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TITLE: Automated Assessment of Visual Photosensitivity in Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: Anat Galor, MD, MSPH

CONTRACTING ORGANIZATION: University of Miami

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14. ABSTRACT In this study, we focus on validating a clinical automated instrument, the Ocular Photosensitivity Analyzer (OPA), to quantify an important sequela of Traumatic Brain Injury (TBI), visual photosensitivity (i.e. photophobia). Additionally, we will also assess the effect of various light filtering eyewear with the OPA to investigate whether specific wavelengths of light have significant impact on the management of visual photosensitivity in TBI subjects. Study Questionnaires will be administered in conjunction with OPA testing to better understand the complex interactions between visual photosensitivity and other TBI associated sequela (Dry Eye, Ocular Pain). We will measure VPT in fifty healthy and fifty TBI subjects via the OPA at Visit#1 (baseline) and Visit#2 (1 month) (both with and without light filtering eyewear, in random order) and correlate VPT to the Study Questionnaires. Twenty study participants have been Recruited, Screened, Enrolled, and Completed Visit#1 as well as nine of those study participants have Completed the Phone Interview and Visit#2.					
15. SUBJECT TERMS Traumatic Brain Injury, Eye, Photophobia, Visual Photosensitivity, Ocular Photosensitivity Analyzer, Visual Photosensitivity Threshold, Pain, Dry Eye, VLSQ-8, Questionnaires					
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1. INTRODUCTION:

Traumatic brain injury (TBI) is a condition with devastating lifelong consequences. Visual photosensitivity, or extreme sensitivity to light, is a common and incapacitating condition associated with TBI. The purpose of this research is to assess visual photosensitivity using a novel instrument, the Ocular Photosensitivity Analyzer (OPA) in healthy and TBI study participants. Additionally, we will administer study questionnaires in conjunction with OPA testing to better understand the complex interactions between visual photosensitivity and other TBI associated sequela. Finally, we will evaluate the effect of various light filtering eyewear with the OPA and explore whether specific wavelengths of light play a significant role in the management of visual photosensitivity in TBI. For conditions such as TBI where increased visual photosensitivity is a prominent feature, quantitative clinical outcome measures are important to establish a baseline, examine disease progression, and evaluate the efficacy of emerging treatments.

2. KEYWORDS:

Traumatic Brain Injury, Eye, Photophobia, Visual Photosensitivity, Ocular Photosensitivity Analyzer, Visual Photosensitivity Threshold, Pain, Dry Eye, Light Sensitivity, VLSQ-8, Questionnaires

3. ACCOMPLISHMENTS:

What were the major goals of the project?

AIM 1: VALIDATE THE OCULAR PHOTSENSITIVITY ANALYZER (OPA) IN HEALTHY AND TRAUMATIC BRAIN INJURY (TBI) SUBJECTS.

AIM 2: DEMONSTRATE THE OPAS ABILITY TO DETECT TREATMENT EFFECT.

Major Tasks	Months	% of Completion
Major Task 1: Clinical Research Study Protocol		
Refine eligibility criteria, exclusion criteria, screening protocol	0-3	100%
Finalize informed consent form and human subjects' protocol	0-3	100%
Coordinate with Site for IRB protocol submission	0-3	100%
Submit amendments (modifications) and protocol deviations to IRB, as needed	As Needed	100%
Coordinate with Site for annual IRB report for continuing review	Annually	
<i>Milestone Achieved: IRB approval obtained</i>	0-3	100%
Submit for HRPO Regulatory Review	2-3	100%
<i>Milestone Achieved: HRPO Regulatory Review approval</i>	2-3	100%
Major Task 2: Training, Checklists, and Assessments		
Coordinate with Sites for training to maintain GCP compliance with protocol	0-3	100%
<i>Milestone Achieved: Research staff trained</i>	0-3	100%
Checklists and flow charts for all study steps, data collection, and database requirements	1	100%

Generate randomization scheme for OPA testing: (1) no filtering (plano lenses (PL)), (2) blue-light blocking lenses (BL), (3) FL-41 lenses (FL) (an established treatment for visual photosensitivity), and (4) gray lenses (GL) (neutral density)	1	100%
<i>Milestone Achieved: Finalized study assessments</i>	0-3	100%
Work with data core and dissemination of findings (abstracts, presentation, publications, DOD)	6-24	10%
<i>Milestone Achieved: Report results from the data analyses</i>	6-24	0%
Major Tasks	Months	% of Completion
Major Task 3: Study Begins		
Source light filtering eyewear: (1) no filtering (plano lenses (PL)), (2) blue-light blocking lenses (BL), (3) FL-41 lenses (FL) (an established treatment for visual photosensitivity), and (4) gray lenses (GL) (neutral density)	1	100%
Begin subject recruitment (healthy/controls)	6-21	38%
Begin subject recruitment (TBI)	6-21	2%
<i>Milestone Achieved: Schedule the first subject first visit, obtain informed consent, screened, and enrolled</i>	6	100%
Administer the VLSQ-8 and Study Questionnaires prior to OPA testing (healthy/controls and TBI) – Visit #1	6-21	20%
Perform baseline OPA testing with and without light filtering eyewear according to the assigned randomization scheme (healthy/controls and TBI) – Visit #1	6-21	20%
<i>Milestone Achieved: Complete subject baseline questionnaires and OPA testing with and without light filtering eyewear (healthy/controls and TBI) – Visit #1</i>	6-21	20%
Assess all subjects at the 1-month timeframe using the OPA with and without light filtering eyewear according to the assigned randomization scheme (healthy/controls and TBI) – Visit #2	6-21	10%
Assess and report all SAEs to IRB, DSMB; enact and see approval for protocol amendments to ensure patient safety, as needed	As needed	
<i>Milestone Achieved: Report findings from baseline – Visit #1 and 1-month – Visit #2 follow-up assessments</i>	3	0%
Major Task 4: Data Analysis		
Coordinate biostatistician/study staff for monitoring data collection rates of VPT and questionnaires and data quality	6-24	30%
Perform all analyses according to specifications, share output and findings with all investigators	6-24	20%
Work with data core and dissemination of findings (abstracts, presentation, publications, DOD)	6-24	20%
<i>Milestone Achieved: Report results from the data analyses</i>	6-24	0%

Projected Quarterly Enrollment:

	Year 1				Year 2				Total
Target Enrollment	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
UM	-	10	15	20	25	30	-	-	100
Target Enrollment (cumulative)	-	10	15	20	25	30	-	-	100

What was accomplished under these goals?

1) Major Activities:

- University of Miami IRB 20200584 was Approved on: June 2, 2020 and the Modification MOD00044812 Review was Completed and Approved on: February 23, 2021 by the University of Miami; the Modifications and Continuing Review MODCR00002619 was Completed and Approved on: March 19, 2021 by the University of Miami.
- Submitted updated approved documents to Michelle Harris from the NIH - FITBIR to begin the process of creating the form structures to input the study data in the FITBIR Data Repository, etc. on March 23, 2021.
- Submitted copies of the IRB Modifications MOD00044812 and MODCR00002619: Modifications and Continuing Review Approval Letters as well as the Approved corresponding documents (UM IRB Protocol V4.0, Information and Consent Form V5.0, UCSD Brief Assessment of Capacity to Consent (UBACC) V1.0, Recruitment Flyer V2.0, Telephone Screening Script V2.0, Study Questionnaires V2.0, Demographics and History Form V1.0, and Visual Photosensitivity Threshold (VPT) Data Sheet V1.0. (see Appendices for Study Questionnaires V2.0) for the University of Miami IRB Protocol 20200584 - E01763.1a - HRPO Approval Memorandum (Proposal Number VR190009, Award Number W81XWH-20-1-0820 - "Automated Assessment of Visual Photosensitivity in Traumatic Brain Injury") to the USAMRMC HRPO on March 29, 2021 via email.

STUDY QUESTIONNAIRES V2.0	VISIT #1	PHONE INTERVIEW	VISIT #2
Visual Light Sensitivity Questionnaire-8 (VLSQ-8)	X		X
DEQ 5	X		X
Ocular Surface Disease Index (OSDI)	X		X
NRS of Pain Intensity	X		X
Neuropathic Pain Symptom Inventory - modified for the eye (NPSI-Eye)	X		X
HIT-6	X		X
Pain History Questionnaire			X
PCS-EN			X
Patient Health Questionnaire (PHQ-9)			X
SF-12V2 OPPERA			X
BTACT (Brief Test of Adult Cognition by Telephone)		X	

- A Phone Interview was scheduled between Visit #1 and Visit #2 to complete some of the Study Questionnaires/Assessments (BTACT) in order to help mitigate unnecessary COVID-19 exposure burden on both the study participants and study team members.
- Sourced/Received the custom manufactured Light Filtering Eyewear with: (1) no filtering (plano lenses (PL)), (2) blue-light blocking lenses (BL), (3) FL-41 lenses (FL) (an established treatment for visual photosensitivity), and (4) gray lenses (GL) (neutral density) mounted on wrap-around frames with the following characteristics: form fitting, with minimal gaps that maximize the field of view while minimizing the intrusion of peripheral lighting.

- Benchtop Testing and Analysis was performed to confirm the spectral filtering characteristics of the Light Filtering Eyewear.



(1) Plano Lenses
(PL) (No Filtering)

(2) Blue-Light Filter
Lenses (BL)

(3) FL-41 Filter
Lenses (FL)

(4) Gray Filter
Lenses (GL)

- Study Team Member Training to Review the Protocol/Procedures, Documents, Administration of Study Questionnaires/Assessments as well as practice using the Devices (i.e. Ocular Photosensitivity Analyzer (OPA), Spot Vision Screener, etc...) and Proper Handling and Disinfecting of the Filtered Eyewear in a Mock Setting was Completed during the month of April 2021.
- Greenphire ClinCard Training for Study Participant Compensation was completed on: April 16, 2021 by Study Team Members.
- Recruitment Activities commenced at the end of April and Phone Screenings commenced in the beginning of May for Healthy Study Participants.
- First Subject First Visit (FSFV) was successfully completed on: May 7, 2021.
- Submitted copies of an additional IRB Modification (MOD00046785) to incorporate the "Greenphire ClinCard" study participant compensation language into the IRB Protocol and ICF was approved by the IRB on April 14, 2021 as well as the Approved corresponding documents (UM IRB Protocol V5.0 and Information and Consent Form V6.0) for the University of Miami IRB Protocol 20200584 - E01763.1a - HRPO Approval Memorandum (Proposal Number VR190009, Award Number W81XWH-20-1-0820 - "Automated Assessment of Visual Photosensitivity in Traumatic Brain Injury") and the HRPO Continuing Review - Submission Form to the USAMRMC HRPO on May 24, 2021 via email.
- Submitted IRB Modification (MOD00049321) which was approved by the IRB on July 12, 2021 to Add a new Study Team Member: Rhiya Mittal, BS.
- An additional Nineteen Study Participants were Recruited, Screened, Enrolled, and Completed Visit #1 (Baseline) at the end of Quarter 4.
- Furthermore, Nine of those Study Participants have Completed the Phone Interview as well as Completed Visit #2 (1 month) at the end of Quarter 4.

2) Specific Objectives:

- **AIM 1: VALIDATE THE OCULAR PHOTOSENSITIVITY ANALYZER (OPA) IN HEALTHY AND TRAUMATIC BRAIN INJURY (TBI) SUBJECTS.** We will measure Visual Photosensitivity Thresholds (VPT) via the Ocular Photosensitivity Analyzer (OPA) at baseline and one-month (both with and without light filtering eyewear, in random order) in (50) healthy and (50) Traumatic Brain Injury (TBI) subjects. Additionally, VPT will be correlated Study Questionnaires.
- **AIM 2: DEMONSTRATE THE OPAS ABILITY TO DETECT TREATMENT EFFECT.** We will evaluate the effect of various light filtering eyewear on VPT ranging from: (1) no filtering (plano lenses (PL)) up to varying filters such as (2) blue-light blocking lenses (BL), (3) FL-41 lenses (FL) (an established treatment for visual photosensitivity), and (4) gray lenses (GL) (neutral density) presented in an randomized order in (50) healthy and (50) TBI subjects. Various light filtering lens tints have been hypothesized to reduce light sensitivity by blocking the shorter light wavelengths implicated in the pathophysiology of visual photosensitivity. Along with demonstrating sensitivity to change with treatment, we will evaluate the effect of various light filtering eyewear on VPT which may provide valuable insights on whether specific wavelengths of light play a significant role in eliciting visual photosensitivity in TBI.

3) Key Outcomes:

- NOTE: Subject Recruitment, Screening, Enrollment, etc.... was rescheduled to commence in late Quarter 3 due to a delay with the procurement of the custom manufactured Light Filtering Eyewear needed to perform the Study Visits.
- Sourced/Received Light Filtering Eyewear - Benchtop Testing and Analysis was performed to confirm the spectral filtering characteristics of the Light Filtering Eyewear.
- First Subject First Visit (FSFV) was successfully completed on: May 7, 2021.
- An additional Nineteen Study Participants were Recruited, Screened, Enrolled, and Completed Visit #1 (Baseline) at the end of Quarter 4.
- Furthermore, Nine of those Study Participants have Completed the Phone Interview as well as Completed Visit #2 (1 month) at the end of Quarter 4.

4) Other Achievements:

- Mariela C. Aguilar, Ph.D. – Received an NIH Loan Repayment Program Award Renewal through the National Eye Institute (NEI) for the period of two years (July 2021 – June 2023) to continue conducting research with: Jean-Marie Parel, Ph.D. and Anat Galor, MD, MSPH (Co-Mentors).

What opportunities for training and professional development has the project provided?

Trainings:

- NIH FITBIR DEEP DIVE Trainings – Completed by Mariela C. Aguilar, Ph.D. and Victoria Graham, BS: Thurs., September 24, 2020 – Submission Tools; Thurs., October 15, 2020 – Introduction to FITBIR; Thurs., October 22, 2020 – Data Dictionary – Data Elements & Form Structures; Thurs., October 29, 2020 – Data Dictionary – Cross-mapping.
- Study Team Member Training to Review the Protocol/Procedures, Documents, Administration of Study Questionnaires/Assessments as well as practice using the Study Devices (i.e. Ocular Photosensitivity Analyzer (OPA), Spot Vision Screener, etc...) and Proper Handling and Disinfecting of the Filtered Eyewear in a Mock Setting was Completed – April 2021 – July 2021.

Professional Development Seminars:

- Bascom Palmer Eye Institute – McKnight Vision Research Seminar – Miranda M. Lim, MD, PhD – Associate Professor of Neurology, Oregon Health & Science University, Staff Neurologist, VA Portland Health Care System, “Sleep, chronic pain, and photosensitivity in TBI: From observation to intervention” on Wednesday, July 7th, 2021 at 12:00 PM ET via Zoom.
- Bascom Palmer Eye Institute – McKnight Vision Research Seminar – Scott D. Mist, Ph.D., LAc – Associate Professor of Anesthesiology and Perioperative Medicine, Oregon Health & Science University, “Light sensitivity as a potential biomarker of central sensitization of pain” on Wednesday, August 25th, 2021 at 12:00 PM ET via Zoom.

How were the results disseminated to communities of interest?

- Anat Galor, MD, MSPH presented project activities at the University of Miami – Department of Public Health Sciences Faculty and Student Speed Networking virtual session via Zoom.

What do you plan to do during the next reporting period to accomplish the goals?

- Continue Healthy Study Participant Recruitment, Screening, Enrollment, and the Ocular Photosensitivity Analyzer (OPA) Testing without and with the Light Filtering Eyewear presented in a randomized order according to the OPA testing randomization scheme for Visit #1 and Visit #2.
- Continue ramping up TBI Study Participant Recruitment, Screening, Enrollment, and the Ocular Photosensitivity Analyzer (OPA) Testing without and with the Light Filtering Eyewear presented in a randomized order according to the OPA testing randomization scheme for Visit #1 and Visit #2.

- Continue performing the Phone Interviews between Visit #1 and Visit #2 to administer the Brief Test of Adult Cognition by Telephone (BTACT) Assessment. NOTE: A Phone Interview was scheduled between Visit #1 and Visit #2 to help mitigate unnecessary COVID-19 exposure burden on both the Study Participants and Study Team Members.
- Perform an Interim Analysis on the OPA and Study Questionnaire data collected once a quarter of the Study Participants have completed Visit #1, Phone Interview, and Visit #2.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

- Utilizing innovative technology such as the Ocular Photosensitivity Analyzer to significantly advance the understanding and diagnosis of visual dysfunction (visual photosensitivity/photophobia) in TBI will enable the development of more robust therapeutic trials for photophobia, a symptom with few therapeutic options.

What was the impact on other disciplines?

- The Ocular Photosensitivity Analyzer (OPA) could potentially be used in other disciplines to investigate visual photosensitivity in populations of patients suffering from various diseases (i.e. migraineurs, individuals suffering from chronic pain, fibromyalgia, etc...). Developing a diagnostic tool to quantify visual photosensitivity will improve our ability to screen patients, quantify disease severity, and monitor disease course over time. Such a machine can also help evaluate the efficacy of emerging therapies to improve the quality of life for those affected.

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. CHANGES/PROBLEMS:

Nothing to Report

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

- Subject Recruitment, Screening, Enrollment, etc.... was rescheduled to commence in late Quarter 3 due to a delay with the procurement of the custom manufactured Light Filtering Eyewear needed to perform the Study Visits.
- We have been ramping up our Recruitment Efforts, Screening, Enrollment, and OPA Testing.
- We have Recruited, Screened, and Enrolled several additional Healthy and TBI Study Participants as well as Completed the Visit #1 since mid-August.
- Additionally, we have Completed the Phone Interviews to administer the BTACT assessment as well as Completed the Visit #2 (1 month) for several Study Participants since mid-August.
- Afterhours and Weekend appointments have been added to the Study Schedule to accommodate more Study Participants and increase Enrollment.

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

- Baksh BS, Garcia JC, Galor A. Exploring the Link Between Dry Eye and Migraine: From Eye to Brain. Eye Brain. 2021 Mar 4;13:41-57. doi: 10.2147/EB.S234073.
Acknowledgement of Federal Support: Yes
- Patel S, Hwang J, Mehra D, Galor A. Corneal Nerve Abnormalities in Ocular and Systemic Diseases. Exp Eye Res. 2021 Jan;202:108284. doi: 10.1016/j.exer.2020.108284.
Acknowledgement of Federal Support: Yes

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers and presentations.

- Anat Galor, MD, MSPH “Photosensitivity: Is it Modifiable?” Presentation at the Annual World Congress of the Society for Brain Mapping and Therapeutics (SBMT), July 8th, 2021.
- Mariela C. Aguilar, Ph.D. “Quantifying Photosensitivity in Healthy and Light Sensitive Subjects” Presentation at the Annual World Congress of the Society for Brain Mapping and Therapeutics (SBMT), July 8th, 2021.

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Anat Galor, MD, MSPH

Project Role: PI

Researcher Identifier (e.g. ORCID ID): 0000-0002-3026-6155

Nearest person month worked: 3.6

Contribution to Project: Dr. Galor has performed work in the development of Clinical Research Study Protocol (refining the eligibility criteria, exclusion criteria, screening protocol), IRB submission, IRB Modification, HRPO regulatory review, and conducted Study Team Member Trainings as well as assisted with Recruitment Activities.

Name: Mariela C. Aguilar, Ph.D.

Project Role: Assistant Scientist – Biomedical Engineer

Researcher Identifier (e.g. ORCID ID): 0000-0003-1891-7813

Nearest person month worked: 6

Contribution to Project: Dr. Aguilar has performed work in the development of Clinical Research Study Protocol (refining the eligibility criteria, exclusion criteria, screening protocol), IRB Submissions (Modifications/Continuing Reviews), HRPO regulatory reviews, FITBIR trainings, Checklists and Flowcharts for all Study Steps, Database requirements, and Filtered Eyewear Sourcing. Additionally, she has conducted the Study Team Member Trainings, performed Recruitment Activities, Phone Screenings, and assisted with the Greenphire ClinCard Activation/Study Compensation for Study Participants (Visit #1/Vist #2) as well as performed several Phone Interviews (BTACT).

Name: Alex Gonzalez, BA

Project Role: Programmer

Researcher Identifier (e.g. ORCID ID): 0000-0002-0774-0031

Nearest person month worked: 1.8

Contribution to Project: Mr. Gonzalez has performed work in the development of Clinical Research Study Protocol, IRB submissions, Checklists and Flowcharts for all study steps, Database requirements, and Filtered Eyewear Sourcing. Additionally, he has conducted the Study Team Member Trainings and performed the Benchtop Testing and Analysis of the Filtered Eyewear to verify the Spectral Filtering Characteristics as well as Enrolled Study Participants and Conducted the Visit #1 – OPA Testing.

Name: Victoria Graham, BS
Project Role: Research Assistant
Nearest person month worked: 1.0
Contribution to Project: Ms. Graham is Research Assistant who has conducted the Study Team Member Trainings and has performed Recruitment Activities as well as Enrolled Study Participants, Conducted the Visit #1 – OPA Testing/Administered Study Questionnaires, as well as Conducted the Visit #2 – OPA Testing/Administered Study Questionnaires.

Name: Rhiya Mittal, BS
Project Role: MD/MPH Student
Researcher Identifier (e.g. ORCID ID): 0000-0002-0584-0848
Nearest person month worked: 1.0
Contribution to Project: Ms. Mittal is an MD/MPH Student who has completed the Study Team Member Trainings and has performed Recruitment Activities as well as Enrolled Study Participants, Conducted the Visit #1 – OPA Testing/Administered Study Questionnaires, Performed Phone Interviews (BTACT), as well as Conducted the Visit #2 – OPA Testing/Administered Study Questionnaires.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

Not Applicable

QUAD CHARTS:

Please see the updated Quad Chart in the Attachments.

9. APPENDICES:

- Study Questionnaires
- A Curriculum Vitae
- Original Copies of Journal Articles

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Visual Light Sensitivity Questionnaire-8 (VLSQ-8)

This questionnaire is designed to detect visual sensitivity to light. Please circle one answer for each question. Choose the response that best describes your situation. Answer all of the questions as if you are wearing your regular glasses or contact lenses. Take as much time as needed to answer each question. All your answers are confidential.

1) In the past month, how often did you have visual light sensitivity outdoors during daylight?

Never Rarely Sometimes Often Always

2) In the past month, how often did you have a sense of glare in your eyes?

Never Rarely Sometimes Often Always

3) In the past month, how often did you have visual light sensitivity from flickering lights or bright colors?

Never Rarely Sometimes Often Always

4) Please rate the severity of the worst visual light sensitivity you experienced in the past month.

None Moderate Severe
1 2 3 4 5

5) When you have sensitivity to light, do you also experience headache?

Never Rarely Sometimes Often Always

6) When you have sensitivity to light, how often is your vision blurry?

Never Rarely Sometimes Often Always

7) How often does sensitivity to light limit your ability to read, watch TV, or use the computer?

Never Rarely Sometimes Often Always

8) In the past month, how often did you need to wear dark glasses on cloudy days or indoors?

Never Rarely Sometimes Often Always

DEQ 5

1. Questions about **EYE DISCOMFORT**:

a. During a typical day in the past month, **how often** did your eyes feel discomfort?

- 0 Never
- 1 Rarely
- 2 Sometimes
- 3 Frequently
- 4 Constantly

b. When your eyes felt discomfort, **how intense was this feeling of discomfort** at the end of the day, within two hours of going to bed?

Never <u>have it</u>	Not at All <u>Intense</u>				Very <u>Intense</u>
0	1	2	3	4	5

2. Questions about **EYE DRYNESS**:

a. During a typical day in the past month, **how often** did your eyes feel dry?

- 0 Never
- 1 Rarely
- 2 Sometimes
- 3 Frequently
- 4 Constantly

b. When your eyes felt dry, **how intense was this feeling of dryness** at the end of the day, within two hours of going to bed?

Never <u>have it</u>	Not at All <u>Intense</u>				Very <u>Intense</u>
0	1	2	3	4	5

3. Question about **WATERY EYES**:

During a typical day in the past month, **how often** did your eyes look or feel excessively watery?

- 0 Never
- 1 Rarely
- 2 Sometimes
- 3 Frequently
- 4 Constantly

Score: $1a + 1b + 2a + 2b + 3 = \text{Total}$
 $\underline{\quad} + \underline{\quad} + \underline{\quad} + \underline{\quad} + \underline{\quad} = \underline{\quad}$

Ocular Surface Disease Index® (OSDI®)²

Ask your patient the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING DURING THE LAST WEEK:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

HAVE PROBLEMS WITH YOUR EYES LIMITED YOU IN PERFORMING ANY OF THE FOLLOWING DURING THE LAST WEEK:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

HAVE YOUR EYES FELT UNCOMFORTABLE IN ANY OF THE FOLLOWING SITUATIONS DURING THE LAST WEEK:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

ADD SUBTOTALS A, B, AND C TO OBTAIN D
(D = SUM OF SCORES FOR ALL QUESTIONS ANSWERED)

(D)

TOTAL NUMBER OF QUESTIONS ANSWERED
(DO NOT INCLUDE QUESTIONS ANSWERED N/A)

(E)

Please turn over the questionnaire to calculate the patient's final OSDI® score.

Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118:615-621

Please think about the intensity of your ocular surface / eye pain.

No pain 0 1 2 3 4 5 6 7 8 9 10 The most intense eye
sensation
imaginable pain sensation

No pain 0 1 2 3 4 5 6 7 8 9 10 The most intense eye
sensation
imaginable pain sensation

No pain 0 1 2 3 4 5 6 7 8 9 10 The most intense eye pain sensation imaginable

No pain sensation imaginable	1	2	3	4	5	6	7	8	9	10	The most intense eye pain sensation
------------------------------	---	---	---	---	---	---	---	---	---	----	-------------------------------------

No pain 0 1 2 3 4 5 6 7 8 9 10 The most intense eye
sensation
imaginable pain sensation

No pain sensation imaginable	1	2	3	4	5	6	7	8	9	10	The most intense eye pain sensation
------------------------------	---	---	---	---	---	---	---	---	---	----	-------------------------------------

Neuropathic Pain Symptom Inventory- modified for the Eye

We wish to know if you feel spontaneous eye pain, that is, pain without any stimulation. For each of the following questions, please select the number that best describes your average spontaneous pain severity during the past 24 hours. Select the number 0 if you have not felt such pain (circle one number only).

1. Does your eye pain feeling like burning?

No	0	1	2	3	4	5	6	7	8	9	10	Worst burning
burning												imaginable

2. Does your eye pain feel like squeezing?

No	0	1	2	3	4	5	6	7	8	9	10	Worst squeezing
squeezing												imaginable

3. Does your eye pain feel like pressure?

No	0	1	2	3	4	5	6	7	8	9	10	Worst pressure
pressure												imaginable

4. During the past 24 hours, your spontaneous pain has been present:

(Select the response that *best describes* your case)

Permanently _____

Between 8-12 hours _____

Between 4-7 hours _____

Between 1-3 hours _____

Less than 1 hour _____

We wish to know if you have brief attacks of eye pain. For each of the following questions, please select the number that best describes the average severity of your painful attacks during the past 24 hours. Select the number 0 if you have not felt such pain (circle one number only).

5. Does your eye pain feel like electric shocks?

No	0	1	2	3	4	5	6	7	8	9	10	Worst electric
electric shocks												shocks imaginable

6. Does your eye pain feel like stabbing?

No	0	1	2	3	4	5	6	7	8	9	10	Worst stabbing
stabbing												imaginable

7. During the past 24 hours, how many of these pain attacks have you had?

(Select the response that *best describes* your case)

More than 20 _____

Between 11-20 _____

Between 6-10 _____

Between 1-5 _____

No pain attack _____

Kalangara JP, Galor A, Levitt RC, Covington DB, McManus KT, Sarantopoulos CD, Felix ER. Characteristics of Ocular Pain Complaints in Patients With Idiopathic Dry Eye Symptoms. Eye Contact Lens. 2017 May;43(3):192-198.

We wish to know if you feel eye pain provoked or increased by wind, light, or contact with cold/hot. For each of the following questions, please select the number that best describes the average severity of your provoked pain during the past 24 hours. Select the number 0 if you have not felt such pain (circle one number only).

8. Is your eye pain provoked or increased by wind?

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst pain imaginable
---------	---	---	---	---	---	---	---	---	---	---	----	-----------------------

9. Is your eye pain provoked or increased by light?

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst pain imaginable
---------	---	---	---	---	---	---	---	---	---	---	----	-----------------------

10. Is your eye pain provoked or increased by contact with something hot or cold (air conditioned/warm weather?)

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst pain imaginable
---------	---	---	---	---	---	---	---	---	---	---	----	-----------------------

We wish to know if you feel abnormal eye sensations. For each of the following questions, please select the number that best describes the average severity of your abnormal sensations during the past 24 hours. Select the number 0 if you have not felt such sensation (circle one number only).

11. Do you feel pins and needles?

No pins & needle	0	1	2	3	4	5	6	7	8	9	10	Worst pins & needle imaginable
------------------	---	---	---	---	---	---	---	---	---	---	----	--------------------------------

12. Do you feel tingling?

No tingling	0	1	2	3	4	5	6	7	8	9	10	Worst tingling imaginable
-------------	---	---	---	---	---	---	---	---	---	---	----	---------------------------

HIT-6™

(VERSION 1.1)

This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches.

To complete, please circle one answer for each question.



1 When you have headaches, how often is the pain severe?

Never Rarely Sometimes Very Often Always

2 How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?

Never Rarely Sometimes Very Often Always

3 When you have a headache, how often do you wish you could lie down?

Never Rarely Sometimes Very Often Always

4 In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?

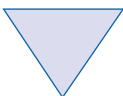
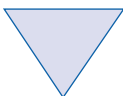
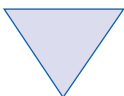
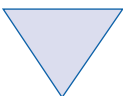
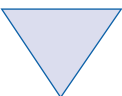
Never Rarely Sometimes Very Often Always

5 In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?

Never Rarely Sometimes Very Often Always

6 In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Never Rarely Sometimes Very Often Always

 +
  +
  +
  +
 
COLUMN 1 **COLUMN 2** **COLUMN 3** **COLUMN 4** **COLUMN 5**
 (6 points each) (8 points each) (10 points each) (11 points each) (13 points each)

To score, add points for answers in each column.

Please share your HIT-6 results with your doctor.

Total Score

Higher scores indicate greater impact on your life.

Score range is 36-78.



HEADACHE IMPACT TEST™

What Does Your Score Mean?

▼ If You Scored 60 or More

Your headaches are having a very severe impact on your life. You may be experiencing disabling pain and other symptoms that are more severe than those of other headache sufferers. Don't let your headaches stop you from enjoying the important things in your life, like family, work, school or social activities.

Make an appointment **today** to discuss your HIT-6 results and your headaches with your doctor.

▼ If You Scored 56 – 59

Your headaches are having a substantial impact on your life. As a result you may be experiencing severe pain and other symptoms, causing you to miss some time from family, work, school, or social activities.

Make an appointment **today** to discuss your HIT-6 results and your headaches with your doctor.

▼ If You Scored 50 – 55

Your headaches seem to be having some impact on your life. Your headaches should not make you miss time from family, work, school, or social activities.

Make sure you discuss your HIT-6 results and your headaches at your next appointment with your doctor.

▼ If You Scored 49 or Less

Your headaches seem to be having little to no impact on your life at this time. We encourage you to take HIT-6 monthly to continue to track how your headaches affect your life.

▼ If Your Score on HIT-6 is 50 or Higher

You should share the results with your doctor. Headaches that are disrupting your life could be migraine.

Take HIT-6 with you when you visit your doctor because research shows that when doctors understand exactly how badly headaches affect the lives of their patients, they are much more likely to provide a successful treatment program, which may include medication.

HIT is also available on the Internet at www.headachetest.com.

The Internet version allows you to print out a personal report of your results as well as a special detailed version for your doctor.

Don't forget to take HIT-6 again or try the Internet version to continue to monitor your progress.

▼ About HIT

The Headache Impact Test (HIT) is a tool used to measure the impact headaches have on your ability to function on the job, at school, at home and in social situations. Your score shows you the effect that headaches have on normal daily life and your ability to function. HIT was developed by an international team of headache experts from neurology and primary care medicine in collaboration with the psychometricians who developed the SF-36® health assessment tool.

HIT is not intended to offer medical advice regarding medical diagnosis or treatment. You should talk to your healthcare provider for advice specific to your situation.

SF-36® is a registered trademark of Medical Outcomes Trust and John E. Ware, Jr.

HIT-6 Scoring Interpretation English Version 1.1

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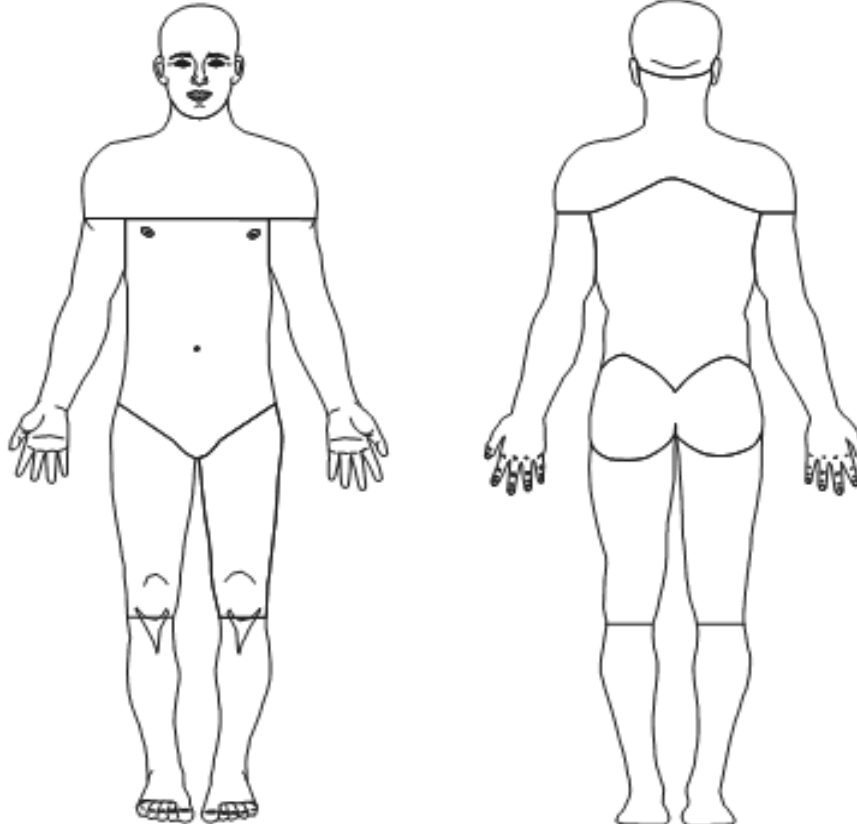
Pain History Questionnaire

A. Do you currently experience persistent pain that has been present for the last 3 months or more?

☐ yes☐ no

IF NO - STOP

B. Please draw on the pictures below to tell us where you have persistent pain.



C. How many different pain problems do you have?

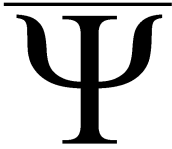
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4
- ☐ 5 or more

Please tell us which of the follow chronic pain conditions you currently have, or have had in the past. Please only tell us about the pain conditions that persisted for AT LEAST 3 months. If you have not had this condition for more than 3 months, please leave the boxes blank.

Condition	Ever	Now
Burning mouth syndrome		
Headaches		
Migraines		
Temporomandibular disorder		
Trigeminal neuralgia pain		
Arthritis		
Low back pain		
Burn pain		
Cancer pain		
Central pain syndrome		
Complex regional pain syndrome / causalgia		

Condition	Ever	Now
Diabetic neuropathy pain		
Fibromyalgia		
Muscle pain		
Sciatica		
Shingles		
Post-surgical pain		
Tendonitis		
Vulvodynia		
Chronic fatigue		
Irritable bowel		
Interstitial cystitis		

Others: _____



PCS-EN

Client No.: _____ Age: _____ Sex: M() F() Date: _____

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

0 – not at all **1** – to a slight degree **2** – to a moderate degree **3** – to a great degree **4** – all the time

When I'm in pain ...

- 1 ☐ I worry all the time about whether the pain will end.
- 2 ☐ I feel I can't go on.
- 3 ☐ It's terrible and I think it's never going to get any better.
- 4 ☐ It's awful and I feel that it overwhelms me.
- 5 ☐ I feel I can't stand it anymore.
- 6 ☐ I become afraid that the pain will get worse.
- 7 ☐ I keep thinking of other painful events.
- 8 ☐ I anxiously want the pain to go away.
- 9 ☐ I can't seem to keep it out of my mind.
- 10 ☐ I keep thinking about how much it hurts.
- 11 ☐ I keep thinking about how badly I want the pain to stop.
- 12 ☐ There's nothing I can do to reduce the intensity of the pain.
- 13 ☐ I wonder whether something serious may happen.

...Total

Updated 11/11

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

27

NAME: _____

DATE: _____

Over the last 2 weeks, how often have you been
bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3

add columns

	+		+	
--	---	--	---	--

(Healthcare professional: For interpretation of TOTAL, TOTAL: _____
please refer to accompanying scoring card).

10. If you checked off *any problems*, how *difficult*
have these problems made it for you to do
your work, take care of things at home, or get
along with other people?

Not difficult at all _____
Somewhat difficult _____
Very difficult _____
Extremely difficult _____

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder

- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder

- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.

Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying **PHQ-9 Scoring Box** to interpret the TOTAL score.
5. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

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Date filled out (mm-dd-yyyy)

			-				-						
--	--	--	---	--	--	--	---	--	--	--	--	--	--

SF-12v2 OPPERA

RESPONDENT ID LABEL

29

Mark(☒) one response for each item and do not skip any items unless specified. If you change your mind, fill the incorrect mark completely and then mark (☒) the new response.

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

		Excellent	Very good	Good	Fair	Poor
1.	In general, would you say your health is:	☐	☐	☐	☐	☐
2.	The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?	Yes, limited a lot	Yes, limited a little	No, not limited at all		
a.	Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.	☐	☐	☐		
b.	Climbing several flights of stairs.	☐	☐	☐		
3.	During the last 4 weeks , how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health ?	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a.	Accomplished less than you would like.	☐	☐	☐	☐	☐
b.	Were limited in the kind of work or other activities.	☐	☐	☐	☐	☐
4.	During the last 4 weeks , how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a.	Accomplished less than you would like.	☐	☐	☐	☐	☐
b.	Did work or other activities less carefully than usual.	☐	☐	☐	☐	☐
5.	During the last 4 weeks , how much did pain interfere with your normal work (including both work outside the home and housework)?	Not at all	A little bit	Moderately	Quite a bit	Extremely
		☐	☐	☐	☐	☐
6.	These questions are about how you feel and how things have been with you during the last 4 weeks . For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the last 4 weeks ...	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a.	Have you felt calm and peaceful?	☐	☐	☐	☐	☐
b.	Did you have a lot of energy?	☐	☐	☐	☐	☐
c.	Have you felt downhearted and depressed?	☐	☐	☐	☐	☐
7.	During the last 4 weeks , how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?	All of the time	Most of the time	Some of the time	A little of the time	None of the time
		☐	☐	☐	☐	☐

STUDY PARTICIPANT ID# _____

DATE: _____

**MIDUS II Cognitive Test Battery
PO1 AG20166 & RO1 AG17920**

**Brief Test of Adult Cognition by Telephone (BTACT)
Margie E. Lachman, Project Leader
Patricia A. Tun, Co-Investigator
Brandeis University
April 2003
(Updated January 2012)**

In this phone interview I will ask you to try and do some exercises that involve remembering and making judgments about words and numbers. Before we begin, I need to tell you a few things. Your participation is completely voluntary. If you prefer not to answer any question, just let me know and we will go on to the next question. The information that you give me will be confidential and used for statistical analysis only. It will be identified only by computer code and at no time will your name or other identifying information be attached to the survey results. Therefore, I won't be able to give any specific feedback.

These tasks are not harmful in any way. The exercises will take about 15 minutes. Do you have any questions about your participation in this study?

We will be tape recording the interview today so that we can score the exercises later. Do I have your permission to go ahead with this?

(If participant seems distracted, or there is noise or commotion in background such as young children, TV or radio, or other people talking, say "It is important that you are able to concentrate without being distracted while we do these exercises. Would it be better for me to call you back another time?" If so, make an appointment for another time.)

First I would like to make sure that you are able to hear me clearly. Please repeat these numbers after me: 2, 8, 3, 6, 9. *(If not loud enough, ask person to speak up clearly.)* Could you hear me clearly?

Now you will hear some words and numbers. Please do not use a paper and pencil for any of the questions. We suggest that you close your eyes while you are doing these to help you concentrate. Some of the questions will be easy for you, and some will be harder. We do not expect anyone to get all of these correct - just do the best you can.

WORD LIST RECALL (1.5 minutes on average)
Rey Auditory-Verbal Learning Test (Lezak, 1983)

I am going to read a list of 15 words. Listen carefully. When I am finished, you are to repeat as many of the words as you can remember. It doesn't matter in what order you repeat them. Just try to remember as many as you can. I will say each word only one time, and I cannot repeat any words. You will have up to one and a half minutes, and I will not say anything until I tell you that your time is up. Do you have any questions? Are you ready?

(Read with one second interval between each word)

DRUM
CURTAIN
BELL
COFFEE
SCHOOL
PARENT
MOON
GARDEN
HAT
FARMER
NOSE
TURKEY
COLOR
HOUSE
RIVER

Now tell me as many words as you can remember.

*(Record words recalled **correctly** by entering the one or two letter code, as well as repetitions of same word and intrusions).*

If person stops before 1 1/2 minutes is up, say, "There's still time left, can you think of any more?"

Good, now let's go on.

DIGITS BACKWARD (2.5 minutes)

WAIS III (1997)

I am going to say some strings of numbers, and when I am done I would like you to repeat them backwards, in the reverse order from which I said them. So if I said “3, 8”, you would say “8, 3”. Do you understand? The sets will get larger as we go.

(Read in monotone, 1 sec per number. Drop your voice on the last digit to indicate it is time to respond. If they get the first trial on one level, move on to the next level. Discontinue after 2 trials missed on a level).

1. 2 - 4 (4 - 2) _____
5 - 7 (7 - 5) _____
2. 6 - 2 - 9 (9 - 2 - 6) _____
4 - 1 - 5 (5 - 1 - 4) _____
3. 3 - 2 - 7 - 9 (9 - 7 - 2 - 3) _____
4 - 9 - 6 - 8 (8 - 6 - 9 - 4) _____
4. 1 - 5 - 2 - 8 - 6 (6 - 8 - 2 - 5 - 1) _____
6 - 1 - 8 - 4 - 3 (3 - 4 - 8 - 1 - 6) _____
5. 5 - 3 - 9 - 4 - 1 - 8 (8 - 1 - 4 - 9 - 3 - 5) _____
7 - 2 - 4 - 8 - 5 - 6 (6 - 5 - 8 - 4 - 2 - 7) _____
6. 8 - 1 - 2 - 9 - 3 - 6 - 5 (5 - 6 - 3 - 9 - 2 - 1 - 8) _____
4 - 7 - 3 - 9 - 1 - 2 - 8 (8 - 2 - 1 - 9 - 3 - 7 - 4) _____
7. 9 - 4 - 3 - 7 - 6 - 2 - 5 - 8 (8 - 5 - 2 - 6 - 7 - 3 - 4 - 9) _____
7 - 2 - 8 - 1 - 9 - 6 - 5 - 3 (3 - 5 - 6 - 9 - 1 - 8 - 2 - 7) _____

Good, now let's go on.

CATEGORY FLUENCY (1.5 minutes)

Drachman & Leavitt (1972)

Now I am going to name a category and you will name things that belong in that category. Let's practice with the category "fruit". You could say peach, or pear. Can you think of any other fruits? (*wait for 2 correct items*). In a moment I will give you another category. When I say begin, you will name all the things from this **new** category you can think of, as fast as you can. You will have one minute to do this. I will let you know when your time is up. The new category is animals. Do you have any questions? Ready?

Begin. (***Time for one minute***). If person stops before 1 minute is up, say "There's still more time, can you think of any more?"

(If person asks whether birds, fish, insects, reptiles, etc. are acceptable, say yes.)

1 – 15 sec.

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

15- 30 sec.

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

30- 45 sec.

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

45-60 sec.

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

Good, now let's go on.

NUMBER SERIES (2.5 minutes)

Salthouse & Prill (1987)

In the next exercise I will read you a series of numbers that may get larger or smaller in value. At the end you will try to figure out what the next number would be. So if the numbers were 2,4,6,8,10, the next number would be 12. After I say each number I will pause for as long as you need, and then you should say “okay” when you are ready for me to go on to the next number in the group. So if I said 2, you should say “okay” when you are ready for me to go on to the next number, then I say 4, you say okay, 6, okay, 8, okay, 10, and at the end I will ask you what you think the next number would be. In this case the next number would be 12, as each number has increased by 2.

Let’s try one for practice: 35 (okay), 30 (okay), 25 (okay), 20 (okay), 15 (okay) **AND** the next number would be....???? (The answer should be 10 as each number has decreased by 5). There will be different patterns, and some of these will be harder than others, so just do the best you can. If you are not sure of the answer, it is okay to guess. Do you have any questions? *(Pause after each of the first 4 items for okay response; after the last item, say **AND** the next number is...?).*

(1) 18, 20, 24, 30, 38.....(48) _____

Okay. Are you ready for another? The next set is:

(2) 81, 78, 75, 72, 69.....(66) _____

Okay. Are you ready for another? The next set is

(3) 7, 12, 16, 19, 21.....(22) _____

Okay. Are you ready for another? The next set is

(4) 28, 25, 21, 16, 10.....(3) _____

Okay. Are you ready for another? The next set is

(5) 20, 37, 18, 38, 16.....(39) _____

Good, let’s move on.

BACKWARD COUNTING (45 seconds)

Next, I would like to see how fast you can count backwards. When I give the signal to begin, start counting backwards from 100 out loud, as fast as you can. So you will say 100, 99, 98 and so on. You will have half a minute. Do you have any questions? I will let you know when the time is up.

Begin *(Time for 30 seconds)*

Record final number reached, and number of errors.

Good, now one more question.

SHORT-DELAY WORD RECALL (40 seconds on average)

Do you remember the very first list of 15 words that I read to you in the beginning? It was the very first thing we did. (WAIT FOR SUBJECT TO RESPOND YES. MAKE SURE THEY UNDERSTAND THAT IT IS THE WORD LIST, NOT THE CATEGORY FLUENCY TEST). I want you to tell me as many of the words from that list as you can. You will have up to one minute. I will tell you when your time is up. (*Record words recalled, including intrusions and repetitions.*) *If person stops before 1 minute is up, say, “there is still more time can you think of any more?”*

DRUM
 CURTAIN
 BELL
 COFFEE
 SCHOOL
 PARENT
 MOON
 GARDEN
 HAT
 FARMER
 NOSE
 TURKEY
 COLOR
 HOUSE
 RIVER

Thank you very much for your help. We appreciate you taking the time to help us with this research project.
 THANK YOU!

Encouraging comments to be used if the person expresses concern about performance:

During the test: “Just do the best you can.”

Remember, we do not expect anyone to get all of these questions correct.”

“Don’t worry. We have deliberately made these questions challenging. If people could get them all right, we would not learn anything. We’re trying to find which questions are harder than others.”

ANAT GALOR

Curriculum Vitae

Last updated: June, 2021

I. PERSONAL

- | | |
|---------------------------------|---|
| 2. Name: | Anat Galor, MD |
| 3. Home Phone: | |
| 4. Office Phone: | 305-326-6000 |
| 5. Home Address: | |
| 6. Primary Appointment: | Dept. of Ophthalmology, University of Miami Miller School of Medicine (Bascom Palmer Eye Institute) |
| 7. Current Academic Rank: | Professor of Ophthalmology |
| 8. Secondary Departments: | Surgical services, Miami Veterans Administration
Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami
Sylvester Cancer Center, University of Miami |
| 9. Citizenship: | USA |
| 10. Visa Type (if non-citizen): | N/A |

II. HIGHER EDUCATION

- | | |
|--------------------------------------|---|
| 11. Institutional: | |
| 6/2011 | University of Miami, Miami, Masters in Science of Public Health |
| 6/2002 | Washington University, St. Louis, Doctor of medicine |
| 6/1997 | Carnegie Mellon University, Pittsburgh, BS, Mechanical Engineering
BA, Biology |
| 12. Non-Institutional: N/A | |
| 13. Certification, licensure: | Florida Medical License, April 2007- present
Diplomate, American Board of Ophthalmology (2009)
<u>Scored in 99%th percentile on written boards.</u> |

III. EXPERIENCE

- | | |
|----------------------|---|
| 14. Academic: | |
| 7/18-present | Tenure awarded. University of Miami. |
| 12/17-present | Secondary appointment at Department of Anesthesiology, Perioperative Medicine and Pain, University of Miami |
| 12/16-present | Secondary appointment at the Sylvester Comprehensive Cancer Center, University of Miami |
| 11/14-present | Bascom Palmer Eye Institute, Associate Professor of Clinical Ophthalmology, University of Miami |
| 11/08-11/14 | Bascom Palmer Eye Institute, Assistant Professor of Clinical Ophthalmology, University of Miami |
| 7/07-10/08 | Bascom Palmer Eye Institute, Cornea Fellowship, Lecturer |
| 7/06-6/07 | Wilmer Eye Institute, Johns Hopkins, Uveitis Fellowship, Lecturer |
| 7/05-6/06 | Cleveland Clinic Cole Eye Institute, Ophthalmology, Chief resident |
| 7/03-6/06 | Cleveland Clinic Cole Eye Institute, Ophthalmology residency |

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- 7/02-6/03 MetroHealth Medical Center (Cleveland), Intern in internal medicine
15. **Hospital Appointments:**
- 7/07- present Jackson Memorial Hospital, Miami
- 1/09- present Miami Veterans Administration Hospital, Miami
- 1/09- present Anne Bates Leach Eye Hospital, Miami
16. **Military:** N/A

IV. PUBLICATIONS

17. Books and monographs published:

1. Nandini Venkateswaran, Carolina Mercado, Sarah C. Wall, **Anat Galor**, Jianhua Wang & Carol L. Karp (2020) High resolution anterior segment optical coherence tomography of ocular surface lesions: A review and handbook, Expert Review of Ophthalmology, DOI: 10.1080/17469899.2021.1851598
2. Paranjpe V, Phung L, **Galor A**. The Tear Film – Anatomy and Physiology. Chapter 14. In *Ocular Fluid Dynamics: From Theory to Clinical Applications*. Editors: Guidoboni G, Sacco R, Harris A. Springer-Birkhauser (New York). 2019. ISBN 978-3-030-25886-3
3. Paranjpe V, Phung L, **Galor A**. The Tear Film – Pathological Conditions. Chapter 15. In *Ocular Fluid Dynamics: From Theory to Clinical Applications*. Editors: Guidoboni G, Sacco R, Harris A. Springer-Birkhauser (New York). 2019. ISBN 978-3-030-25886-3
4. **Galor A**, Goldhardt R. *Ophthalmology for the Internist* in Baliga RR (editor). Textbook of Internal Medicine: An Intensive Board Review Book with 1480 Multiple Choice Questions 1st Kindle Edition, Blendon-Miller, An imprint of MasterMedFacts LLC, March 2018.
5. Ezuddin N, Avila S, **Galor A**. New diagnostics modalities for dry eye disease. In Ocular Surface Disease: A case based update. Ed. Ali Djalilian, MD. Springer, Cham, Switzerland, 139-150. 2018.
6. Patel R, Yoo SH, Karp CL, **Galor A**. Cataract Surgery After Refractive Surgery. Int Ophthalmol Clin. 2016 Spring;56(2):171-82. (Senior and corresponding author).
7. **Galor A**, Karp CL. Ocular surface tumors. *Manual de Oftalmología*. 2016. Editor: Gabriela Junco .
8. Murillo JC, **Galor A**, Karp CL. Ultra-high resolution optical coherence tomography for ocular surface tumors. In: *Essentials of OCT in Ocular Disease*. Agarwal A, Kumar D. (eds). Thieme: New York. 2015. <https://www.amazon.com/Essentials-Ocular-Disease-Amar-Agarwal/dp/1626230986>
9. **Galor A**. Diagnosis and management of ocular surface disease. In *Advances in Medical and Surgical Cornea* (Jeng, editor). Springer New York. 2014. Pages 1-10.
10. **Galor A**, Jeng B, Singh AD. Surgical techniques. In: Pe'er J, Singh AD, (eds) *Clinical Ophthalmic Oncology: Eyelid and Conjunctival Tumors*, 2nd Edition. Philadelphia, Springer. 2013. Chapter 21: 221-228.
11. **Galor A**. Section 3: Cornea/external disease. In: Russell SR, Rockwood EJ, eds. *ProVision Series 5: Ophthalmic Multiple-Choice Questions With Discussions*. San Francisco: American Academy of Ophthalmology; 2012. 37-69, 229-248.
12. Pouyeh B, **Galor A**, Miller D, Alfonso E. In Copeland RA, Afshari NA (Ed.) Chapter 25: Fungal keratitis. *Principles and Practice of Cornea*. Jaypee Brothers Medical Publishers, New Delhi, India. 2013. 295-308. (Corresponding author)
13. **Galor A**, Gregori NZ, Pelletier J, Goldhardt R, Junk A, Wellik S. Update on Eye Care Issues in Veterans. In McCleod M , Hewitt CS (eds). *Veterans: Health Issues, Coping Strategies and Benefits*. Nova Science Publishers, Inc. New York 2012, pp 45-64. (Corresponding author)
14. **Galor A**, Thorne JE, Jabs DA. Chapter 26: Ocular Manifestations of the Rheumatic Diseases. In: Tasman W, Jaeger EA (eds)) *Duane's Ophthalmology* 2011 edition. Philadelphia, Lippincott Williams & Wilkins, 2011, Volume 5.
15. Alfonso E, **Galor A**, Miller D. Fungal keratitis. In: Krachmer JH, Mannis MJ, Holland EJ (eds). *Cornea* 3rd edition, Mosby Elsevier, 2011, pp. 1009-22.
16. **Galor A**, Yoo SH. Microincision phacoemulsification and posterior chamber lens implantation. In: Dunn

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Curriculum Vitae

- JP. (ed) *Basic Techniques in Ophthalmic Surgery*. San Francisco, American Academy of Ophthalmology, 2009, pp. 88-91.
17. Perez VL, **Galor A**, Langston DP. Uveal tract, iris, ciliary body, and choroid. In: Langston DP ed (ed) *Manual of Ocular Diagnosis and Therapy*, 6th edition, Philadelphia, Lippincott Williams & Wilkins, 2008, pp. 206-258.
 18. **Galor A**, Jeng B. Surgical techniques. In: Singh AD, Damato BE, Pe'er J, Murphree AL, Perry JD, (eds) *Clinical Ophthalmic Oncology*. Philadelphia, Mosby Elsevier. 2007, pp. 158-161.
 19. **Galor A**, Kaiser P, Perez VL. Ocular histoplasmosis. In: Huang D, Kaiser PK, Lowder CY, Traboulsi, EI (eds). *Atlas of Posterior Segment Images*. Philadelphia, Mosby Elsevier. 2006, pp 359-365.

18. Juried or refereed journal articles or exhibitions:

EDITORIALS

1. **Galor A**. Why Internists Should Care About Dry Eye Disease. J Clin Med. 2020 Feb 15;9(2).
2. **Galor A**. Painful Dry Eye Symptoms: A Nerve Problem or a Tear Problem? Ophthalmology. 2019 May;126(5):648-651.
2. Albin T, Callaway NF, Jaffe GJ, Feuer W, Davis J, Goldstein D, Lowder C, Lin P, Nguyen Q, Srivastava S, Callanan D, **Galor A**, Goldhardt R, Flynn H Jr MUST Beg to Differ. Ophthalmic Surg Lasers Imaging Retina. 2019 May 1;50(5):266-268.

PEER REVIEWED PUBLICATIONS:

1. Watane A, Cavuoto KM, Rojas M, Dermer H, O Day J, Banerjee S, **Galor A**. Fecal Microbial Transplant in Individuals with Immune-mediated Dry Eye. Am J Ophthalmol. 2021 Jun 29:S0002-9394(21)00348-2. (Senior and corresponding author)
2. Chacko G, Patel S, **Galor A**, Kumar N. Heat Exposure and Multiple Sclerosis-A Regional and Temporal Analysis. Int J Environ Res Public Health. 2021 Jun 2;18(11):5962.
3. Levine H, Hwang J, Dermer H, Mehra D, Feuer W, **Galor A**. Relationships between activated dendritic cells and dry eye symptoms and signs. Ocul Surf. 2021 Jun 6;21:186-192. (Senior and corresponding author)
4. Mehra D, Mangwani-Mordani S, Acuna K, C Hwang J, R Felix E, **Galor A**. Long-Term Trigeminal Nerve Stimulation as a Treatment for Ocular Pain. Neuromodulation. 2021 May 4. (Senior and corresponding author)
5. Aboumourad RJ, **Galor A**, Karp CL. Case Series: High-resolution Optical Coherence Tomography as an Optical Biopsy in Ocular Surface Squamous Neoplasia. Optom Vis Sci. 2021 May 1;98(5):450-455.
6. Patel S, Kaplan C, **Galor A**, Kumar N. The Role of Temperature Change, Ambient Temperature, and Relative Humidity in Allergic Conjunctivitis in a US Veteran Population. Am J Ophthalmol. 2021 May 12:S0002-9394(21)00272-5.
7. Cavuoto KM, **Galor A**, Banerjee S. mOcular Surface Microbiome Alterations Are Found in Both Eyes of Individuals With Unilateral Infectious Keratitis. Transl Vis Sci Technol. 2021 Feb 5;10(2):19.
8. Gomez A, Serrano A, Salero E, Tovar A, Amescua G, **Galor A**, Keane RW, Pablo de Rivero Vaccari J, Sabater AL. Tumor necrosis factor-alpha and interferon-gamma induce inflammasome-mediated corneal endothelial cell death. Exp Eye Res. 2021 Apr 17;207:108574.
9. Jabs DA, Denniston AK, **Galor A**, Lightman S, McCluskey P, Oden N, Palestine AG, Rosenbaum JT, Saleem SM, Thorne JE, Trusko BE; Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for tubulointerstitial nephritis with uveitis syndrome. Am J Ophthalmol. 2021 Apr 9:S0002-9394(21)00166-5.
10. Jabs DA, Caspers L, Chee SP, **Galor A**, Goldstein D, McCluskey P, Murray PI, Oden N, Palestine AG, Rosenbaum JT, Thorne JE, Trusko BE; Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for cytomegalovirus anterior uveitis. Am J Ophthalmol. 2021 Apr 9:S0002-9394(21)00185-9

Anat Galor, MD
Curriculum Vitae

11. Patel S, Tohme N, Gorrin E, Kumar N, Goldhagen B, **Galor A**. Prevalence and risk factors for chalazion in an older veteran population. *Br J Ophthalmol*. 2021 Mar 31;bjophthalmol-2020-318420. *(Senior and corresponding author)*
12. Baksh BS, Zayan KL, Goldhardt R, Felix ER, Klimas N, **Galor A**. Ocular manifestations and biomarkers of Gulf War Illness in US veterans. *Sci Rep*. 2021 Mar 22;11(1):6548. *(Senior and corresponding author)*
13. Baksh BS, Morkin M, Felix E, Karp CL, **Galor A**. Ocular Pain Symptoms in Individuals With and Without a History of Refractive Surgery: Results From a Cross-Sectional Survey. *Cornea*. 2021 Feb 8. *(Senior and corresponding author)*
14. Rainer QC, Rodriguez AA, Bajic P, **Galor A**, Ramasamy R, Masterson TA. Implications of Calcification in Peyronie's Disease, A Review of the Literature. *Urology*. 2021 Jan 18:S0090-4295(21)00058-3.
15. Dermer H, Hwang J, Mittal R, Cohen A, **Galor A**. Corneal sub-basal nerve plexus microneuromas in individuals with and without dry eye. *Br J Ophthalmol*. 2021 Jan 4;bjophthalmol-2020-317891. *(Senior and corresponding author)*
16. Hwang J, Karanam V, Wang J, Feuer WJ, Garg RK, Tamariz L, **Galor A**. Conjunctival Vessels in Diabetes Using Functional Slit Lamp Biomicroscopy. *Cornea*. 2020 Dec 16. *(Senior and corresponding author)*
17. Laura D, Lee Y, Farhangi M, Salamo O, Mirsaeidi M, Goldhardt R, **Galor A**. Ocular Manifestations of Sarcoidosis in a South Florida Population. *Clin Ophthalmol*. 2020 Nov 2;14:3741-3746. *(Senior and corresponding author)*
18. Venkateswaran N, Hwang J, Rong AJ, Levitt AE, Diel RJ, Levitt RC, Sarantopoulos KD, Lee WW, **Galor A**. Periorbital botulinum toxin A improves photophobia and sensations of dryness in patients without migraine: Case series of four patients. *Am J Ophthalmol Case Rep*. 2020 Jul 4;19:100809. *(Senior and corresponding author)*
19. Soifer M, Mousa HM, Stinnett SS, **Galor A**, Perez VL. Matrix metalloproteinase 9 positivity predicts long term decreased tear production. *Ocul Surf*. 2020 Oct 21:S1542-0124(20)30159-2.
20. Levitt AE, **Galor A**, Small L, Feuer W, Felix ER. Pain sensitivity and autonomic nervous system parameters as predictors of dry eye symptoms after LASIK. *Ocul Surf*. 2020 Oct 20:S1542-0124(20)30160-9. *(Senior and Corresponding author)*.
21. Rock S, **Galor A**, Kumar N. Indoor Airborne Microbial Concentration and Dry Eye. *Am J Ophthalmol*. 2020 Oct 13:S0002-9394(20)30563-8.
22. Cheng AM, Hwang J, Dermer H, **Galor A**. Prevalence of Ocular Demodicosis in an Older Population and Its Association With Symptoms and Signs of Dry Eye. *Cornea*. 2020 Sep 21. *(Senior and Corresponding author)*.
23. Ramos-Betancourt N, Field MG, Davila-Alquisiras JH, Karp CL, Hernández-Zimbrón LF, García-Vázquez R, Vazquez-Romo KA, Wang G, Fromow-Guerra J, Hernandez-Quintela E, **Galor A**. Whole exome profiling and mutational analysis of Ocular Surface Squamous Neoplasia. *Ocul Surf*. 2020 Jul 24;18(4):627-632.
24. Huang A, Janecki J, **Galor A**, Rock S, Menendez D, Hackam AS, Jeng BH, Kumar N. Association of the Indoor Environment With Dry Eye Metrics. *JAMA Ophthalmol*. 2020 Aug 1;138(8):867-874.
25. Zayan K, Aggarwal S, Felix E, Levitt R, Sarantopoulos K, **Galor A**. Transcutaneous Electrical Nerve Stimulation for the Long-Term Treatment of Ocular Pain. *Neuromodulation*. 2020 Jul 21;35:1-10. *(Senior and Corresponding author)*.
26. Idarraga MA, Guerrero JS, Mosle SG, Miralles F, **Galor A**, Kumar N. Relationships Between Short-Term Exposure to an Indoor Environment and Dry Eye (DE) Symptoms. *J Clin Med*. 2020 May 2;9(5):1316. *(Corresponding author)*.
27. Liu Z, Karp CL, **Galor A**, Ai Bayyat GJ, Jiang H, Wang J. Role of optical coherence tomography angiography in the characterization of vascular network patterns of ocular surface squamous neoplasia. *Ocul Surf*. 2020 Apr 25. pii: S1542-0124(20)30062-8.

Anat Galor, MD
Curriculum Vitae

28. Mendez R, Watane A, Farhangi M, Cavuoto KM, Leith T, Budree S, **Galor A**, Banerjee S. Gut microbial dysbiosis in individuals with Sjögren's syndrome. *Microb Cell Fact*. 2020 Apr 15;19(1):90.
29. Farhangi M, Cheng AM, Baksh B, Sarantopoulos CD, Felix ER, Levitt RC, **Galor A**. Effect of non-invasive intranasal neurostimulation on tear volume, dryness and ocular pain. *Br J Ophthalmol*. 2020 Sep;104(9):1310-1316. (*Senior and Corresponding author*).
30. Hubschman S, Rojas M, Kalavar M, Kloosterboer A, Sabater AL, **Galor A**. Association Between Early Sjögren Markers and Symptoms and Signs of Dry Eye. *Cornea*. 2020 Mar;39(3):311-315. (*Senior and Corresponding author*).
31. Dermer H, Theotoka D, Lee CJ, Chhadva P, Hackam AS, **Galor A**, Kumar N. Total Tear IgE Levels Correlate with Allergenic and Irritating Environmental Exposures in Individuals with Dry Eye. *J Clin Med*. 2019 Oct 4;8(10). (*Corresponding author*).
32. Naranjo A, Arboleda A, Martinez JD, Durkee H, Aguilar MC, Relhan N, Nikpoor N, **Galor A**, Dubovy SR, Leblanc R, Flynn HW Jr, Miller D, Parel JM, Amescua G. Rose Bengal Photodynamic Antimicrobial Therapy (RB-PDAT) for Patients with Progressive Infectious Keratitis: A Pilot Clinical Study. *Am J Ophthalmol*. 2020 Apr 7. pii: S0002-9394(20)30054-4.
33. Small LR, **Galor A**, Felix ER, Horn DB, Levitt RC, Sarantopoulos CD. Oral Gabapentinoids and Nerve Blocks for the Treatment of Chronic Ocular Pain. *Eye Contact Lens*. 2020 May;46(3):174-181. (*Senior and Corresponding author*).
34. **Galor A**, Patel S, Small LR, Rodriguez A, Venincasa MJ, Valido SE, Feuer W, Levitt RC, Sarantopoulos CD, Felix ER. Pregabalin Failed to Prevent Dry Eye Symptoms after Laser-Assisted in Situ Keratomileusis (LASIK) in a Randomized Pilot Study. *J Clin Med*. 2019 Sep 1;8(9). (*Senior and Corresponding author*).
35. Tran AQ, Venkateswaran N, **Galor A**, Karp CL. Utility of high-resolution anterior segment optical coherence tomography in the diagnosis and management of sub-clinical ocular surface squamous neoplasia. *Eye Vis (Lond)*. 2019 Aug 27;6:27.
36. Tirpack AR, Vanner E, Parrish JM, **Galor A**, Hua HU, Wellik SR. Dry Eye Symptoms and Ocular Pain in Veterans with Glaucoma. *J Clin Med*. 2019 Jul 22;8(7).
37. Kaplan C, **Galor A**, Blackwelder P, Hackam AS, Jeng BH, Menendez D, Kim SJ, Kumar N. Human Ocular Surface Particulate Composition in the Clinical Versus Home Environment. *Cornea*. Oct;38(10):1266-1272.
38. Cavuoto KM, **Galor A**, Banerjee S. Anatomic Characterization of the Ocular Surface Microbiome in Children. *Microorganisms*. 2019 Aug 14;7(8). pii: E259.
39. Patel S, Felix ER, Levitt RC, Sarantopoulos CD, **Galor A**. Dysfunctional Coping Mechanisms Contribute to Dry Eye Symptoms. *J Clin Med*. 2019 Jun 24;8(6). (*Senior and Corresponding author*).
40. Venkateswaran N, Mercado C, Tran AQ, Garcia A, Diaz PFM, Dubovy SR, **Galor A**, Karp CL. The use of high resolution anterior segment optical coherence tomography for the characterization of conjunctival lymphoma, conjunctival amyloidosis and benign reactive lymphoid hyperplasia. *Eye Vis (Lond)*. 2019 Jun 18;6:17.
41. Karp CL, Mercado C, Venkateswaran N, Ruggeri M, **Galor A**, Garcia A, Sivaraman KR, Fernandez MP, Bermudez A, Dubovy SR. Use of High-Resolution Optical Coherence Tomography in the Surgical Management of Ocular Surface Squamous Neoplasia: A Pilot Study. *Am J Ophthalmol*. 2019 Jun 1. pii: S0002-9394(19)30249-1.
42. Segev F, Geffen N, **Galor A**, Cohen Y, Gefen R, Belkin A, Arieli Y, Epshtein S, Oren A, Harris A. Dynamic assessment of the tear film muco-aqueous and lipid layers using a novel tear film imager (TFI). *Br J Ophthalmol*. 2020 Jan;104(1):136-141.
43. Farhangi M, Diel RJ, Buse DC, Huang AM, Levitt RC, Sarantopoulos CD, Felix ER, **Galor A**. Individuals with migraine have a different dry eye symptom profile than individuals without migraine. *Br J Ophthalmol*. 2020 Feb;104(2):260-264. (*Senior and Corresponding author*).

Anat Galor, MD
Curriculum Vitae

44. Gregori NZ, Rodriguez M, Staropoli PC, Karli SZ, **Galor A**, Wellik SR, Goldhardt R, Shi W, Junk AK. Visual and anatomic outcomes of cataract surgery with intraoperative or postoperative complications in a teaching institution. *Can J Ophthalmol*. 2019 Jun;54(3):382-387.
45. Smith LM, Lamba S, Karp CL, **Galor A**. Epidemiology of ocular surface squamous neoplasia in veterans: a retrospective case-control study. *Eye Vis (Lond)*. 2019 May 14;6:14. (*Senior and Corresponding author*).
46. Goldhardt R, Batawi HIM, Rosenblatt M, Lollett IV, Park JJ, **Galor A**. Effect of Anti-Vascular Endothelial Growth Factor Therapy on Corneal Nerves. *Cornea*. 2019 May;38(5):559-564.
47. Farhangi M, Feuer W, **Galor A**, Bouhassira D, Levitt RC, Sarantopoulos CD, Felix ER. Modification of the Neuropathic Pain Symptom Inventory for use in eye pain (NPSI-Eye). *Pain*. 2019 Jul;160(7):1541-1550.
48. Dermer H, **Galor A**, Hackam AS, Mirsaedi M, Kumar N. Impact of seasonal variation in meteorological conditions on dry eye severity. *Clin Ophthalmol*. 2018 Nov 29;12:2471-2481. (*Corresponding author*).
49. Martinez JD, **Galor A**, Amescua G, Ramos-Betancourt N, Beltrán F, Babayán Sosa A, Santacruz Valdés C, Ramírez-Assad C, Mora Juárez E, Hernández-Quintela E. Transcultural validation of the 5-Item Dry Eye Questionnaire for the Mexican population. *Int Ophthalmol*. Oct;39(10):2313-2324.
50. Paranjpe V, Tan J, Nguyen J, Lee J, Allegood J, **Galor A**, Mandal N. Clinical signs of meibomian gland dysfunction (MGD) are associated with changes in meibum sphingolipid composition. *Ocul Surf*. 2018 Dec 12. pii: S1542-0124(18)30196-4. (*Corresponding author*).
51. Diel RJ, Hwang J, Kroeger ZA, Levitt RC, Sarantopoulos CD, Sered H, Felix ER, Martinez-Barrizonte J, **Galor A**. Photophobia and sensations of dryness in patients with migraine occur independent of baseline tear volume and improve following botulinum toxin A injections. *Br J Ophthalmol*. 2019 Aug;103(8):1024-1029. (*Senior and Corresponding author*).
52. Cavuoto KM, Banerjee S, Miller D, **Galor A**. Composition and Comparison of the Ocular Surface Microbiome in Infants and Older Children. *Transl Vis Sci Technol*. 2018 Nov 30;7(6):16.
53. Venkateswaran N, Mercado C, **Galor A**, Karp CL. Comparison of topical 5-fluorouracil and interferon alfa-2b as primary treatment modalities for ocular surface squamous neoplasia. *Am J Ophthalmol*. 2019 Mar;199:216-222.
54. Karanam VC, Tamariz L, Batawi H, Wang J, Galor A. Functional slit lamp biomicroscopy metrics correlate with cardiovascular risk. *Ocul Surf*. 2019 Jan;17(1):64-69.
55. Mercado CL, Pole C, Wong J, Batlle JF, Roque F, Shaikh N, Murillo JC, **Galor A**, Karp CL. Surgical versus medical treatment for ocular surface squamous neoplasia: A quality of life comparison. *Ocul Surf*. 2018 Sep 11. pii: S1542-0124(18)30068-5.
56. Yesilirmak N, Chhadva P, Cabot F, **Galor A**, Yoo SH. Post-Laser In Situ Keratomileusis Epithelial Ingrowth: Treatment, Recurrence, and Long-Term Results. *Cornea*. 2018 Dec;37(12):1517-1521.
57. Sajjani R, Raia S, Gibbons A, Chang V, Karp CL, Sarantopoulos CD, Levitt RC, **Galor A**. Epidemiology of Persistent Postsurgical Pain Manifesting as Dry Eye-like Symptoms After Cataract Surgery *Cornea*. 2018 Dec;37(12):1535-1541. (*Senior and Corresponding author*).
58. Cavuoto KM, Mendez R, Miller D, **Galor A**, Banerjee S. Effect of clinical parameters on the ocular surface microbiome in children and adults. *Clin Ophthalmol*. 2018 Jul 2;12:1189-1197.
59. Dutca LM, Rudd D, Robles V, **Galor A**, Garvin MK, Anderson MG. Effects of sustained daily latanoprost application on anterior chamber anatomy and physiology in mice. *Sci Rep*. 2018 Aug 30;8(1):13088.
60. Yim M, **Galor A**, Nanji A, Joag M, Palioura S, Feuer W, Karp CL. Ability of novice clinicians to interpret high-resolution optical coherence tomography for ocular surface lesions. *Can J Ophthalmol*. 2018 Apr;53(2):150-154.
61. Sayed-Ahmed I, Murillo JC, Monsalve P, Ulloa JP, Fernandez MP, Wong J, Elgart G, **Galor A**, Dubovy SR, Karp CL. Blue Nevus of the Ocular Surface: Clinical Characteristics, Pathologic Features, and Clinical Course. *Ophthalmology*. 2018 Aug;125(8):1189-1198.

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62. Batawi H, Lollett IV, Maliakal C, Wellik SR, Anderson M, Feuer W, Karp CL, **Galor A**. A Comparative Study of Central Corneal Epithelial, Stromal, and Total Thickness in Males With and Without Primary Open-Angle Glaucoma. *Cornea*. 2018 Jun;37(6):712-719. *(Senior and Corresponding author)*.
63. Iglesias E, Sajjani R, Levitt RC, Sarantopoulos CD, **Galor A**. Epidemiology of Persistent Dry Eye-Like Symptoms After Cataract Surgery. 2018 Jul;37(7):893-898. *(Senior and Corresponding author)*.
64. **Galor A**, Small L, Feuer W, Levitt RC, Sarantopoulos KD, Yosipovitch G. The Relationship Between Ocular Itch, Ocular Pain, and Dry Eye Symptoms (An American Ophthalmological Society Thesis). *Trans Am Ophthalmol Soc*. 2018 Jan 17;115:T5. *(Senior and Corresponding author)*.
65. Lee CJ, Levitt RC, Felix ER, Sarantopoulos CD, **Galor A**. Evidence that dry eye is a comorbid pain condition in a U.S. veteran population. *Pain Rep*. 2017 Nov 20;2(6):e629.
66. Stringham J, Ashkenazy N, **Galor A**, Wellik SR. Barriers to Glaucoma Medication Compliance Among Veterans: Dry Eye Symptoms and Anxiety Disorders. *Eye Contact Lens*. 2018 Jan;44(1):50-54.
67. Diel RJ, Kroeger ZA, Levitt RC, Sarantopoulos C, Sered H, Martinez-Barrizonte J, **Galor A**. Botulinum Toxin A for the Treatment of Photophobia and Dry Eye. *Ophthalmology*. 2018 Jan;125(1):139-140. *(Senior and Corresponding author)*.
68. Sivanesan E, Levitt RC, Sarantopoulos CD, Patin D, **Galor A**. Noninvasive Electrical Stimulation for the Treatment of Chronic Ocular Pain and Photophobia. *Neuromodulation*. 2018 Dec;21: 727-734. *(Senior and Corresponding author)*.
69. Chang VS, Rose TP, Karp CL, Levitt RC, Sarantopoulos C, **Galor A**. Neuropathic-Like Ocular Pain and Nonocular Comorbidities Correlate With Dry Eye Symptoms. *Eye Contact Lens*. 2018 Nov;44 Suppl 2:S307-S313. *(Senior and Corresponding author)*.
70. Swaminathan SS, Field MG, Sant D, Wang G, **Galor A**, Dubovy SR, Harbour JW, Karp CL. Molecular Characteristics of Conjunctival Melanoma Using Whole-Exome Sequencing. *JAMA Ophthalmol*. 2017 Dec 1;135(12):1434-1437.
71. Zhang L, Mercado C, **Galor A**, Holland EJ, Wang G, Karp CL. Challenging Treatment of Ocular Surface Squamous Neoplasia in Patients with Atopic Disease. *Ocul Immunol Inflamm*. 2017 Nov 30;1-6.
72. Atallah M, Joag M, **Galor A**, Amescua G, Nanji A, Wang J, Perez VL, Dubovy S, Karp CL. Role of high resolution optical coherence tomography in diagnosing ocular surface squamous neoplasia with coexisting ocular surface diseases. *Ocul Surf*. 2017 Oct;15(4):688-695.
73. Ahmad S, Lopez M, Attala M, **Galor A**, Stanciu NA, Miller D, Suh L, Albin T, Perez VL, Karp CL, Davis JL, Alfonso E, Forster RK, Amescua G. Interventions and Outcomes in Patients with Infectious Pseudomonas scleritis: A 10-Year Perspective. *Ocul Immunol Inflamm*. 2017 Oct 17:1-8.
74. Staropoli PC, Gregori NZ, Junk AK, **Galor A**, Goldhardt R, Goldhagen BE, Shi W, Feuer W. Surgical Simulation Training Reduces Intraoperative Cataract Surgery Complications Among Residents. *Simul Healthc*. 2018 Feb;13(1):11-15.
75. Lee CJ, Felix ER, Levitt RC, Eddy C, Vanner EA, Feuer WJ, Sarantopoulos CD, **Galor A**. Traumatic brain injury, dry eye and comorbid pain diagnoses in US veterans. *Br J Ophthalmol*. 2018 May;102(5):667-673. *(Senior and Corresponding author)*.
76. Ong ES, Felix ER, Levitt RC, Feuer WJ, Sarantopoulos CD, **Galor A**. Epidemiology of discordance between symptoms and signs of dry eye. *Br J Ophthalmol*. 2018 May;102(5):674-679. *(Senior and Corresponding author)*.
77. Avula A, **Galor A**, Blackwelder P, Carballosa-Gautam M, Hackam AS, Jeng B, Kumar N. Application of Scanning Electron Microscopy With Energy-Dispersive X-Ray Spectroscopy for Analyzing Ocular Surface Particles on Schirmer Strips. 2017 Jun;36(6):752-756.
78. Batawi H, Shalabi N, Joag M, Koru-Sengul T, Rodriguez J, Green PT, Campigotto M, Karp CL, **Galor A**. Sub-basal Corneal Nerve Plexus Analysis Using a New Software Technology. *Eye Contact Lens*. 2018 Sep;44 Suppl 1:S199-S205. *(Senior and Corresponding author)*.
79. Murillo JC, **Galor A**, Wu MC, Kye NK, Wong J, Ahmed IO, Joag M, Shalabi N, Lahners W, Dubovy S, Karp CL. Intracorneal and Intraocular Invasion of Ocular Surface Squamous Neoplasia after Intraocular

Anat Galor, MD
Curriculum Vitae

- Surgery: Report of Two Cases and Review of the Literature. *Ocul Oncol Pathol*. 2017 Jan;3(1):66-72.
80. **Galor A**, Seiden BE, Park JJ, Feuer WJ, McClellan AL, Felix ER, Levitt RC, Sarantopoulos CD, Wallace DM. The Association of Dry Eye Symptom Severity and Comorbid Insomnia in US Veterans. *Eye Contact Lens*. 2018 Sep;44 Suppl 1:S118-S124. (*Senior and Corresponding author*).
 81. Ashkenazy N, Karp CL, Wang G, Acosta CM, **Galor A**. Immunosuppression as a Possible Risk Factor for Interferon Nonresponse in Ocular Surface Squamous Neoplasia. *Cornea*. 2017 Apr;36(4):506-510. (*Senior and Corresponding author*).
 82. Crane AM, Feuer W, Felix ER, Levitt RC, McClellan AL, Sarantopoulos KD, **Galor A**. Evidence of central sensitisation in those with dry eye symptoms and neuropathic-like ocular pain complaints: incomplete response to topical anaesthesia and generalised heightened sensitivity to evoked pain.. *Br J Ophthalmol*. 2017 Sep;101(9):1238-1243. (*Senior and corresponding author*).
 83. Chen W, Batawi HI, Alava JR, **Galor A**, Yuan J, Sarantopoulos CD, McClellan AL, Feuer WJ, Levitt RC, Wang J. Bulbar conjunctival microvascular responses in dry eye. *Ocul Surf*. 2017 Apr;15(2):193-201. (*Corresponding author*).
 84. Ong ES, Alghamdi YA, Levitt RC, McClellan AL, Lewis G, Sarantopoulos CD, Felix ER, **Galor A**. Longitudinal Examination of Frequency of and Risk Factors for Severe Dry Eye Symptoms in US Veterans. *JAMA Ophthalmol*. 2016 Dec 22. (*Senior and corresponding author*).
 85. **Galor A**, Levitt RC, McManus KT, Kalangara JP, Seiden BE, Park JJ, Covington DB, Sarantopoulos CD, Felix ER. Assessment of Somatosensory Function in Patients With Idiopathic Dry Eye Symptoms. *JAMA Ophthalmol*. 2016 Nov 1;134(11):1290-1298. (*Senior and corresponding author*).
 86. Rodriguez M, Yesilirmak N, Chhadva P, Goldhagen B, Karp C, **Galor A**. High-Resolution Optical Coherence Tomography in the Differentiation of Inflammatory Versus Noninflammatory Peripheral Corneal Thinning. *Cornea*. 2017 Jan;36(1):48-52. (*Senior and corresponding author*).
 87. Martinez JD, **Galor A**, Ramos-Betancourt N, Lisker-Cervantes A, Beltrán F, Ozorno-Zárate J, Sánchez-Huerta V, Torres-Vera MA, Hernández-Quintela E. Frequency and risk factors associated with dry eye in patients attending a tertiary care ophthalmology center in Mexico City. *Clin Ophthalmol*. 2016 Jul 21;10:1335-42.
 88. Alghamdi YA, Camp A, Feuer W, Karp CL, Wellik S, **Galor A**. Compliance and Subjective Patient Responses to Eyelid Hygiene. *Eye Contact Lens*. 2017 Jul;43(4):213-217. (*Senior and corresponding author*).
 89. Spierer O, Felix ER, McClellan AL, Parel JM, Gonzalez A, Feuer WJ, Sarantopoulos CD, Levitt RC, Ehrmann K, **Galor A**. Corneal Mechanical Thresholds Negatively Associate With Dry Eye and Ocular Pain Symptoms. *Invest Ophthalmol Vis Sci*. 2016 Feb 1;57(2):617-25. (*Senior and corresponding author*).
 90. Walter SD, Gronert K, McClellan AL, Levitt RC, Sarantopoulos KD, **Galor A**. ω-3 Tear Film Lipids Correlate With Clinical Measures of Dry Eye. *Invest Ophthalmol Vis Sci*. 2016 May 1;57(6):2472-8. (*Senior and corresponding author*).
 91. Crane AM, Levitt RC, Felix ER, Sarantopoulos KD, McClellan AL, **Galor A**. Patients with more severe symptoms of neuropathic ocular pain report more frequent and severe chronic overlapping pain conditions and psychiatric disease. *Br J Ophthalmol*. 2017 Feb;101(2):227-231. (*Senior and corresponding author*).
 92. Tran KD, Falcone MM, Choi DS, Goldhardt R, Karp CL, Davis JL, **Galor A**. Epidemiology of Herpes Zoster Ophthalmicus: Recurrence and Chronicity. 2016 Jul;123(7):1469-75. (*Senior and corresponding author*).
 93. Joag MG, Sise A, Murillo JC, Sayed-Ahmed IO, Wong JR, Mercado C, **Galor A**, Karp CL. Topical 5-Fluorouracil 1% as Primary Treatment for Ocular Surface Squamous Neoplasia. 2016 Jul;123(7):1442-8.
 94. Alghamdi YA, Mercado C, McClellan AL, Batawi H, Karp CL, **Galor A**. Epidemiology of Meibomian Gland Dysfunction in an Elderly Population. 2016 Jun;35(6):731-5. (*Senior and corresponding author*).
 95. Kalangara JP, **Galor A**, Levitt RC, Covington DB, McManus KT, Sarantopoulos CD, Felix ER.

Anat Galor, MD
Curriculum Vitae

- Characteristics of Ocular Pain Complaints in Patients With Idiopathic Dry Eye Symptoms. *Eye Contact Lens*. 2017 May;43(3):192-198.
96. Chhadva P, McClellan AL, Alabiad CR, Feuer WJ, Batawi H, **Galor A**. Impact of Eyelid Laxity on Symptoms and Signs of Dry Eye Disease. *Cornea*. 2016 Apr;35(4):531-5. (*Senior and corresponding author*).
 97. Lanza NL, McClellan A, Batawi H, Felix ER, Sarantopoulos KD, Levitt RC, **Galor A**. Dry Eye Profiles in Patients with a Positive Elevated Surface Matrix Metalloproteinase 9 Point-of-Care Test Versus Negative Patients. *Ocul Surf*. 2016 Apr;14(2):216-23. (*Senior and corresponding author*).
 98. Moon CS, Nanji AA, **Galor A**, McCollister KE, Karp CL. Surgical versus Medical Treatment of Ocular Surface Squamous Neoplasia: A Cost Comparison. 2016 Mar;123(3):497-504.
 99. **Galor A**, Covington D, Levitt AE, McManus KT, Seiden B, Felix ER, Kalangara J, Feuer W, Patin DJ, Martin ER, Sarantopoulos KD, Levitt RC. Neuropathic ocular pain due to dry eye is associated with multiple comorbid chronic pain syndromes. *J Pain*. 2016 Mar;17(3):310-8. (*Senior and corresponding author*).
 100. **Galor A**, Felix ER, Sarantopoulos CD, Martin ER, Levitt RC. Aging and dry eye: Age-related changes in the function of the corneal somatosensory system likely underlie dry eye symptoms. *J Pain Relief* 2015, 4:176. (*Senior and corresponding author*).
 101. **Galor A**, Batawi H, Felix ER, Margolis TP, Sarantopoulos KD, Martin ER, Levitt RC. Incomplete response to artificial tears is associated with features of neuropathic ocular pain. 2016 Jun;100(6):745-9. (*Senior and corresponding author*).
 102. **Galor A**, Garg N, Nanji A, Joag M, Nuovo G, Palioura S, Wang G, Karp CL. Human Papilloma Virus Infection Does Not Predict Response to Interferon Therapy in Ocular Surface Squamous Neoplasia. *Ophthalmology*. 2015 Nov;122(11):2210-5.
 103. **Galor A**, Karp CL, Sant D, Joag M, Shalabi N, Gustafson CB, Wang G. Whole Exome Profiling of Ocular Surface Squamous Neoplasia. *Ophthalmology*. 2016 Jan;123(1):216-217.
 104. Levitt AE, McManus KT, McClellan AL, Davis JL, Goldhardt R, **Galor A**. Ocular Inflammation in the Setting of Concomitant Systemic Autoimmune Conditions in an Older Male Population. *Cornea*. 2015 Jul;34(7):762-7. (*Senior and corresponding author*).
 105. Chhadva P, Lee T, Sarantopoulos CD, Hackam AS, McClellan AL, Felix ER, Levitt RC, **Galor A**. Human Tear Serotonin Levels Correlate with Symptoms and Signs of Dry Eye. *Ophthalmology*. 2015 Aug;122(8):1675-80. (*Senior and corresponding author*).
 106. Nanji AA, Sayyad FE, **Galor A**, Dubovy S, Karp CL. High-Resolution Optical Coherence Tomography as an Adjunctive Tool in the Diagnosis of Corneal and Conjunctival Pathology. *Ocul Surf*. 2015 Jul;13(3):226-35.
 107. Chhadva P, Alexander A, McClellan AL, McManus KT, Seiden B, **Galor A**. The impact of conjunctivochalasis on dry eye symptoms and signs. *Invest Ophthalmol Vis Sci*. 2015 May 1;56(5):2867-71. (*Senior and corresponding author*).
 108. Kumar N, Feuer W, Lanza NL, **Galor A**. Seasonal Variation in Dry Eye. 2015 Aug;122(8):1727-9. (*Senior and corresponding author*).
 109. Camp A, Wellik SR, Tzu JH, Feuer W, Arheart KL, Sastry A, **Galor A**. Dry eye specific quality of life in veterans using glaucoma drops. *Cont Lens Anterior Eye*. 2015 Jun;38(3):220-5. (*Senior author*).
 110. **Galor A**, Felix ER, Feuer W, Shalabi N, Martin ER, Margolis TP, Sarantopoulos CD, Levitt RC. Dry eye symptoms align more closely to non-ocular conditions than to tear film parameters. 2015 Aug;99(8):1126-9. (*Senior and corresponding author*).
 111. Ansari Z, Singh R, Alabiad C, **Galor A**. Prevalence, Risk Factors, and Morbidity of Eye Lid Laxity in a Veteran Population. *Cornea*. 2015 Jan;34(1):32-6. (*Senior and corresponding author*).
 112. **Galor A**, Zlotcavitch L, Walter SD, Felix ER, Feuer W, Martin ER, Margolis TP, Sarantopoulos KD, Levitt RC. Dry eye symptom severity and persistence are associated with symptoms of neuropathic pain. *Br J Ophthalmol*. 2015 May;99(5):665-8. (*Senior and corresponding author*).

Anat Galor, MD
Curriculum Vitae

113. **Galor A**, Diane Zheng D, Arheart KL, Lam BL, McCollister KE, Ocasio MA, Fernandez CA, Lee DJ. Influence of Socio-Demographic Characteristics on Eye Care Expenditure: Data from the Medical Expenditure Panel Survey 2007. *Ophthalmic Epidemiol.* 2015 Feb;22(1):28-33.
114. Tzu JH, Shah CT, **Galor A**, Junk AK, Sastry A, Wellik SR. Refractive Outcomes of Combined Cataract and Glaucoma Surgery. *J Glaucoma.* 2015 Feb;24(2):161-4.
115. Junk AK, Dunn EN, **Galor A**, Wellik SR, Pelletier J, Gregori NZ, Feuer W. Cumulative probability and risk analysis for Nd:YAG laser capsulotomy. *World J Ophthalmol* 2014 August 12; 4(3): 82-86.
116. Amescua G, Atallah M, Nikpoor N, **Galor A**, Perez VL. Modified Simple Limbal Epithelial Transplantation Using Cryopreserved Amniotic Membrane for Unilateral Limbal Stem Cell Deficiency. *Am J Ophthalmol.* 2014 Sep;158(3):469-75.
117. Azcarate PM, Venincasa VD, Feuer W, Stanczyk F, Schally AV, **Galor A**. Androgen Deficiency and Dry Eye Syndrome in the Aging Male. *Invest Ophthalmol Vis Sci.* 2014 Jul 3;55(8):5046-53. (*Senior and corresponding author*).
118. Shalabi N, Karp CL, Aziz H, Jeng BH, **Galor A**. Superficial epithelial keratectomy, cautery, and amniotic membrane transplant for the treatment of painful bullous keratopathy in eyes with poor visual potential. *Cornea.* 2014 Jul;33(7):755-9. (*Senior and corresponding author*).
119. **Galor A**, Gardener H, Pouyeh B, Feuer W, Florez H. Effect of a Mediterranean dietary pattern and vitamin D levels on Dry Eye syndrome. *Cornea.* 2014 May;33(5):437-41. (*Senior and corresponding author*).
120. Nanji AA, Moon CS, **Galor A**, Sein J, Oellers P, Karp CL. Surgical versus Medical Treatment of Ocular Surface Squamous Neoplasia: A Comparison of Recurrences and Complications. *Ophthalmology.* 2014 May;121(5):994-1000.
121. **Galor A**, Kumar N, Feuer W, Lee DJ. Environmental factors affect the risk of dry eye syndrome in a United States veteran population. *Ophthalmology.* 2014 Apr;121(4):972-3. (*Senior and corresponding author*).
122. Thomas BJ, **Galor A**, Nanji AA, El Sayyad F, Wang J, Dubovy SR, Joag MG, Karp CL. Ultra high-resolution anterior segment optical coherence tomography in the diagnosis and management of ocular surface squamous neoplasia. *Ocul Surf.* 2014 Jan;12(1):46-58.
123. Modi YS, Qurban Q, Zlotcavitch L, Echeverri RJ, Feuer WJ, Florez HJ, **Galor A**. Ocular surface symptoms in veterans returning from Operation Iraqi Freedom and Operation Enduring Freedom. *Invest Ophthalmol Vis Sci.* 2014 Feb 3;55(2):650-3. (*Senior and corresponding author*).
124. See C, Bilonick RA, Feuer W, **Galor A**. Comparison of two methods for composite score generation in dry eye syndrome. *Invest Ophthalmol Vis Sci.* 2013 Sep 19;54(9):6280-6. (*Senior and corresponding author*).
125. McClellan AJ, McClellan AL, Pezon CF, Karp CL, Feuer W, **Galor A**. Epidemiology of Ocular Surface Squamous Neoplasia in a Veterans Affairs Population. *Cornea.* 2013 Oct;32(10):1354-8. (*Senior and corresponding author*).
126. Canto AP, Chhadva P, Cabot F, **Galor A**, Yoo SH, Vaddavalli PK, Culbertson WW. Comparison of IOL Power Calculation Methods and Intraoperative Wavefront Aberrometer in Eyes After Refractive Surgery. *J Refract Surg.* 2013 Jul;29(7):484-9. (*Corresponding author*).
127. Crane AM, Feuer W, **Galor A**. C-reactive protein levels and tear function parameters. *Ophthalmology.* 2013 May;120(5):1099-1099.e1. (*Senior and corresponding author*).
128. Fernandez CA, **Galor A**, Arheart KL, Musselman DL, Venincasa VD, Florez HJ, Lee DJ. Dry Eye Syndrome, Posttraumatic Stress Disorder, and Depression in an Older Male Veteran Population. *Invest Ophthalmol Vis Sci.* 2013 May 1;54(5):3666-72. (*Senior and corresponding author*).
129. Hurmeric V, Vaddavalli P, **Galor A**, Perez VL, Roman JS, Yoo SH. Single and multiple injections of subconjunctival ranibizumab for early, recurrent pterygium. *Clin Ophthalmol.* 2013;7:467-73.
130. Anwar Z, **Galor A**, Albini TA, Miller D, Perez VL, Davis JL. The Diagnostic Utility of Anterior Chamber Paracentesis with Polymerase Chain Reaction in Anterior Uveitis. *American J Ophthalmology*

Anat Galor, MD
Curriculum Vitae

- Am J Ophthalmol. 2013 May;155(5):781-786.
131. **Galor A**, Feuer W, Lee DJ, Florez H, Venincasa VD, Perez VL. Ocular surface parameters in older male veterans. *Invest Ophthalmol Vis Sci*. 2013 Feb 19;54(2):1426-33. (*Senior and corresponding author*).
 132. Venincasa VD, **Galor A**, Feuer W, Lee DJ, Florez H, Venincasa MJ. Long-Term Effects of Cataract Surgery on Tear Film Parameters. *Scientific World Journal*. 2013;2013:643764 (*Senior and corresponding author*).
 133. Lee BW, **Galor A**, Feuer WJ, Pouyeh B, Pelletier JS, Vaddavalli PK, Lemelman BT, See C, Yoo SH. Agreement Between Pentacam and IOLMaster in Patients Undergoing Toric IOL Implantation. *J Refract Surg*. 2013 Feb;29(2):114-20. (*Senior and corresponding author*).
 134. Martinez JD, **Galor A**, Perez VL, Karp CL, Yoo SH, Alfonso EC. Endothelial Graft Failure After Contralateral Autologous Corneal Transplantation. *Cornea*. 2013 Jun;32(6):745-50. (*Senior and corresponding author*).
 135. Oellers P, Karp CL, Sheth A, Kao AA, Abdelaziz A, Matthews JL, Dubovy SR, **Galor A**. Prevalence, Treatment, and Outcomes of Coexistent Ocular Surface Squamous Neoplasia and Pterygium. *Ophthalmology*. 2013 Mar;120(3):445-50.
 136. Hodson KL, **Galor A**, Karp CL, Davis JL, Albin TA, Perez VL, Miller D, Forster RK. Epidemiology and Visual Outcomes in Patients With Infectious Scleritis. *Cornea*. 2013 Apr;32(4):466-72. (*Senior and corresponding author*).
 137. **Galor A**, Zheng DD, Arheart KL, Lam BL, Perez VL, McCollister KE, Ocasio M, McClure LA, Lee DJ. Dry Eye Medication Use and Expenditures: Data from the Medical Expenditure Panel Survey 2001 to 2006. *Cornea*. 2012 Dec;31(12):1403-7. (*Corresponding author*).
 138. Kao AA, **Galor A**, Karp CL, Abdelaziz A, Feuer WJ, Dubovy SR. Clinicopathologic Correlation of Ocular Surface Squamous Neoplasms at Bascom Palmer Eye Institute: 2001 to 2010. *Ophthalmology*. 2012 Sep;119(9):1773-6.
 139. McCollister KE, Zheng DD, Fernandez CA, Lee DJ, Lam BL, Arheart KL, **Galor A**, Ocasio M, Muennig P. Racial Disparities in Quality-Adjusted Life-Years Associated With Diabetes and Visual Impairment. *Diabetes Care*. 2012 Aug;35(8):1692-4.
 140. Henry CR, Canto AP, **Galor A**, Vaddavalli PK, Culbertson WW, Yoo SH. Epithelial Ingrowth Under LASIK Flap: Clinical Characteristics, Risk Factors, and Visual Outcomes in Patients Requiring Flap Lift. *Refract Surg*. 2012 Jun 18;1-5. (*Senior and corresponding author*).
 141. **Galor A**, Karp CL, Oellers P, Kao AA, Abdelaziz A, Feuer W, Dubovy SR. Predictors of Ocular Surface Squamous Neoplasia Recurrence after Excisional Surgery. *Ophthalmology*. 2012 Oct;119(10):1974-81.
 142. **Galor A**, Feuer W, Lee DJ, Florez H, Faler AL, Zann KL, Perez VL. Depression, Post-traumatic Stress Disorder, and Dry Eye Syndrome: A Study Utilizing the National United States Veterans Affairs Administrative Database. *Am J Ophthalmol*. 2012 Aug;154(2):340-346.e2. (*Senior and corresponding author*).
 143. Zheng DD, Christ SL, Lam BL, Arheart KL, **Galor A**, Lee DJ. Increased Mortality Risk among the Visually Impaired: The Roles of Mental Well-Being and Preventive Care Practices. *Invest Ophthalmol Vis Sci*. 2012 May 14;53(6):2685-92.
 144. Pouyeh B, Viteri E, Feuer W, Lee DJ, Florez H, Fabian JA, Perez VL, **Galor A**. Impact of ocular surface symptoms on quality of life in a United States Veterans Affairs population. *Am J Ophthalmol*. 2012 Jun;153(6):1061-1066. (*Senior and corresponding author*).
 145. Kieval JZ, Karp CL, Shousha MA, **Galor A**, Hoffman RA, Dubovy SR, Wang J. Ultra-High Resolution Optical Coherence Tomography for Differentiation of Ocular Surface Squamous Neoplasia and Pterygia. *Ophthalmology*. 2012 Mar;119(3):481-6.
 146. Pouyeh B, **Galor A**, Junk AK, Pelletier J, Wellik SR, Gregori NZ, Trentacoste J. Surgical and refractive outcomes in cataract surgery with toric intraocular lens implantation in a resident-teaching institution. *J Cataract Refract Surg*. 2011 Sep;37(9):1623-8. (*Senior and corresponding author*).

Anat Galor, MD
Curriculum Vitae

147. **Galor A**, Feuer W, Lee DJ, Florez H, Carter D, Pouyeh B, Prunty WJ, Perez VL. Prevalence and Risk Factors of Dry Eye Syndrome in a United States Veterans Affairs Population. *Am J Ophthalmol*. 2011 Sep;152(3):377-384.e2 (*Senior and corresponding author*).
148. Madow B, **Galor A**, Feuer WJ, Altaweel MM, Davis JL. Validation of a Photographic Vitreous Haze Grading Technique for Clinical Trials in Uveitis. *Am J Ophthalmol*. 2011 Aug;152(2):170-176.e1.
149. Leder HA, Jabs DA, **Galor A**, Dunn JP, Thorne JE. Periocular Triamcinolone Acetonide Injections for Cystoid Macular Edema Complicating Noninfectious Uveitis. *Am J Ophthalmol*. 2011 Sep;152(3):441-448.e2.
150. Hurmeric V, Yoo SH, Karp CL, **Galor A**, Vajzovic L, Wang J, Dubovy SR, Forster RK. In Vivo Morphologic Characteristics of Salzmann Nodular Degeneration with Ultra-High-Resolution Optical Coherence Tomography. *Am J Ophthalmol*. 2011 Feb;151(2):248-56.e2
151. Karp CL, **Galor A**, Lee Y, Yoo SH. Pegylated interferon alpha 2b for treatment of ocular surface squamous neoplasia: a pilot study. *Ocul Immunol Inflamm*. 2010 Aug;18(4):254-60.
152. Karp CL, **Galor A**, Chhabra S, Barnes SD, Alfonso EC. Subconjunctival/Perilesional Recombinant Interferon alpha2b for Ocular Surface Squamous Neoplasia A 10-Year Review. *Ophthalmology*. 2010 Dec;117(12):2241-6.
153. **Galor A**, Feuer W, Kempen JH, Kaçmaz RO, Liesegang TL, Suhler EB, Foster CS, Jabs DA, Levy-Clarke GA, Nussenblatt RB, Rosenbaum JT, Thorne JE. Adverse effects of smoking on patients with ocular inflammation. *Br J Ophthalmol*. 2010 Jul;94(7):848-53.
154. **Galor A**, Yoo SH, Piccoli FV, Schmitt AJ, Chang V, Perez VL. Phase I study of subconjunctival ranibizumab in patients with primary pterygium undergoing pterygium surgery. *Am J Ophthalmol*. 2010 Jun;149(6):926-931.
155. **Galor A**, Gonzalez M, Goldman D, O'Brien TP. Intraocular lens exchange surgery in dissatisfied patients with refractive intraocular lenses. *J Cataract Refract Surg*. 2009 Oct;35(10):1706-10.
156. **Galor A**, Davis JL, Flynn HW Jr, Feuer WJ, Dubovy SR, Setlur V, Kesen MR, Goldstein DA, Tessler HH, Ganelis IB, Jabs DA, Thorne JE. Sympathetic Ophthalmia: Incidence of Ocular Complications and Vision Loss in the Sympathizing Eye. *Am J Ophthalmol*. 2009 Nov;148(5):704-710.
157. Mucci JJ, Utz VM, **Galor A**, Feuer W, Jeng BH. Recurrence rates of herpes simplex virus keratitis in contact lens and non-contact lens wearers. *Eye Contact Lens*. 2009 Jul;35(4):185-7.
158. **Galor A**, Karp CL, Chhabra S, Barnes S, Alfonso EC. Topical Interferon Alpha 2b Eye Drops for Treatment of Ocular Surface Squamous Neoplasia: A Dose Comparison Study. *Br J Ophthalmol*. 2010 May;94(5):551-4.
159. **Galor A**, Jabs DA, Leder HA, Kedhar SR, Dunn JP, Peters GB III, Thorne JE. Comparison of antimetabolite drugs as corticosteroid-sparing therapy for noninfectious ocular inflammation. *Ophthalmology*. 2008 Oct;115(10):1826-32.
160. Jeng BH, **Galor A**, Lee MS, Hollyfield JG, Schoenfield L, McMahon JT, Langston RHS. Amantadine induced corneal edema: potentially irreversible even after cessation of the medication. *Ophthalmology*. 2008 Sep;115(9):1540-4.
161. Amescua G, Collings F, Sidani A, Bonfield TL, Rodriguez JP, **Galor A**, Medina C, Yang X, Perez VL. Effect of CXCL-1/KC production in high risk vascularized corneal allografts on T cell recruitment and graft rejection. *Transplantation*. 2008 Feb 27;85(4):615-625.
162. **Galor A**, Lowder CY, Perez VL, Kaiser PK, Sears JE. Efficacy of surgical drainage of chronic serous retinal detachment in uveitis patients. *Retina*. 2008 Feb;28(2):282-8.
163. **Galor A**, Margolis R, Oswaldo BFM, Perez VL, Kaiser PK, Sears JE, Lowder CY, Smith SD. Adverse events after intravitreal triamcinolone in patients with and without uveitis. *Ophthalmology*. 2007 Oct;114(10):1912-8.
164. **Galor A**, Lee MS, Singh AD, Perez VL, Peereboom DM, Ference SJ, Stevens GHJ. Blood brain barrier disruption maculopathy. *American Journal of Ophthalmology*. 2007 Jul;144(1):45-49.
165. **Galor A**, Margolis R, Kaiser PK, Lowder CY. Vitreous band formation and the sustained-Release,

Anat Galor, MD
Curriculum Vitae

- intravitreal, fluocinolone acetonide (Retisert™) implant. Archives of Ophthalmology. 2007 Jun;125(6):836-8.
166. Brasil OF, Smith SD, **Galor A**, Lowder CY, Sears JE, Kaiser PK. Predictive factors for short term visual outcome after intravitreal triamcinolone acetonide injection for diabetic macular edema: an OCT study. British Journal of Ophthalmology. 2007 Jun;91(6):761-5.
 167. **Galor A**, Perez VL, Lowder CY. Differential effectiveness of etanercept and infliximab in the treatment of ocular inflammation. Ophthalmology. 2006 Dec;113(12):2317-23.
 168. Lee MS, Smith SD, **Galor A**, Hoffman GS. Antiplatelet and anticoagulant therapy in patients with giant cell arteritis. Arthritis and Rheumatism. 2006 Oct;54(10):3306-9.
 169. Grigsby PW, **Gal-or A**, Michalski JM, Doherty GM. Childhood and adolescent thyroid carcinoma. Cancer. 2002 Aug 15;95(4):724-9.

PEER REVIEWED CASE REPORTS:

1. Quan AV, Huang AM, **Galor A**. Ciprofloxacin Corneal Deposits With Complete Dissipation After Switching to Moxifloxacin. JAMA Ophthalmol. 2020 Mar 1;138(3):e190921. (*Senior author*).
2. Cohen AK, Theotoka D, **Galor A**. Epipremnum aureum Keratopathy: Case Report and Review of the Literature. Eye Contact Lens. 2020 Sep;46(5):e33-e39. (*Senior and corresponding author*).
3. Wang YE, **Galor A**, Junk AK. Supraciliary Microstent Revision in a Patient With Corneal Edema and Primary Open Angle Glaucoma: A Case Report. J Glaucoma. 2020 Jan;29(1):e3-e6.
4. AlBaiyyat GJ, Venkateswaran N, Arreaza D, Dubovy SR, **Galor A**, Karp CL. Spontaneous regression of conjunctival keratoacanthoma. BMJ Case Rep. 2019 Jul 11;12(7).
5. Tran AQ, Yannuzzi NA, Motulsky EH, Zhou XY, **Galor A**, Dubovy SR, Rosenfeld PJ, Lam BL. Swept-Source Optical Coherence Tomography Angiography of an Amalric Choroidal Infarction in a Rare Presentation of Giant Cell Arteritis With Bilateral Corneal Edema. Ophthalmic Surg Lasers Imaging Retina. 2018 Oct 1;49(10):e157-e160.
6. Duerr ER, Chang A, Venkateswaran N, Goldhardt R, Levitt RC, Gregori NZ, Sarantopoulos CD, **Galor A**. Resolution of pain with periocular injections in a patient with a 7-year history of chronic ocular pain. Am J Ophthalmol Case Rep. 2019 Feb 12;14:35-38. (*Senior and corresponding author*).
7. Venkateswaran N, **Galor A**. Rosette-Shaped Cataract Due to Lightning Injury. JAMA Ophthalmol. 2018 Jan 11;136(1):e175719.
8. Palioura S, Sivaraman K, Joag M, Sise A, Batlle JF Jr, Miller D, Espana EM, Amescua G, Yoo SH, **Galor A**, Karp CL. Candida Endophthalmitis After Descemet Stripping Automated Endothelial Keratoplasty With Grafts From Both Eyes of a Donor With Possible Systemic Candidiasis. Cornea. 2018 Apr;37(4):515-518.
9. Phung L, Lollett IV, Goldhardt R, Davis JL, Young L, Ascherman D, **Galor A**. Parallel ocular and serologic course in a patient with early Sjogren's syndrome markers. Am J Ophthalmol Case Rep. 2017 Oct 6;8:48-52. (*Senior and corresponding author*).
10. Joag MG, Gupta A, **Galor A**, Dubovy SR, Bermudez-Magner JA, Wang J, Karp CL. Conjunctival Intraepithelial Neoplasia with Mucoepidermoid Differentiation: A Case Report of a Subtle Lesion. Ocul Oncol Pathol. 2015 Jun;1(4):278-82.
11. Shalabi N, **Galor A**, Dubovy SR, Thompson J, Bermudez-Magner JA, Karp CL. Atypical Fibroxanthoma of the Conjunctiva in Xeroderma Pigmentosum. Ocul Oncol Pathol. 2015 Jun;1(4):254-8.
12. Chhadva P, Cabot F, **Galor A**, Karp CL, Yoo SH. Long-term Outcomes of Flap Amputation After LASIK. J Refract Surg. 2016 Feb 1;32(2):136-7.
13. Batawi H, Kothari N, Camp A, Bernhard L, Karp CL, **Galor A**. Spontaneous Corneal Hydrops in a Patient with a Corneal Ulcer. Case Rep Ophthalmol. 2016 Jan 14;7(1):49-53. (*Senior and corresponding author*).
14. Pole C, Sise A, Joag M, **Galor A**, Bermudez-Magner JA, Dubovy S, Karp CL. High-Resolution Optical Coherence Tomography Findings of Lisch Epithelial Corneal Dystrophy. 2016 Mar;35(3):392-4.

Anat Galor, MD
Curriculum Vitae

15. Read SP, Rodriguez M, Dubovy S, Karp CL, **Galor A**. Treatment of Refractory Filamentary Keratitis With Autologous Serum Tears. *Eye Contact Lens*. 2017 Sep;43(5):e16-e18. (*Senior and corresponding author*)
16. Tourkmani AK, Martinez JD, Berrones D, Juárez-Domínguez BY, Beltrán F, **Galor A**. Brown-McLean Syndrome in a Pediatric Patient. *Case Rep Ophthalmol*. 2015 Apr 24;6(1):139-42.
17. Chhadva P, Cabot F, **Galor A**, Yoo SH. Long-Term Outcomes of Radial Keratotomy, Laser In Situ Keratomileusis, and Astigmatic Keratotomy Performed Consecutively over a Period of 21 Years. *Case Rep Ophthalmol Med*. 2015;2015:592495.
18. Shalabi N, **Galor A**, Dubovy SR, Thompson J, Bermudez-Magner JA, Karp CL. Atypical Fibroxanthoma of the Conjunctiva in Xeroderma Pigmentosum. *Ocul Oncol Pathol* 2015;1:254-258.
19. Joag MG, **Galor A**, Karp CL. Delayed expulsive choroidal hemorrhage after penetrating keratoplasty. *Ophthalmic Surg Lasers Imaging Retina*. 2015 Feb 1;46(2):289-92.
20. **Galor A**, Eberhard ML. Follow-up on anterior chamber angiostrongyliasis. *JAMA Ophthalmol*. 2014 Aug;132(8):1029-30.
21. Crane AM, Weiss M, **Galor A**. Anterior chamber angiostrongyliasis. *JAMA Ophthalmol*. 2013 Jul 1;131(7):951-2.
22. Shah AA, Modi Y, Thomas B, Wellik SR, **Galor A**. Brimonidine Allergy Presenting as Vernal-like Keratoconjunctivitis. *J Glaucoma*. 2013 Apr 29. (*Senior and corresponding author*)
23. Hurmeric V, Yoo SH, **Galor A**, Canto AP, Wang J. Atypical presentation of Salzmann nodular degeneration diagnosed with ultra-high-resolution optical coherence tomography. *Ophthalmic Surg Lasers Imaging*. 2011 Dec 8;42 Online:e122-5.
24. Cavuoto K, **Galor A**, Dubovy SR, Gregori N, McCarthy M. Subconjunctival Masses Associated With Central Nervous System Rosai-Dorfman Disease. *Cornea*. 2011 Feb;30(2):237-40. (*Senior and corresponding author*)
25. **Galor A**, Yoo SH. Corneal Melt While Using Topical Bevacizumab Eye Drops. *Ophthalmic Surg Lasers Imaging*. 2010 Mar 9;1-3.
26. **Galor A**, Karp CL, Forster RK, Dubovy SR, Gaunt ML, Miller D. Subconjunctival mycetoma after sub-Tenon's corticosteroid injection. *Cornea*. 2009 Sep;28(8):933-5.
27. Kymionis GD, Ide T, **Galor A**, Yoo SH. Femtosecond-assisted anterior lamellar corneal staining-tattooing in a blind eye with leukocoria. *Cornea*. 2009 Feb;28(2):211-3.
28. **Galor A**, Leder HA, Thorne JE, Dunn JP. Transient band keratopathy associated with ocular inflammation and systemic hypercalcemia. *Clinical Ophthalmology*. 2008;2(3) 645–647.
29. **Galor A**, Georgy M, Leder HA, Dunn JP, Peters GB. Papillary conjunctivitis associated with Kikuchi's disease. *Cornea*. 2008 Sep;27(8):944-6..
30. Leder HA, **Galor A**, Thorne JE, Jabs DA. Disappearance of classic birdshot spots after immunosuppression with tacrolimus and mycophenolate mofetil. *British Journal of Ophthalmology*. 2008 Feb;92(2):291.
31. Leder HA, **Galor A**, Peters GB, Kedhar SR, Dunn JP, Thorne JE. Resolution of conjunctival Kaposi sarcoma after institution of highly active antiretroviral therapy alone. *British Journal of Ophthalmology*. 2008 Jan;92(1):151
32. **Galor A**, Thorne JE, Jabs DA. Rheumatic disease and scleritis. *Ophthalmology*. 2007 Jun;114(6):1232.
33. **Galor A**, Hall GS, Procop GW, Tuohy M, Millstein ME, Jeng BH. Rapid species determination of nocardia keratitis using pyrosequencing technology. *American Journal of Ophthalmology*. 2007 Jan;143(1):182-3.
34. **Galor A**, Perry JD, Ratliff N, Kaiser PK, Bakri S, and Lee MS. Failure of imaging to detect optic nerve avulsion: an explanation based on histopathology. *Eye*. 2006 Aug;20(8):965-7.
35. **Galor A**, Lee M. Slowly progressive vision loss in giant cell arteritis. *Archives of Ophthalmology*. 2006 Mar;124(3):416-8.
36. **Galor A**, O'Brien T. Rituximab treatment for relapsed autoimmune hemolytic anemia in Evans

syndrome. International Journal of Hematology. 2003; Nov;78(4):335-6.

19. Other works, publications, and abstracts:

REVIEWS:

1. Mittal R, Patel S, **Galor A**. Alternative therapies for dry eye disease. Curr Opin Ophthalmol. 2021 Jul 1;32(4):348-361. *(Senior and corresponding author)*
2. Kim M, Lee Y, Mehra D, Sabater AL, **Galor A**. Dry eye: why artificial tears are not always the answer. BMJ Open Ophthalmol. 2021 Apr 8;6(1):e000697. *(Senior and corresponding author)*
3. Mittal R, Patel S, **Galor A**. Alternative therapies for dry eye disease. Curr Opin Ophthalmol. 2021 Jul 1;32(4):348-361. *(Senior and corresponding author)*
4. Baksh BS, Garcia JC, **Galor A**. Exploring the Link Between Dry Eye and Migraine: From Eye to Brain. Eye Brain. 2021 Mar 4;13:41-57. *(Senior and corresponding author)*
5. Hwang J, Dermer H, **Galor A**. Can in vivo confocal microscopy differentiate between sub-types of dry eye disease? A review. Clin Exp Ophthalmol. 2021 Mar 26. *(Senior and corresponding author)*
6. Shah AM, **Galor A**. Impact of Ocular Surface Temperature on Tear Characteristics: Current Insights. Clin Optom (Auckl). 2021 Feb 15;13:51-62. *(Senior and corresponding author)*
7. Mandell JT, Idarraga M, Kumar N, Galor A. Impact of Air Pollution and Weather on Dry Eye. J Clin Med. 2020 Nov 20;9(11):3740. *(Senior and corresponding author)*
9. Mehra D, **Galor A**. Digital Screen Use and Dry Eye: A Review. Asia Pac J Ophthalmol (Phila). 2020 Dec;9(6):491-497. *(Senior and corresponding author)*
10. Patel S, Hwang J, Mehra D, **Galor A**. Corneal Nerve Abnormalities in Ocular and Systemic Diseases. Exp Eye Res. 2020 Oct 10:108284. *(Senior and corresponding author)*
11. Mehra D, Cohen NK, **Galor A**. Ocular Surface Pain: A Narrative Review. Ophthalmol Ther. 2020 Sep;9(3):1-21. *(Senior and corresponding author)*
12. Diel RJ, Mehra D, Kardon R, Buse DC, Moulton E, **Galor A**. Photophobia: shared pathophysiology underlying dry eye disease, migraine and traumatic brain injury leading to central neuroplasticity of the trigeminothalamic pathway. Br J Ophthalmol. 2021 Jun;105(6):751-760. *(Senior and corresponding author)*
13. Dermer H, Lent-Schochet D, Theotoka D, Paba C, Cheema AA, Kim RS, **Galor A**. A Review of Management Strategies for Nociceptive and Neuropathic Ocular Surface Pain. Drugs. 2020 Apr;80(6):547-571. *(Senior and corresponding author)*
14. Kloosterboer A, Dermer H, **Galor A**. Diagnostic tests in dry eye, Expert Review of Ophthalmology, 14:4-5, 237-246, 2019. *(Senior and corresponding author)*
15. Watane A, Cavuoto KM, Banerjee S, **Galor A**. The Microbiome and Ocular Surface Disease. Current Ophthalmology Reports volume 7, pages196–203 (2019).
16. Tanenbaum RE, **Galor A**, Dubovy SR, Karp CL. Classification, diagnosis, and management of conjunctival lymphoma. Eye Vis (Lond). 2019 Jul 27;6:22.
17. Paranjpe V, **Galor A**, Monsalve P, Dubovy SR, Karp CL. Salzmann nodular degeneration: prevalence, impact, and management strategies. Clin Ophthalmol. 2019 Jul 25;13:1305-1314.
18. Al Bayyat G, Arreaza-Kaufman D, Venkateswaran N, **Galor A**, Karp CL. Update on pharmacotherapy for ocular surface squamous neoplasia. Eye Vis (Lond). 2019 Aug 12;6:24.
19. Theotoka D, Morkin MI, **Galor A**, Karp CL. Update on Diagnosis and Management of Conjunctival Papilloma. Eye Vis (Lond). 2019 Jun 18;6:18.
20. Cavuoto KM, Stradiotto AC, Galor A. Role of the ocular surface microbiome in allergic disease. Curr Opin Allergy Clin Immunol. 2019 Oct;19(5):482-487.
21. Cavuoto KM, Banerjee S, **Galor A**. Relationship between the microbiome and ocular health. Ocul Surf. 2019 Jul;17(3):384-392. *(Senior author)*.
22. Patel N, Venkateswaran N, Wang Z, **Galor A**. Ocular involvement in atopic disease: a review. Curr Opin Ophthalmol. 2018 Nov;29(6):576-581. *(Senior and Corresponding author)*.

Anat Galor, MD
Curriculum Vitae

23. Aggarwal S, Galor A. What's new in dry eye disease diagnosis? Current advances and challenges. *F1000Res*. 2018 Dec 19;7. (*Senior and Corresponding author*).
24. Gibbons A, **Galor A**. Current vaccines for the prevention of herpes zoster. *Curr Opin Ophthalmol*. 2018 Jul;29(4):355-359. (*Senior and Corresponding author*).
25. Venkateswaran N, **Galor A**, Wang J, Karp CL. Optical coherence tomography for ocular surface and corneal diseases: a review. *Eye Vis (Lond)*. 2018 Jun 12;5:13.
26. Akinsoji E, Goldhardt R, **Galor A**. A Glimpse into Uveitis in the Aging Eye: Pathophysiology, Clinical Presentation and Treatment Considerations. *Drugs Aging*. 2018 May;35(5):399-408. (*Senior and Corresponding author*).
27. Lollett IV, **Galor A**. Dry eye syndrome: developments and lifitegrast in perspective. *Clin Ophthalmol*. 2018 Jan 15;12:125-139. (*Senior and Corresponding author*).
28. Chhadva P, Goldhardt R, **Galor A**. Meibomian Gland Disease: The Role of Gland Dysfunction in Dry Eye Disease. *Ophthalmology*. 2017 Nov;124(11S):S20-S26. (*Senior and Corresponding author*).
29. **Galor A**, Moein HR, Lee C, Rodriguez A, Felix ER, Sarantopoulos KD, Levitt RC. Neuropathic pain and dry eye. *Ocul Surf*. 2018 Jan;16(1):31-44. (*Senior and Corresponding author*).
30. Chhadva P, Goldhardt R, **Galor A**. Meibomian Gland Disease: The Role of Gland Dysfunction in Dry Eye Disease. *Ophthalmology*. 2017 Nov;124(11S):S20-S26. (*Senior and Corresponding author*).
31. Andersen HH, Yosipovitch G, **Galor A**. Neuropathic symptoms of the ocular surface: dryness, pain, and itch. *Curr Opin Allergy Clin Immunol*. 2017 Oct;17(5):373-381. (*Senior and Corresponding author*).
32. Levitt AE, **Galor A**, Chowdhury AR, Felix ER, Sarantopoulos CD, Zhuang GY, Patin D, Maixner W, Smith SB, Martin ER, Levitt RC. Evidence that Dry Eye Represents a Chronic Overlapping Pain Condition. *Mol Pain*. 2017 Jan-Dec;13.
33. Belmonte C, Nichols JJ, Cox SM, Brock JA, Begley CG, Bereiter DA, Dartt DA, **Galor A**, Hamrah P, Ivanusic JJ, Jacobs DS, McNamara NA, Rosenblatt MI, Stapleton F, Wolffsohn JS. TFOS DEWS II pain and sensation report. *Ocul Surf*. 2017 Jul;15(3):404-437.
34. Nanji AA, Mercado C, **Galor A**, Dubovy S, Karp CL. Updates in Ocular Surface Tumor Diagnostics. *Int Ophthalmol Clin*. 2017 Summer;57(3):47-62.
35. Sayed-Ahmed IO, Palioura S, **Galor A**, Karp CL. Diagnosis and Medical Management of Ocular Surface Squamous Neoplasia. *Expert Rev Ophthalmol*. 2017;12(1):11-19.
36. **Galor A**, Levitt RC, Felix ER, Sarantopoulos CD. What can photophobia tell us about dry eye? *Expert Review of Ophthalmology* 2016;11:321-24. (*Senior and corresponding author*).
37. Lanza NL, Valenzuela F, Perez VL, **Galor A**. The Matrix Metalloproteinase 9 Point-of-Care Test in Dry Eye. *Ocul Surf*. 2016 Apr;14(2):189-95. (*Senior and corresponding author*).
38. Kalangara JP, **Galor A**, Levitt RC, Felix ER, Alegret R, Sarantopoulos CD. Burning Eye Syndrome: Do Neuropathic Pain Mechanisms Underlie Chronic Dry Eye? *Pain Med*. 2016 Apr;17(4):746-55.
39. Levitt AE, **Galor A**, Weiss JS, Felix ER, Martin ER, Patin DJ, Sarantopoulos KD, Levitt RC. Chronic dry eye symptoms after LASIK: parallels and lessons to be learned from other persistent post-operative pain disorders. *Mol Pain*. 2015 Apr 21;11(1):21.
40. Ezuddin NS, Alawa KA, **Galor A**. Therapeutic Strategies to Treat Dry Eye in an Aging Population. *Drugs Aging*. 2015 Jul;32(7):505-13. (*Senior and corresponding author*).
41. **Galor A**, Levitt RC, Felix ER, Sarantopoulos CD. Understanding the true burden of dry eye disease. *Expert Review of Ophthalmology* 2015;10:403-05.
42. Ames P, **Galor A**. Cyclosporine ophthalmic emulsions for the treatment of dry eye: a review of the clinical evidence. *Clin Investig (Lond)*. 2015;5(3):267-285. (*Senior and corresponding author*).
43. **Galor A**, MGD: Definition Versus Dry Eye Disease, Risk Factors, Current Ophthalmology Reports, 2014;2, 58-64.
44. **Galor A**, Levitt RC, Felix ER, Martin ER, Sarantopoulos CD. Neuropathic ocular pain: an important yet underevaluated feature of dry eye. *Eye (Lond)*. 2015 Mar;29(3):301-12.
45. Wong JR, Nanji AA, **Galor A**, Karp CL. Management of conjunctival malignant melanoma: a review and

Anat Galor, MD
Curriculum Vitae

- update. *Expert Rev Ophthalmol*. 2014 Jun;9(3):185-204.
46. Huang, LC, Wong JR, Alonso-Llamazares J, Nousari CH, Perez VL, Amescua G, Karp CL, **Galor A**. Pseudopemphigoid as caused by topical drugs and pemphigus disease. *World J Ophthalmol* 2015 February 12; 5(1): 1-15. (*Senior and corresponding author*).
 47. Wong JR, Nanji AA, **Galor A**, Karp CL. Management of conjunctival malignant melanoma: a review and update. *Expert Rev Ophthalmol*. 2014 Jun;9(3):185-204.
 48. Shah AA, Yoo SH, **Galor A**. Astigmatism Management in Patients after Corneal Transplant. In *Astigmatism: Types, Diagnosis and Treatment Options*. Editor Reuben Buckley. Series: Eye and Vision Research Developments. Nova Science Publisher. 2014. (*Senior and corresponding author*).
 49. **Galor A**, Goldhardt R, Wellik SR, Gregori NZ, Flynn HW. Management strategies to reduce risk of postoperative infections. *Curr Ophthalmol Rep*. 2013 Dec;1(4). (*Senior and corresponding author*).
 50. Al-Mohtaseb Z, **Galor A**, and Perez VL. Dry Eyes and Menopause: But Don't Forget Men. *Ocular Surface News*. August 16, 2013.
http://www.visioncareprofessional.com/emails/OSN/issue_081613.asp
 51. **Galor A**, Wellik S, Gregori NZ, Goldhardt R. Management strategies to reduce risk of postoperative infections. *Current Ophthalmology Reports*. *Curr Ophthalmol Rep*. 2013 Dec;1(4). (*Senior and corresponding author*).
 52. Vu S, Karp CL, **Galor A**, Wester SD. OCT can be useful in diagnosis of conjunctival lymphangiectasis. *Ocular Surgery News U.S. Edition*, May 25, 2013
 53. Ansari Z, Miller D, **Galor A**. Current Thoughts in Fungal Keratitis: Diagnosis and Treatment. *Curr Fungal Infect Rep*. 2013 Sep 1;7(3):209-218.
 54. **Galor A**, Perez VL. Advanced medical therapy for dry eye syndrome. *Advanced Ocular Care*. May/June 2013; 52-55.
 55. Anwar Z, Wellik SR, **Galor A**. Glaucoma therapy and ocular surface disease: current literature and recommendations. *Curr Opin Ophthalmol*. 2013 Mar;24(2):136-43. (*Senior author*)
 56. Sein J, **Galor A**, Sheth A, Kruh J, Pasquale LR, Karp CL. Exfoliation syndrome: new genetic and pathophysiologic insights. *Curr Opin Ophthalmol*. 2013 Mar;24(2):167-74.
 57. Pouyeh B, **Galor A**, Miller D, Alfonso E. New Horizons in One of Ophthalmology Challenges: Fungal Keratitis. *Expert Rev Ophthalmol*. 2011;6(5):529-540. (*Corresponding author*)
 58. **Galor A**, Miller D, Alfonso EC. Epidemiology, clinical features, diagnosis, and management of patients with fungal keratitis. *Vision Pan-America*. Issue X, No. 3, September 2011: 68-71. (*Corresponding author*)
 59. **Galor A**, Lee DJ. Effects of Smoking on Ocular Health. *Current Opinion in Ophthalmology*. 2011 Nov;22(6):477-82. (*Corresponding author*)
 60. Amescua G, **Galor A**, Perez VL. Enfermedades inflamatorias de la epiesclera y esclera. Review of Ophthalmology: Mexico. Segunda Edicion 2010. Volumen 38. Pages 32-35.
 61. **Galor A**, Jeng B. The red eye: a primer for the internist. *Cleveland Clinic Journal of Medicine*. 2008, Feb;75(2):137-44.
 62. **Galor A**, Thorne JE. Scleritis and peripheral ulcerative keratitis. *Rheumatic Disease Clinics of North America*. 2007 Nov;33(4):835-54.
 63. Thorne JE, **Galor A**. Cytomegalovirus retinitis. *Expert Review of Ophthalmology*. 2007 Aug, 2(4):583-595.
 64. **Galor A**, Jeng, B, Singh A. Current management of corneal abrasion: an evidence based review. *Comprehensive Ophthalmology Update*. 2005 March-April;5(2):105-111.

EYE WIKI

1. http://eyewiki.org/Anterior_segment_optical_coherence_tomography_for_various_ocular_surface_lesions_and_corneal_pathologies

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MEDIA COVERAGE:

1. <https://rarediseases.org/rare-diseases/neuropathic-ocular-pain/>
2. <https://www.aarp.org/health/conditions-treatments/info-2019/should-you-get-lasik-surgery.html>
<https://www.aarp.org/health/conditions-treatments/info-2019/should-you-get-lasik-surgery.html?intcmp=AE-HP-BB>
3. Dry eye. <https://www.xconomy.com/san-diego/2018/06/12/in-digital-device-boom-tear-film-sees-window-for-dry-eye-treatment/>
4. Asymptomatic dry eye. *Ophthalmology Management*. Wendy Lyons Sunshine
5. Dry eye and allergies: <http://www.medscape.com/viewarticle/834748>
<http://www.sciencedaily.com/releases/2015/04/150423182400.htm>
6. Dry eye and air pollution: <http://www.medscape.com/viewarticle/815040>
7. Dry eye and veteran health: <http://consumer.healthday.com/mental-health-information-25/depression-news-176/undiagnosed-eye-problems-plague-some-u-s-veterans-670560.html>

MEETING PRESENTATIONS:

1. Rodriguez D, Levitt R, Felix ER, **Galor A**. ABSTRACT ID: 30068049 TITLE: Dry eye (DE) disease GWAS identifies genomic variants correlated with symptom severity and comorbidities, but not DE signs. Poster presentation. Nov. 12-15 - AAO 2021 New Orleans
2. Huang A, Felix ER, **Galor A**. ABSTRACT ID: 30068197 TITLE: Role of conditioned pain modulation in dry eye. Paper presentation. Nov. 12-15 - AAO 2021 New Orleans
3. Mehra D, Moulton E, Felix ER, **Galor A**. ABSTRACT ID: 30068199. TITLE: fMRI Activity and Modulation of Central Photophobia Pathways in Dry Eye Patients. Poster presentation. Nov. 12-15 - AAO 2021 New Orleans
4. Mehra D, **Galor A**. Long-Term Trigeminal Nerve Stimulation as a Treatment for Ocular Pain. Poster presentation for AOS May 21 – 23, 2021 virtual meeting.
5. Levine H, Hwang J, Dermer H, Mehra D, **Galor A**. Relationships between activated Dendritic Cells and Dry Eye Symptoms and Signs. ARVO virtual meeting 2021. Award recipient.
6. Theotoka D, Liu Z, Wall S, **Galor, A**, Wang, J, Jiang H, Karp CL. Alterations of Vascular Network Patterns in Ocular Surface Squamous Neoplasia With Topical Medical Therapy Detected Via OCTA. 30065538. AAO 2021. Virtual meeting.
7. Naranjo A, Pirakitikulr N, Martinez JD, Amescua G, **Galor A**, Dubovy SR. Clinicopathologic correlations of retrocorneal membranes associated with lamellar corneal graft failure. Abstract Number: 30064974. AAO 2021. Virtual meeting.
8. Hwang, J, Dermer H, **Galor A**. Corneal Microneuromas: Markers of Neuropathic Corneal Pain? Abstract Number: 30064045. AAO 2021. Virtual meeting.
9. Staropoli PC, **Galor A**. Transcutaneous Electrical Nerve Stimulation for the Long-Term Treatment of Ocular Pain. ASCRS. Boston 2020. Second place in resident and fellow poster category.
10. Idarraga M, Guerrero J, **Galor A**, Kumar N. Short-term exposure to indoor environment and the severity of dry eye symptoms. Abstract Number: 3357519. ARVO 2020. Baltimore, MD.
11. Wall S, Theotoka D, Friehmann A, **Galor A**, Karp CL. Anterior Segment High Resolution Optical Coherence Tomography (HR-OCT) as a Diagnostic Tool for Clinically Ambiguous Ocular Surface Lesions. Abstract Number: 3362829. ARVO 2020. Baltimore, MD.
12. Rock S, Kumar, N, **Galor, A**. Indoor Airborne Microbial Concentration and Dry Eye. Abstract Number: 3357116. ARVO 2020. Baltimore, Maryland.
13. Naranjo A, Pirakitikulr N, Martinez JD, Amescua G, **Galor A**, Dubovy SR. Characterization of fibrocellular retrocorneal membranes associated with lamellar corneal graft failure. Abstract Number: 3366550. ARVO 2020. Baltimore, MD.
14. Mangwani-Mordani S, **Galor A**, Goldhardt R. Use of Transcutaneous Supraorbital Nerve Stimulation with Cefaly® Device in Patients with Chronic Ocular Pain and Dry Eye Case Series. Abstract number:

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3355149. ARVO 2020. Baltimore.
15. Miralles, F., Kumar, N., **Galor, A.** "Indoor Carbon Monoxide and Ocular Surface Inflammation." Abstract Number: 3366590. ARVO 2020. Baltimore, MD.
16. Patel S, **Galor A**, Kumar N. The Effects of Temperature Change on Allergic Conjunctivitis. Abstract Number: 3356626. ARVO 2020. Baltimore, MD.
17. Hwang J, Karanam V, Goldhardt R, Feuer W, Tamariz L, Wang J, **Galor A.** Conjunctival hemodynamic changes in diabetes. Abstract Number: 3359127. ARVO 2020. Baltimore, Maryland.
18. Zayan K, **Galor A**, Aggarwal S, Sarantopoulos K, Felix E, Goldhardt R. Transcutaneous Electrical Nerve Stimulation for the Long-Term Treatment of Ocular Pain. Abstract Number: 3357323. ARVO 2020. Baltimore, MD.
19. **Galor A**, Nau J. 3347680, ONSET-1 Phase 2b study of OC-01 Nasal Spray for the Treatment of the Signs and Symptoms of Dry Eye, 2020 ARVO Annual Meeting. May 3-7. Baltimore, MD.
20. Baksh B, Goldhardt R, **Galor A.** "Could the Nerve Fiber Layer Serve as a Biomarker of Gulf War Illness?" North American Neuro-Ophthalmology Society 46th Annual Meeting, March 7-12, 2020 Amelia Island, FL
21. Han E, Paranjpe V, and **Galor A.** Demographics and socioeconomic status are associated with low vision and perception of vision limiting daily activities. American Academy of Ophthalmology Annual Meeting, San Francisco, California. October 2019.
22. Farhangi M, Chang A, **Galor A.** 30060254 Effect of Noninvasive Intranasal Neurostimulation on Tear Volume, Dryness and Ocular Pain by Dry Eye Subtype. AAO meeting. San Francisco 2019.
23. Huang A, Kumar N, **Galor A.** 30060337 Impact of the Personal Microenvironment on Dry Eye Metrics. AAO meeting. San Francisco 2019.
24. Hwang J, **Galor A.** 30059675 Conjunctival Blood Flow Metrics Correlate With Diabetes-Related Complications. AAO meeting. San Francisco 2019.
25. Venkateswaran N, Hwang J, Rong A, Levitt A, Levitt RC, Lee W, **Galor A.** 30060805 OnabotulinumtoxinA Improves Photophobia and Sensations of Dryness Independent of Ocular Surface Parameters in Patients With Neuropathic-Like Dry Eye Without a history of Migraine. AAO meeting. San Francisco 2019.
26. **Galor A**, Yoel Cohen, Yoel Arieli, Shlomi Epshtin, Raanan Gefen, Alon Harris 0293: Blink dynamics in healthy versus dry eye subjects as assessed by a novel device. Thu, May 02. ARVO 2019. Vancouver. Canada.
27. Rojas M, Felix E, Small L, Goldhardt R, **Galor A.** Autonomic Function Testing and After-sensations as Predictors for Post-operative Dry Eye Symptoms after Laser-Assisted in Situ Keratomileusis. 5202. ARVO 2019. Vancouver, Canada.
28. Gefen R, Segev F, Geffen N, **Galor A**, Cohen Y, Arieli Y, Epshtin S, Harris A. A new hyperspectral imaging method to evaluate dry eye disease – 3D-WLT study results. Posterboard#: Abstract Number: 6780 - B0304. ARVO 2019. Vancouver, Canada.
29. Small L, Mendez R, Farhangi M, Cavuoto KM, Budree S, **Galor A**, Banerjee S. Gut dysbiosis in individuals with and without Sjögren's disease. Abstract Number: 5204. ARVO 2019. Vancouver, Canada.
30. Paranjpe V, Rabinovich EP, Sharma N, Srivastava A, **Galor A**, Hackam A, Jeng bH, Kumar N. Solid fuel exposure and the development of cataracts. Abstract Number: 4254. ARVO 2019. Vancouver, Canada.
31. Venkateswaran N, Hwang J, Rong A, Levitt A, Levitt RC, Lee W, **Galor A.** Onabotulinum toxin A improves photophobia and sensations of dryness independent of ocular surface parameters. Abstract Number: 6757 - B0281. ARVO 2019. Vancouver, Canada.
32. Huang A, Menendez DM, **Galor A**, Kumar N. Impact of bioaerosols and particulate matter on dry eye symptoms and signs. Abstract Number: 2773 - B0523. ARVO 2019. Vancouver, Canada.

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33. Rothfield L, Hubschman S, Rojas M, Goldhardt R, **Galor A**. ASSOCIATION BETWEEN EARLY SJOJREN MARKERS AND SYMPTOMS AND SIGNS OF DRY EYE. Abstract Number: 2762 - B0512. ARVO 2019. Vancouver, Canada.
34. Kaplan C, **Galor A**, Blackwelder P, Hackam A, Jeng BH, Menendez D, Kumar N. Human Ocular Surface Particulate Composition: Home vs. Clinical Environment. Abstract Number: 1746 ARVO 2019. Vancouver, Canada.
35. Betancourt NR, Field MG, Wang G, Karp CL, Dávila-Alquisiras JH, Hernandez-Zimbrón LF, García-Vazquez R, Vazquez Romo KA, Hernandez-Quintela E, Fromow-Guerra J, **Galor A**. Whole Exome Profiling and Mutational Analysis of Ocular Surface Squamous Neoplasia. Abstract Number: 3554 - A0595. ARVO 2019. Vancouver, Canada.
36. Bussies P, Diel R, **Galor A**. Efficacy of Autologous Serum Tears for the Treatment of Ocular Surface Disease. Abstract Number: 2098 - B0396. ARVO 2019. Vancouver, Canada.
37. Chen Y, Levine H, Quan A, Goldhardt R, Galor A. Subconjunctival bevacizumab injections in the management of impending recurrent pterygium. Abstract Number: 6269 - B0250. ARVO 2019. Vancouver, Canada.
38. Monsalve P, Garcia AL, Zhou XY, Elgart SW, Karp CL, Johnson TE, Galor A, Dubovy S. Atypical Fibroxanthoma Affecting the Ocular Surface and Adnexa: A Case Series. Abstract Number: 3574 - A0615. ARVO 2019. Vancouver, Canada.
39. Garcia AL, Monsalve P, Wester ST, Lee W, Tse DT, Karp CL, Galor A, Dubovy S. Extranodal Rosai-Dorfman disease of the eye and ocular adnexa: A clinicopathologic series of 8 cases. Abstract Number: 3579 - A0620. ARVO 2019. Vancouver, Canada.
40. Janecki J, **Galor A**, Hackam A, Jeng BH, Kumar N. Impact of the personal microenvironment on dry eye metrics. Abstract Number: 2742 - B0492. ARVO 2019. Vancouver, Canada.
41. Pirakitikulr N, Martinez JD, Garcia AL, Goldhardt R, Dubovy S, Amescua G, **Galor A**. Myofibroblastic membranes after corneal surgery: a clinical histopathologic correlation study. Abstract Number: 6297 - B0348. ARVO 2019. Vancouver, Canada.
42. Quan A; Patel N; Pirakitikulr N; Laura D; Fan K, **Galor A**. Oral Tacrolimus for the Treatment of Refractory Atopic Keratoconjunctivitis and Dermatitis. ASCRS Paper ID 55838. San Diego, CA. May 6, 2019
43. Venkateswaran, N; Hwang J; Rong A; Levitt A; **Galor A**; Lee W. Onabotulinum Toxin a Improves Photophobia and Sensations of Dryness Independent of Ocular Surface Parameters. ASCRS Paper ID 53254. San Diego, CA. May 6, 2019
44. Rojas M, Small L, **Galor A**. Pregabalin for the Prevention of Dry Eye Symptoms after Laser-Assisted in Situ Keratomileusis: A Pilot Study. ASCRS Paper ID 57472. San Diego, CA. May 4, 2019.
45. Aggarwal S, **Galor A**. Transcutaneous Electrical Nerve Stimulation for Treatment of Neuropathic Corneal Pain. ASCRS Paper ID 56410. San Diego, CA. May 6, 2019.
46. **Galor A**, Gefen R, Harris A. Dynamic assessment of the Tear Film Muco-Aqueous and Lipid Layers Using a Novel Tear Film Imager (TFI). OMIG meeting. AAO, Chicago, IL, October 26, 2018.
47. Hwang J, Diel R, Levitt R, Sarantopoulos CD, Felix ER, **Galor A**. Botulinum toxin A improves photophobia and sensations of dryness independent of ocular surface parameters. OMIG meeting. AAO, Chicago, IL, October 26, 2018.
48. Paranjpe V, **Galor A**. Socioeconomic Factors Are Associated with Access to Cataract Surgery in the United States. Poster presented at: The American Academy of Ophthalmology Annual Meeting, Chicago, IL. October 27-30, 2018.
49. Lara D. Fan K. Goldhardt R, Mirsaeidi, M, **Galor A**. # 2920911, Ocular manifestations of sarcoidosis in a South Florida population. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
50. Cavuoto K, **Galor A**, Miller D, Banerjee S. # 2915825, Determining the Ideal Swab Material for Analyzing the Ocular Surface Microbiome. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.

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51. Goldhardt R, Batawi H, **Galor A.** # 2925912, In Vivo Confocal Microscopy of Corneal Nerves in Patients Receiving Intravitreal Anti-VEGF. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
52. Small L, Levitt RC, Sarantopoulos KD, **Galor A.** # 2925844, Periocular nerve blocks for the treatment of ocular pain. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
53. Paranjpe V, Mandal N, Tan, J, Nguyen J, Lee, JY, **Galor A.** # 2903993, Associations between meibum quality and sphingolipid quantity and composition. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
54. Gibbons, A; Iglesias E; Sajani R; Levitt, RC; Sarantopoulos KD; **Galor A.** # 2903095, Epidemiology of persistent dry eye-like symptoms after cataract surgery. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
55. Venkateswaran N, **Galor A,** Karp C. # 2919700, Application of high resolution anterior segment optical coherence tomography for non-invasive diagnosis and differentiation of benign lymphoid hyperplasia, conjunctival lymphoma and conjunctival amyloidosis. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
56. Sajani RS, Allister G, Chang V, Levitt RC, **Galor A.** # 2906282, Epidemiology of persistent post-surgical pain manifesting as dry eye symptoms after cataract surgery. 2018 ARVO Annual Meeting, April 29 - May 3, 2018 in Honolulu, Hawaii.
57. Venkateswaran N, Tran VA, **Galor A,** Karp CL. The use of ultra-high resolution anterior segment optical coherence tomography for the diagnosis and differentiation of benign lymphoid hyperplasia, conjunctival lymphoma and conjunctival amyloidosis, in Washington DC. Paper presentation - Young Eye Surgeons (YES) Best Papers and Posters by Residents and Fellows session on Sunday, April 15th Paper presentation Tuesday April 17th Ocular Surface/Pterygium, AMT session.
58. Tran VA, Venkateswaran N, **Galor A,** Karp CL. Treatment of Clinically Occult Subclinical Ocular Surface Squamous Neoplasia Using High Resolution Anterior Segment Optical Coherence Tomography. 2018 ASCRS Annual Meeting, April 15, 2018 in Washington DC.
59. Lee C, Felix ER, Sarantopoulos CS, Levitt RC, **Galor A.** 30051997 Dry Eye Associated with Chronic Pain Conditions in the U.S. Veteran Population. AAO meeting paper presentation 2018. New Orleans.
60. Ong E, Felix ER, Sarantopoulos CS, Levitt RC, **Galor A.** 30051484 Epidemiology of Discordance between Symptoms and Signs of Dry Eye. AAO meeting poster presentation 2018. New Orleans.
61. Cavuoto K, Miller D, Banerjee S, **Galor A.** 30052008 Ocular Surface Microbial Signatures Change with Age. AAO meeting poster presentation 2018. New Orleans.
62. Hatim B, Rodriguez A, Felix ER, Sarantopoulos CS, Levitt RC, **Galor A.** 30052182 Assessment of Central Sub-basal Corneal Nerve Plexus in patients with Multiple Comorbid Chronic Pain Syndromes. AAO meeting poster presentation 2018. New Orleans.
63. Aguilar M, Asfour SS, Lam BL, **Galor A,** Gregori NZ, Gonzalez A, Rowaan CJ, Durkee, HA, Rosa RP, Parel JMA. #2691838, B0023: Quantifying Visual Photosensitivity in Veterans with Traumatic Brain Injury. ARVO, Baltimore. May 2017.
64. Diel R, Galor, Kroeger ZA, Sered H, **Galor A.** #2678037, A0355, Botulinum toxin for the treatment of photophobia in chronic migraine patients. ARVO, Baltimore. May 2017.
65. Cavuoto K, Miller D, **Galor A,** Alfonso EC, Chang TC, Osigian P, Carla J. Relationship between the Ocular Surface and the Head and Neck Microbiomes in Children. ARVO, Baltimore. May 2017.
66. Rodriguez M, Gregori N, Junk AK, **Galor A,** Wellik S, Goldhardt, R, Staropoli P, Phung, L, She W. The impact of cataract surgery on eyes with epiretinal membranes. ARVO, Baltimore. May 2017.
67. Small L, Felix ER, Levitt RC, Sarantopoulos C, Galor A. A0239: The epidemiology of ocular itch by dry eye symptoms and signs. ARVO, Baltimore. May 2017.
68. Swaminathan S, Sant D, Wang G, **Galor A,** Harbour WJ, Dubovy S, Karp CL. B0621: Whole Exome Sequencing of Conjunctival Melanoma. ARVO, Baltimore. May 2017.
69. Mercado C, **Galor A,** Karp CL. B0628: Immunosuppression as a possible risk factor for interferon non-

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- response in ocular surface squamous neoplasia. ARVO, Baltimore. May 2017.
70. Zhang L, Mercado C, **Galor A**, Wang G, Karp CL. A0179: Atopy and Ocular Surface Squamous Neoplasia. ARVO, Baltimore. May 2017.
 71. Lee C, Felix ER, Levitt RC, Sarantopoulos C, **Galor A**. The link between pain syndromes and dry eye in patients with traumatic brain injury. Paper presentation. ARVO, Baltimore. May 2017.
 72. Cavuoto K, Miller D, **Galor A**, Alfonso EC, Chang TC, Osigian P, Carla J. Ocular Surface Microbiome in Children. Session: Cataract Surgery, Congenital Cataracts, and IOL Power Calculations. May 8, 2017. ASCRS, Los Angeles, CA, 2017.
 73. Chang V, Karp CL, Rose T, **Galor A**. ID: 31670. Dry Eye Symptoms Correlate With Non-Ocular Conditions. ASCRS, Los Angeles, CA, May 5-9, 2017.
 74. Mercado CL, Pole C, Wong JR, Shaikh N, Battle JF, Murillo JC, **Galor A**, Karp CL. Surgical versus Medical treatment for ocular surface squamous neoplasia: A Quality of life comparison. *American Academy of Ophthalmology (AAO) Annual Meeting*. Chicago, IL – October 2016
 75. **Galor A**, Felix ER, Levitt RC, Sarantopoulos KD. 30047203: Somatosensory function in patients with idiopathic dry eye symptoms. *American Academy of Ophthalmology (AAO) Annual Meeting*. Chicago, IL – October 2016
 76. Goldhardt R, Hatim B, **Galor A**. 30047709: In Vivo Confocal Microscopy of Human Nerves in Patients Receiving Intravitreal Anti-VEGF. *American Academy of Ophthalmology (AAO) Annual Meeting*. Chicago, IL – October 2016
 77. Cabot F, Parel JM, Yoo S, Karp CK, **Galor A**, Aguilar M, Chhadva P, Mote KL, Alawa KA, Joag M, Durkee HA. Improving ophthalmology resident surgical training using novel 3D printed eye models for teaching corneal suturing. *American Academy of Ophthalmology (AAO) Annual Meeting*. Chicago, IL – October 2016
 78. Hatim B, Wellik S, Junk A, Anderson M, **Galor A**. 30048470: Evaluation of epithelial and stromal central corneal thickness in primary open angle glaucoma and non-glaucoma patients. *American Academy of Ophthalmology (AAO) Annual Meeting*. Chicago, IL – October 2016
 79. Chhadva P, Seiden B, Park JJ, McClellan AL, Felix ER, Sarantopoulos CD, Levitt RC, Wallace DM, **Galor A**. The Association of Dry Eye and Insomnia. *American Academy of Ophthalmology (AAO) Annual Meeting*. Chicago, IL – October 2016
 80. **Galor A**, Felix ER, Levitt RC, Sarantopoulos KD. Dry Eye: Neuropathic pain: a missing piece of the dry eye puzzle. XXII Biennial Meeting of the International Society for Eye Research, taking place from September 25 – 29, 2016 in Tokyo, Japan.
 81. **Galor A**, Felix ER, Levitt RC, Sarantopoulos KD. Expanding the functions of ocular surface innervation: photophobia and photoallodynia: Clinical relevance of photophobia in dry eye. XXII Biennial Meeting of the International Society for Eye Research, taking place from September 25 – 29, 2016 in Tokyo, Japan.
 82. Yim M, **Galor A**, Karp C. # 2438052, Ability of novice clinicians to use the high resolution ocular coherence tomography to assess lesions of the ocular surface, 2016 ARVO Annual Meeting, Research: A Vision of Hope, May 1-5, 2016, in Seattle, Washington.
 83. Alawa, Karam Al-Rahman, **Galor A**. # 2450888, Assessment of corneal suturing performance on novel 3D-printed ophthalmic teaching models using a custom photogrammetry-based software, 2016 ARVO Annual Meeting, Research: A Vision of Hope, May 1-5, 2016, in Seattle, Washington.
 84. Levitt A, **Galor A**. # 2450283, Microvascular responses of the bulbar conjunctiva in dry eye, 2016 ARVO Annual Meeting, Research: A Vision of Hope, May 1-5, 2016, in Seattle, Washington.
 85. Bilonik R, **Galor A**. # 2447409, A Structural Equation Model (SEM) Relating Eye Pain (EP) and Ocular Surface Measurements (OSMs), 2016 ARVO Annual Meeting, Research: A Vision of Hope, May 1-5, 2016, in Seattle, Washington.
 86. **Galor A**. # 2447340, Does dry eye severity correlate with somatosensory function in the V1 distribution of the trigeminal nerve? 2016 ARVO Annual Meeting, Research: A Vision of Hope, May 1-5, 2016, in Seattle, Washington.

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87. Cabot F, Joag M, Alawa K, Chhadva P, Durkee H, Aguilar M, **Galor A**, Parel JM, Yoo SH, Karp C. Assessment of Corneal Suturing Performance Using Novel 3D-Printed Ophthalmic Teaching Models. ASCRS Paper Session 3-L CATARACT: Epidemiology, Techniques, Outcomes, ASCRS Paper ID 21813. New Orleans, May 9, 2016.
88. Kothari N, Levitt RC, McClellan A, **Galor A**. Elevated CRP is associated with multiple chronic comorbid pain conditions and neuropathic ocular pain. ASCRS Paper Session CORNEA: Conjunctival Disease and Corneal Imaging. Paper ID 22064. New Orleans, May 9, 2016.
89. Crane A, Levitt RC, Felix ER, Sarantopoulos KD, **Galor A**. Patients with More Severe Symptoms of Neuropathic Ocular Pain Exhibit More Frequent and Severe Centralized Pain Conditions and Psychiatric Disease ASCRS Paper Session 2-A CORNEA Dry Eye: MGD and Aqueous Tear Deficiency. ASCRS Paper ID 23019. New Orleans, May 8, 2016.
90. Tran KD, Falcone MM, Choi DS, Goldhardt R, Karp CL, Davis JL, **Galor A**. Epidemiology of Herpes Zoster Ophthalmicus: Recurrence and Chronicity. OMIG meeting. AAO 2015. Las Vegas.
91. Palioura S, Sivaraman K, Sise A, Batlle J, Miller D, Amesuca G, **Galor A**, Karp CL. Fungal endophthalmitis after Descemet Stripping Automated Endothelial Keratoplasty Due to Endogenously Infected Grafts from the Same Donor. OMIG meeting. AAO 2015. Las Vegas.
92. Chang VS, Lanza NL, Valenzuela F, Perez VL, **Galor A**. Dry Eye Profiles in Patients with a Positive Elevated Surface Matrix Metalloproteinase 9 Point of Care Test versus Negative Patients. OMIG meeting. AAO 2015. Las Vegas.
93. Batawi H, Covington D, McManus KT, Seiden B, Felix ER, Kalangara J, Feuer W, Patin D, Marin ER, Sarantopoulos KD, Levitt RC, **Galor A**. Features of Neuropathic Ocular Pain in Dry Eye are Associated with Chronic Comorbid Pain Syndromes (CPS). OMIG meeting. AAO 2015. Las Vegas.
94. Joag M, Sise A, Murillo JC, Osama-Sayed Ahmed I, Wong J, Mercado C, **Galor A**, Karp CL. Topical 5-Fluorouracil (5FU) 1% in the treatment of ocular surface squamous neoplasia. EBAA meeting. AAO 2015. Las Vegas.
95. Chhadva P, Yesilirmak N, **Galor A**, Cabot F, Yoo SH. Post-LASIK Epithelial Ingrowth: Correction, Recurrence, and Long-term Follow-up. Meeting Presentation. AAO 2015. Las Vegas.
96. Atallah M, Joag M, **Galor A**, Amescua G, Nani A, Karp CL. Role of Ultra-High Resolution Optical Coherence Tomography (UHR-OCT) in the Diagnosis of Ocular Surface Squamous Neoplasia (OSSN) in Complex Ocular Surface Diseases. Meeting Presentation. AAO 2015. Las Vegas.
97. Palioura S, **Galor A**, Garg N, Nanji A, Joag M, Nuovo G, Wang G, Karp CL. Human papillomavirus infection does not predict response to interferon therapy in ocular surface squamous neoplasia. Meeting Poster. AAO 2015. Las Vegas.
98. Choi D, Goldhardt R, **Galor A**. Let's give it a shot. SPEIO meeting. AAO 2015. Las Vegas.
99. Tran KD, **Galor A**, Goldhardt R. Looking for love in all the wrong places. SPEIO meeting. AAO 2015. Las Vegas.
100. Ahmed S, **Galor A**, Karp CL, Sant D, Joag M, Shalabi N, Gustafson CB, Wang G. Whole Exome Profiling of Ocular Surface Squamous Neoplasia. SPEIO meeting. AAO 2015. Las Vegas.
101. Dixit L, **Galor A**, Karp CL. Differentiation of conjunctival amyloid and lymphoma by high resolution anterior segment OCT. SPEIO meeting. AAO 2015. Las Vegas.
102. Alghamdi Y, Shalabi N, McClellan A, **Galor A**. Meibomian gland dysfunction and hypercholesterolemia. The Association for Research and Vision in Ophthalmology (ARVO). Denver, CO – May 2015.
103. Batawi H, Levitt RC, Felix E, Margolis TP, Sarantopoulos C, Martin E R, **Galor A**. Incomplete Response To Artificial Tears is Associated With Self-reported Features of Neuropathic Ocular Pain. The Association for Research and Vision in Ophthalmology (ARVO). Denver, CO – May 2015.
104. Gibbons A, Lanza N, Valenzuela F, Perez V, **Galor A**. Dry eye profiles in patients with a positive elevated surface matrix metalloproteinase 9 point of care test versus negative patients The Association for Research and Vision in Ophthalmology (ARVO). Denver, CO – May 2015.

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105. McClellan A, Spierer O, Ehrmann K, Parel JM, Gonzalez A, Felix E, Feuer WJ, Sarantopoulos C, Levitt R, **Galor A**. Corneal Mechanical Hypersensitivity is Correlated with Wind Hyperalgesia, Ocular Symptoms, and Systemic Complaints. The Association for Research and Vision in Ophthalmology (ARVO). Denver, CO – May 2015.
106. Chhadva P, Lee T, Hackam AS, McClellan A, Sarantopoulos KD, Felix ER, Levitt RC, **Galor A**. Human Tear Serotonin Levels and Neuropathic Ocular Pain in Dry Eye. The Association for Research and Vision in Ophthalmology (ARVO). Denver, CO – May 2015.
107. Chhadva P, Alexander A, McClellan AL, **Galor A**, "The Impact of Conjunctivochalasis on Dry Eye Symptoms", poster presentation. World Cornea Congress VII of ASCRS 2015. April 2015 - San Diego, CA
108. Walter S, Levitt R, Gronert K, **Galor A**. Correlation Between Arachadonic Acid–Derived Tear–Film Lipids and Ocular Surface Disease in Dry Eye. Presentation Date Sunday, April 19, 2015. San Diego, CA.
109. Alghamdi Y, Shalabi N, McClellan A, **Galor A**. Title for Printed Programs Epidemiology of Meibomian Gland Dysfunction in Elderly Population. ASCRS Paper ID 16899. Presentation Date Sunday, April 19, 2015. San Diego, CA.
110. Cabot F, Chhadva P, Yesilirmak N, **Galor A**, Yoo S. ASCRS Paper Assessment of IOL Centration 1 Day and 1 Month After Cataract Surgery. Presentation Date Sunday, April 19, 2015. San Diego, CA.
111. Stringham J, Ashkenazi N, **Galor A**, Wellik S. ASCRS Paper Barriers to Glaucoma Medication Compliance Among Veterans: Dry Eye Symptoms and Anxiety Disorders. Presentation Date Saturday, April 18, 2015. ASCRS Paper ID 15529. San Diego, CA.
112. Kaakour AH, Cabot F, Yesilirmak N, Chhadva P, **Galor A**, Yoo S. ASCRS Paper Inter-Device Agreement in Keratometric Readings Measured With Scheimpflug-Based Topography and Ray-Tracing Technology. Presentation Date Sunday, April 19, 2015, ASCRS Paper ID 17453, San Diego, CA.
113. Chhadva P, Cabot F, **Galor A**, Yoo S. Long-Term Outcomes of Flap Amputation After LASIK. ID: 17420. ASCRS Symposium, April 17–21, 2015, San Diego, CA.
114. Read, S, **Galor A**. Treatment of Refractory Filamentary Keratopathy After LASIK With Autologous Serum Tears, ID: 15391. April 17–21, 2015, San Diego, CA.
115. Junk A, **Galor A**. Open Sky Anterior Segment Surgery: Cataract, Glaucoma and Cornea. ASCRS Film program for the ASCRS ASOA Symposium and Congress. San Diego, 2015.
116. Camp A, **Galor A**, Wellik S. The epidemiology of meibomian gland disease in those with and without glaucoma drops. American glaucoma society meeting. San Diego 2015.
117. Zlotcavitch L, Felix ER, Feuer W, Martin ER, Margolis TP, Sarantopoulos KD, Levitt RC, **Galor A**. Characterization of Ocular Pain Features in Dry Eye. Ocular microbiology and immunology group (OMIG) meeting at AAO, Chicago 2014.
118. Walter S, Felix ER, Feuer W, Martin ER, Margolis TP, Sarantopoulos KD, Levitt RC, **Galor A**. Dry Eye Symptom Severity and Persistence are Associated with Symptoms of Neuropathic Pain. Ocular microbiology and immunology group (OMIG) meeting at AAO, Chicago 2014.
119. Galor A, Felix ER, Feuer, W, Shalabi N, McClellan AL, Patin DJ, Martin ER, Margolis TP, Sarantopoulos KD, Levitt RC. Dry eye symptoms align more closely to non-ocular complaints than to tear film parameters. AAO annual meeting, Chicago 2014.
120. Moon C, Nanji A, **Galor, A**, Karp CL. Surgical versus medical treatment of ocular surface squamous neoplasia: A comparison of costs. AAO annual meeting, Chicago 2014.
121. Murillo JC, Joag MG, Sayed-Ahmed IO, Nanji A, Shalabi NM, **Galor A**, Karp C. Ultra-High Resolution Optical Coherence Tomography for the Differentiation of Ocular Surface Squamous Neoplasia and Melanoma. 2014 ISIE/Imaging Conference, Saturday, May 3, 2014, Orlando, FL.
122. Joag MG, Sayed-Ahmed IO, Nanji A, Shalabi NM, **Galor A**, Karp C. Confocal microscopy for the analysis of the sub-basal corneal nerves. 2014 ISIE/Imaging Conference, Saturday, May 3, 2014, Orlando, FL.

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123. Atallah M, Sayed-Ahmed IO, Nanji A, Shalabi NM, **Galor A**, Amescua G, Karp C. Role of Ultra High Resolution Optical Coherence Tomography (UHR-OCT) in the Diagnosis of Ocular Surface Squamous Neoplasia (OSSN) in Complex Ocular Surface Diseases. 2014 ISIE/Imaging Conference, Saturday, May 3, 2014, Orlando, FL.
124. Joag MG; Wong J; Murillo JC; Sayed-Ahmed IO; Nanji A; Shalabi NM; **Galor A**; Karp CL. The Bioniko ophthalmic surgery model: an innovative approach for teaching capsulorhexis. 1295. ARVO, Orlando 2014.
125. Ansari Z; Singh R; Dang S; Alabiad C; **Galor A**. Prevalence, risk factors, and morbidities of eye lid laxity in a Veteran population. 1493 - C0132. ARVO, Orlando 2014.
126. Sayed-Ahmed IO, Wong J, Murillo JC, Joag MG, Shalabi NM, Nanji A, **Galor A**, Karp CL. Blue Nevus of the Ocular Surface. 1498 - C0137. ARVO, Orlando 2014.
127. Zlotcavitch L; Modi Y; Qurban Q; Echeverri R; Feuer WJ; Florez H; **Galor A**. Ocular surface symptoms in veterans returning from Operation Iraqi Freedom and Operation Enduring Freedom. 1998 - B0297. ARVO, Orlando 2014.
128. Nanji A; **Galor A**; Feuer WJ; Wong J; Joag MG; Murillo JC; Sayed-Ahmed IO, Shalabi NM; Karp CL. Evaluation of high resolution optical coherence tomography among novice users in the diagnosis of ocular surface squamous neoplasia. 2448 - B0233. ARVO, Orlando 2014.
129. Martinez JD; Tourkmani-Masri AK; **Galor A**; Beltran F. Brown-McLean syndrome in a pediatric patient and literature review. 2799 - A0384. ARVO, Orlando 2014.
130. Gonzalez A; Ehrmann K; Rowaan C; Lee W; Aguilar MC; McClellan AL; Shalabi NM; **Galor A**; Parel JMA. Age-Related Corneal Sensitivity assessed with a modified BHVI-Belmonte Aesthesiometer: a preliminary study. 3649 - A0163. ARVO, Orlando 2014.
131. Shalabi NM; Tuzhikov AI; **Galor A**; Dong Q; Panchin AU; Thanathanee O; Van Gelder R; O'Brien TP; Shestopalov V. Experimental approaches in the analysis of microbial community in ocular samples. 6288 - B0207. ARVO, Orlando 2014.
132. Walter S, **Galor A**, Wellik SR. Glaucoma Medications Differentially Affect Dry Eye Incidence. ASCRS, Boston 2014.
133. Nanji AA, Moon CS, **Galor A**, Sein J, Oellers P, Karp CL. Surgical vs. Medical Treatment of Ocular Surface Squamous Neoplasia: A Comparison of Recurrences and Complications. Cornea Society meeting, AAO meeting, New Orleans 2013.
134. Murillo JC, **Galor A**, Karp CL. Corneal and Intraocular Invasion of Ocular Surface Squamous Neoplasia After Intraocular Surgery". OMIG meeting, New Orleans 2013.
135. Shalabi N, Karp CL, Aziz H, Jeng B, **Galor A**. Superficial keratectomy, cautery, amniotic membrane transplant for the treatment of painful bullous keratopathy in eyes with poor visual potential. OMIG meeting, New Orleans 2013.
136. McClellan AJ, McClellan AL, Pezon CF, Karp CL, Feuer W, **Galor A**. Epidemiology of Ocular Surface Squamous Neoplasia in a Veterans Affairs Population. OMIG meeting, New Orleans 2013.
137. Nikpoor N, Gregori NZ, Goldhardt R, **Galor A**. Setting the mood. SPEIO meeting, New Orleans 2013.
138. McClellan A, Gregori, NZ, Goldhardt R, **Galor A**. Infection vs inflammation? SPEIO meeting, New Orleans 2013.
139. **Galor A**, Invited Panelist: Cornea Original Paper Session Panelist (DMEK) AAO meeting, New Orleans 2013.
140. **Galor A**, Kumar N, Feuer W, Florez H, Lee DJ. Environmental Factors and Dry Eye Syndrome: A Study Utilizing the National United States Veterans Affairs Administrative Database. AAO meeting, New Orleans 2013.
141. Nanji AA, Moon CS, **Galor A**, Sein J, Oellers P, Karp CL. Surgical vs. Medical Treatment of Ocular Surface Squamous Neoplasia: A Comparison of Recurrences and Complications. AAO meeting, New Orleans 2013.
142. Morkin M, **Galor A**. Hanging by a thread. VISTA meeting at ARVO, Seattle 2013.

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143. Martínez JD, Bentancourt NR, **Galor A**, Beltran Diaz de la Vega F, Ozorno Zarate J, Sanches Huerta V, Torres MA. Frequency and Risk Factors Associated with Ocular Surface Disease in Patients Attending a Tertiary Care Ophthalmology Center in Mexico City. Pan-American Research Day, Seattle, 2013.
144. Martínez JD, Bentancourt NR, **Galor A**, Beltran Diaz de la Vega F, Ozorno Zarate J, Sanches Huerta V, Torres MA. Frequency and Risk Factors Associated with Ocular Surface Disease in Patients Attending a Tertiary Care Ophthalmology Center in Mexico City. ARVO meeting, Seattle 2013.
145. **Galor A**, Venincasa VD, Feuer W, Lee DJ, Florez H, Venincasa MJ. Long-Term Effects of Cataract Surgery on Tear Film Parameters. ARVO meeting, Seattle 2013.
146. Chhadva P, Canto APFS, **Galor A**, Yoo S, Vaddavalli P, Cabot F, Culbertson W. Comparison of IOL Calculation Methods and Intraoperative Wavefront in Eyes That Have Undergone Refractive Surgery. Eastern-Atlantic Student Research Forum, Miami FL 2013.
147. Tzu J, **Galor A**, Wellik S. Quality Of Life In Veterans Using Glaucoma Drops: Health Care Disparities. American Glaucoma Society annual meeting, San Francisco 2013.
148. **Galor A**, Ashley C, Feuer W. The relationship between C-reactive protein (CRP) and tear film parameters. Ocular microbiology and immunology group (OMIG) meeting at AAO, Chicago 2012.
149. El Sayyad F, **Galor A**, Dubovy SR, Karp CL. Anterior Segment OCT for Imaging of Ocular Surface Lesions. Cornea Society/EBAA Meeting, Chicago 2012.
150. **Galor A**, Feuer W, Lee DJ, Perez VL. Depression, Post Traumatic Stress Disorder, and Dry Eye Syndrome. 2012 Joint Meeting of the American Academy of Ophthalmology and the Asia-Pacific Academy of Ophthalmology. Chicago 2012. PO053.
151. Canto APFS, Chhadva P, **Galor A**, Yoo S, Vaddavalli P, Cabot F, Culbertson W. Comparison of IOL Calculation Methods and Intraoperative Wavefront in Eyes That Have Undergone Refractive Surgery. Abstract #: 101679. 2012 Refractive Surgery Subspecialty Day Meeting of the International Society of Refractive Surgery (ISRS). Chicago, IL, USA. 2012
152. Young R, Goldhardt R, Gregori NZ, **Galor A**. A Bird in Hand. SPEIO meeting at AAO. Chicago, 2012
153. Fernandez, CA, **Galor A**, Arheart KL, Florez H, Musselman D, Lee DJ. Dry Eye Syndrome, Posttraumatic Stress Disorder (PTSD), and Depression in Older Male Veterans. American Public Health Association Student Assembly Latebreakers. Paper #273895. APHA 140th annual meeting. San Francisco, 2012.
154. Karp CL, **Galor A**, Oellers P, Kao AA, Abdelaziz A, Feuer W, Dubovy SR. Predictors of ocular surface squamous neoplasia recurrence after exisional surgery. ARVO meeting, Ft. Lauderdale, 2012.
155. Martinez JD, **Galor A**, Perez VL, Karp CL, Yoo SH, Alfonso EC. Endothelial Graft Failure after Contralateral Autologous Corneal Transplantation. ARVO meeting, Ft. Lauderdale, 2012. Travel award recipient.
156. Dunn E, **Galor A**, Junk A, Wellik S, Pelletier J, Gregori NZ. Cumulative Probability and Risk Analysis for Nd:YAG Laser Posterior Capsulotomy After Phacoemulsification. ARVO meeting, Ft. Lauderdale, 2012.
157. Fernandez CA. **Galor A**. Zheng DD, Arheart KL, Lam BL, McCollister KE, Ocasio MA, Lee DJ. Influence of Demographic Characteristics on Eye Care Expenditures: Data from the Medical Expenditure Panel Survey 2007. ARVO meeting, Ft. Lauderdale, 2012.
158. Shah C, Tzu J, **Galor A**, Junk AK, See CW, Wellik SR. Refractive Outcomes of Combined Cataract and Glaucoma Surgery at a VA Hospital. ARVO meeting, Ft. Lauderdale, 2012.
159. Canto A, Henry C, **Galor A**, Yoo SH. Epithelial Ingrowth Under LASIK Flap: Characteristics, Associated Factors And Visual Outcomes In Patients Requiring Flap Lift. ARVO meeting, Ft. Lauderdale, 2012. Travel award recipient.
160. Hurmeric V, Vaddavalli, P, **Galor A**, Yoo SH. The Effect Of Single And Multiple Injections Of Subconjunctival Ranibizumab In Patients With Recurrent Pterygium. ARVO meeting, Ft. Lauderdale, 2012.

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161. Craig S, Pouyeh B, Bilonick RA, **Galor A**. Composite Index Scores for Dry Eye Syndrome: a Comparative Approach. ARVO meeting, Ft. Lauderdale, 2012. Travel award recipient.
162. Oellers P, Karp, CL, Sheth A, Kao AA, Abdelaziz A, Dubovy SR, **Galor A**. Incidence, treatment and outcomes of ocular surface squamous neoplasia associated with pterygium. ARVO meeting, Ft. Lauderdale, 2012.
163. Wellik S, Pouyeh B, Guan H, **Galor A**. Impact Of Ocular Surface Disease On Quality Of Life In Glaucoma Patients. ARVO meeting, Ft. Lauderdale, 2012.
164. Guan H, Wellik S, Pouyeh B, **Galor A**. Impact Of Ocular Surface Disease On Quality Of Life In Glaucoma Patients. Miami VA meeting, Miami, 2012.
165. Tzu J, Shah C, **Galor A**, Junk AK, See C, Wellik SR. Refractive Outcomes of Combined Cataract and Glaucoma Surgery at a VA Hospital. Miami VA meeting, Miami, 2012.
166. Dunn E, **Galor A**, Junk A, Wellik S, Pelletier J, Gregori NZ. Cumulative Probability and Risk Analysis for Nd:YAG Laser Posterior Capsulotomy After Phacoemulsification. Miami VA meeting, Miami, 2012.
167. McCollister A, **Galor A**, Feuer W, Lee D, Faler A, Florez H, Perez VL. Depression, Post Traumatic Stress Disorder and Dry Eye Syndrome: A Study Utilizing the National United States Veterans Affairs Administrative Database. Miami VA meeting, Miami, 2012.
168. Junk A, Dunn E, **Galor A**, Wellik S, Pelletier J, Gregori NZ. Cumulative Probability and Risk Analysis for Nd:YAG Laser Posterior Capsulotomy After Phacoemulsification. Association of VA Surgeons meeting, Miami Beach, 2012.
169. **Galor A**, Martinez J, Perez VL, Karp CL, Yoo SH, Alfonso EC. Endothelial Graft Failure after Contralateral Autologous Corneal Transplantation. Association of VA Surgeons meeting, Miami Beach, 2012.
170. Tzu J, Shah C, **Galor A**, Junk AK, See C, Wellik SR. Refractive Outcomes of Combined Cataract and Glaucoma Surgery at a VA Hospital. ASCRS, Chicago, 2012.
171. Henry C, Canto A, **Galor A**, Yoo S. Epithelial Ingrowth Under LASIK Flap: Clinical Characteristics, Risk Factors, and Visual Outcomes in Patients Requiring Flap Lift. ASCRS, Chicago, 2012.
172. Weiss M, **Galor A**. Anterior chamber worm, SPEIO meeting, AAO, Orlando, 2011.
173. Oellers P, Miller D, Karp CL, **Galor A**, Alfonso EC. Acanthamoeba keratitis with polymicrobial infections, OMIG meeting, AAO, Orlando, 2011.
174. Kao AA, **Galor A**, Karp CL, Dubovy SR. Clinicopathologic Correlation of Ocular Surface Squamous Neoplasms at Bascom Palmer Eye Institute: 2001 – 2010, OMIG meeting, AAO, Orlando, 2011.
175. **Galor A**, Feuer W, Lee DJ, Florez H, Carter D, Prunty WJ, Perez VL. Prevalence and risk factors of dry eye syndrome in a veteran population. ARVO meeting, Ft. Lauderdale, 2011.
176. Viteri E, Pouyeh B, **Galor A**, Lee DJ, Florez H, Fabian J, Perez VL. Prevalence And Morbidity Of Ocular Surface Symptoms In A Veteran Population. ARVO meeting, Ft. Lauderdale, 2011.
177. Pouyeh B, **Galor A**, Junk AK, Pelletier J, Wellik SR, Gregori NZ, Trentacoste J. Surgical and refractive outcomes in cataract surgery with toric intraocular lens implantation in a resident-teaching institution. ARVO meeting, Ft. Lauderdale, 2011.
178. Hodson K, **Galor A**, Karp CL, Davis JL, Albini TA, Perez VL, Miller D, Forster RK. Diagnosis, Treatment, and Outcomes of Patients with Infectious Scleritis: a 20-year review. ARVO meeting, Ft. Lauderdale, 2011.
179. Kao A, **Galor A**, Karp CL, Dubovy SR. Pathologic Characteristics of Ocular Surface Squamous Neoplasm at Bascom Palmer Eye Institute: 2001 - 2010. ARVO meeting, Ft. Lauderdale, 2011.
180. Davis JL, **Galor A**, Ruiz P, Amador A, Albini TA. Simultaneous Cytokine and Cytofluorographic Analysis of Aqueous Humor in Active Uveitis. ARVO meeting, Ft. Lauderdale, 2011.
181. Lemelman B, Lee B, **Galor A**, Feuer W, Pouyeh B, Pelletier J, Vaddavalli P, Yoo SH. Agreement Between Pentacam and IOLMaster in Patients Undergoing Toric Intraocular Lens Implantation. ARVO meeting, Ft. Lauderdale, 2011.
182. Ocasio M, **Galor A**, Zheng DD, Arheart KL, Lam BL, Perez VL, McCollister KE, McClure LA, Lee

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- DJ. Dry Eye Medication Use and Expenditures: Data from the Medical Expenditure Panel Survey 2001-2006. ARVO meeting, Ft. Lauderdale, 2011.
183. Karp CL, Kieval JZ, Abou Shousha M, **Galor A**, Hoffman RA, Dubovy SR, Wang J. Ultra-High Resolution Optical Coherence Tomography for Differentiation of Ocular Surface Squamous Neoplasia and Pterygia. ARVO meeting, Ft. Lauderdale, 2011.
 184. Abou Shousha M, Perez V, Feuer W, **Galor A**, Wang J. Epithelial Irregularity Factor (EIF): A new diagnosis of dry eye syndrome. ACSRS meeting, San Diego, 2011.
 185. Fishler J, Hurmeric V, **Galor A**, Yoo SH, Perez VL. Subconjunctival ranibizumab for recurrent pterygium. ACSRS meeting, San Diego, 2011.
 186. Hodson K, **Galor A**, Karp CL, Albin TA, Perez VL, Davis J, Miller D, Forster RK. Diagnosis, Treatment, and Outcomes of Patients with Infectious Scleritis. OMIG meeting at AAO meeting, Chicago, 2010.
 187. Perez V, Abou Shousha M, Feuer W, **Galor A**, Wang J. Epithelial Irregularity Factor (EIF): A new diagnosis of dry eye syndrome. Tear film and ocular surface society (TFOS) meeting, Florence, Italy, 2010.
 188. **Galor A**, Feuer W, Kempen JH, Kaçmaz RO, Liesegang TL, Suhler EB, Foster CS, Jabs DA, Levy-Clarke, GA, Nussenblatt, RB, Rosenbaum JT, Thorne FE. Adverse effects of smoking on patients with ocular inflammation. ARVO. 2010
 189. Driscoll D, **Galor A**, Yoo SH, Piccoli FVR, Schmitt AJ, Chang V, Perez VL. Ranibizumab for the Inhibition of Neovascularization in the Cornea in High Risk Corneal Transplant Surgery. ACSRS meeting, Boston, 2010.
 190. **Galor A**, Davis JL, Flynn HW, Feuer W, Dubovy SR, Setlur V, Kesen MR, Goldstein DA, Tessler HH, Bykhovskaya Ganelis I, Jabs DA, Thorne JE. Sympathetic ophthalmia: Incidence of ocular complications and vision loss in the sympathizing eye. ARVO. 2009
 191. Gonzalez M, **Galor A**, Goldman D, O'Brien TP. Outcomes after intraocular lens exchange surgery in dissatisfied patients with refractive intraocular lenses. ARVO. 2009
 192. **Galor A**, Davis JL, Flynn HW, Feuer W, Dubovy SR, Setlur V, Kesen MR, Goldstein DA, Tessler HH, Bykhovskaya Ganelis I, Jabs DA, Thorne JE. Sympathetic ophthalmia: Incidence of ocular complications and vision loss in the sympathizing eye. AAO meeting, Atlanta. 2008.
 193. Barnes SD, Karp CL, Chabra S, **Galor A**, Alfonso EC. Subconjunctival/perilesional Recombinant Interferon Alpha 2b for Ocular Surface Squamous Neoplasia: a 10 year review. OMIG meeting at AAO meeting, Atlanta. 2008.
 194. **Galor A**, Karp CL, Chhabra S, Barnes S, Alfonso EC. Topical Interferon Alpha 2b Eye Drops for Treatment of Ocular Surface Squamous Neoplasia: A Dose Comparison Study. OMIG meeting at AAO meeting, Atlanta. 2008.
 195. Leder HA, Jabs DA, **Galor A**, Kedhar SR, Dunn FP, Peters GB, Thorne JE. Posterior subtenons corticosteroid injections for cystoid macular edema complicating noninfectious uveitis. ARVO. 2008.
 196. **Galor A**, Karp C. Pegylated interferon alpha 2b for treatment of ocular surface squamous neoplasia: A pilot study. ARVO. 2008.
 197. **Galor A**, Jabs DA, Leder HA, Kedhar SR, Dunn JP, Peters GB III, Thorne JE. Comparison of antimetabolite therapies for noninfectious ocular inflammation. AAO Meeting, New Orleans. 2007.
 198. **Galor A**, Jabs DA, Leder HA, Kedhar SR, Dunn JP, Peters GB III, Thorne JE. Comparison of antimetabolite therapies for noninfectious ocular inflammation. American Uveitis Society meeting at ARVO. 2007.
 199. Lowder CY, **Galor A**, Margolis R, Kaiser PK. Complications associated with the intravitreal, fluocinolone acetonide implant (Retisert™). ARVO meeting. 2007.
 200. **Galor A**, Ference SF, Singh AD, Lee MS, Stevens GHJ, Perez VL, Peereboom DM. Maculopathy as a complication of blood brain barrier disruption in patients with CNS lymphoma. ARVO meeting. 2007.

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201. Mucci J, Miraldi VA, **Galor A**, Jeng BH. Recurrence rates of herpes simplex virus keratitis in contact lens wears compared to non-contact lens wearers. Ocular Microbiology and Immunology Group, AAO Meeting, Las Vegas. 2006.
202. **Galor A**, Lowder CY, Perez VL, Kaiser PK, Sears JE. Surgical management of long-standing retinal detachments associated with uveitis: a pilot study. American Uveitis Society Winter Meeting, Colorado. 2006.
203. **Galor A**, Brasil OFM, Smith S, Bakri S, Sears JE, Kaiser PK, Lowder CY. Comparison of adverse events from intravitreal triamcinolone in patients with and without uveitis. AAO Meeting, Chicago. 2005.
204. **Galor A**, Carlson EC, Amescua G, Yang X, Perez VL. The immunological milieu of vascularized high risk corneas. Resident day presentation. Cole Eye Institute. 2005.
205. **Galor A**, Meisler D, Yang X, Perez VL. The immunological milieu of human high risk corneal transplant recipients. ARVO meeting. 2005.
206. **Galor A**, Perez VL, Lowder CY. Differential effectiveness of etanercept and infliximab in the treatment of ocular inflammation. American Uveitis Society Winter meeting, Utah. 2005.
207. **Galor A**, Carlson EC, Rodriguez JP, Yang X, Perez VL. Differential migration of inflammatory cells in the vascularized high risk cornea. ARVO meeting. 2004.

NON-PEER REVIEWED PUBLICATIONS

1. <https://atlasofscience.org/> Uveitis and aging.
2. Eye world interview. <http://eyeworld.org/article-newer-dry-eye-diagnostic-tools-show-promise>
3. Vu S, Karp CL, **Galor A**, Wester ST. OCT can be useful in diagnosis of conjunctival lymphangiectasis. Ocular Surgery News U.S. Edition, May 25, 2013
4. **Galor A**, Lowder CY, Jeng BH. Sudden onset of bilateral corneal edema and blurry vision. Eysenet 2007 Jan:41-2.
5. **Galor A**, Lowder CY. Steroid therapy and the eye. Focal Points. 2006 Sept;24(7):10-13.
6. **Galor A**, Perez VL. Ophthalmic puzzler: syphilitic anterior uveitis. Ophthalmology Update. 2005; Fall: 7-8.
7. **Galor A**, Singh A. Ophthalmic puzzler: Indeterminate choroidal melanocytic lesion. Ophthalmology Update. 2005; Winter: 7-9.
8. **Galor A**, Singh A. Ophthalmic puzzler: pediatric choroidal melanoma. Ophthalmology Update. 2004; Winter: 7-9.

20. Other works accepted for publication:

V. PROFESSIONAL

21. Funded Research Performed:

07/20-06/22	Observational Study of Conjunctivitis in the Setting of DUPIXENT® Treatment for Atopic Dermatitis. Dr. Galor. Regeneron
03/21-02/23	Study of efficacy and safety of SAF312 eye drops in subjects with post-operative chronic ocular surface pain (COSP). Dr. Galor. Novartis.
09/20-08/25	Biomarkers of ocular pain after refractive surgery. Dr. Galor/Aicher. R61 NS114960-01A1. NEI
07/20-06/22	Automated Assessment of Visual Photosensitivity in Traumatic Brain Injury. Dr. Galor. VR190009, DOD
04/20-03/24	Neural mechanisms of ocular pain. Principal Investigator Dr. Galor, Total direct costs \$650,000 funded by the Department of Veterans Affairs, CSRD
04/20-03/24	Lipid Mediators in Meibomian Gland Disease. Principal Investigators Drs. Galor and Mandel, Total direct costs \$1M funded by the Department of Veterans Affairs, BLRD

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04/20-03/23	Gulf War Illness: Eye-Brain connection. Funded by the DOD.
06/18-05/19	SAC internal grant. FMT for Sjogrens. \$25,000
09/17-08/19	Sjogrens syndrome (SS) foundation, \$50,000 pilot award to study FMT for SS
04/17-03/22	ZEDS, U of Miami site, funded by NEI, Steering committee member
09/16-08/21	Micro-environment and dry eye: Principal Investigators Drs Galor and Kumar, Total direct costs \$1.7M funded by NEI (R01EY026174)
01/16-12/20	Neuropathic pain: A missing piece of the dry eye puzzle. Principal Investigator Dr. Galor, Total direct costs \$650,000 funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research EPID-006-15S
01/17-12/17	2016 ARVO Foundation/Collaborative Research Fellowship with Nalle Ramos from the Asociacion para Evitar la Ceguera en México (APEC), \$10,000.
03/16-02/17	LASIK-induced Neuropathic Pain: New Paradigms for Perioperative Management of Corneal Nerve Injury and Dry Eye. Principal Investigator Dr. Galor, Total direct costs \$50,000 provided by the University of Miami, CTSI program.
12/14-12/15	The environment and dry eye. Principal Investigator Dr. Galor, Total direct costs \$10,000 provided by the University of Miami.
10/10-10/15	The Scope of Dry Eye Syndrome in a Veteran Population, Principal Investigator Dr. Galor, Total direct costs \$1,100,000 provided by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research and Development's Career Development Award CDA-2-024-10S, 75% effort
07/13-06/14	Identification of tumor and patient characteristics that predict interferon treatment success in ocular surface squamous neoplasia. Principal Investigator Dr. Galor, Total direct costs \$40,000 provided by the Stanley Glaser award, University of Miami.
10/12-10/14	The ocular microbiome and dry eye syndrome, Principal Investigator Russ Van Gelder, Total direct costs \$60,000 provided by an Alcon grant, 5% effort
11/08-06/11	Analysis of Intraocular Fluids in Patients with Uveitis, Principal Investigator: Janet Davis, Total direct costs \$70,000 provided by Bascom Palmer and the Jaime Marti Foundation, 10% effort
11/08-06/11	Ranibizimab in the treatment of pterygium and high risk corneal transplantation, Principal Investigator: Sonia Yoo, Total direct costs \$25,000 provided by Genentech, 10% effort

22. Reviewer and Editorial responsibilities:

Book Editor

2020	<i>Gut microbiome and dry eye: What's the connection (Published by Elsevier)</i>
2020	<i>Dry Eye Diseases (Published by Elsevier)</i>

Special issue Editor

2020	<i>Current Ophthalmology Reports: Ocular surface</i>
2020	<i>Frontiers in Pharmacology: Eye Pain: Etiology and Therapeutic Approaches</i>
2020	<i>Journal of Clinical Medicine: Dry Eye Syndrome: Climate, environment, and disease</i>
2019	<i>Journal of Clinical Medicine: Dry Eye Syndrome: New Insights on Epidemiology and Management</i>

Section Editor for

2020-present	<i>Clinical and Experimental Ophthalmology</i>
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2019-present	<i>Eye and Contact Lens</i>
2019-present	<i>British Medical Journal Ophthalmology</i>
2018-present	<i>Ophthalmology</i>
2018-present	<i>British Journal of Ophthalmology</i>
2018-present	<i>Ocular Surface</i>

Reviewer for

American Journal of Ophthalmology
American Journal of Ophthalmology Case Reports
Ophthalmology
Ophthalmology Science
JAMA Ophthalmology
British Journal of Ophthalmology
Ocular Surface
IOVS
Eye
Cornea
Ocular Immunology and Inflammation
BMC Ophthalmology
Eye and Contact Lens
Case reports in ophthalmology
European Journal of Pain

23. Professional and Honorary Participation in National Organizations:

2018-present	AMPC committee, ARVO, representative of Cornea section.
2018-present	Study section member and chair of the NEI ZRG1 BDCN J 81 group.
2018-present	Council position for the Ocular Microbiology and Immunology Group
2018-2020	AAO Focal Points committee
2018-present	AAO corneal abstract and instructional course committee
2013-present	ARVO (The Association for Research in Vision and Ophthalmology) CME committee
2013-present	ONE (Ophthalmic News and Education network) editorial committee member, AAO (American Academy of Ophthalmology), chair of cornea section
2010-present	Tear Film Ocular Surface Society (member)
2010-2017	Self-assessment committee, American Academy of Ophthalmology: responsibilities include writing cornea/external disease questions to assist ophthalmologists in preparing for the board and Maintenance of Competency (MOC) examinations
2009-present	Ocular Microbiology and Immunology Group (past-president)
2009-present	Society of HEED fellows (member)
2009-present	Miami Ophthalmology Society (member)
2006-present	American Uveitis Society (member)
2003-present	American Academy of Ophthalmology (AAO) (member)
2003-present	Association for Research in Vision and Ophthalmology (ARVO) (member)
2010-2015	ISTA's Women Leadership Forum, AAO (member)

24. Honors and Awards

2020	2020 Ludwig Von Sallmann Clinician-Scientist Award recipient, ARVO
2018	Induction into the American Ophthalmology Society
2017	American Academy of Ophthalmology's <i>Senior Achievement Award</i>
2016	Selected to participate in AAO Leadership Development Program

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2015	Chhadva, P. Best paper award AAO “Post-LASIK Epithelial Ingrowth: Correction, Recurrence, and Long-term Follow-up. Meeting Presentation” Senior mentor
2015	Chhadva, P. First Place Clinical Science Presentation “ <i>The Impact of Eyelid Laxity on Dry Eye</i> ” Senior mentor
2015	Shalabi, N. First Place Young Investigator Clinical Science Presentation “ <i>Confocal microscopy for the analysis of the sub-basal corneal nerves</i> ” Senior mentor
2014	AAO paper “ <i>Dry eye symptoms align more closely to non-ocular complaints than to tear film parameters</i> ” poster award
2013	AAO paper on dry eye and environment highlighted in press release as “new and newsworthy”
2013	McClellan, A. First Place Young Investigator Clinical/Health Services Presentation “ <i>Epidemiology of OSSN in veteran population</i> ” Senior mentor
2012	AAO paper on dry eye in veterans highlighted in press release as “new and newsworthy”
2012	Guan H. First Place Young Investigator Clinical/Health Services Presentation “ <i>Impact Of Ocular Surface Disease On Quality Of Life In Glaucoma Patients</i> ” Senior mentor
2010	Professor of the Year Award, Bascom Palmer Eye Institute, awarded by the BPEI residents for outstanding teaching
2010	American Academy of Ophthalmology’s <i>Achievement Award</i>
2007	Herminia Greig Memorial Award, Bascom Palmer Eye Institute
2007	ARVO travel grant
2006	HEED fellowship recipient
2006	Highest resident quiz score, Cole Eye Institute
2006	Highest OKAP score award, Cole Eye Institute
2005	Travel grant for best abstract, TNF & Beyond Summit, CCF
2005	Highest resident quiz score, Cole Eye Institute
2005	Highest OKAP score award, Cole Eye Institute
2004	Resident day research award for best paper, Cole Eye Institute
2004	Highest OKAP score award, Cole Eye Institute
2002	Alpha Omega Alpha, Washington University
2002	Glasgow Memorial achievement – for graduating in top10% of class
2002	Max and Evelyn grand prize – excellence in ophthalmic research
2002	John Kirk Scholastic award – high scholastic standing
2002	Alumni scholarship – full tuition scholarship to student with highest rank
2001	Steven Dresler prize – excellence in community service
2000	Dr. Margaret Smith award – outstanding women in medicine
1999	Carl and Gerty Cori prize – performance in Biochemistry
1997	Phi Beta Kappa, Carnegie Mellon University
1997	Bennett award – for excellence in mechanical engineering
1997	University honors and college research honors
1997	Mortar Board – national senior service honor society

25. Post-Doctoral Fellowships: N/A

26. Other Professional Activities (e.g. papers presented; performances; conference proceedings; seminar or conference panel member; catalogue work; etc)

Visiting Professorships

1. UC Davis- March 4, 2022
2. UT Health San Antonio Cornea Day-9/24/2021—Virtual presentation
3. UCSF/Proctor - Dept of Ophthalmology, April 28, 2021—Virtual presentation
4. UT Austin Dell Medical School - Dept of Ophthalmology, January 14, 2021—Virtual presentation

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5. University of Utah, January 15, 2021—Virtual presentation
6. University of Iowa, July 15, 2020—Virtual presentation
7. Augusta University, June 12, 2020—Cancelled due to COVID19
8. UT Southwestern, June 4, 2020—Cancelled due to COVID19
9. UC Davis, April 24, 2020—Cancelled due to COVID19
10. École d'Optométrie/School of Optometry, Université de Montréal, November 11, 2019
11. Stony Brook University, New York October 17, 2019
12. Schepens Eye Research Institute /Mass Eye and Ear Distinguished lecture, Boston, February 22, 2019
13. University of Iowa, Department of Ophthalmology, December 7, 2018
14. Indiana University Department of Ophthalmology, November 7, 2018
15. University of San Francisco, October 18, 2018.
16. Center for Pain and the Brain at Boston Children's Hospital, David Borsook, October 8, 2018.
17. Physiology & Pharmacology department at OHSU, Sue Aicher, November 2, 2017.
18. Proctor Foundation, June 10, 2017.
19. Wills Eye Hospital. April 12, 2017
20. Case Western Reserve University. March 31, 2017
21. University of Maryland. September 20, 2016
22. Virginia Society of Eye Physicians and Surgeons. June 4, 2016
23. University of Seattle. April 16-17, 2016.

Courses Director

1. Ocular Surface Masqueraders: What Not to Miss and How Not to Miss It, AAO, Virtual meeting, November 15, 2020.
2. Evaluation and Management of Painful Dry eye Symptoms: Nerves vs tears, AAO, Virtual meeting, November 15, 2020.
3. Ocular Surface Masqueraders: What Not to Miss and How Not to Miss It, AAO, San Francisco, October 14, 2019.
4. Evaluation and Management of Painful Dry eye Symptoms: Nerves vs tears, AAO, San Francisco, October 13, 2019.
5. Ecourse director: Ocular Pain: An Important Yet Under-Evaluated Feature of Dry Eye. AAO website, 2018.
6. Ocular Surface Pain: Principles and Practice, AAO, Chicago, October 28, 2018.
7. Ocular Surface Pain: Principles and Practice, AAO, New Orleans, November 17, 2017.
8. Ocular Surface Pain: Principles and Practice, AAO, Chicago, October 17, 2016.

Didactic Lectures

1. Invited lecture, Heidelberg Engineering. What can my confocal do for me? September 21, 2021. Virtual presentation.
2. Invited lecture, 8th Annual World Congress of SBMT (Society of Brain Mapping and Therapeutics), July 8, 2021. Los Angeles, California.
3. Invited lecture, EUDEC 2021: European Dry Eye Congress: Paris. June 18-19, 2021
4. Invited lecture, Knapp Symposium AOS 2021: COVID19 and the eye. Naples, May 21, 2021
5. Invited lecture, The microbiome and dry eye. Bowman's Club. March 26, 2021
6. Invited lecture, University of Miami Anesthesia Department, Chronic Ocular Pain: Real, Often Misdiagnosed And Difficult To Treat, March 4, 2021
7. Invited lecture, The environment and the eye. BPEI corneal consultation. February 27, 2021
8. Invited lecture, Pain and sensation. ADVANCES IN DIAGNOSIS AND MANAGEMENT FOR DRY EYE: Understanding better the Dry Eye Workshop Study (DEWS II), transmitted in Mexico and Latin America. February 27, 2021.

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9. Invited lecture, Neuropathic pain. Cornea virtual summit, December 12, 2020.
10. Course participant. Ocular pain. US Association for the Study of Pain Meeting. December 9, 2020.
11. Invited lecture, CURSO meeting, Bascom Palmer Eye Institute, November 21, 2020,
12. Invited lecture, Dry eye 360: Role of environment on the ocular surface, November, 3, 2020, Virtual meeting, Journal of Clinical Medicine lecture series.
13. Invited lecture, Neuropathic Ocular Pain - Real, Often Misdiagnosed & Difficult to Treat, Oct 29, 2020, Joint meeting with Dr. Nigel Baker at the Queen Elizabeth Hospital in Barbados.
14. Invited lecture, Dry Eye "Desert!" 2020 Course! October 18, 2020, Virtual meeting put on by Dr. Ashiyana Nariani, MD, MPH in Maharashtra India.
15. Invited lecture, Ocular pain and dry eye: What's the connection? Portland Oregon VAMC, October 14, 2020.
16. Invited lecture, The Emirates Society of Ophthalmology, September 12, 2021.
17. Invited lecture, Tear Film and Ocular Surface Society Meeting 2020, September 9-12, 2020, Cernobbio, Italy.—cancelled due to COVID19.
18. Invited lecture, Association of Contact Lens Educators. May 29, 2020, Nova Southeastern University, Florida. —cancelled due to COVID19.
19. Mini-symposium organizer, Ocular Pain, ARVO, May 3rd, 2020. Baltimore. —cancelled due to COVID19.
20. Invited lecture, Bowman's conference. March 27, 2020, Liverpool, England. —cancelled due to COVID19.
21. Invited lecture, Cornea Gordon Research Conference. February 16-21, 2020, Lucca, Italy.
22. Invited lecture, Ocular Surface Workshop 2020. January 13-19, 2020, Hyderabad, India.
23. Participant. Cornea day at AAO, San Francisco, CA. October 11, 2019.
24. Participant. Management of Common Allergic and Immunologic Diseases of the Conjunctiva and Cornea. AAO, San Francisco, October 14, 2019.
25. Participant. Cornea fellowship summit. September 5-8, 2018. Atlanta, GA.
26. Invited lecture, SSO (Societe Suisse d'Ophthalmologie) Annual Meeting 2019. August 29-30, 2019, Interlaken, Switzerland
27. Invited lectures, Clínica Barraquer de Bogotá Cornea meeting, August 22-25, 2019 Bogota, Columbia.
28. Invited lectures, Georgia Society of Ophthalmology, Amelia Island, August 2-4, 2019.
29. Invited lectures, 35rd Pan-American Congress of Ophthalmology 2019, May 25-28, Cancun, Mexico.
30. Participant. Climate and Health Symposium, May 11, 2019, Miami, FL.
31. Invited lecture, New advances in keratoconus, March 23, 2019, Bascom Palmer Eye Institute, Miami, FL.
32. Invited lecture, Birmingham Corneal Meeting, March 9, 2019, Birmingham, England.
33. Invited lecture, Interactive Consultations in Cornea and Refractive Surgery, Feb 22, 2019, Bascom Palmer Eye Institute, Miami, FL.
34. Invited lecture, EnVision Summit, February 15-18, 2019, San Juan, Puerto Rico.
35. Invited lecture, I Curso Bascom Palmer Eye Institute Ecuador, January 10-14, 2019, Cuenca, Ecuador
36. Invited lecture, XL Inter-American Course in Clinical Ophthalmology, Nov 4-7, 2018, DoubleTree by Hilton Hotel, Miami, FL
37. Participant. Cornea day at AAO. October 27, 2019. Chicago, IL.
38. Participant. Cornea fellowship summit. September 6-8, 2018. Tampa, FL.
39. Invited lecture. National Medical Association. August 14, 2018. Orlando, FL.
40. Invited lecture. Paraguayan Ophthalmology Society. August 2-3, 2018. Asunción.
41. Invited lecture. North Carolina Retina Associates, April 25, 2018.
42. Participant. Cornea Day, ASCRS, April 13, 2018.
43. Invited lecture. Interactive Consultations in Cornea and Refractive Surgery, Bascom Palmer, February 23-24, 2018.
44. Invited lecture. Sarcoidosis patient advocacy day, University of Miami, February 24, 2018.

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45. Invited lecture, XXXVII Inter-American Course in Clinical Ophthalmology Nov 19, 2017, InterContinental Hotel, Miami, FL
46. Invited lectures, 33rd Pan-American Congress of Ophthalmology 2017, August 9-11, Lima, Peru.
47. Invited lecture, Ocular Surface Diseases Course 2017, Mar 18 2017, Bascom Palmer Eye Institute, Miami, FL.
48. Invited lecture, Ophthalmology Exchange Meeting 3rd March 2017, London, England.
49. Invited lecture, PanCornea International Congress. February 24 - 25, 2017. Miami FL.
50. Invited lecture, Interactive Consultations in Cornea and Refractive Surgery, Feb 3 - Feb 4 2017, Bascom Palmer Eye Institute, Miami, FL
51. Invited lecture, *Ophthalmology Congress*. Quito, Equator, January 13, 2017.
52. Invited lecture, XXXVIII Inter-American Course in Clinical Ophthalmology October 30, 2016. Trump Hotel Doral, Miami, FL
53. Reconstruccion de cornea y superficie ocular: Ciudad de Mexico, October 27-29 2016
54. New Developments in Dry Eye Diagnosis and Treatment: Ocular microbiome in dry eye, *Cornea sub-specialty day*, AAO, Chicago, IL, October 15, 2016.
55. AAO-OMIG (Ocular Microbiology and Immunology Group) Joint Symposium entitled Rethinking The Ophthalmologists' Approach to Inflammatory Diseases of the Ocular Surface, Chicago, October 18, 2016.
56. Neuropathic pain: a missing piece of the dry eye puzzle, *Dry eye session*, XXII Biennial Meeting of the International Society for Eye Research, September 25-29, 2016 | Tokyo, Japan
57. Clinical relevance of photophobia in dry eye. *Expanding the functions of ocular surface innervation: photophobia and photoallodynia*. XXII Biennial Meeting of the International Society for Eye Research, September 25-29, 2016 | Tokyo, Japan
58. Diagnosis and management of corneal somatosensory dysfunction. *Neuropathic pain session*. Tear film and ocular surface society meeting, Montpellier, France, September, 8, 2016.
59. Invited lecture, *Video Conferencia Congreso Nacional de Oftalmología*. Venezuela, June 16, 2016
60. Invited lecture, *XXII Biennial Meeting of the International Society for Eye Research*, Tokyo, Japan. September 25 – 29, 2016
61. Invited lecture, *Keynote Speaker in the 8th International Conference on the Tear Film & Ocular Surface: Basic Science and Clinical Relevance*, Montpellier, France. September 7- 10, 2016.
62. Invited lecture, *La Oftalmología de hoy. Un Curso Del Bascom Palmer Eye Institute and Sociedad Peruana De Oftalmología*. Lima, Peru. June 10, 2016.
63. Invited lecture, *Ocular Surface Diseases Course 2016*. BPEI. April 16, 2016.
64. Invited lecture, *Interactive Consultations in Cornea and Refractive Surgery*. BPEI. March 4-5, 2016.
65. Invited lecture, *BPEI-FOLA-Barraquer-Course*, Santiago, Chile, December 3-4, 2015.
66. Invited lecture, *XXXVII Curso Interamericano*, Miami, November 22, 2015.
67. Invited lecture, *Cornea sub-specialty day*. Adenoconjunctivitis. AAO 2015 November 14, 2015.
68. Invited lecture, *Centro Mexicano de Córnea y Cirugía Refractiva A.C*, Cancun, Mexico. September 14-16, 2015.
69. Invited lecture, *XXXI Pan-American Congress of Ophthalmology*, Bogota, Columbia. August 5-8, 2015.
70. Invited lecturer, *Association for Ocular Pharmacology and Therapeutics meeting*, Dry eye and Aging, Charleston, SC, February 27, 2015.
71. Invited lecturer, *52nd Actualization Course in Ophthalmology*, Mexico City, Mexico, February 18-21, 2015.
72. Conference presenter and session organizer/moderator: *XXXVI Curso Interamericano*, Miami, October 26, 2014.
73. Skills Transfer Instructor “*Microsurgical Suturing Techniques*”, American Academy of Ophthalmology annual meeting, Chicago, November, 2014.
74. Conference presenter, *Cornea 2014: Restocking the Toolbox: Concepts and Techniques for the Toughest Jobs: Anti-angiogenesis Therapy*. Corneal subspecialty day. AAO Chicago, 10/18/2014.

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75. Invited lecturer for webinar, *Pan-American Association of Ophthalmology (PAAO) "Neuropathic pain: a missing piece of the dry eye puzzle?"* September 8, 2014.
76. Invited lecturer, Tel hashomer hospital, Tel Aviv Israel *"Neuropathic pain: a missing piece of the dry eye puzzle?"* July 10, 2014.
77. Invited lecturer, *23rd Pan-American Regional Course*, Punta del Este, Uruguay, May 29 - 31 2014
78. Invited lecturer, *Bascom Palmer Eye Institute & Fundación Oftalmológica Los Andes*. Santiago, Chile, December 5 - 7, 2013.
79. Conference presenter *"Oops I didn't mean for that to happen, now what?"* XXXV Curso Interamericano, Miami, November 24, 2010.
80. Skills Transfer Instructor *"Microsurgical Suturing Techniques"*, American Academy of Ophthalmology annual meeting, New Orleans, November, 2013.
81. Dry eye syndrome and glaucoma. CME event at the AAO meeting, New Orleans 2013.
82. Invited lecturer, *XXX Pan-American Congress of Ophthalmology & XXXVII Brazilian Congress of Ophthalmology*. August 7 - 10, 2013 Rio de Janeiro, Brazil.
83. Visiting Professor, *The 11th annual John Dickerson Memorial Ophthalmic lecture*, Norfolk, VA, May 3-4, 2013.
84. Skills Transfer Instructor *"Microsurgical Suturing Techniques"*, American Academy of Ophthalmology annual meeting, Chicago, November 12, 2012.
85. Invited lecturer, *18th International Course on Cornea and Refractive Surgery*, Cancun, Mexico, August 8-11, 2012.
86. Invited lecturer, *Masters in Ophthalmology 2012*, Orlando, Florida, June 22, 2012.
87. Invited lecturer, *Sociedad Puertorriquena de Oftalmologia 43rd Annual Congress*, San Juan, Puerto Rico, May 25-28, 2012.
88. Invited lecturer, *VIII Uruguayan National Ophthalmology Congress & International Course of Bascom Palmer Eye Institute*, Montevideo, Uruguay, November 30, 2011.
89. Invited lecturer, *XIV Peruvian Prevention of Blindness Congress & XIII Regional Congress of Ophthalmology*, Arequipa, Peru, September 30, 2011.
90. Conference presenter *"Dry eye syndrome – men also have it"* XXXIV Curso Interamericano, Miami, October 31, 2011.
91. Skills Transfer Instructor *"Microsurgical Suturing Techniques"*, American Academy of Ophthalmology annual meeting, Orlando, October 25, 2011.
92. Conference presenter *"Refractive surgery after penetrating keratoplasty"* XXXIII Curso Interamericano, Miami, October 30, 2010.
93. Conference presenter *"Persistent inflammation after cataract surgery"* Cataract and refractive surgery conference, Miami, February 26, 2010.
94. Conference presenter *"Epidemiology of blepharitis"* 5th International Conference in Ocular Infections, Palm Beach, February 20, 2010.
95. Conference presenter *"The young endothelium"* Cataract and refractive surgery conference, Miami, February 6, 2009.
96. Conference presenter *"The unstable lens"* Cataract and refractive surgery conference, Miami, February 8, 2008.

Professional Service

National Responsibilities:

Grant review process

- | | |
|--------------|--|
| 2019-2020 | Ad hoc reviewer for National Science Center, Poland |
| 2017-present | Member of the Ocular Surface, Cornea, and Refractive Error special emphasis panel, NEI 10/2020; 2/2020; 3/2019 05/2019 ZRG1 BDCN-J (81), chair of section 11/2020 ZRG1 BDCN-J (91) |

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- 2/2021 PED2
2017-present Ad hoc reviewer for the CSRD and BLRD VA study sections
2017-present Ad hoc reviewer for The French National Research Agency

National service

- 2020-present Executive committee, TFOS DEWS III Workshop
2018-present Cornea section representative, *Association for Vision and Research in Ophthalmology*
2017-present Focal point member, *American Academy of Ophthalmology*
2017-present AAO Annual Meeting Program Committee
2017-2018 Cornea sub-specialty day sub-committee, ASCRS
2015-2017 President, *Ocular Microbiology and Immunology Group*
2014-2018 Pain and sensation sub-committee member, TFOS DEWS II Workshop
2013-present Mentor for the annual Heed Ophthalmic Foundation Residents Retreat, Chicago IL
2013-present Continuing medical education committee member, ARVO. The CME committee is advisory in nature and serves to ensure that ARVO's continuing medical education program meets or exceeds the Essential Areas and policies of the ACCME and AMA.
2013-present Ophthalmic News and Education (ONE) assistant senior editor, cornea, AAO. The ONE network provides a single source of ophthalmic news and education for ophthalmologists around the world. The role of the committee members include: providing breaking news, reports from meetings, journal studies, information on new drugs, technologies and procedures, review of Academy content and advice as to what additional educational materials are needed in each area.
2013-present Assistant Senior Editor Cornea, ONE network for *American Academy of Ophthalmology*
2011-present Examiner for the oral board examination; *American Board of Ophthalmology*
2011-2017 Member of the Self Assessment Committee for the *American Academy of Ophthalmology* responsibilities include writing cornea/external disease to assist ophthalmologists in preparing for the board and Maintenance of Competency (MOC) examinations

Advocacy

- 2019 Mid-year forum for the American Academy of Ophthalmology, April 11-12. Washington DC
2018 Mid-year forum for the American Academy of Ophthalmology, April 18-21. Washington DC
2017 Dry Eye Research Advocates, sponsored by TFOS, National Alliance for Eye and Vision Research (NAEVR)/Alliance for Eye and Vision Research (AEVR), Washington DC
2016 Mid-year forum for the American Academy of Ophthalmology, Washington DC

VI. TEACHING

27. **Teaching Awards Received:** Professor of the Year, 2010
28. **Teaching Specialization**

Online education: Ocular pain content development in conjunction with AAO in the form of CME based case problem based learning. Launched on the AAO website October 2016.

Clinical Supervision and Teaching

- 2009-present Participate in cataract skills transfer course bi-yearly, Bascom Palmer Eye Institute.
2009-present Staffing residents in OR and clinics at the Veterans Administration hospital, Miami
1 day per week outpatient clinic, 1 day per week in operating room.
2009-present Weekly cornea/uveitis lecture for first and second year residents on VA rotation,

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- Mondays 5-6 pm
- 2009-present Supervise medical students during their VA ophthalmology rotation and serve as the director of the VA eye clinic medical student rotation,
<https://sites.google.com/site/ophthalmologymdr861/home>
- 2009-present Teach corneal to the 3rd and 4th year medical students during their ophthalmology rotation at Bascom Palmer Eye Institute, 6 lectures/year
- 2009-present Teach 2nd year students during their ophthalmology course, one a year
- 2009-present Teach residents during the 7 am lecture series/ 3x year
- 2015-2016 Small group leader for 1st year MD/MPH students

National cataract skills transfer activities

- 15th Annual Harvard Ophthalmology Intensive Cataract Surgical Training Course. May 17-18, 2019. Boston, MA
- 13th Annual Harvard Ophthalmology Intensive Cataract Surgical Training Course. May 20-21, 2017. Boston, MA
- 12th Annual Harvard Ophthalmology Intensive Cataract Surgical Training Course. May 21-22, 2016. Boston, MA

Trainee research supervision (topic; student name; date)

Medical student supervision

1. *OCT as a biomarker for Gulf War Illness*. Brandon Baksh, 6/19-present. In Progress
2. *Gut microbiome dysbiosis in Sjogrens*, Kelly Acuna, 12/19-present. In Progress
3. *TENS for ocular pain*, Meghana Kalavar, 12/19-present. In Progress
4. *MMP levels in GVHD*, Justin Konje Achua, 12/19-present. In Progress
5. *Neural mechanisms of photophobia*, Jodi Hwang, 12/19-present. In Progress
6. *Diabetes and functional slit lamp biomicroscopy*. Jodi Hwang. 10/2018-present. In Progress
7. *Inflammation as a predictor of cyclosporine response*. Kristen Zayan. 8/2018-present. In Progress
8. *Quantitative sensory testing in photophobia*. Daniel Rodriguez. 12/2018-present. In Progress
9. *Epidemiology of chalazion*. Sneha Patel. 7/2017-present. In Progress
10. *Autologous serum tears for the treatment of dry eye*. Parker Lloyd Bussies, Despoina Theotoka, 7/2017-present. In Progress
11. *Corneal densitometry values in VZO*. Joshua Hansen 7/2017-present. In Progress
12. *Gut microbiome in Sjogrens*. Arjun Watane, Monika Farhangi. 10/2017-present. In Progress
13. *Confocal nerve parameters and dry eye*. Harrison Dermer; 7/2017-present. In Progress
14. *Real world experience with TENS for ocular pain*.
15. *Botulinum toxin for the treatment of photophobia*. Kristen Zayan. 7/2018- present. Favorable review Neuromodulation.
16. *Coping mechanisms in dry eye*. Sneha Bhupendrakumar Patel. 9/2018-8/2019. Published in Clinical J of Medicine.
17. *Early markers of Sjögrens in dry eye*. Sasha Hubschman. 8/2018-11/2019. Published Cornea
18. *Epidemiology of OSSN in veterans*. Logan M Smith. 7/2017-8/2018. Published Eye and Vision
19. *TrueTear for the treatment of dry eye*. Monika Farhangi. 6/2018-9/1019. Published BJO
20. *IgE levels in the tears of dry eye patients*. Harrison Dermer; 03/2017-8/2019; Published in Journal of Clinical Medicine.

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21. *Pregabalin for the prevention of dry eye symptoms after LASIK.* Michael Venincasa and Stephen E Valido. 5/2017-8/2019; Published in Journal of Clinical Medicine
22. *Ocular pain in those using glaucoma drops.* Hua Hong-Uyen Thanh and James Parrish. 6/2015-9/2019; Published in Journal of Clinical Medicine
23. *Meibum lipid composition and dry eye.* Vikram Paranjpe, 6/2016-1/2019; Published Ocular Surface
24. *Quality of life in patients undergoing treatment for OSSN.* James Wong; Carolina Mercado; 12/2013-7/2018. Published, Ocular Surface.
25. *Seasons and dry eye.* Harrison Dermer; 1/2017-12/2018. Published Clinical Ophthalmology.
26. *Dry eye symptoms after cataract surgery.* Ravin Sajani, 7/2017-7/2018. Published Cornea.
27. *A comparative study of central corneal epithelial, stromal and total thickness in primary open angle glaucoma patients and non-glaucoma patients.* Cima P Maliakal, 7/2016-1/2018; Published, Cornea
28. *Atopic Disease Associated With Poorer Prognosis In Ocular Surface Squamous Neoplasia,* Lilly Zhang, 7/2016-1/2018; Published Ocul Immunol Inflamm.
29. *Botulinum toxin for the treatment of photophobia.* Ryan Diel and Zachary Kroeger, 7/2016-1/2018; Published Ophthalmology
30. *Central sensitization: A link between traumatic brain injury and dry eye.* Charity Lee; 6/2015-1/2018; Published BJO.
31. *Dry eye symptoms in OEF/OIF clinics.* Vikram Paranjpe. 6/2015-1/2018
32. *Blue nevus of the ocular surface,* James Wong; Carolina Mercado, Ibrahim Osama, 11/2013- 1/2018. Published Ophthalmology.
33. *Risk factors for dry eye discordance.* Erin Ong; 7/16-1/2017; Published BJO
34. *Longitudinal Examination of Frequency of and Risk Factors for Severe Dry Eye Symptoms in US Veterans.* Erin Ong; 7/2016-1/2017; Published in JAMA Ophthalmology.
35. *The Association of Dry Eye Symptom Severity and Comorbid Insomnia in US Veterans.* Benjamin Ethan Seiden; Published in Eye and Contact Lens.
36. *Immunosuppression as a Possible Risk Factor for Interferon Nonresponse in Ocular Surface Squamous Neoplasia.* Noy Ashkenazy, noyashkenazy@gmail.com; Published in Cornea.
37. *Dry eye cases.* Nisreen Ezuddin 06/2015-1/2017. Published in Ocular Surface Disease (Book Chapter)
38. *Chronic dry eye symptoms after LASIK: parallels and lessons to be learned from other persistent post-operative pain disorders.* Alexandra Levitt, MS II; 7/2013-9/2015. Published in Molecular Pain
39. *Ocular surface symptoms and quality of life in patients using glaucoma drops.* Noy Ashkenazi; 12/2013-2015. Published in Eye and contact lens.
40. *Impact of Eyelid Laxity on Symptoms and Signs of Dry Eye Disease.* Priyanka Chhadva; 03/2015-2/2016. Published in Cornea
41. *The Matrix Metalloproteinase 9 Point-of-Care Test in Dry Eye and Dry Eye Profiles in Patients with a Positive Elevated Surface Matrix Metalloproteinase 9 Point-of-Care Test Versus Negative Patients.* Nicole Lanza 03/15-2/2016. Published in Ocular Surface.
42. *The Impact of Conjunctivochalasis on Dry Eye Symptoms and Signs,* Priyanka Chhadva; 03/15-12/2015. Published in IOVS
43. *Human papillomavirus in ocular surface squamous carcinoma does not predict response to interferon treatment.* Nisha Garg; 02/2015-2015. Published in Ophthalmology
44. *Tear serotonin levels in dry eye syndrome.* Priyanka Chhadva; 12/2013-12/2015. Published in Ophthalmology
45. *Epidemiology of anterior segment inflammation in patients with autoimmune disease.* Alexandra Levitt, MS II; 7/2013-3/2015. Published in Cornea
46. *Seasonality and dry eye.* Nicole Lanza. 10/2014-3/2015, Published in Ophthalmology
47. *Cyclosporine ophthalmic emulsions for the treatment of dry eye - a review of the clinical evidence.* Philip Ames; 10/2014-2/2015. Published in Future Science
48. *Pseudopemphigoid as caused by topical drugs and pemphigus disease.* Laura Huang; Published World

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J Ophthalmol.

49. *Management of conjunctival malignant melanoma: a review and update.* James Wong; 8/2014-12/2014. Published in Expert Rev Ophthalmol
50. *Ocular pain in dry eye syndrome.* Leonid Zlotcavitch; 12/2013-12/2014. Published in BJO
51. *Dry eye associated morbidity from glaucoma medications.* Ananth Sastry; 7/2013-12/2014. Published in Eye and Contact Lens.
52. *Prevalence, risk factors, and morbidities of eye lid laxity in a veteran population* Zubair Ansari; 7/2013-12/2014. Published in Cornea.
53. *Androgen Deficiency and Dry Eye Syndrome in the Aging Male* Patrick Azcarate; 7/2013-12/2014. Published in IOVS.
54. *Ocular surface symptoms in veterans returning from Operation Iraqi Freedom and Operation Enduring Freedom.* Leonid Zlotcavitch; 8/2013-12/2013. Published in IOVS.
55. *Current Thoughts in Fungal Keratitis: Diagnosis and Treatment.* Zubair Ansari; 12/2012-7/2013. Published in Curr Fungal Infect Rep.
56. *OCT can be useful in diagnosis of conjunctival lymphangiectasis.* Sawlar Vu; 12/2012-07/2013. Published in Ocular Surface News.
57. *Outcomes after combined cataract and glaucoma surgery,* Ananth Sastry; 8/2011-7/2013. Published in J Glaucoma.
58. *Calculation Methods and Intraoperative Wavefront in Eyes That Have Undergone Refractive Surgery.* Priyanka Chhadva; 1/2012-8/2013. Published in J Refract Surg.
59. *Composite score formulation in dry eye syndrome;* Craig See; 8/2011-8/2013. Published in IOVS.
60. *Comparison of outcomes between interferon and surgery in the treatment of OSSN;* Julia Sein,; 6/2011-7/2013. Published in Ophthalmology.
61. *Anterior chamber Angiostrongyliasis,* Ashley Crane, MS IV; 2/2012-1/2013. Published in JAMA Ophthalmology.
62. *C-reactive protein and dry eye syndrome,* Ashley Crane; 7/2012-1/2013. Published in Ophthalmology.
63. *Long-term effects of cataract surgery on tear film parameters,* Vincent D Venincasa; 7/2012-12/2012. Published in Scientific World Journal.
64. *The diagnostic utility of anterior chamber paracentesis in anterior uveitis,* Zane Anwar; 7/2012-12/2012. Published in Am J Ophthalmol.
65. *Ocular surface disease in glaucoma,* Zane Anwar; 7/2012-12/2012. Published in Curr Opin Ophthalmol.
66. *Comparison of Pentacam and IOL Master for preoperative planning in patients undergoing a toric IOL,* Benjamin Lemelman; 10/2010-6/2012. Published in J Refract Surg.
67. *Refractive Outcomes of Combined Cataract and Glaucoma Surgery.* Christopher Shah; 8/2011-6/2012. Published in J Glaucoma.
68. *Incidence of YAG capsulotomy in a resident-teaching institution;* Evan Dunn; 6/2011-6/2012. Published in World Journal of Ophthalmology
69. *Endothelial Graft Failure after Contralateral Autologous Corneal Transplantation,* Jaime Martinez; 8/2011-12/2011 Published in Cornea.
70. *Ocular surface symptoms in veteran patients,* Eduardo Viteri; 8/2010-6/2011. Published in Am J Ophthalmol.
71. *Morbidity of ocular surface symptoms in a veteran population;* Ehsan Mozayan; 6/2010-7/2010. Published in Am J Ophthalmol.

Resident supervision

1. *Contractile anterior segment membranes as a cause of DSAEK failure.* Nathan Pirakitikulr, 7/18-present. In Progress.
2. *Conjunctival keratoacanthoma.* Nandini Venkateswaran, 7/17-present. In Progress.

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3. *Ocular sarcoidosis*, Kenneth Fan and Diana Laura, 7/17-present. In Progress.
4. *Clinical outcomes of conjunctival melanoma*, Eric Hansen, Carolina Mercado, Nandini Venkateswaran, Basil Williams; 07/13-present. In Progress
5. *Amyloid versus lymphoma: An OCT study*. Nandini Venkateswaran, 7/17-8/19. Published Eye and Vision.
6. *Clinical versus OCT exams for ocular surface squamous neoplasia*. Nandini Venkateswaran and Van Anne Tran, 7/17-8/19. Published Eye and Vision.
7. *5FU versus interferon for the treatment of ocular surface squamous neoplasia*. Nandini Venkateswaran, 7/16-12/2018. Published, AJO.
8. *Genetics of conjunctival melanomas*, Swarup Swamanathan, 07/16-1/2018. Published in JAMA.
9. *Orbital ocular surface squamous neoplasia*; Benjamin Erickson; 07/13-1/2018.
10. *Utility of high resolution OCT in management of ocular surface lesions*. Michael Yim; 10/14-1/2018. Published Canadian Journal of Ophthalmology.
11. *Evidence of central sensitisation in those with dry eye symptoms and neuropathic-like ocular pain complaints: incomplete response to topical anaesthesia and generalised heightened sensitivity to evoked pain*. Ashley Crane, 1/2016. Published in British Journal of Ophthalmology.
12. *Assessment of Somatosensory Function in Patients With Idiopathic Dry Eye Symptoms*. Derek Covington (Anesthesia Resident, 07/2015-12/2016); Published in JAMA Ophthalmology.
13. *High-Resolution Optical Coherence Tomography in the Differentiation of Inflammatory Versus Noninflammatory Peripheral Corneal Thinning*, Marianeli Rodriguez; 07/2016-12/2016. Published in Cornea
14. *Patients with more severe symptoms of neuropathic ocular pain report more frequent and severe chronic overlapping pain conditions and psychiatric disease..* Ashley Crane; 11/2015-12/2016. Published in British Journal of Ophthalmology.
15. *Ocular surface symptoms and quality of life in patients using glaucoma drops*. Jack Stringham; 12/2013-2/2016. Published in Eye and Contact Lens.
16. *Lid hygiene for the treatment of dry eye: who responds?* Andrew Camp; 10/2014-3/2016. Published in Eye and Contact Lens.
17. *ω -3 Tear Film Lipids Correlate With Clinical Measures of Dry Eye*. Scott Walters; 7/2013-5/2016. Published in IOVS
18. *Epidemiology of Herpes Zoster Ophthalmicus: Recurrence and Chronicity*. Kimberly Tran; 10/2014-5/2016. Published in Ophthalmology.
19. *Neuropathic ocular pain due to dry eye is associated with chronic comorbid pain syndromes*. Derek Covington (anesthesia resident) 10/2014-2/2016. Published in Journal of Pain
20. *Autologous serum tears for the treatment of filamentary keratopathy*. Sarah Read; 07/2014-12/2015. Published Eye contact lens.
21. *Burning Eye Syndrome: Do neuropathic pain mechanisms underlie chronic dry eye?* Jerry Kalangara (anesthesia resident); 12/2013-12/2014. Published Pain medicine
22. *Prevalence and risk factors of dry eye in patients using glaucoma medications*; Scott Walters; 07/2013-12/2014. Presented at ASCRS 2014.
23. *Quality of life disparities in veterans using glaucoma drops*, Jonathan Tzu; 8/2012-12/2014. Published to Eye and Contact Lens.
24. *Treatment of ocular exposure in ICU patients*; Neda Nikpoor. 07/2013-05/2014. Presented at Residents day 2014.
25. *Superficial Keratectomy, Cautery, Amniotic Membrane transplant for the Treatment of Painful Bullous Keratopathy in Eyes with Poor Visual Potential*, Hassan Aziz; 05/1202-12/2013. Published in Cornea.
26. *Ocular surface symptoms in veterans returning from Operation Iraqi Freedom and Operation Enduring Freedom*; Yasha Modi; 07/2013-12/2013. Published in IOVS
27. *Ultra high-resolution anterior segment optical coherence tomography in the diagnosis and*

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- management of ocular surface squamous neoplasia.*, Benjamin Thomas; 2/2012-12/2013. Published in Ocular Surface.
28. *Epidemiology of Ocular Surface Squamous Neoplasia in a Veterans Affairs Population.* Andrew McClellan; 7/2012-8/2013. Published in Cornea.
 29. *Outcomes after combined cataract and glaucoma surgery,* Jonathan Tzu; 8/2011-8/2013. Published in J Glaucoma.
 30. *An Atypical Allergy to Brimonidine.* Yasha Modi; 11/2012-3/2013. Published in J Glaucoma.
 31. *Comparison of Pentacam and IOL Master for preoperative planning in patients undergoing a toric IOL,* Bradford Lee; 10/2010-12/2012. Published in J Refract Surg.
 32. *Outcomes after flap lift for epithelial ingrowth,* Christopher Henry; 9/2011-6/2012. Published in J Refract Surg.

Fellow research supervision

1. *Pain sensitivity and autonomic function as predictors of dry eye symptoms after LASIK.* Mario Rojas. 07/2018-present. In Progress.
2. *Perioperative mapping of OSSN.* Kavitha Sivaraman. 10/2014-9/18. Published in AJO.
3. *SEM for direct quantification of ocular surface exposure to air pollution.* 10/2017-4/2019 Published Cornea.
4. *Ocular pain characteristics in patients presenting to a comprehensive clinic.* Victoria Chang, 06/2015-1/2018. Published Eye and Contact lens.
5. *Confocal microscopy and anti-VEGF injections,* Hatim Batawi; 10/14-present. Published, Cornea.
6. *Conjunctival amyloidosis.* Lena Dixit, 6/2015-12/2017. Presented ARVO.
7. *Genetics of OSSN,* Afshan Nanji, Madhura Joag; 7/2013-1/2016. Published in Ophthalmology
8. *Characteristics of Ocular Pain Complaints in Patients With Idiopathic Dry Eye Symptoms.* Jerry Kalangera (Anesthesia Resident). 1/2015-2/2016. Published in Eye and Contact Lens.
9. *Cataract Surgery After Refractive Surgery.* Ravi Patel (Cornea Fellow 2015-16). Published in International Ophthalmology Clinics.
10. *Frequency and risk factors associated with dry eye in patients attending a tertiary care ophthalmology center in Mexico City.* Jaime Martinez 7/2015-10/2016. Published in Clinical Ophthalmology.
11. *Bulbar conjunctival microvascular responses in dry eye.* Hatim Batawi; 07/2015-1/2017. Published in Ocular Surface.
12. *Compliance and Subjective Patient Responses to Eyelid Hygiene.* 8/2015- 5/2016. Yousef Alghamdi, Published in Eye and Contact Lens
13. *Epidemiology of MGD in a veteran population.* 8/2012- 2/2016. Yousef Alghamdi, Published in Cornea
14. *5FU for the treatment of OSSN,* Madhura Joag and Adam Sise, 07/2013- 02/2016. Published in Ophthalmology
15. *Corneal and Intraocular Invasion of Ocular Surface Squamous Neoplasia After Intraocular Surgery. Report of two cases and review of the literature.* Juan Carlos Murillo, 07/2013- 4/2016. Published in Ocular Oncology and Pathology
16. *Cost of medical versus surgical treatment of ocular surface squamous neoplasia.* Christina Moon, 7/2012- 2015. Published in Ophthalmology.
17. *Human papillomavirus in ocular surface squamous carcinoma does not predict response to interferon treatment,* Afshan Nanji and Madhura Joag, 7/2013-2015. Published in Ophthalmology
18. *RTVue in the evaluation of conjunctival lesions.* Fouad El Sayyad and Afshan Nanji, 7/2012- 12/2014. Published in Ocular Surface.
19. *Delayed expulsive choroidal hemorrhage after penetrating keratoplasty..* Madhura Joag, 07/2013-12/2014. Published in Ophthalmic Surg Lasers Imaging Retina
20. *ORange intraoperative aberrometer for post refractive patients,* Ana Canto, 12/11-7/13. Published in J Refract Surg.

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21. *Outcomes after flap lift for epithelial ingrowth*, Christopher Henry and Ana Canto, clinical fellow; 9/2011-6/2012. Published in J Refract Surg.
22. *Medical versus surgical management of ocular surface squamous neoplasia*. Afshan Nanji, 12/2011-6/2012; Published in Ophthalmology.
23. *Ranibizumab for the treatment of early pterygium recurrence*, Pravin Vaddavalli and Volkan Hurmeric, 8/2009-6/2012. Published in Clinical Ophthalmology.
24. *Surgical and refractive outcomes in resident-performed cataract surgery utilizing toric intraocular lenses*; Bozorgmehr Pouyeh; 6/2010-6/2011. Published in Am J Ophthalmol.
25. *Clinicopathologic Correlation of Ocular Surface Squamous Neoplasms at Bascom Palmer Eye Institute: 2001 - 2010*, Andrew Kao; 10/2010-6/2011. Published in Ophthalmology.
26. *Infectious Scleritis*; Kelly Hodson, pre-residency fellow; 8/2010-6/2011 Published in Cornea.

Faculty mentorship

1. *TBI and photophobia*. Mariela Aguilar, PHD; 8/19-present: Published in Cornea.
2. *Management strategies for ocular pain*. Leslie Small, OD; 7/17-8/19: Published in Eye and Contact Lens.
3. *Defining the ocular microbiome in children and adults*; Kara Cavuoto; 7/16-present; In Progress.
Mentor on her K23 application.

Supervision of Grand rounds presentations:

1. Ophthalmology grand rounds discussant "*Diablito does not wear Prada*" presenter Shanlee Stevens, MD September 10, 2020. (OSSN in atopy)
2. Ophthalmology grand rounds discussant "Reading between the lines" presenter Caroline Lieux, MD August 20, 2020. (Recurrent erosion syndrome in lattice corneal dystrophy)
3. Ophthalmology grand rounds discussant "*Suffering from Success.*" presenter Wade Reddick, MD December 19, 2019. (GVHD)
4. Ophthalmology grand rounds discussant "*Cardi A.*" presenter Benjamin Fowler, MD September 19, 2019. (Nocardia keratitis)
5. Ophthalmology grand rounds discussant "*Here comes the sun*" presenter Humberto Salazar, MD September 5, 2019. (ASOCT imaging for OSSN)
6. Ophthalmology grand rounds discussant "*Bad Blood*" presenter Anne Kunkler, MD August 22, 2019. (HLAB27 anterior uveitis)
7. Ophthalmology grand rounds discussant "*Looking at your viral eyes*" presenter Diana Laura, MD August 15, 2019. (Adenovirus conjunctivitis)
8. Ophthalmology grand rounds discussant "*So Basic*" presenter Patrick Staropoli, MD August 15, 2019. (Chemical injury)
9. Ophthalmology grand rounds discussant "*The way you make me feel*" presenter Michelle Latting, MD August 1, 2019. (Neurotrophic keratitis treated with topical NGF)
10. Ophthalmology grand rounds discussant "*Surfer's Eye*" presenter Ying Chen, MD June 6, 2019. (Pterygium)
11. Ophthalmology grand rounds discussant "*Roid Rage*" presenter Alex Levitt, MD March 14, 2019. (Corneal keloid)
12. Ophthalmology grand rounds discussant "*The Pain Killers*" presenter Eric Duerr, MD October 18, 2018. (Management of neuropathic ocular pain)
13. Ophthalmology grand rounds discussant "*Healing with feeling*" presenter Nathan Pirakitikulr, MD Sept 20, 2018. (Management of neurotrophic keratitis)
14. Ophthalmology grand rounds discussant "*Getting rejected*" presenter Kenneth Fan, MD June 7, 2018. (Management of allograft rejection in corneal transplant)
15. Ophthalmology grand rounds discussant "*Lumps and Bumps*" presenter Ying Chen, MD February 22,

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2018. (Corneal lesions in NF1)
16. Ophthalmology grand rounds discussant "*Eye want to be one less*" presenter Diana Laura, MD January 18, 2018. (Conjunctival papilloma)
17. Ophthalmology grand rounds discussant "*Neither corny nor funny*" presenter Kenny Fan, MD October 12, 2017. (Fungal keratitis)
18. Ophthalmology grand rounds discussant "*Pro VI*" presenter Eric Deurr, MD August 31, 2017. (VZO)
19. Ophthalmology grand rounds discussant "*All that glitters is not gold*" presenter Jonathan Russell, MD August 3, 2017. (Synchysis scintillans)
20. Ophthalmology grand rounds discussant "*Here comes the sun*" presenter Nicolas Yannuzzi, MD July 27, 2017. (Porphyria)
21. Ophthalmology grand rounds discussant "*The price of beauty*" presenter Dan Choi, MD February 2, 2017. (Cosmetic conjunctival surgery)
22. Ophthalmology grand rounds discussant "*Muffin top*" presenter Nicolas Yannuzzi, MD February 11, 2016. (Conjunctival chalasis)
23. Ophthalmology grand rounds discussant "*Out of Place*" presenter Nimish Patel, MD January 14, 2016. (Atopic conjunctivitis)
24. Ophthalmology grand rounds discussant "*Let's give it a shot*" presenter Dan Choi, MD November 5, 2015.
25. Ophthalmology grand rounds discussant "*Blinded by the light*" presenter Eric Hansen, MD October 29, 2015. (Photophobia)
26. Ophthalmology grand rounds discussant "*Restoring balance*" presenter Nikisha Kotari, MD August 13, 2015. (Amantadine toxicity)
27. Ophthalmology grand rounds discussant "*Peripheral mysteries*" presenter Marianeli Rodriguez, MD January 8, 2015. (Peripheral keratitis)
28. Ophthalmology grand rounds discussant "*Pumped up tricks by zoster the people*" presenter Daniel Choi, MD November 6, 2014. (VZO)
29. Ophthalmology grand rounds discussant "*Its not a tumor*" presenter Andrew Camp, MD September 25, 2014. (Pterygium)
30. Ophthalmology grand rounds discussant "*Musical Chairs*" presenter Ashley Crane, MD August 21, 2014. (Corneal cautery and AMT for the treatment of painful bullous keratopathy)
31. Ophthalmology grand rounds discussant "*Stinkeye*" presenter Andrew McClellan, MD July 24, 2014.
32. Ophthalmology grand rounds discussant "*Tip of the iceberg*" presenter Daniel Churgin, MD July 17, 2014.
33. Ophthalmology grand rounds discussant "*All that is superficial is not plastics*" presenter Hassan Aziz, MD April 17, 2014. (Cautery/AMT as treatment for painful bullous keratopathy)
34. Ophthalmology grand rounds discussant "*Growing, growing, gone?*" presenter Korey Jaben, MD March 20, 2014
35. Ophthalmology grand rounds discussant "*To Creep or Not to Creep*" presenter Basil Williams, MD October 31, 2013 (HSV keratitis)
36. Ophthalmology grand rounds discussant "*If at first you don't succeed dry dry again*" presenter Sarah Read, MD August 29, 2013 (Filamentary conjunctivitis)
37. Ophthalmology grand rounds discussant "*Moody Moles*" presenter Andrew McClellan, MD August 1, 2013 (Blue nevus of the conjunctiva)
38. Ophthalmology grand rounds discussant "*Two birds with one stone*" presenter Korey Jaben, MD January 24, 2013 (corneal dystrophy)
39. Ophthalmology grand rounds discussant "*A bird in hand*" presenter Ryan Young, MD December 6, 2012 (Candida endophthalmitis)
40. Ophthalmology grand rounds discussant "*I'm too steep*" presenter Audrey Ko, MD September 13, 2012 (Managing astigmatism after corneal transplant)

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41. Ophthalmology grand rounds discussant "*What a blast*" presenter: Sara Grace, MD August 30, 2012
42. Ophthalmology grand rounds discussant "*What would Ben Stein say*" presenter: Yasha Modi, MD May 31, 2012 (glaucoma medication associated ocular surface disease)
43. Ophthalmology grand rounds discussant "*That's what she said...*" presenter: Daniel Chao, MD May 16, 2012
44. Ophthalmology grand rounds discussant "*Chopsticks: A cautionary tale*" presenter: Christopher Henry, MD March 15, 2012 (Trauma after LASIK)
45. Ophthalmology grand rounds discussant "*Another Tequila Sunrise*" presenter: Matthew Weiss, MD July 28, 2011
46. Ophthalmology grand rounds discussant "*Epic Failure*" presenter: Ashkan Abbey, MD June 2, 2011 (Autologous corneal transplantation)
47. Ophthalmology grand rounds discussant "*Give me a word, any word, and I show you that the root of that word is Greek*" presenter: Anil Vedula, MD January 13, 2011
48. Ophthalmology grand rounds discussant "*The case of the unblanched soldier*" presenter: Marco Gonzalez, MD August 12, 2010
49. Ophthalmology grand rounds discussant "*Don't forget to smell the roses*" presenter: David Samimi, MD January 28, 2010 (Rosacea)
50. Ophthalmology grand rounds discussant "*It's all in the jeans*" presenter: David Weiss, MD December 3, 2009 (HLA-B27)
51. Ophthalmology grand rounds discussant "*Connecting the dots*" presenter: Kara Cavouto, MD December 3, 2009 (Rosai Dorfman)
52. Ophthalmology grand rounds discussant "*Are you inquisita about bullosa acquisita?*" presenter: Lejla Mutapcic, MD January 15, 2009 (cicatizing conjunctivitis)

Supervision of Resident Day Projects:

- 2017 Resident's day: Nandini Venkateswaran MD, 5-FU versus Interferon for the treatment of primary ocular surface squamous neoplasia
- 2016 Resident's day: Ashley M. Crane, MD, Patients with more Severe Symptoms of Neuropathic Ocular Pain Report more Frequent and Severe Chronic Overlapping Pain Conditions and Psychiatric Disease
- 2016 Resident's day: Zubair A. Ansari, MD; Bulbar Conjunctival Microvascular Responses in Dry Eye
- 2016 Resident's day: Victoria S. Chang, MD, Dry Eye Symptoms Correlates with Non- Ocular Conditions
- 2015 Resident's day: Jack Stringham, MD, Dry eye symptoms and quality of life in patients using glaucoma drops.
- 2015 Resident's day: Scott Walter, MD, Lipid mediators and dry eye.
- 2015 Resident's day: Michael Yim, MD, Utility of UHR-OCT in the management of ocular surface lesions
- 2015 Resident's day: Kimberley Tran, MD, The epidemiology of HZO in the veteran population
- 2015 Resident's day: Andrew Camp, MD, Lid hygiene for dry eye: Who gets better?
- 2015 Resident's day: Sotiria Palioura, MD, HPV in OSSN
- 2014 Resident's day: Eric Hansen, MD, Conjunctival melanoma.
- 2014 Resident's day: Neda Nikpoor, MD, Ophthalmology practice patterns of ICU nurses.
- 2013 Resident's day: Andrew McClellan, MD, The epidemiology of ocular surface squamous neoplasia in a Veterans Affairs population.
- 2013 Resident's day: Cristina Moon, MD, Medical versus surgical management of ocular surface squamous neoplasia: comparison of cost.
- 2013 Resident's day: Afshan Nanji, MD, Medical versus surgical management of ocular surface squamous neoplasia: comparison of efficacy and side effects.
- 2012 Resident's day: Benjamin Thomas, MD, Ultrahigh resolution Optical Coherence Tomography for the evaluation of complex ocular surface lesions.
- 2011 Resident's day: Bradford Lee, MD, Agreement Between Pentacam and IOLMaster in Patients

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Undergoing Toric Intraocular Lens Implantation.

2011 Resident's day: Andrew Kao, MD, Clinicopathologic Correlation of Ocular Surface Squamous Neoplasms at Bascom Palmer Eye Institute: 2001 - 2010

2010 Resident's day: Jane Fishler, MD, Subconjunctival ranibizumab for recurrent pterygium.

2010 Resident's day: Natalie Stanciu, MD, Ultra-High Resolution Optical Coherence Tomography for Differentiation of Ocular Surface Squamous Neoplasia and Pterygia.

28. Thesis and Dissertation Supervision

2016 MSPH thesis: Hatim Batawi, MD, Evaluation of central corneal epithelial, stromal and total thickness in primary open angle glaucoma patients and non-glaucoma patients

2016 MPH capstone: Yousef Alghamdi MD, Compliance and Subjective Patient Responses to Eyelid Hygiene.

2015 MSPH thesis: Nabeel Shalabi, MD, Confocal microscopy for the analysis of the sub-basal corneal nerves.

VII. SERVICE

29. University Committee and Administrative Responsibilities:

2014-present	Cornea lecture organizer, Bascom Palmer Eye Institute
2014-present	ESRF Alving Judge
2013-present	Research budget committee, Miami VAMC
2013-present	Research equipment committee, Miami VAMC
2013-present	Corneal co-fellowship director, Bascom Palmer Eye Institute
2009-present	Medical student lecturer, Bascom Palmer Eye Institute
2008-present	Medical student coordinator of ophthalmology rotation at the Miami VAMC
2014-2018	IRB committee member and sub-chair, Miami VAMC
2014-2015	Eye surgery infection prevention workforce, Miami VAMC
2011-2013	Surgical eye flow committee, Miami VAMC (chair)

30. National service:

Listed above under Professional Service

31. Community Activities:

01/09-06/09	Community based participatory research evaluating environmental concerns in Liberty City, Miami
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Exploring the Link Between Dry Eye and Migraine: From Eye to Brain

This article was published in the following Dove Press journal:
Eye and Brain

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Abstract: Dry eye and migraine are common diseases with large societal and economic burdens that have recently been associated in the literature. This review outlines the link between dry eye and migraine, which may have implications for reducing their respective burdens. We highlight possible shared pathophysiology, including peripheral and central sensitization, as the potential link between dry eye and migraine. Finally, therapies targeting similar pathophysiological mechanisms between dry eye and migraine are discussed.

Keywords: dry eye, migraine, brain, sensitization

Introduction

Awareness of dry eye has increased in recent years including its association with specific diseases, such as migraine headaches. However, our understanding of the link between dry eye and migraine is contingent on what is currently known about them as separate diseases. Specifically, dry eye and migraine are both highly prevalent in the population. The prevalence of dry eye ranges from 5% to 50% in the worldwide population, depending on disease definition and population studied, with an overall estimated societal economic burden of \$55.4 billion in the United States.¹ As with dry eye, the prevalence of migraine headache is also high. In western countries, the lifetime prevalence of migraine is up to 9.5% in males and 25% in females.² The societal economic burden of migraine in the United States is estimated at \$36 billion.³ Thus, migraine headaches and dry eye are important health concerns, and their association warrants further exploration. Understanding shared connections between the two diseases may provide insight into shared pathophysiology and treatments, with a potential decrease in disease morbidity.

To understand the link between dry eye and migraine, we must first define them as separate diseases. Dry eye is defined by the Tear Film and Ocular Surface Society Dry Eye Workshop II as

a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.⁴

The symptoms of dry eye are variable and can include sensations of “dryness”, “grittiness”, “burning” and “stinging”, to name a few.⁵ Individuals may also report that these sensations are spontaneous and/or evoked by wind or light.⁵ Others complain of visual phenomena, such as blurry or fluctuating vision.⁶ Dry eye

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symptoms are commonly assessed in the clinic with specific questionnaires, such as Dry Eye Questionnaire-5 (DEQ-5; range 0–22)⁷ and Ocular Surface Disease Index (OSDI; range, 0–100),⁸ which incorporate many of the above complaints. The DEQ-5 focuses on intensity and frequency of dryness and discomfort, along with tearing, while the OSDI considers spontaneous and evoked pain, visual complaints, and impact on daily activities. These questionnaires lump responses and generate severity scores, with DEQ-5 scores ≥ 6 considered indicative of any dry eye symptoms⁷ and scores ≥ 12 considered severe symptoms. OSDI scores are interpreted as normal=0–12, mild=12–32, and severe=33–100.⁹ Of note, these severity scales incorporate a number of different aspects of dry eye to reach a final score, including pain, visual complaints, tearing, and activity limitations. Given that specific symptoms may be driven by different contributors, other questionnaires have been developed to specifically assess for ocular pain complaints, including the Ocular Pain Assessment Survey (OPAS), a 28-question survey, that focuses on intensity of eye pain, non-eye related pain, and aggravating factors,¹⁰ and the Neuropathic Pain Symptom Inventory-Eye (NPSI-Eye; range, 0–100), which focuses on neuropathic pain features, inquiring about descriptors such as burning pain and evoked pain to wind and light.¹¹

In addition to symptoms, clinical signs are also included under the purview of dry eye. The tear film is composed of 2 layers, a thicker muco-aqueous layer that interacts with the corneal epithelium, and a thinner lipid layer that sits on top of the muco-aqueous layer and inhibits its evaporation.¹² Broadly speaking, dry eye is sub-grouped into categories by dysfunction in these two layers, that is aqueous tear deficient and evaporative dry eye.¹³ Signs of aqueous deficiency include decreased tear volume, assessed by examining the tear meniscus under the slit lamp examination or with the Phenol Red Thread (PRT) test, and reduced tear production, assessed with Schirmer strips (strips of paper placed in the corner of the eye and left in place for 5 minutes, mm of wetting recorded). The main sign of evaporative deficiency is a rapid tear break up time (TBUT, measured in seconds until a black spot appears in the tear film), which can occur with a dysfunctional lipid layer. However, any tear abnormality, including aqueous deficiency, can result in a rapid TBUT. Furthermore, the sub-types co-exist and individuals may present with both aqueous and evaporative deficiency. Punctate epithelial erosions, which are

small disruptions in the corneal epithelium visualized with vital dyes such as sodium fluorescein, rose bengal, or lissamine green, can be seen in both dry eye sub-types and with other ocular surface abnormalities (eg anatomic abnormalities of the eyelid, conjunctivae, or cornea).

The lipid layer is produced by the Meibomian glands (MG) in the upper and lower eyelids. Eyelid abnormalities such as plugging of the MG orifices, MG atrophy, and production of a thicker than normal lipid product (eg abnormal meibum quality) can accompany signs of tear dysfunction.¹⁴ Point of care tests have also been developed to assess tear composition and inflammation and can specifically evaluate tear osmolarity (TearLab, San Diego)¹⁵ and ocular surface inflammation (matrix metalloproteinase-9, Inflammadry, Quidel Corporation, San Diego)¹⁶ in the clinical setting. Some individuals with clinical tear film abnormalities will have high or unstable tear osmolarity levels and/or detectable inflammation on their ocular surface.

A challenge in evaluating dry eye is that the symptoms and signs of disease are often disparate.^{17,18} The presenting symptoms of dry eye can vary even in the same individual and are frequently discordant from the clinical signs and their severity, which can make the diagnosis and management of dry eye difficult. For example, a systematic review of 33 studies assessing associations between dry eye symptoms and signs found that out of 175 individual symptom-sign analyses, only 42 (24%) were significantly correlated with one another. This study also found that the majority (129/148; 87%) of individual analyses reporting correlation coefficients were in the low-to-moderate range (–0.4 to 0.4).¹⁷ In addition, the lack of a single objective test with which to evaluate dry eye signs and the low repeatability of tests (eg Schirmer) contributes to the complexity of the disorder.

One of the reasons it is important to screen for dry eye is that dry eye symptoms have a negative impact on individuals' lives as they decrease the ability to work and carry out activities of daily living.¹⁹ For example, a study recruited 56 individuals with a dry eye diagnosis (International Classification of Diseases, Ninth Revision, ICD-9, codes) for assessment of ophthalmic and quality of life parameters. This study found that individuals with severe dry eye disease (composite score of symptoms [9-level subjective facial expression scale] and signs [Schirmer and corneal surface staining]) had quality of life scores (measured by the time trade-off method) in the range of severe (class III/IV) angina (mean utility

score, range 0 to 1, lower values indicate worse quality of life: 0.72 for severe dry eye disease and 0.71 for class III/IV angina).²⁰ In addition, dry eye symptoms have a negative impact on mental health and several studies have linked depression and anxiety to dry eye.^{21,22} Finally, individuals with dry eye have sleep abnormalities. For example, a meta-analysis of 17 studies found that individuals with dry eye symptoms or disease (diagnosed using varying criteria across studies) or primary Sjogren's syndrome had worse sleep quality scores (using Pittsburgh Sleep Quality Index) compared to controls (weighted mean difference=1.69, 95% confidence interval (CI): 0.82–2.56).²³ Taken together, dry eye is a debilitating disease with profound impacts on social functioning and perception of life quality.

Similar to dry eye, migraine is a prevalent condition in the general population.² The International Headache Society (IHS) defines migraine as a “recurrent headache disorder manifesting in attacks lasting 4–72 hours”.²⁴ Migraine headaches are characterized by unilateral location and pulsating quality and can include nausea, photophobia, and/or phonophobia. Migraine attacks are classified into those with or without aura. Migraine with aura involves reversible prodromal symptoms, such as visual, sensory, or other central nervous system disturbance lasting a few minutes.²⁴ Migraine can also be separated into chronic and episodic. Chronic migraine is characterized as occurring ≥ 15 days per month for three months, which, on at least eight days per month, has features of migraine, while episodic migraine occurs less than 15 days per month.²⁴

As with dry eye, migraine symptoms can be debilitating and decrease quality of life.²⁵ An observational study of 102 individuals with migraine found disability and health-related quality of life scores were significantly lower than the general population.²⁶ Similarly, a retrospective cross-sectional survey study of 80,600 European patients found lower health-related quality of life and decreased work productivity among those with ≥ 4 monthly migraine headaches compared to non-migraine controls.²⁷ Interestingly, lower quality of life scores among those with migraine closely associate with dry eye symptoms. In a cross-sectional survey-based study of 62 individuals with migraine, visual function (measured via visual functioning questionnaire-25) and overall quality of life (measured via headache impact test-6) correlated with dry eye symptoms (measured via OSDI score).²⁸ Together, these data show that both dry eye, migraine,

and perhaps their interaction, have significant negative impacts on patient quality of life. Thus, in this review, we explore the association between dry eye and migraine with the goal of illuminating overlapping pathophysiology and potential therapies. To do so, we reviewed recent studies that investigated the relationship between dry eye and migraine.

Methods

A PubMed search was conducted using the terms “dry eye” AND “migraine”. All published scientific articles were considered including original research, meta-analyses, and systematic reviews. All searches were limited to the English language. Eligible articles were reviewed and summarized.

Clinical Associations Between Dry Eye and Migraine Epidemiology of Dry Eye, Migraine, and Their Co-Existence

Dry eye and migraine are co-morbid. Using survey data from a Korean population-based cross-sectional study of 14,329 participants, the prevalence of migraine and dry eye diagnosis was found to be similar among participants: 24.2% reported migraine headaches (positive answer to “Do you have, or have you ever experienced migraine [pulsatile pain unilaterally in your head]?”), 22.6% reported a dry eye diagnosis (positive answer to “Have you ever been diagnosed with dry eye by an ophthalmologist?”), and 37.1% reported dry eye symptoms (positive answer to “Do your eyes tend to be dry, with a foreign body sensation including itching and burning or sandy feeling lately?”).²⁹ Furthermore, the frequency of dry eye diagnosis was found to be higher in those with migraine. Of those with migraine, 14.4% reported a dry eye diagnosis compared to 8.2% without migraine, $p < 0.0001$. Similarly, of those with migraine, 22% reported dry eye symptoms compared to 15.1% without migraine, $p < 0.0001$.²⁹ While limitations of this study included the use of data assessed via questionnaires, other studies have reported similar results. In a hospital-based case-control study of 72,969 individuals from University of North Carolina-affiliated hospitals, individuals with migraine and dry eye were identified using International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) codes. The prevalence of a migraine or dry eye diagnosis was 7.3% and 13.2%, respectively. Again, individuals with migraine had a higher frequency of a co-morbid dry eye

diagnosis. Of those with migraine, 19.6% had a dry eye diagnosis compared to 12.7% without migraine.³⁰

Looking at the data as odds ratios (OR), in the population-based questionnaire study of 14,329 Korean individuals, after adjusting for confounders, the presence of migraine was found to increase the odds of a dry eye diagnosis 1.58 fold (95% confidence interval (CI) 1.34–1.86) and the odds of dry eye symptoms 1.3 fold (95% CI, 1.15–1.50).²⁹ In the study of 72,969 individuals from North Carolina, the presence of migraine increased the odds of a dry eye diagnosis 1.42 fold (95% CI, 1.20–1.68). The association was strongest among women ≥ 65 years old (OR, 2.47; 95% CI, 1.75–3.47).³⁰

Other studies have investigated the reverse relationship, that is the odds of migraine in individuals with dry eye. In a large Taiwanese study using ICD-9 codes ($n=48,028$), the presence of a dry eye diagnosis increased the odds of a migraine diagnosis 1.76 fold (95% CI, 1.57–1.98), after adjusting for co-morbidities.³¹ While these studies suggest a reciprocal relationship between dry eye and migraine, they are limited by their retrospective or cross-sectional nature and reliance on ICD coding and questionnaires for migraine and dry eye diagnosis. This is especially relevant as dry eye is a heterogeneous disease and it is unclear which combination of symptoms and/or signs led to the coded diagnosis. Overall, these studies suggest that dry eye and migraine are common conditions and that individuals with migraine are more likely to have dry eye symptoms and carry a dry eye diagnosis compared to those without. However, a limitation of the studies is that they did not look at dry eye signs and as such, it is difficult to understand what component of dry eye is most closely related to migraine.

Dry Eye Characteristics Among Individuals with Migraine

To further explore relationships between dry eye and migraine, several smaller studies investigated associations between migraine and dry eye symptoms and signs. In a cross-sectional study of South Florida veterans seen in a dry eye clinic, 31 individuals with migraine (defined via the American Migraine Study/American Migraine Prevalence and Prevention (AMS/AMPP) migraine diagnostic module)³² were compared to 219 individuals without migraine. Migraineurs had significantly higher dry eye symptom scores (via OSDI) but similar tear metrics (TBUT, corneal staining, tear production) compared to controls.³³ Interestingly, NSPI-Eye scores, assessing for

neuropathic features of eye pain, were also higher among individuals with migraine compared to controls. These data suggest dry eye symptoms, but not dry eye signs, are related to migraine. This conclusion is supported by other studies, as well. One observational study of Turkish individuals seen in a dry eye clinic compared 33 individuals with migraine to 33 controls. Migraine was diagnosed by different neurologists. Dry eye symptoms were assessed using OSDI and dry eye signs using TBUT, corneal staining, and Schirmer test. Migraineurs had significantly higher dry eye symptoms, lower TBUT, and Schirmer scores, and higher corneal staining compared to controls.³⁴ However, Schirmer scores were within normal limits in both groups (mean >10 mm/5 min) and thus the clinical relevance of the differences in values is unclear. Similar findings were reported in another study of 46 Turkish patients with migraine and 50 controls that were assessed for Sjogren's Syndrome, dry eye symptoms (via OSDI), and dry eye signs (TBUT, Schirmer) in a rheumatology clinic.³⁵ Migraine was diagnosed by the referring neurologist. In this study, individuals with migraine had significantly higher dry eye symptoms and lower TBUT and Schirmer scores compared to controls, however again, Schirmer results were still within normal limits (mean >10 mm/5 min). Another case-control study performed in a United States ophthalmology clinic assessed dry eye symptoms and signs and corneal nerve parameters in 19 individuals with chronic migraine. This study used 30 controls from a normative dataset for corneal nerve comparisons, but no control data were included for dry eye parameters. Chronic migraine was defined by the International Headache Society guidelines. Dry eye symptoms via measured DEQ-5 were abnormal in all subjects (DEQ-5 >6), but tear parameters were within normal limits among all individuals with chronic migraine (data not reported).³⁶ Interestingly, corneal nerve fiber density was significantly lower in individuals with migraine compared to controls (48 ± 23 vs 71 ± 15 fibers/mm²). However, given the lack of standard nomograms for corneal nerve fiber density, the interpretation of this finding is uncertain. Together, these studies point to dry eye symptoms being more closely related to migraine than dry eye signs.

Migraine Characteristics Among Individuals with Dry Eye

As above, while some studies evaluated dry eye characteristics in individuals with migraine, other studies evaluated

whether specific migraine characteristics were more closely associated with dry eye. A Turkish study that evaluated 58 individuals with migraine reported that the odds of having dry eye (defined if 2 of 3 criteria met: OSDI >33, TBUT <10 seconds or Schirmer <10 mm/5 min) were 5.03 times higher in those with migraine and aura compared to those without aura (95% CI, 1.42–17.83).³⁷ These data suggest that migraine with aura is more closely associated with aspects of dry eye than migraine without aura.

In addition to aura, the lifetime duration of migraine has also been explored in its relationship to dry eye. In the above Turkish study, individuals with a dry eye diagnosis had a longer median lifetime duration of migraine compared to those without a diagnosis (10 vs 6 years, $p=0.01$).³⁷ Similarly, another Turkish study of 46 individuals with migraine (diagnosed by a neurologist) found that migraine lifetime duration correlated with both dry eye symptom severity (OSDI score) ($r=0.3$, $p=0.01$), tear stability (TBUT: $r=-0.23$, $p=0.05$), and tear production (Schirmer: $r=-0.28$, $p=0.01$). Of note, the negative correlations imply that longer duration of migraine associated with faster break-up time and lower tear production.³⁵ Taken together, these studies suggest that migraine with aura and longer disease duration are associated with aspects of dry eye. However, it is important to note that definitions of dry eye were not uniform among studies, and migraine criteria were not always clearly outlined.

Photophobia is a Feature of Both Dry Eye and Migraine

Thus far, we have discussed associations between dry eye and migraine. However, the diseases also share a common feature, that is, the presence of photophobia. Although photophobia is variably defined in the literature, in this review, photophobia refers to light-induced neurological symptoms, which usually emerge in the form of (i) increased sensitivity to light or glare, (ii) intensification of headache and (iii) ocular pain or discomfort.³⁸ With regards to dry eye, our group reported that 75% of 236 veterans with dry eye symptoms (DEQ-5 score ≥ 6) reported pain sensitivity to light (defined as score ≥ 1 on a 0–10 numerical rating scale (NRS)).³⁹ In another study, we found that of 102 South Florida veterans, individuals with persistent dry eye symptoms (DEQ-5 score ≥ 6 over a 2-year period) were more likely to report photophobia compared to those without persistent symptoms (OR, 15.6; 95% CI, 2.0 to 123, $p=0.009$).⁴⁰

Our data suggest that photophobia is a common feature in individuals with dry eye symptoms, and in fact, presence and severity of photophobia is the first question on the OSDI.

Photophobia is also a common feature in migraine. In a cross-sectional survey of 6045 respondents in the Migraine in America: Symptoms and Treatment Study, 49.1% reported photophobia as the ‘most bothersome symptom’.⁴¹ In a retrospective cross-sectional study of 117 individuals with chronic migraine (≥ 15 headache days/month), 80% rated their photophobia (via 0–10 NRS) as severe (a score of $\geq 7/10$; mean 7.91 ± 2.05).⁴² Together, the data demonstrate that photophobia is a feature of both dry eye and migraine. The presence of photophobia in both diseases has implications for shared pathophysiology and treatments as discussed later in the review.

Neural Pathways Mediating Photophobia

Studies have explored the neural circuitry underlying photophobia, both in the context of dry eye⁴³ and migraine.⁴⁴ One pathway involves light-evoked signals in rod and cone cells that are transmitted to retinal ganglion cells (RGC) via amacrine and bipolar cells. Some signals in RGCs are transmitted to the olivary pretectal nucleus (OPN), then to the superior salivatory nucleus, and subsequently to the sphenopalatine ganglion, which stimulates parasympathetic-mediated vasodilation of ocular⁴⁵ and dural³⁸ vessels that are innervated by trigeminal afferents. Trigeminal signals subsequently travel to the trigeminal nucleus caudalis, posterior thalamus, and cortical structures (Figure 1).³⁸ Evidence for this pathway comes from immunocytochemistry experiments in rats that demonstrated light-evoked neuronal activity in the trigeminal brainstem, which was reduced after intravitreal injection of norepinephrine. These data suggest that constriction of ocular blood vessels by norepinephrine plays a role in light-evoked neuronal activity, thus implicating ocular vasculature in the trigeminal brainstem pathway of photophobia.⁴⁵ A mouse study similarly found a trend for reduced blue-light aversion behavior (measured by amount of time mice spent in the illuminated portion of a box) after intravitreal injection of norepinephrine, but the reduction did not reach statistical significance.⁴⁶

A second neural pathway involves light-sensitive neurons in the posterior thalamus, specifically the lateral

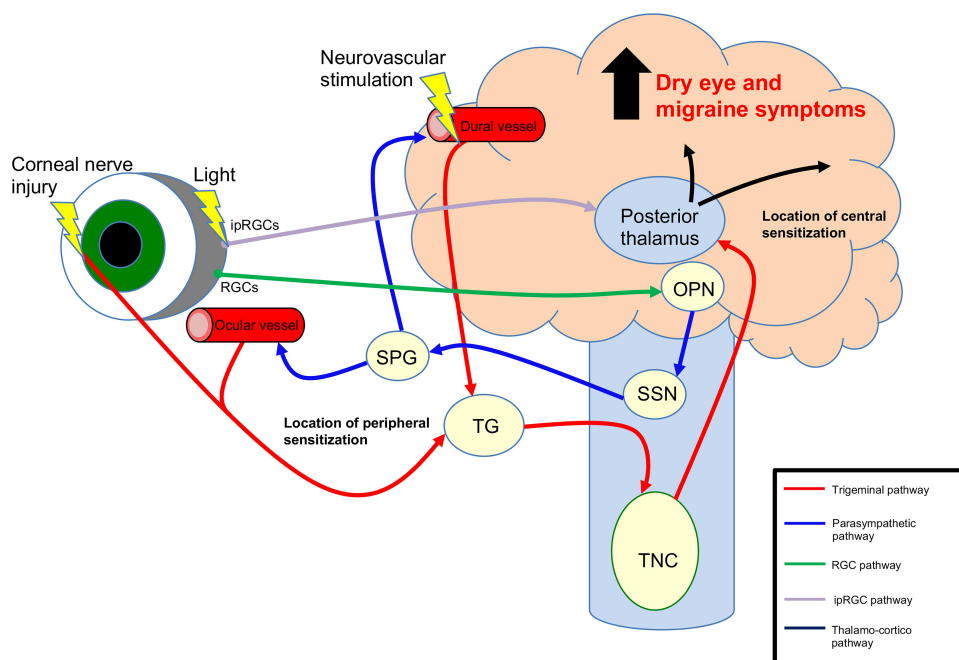


Figure 1 Selected photophobia neural pathways in dry eye and migraine. Light evokes signals from rod and cone cells that are transmitted via amacrine and bipolar cells (not shown) to retinal ganglion cells (RGC), which project to the olivary pretectal nucleus (OPN, green line). Blue line: parasympathetic signals travel from the OPN to the superior salivatory nucleus (SSN), then to the sphenopalatine ganglion (SPG), and ocular and dural vessels to mediate vasodilation. Red line: afferent trigeminal signals from cornea (stimulated by corneal disruptions), ocular vessels, and dural vessels (stimulated by vasodilation) travel to the trigeminal ganglion (TG) then to the trigeminal nucleus caudalis (TNC) and finally the posterior thalamus. Alternatively, light-evoked signals from intrinsically photosensitive RGCs (ipRGC) travel directly to the posterior thalamus (purple line). Black line: signals from the posterior thalamus travel to somatosensory and visual cortices to mediate dry eye and migraine symptoms. Note other pathways of photophobia that involve the hypothalamus and retinal rod and cone cells are not depicted.

posterior (LP) and posterior nuclei (PO),³⁸ which receives input from both intrinsically photosensitive RGCs (ipRGC) and dural trigeminal afferents, and subsequently send signals to somatosensory and visual cortices (Figure 1).^{38,47} Evidence for this pathway comes from a rat study using electrophysiologic and histopathologic techniques which demonstrated that cell bodies and dendrites of dura- and light-sensitive neurons in the posterior thalamus were in close apposition to axons originating from ipRGCs.⁴⁸ Other studies have further connected the posterior thalamic nuclei to photophobia. A mouse model found that stimulation of posterior thalamic nuclei (LP and PO nuclei) by optogenetics or injection of calcitonin gene-related peptide (CGRP)⁴⁹ triggered light aversive behavior.⁵⁰ Beyond these two pathways, other postulated, but less well studied pathways in photophobia involve the hypothalamus, retinal rod and cone cells, and the iris.^{47,51,52}

Dry Eye and Migraine Share Underlying Pathophysiology

The clinical overlap between dry eye symptoms and migraine, including the presence of photophobia, suggests pathophysiological links between them. One unifying theory is that dry

eye symptoms and migraine involve abnormal peripheral trigeminal nerve activation with subsequent peripheral and central sensitization. Peripheral sensitization is defined as “increased responsiveness and reduced threshold of nociceptive neurons in the periphery to the stimulation of their receptive fields”⁵³ and below we focus on corneal peripheral nerve abnormalities that have been described in dry eye and migraine. Central sensitization is defined as “increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input”⁵³ and below we focus on changes in secondary and tertiary nerves that connect corneal afferents to higher cortical areas.

Tests Used to Evaluate Nerve Abnormalities in Dry Eye and Migraine in Animal Models and Humans

In animals, peripheral nerve function is often evaluated via electrophysiological recordings of polymodal (~70%), mechano- (10–15%), and cold thermoreceptors (10–15%) within corneal nerves or via recordings in ciliary nerves.^{54–56} Polymodal nociceptors respond to mechanical force, heat, chemical irritants and inflammatory mediators,⁵⁷ mechanoreceptors to mechanical forces, and cold thermoreceptors to

temperature drop and changes in tear osmolarity.⁵⁸ Electrophysical recordings are also used to evaluate central nerve function along trigeminal pathways, such as in the trigeminal nucleus caudalis.⁵⁹ Corneal sensitivity is also tested in animals with von Frey filaments, where increasing force is used to contact the central cornea until a blink-response is elicited.⁵⁵

In humans, electrophysiological recordings of corneal and central nerves are not feasible. As such, clinicians have developed several tests that evaluate corneal nerve pathway function. In the clinic, corneal sensitivity is typically qualitatively checked with a cotton tip or dental floss (rated as 0=absent, 1=reduced, 2=normal, 3, increased). In the research arena, corneal sensitivity can be quantitatively assessed using a Cochet-Bonnet esthesiometer where a nylon monofilament 6 cm in length is used to contact the ocular surface and then retracted in 0.5-cm increments until corneal sensation is felt. For this test, a higher result corresponds to a higher corneal sensitivity.⁶⁰ Alternatively, a Belmonte esthesiometer utilizes a non-contact air jet to provide the stimulus, which can either be mechanical (variable airflow), thermal (hot or cold pulses), or chemical (varying CO₂ concentrations). In contrast to Cochet-Bonnet, lower values with the Belmonte esthesiometer correspond to increasing sensitivity. The presence of hypo- or hyper-sensitivity suggests abnormalities in the corneal nerve pathway, although it is not possible to determine if the abnormality is in peripheral and/or central nerves. Overall, a wide range of corneal sensitivity values has been found in individuals with and without dry eye.⁶¹ One study of 403 individuals with dry eye symptoms (DEQ5 ≥ 6) found a mean corneal mechanical detection threshold (using Belmonte esthesiometer) of 87 ± 46 mL/min, with a 10th percentile of 40 mL/min and a 90th percentile of 145 mL/min. Twenty-four percent of individuals had values that fell at or outside this range, 13% (n=51) were hypersensitivity (≤ 40 mL/min) and 11% (n=46) hyposensitive (≥ 145 mL/min).⁶¹

Peripheral nerve structure can be assessed using *in vivo* confocal microscopy (IVCM). IVCM images can be used to examine corneal subbasal nerves for density, branching, beading, tortuosity, and abrupt termination with swelling (termed microneuroma).⁶² IVCM, however, has limitations in that it lacks built-in software to analyze nerve parameters, there are no normative databases with which to compare values across populations, it provides a small field of view, and it is difficult to scan the exact same location over time.⁶³

In humans, certain symptom profiles suggest central abnormalities including the presence of allodynia (pain due to a stimulus that does not normally provoke pain,⁵³ such as with light), hyperalgesia (increased pain from a stimulus that normally provokes pain,⁵³ such as with wind) and expansion of the receptive fields (such as pain to light touch of the periocular skin).^{43,64} The proparacaine challenge is another clinical test used to detect central abnormalities. Individuals are first asked to rate their ocular pain intensity (typically on a 0–10 scale) immediately prior to placement of topical anesthetic. After one drop is instilled in each eye and 30 seconds to 2 minutes have passed (different investigators use different time periods), ocular pain is reassessed. Elimination of pain suggests nociceptive or peripheral contributors to pain while persistence of pain suggests central or non-ocular contributors. A limitation of this test is that it is not informative if no pain is present at the start of testing. In the research arena, brain functional studies⁶⁵ and quantitative sensory testing have been used to identify central abnormalities in trigeminal pathways.⁶⁶

Abnormalities in Peripheral Nerves Have Been Detected in Dry Eye and Migraine

The literature suggests that both dry eye symptoms and migraine pain are driven in part by peripheral sensitization.^{67,68} In dry eye, peripheral injury and activation may result from a number of sources including chronic epithelial disruptions, high tear osmolarity, ocular surface inflammation, and/or surgically induced nerve injury (eg refractive surgery).⁶⁷ On the other hand, initiators of peripheral nerve injury in migraine remain controversial.⁶⁹

Electrophysiology studies have detected corneal nerve abnormalities in dry eye. In a guinea-pig model of aqueous tear deficiency using lacrimal gland excision, changes in peripheral nerve function were detected in mechanoreceptor spontaneous activity at 1 week post-surgery (0.30 ± 0.22 vs 0.02 ± 0.02 impulses/second, $p < 0.05$) and cold-thermoreceptor spontaneous activity at 4 weeks post-surgery (13.22 ± 1.00 vs 10.27 ± 0.78 impulses/second, $p < 0.05$) compared to sham controls. Furthermore, a change in cold-thermoreceptor thresholds was observed 4 weeks post-surgery (32.42 ± 0.14 vs 29.87 ± 0.35 °C, respectively, $p < 0.05$) compared to controls, indicating increased sensitivity to cooling.⁵⁶ In a mouse model, lacrimal gland excision resulted in an

increase in spontaneous ciliary nerve activity compared to sham controls (86.8 ± 7.6 vs 43.4 ± 4.9 impulses/sec, $p < 0.001$). Concomitantly, corneal mechanical thresholds decreased (implying increased sensitivity) compared to sham controls (0.012 ± 0.001 vs 0.028 ± 0.002 g, $p < 0.0001$).⁷⁰ Together, the studies demonstrate that the initiation of aqueous tear deficiency causes a change in corneal nerve function, manifesting as hypersensitivity. Unfortunately, corneal nerve electrophysiology studies in migraine animal models are lacking.

Alterations in corneal nerves structure and function have also been reported in various dry eye populations compared to controls. Overall, most studies have reported decreased corneal nerve density and sensitivity in individuals with aqueous tear deficiency and Sjögren's syndrome but not in individuals with evaporative dry eye.⁶² For example, an Italian study examined corneal nerves in 39 individuals with symptomatic aqueous tear deficiency (low TBUT, corneal staining, low Schirmer) compared to 30 controls. They found significantly lower corneal nerve fiber density and length, but higher width in the dry eye vs control group (respectively, 20.5 ± 8.7 vs 25 ± 6.7 n/mm², $p = 0.008$; 12.6 ± 4.4 vs 14.5 ± 2.9 mm/mm², $p = 0.02$; 0.021 ± 0.001 vs 0.019 ± 0.001 mm/mm², $p < 0.001$).⁷¹ For corneal sensitivity, an American study of 33 individuals with symptomatic aqueous tear deficiency (OSDI >20, TBUT ≤ 7 seconds, tear meniscus height <220 μ m) found decreased sensitivity (measured via Cochet-Bonnet) compared to 10 healthy controls (3.6 ± 1.6 vs 5.5 ± 0.83 cm, $p < 0.05$). Similar to density, individuals with other dry eye sub-types (Meibomian gland dysfunction and conjunctivochalasis) did not have differences in corneal sensitivity compared to controls.⁷² Together, the above studies suggest that individuals with aqueous tear deficiency have lower nerve densities and sensitivity than controls, but that these differences are not as robust in other dry eye sub-types.

Corneal nerve alternations have also been documented in migraine. A Chinese study examined corneal nerves in 10 individuals with episodic migraine and 10 controls. Corneal nerve branching and tortuosity were significantly increased in individuals with migraine compared to controls (91 ± 13.8 vs 75 ± 14.2 branches/mm², $p = 0.03$ and 2.3 ± 4.6 vs 1.6 ± 0.5 , $p = 0.01$, respectively).⁷³ Photophobia has also been linked to peripheral corneal nerve abnormalities. In a prospective Indian study, individuals with chronic migraine and photophobia ($n = 36$) had significantly lower subbasal nerve parameters, including

corneal nerve fiber length (14.8 ± 4.0 vs 18.1 ± 3.3 mm/mm², $p = 0.007$), compared to those with migraine but no photophobia ($n = 24$).⁷⁴

Individuals with migraine have also been found to have increased corneal sensitivity compared to controls. One Turkish study compared 58 individuals with chronic migraine to 30 controls. Corneal sensitivity (measured by Cochet-Bonnet) in the nasal region was higher (increased sensitivity) in the migraine vs control group [median (IQR); 5.5 (5.25 – 6.0) vs 5.37 (5.0 – 5.75) cm, $p = 0.02$]. Interestingly, in individuals with unilateral migraine, corneal sensitivity was higher in the affected vs unaffected side (median (IQR); 5.4 (5.0 – 5.7) vs 5.3 (5.0 – 5.65), $p = 0.049$).⁷⁵ The data on sensitivity, however, are limited in that the Cochet-Bonnet can only measure sensitivity up to 6 cm and most healthy individuals can detect the filament when fully extended. No studies have evaluated corneal sensitivity in migraine with Belmonte esthesiometry which has a wider testing range. Overall, while not as robust as for dry eye, studies demonstrate that individuals with migraine have changes in their corneal nerve structure and function compared to controls.

Abnormalities in Central Nerves Have Been Detected in Dry Eye and Migraine

The literature suggests that both dry eye symptoms and migraine pain are driven in part by central sensitization. Given that corneal nerve fibers project to the trigeminal brainstem region, studies have used this region to investigate central nerve changes in dry eye.⁷⁰ In a lacrimal gland excision mouse model, an increase in spontaneous firing rate of trigeminal subnucleus interpolaris/caudalis (Vi/Vc) neurons was noted compared to sham controls (6.4 ± 1.9 vs 2.9 ± 1.4 Hz, $p < 0.05$). Additionally, periocular cutaneous receptive field areas of Vi/Vc and Vc/C1 units were significantly enlarged compared to sham controls.⁵⁹ These data suggest that aqueous tear deficiency can lead to central nerve abnormalities.

As with dry eye, central nerve abnormalities have been demonstrated in migraine. In a rat model of migraine using dural stimulation with an “inflammatory soup” (i.e histamine, serotonin, bradykinin), electrophysiologic recordings from trigeminovascular neurons in the posterior thalamus showed an increased firing rate and increased magnitude of responses to pressure, pinch, cephalic and extracephalic brush after dural stimulation compared to baseline. In contrast, control animals (dura stimulated

with fluid) showed no change in responsiveness after stimulation compared to baseline.⁷⁶

Central abnormalities have also been noted in humans with dry eye and migraine. With regards to dry eye, a cross-sectional study of 224 South Florida veterans with dry eye symptoms (DEQ-5 ≥ 6) found that 18 (41%) had persistent ocular pain (0–10 NRS) after topical anesthesia placement. Individuals with persistent ocular pain also had worse dry eye symptoms (DEQ-5, 14.6 ± 3.7 vs 12.7 ± 3.3 , $p=0.001$) and photophobia intensity (5.6 ± 3.1 vs 3.2 ± 3.2 , $p<0.0005$, 0–10 NRS scale) compared to individuals without pain after topical anesthesia.⁷⁷ These data highlight multiple clinical features suggestive of central abnormalities in individuals with dry eye symptoms. However, brain imaging studies would provide stronger evidence of central nerve abnormalities. While lacking for aqueous tear deficiency, a case report of functional magnetic resonance imaging (fMRI) in an individual with contact lens overuse (one contributor to dry eye)⁷⁸ and photophobia reported activation at the level of the trigeminal ganglion, trigeminal nucleus caudalis, and thalamus when presented with 6-second blocks of light.⁶⁵ The strength of this report is that it links corneal epithelial cell disruption to photophobia to activation of central trigeminal pathways. However, more imaging studies in a variety of dry eye sub-types are needed to supplement these findings. Quantitative sensory testing has also been applied to the study of dry eye, with higher dry eye symptoms associated with enhanced temporal summation and the presence of after-sensations, both of which suggest central contributions to symptoms.⁶⁶

Similar to dry eye, central abnormalities have been found in individuals with migraine pain.⁷⁹ In a Chinese study of 16 individuals with chronic migraine, 18 with episodic migraine, and 18 controls, individuals with chronic migraine demonstrated increased resting-state functional connectivity between bilateral amygdala and several brain regions compared to those with episodic migraine on fMRI. Compared to controls, those with chronic migraine had decreased functional connectivity between the right amygdala and several brain regions, whereas those with episodic migraine had increased functional connectivity in the left amygdala.⁸⁰ In a Korean study, 19 individuals with chronic migraine had increased resting-state functional connectivity between pain processing areas and the dorsal raphe nucleus compared to 45 individuals with episodic migraine on fMRI.⁸¹ Together, these studies demonstrate central abnormalities in animal

models and humans with migraine, with greater abnormalities noted in individuals with chronic vs episodic migraine.

Inflammation is an important contributor to peripheral and central nerve abnormalities in dry eye and migraine.

Inflammatory mediators likely contribute to the development of peripheral and central sensitization in individuals with dry eye and migraine. For example, CGRP, a neuropeptide involved in neurogenic inflammation, as well as cardiovascular, gastrointestinal and endocrine processes,⁴³ has been associated with changes in nerve function in dry eye and migraine. In a rat model of corneal abrasion using heptanol, CGRP increased in peripheral corneal nerves at one week (measurement at 24 hours was limited by the abrasion) and in the trigeminal ganglion at 24 hours compared to controls. Concomitantly, rats displayed corneal hyperalgesia (increased eye wipes after corneal application of menthol) at 24 hours compared to controls. Both CGRP levels and hyperalgesia decreased to baseline at 1 week. These results suggest an association between CGRP and peripheral nerve function.⁸²

Inflammatory mediators have also been found to increase in the central nervous system in dry eye. In a mouse model of lacrimal gland excision, increased mRNA levels of pro-inflammatory markers were noted in the trigeminal ganglion and brainstem compared to sham controls 21 days post-surgery. Similar to the rat model, these mice also exhibited corneal hypersensitivity after injury. Additionally, increased spontaneous electrical activity in their ciliary nerve was noted compared to controls. Centrally, increased synaptic plasticity in the trigeminal brainstem complex (measured using immunofluorescence of presynaptic zone components) was observed at 21 days.⁷⁰ This study demonstrates an association between aqueous tear deficiency, inflammation in central trigeminal pathways, and peripheral and central nerve abnormalities.

Human studies also support the link between inflammation and corneal nerve abnormalities. A Turkish study of 37 individuals with dry eye symptoms and signs (TBUT <7 seconds, corneal staining, Schirmer <10 mm) measured corneal sensitivity (via Cochet-Bonnet) before and after topical cyclosporine 0.05% (an anti-inflammatory agent). Corneal sensitivity increased post vs pre cyclosporine therapy (58.8 ± 2.1 vs 52.1 ± 5.5 mm, $p<0.001$).⁸³ These data suggest that inflammation impacts corneal nerve sensitivity in dry eye.

Inflammation, specifically CGRP, has also been linked to nerve abnormalities in migraine.⁴⁹ For example, a rat model

of migraine (recurrent administration of nitroglycerin) found that CGRP-immunoreactive fibers significantly increased in the trigeminal nucleus caudalis compared to controls. This was clinically accompanied by thermal hyperalgesia (withdrawal latency after infrared radiation on hind paw). Furthermore, hyperalgesia was ameliorated by knocking down CGRP with short hairpin RNA.⁸⁴ In a rat model of migraine (glass micropipette inserted into the visual cortex), a propagating wave of depolarization was induced with a resultant increase in the firing rate of spinal trigeminal nucleus neurons.⁸⁵ The increased firing rate was blocked when rats were pretreated with a CGRP-blocking antibody.⁸⁶ These data demonstrate that CGRP impacts nerve sensitivity in migraine.

CGRP has also been linked to migraine in humans. In a placebo-controlled, cross-over study of 13 individuals with migraine, intravenous CGRP induced migraine-like attacks in 10 individuals compared to 0 after placebo (isotonic saline), $p=0.002$. Median peak headache intensity score (NRS scale 0 to 10) was 5 (5–9) after CGRP compared to 2 (0–4) after placebo ($p=0.004$).⁸⁷ The effectiveness of anti-CGRP antibodies in treating migraine provides further support for the role of CGRP in migraine pathophysiology.⁸⁸ Together, the above studies support the interaction between CGRP and nerve function in migraine.

CGRP is Also Related to Light Sensitivity, Independent of Dry Eye and Migraine

CGRP can induce light sensitivity. In wild-type mice, peripheral (intraperitoneal) and central (intracerebroventricular) injection of CGRP induced light-aversive behavior (time spent in illuminated portion of a light/dark box). Furthermore, an anti-CGRP monoclonal antibody attenuated light aversion after the peripheral injection of CGRP.⁸⁹ In transgenic mice that overexpressed the CGRP receptor, central, but not peripheral, CGRP administration induced light aversion. In another mouse model, peripheral injection of CGRP produced spontaneous pain (measured by a squint assay) both in complete darkness and in bright light.⁹⁰ Together, these studies support the role of CGRP in pain and photophobia via multiple mechanisms.

Light Can Trigger Corneal Inflammation and Nerve Abnormalities

In a mouse model, blue light, but not yellow light, increased corneal sensitivity (via von Frey hair test) 3 hours post vs pre exposure. Exposure to blue light also

led to observable changes on in-vivo confocal microscopy including activation of the superficial corneal epithelium (defined as the appearance of hyperreflective nuclei), increased numbers of dendritic (inflammatory) cells in the sub-basal plexus, and increased numbers of keratocytes in the stroma.^{91,92} Additionally, blue-light increased inflammation in both the trigeminal ganglia and spinal trigeminal nucleus, as measured by mRNA expression of cFOS and ATF3.⁴⁶ These data suggest that the pathophysiology of dry eye and migraine is complex with multiple potential entry points (light, aqueous tear deficiency, corneal epithelial damage, cortical disruptions) that lead to inflammation and nerve abnormalities in multiple compartments (peripheral and central).

Practical Implications for Diagnosing Dry Eye and Migraine

The overlap between dry eye and migraine has potential implications in the evaluation and treatment of individuals with these two diseases as illustrated in Figure 2. First, eye care providers should ask individuals with dry eye about comorbid headache and primary care doctors and neurologists should ask individuals with migraine about symptoms of dry eye. If present, appropriate referrals can be made.

Second, given shared pathophysiology involving nerve dysfunction, eye care providers should think about nerve status when evaluating an individual with dry eye symptoms. This includes assessing for ocular pain via standardized questionnaires (eg NRS, Neuropathic Pain Symptom Inventory-Eye [NPSI-Eye]) and evaluating nerve structure and function clinically. The presence of cutaneous allodynia can be assessed by evaluating for pain to touch around the eyes. In addition, corneal sensitivity can be qualitatively checked with a cotton tip or dental floss (generally rated as 0=absent, 1=reduced, 2=normal, 3, increased). The proparacaine test can help differentiate between nociceptive pain (“pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors”)⁵³ or peripheral neuropathic pain vs centrally mediated or non-ocular pain.⁷⁷

Corneal nerves can be imaged with IVCN and certain nerve findings have been reported to suggest the presence of peripheral neuropathic pain. Specifically, one retrospective study found that in individuals with clinical suspected neuropathic pain, nerves in the subbasal layer abruptly terminated with hyperreflective enlargements.⁹³ This finding was termed microneuroma based on similar findings in

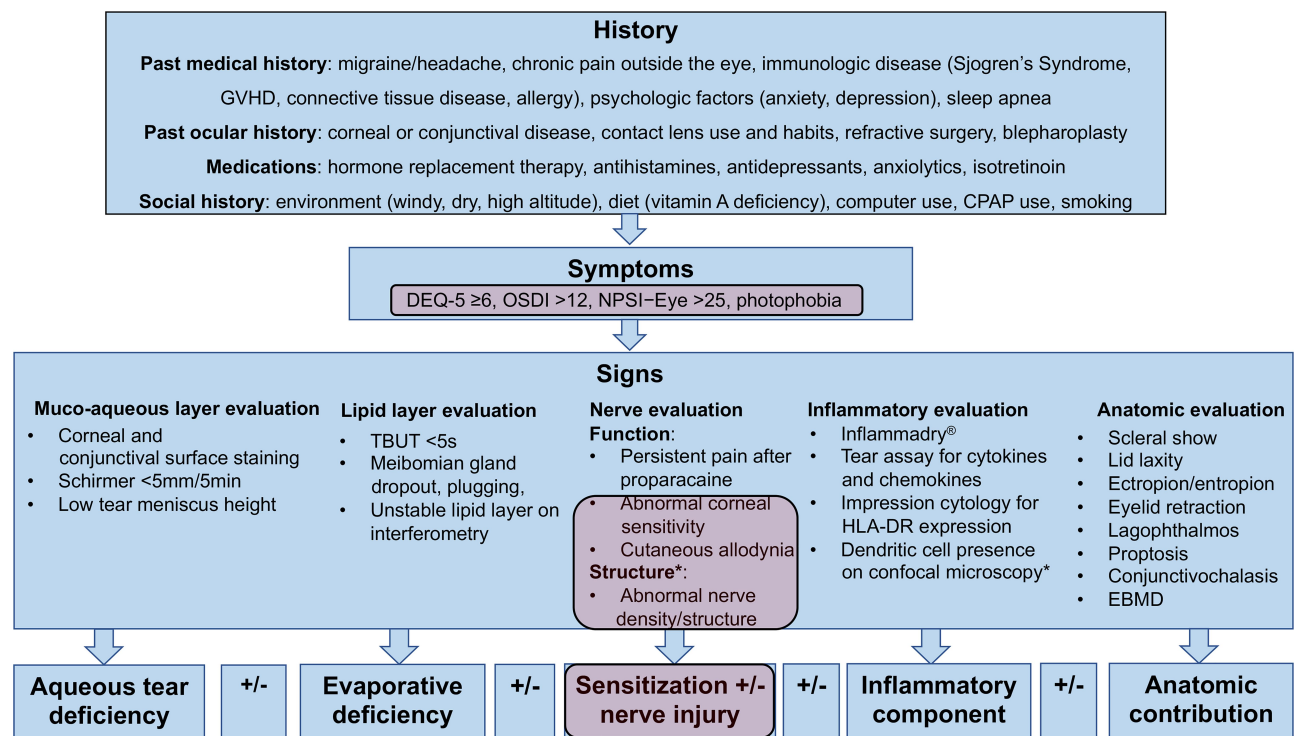


Figure 2 Clinical assessment of patients with dry eye. Purple boxes indicate phenotypes that overlap with migraine. *Nerve structure findings using in-vivo confocal microscopy.

Abbreviations: GVHD, graft versus host disease; DEQ-5, Dry Eye Questionnaire-5; OSDI, Ocular Surface Disease Index; NRS, numerical rating scale; NPSI-Eye, Neuropathic Pain Symptom Inventory-Eye; TBUT, tear break up time; EBMD, epithelial basement membrane dystrophy.

animal models.⁹⁴ Microneuromas were observed in all subjects with ocular pain (n=30), but were not present in any subjects without pain (n=30).⁹³ Other studies, however, failed to replicate these findings in other dry eye populations.⁹⁵

Understanding nerve status in an individual patient may help explain their clinical presentation as different sensitivity profiles have been described in different dry eye populations (eg hyposensitivity in aqueous tear deficiency, hypersensitivity in individual with presumed neuropathic ocular pain⁹⁶ and/or migraine).⁷⁵ This heterogeneity may explain the disconnect often seen between dry eye symptoms and signs, as nerve function drives sensation, and thus symptomatic interpretation, of dry eye signs (decreased tear volume, rapid tear evaporation). Understanding nerve status can also help tailor an individualized treatment plan.

An Updated Paradigm for the Treatment of Dry Eye Based on Data in Migraine

The current paradigm for managing dry eye is to target tear dysfunction. This new paradigm suggests that when

this approach does not sufficiently relieve dry eye symptoms, therapies targeting nerve dysfunction should be considered. Given similarities between dry eye and migraine, therapies that are of benefit in migraine may be beneficial in dry eye.

Anti-Inflammatory Therapy

Anti-inflammatory medications are a first-line treatment in dry eye and migraine.^{69,97} Specifically, in dry eye, short-term topical corticosteroids, and long-term cyclosporine and lifitegrast are first-line agents.⁶⁷ Decreasing ocular surface inflammation may improve tear composition and dry eye symptoms.⁹⁸ However, similar to migraine,⁹⁹ not all patients with dry eye respond to anti-inflammatory therapy.¹⁰⁰ Interestingly, baseline nerve status may predict who responds to anti-inflammatory therapy. In an American study, 60 individuals with dry eye (OSDI>22, corneal staining, meibomian gland dysfunction) were grouped by subbasal corneal nerve length (<16.84 (n=9) vs ≥16.84 mm/mm², n=11). Symptoms and signs in individuals with higher baseline SNFL improved 4 weeks after starting loteprednol (Symptom Assessment in Dry Eye, SANDE: 60.1 ± 17.4 vs 50.0 ± 22.7, p=0.04 and corneal

staining: 6.7 ± 3.2 vs 4.6 ± 2.9 , $p=0.01$) while those with low baseline nerve length showed no improvement.¹⁰⁰ In patients who fail anti-inflammatory therapies, other therapies need to be considered.

Oral Nerve Modulators

In individuals with features suggestive of centrally mediated pain (peri-ocular allodynia to light touch, photophobia, persistent pain after anesthesia), systemic nerve modulators should be considered. Oral nerve modulators have been effective for migraine prevention including, serotonin and norepinephrine reuptake inhibitors and tricyclic antidepressants (TCAs),²⁵ and for aborting acute migraine attacks, such as triptans.¹⁰¹ Given similar pathophysiology to migraine, patients with dry eye may also benefit from oral nerve modulators. Indeed, gabapentin and pregabalin, both $\alpha 2\gamma$ ligands, have been examined in dry eye. These agents are thought to exert their effect by reducing voltage-gated calcium channel currents in the central nervous system leading to decreased excitatory neurotransmission.¹⁰² A case series evaluated the efficacy of $\alpha 2\gamma$ ligands in 8 individuals with ocular pain unresponsive to topical therapies. Gabapentin was escalated to a dose of 600–900 mg three times daily and pregabalin to 150 mg twice in the study. Two individuals reported complete pain relief after adding a $\alpha 2\gamma$ ligand to their multi-modal regimen while 3 individuals reported significant relief.¹⁰² Interestingly, the 2 individuals with complete pain relief were also on concomitant duloxetine. This study demonstrates that $\alpha 2\gamma$ ligands may alleviate ocular pain in dry eye as part of a multi-modal regimen. However, additional studies are needed.

As with migraine, groups have studied the impact of TCAs in nerve-related ocular pain. TCAs inhibit central and peripheral serotonin and norepinephrine reuptake as well as cholinergic, histaminergic, and sodium channels.⁹⁸ In a retrospective cohort study of 30 patients who failed other therapies and had persistent pain after anesthesia, nortriptyline (at least 4 weeks of use, started at 10 mg and increased up to 100 mg based on response and tolerability) improved ocular pain in the last 24-hours (measured via NRS) from 5.7 ± 2.1 to 3.6 ± 2.1 after 10.5 ± 9.1 months ($p<0.0001$) of use. In addition, quality of life score (via an OPAS sub-score) improved from 6.0 ± 2.5 to 4.3 ± 2.4 ($p=0.019$).¹⁰³ Taken together, the above studies suggest that in individuals with dry eye symptoms and clinical features suggestive of central nerve abnormalities, oral nerve modulators may improve ocular pain symptoms.

However, in patients with either dry eye or migraine who show no or partial response to oral therapies, adjuvant approaches may be considered.

Adjuvant Approaches

Adjuvant therapies are often employed in migraine and may also be beneficial in the treatment of dry eye. For example, botulinum toxin is an approved medication in migraine¹⁰⁴ and has been explored in dry eye. Botulinum toxin is thought to target pain responses by reducing facial muscle contraction and thus decreasing trigeminal afferent signaling as well as by reducing synaptic release of CGRP.⁴² In migraine, a Cochrane meta-analysis of 26 double-blind randomized controlled trials found that botulinum toxin treatment reduced the frequency of migraine (mean difference = -2.39 migraine days/month; 95% CI, -4.02 to -0.76) and migraine severity (measured by NRS 0–10; mean difference = -3.30 ; 95% CI, -4.16 to -2.45) compared to placebo in those with episodic or chronic migraine.¹⁰⁵ In dry eye, a retrospective study of 117 South Florida veterans with chronic migraine (≥ 15 headaches or headache days/month) found that botulinum toxin A (mean units injected: 114.4 ± 24.5) improved migraine pain (mean change = -3.43 ; 95% CI, -3.95 to -2.92 ; $p<0.001$), photophobia (mean difference = -2.64 ; 95% CI, -3.18 to -2.11 ; $p<0.001$), and dry eye symptoms (mean difference = -0.716 ; 95% CI, -1.18 to -0.249 ; $p=0.003$) (all measured via NRS 0–10) compared to pre-injection scores.¹⁰⁶ This effect was found to be independent of tear volume,⁴² suggesting that mechanisms beyond tear dysfunction drive eye symptoms. In 4 individuals with dry eye symptoms without migraine, a modified botulinum toxin A protocol (35 units in 7 sites) improved photophobia and dry eye symptoms 1 month post vs pre injection.¹⁰⁷ Together, these data suggest that botulinum toxin A may improve photophobia and dry eye symptoms in individuals with and without migraine.

Another adjuvant treatment with success in migraine is device neuromodulation, and this entity has also been studied in dry eye. Specifically, transcutaneous electrical nerve stimulation (TENS) uses pulsed low voltage electrical currents across the intact surface of the skin to stimulate peripheral nerves.¹⁰⁸ TENS has been postulated to improve pain by stimulating deep sensory afferents that secondarily inhibit nociceptive input via gate control theory.¹⁰⁸ As applied to ocular pain, TENS may stimulate deep A β fibers in the V1 and V2 distribution and block nociceptive input from unmyelinated C fibers. In terms of migraine, one meta-analysis of four studies using different

TENS devices, Cefaly (company, location), LH202H Han Electrostimulator (company, location), GammaCore® (company, location), HANS-200A machine (company, location), with varying protocols (five times weekly, daily, three times daily) found that TENS significantly reduced monthly headache days (standard mean difference= -0.48; 95% CI, -0.73 to -0.23; $p<0.001$) and analgesic intake (standard mean difference= -0.78; 95% CI, -1.14 to -0.42; $p<0.001$) compared to sham TENS (TENS device was applied with far less electrical stimulation or none at all).¹⁰⁸ Similar to migraine, TENS has also shown promise in dry eye. In a retrospective study of 10 individuals with ocular pain, some of which had dry eye signs, an RS4i (RS medical, Vancouver) was used at varying intervals (range 3–21 times weekly) for a median of 6.5 months (range: 3–14 months). Overall, pain scores (one-week recall measured via NRS 0–10) decreased by 27.4% ($p=0.02$) post- vs pre-treatment.¹⁰⁹ Together, these data suggest that TENS may be incorporated as an adjunct treatment in individuals with dry eye and migraine.

Another modality less frequently used in migraine is the blockage of peripheral nerve afferents with local anesthetic.¹⁰² In migraine, a meta-analysis of 33 articles showed that blockade of the greater occipital nerve was associated with a significant decrease in the number of headache days (pooled mean difference in headache days= -3.6; 95% CI, -1.39 to -5.81) and headache severity (pooled mean difference in pain scores= -2.2; 95% CI, -1.56 to -2.84).¹¹⁰ This approach may also benefit patients with ocular pain when applied to trigeminal nerve afferents. A retrospective series of eleven individuals who failed conservative therapy for dry eye and ocular pain reported outcomes after periocular nerve block with 4 mL of 0.5% bupivacaine mixed with 1 mL of 80 mg/mL methylprednisolone acetate targeting the supraorbital, supratrochlear, infratrochlear, and infraorbital nerves. Seven of 11 individuals experienced pain relief after nerve block lasting hours to months and five individuals underwent repeat nerve blocks.¹⁰² Of note, four of the seven individuals who responded to nerve blocks had ocular surgery as the pain trigger, whereas this was the case for one of the four non-responders. The above studies suggest that nerve blocks may benefit some patients with refractory ocular pain. However, these data are limited by their observational nature and limited number of subjects.

In addition to trigeminal afferent blockade, other nerve block sites have shown promise for treatment of migraine

and dry eye, such as sphenopalatine ganglion (SPG) blocks.^{111,112} In fact, some ocular pain is thought to be mediated by parasympathetic fibers, whose presence has been documented on the cornea.¹¹³ Although biologic plausibility exists, studies are needed to evaluate the effects of SPG blocks in individuals with dry eye symptoms and ocular pain. Overall, the data presented in this section support the use of nerve blocks in appropriate individuals, especially those with surgically induced chronic ocular pain.

Conclusions

To conclude, this review discusses potential links between dry eye and migraine, prompted by an association between the two diseases in the literature. This information can be used to better understand pathophysiological mechanisms and develop targeted treatments by applying therapies successful in reducing migraine pain to dry eye. Neuronal injury leading to peripheral and central sensitization through trigeminal pathways are important mechanisms in some individuals with dry eye symptoms. Clinically, these individuals may manifest as hyperalgesia (evoked pain with wind), photophobia, and expansions of the receptive field (pain to light touch of the skin around the eye). These data highlight the need to test for nerve function in individuals with dry eye and consider the use of therapies that target nerve abnormalities in appropriate individuals.

Disclosure

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References

- McDonald M, Patel DA, Keith MS, Snedecor SJ. Economic and humanistic burden of dry eye disease in Europe, North America, and Asia: a systematic literature review. *Ocul Surf*. 2016;14(2):144–167. doi:10.1016/j.jtos.2015.11.002

2. Younger DS. Epidemiology of migraine. *Neurol Clin.* 2016;34(4):849–861. doi:10.1016/j.ncl.2016.06.011
3. Bonafede M, Sapra S, Shah N, Tepper S, Cappell K, Desai P. Direct and indirect healthcare resource utilization and costs among migraine patients in the United States. *Headache.* 2018;58(5):700–714. doi:10.1111/head.13275
4. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. *Ocul Surf.* 2017;15(3):276–283. doi:10.1016/j.jtos.2017.05.008
5. Kalangara JP, Galor A, Levitt RC, et al. Characteristics of ocular pain complaints in patients with idiopathic dry eye symptoms. *Eye Contact Lens.* 2017;43(3):192–198. doi:10.1097/ICL.0000000000000249
6. Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II epidemiology report. *Ocul Surf.* 2017;15(3):334–365.
7. Chalmers RL, Begley CG, Caffery B. Validation of the 5-Item Dry Eye Questionnaire (DEQ-5): discrimination across self-assessed severity and aqueous tear deficient dry eye diagnoses. *Cont Lens Anterior Eye.* 2010;33(2):55–60. doi:10.1016/j.clae.2009.12.010
8. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the ocular surface disease index. *Arch Ophthalmol.* 2000;118(5):615–621. doi:10.1001/archophth.118.5.615
9. Miller KL, Walt JG, Mink DR, et al. Minimal clinically important difference for the ocular surface disease index. *Arch Ophthalmol.* 2010;128(1):94–101. doi:10.1001/archophthol.2009.356
10. Qazi Y, Hurwitz S, Khan S, Jurkunas UV, Dana R, Hamrah P. Validity and reliability of a Novel Ocular Pain Assessment Survey (OPAS) in quantifying and monitoring corneal and ocular surface pain. *Ophthalmology.* 2016;123(7):1458–1468. doi:10.1016/j.ophtha.2016.03.006
11. Farhangi M, Feuer W, Galor A, et al. Modification of the Neuropathic Pain Symptom Inventory for use in eye pain (NPSI-Eye). *Pain.* 2019;160(7):1541–1550. doi:10.1097/j.pain.0000000000001552
12. Willcox MDP, Argueso P, Georgiev GA, et al. TFOS DEWS II tear film report. *Ocul Surf.* 2017;15(3):366–403.
13. Nelson JD, Craig JP, Akpek EK, et al. TFOS DEWS II Introduction. *Ocul Surf.* 2017;15(3):269–275. doi:10.1016/j.jtos.2017.05.005
14. Chhadva P, Goldhardt R, Galor A. Meibomian gland disease: the role of gland dysfunction in dry eye disease. *Ophthalmology.* 2017;124(11):S20–S26. doi:10.1016/j.ophtha.2017.05.031
15. Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II diagnostic methodology report. *Ocul Surf.* 2017;15(3):539–574.
16. Lanza NL, Valenzuela F, Perez VL, Galor A. The matrix metalloproteinase 9 point-of-care test in dry eye. *Ocul Surf.* 2016;14(2):189–195. doi:10.1016/j.jtos.2015.10.004
17. Bartlett JD, Keith MS, Sudharshan L, Snedecor SJ. Associations between signs and symptoms of dry eye disease: a systematic review. *Clin Ophthalmol (Auckland, NZ).* 2015;9:1719–1730. doi:10.2147/OPHTH.S89700
18. Ong ES, Felix ER, Levitt RC, Feuer WJ, Sarantopoulos CD, Galor A. Epidemiology of discordance between symptoms and signs of dry eye. *Br J Ophthalmol.* 2018;102(5):674–679. doi:10.1136/bjophthalmol-2017-310633
19. Pouyeh B, Viteri E, Feuer W, et al. Impact of ocular surface symptoms on quality of life in a United States veterans affairs population. *Am J Ophthalmol.* 2012;153(6):1061–1066 e1063. doi:10.1016/j.ajo.2011.11.030
20. Schiffman RM, Walt JG, Jacobsen G, Doyle JJ, Lebovics G, Sumner W. Utility assessment among patients with dry eye disease. *Ophthalmology.* 2003;110(7):1412–1419. doi:10.1016/S0161-6420(03)00462-7
21. Fernandez CA, Galor A, Arheart KL, et al. Dry eye syndrome, posttraumatic stress disorder, and depression in an older male veteran population. *Invest Ophthalmol Vis Sci.* 2013;54(5):3666–3672. doi:10.1167/iov.13-11635
22. Labbe A, Wang YX, Jie Y, Baudouin C, Jonas JB, Xu L. Dry eye disease, dry eye symptoms and depression: the Beijing Eye Study. *Br J Ophthalmol.* 2013;97(11):1399–1403. doi:10.1136/bjophthalmol-2013-303838
23. Au NH, Mather R, To A, Malvankar-Mehta MS. Sleep outcomes associated with dry eye disease: a systematic review and meta-analysis. *Can J Ophthalmol.* 2019;54(2):180–189. doi:10.1016/j.cjco.2018.03.013
24. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia.* 2018;38(1):1–211. doi:10.1177/0333102417738202
25. Burch RC, Buse DC, Lipton RB. Migraine: epidemiology, Burden, and Comorbidity. *Neurol Clin.* 2019;37(4):631–649. doi:10.1016/j.ncl.2019.06.001
26. Leonardi M, Raggi A, Bussone G, D'Amico D. Health-related quality of life, disability and severity of disease in patients with migraine attending to a specialty headache center. *Headache.* 2010;50(10):1576–1586. doi:10.1111/j.1526-4610.2010.01770.x
27. Vo P, Fang J, Bilitou A, Laflamme AK, Gupta S. Patients' perspective on the burden of migraine in Europe: a cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom. *J Headache Pain.* 2018;19. doi:10.1186/s10194-018-0907-6
28. Ozudogru S, Neufeld A, Katz BJ, et al. Reduced visual quality of life associated with migraine is most closely correlated with symptoms of dry eye. *Headache.* 2019;59(10):1714–1721. doi:10.1111/head.13662
29. Yang S, Kim W, Kim HS, Na KS. Association between migraine and dry eye disease: a nationwide population-based study. *Curr Eye Res.* 2017;42(6):837–841. doi:10.1080/02713683.2016.1262876
30. Ismail OM, Poole ZB, Bierly SL, et al. Association between dry eye disease and migraine headaches in a large population-based study. *JAMA Ophthalmol.* 2019;137(5):532–536. doi:10.1001/jamaophthalmol.2019.0170
31. Wang TJ, Wang JJ, Hu CC, Lin HC. Comorbidities of dry eye disease: a nationwide population-based study. *Acta Ophthalmol.* 2012;90(7):663–668. doi:10.1111/j.1755-3768.2010.01993.x
32. Buse DC, Manack AN, Fanning KM, et al. Chronic migraine prevalence, disability, and sociodemographic factors: results from the American migraine prevalence and prevention study. *Headache.* 2012;52(10):1456–1470. doi:10.1111/j.1526-4610.2012.02223.x
33. Farhangi M, Diel RJ, Buse DC, et al. Individuals with migraine have a different dry eye symptom profile than individuals without migraine. *Br J Ophthalmol.* 2020;104(2):260–264. doi:10.1136/bjophthalmol-2018-313471
34. Koktekir BE, Celik G, Karalezli A, Kal A. Dry eyes and migraines: is there really a correlation? *Cornea.* 2012;31(12):1414–1416. doi:10.1097/ICO.0b013e318247ec2a
35. Sarac O, Kosekahya P, Yildiz Tasci Y, et al. The prevalence of dry eye and sjogren syndrome in patients with migraine. *Ocul Immunol Inflamm.* 2017;25(3):370–375. doi:10.3109/09273948.2015.1132739
36. Kinard KI, Smith AG, Singleton JR, et al. Chronic migraine is associated with reduced corneal nerve fiber density and symptoms of dry eye. *Headache.* 2015;55(4):543–549. doi:10.1111/head.12547
37. Celikbilek A, Adam M. The relationship between dry eye and migraine. *Acta Neurol Belg.* 2015;115(3):329–333. doi:10.1007/s13760-014-0359-y
38. Nosedá R, Copenhagen D, Burstein R. Current understanding of photophobia, visual networks and headaches. *Cephalalgia.* 2018;39(13):1623–1634. doi:10.1177/0333102418784750

39. Galor A, Levitt RC, Felix ER, Sarantopoulos CD. What can photophobia tell us about dry eye? *Expert Rev Ophthalmol.* 2016;11(5):321–324. doi:10.1080/17469899.2016.1222905
40. Galor A, Zlotcavitch L, Walter SD, et al. Dry eye symptom severity and persistence are associated with symptoms of neuropathic pain. *Br J Ophthalmol.* 2015;99(5):665–668. doi:10.1136/bjophthalmol-2014-306057
41. Munjal S, Singh P, Reed ML, et al. Most bothersome symptom in persons with migraine: results from the Migraine in America Symptoms and Treatment (MAST) study. *Headache.* 2020;60(2):416–429. doi:10.1111/head.13708
42. Diel RJ, Hwang J, Kroeger ZA, et al. Photophobia and sensations of dryness in migraine patients occur independent of baseline tear volume and improve following botulinum toxin A injections. *Br J Ophthalmol.* 2019;103(8):1024–1029. doi:10.1136/bjophthalmol-2018-312649
43. Diel RJ, Mehra D, Kardon R, Buse DC, Moulton E, Galor A. Photophobia: shared pathophysiology underlying dry eye disease, migraine and traumatic brain injury leading to central neuroplasticity of the trigeminothalamic pathway. *Br J Ophthalmol.* 2020; bjophthalmol-2020-316417.
44. Brennan KC, Pietrobon D. A systems neuroscience approach to migraine. *Neuron.* 2018;97(5):1004–1021. doi:10.1016/j.neuron.2018.01.029
45. Okamoto K, Thompson R, Tashiro A, Chang Z, Bereiter DA. Bright light produces Fos-positive neurons in caudal trigeminal brainstem. *Neuroscience.* 2009;160(4):858–864. doi:10.1016/j.neuroscience.2009.03.003
46. Marek V, Reboussin E, Dégardin-Chicaud J, et al. Implication of melanopsin and trigeminal neural pathways in blue light photosensitivity in vivo. *Front Neurosci.* 2019;13:497. doi:10.3389/fnins.2019.00497
47. Burstein R, Nosedá R, Fulton AB. Neurobiology of photophobia. *J Neuroophthalmol.* 2019;39(1):94–102. doi:10.1097/WNO.0000000000000766
48. Nosedá R, Kainz V, Jakubowski M, et al. A neural mechanism for exacerbation of headache by light. *Nat Neurosci.* 2010;13(2):239–245. doi:10.1038/nn.2475
49. Wattiez A-S, Sowers LP, Russo AF. Calcitonin gene-related peptide (CGRP): role in migraine pathophysiology and therapeutic targeting. *Expert Opin Ther Targets.* 2020;24(2):91–100. doi:10.1080/14728222.2020.1724285
50. Sowers LP, Wang M, Rea BJ, et al. Stimulation of posterior thalamic nuclei induces photophobic behavior in mice. *Headache.* 2020;60(9):1961–1981. doi:10.1111/head.13917
51. Bernstein CA, Nir -R-R, Nosedá R, et al. The migraine eye: distinct rod-driven retinal pathways' response to dim light challenges the visual cortex hyperexcitability theory. *Pain.* 2019;160(3):569–578. doi:10.1097/j.pain.0000000000001434
52. Xue T, Do MTH, Riccio A, et al. Melanopsin signalling in mammalian iris and retina. *Nature.* 2011;479(7371):67–73. doi:10.1038/nature10567
53. IASP terminology; 2018. Available from: <http://www.iasp-pain.org/terminology>. Accessed February 22, 2021.
54. Belmonte C. Pain, dryness, and itch sensations in eye surface disorders are defined by a balance between inflammation and sensory nerve injury. *Cornea.* 2019;38:S11–S24. doi:10.1097/ICO.0000000000002116
55. Joubert F, Acosta M, Gallar J, et al. Effects of corneal injury on ciliary nerve fibre activity and corneal nociception in mice: a behavioural and electrophysiological study. *Eur J Pain.* 2019;23(3):589–602. doi:10.1002/ejp.1332
56. Kovács I, Luna C, Quirce S, et al. Abnormal activity of corneal cold thermoreceptors underlies the unpleasant sensations in dry eye disease. *Pain.* 2016;157(2):399–417. doi:10.1097/j.pain.0000000000000455
57. Yang AY, Chow J, Liu J. Corneal innervation and sensation: the eye and beyond. *Yale J Biol Med.* 2018;91:13–21.
58. Parra A, Madrid R, Echevarria D, et al. Ocular surface wetness is regulated by TRPM8-dependent cold thermoreceptors of the cornea. *Nat Med.* 2010;16(12):1396–1399. doi:10.1038/nm.2264
59. Rahman M, Okamoto K, Thompson R, Katagiri A, Bereiter DA. Sensitization of trigeminal brainstem pathways in a model for tear deficient dry eye. *PAIN.* 2015;156(5):942–950. doi:10.1097/j.pain.000000000000135
60. Mehra D, Cohen NK, Galor A. Ocular surface pain: a narrative review. *Ophthalmol Ther.* 2020;9(3):1–21. doi:10.1007/s40123-020-00263-9
61. Galor A, Felix ER, Feuer W, Levitt RC, Sarantopoulos CD. Corneal nerve pathway function in individuals with dry eye symptoms. *Ophthalmology.* 2020. doi:10.1016/j.ophtha.2020.07.061
62. Patel S, Hwang J, Mehra D, Galor A. Corneal nerve abnormalities in ocular and systemic diseases. *Exp Eye Res.* 2020;202:108284. doi:10.1016/j.exer.2020.108284
63. Kowtharapu BS, Winter K, Marfurt C, et al. Comparative quantitative assessment of the human corneal sub-basal nerve plexus by in vivo confocal microscopy and histological staining. *Eye.* 2017;31(3):481–490. doi:10.1038/eye.2016.220
64. Harte SE, Harris RE, Clauw DJ. The neurobiology of central sensitization. *J Appl Biobehav Res.* 2018;23(2):e12137.
65. Moulton EA, Becerra L, Borsook D. An fMRI case report of photophobia: activation of the trigeminal nociceptive pathway. *Pain.* 2009;145(3):358–363. doi:10.1016/j.pain.2009.07.018
66. Galor A, Levitt RC, McManus KT, et al. Assessment of somatosensory function in patients with idiopathic dry eye symptoms. *JAMA Ophthalmol.* 2016;134(11):1290–1298. doi:10.1001/jamaophthalmol.2016.3642
67. Galor A, Moein H-R, Lee C, et al. Neuropathic pain and dry eye. *Ocul Surf.* 2018;16:31–44. doi:10.1016/j.jtos.2017.10.001
68. Burstein R, Nosedá R, Borsook D. Migraine: multiple processes, complex pathophysiology. *J Neurosci.* 2015;35(17):6619–6629. doi:10.1523/JNEUROSCI.0373-15.2015
69. Charles A. The pathophysiology of migraine: implications for clinical management. *Lancet Neurol.* 2018;17(2):174–182. doi:10.1016/S1474-4422(17)30435-0
70. Fakh D, Zhao Z, Nicolle P, et al. Chronic dry eye induced corneal hypersensitivity, neuroinflammatory responses, and synaptic plasticity in the mouse trigeminal brainstem. *J Neuroinflammation.* 2019;16(1):268. doi:10.1186/s12974-019-1656-4
71. Giannaccare G, Pellegrini M, Sebastiani S, Moscardelli F, Versura P, Campos EC. In vivo confocal microscopy morphometric analysis of corneal subbasal nerve plexus in dry eye disease using newly developed fully automated system. *Graefes Arch Clin Exp Ophthalmol.* 2019;257(3):583–589. doi:10.1007/s00417-018-04225-7
72. Rahman EZ, Lam PK, Chu C-K, Moore Q, Pflugfelder SC. Corneal sensitivity in tear dysfunction and its correlation with clinical parameters and blink rate. *Am J Ophthalmol.* 2015;160(5):858–866.e855. doi:10.1016/j.ajo.2015.08.005
73. Shen F, Dong X, Zhou X, Yan L, Wan Q. Corneal subbasal nerve plexus changes in patients with episodic migraine: an in vivo confocal microscopy study. *J Pain Res.* 2019;12:1489–1495. doi:10.2147/JPR.S196705
74. Shetty R, Deshmukh R, Shroff R, Dedhiya C, Jayadev C. Subbasal nerve plexus changes in chronic migraine. *Cornea.* 2018;37(1):72–75. doi:10.1097/ICO.0000000000001403
75. Aykut V, Elbay A, Esen F, Kocaman G, Savran Elilob E, Oguz H. Patterns of altered corneal sensation in patients with chronic migraine. *Eye Contact Lens.* 2018;44:S400–S403. doi:10.1097/ICL.0000000000000553

76. Burstein R, Jakubowski M, Garcia-Nicas E, et al. Thalamic sensitization transforms localized pain into widespread allodynia. *Ann Neurol*. 2010;68(1):81–91. doi:10.1002/ana.21994
77. Crane AM, Feuer W, Felix ER, et al. Evidence of central sensitisation in those with dry eye symptoms and neuropathic-like ocular pain complaints: incomplete response to topical anaesthesia and generalised heightened sensitivity to evoked pain. *Br J Ophthalmol*. 2017;101(9):1238–1243. doi:10.1136/bjophthalmol-2016-309658
78. Gomes JAP, Azar DT, Baudouin C, et al. TFOS DEWS II iatrogenic report. *Ocul Surf*. 2017;15(3):511–538.
79. Filippi M, Messina R. The chronic migraine brain: what have we learned from neuroimaging? *Front Neurol*. 2020;10:1356. doi:10.3389/fneur.2019.01356
80. Chen Z, Chen X, Liu M, Dong Z, Ma L, Yu S. Altered functional connectivity of amygdala underlying the neuromechanism of migraine pathogenesis. *J Headache Pain*. 2017;18(1):7. doi:10.1186/s10194-017-0722-5
81. Lee MJ, Park B-Y, Cho S, Kim ST, Park H, Chung C-S. Increased connectivity of pain matrix in chronic migraine: a resting-state functional MRI study. *J Headache Pain*. 2019;20(1):29. doi:10.1186/s10194-019-0986-z
82. Hegarty DM, Hermes SM, Morgan MM, Aicher SA. Acute hyperalgesia and delayed dry eye after corneal abrasion injury. *Pain Rep*. 2018;3(4):e664–e664. doi:10.1097/PR9.00000000000000664
83. Tokar E, Asfuroglu E. Corneal and conjunctival sensitivity in patients with dry eye: the effect of topical cyclosporine therapy. *Cornea*. 2010;29(2):133–140. doi:10.1097/ICO.0b013e3181acf68d
84. Zhang Y, Zhang Y, Tian K, et al. Calcitonin gene-related peptide facilitates sensitization of the vestibular nucleus in a rat model of chronic migraine. *J Headache Pain*. 2020;21(1):72. doi:10.1186/s10194-020-01145-y
85. Zhang X, Levy D, Kainz V, Nosedá R, Jakubowski M, Burstein R. Activation of central trigeminovascular neurons by cortical spreading depression. *Ann Neurol*. 2011;69(5):855–865. doi:10.1002/ana.22329
86. Melo-Carrillo A, Nosedá R, Nir -R-R, et al. Selective inhibition of trigeminovascular neurons by fremanezumab: a humanized monoclonal anti-CGRP antibody. *J Neurosci*. 2017;37(30):7149–7163. doi:10.1523/JNEUROSCI.0576-17.2017
87. Christensen CE, Younis S, Deen M, Khan S, Ghanizada H, Ashina M. Migraine induction with calcitonin gene-related peptide in patients from erenumab trials. *J Headache Pain*. 2018;19(1):105. doi:10.1186/s10194-018-0927-2
88. Urits I, Jones MR, Gress K, et al. CGRP antagonists for the treatment of chronic migraines: a comprehensive review. *Curr Pain Headache Rep*. 2019;23(5):29. doi:10.1007/s11916-019-0768-y
89. Mason BN, Kaiser EA, Kuburas A, et al. Induction of migraine-like photophobic behavior in mice by both peripheral and central CGRP mechanisms. *J Neurosci*. 2017;37(1):204–216. doi:10.1523/JNEUROSCI.2967-16.2016
90. Rea BJ, Wattiez A-S, Waite JS, et al. Peripherally administered calcitonin gene-related peptide induces spontaneous pain in mice: implications for migraine. *Pain*. 2018;159(11):2306–2317. doi:10.1097/j.pain.0000000000001337
91. Aggarwal S, Kheirikhah A, Cavalcanti BM, Cruzat A, Jamali A, Hamrah P. Correlation of corneal immune cell changes with clinical severity in dry eye disease: an in vivo confocal microscopy study. *Ocul Surf*. 2020;19:183–189. doi:10.1016/j.jtos.2020.05.012
92. Matsumoto Y, Ibrahim OMA. Application of in vivo confocal microscopy in dry eye disease. *Invest Ophthalmol Vis Sci*. 2018;59(14):DES41–DES47. doi:10.1167/iovs.17-23602
93. Moein H-R, Akhlaq A, Dieckmann G, et al. Visualization of microneuromas by using in vivo confocal microscopy: an objective biomarker for the diagnosis of neuropathic corneal pain? *Ocul Surf*. 2020;18(4):651–656. doi:10.1016/j.jtos.2020.07.004
94. Stepp MA, Pal-Ghosh S, Downie LE, et al. Corneal epithelial “neuromas”: a case of mistaken identity? *Cornea*. 2020;39(7):930–934. doi:10.1097/ICO.0000000000002294
95. Dermer H, Hwang J, Mittal R, Cohen A, Galor A. Corneal sub-basal nerve plexus microneuromas in individuals with and without dry eye. *Br J Ophthalmol*. 2021;bjophthalmol-2020-317891. doi:10.1136/bjophthalmol-2020-317891
96. Spierer O, Felix ER, McClellan AL, et al. Corneal mechanical thresholds negatively associate with dry eye and ocular pain symptoms. *Invest Ophthalmol Vis Sci*. 2016;57(2):617–625. doi:10.1167/iovs.15-18133
97. Silbert JA, Bitton E, Bhagat K. Advances in diagnosis and management of dry eye disease. *Adv Ophthalmol Optom*. 2019;4:13–38. doi:10.1016/j.yaoo.2019.04.002
98. Dieckmann G, Goyal S, Hamrah P. Neuropathic corneal pain: approaches for management. *Ophthalmology*. 2017;124(11):S34–s47. doi:10.1016/j.ophtha.2017.08.004
99. Ong JJY, De Felice M. Migraine treatment: current acute medications and their potential mechanisms of action. *Neurotherapeutics*. 2018;15(2):274–290. doi:10.1007/s13311-017-0592-1
100. Kheirikhah A, Dohlman TH, Amparo F, et al. Effects of corneal nerve density on the response to treatment in dry eye disease. *Ophthalmology*. 2015;122(4):662–668. doi:10.1016/j.ophtha.2014.11.006
101. Konstantinos S, Vikelis M, Rapoport A. Acute care and treatment of migraine. *J Neuro Ophthalmol*. 2020;40(4):472–484. doi:10.1097/WNO.0000000000001053
102. Small LR, Galor A, Felix ER, Horn DB, Levitt RC, Sarantopoulos CD. Oral gabapentinoids and nerve blocks for the treatment of chronic ocular pain. *Eye Contact Lens*. 2020;46(3):174–181. doi:10.1097/ICL.0000000000000630
103. Ozmen MC, Dieckmann G, Cox SM, et al. Efficacy and tolerability of nortriptyline in the management of neuropathic corneal pain. *Ocul Surf*. 2020;18(4):814–820. doi:10.1016/j.jtos.2020.08.006
104. Janis JE, Barker JC, Palettas M. Targeted peripheral nerve-directed onabotulinumtoxin A injection for effective long-term therapy for migraine headache. *Plast Reconstr Surg Glob Open*. 2017;5(3):e1270. doi:10.1097/GOX.0000000000001270
105. Herd CP, Tomlinson CL, Rick C, et al. Cochrane systematic review and meta-analysis of botulinum toxin for the prevention of migraine. *BMJ Open*. 2019;9(7):e027953. doi:10.1136/bmjopen-2018-027953
106. Diel RJ, Kroeger ZA, Levitt RC, et al. Botulinum toxin A for the treatment of photophobia and dry eye. *Ophthalmology*. 2018;125(1):139–140. doi:10.1016/j.ophtha.2017.09.031
107. Venkateswaran N, Hwang J, Rong AJ, et al. Periorbital botulinum toxin A improves photophobia and sensations of dryness in patients without migraine: case series of four patients. *Am J Ophthalmol Case Rep*. 2020;19:100809. doi:10.1016/j.ajoc.2020.100809
108. Tao H, Wang T, Dong X, Guo Q, Xu H, Wan Q. Effectiveness of transcutaneous electrical nerve stimulation for the treatment of migraine: a meta-analysis of randomized controlled trials. *J Headache Pain*. 2018;19(1):42. doi:10.1186/s10194-018-0868-9
109. Zayan K, Aggarwal S, Felix E, Levitt R, Sarantopoulos K, Galor A. Transcutaneous electrical nerve stimulation for the long-term treatment of ocular pain. *Neuromodulation*. 2020;23(6):871–877. doi:10.1111/ner.13146
110. Shauly O, Gould DJ, Sahai-Srivastava S, Patel KM. Greater occipital nerve block for the treatment of chronic migraine headaches: a systematic review and meta-analysis. *Plast Reconstr Surg*. 2019;144(4):943–952. doi:10.1097/PRS.00000000000006059

111. Cady R, Saper J, Dexter K, Manley HR. A double-blind, placebo-controlled study of repetitive transnasal sphenopalatine ganglion blockade with tx360((R)) as acute treatment for chronic migraine. *Headache*. 2015;55(1):101–116. doi:10.1111/head.12458
112. Mehta D, Leary MC, Yacoub HA, et al. The effect of regional anesthetic sphenopalatine ganglion block on self-reported pain in patients with status migrainosus. *Headache*. 2019;59(1):69–76. doi:10.1111/head.13390
113. Chen W, Batawi HIM, Alava JR, et al. Bulbar conjunctival microvascular responses in dry eye. *Ocul Surf*. 2017;15(2):193–201. doi:10.1016/j.jtos.2016.12.002

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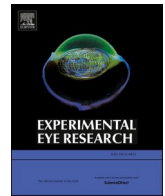
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Corneal Nerve Abnormalities in Ocular and Systemic Diseases

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ABSTRACT

The trigeminal nerve gives rise to the corneal subbasal nerve system, which plays a crucial role in sensations of touch, pain, and temperature and in ocular healing processes. Technological advancements in instruments, in particular in vivo confocal microscopy and aesthesiometry, have allowed for the structural and functional evaluation of corneal nerves in health and disease. Through application of these technologies in humans and animal models, structural and functional abnormalities have been detected in several ocular and systemic disorders, including dry eye disease (DED), glaucoma, migraine, and fibromyalgia. However, studies across a number of conditions have found that structural abnormalities do not always relate to functional abnormalities. This review will discuss instruments used to evaluate corneal nerves and summarize data on nerve abnormalities in a number of ocular and systemic conditions. Furthermore, it will discuss potential treatments that can alleviate the main manifestations of nerve dysfunction, namely ocular surface pain and persistent epithelial defects.

1. Introduction

The cornea is among the most densely innervated tissues in the body, containing a rich supply of nerve fibers. For the past several decades, studies examining the anatomy of this system have provided insight into the architecture and ultrastructure of the corneal subbasal nerve system in health and disease. A number of studies have reported corneal nerve structural and functional abnormalities in the setting of various ocular and systemic diseases. This review will summarize these data and discuss treatments that can combat symptoms and signs of corneal nerve dysfunction, namely chronic ocular surface pain and loss of epithelial integrity. (see [Table 1](#))

2. Methods of studying structure and function

2.1. Structure of corneal nerves

The cornea is the most densely innervated tissue in the body. Corneal sensory nerves originate from the ophthalmic division of the trigeminal nerve system, travel in the nasociliary nerve and its long ciliary nerve branches, and finally branching into nerve fibers that penetrate and innervate the cornea ([Yang et al., 2018](#)). The majority of our early understanding of corneal nerve morphology and ultrastructure came from

microscopic observations of stained corneas, and descriptions of corneal nerve ultrastructure using electron microscopic techniques ([Erie et al., 2009](#)). By combining finds of early light and electron microscopy studies with more recent in vivo confocal microscopy (IVCM) findings, the morphology of the human corneal subbasal nerve system has been studied in detail ([Müller et al., 1996, 2003](#)). The corneal subbasal nerve system has approximately 6–8 nerve bundles per microscopic image. With this information, the total corneal surface area of the subbasal nerve system is estimated at 90 mm² with 5400–7200 nerve bundles. Each bundle then separates into numerous side branches, each containing 3–7 individual axons, with an estimated 19,000–44,000 total axons. Each nerve fiber houses 10–20 nerve terminals, and thus it is estimated that there are 315,000–630,000 nerve terminals in the cornea, or approximately 7000 per mm ([Erie et al., 2009](#)).

Several confocal microscopes have been used to study corneal nerve anatomy, including those that use a slit principle (e.g. ConfoScan 4; Nidek), tandem-scanning microscopes with a rotating disc (e.g. Tandem Scanning; Reston), and laser-utilizing microscopes (e.g. Heidelberg Retina Tomograph (HRT); Heidelberg). Strengths of IVCM include the ability to image corneal nerves non-invasively with high resolution (dimensional resolution of 1–2 µm laterally and 5–10 µm axially and with a magnification of up to 600×) ([Jalbert et al., 2003](#)). Draw-backs include a small field of view, difficulties in scanning the peripheral

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Table 1
Selected findings of quantitative IVCN in health and disease.

Disease	Authors	Instrument	Nerve Density (disease vs. healthy)	Nerve Count (disease vs. healthy)	Tortuosity (disease vs. healthy)	Sensitivity (disease vs. healthy)
Healthy	1) Niederer RL et al. (Niederer et al., 2007) 2) Parissi M et al. (Parissi et al., 2013) 3) Golebiowski B et al. (Golebiowski et al., 2011)	1) Laser-scanning 2) Laser-scanning	1) 20,300 ± 6500 µm/mm ² (5000–35,000) 2) 19,000 ± 4500 µm/mm ² (13,400–23,400); p < 0.0001			3) Cochet-Bonnet (5.50 ± 0.80 cm) and Belmonte (64.40 ± 29.40 mL/min)
DED (Non-Sjögren, Non-GvHD)	1) Labbé et al. (Labbé et al., 2012) [ATD] 2) Choi et al. (Choi, 2015) [ATD] 3) Labbé et al. (Labbé et al., 2013) [ATD] 4) Rahman et al. (Rahman et al., 2015) [ATD] 5) Shetty et al. [Evaporative] (Shetty et al., 2016) 6) Khamar et al. [Evaporative] (Khamar et al., 2019) 7) De Paiva et al. (Sade De Paiva and Pflugfelder, 2004)	1) Laser-scanning 2) Laser-scanning 3) Laser-scanning 5) Laser-scanning 6) Laser-scanning	[↓] 1) 9426 ± 2640 vs. 15,956 ± 2431 µm/mm (Erie et al., 2009); p < 0.0001 [↓] 2) 9884 ± 2548 vs. 12,030 ± 2203 µm/mm ² , p < 0.005 [–] 5) 27.20 ± 0.60 vs. 28.60 ± 0.80 nerves/mm ² [frame of 400 × 400 µm]; p > 0.05 [–] 6) ~30 nerves/mm ² for both groups, p > 0.05	[↓] 3) 34.91 ± 8.08 vs. 45.87 ± 4.21 nerves/mm ² [frame = 400 × 400 µm], p < 0.001)	[↑] 2) 3.70 ± 0.50 vs. 1.60 ± 0.60, p < 0.001 [↑] 3) 3.01 ± 0.49 vs. 1.94 ± 0.46, p < 0.001	[↓] 1) Cochet Bonnet (5.00 ± 0.83 vs. 5.89 ± 0.22 cm, p = 0.01) [↓] 4) Cochet Bonnet (3.60 ± 1.70 vs. 5.50 ± 0.83 cm; p < 0.05) [↑] 7) Belmonte (34.60 ± 21.09 vs. 61.50 ± 20.07 mL/min, p < 0.05)
Glaucoma	1) Saini M et al. (Saini et al., 2017) 2) Gatzoufas et al. (Gatzoufas et al., 2014) 3) Ranno et al. (Ranno et al., 2011)	1) Slit-scanning 2) Laser-scanning 3) Laser-scanning	[↓] 1) 6883.94 ± 1798.03 vs. 12,273.15 ± 3516.04 µm/mm (Erie et al., 2009), p = 0.001 [↓] 2) 2108 ± 692 vs. 2642 ± 484 µm/frame (frame = 0.06 mm (Erie et al., 2009)) p = 0.003 [↓] 3) 448.9 ± 409.3 vs. 2258.4 ± 989.0 µm/frame [frame 460 × 345 µm], p < 0.001	[↓] 1) 3.58 ± 0.99 vs. 5.40 ± 1.70 nerves/frame (frame = 0.16 mm ²), p = 0.001 [↓] 2) 12.30 ± 4.20 vs. 15.40 ± 3.0 nerves/frame, p = 0.02 [↓] 3) 2.50 ± 0.70 vs. 2.90 ± 0.90 nerves/frame, p = 0.01	[↑] 2) 1.90 ± 0.40 vs. 1.70 ± 0.20, p = 0.10 [↑] 3) 2.60 ± 1.0 vs. 2.00 ± 0.80, p = 0.01	[–] 1) Cochet-Bonnet (4.68 ± 0.44 vs. 5.07 ± 0.37 cm, p = 0.08) [–] 2) Cochet-Bonnet (5.80 ± 0.20 vs. 5.80 ± 0.20 cm, p = 0.20)
NK	1) Moein H-R et al. (Moein et al., 2018) 2) Hamrah P et al. (Hamrah et al., 2010)	1) Slit-scanning 2) Laser-scanning	[↓/↓] 1) Affected 1400 ± 600 µm/mm ² vs. contralateral 6400 ± 700 µm/mm ² vs. control 14,100 ± 1600 µm/mm ² ; all P < 0.001 [↓] 2) 448.9 ± 409.3 vs. 2258.4 ± 989.0 µm/frame [frame 460 × 345 µm], p < 0.001	[↓] 2) 5.2 ± 4.5 vs. 13.1 ± 3.8 nerves/frame, p < 0.001		[↓/–] 1) Cochet Bonnet (affected 2.60 ± 0.60 cm vs. 6.00 ± 0.00, p < 0.001) vs. contralateral eyes (5.40 ± 0.20 vs. 5.20 ± 0.20, p = 0.26) [↓] 2) Cochet Bonnet (3.30 ± 1.90 vs. 6.00 ± 0 cm, p < 0.05)
Migraine	1) Kinard KI et al. (Kinard et al., 2015) 2) Shetty R et al. (Shetty et al., 2018) 3) Aykut V et al. (Aykut et al., 2018a)	1) Laser-scanning 2) Laser-scanning	[↓] 1) 48.40 ± 23.50 vs. 71.00 ± 15.00 nerves/mm ² [frame = 300 × 300 µm], p < 0.001 [–/–] 2) 24,690 ± 8120 migraine and photophobia vs. 28,640 ± 6890 migraine alone vs. 24,280 ± 6660 µm/mm ² controls, p = 0.13	[↓/–] 2) 14.76 ± 3.98 migraine and photophobia vs. 18.13 ± 3.33 migraine alone vs. 17.26 ± 4.29 mm/mm ² controls, p = 0.01		[↑] 3) Cochet Bonnet (5.40 vs. 5.30 mm, p = 0.049)
Fibromyalgia	1) Erkan Turan et al. (Erkan Turan et al., 2018) 2) Ramírez M et al. (Ramírez et al., 2015) 3) Aykut V et al. (Erkan Turan et al., 2018)	1) Laser-scanning 2) Slit-scanning	[↓] 1) 1563 ± 620 vs. 2545 ± 973 µm/frame [frame = 450 × 340 µm], p < 0.001 [↓] 2) 85 ± 29 vs. 107 ± 26 nerves/mm ² [frame = 340 × 255 µm], p = 0.02	[↓] 1) 5.00 ± 1.80 vs. 10.30 ± 2.10 nerves/frame, p < 0.001		[–] 3) Cochet Bonnet (0.4 g/mm ² in both groups, p = 1.0) [Overall ↑] 4) Cochet Bonnet (central (6.00 vs. 5.50 cm, p = 0.03), superior (5.75 vs. 5.00 cm, p = 0.005), inferior (5.389 vs. 4.603 cm, p < 0.001), temporal (5.500 vs. 5.40 cm, p = 0.28), nasal (5.44 vs. 5.37 cm, p = 0.52)

(continued on next page)

cornea, and inability to scan in the exact same area over time (Petroll and Robertson, 2015; Shaheen et al., 2014). Furthermore, trained operators are needed to operate the instruments, and there are no built-in software programs that automatically quantify corneal nerve density and structural parameters such as beading, tortuosity, and micro-neuromas. As such, studies have relied on different secondary image analyses programs (e.g. Image J, EpiView, etc.) to process images and quantify parameters of interest. Furthermore, there are no age-adjusted nomograms available for corneal nerve parameters, as there are for optical coherence tomography (OCT).

Several subbasal nerve attributes have been examined through the use of IVCM, including nerve density (nerves visible within a defined area [$\mu\text{m}/\text{mm}^2$ or mm/mm^2] or, to a lesser extent total number of nerves within a frame), nerve fiber length (which relates to density of nerves present in a frame and has been used as a proxy for nerve density in a minority of studies, measured in mm/mm^2), total nerve count (approximate number of identifiable subbasal nerve fibers per frame), and nerve tortuosity (twisting of the nerves, evaluated on a Likert grade scale or by tortuosity coefficient) among other variables (Patel and McGhee, 2009).

Unfortunately, there are several challenges when comparing subbasal nerve attributes across IVCM literature. First, the structural properties and functional capabilities of the different microscopes impact attribute readings. For example, field brightness and image contrast both impact the appearance of nerves. These features are maximized with laser- and slit-scanning IVCM, and as such they are preferred over tandem-scanning instruments for analyzing subbasal attributes. Magnification differences also impact nerve measurements, with limited magnification of tandem-scanning instruments in comparison to higher magnification with laser and slit-scanning IVCM. As such, it is not possible to compare nerve densities between studies that used different types of microscopes. Another challenge is the use of different units to express quantified findings (e.g. nerve density has been reported in $\mu\text{m}/\text{mm}$ (Erie et al., 2009), $\mu\text{m}/\text{frame}$, and $\text{nerves}/\text{mm}^2$) (Erie et al., 2009; Alhatem et al., 2012). In order to alleviate some of this burden, throughout this review, we give information on the type of IVCM used, standardize units across cited literature, and included frame dimensions or image area to aid in comparisons across studies.

Tandem-scanning instruments have a small aperture (30 μm), narrow depth of field (7–11 μm), and limited magnification, and thus have

difficulty in telling apart objects <5 μm in size. For this reason, the instrument is better suited to image the anterior stroma, but has poor resolution for sub-basal nerves. One study of 65 healthy individuals (mean age 46 ± 19 years, range 15–79) quantified central sub-basal corneal nerve density with a tandem-scanning instrument and reported a mean density of $8404 \pm 2012 \mu\text{m}/\text{mm}^2$ (range 4735–14,018 $\mu\text{m}/\text{mm}^2$) (Erie et al., 2005). Slit-scanning microscopes have wider apertures (e.g. as high as 300 μm) and a larger depth of field (10–26 μm), and this allows for improved resolution of corneal nerve density. Two studies utilizing this technology in healthy individuals ($n = 60$, age <35 or >50 years) (Patel et al., 2009) and ($n = 14$, mean age 32 years, range 19–42) Oliveira-Soto and Efron, 2001 reported a mean density of $14,731 \pm 6056 \mu\text{m}/\text{mm}^2$ and $11,110 \mu\text{m}/\text{mm}^2$ respectively, which are both higher than tandem-scanning measurements. Finally, through use of a pinhole aperture (1 μm) and ultra-small depth of field (4–7 μm), the laser-scanning microscope offers the highest-contrast and resolution for examining and quantifying corneal nerves. A study of 85 healthy individuals (mean age 38 ± 16 years, range 18–87) estimated central sub-basal corneal nerve density at $20,300 \pm 6500 \mu\text{m}/\text{mm}^2$ (range 5000–35,000 $\mu\text{m}/\text{mm}^2$) (Niederer et al., 2007). Another study of 106 healthy subjects (mean age 50, range 15–88) reported a mean subbasal nerve density of $19,000 \pm 4500 \mu\text{m}/\text{mm}^2$ (range 13,400 to 23,400 $\mu\text{m}/\text{mm}^2$) (Parissi et al., 2013). While these values are on average higher than both tandem and slit-scanning instruments, there were overlap in values between all 3 instruments, demonstrating a wide variability of measurements even in healthy individuals.

Other differences also exist between the instruments. With the Confoscan devices (Nidek), the lens (40x) directly contacts the eye through a gel interphase (such as Genteal, Novartis). With the HRT devices, a disposable plastic cap (TomoCap) is placed on top of the Rostock Cornea Module lens which then contacts the eye through a gel interphase that is placed between the plastic cap and lens and over the cap. Furthermore, the Confoscan uses a bright light source to image corneal nerves, which some individuals find uncomfortable, while the HRT does not require a bright light source due to its reliance on laser technology (Fig. 1).

While this review focuses on confocal microscopy studies, other neuroimaging devices (e.g. Computed Tomography (CT), Optical Coherence Tomography (OCT), and Magnetic Resonance Imaging (MRI)) and neuro-marker indices have also contributed to our

Table 1 (continued)

Disease	Authors	Instrument	Nerve Density (disease vs. healthy)	Nerve Count (disease vs. healthy)	Tortuosity (disease vs. healthy)	Sensitivity (disease vs. healthy)
Diabetes	4) Gallar J et al. (Aykut et al., 2018b)					
	1) Mocan MC et al. (Mocan et al., 2006)	1) Slit-scanning	[1] 1) 39.70 ± 13.20 vs. 58.50 ± 12.40 nerves/ mm^2 [frame = $450 \times 340 \mu\text{m}$], $p < 0.001$		[1] 1) 2.49 ± 0.89 vs. 1.71 ± 0.55 , $p = 0.001$	[1] 2) Belmonte (1.48 ± 0.10 vs. 0.72 ± 0.02 mbars, $p < 0.001$)
	2) Tavakoli M et al. (Tavakoli et al., 2011)	2) Slit-scanning	[1] 2) 27.02 ± 1.16 vs. 40.78 ± 2.64 nerves/ mm^2 [frame = 768×576 pixels], $p < 0.001$		[1] 2) 25.69 ± 1.05 vs. 19.77 ± 1.35 , tortuosity coefficient, $p < 0.001$	[1] 3) Cochet-Bonnet (4.77 ± 1.31 vs. 5.74 ± 0.53 cm, $p < 0.0001$)
TED	3) Saito J et al. (Saito et al., 2003)					
	1) Kocabeyoglu S et al. (Kocabeyoglu et al., 2015)	1) Laser-scanning	[1] 1) 958 ± 394 vs. $1416 \pm 744 \mu\text{m}/\text{frame}$, [frame = $200 \times 300 \mu\text{m}$], $p < 0.001$	[1/1] 2) Active vs. Inactive vs. control (3.29 ± 1.13 vs. 3.28 ± 1.21 vs. 5.04 ± 0.83 nerves/frame, $p < 0.001$)	[1] 1) 2.7 ± 0.8 vs. 1.6 ± 0.6 , grade, $p < 0.001$	[–] 2) Belmonte (5.67 ± 0.42 vs. 5.43 ± 0.82 vs. 5.85 ± 0.39 mL/min, $p = 0.12$)
	2) Villani E et al. (Villani et al., 2010)	2) Laser-scanning	[1/1] 3) Active vs. Inactive vs. control (12.30 ± 4.70 and 17.20 ± 6.20 vs. 28.40 ± 6.70 nerves/ mm^2 [frame = $400 \times 400 \mu\text{m}$], $p < 0.001$)	[1/1] 3) Active vs. Inactive vs. control (10.4 ± 3.0 and 12.3 ± 3.1 vs. 17.6 ± 3.6 mm/ mm^2 , $p < 0.001$)	[1/1] 2) Active vs. Inactive vs. control (2.49 ± 0.91 vs. 2.58 ± 0.96 vs. 1.33 ± 0.64 , grade, $p < 0.001$)	[1] 2) Belmonte (inactive TED only - 5.46 ± 0.47 vs. 5.80 ± 0.32 cm, $p = 0.022$)
	3) Wu L-Q et al. (Wu et al., 2019)					

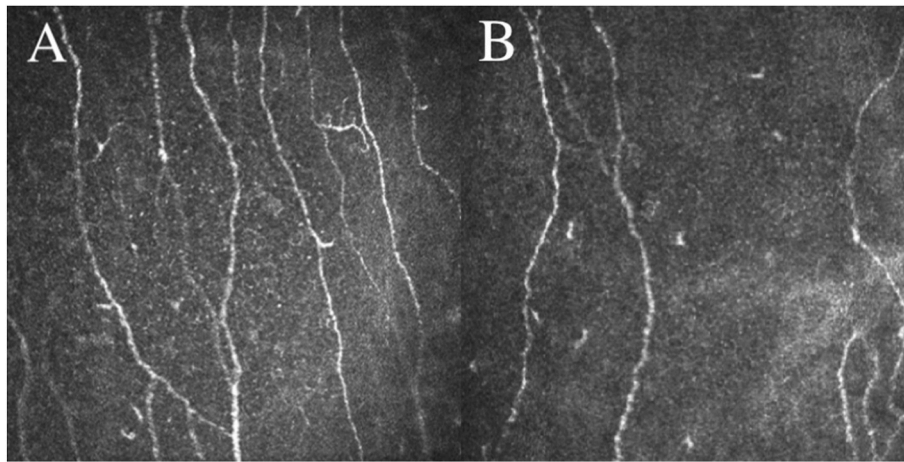


Fig. 1. In Vivo Confocal Microscopy Image of Sub-basal Nerves (Heidelberg Retina Tomograph/Cornea Rostock Module by Heidelberg Engineering, Heidelberg, Germany) depicting A) a normal nerve pattern with few dendritic cells (circled) in a healthy patient without ocular disease. B) Nerves with decreased density, increased tortuosity, and dendritic cells (circled) in a patient with dry eye disease.

understanding of ocular nerve architecture (Prasad, 2014). For example, a French study developed a full-field OCT system to image the cornea and showed that the technology could image the nerve plexus at a resolution of 1.7 μm and large field-of-view of 1.26 mm $\times$ 1.26 mm (Mazlin et al., 2018). Neuromarker applications are in a more premature state, but preclinical studies have identified specific molecules whose levels fluctuate in states of pathology and with wound healing, and may in the future be used to evaluate corneal nerve status. For example, one study treated rabbits with a combination of docosahexaenoic acid (DHA) and pigment epithelial-derived factor (PEDF) after lamellar keratectomy. Several neuropeptides were found to be significantly lower post-injury compared to baseline, and returned to normal levels as nerves regenerated, including β III-tubulin, substance P, and calcitonin gene-related peptide (CGRP) (Cortina et al., 2011). However, IVCN is by far the most prevalent diagnostic tool for studying corneal nerve anatomy, but with time, other technologies may be incorporated into clinical practice.

2.2. Function of corneal nerves

Results of early nerve tracing studies found that most nerve fibers are derived from the ophthalmic branch of the trigeminal nerve (with the exception of the inferior cornea, which receives some input from the maxillary branch), and that these fibers are mainly sensory in nature (Shaheen et al., 2014). The innervation of the cornea and bulbar conjunctiva is provided by a relatively small number of primary sensory neurons located in the ipsilateral trigeminal ganglion (Marfurt et al., 1989). Based on immunohistochemical staining, several different types of corneal nerves utilizing various neuropeptides exist (Yang et al., 2018). The majority (70%) are polymodal nociceptors that are activated by near-noxious mechanical stimuli, heat, exogenous chemical irritants, and endogenous chemical mediators. A minority of nerves (20%) are mechanonociceptors that respond to mechanical forces of a magnitude close to that required to damage corneal epithelial cells. Finally, a minority (10%) of the cold-sensitive receptors exist, which discharge spontaneously at rest, are silenced upon increased temperature, and increase their firing rate when corneal surface temperature decreases (Shaheen et al., 2014; Belmonte et al., 1994; Bessou and Perl, 1969).

Corneal function is most often tested in humans by evaluating corneal sensitivity. This can be tested qualitatively in the clinical arena with a cotton tip applicator or dental floss, with sensation graded as absent, decreased, normal, or increased. In research, the two devices that have been used to measure corneal sensitivity are the Cochet-Bonnet aesthesiometer and the non-contact Belmonte aesthesiometer. The Cochet-Bonnet aesthesiometer has a nylon filament which is

extended to 6 cm and directly contacts the central cornea. The filament is then retracted by 0.5 cm until the individual detects the stimulus. The Cochet-Bonnet thus measures mechanical detection thresholds. In comparison, the Belmonte aesthesiometer propels jets of air at various intensities (with or without intermixed CO_2 and at varying temperatures) and can thus test mechanical, chemical, and thermal detection and pain thresholds (Fig. 2). Of note, the Cochet-Bonnet's nylon filament exerts pressure on a small fixed corneal area while the area of the Belmonte aesthesiometer is larger and non-uniform (Golebiowski et al., 2011). When interpreting sensitivity values, it is important to remember that a **higher** value on Cochet-Bonnet indicates higher sensitivity, with a value of 6 cm representing the upper limit of testing while in contrast, a **lower** value on Belmonte indicates a higher sensitivity.

Both instruments have limitations. The Cochet-Bonnet can only produce a mechanical stimulus by touching the cornea directly and thus requires sterilization of the filament, can be impacted by room humidity and temperature, and has a small stimulus intensity range and problems with reproducibility given variabilities in placement and replication of force and aging of the nylon with time. For example, one Canadian study reported that the rigidity of the Cochet-Bonnet nylon filament changed with varying environmental humidity, with an average exerted force loss of 12% and 15% with every 10% increase in humidity for the 0.08 mm and 0.12 mm filaments, respectively ($p < 0.001$) (Lum and Murphy, 2018). Limitations of the Belmonte aesthesiometer include that it is not commercially available, it is relatively large and bulky, and its sensitivity measurements take longer to obtain than the Cochet-Bonnet. Additionally, variations between machines and composition and mode of stimulation make comparisons between studies challenging.

In an Australian study of 18 healthy subjects (mean age 34.40 ± 8.09 years, sex distribution not specified), mean detection thresholds using Cochet-Bonnet and Belmonte aesthesiometers were 5.50 ± 0.80 cm and 64.40 ± 29.40 mL/min, respectively. However, 56% of the measurements were beyond the maximum threshold of the Cochet-Bonnet (individuals felt the stimulus when the thread was at its full length of 6 cm), while all values were within the testing range of the Belmonte aesthesiometer (Golebiowski et al., 2011). Near identical results were reported in a British study of 17 healthy subjects (mean age = 20.3 years, range = 19–26) where 61% of subjects felt the stimulus at 6 cm, while none of the sensitivity thresholds reached the maximum Belmonte stimulus intensity (Murphy et al., 1998).

Of note, both instruments have been found to be more reproducible when tested in the central cornea as opposed to the conjunctiva. For example, a Welsh study testing the Cochet-Bonnet on 20 healthy individuals (mean age 30 years, range 22–56) reported reasonable



Fig. 2. Testing corneal mechanical detection thresholds using a modified Belmonte aesthesiometer.

repeatability when sensitivity was measured in the central cornea (coefficient of repeatability (CoR) = $\pm 0.23 \text{ g/mm}^2 \sim 1/3$ of corneal threshold value) but not in the inferior conjunctiva (CoR = $\pm 12.78 \text{ g/mm}^2$) (Chao et al., 2015). Interestingly, another Welsh study of 14 healthy individuals (mean age 32 years, range 24–39) found better reproducibility of Belmonte aesthesiometer in the central cornea (CoR = 16.10 mL/min, less than 1/4 of corneal threshold value), followed by the inferior cornea (CoR = 19.0 mL/min) and inferior conjunctiva (CoR = 25.90 mL/min). (Stapleton et al., 2004).

3. Ocular diseases associated with nerve abnormalities

3.1. Dry eye disease (DED)

DED is defined as a “disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play

etiological roles.” (Craig et al., 2017) Engrained in this definition is disease heterogeneity, as DED can be subtyped into aqueous tear deficiency (ATD), evaporative, and mixed sub-types. In addition, DED can occur as an isolated eye disease or in the setting of systemic abnormalities, such as Sjögren’s and Graft Versus Host Disease (GVHD). Corneal nerve abnormalities have been associated with DED in several studies, with some studies specifying disease sub-type (Alhatem et al., 2012). An important point to consider when comparing DED studies is that studies often define DED slightly differently, which can make interpretation and comparison of findings across studies difficult (Kloosterboer et al., 2019). Overall, while many studies have detected statistically significant differences in subbasal nerve attributes between subjects with DED and healthy controls, similar to what has been reported in healthy individuals, there is wide overlap in nerve measurement values across both groups, demonstrating the heterogeneity of nerve anatomy between individuals with and without disease.

A. Aqueous tear deficiency (ATD).

The majority of studies focusing on ATD have reported decreased

nerve densities in individuals with DED compared to healthy controls. For example, a French study examined 12 subjects with ATD (irritation, tear instability, staining ≥ 2 , Schirmer ≤ 10 mm) and 10 controls via laser-scanning IVCN and reported that nerve density was lower in the ATD group compared to controls (9426 ± 2640 vs. $15,956 \pm 2431$ $\mu\text{m}/\text{mm}$ (Erie et al., 2009); $p < 0.0001$) (Labbé et al., 2012). Near identical findings were described in a Korean study on 40 patients with ATD (symptoms, TBUT < 5 s, Schirmer < 10 mm) and 18 controls utilizing laser-scanning IVCN, which found lower density (9884 ± 2548 vs. $12,030 \pm 2203$ $\mu\text{m}/\text{mm}^2$, $p < 0.005$) and higher tortuosity (3.70 ± 0.50 vs. 1.60 ± 0.60 , $p < 0.001$) in the DED group (Choi, 2015). Other studies have used lower nerve counts as a surrogate of nerve density and reporting corroborating results, although these measures are not directly translatable. Exemplifying this point, a Chinese study using laser-scanning IVCN on 43 subjects with ATD (irritation, TBUT < 10 s, Schirmer < 5 mm) and 14 controls reported lower nerve counts (34.91 ± 8.08 vs. 45.87 ± 4.21 nerves/ mm^2 [frame = 400×400 μm], $p < 0.001$) and higher tortuosity (3.01 ± 0.49 vs. 1.94 ± 0.46 , $p < 0.001$) in the ATD group (Labbé et al., 2013). In a similar manner, an Italian study using laser-scanning IVCN on 15 subjects with ATD (defining specifications not provided) reported lower nerve counts compared to 15 controls (3.90 ± 0.50 vs. 5.80 ± 1.30 nerves/frame, $p < 0.001$) (Villani et al., 2013). Diverging from these many findings, a Chinese study on 38 individuals with ATD ($n = 8$ Sjögren's, $n = 30$ without) reported higher nerve density in the non-Sjögren's ATD group (symptoms, staining, Schirmer test ≤ 8 mm) compared to controls (1423.5 ± 609.5 vs. 1315.70 ± 664.70 $\mu\text{m}/\text{frame}$ [frame = 340×255 μm], $p = 0.50$), although differences between groups were not statistically significant (Zhang et al., 2005). Beyond discrepancies between studies, as mentioned above, another reality of these reported findings is the overlap in nerve density values across studies between subjects with and without ATD.

B. Evaporative Deficiency.

Contrasting with the findings reported in studies focusing on ATD, differences in nerve densities between patients with evaporative DED and healthy patients have not been reported in current literature. In an Indian study of 52 subjects with evaporative DED (high Ocular Surface Disease Index [OSDI], low tear breakup time [TBUT], normal Schirmer's; specific cutoffs not provided) and 43 healthy controls using laser-scanning IVCN, no differences in nerve fiber density were found (27.20 ± 0.60 vs. 28.60 ± 0.80 nerves/ mm^2 [frame of 400×400 μm]; $p > 0.05$) (Shetty et al., 2016). These findings were supported by another Indian study on 47 subjects with evaporative DED (symptoms, TBUT < 10 s, and Schirmer > 10 mm/5 min) and 33 controls using laser-scanning IVCN, which reported no significant difference in nerve fiber density (~ 30 nerves/ mm^2 for both groups, $p > 0.05$) amongst groups (Khamar et al., 2019).

Data on corneal sensitivity has been inconsistent in DED studies. Of note, when interpreting sensitivity studies, it is important that many studies did not differentiate ATD vs. evaporative DED in its experimental subjects, and as such, it is difficult to examine whether these inconsistencies in findings may be attributed to DED sub-type. Regardless, most studies examining individuals with DED have reported decreased sensitivity compared to controls. For example, the French study discussed above which examined 12 subjects with ATD and 10 controls reported lower sensitivity in the DED group (5.0 ± 0.83 vs. 5.89 ± 0.22 cm, $p = 0.01$) using Cochet-Bonnet (Labbé et al., 2012). Similarly, an American study examining 10 subjects with ATD (OSDI > 20 , TBUT ≤ 7 s, tear meniscus height < 220 μm via optical coherence tomography) reported hypoesthesia in comparison to 10 healthy subjects (3.6 ± 1.7 vs. 5.5 ± 0.83 cm; $p < 0.05$) using Cochet-Bonnet (Rahman et al., 2015). Similar findings have been described in studies utilizing Belmonte aesthesiometer. A Spanish study on 10 subjects with DED (symptoms, Schirmer's < 10 mm) and 10 controls also noted hypoesthesia (higher mechanical threshold) in the DED group (134 ± 24 vs. 78 ± 12 mL/min, $p = 0.021$) using Belmonte (Benítez-del-Castillo et al., 2007). In another

Spanish study on 44 individuals with DED (symptoms, TBUT ≤ 6 s) and 42 controls, hypoesthesia was again noted on Belmonte in the DED group, specifically to mechanical (152.6 ± 33.8 vs. 109.0 ± 23.3 mL/min, $p < 0.001$), chemical (23.90 ± 4.30 vs. 16.40 ± 3.10 %CO₂, $p < 0.001$), heat ($+0.34 \pm 0.13$ vs. $+0.26 \pm 0.05$ °C, $p < 0.001$), and cold ($-0.14 \pm 0.15^*$ vs. -0.05 ± 0.04 °C, $p < 0.001$) stimuli. However, comparison of results from this study is difficult because the disease group included individuals with Sjögren's-associated DED ($n = 14$ of 44) (Bourcier et al., 2005). Diverging from this literature, other studies have found that individuals with DED are hypersensitive compared to healthy controls. In particular, an American study that examined 20 individuals with DED (symptoms, TBUT ≤ 5 , fluorescein staining ≥ 2) and 20 controls via Belmonte noted hyperesthesia (lower mechanical threshold) in the DED group (34.60 ± 21.09 vs. 61.50 ± 20.07 mL/min, $p < 0.05$). (Sade De Paiva and Pflugfelder, 2004).

Animal studies support the findings of decreased nerve fiber density and decreased corneal sensitivity that have been reported in most DED studies. One study exposed mice to environmental stress (fan) for 5 h/day for 3 days (humidity $25\% \pm 5\%$) and found lower nerve fiber density post vs. pre stress (2813 ± 762 to 1898 ± 286 pixels/frame; $p = 0.007$). However, tortuosity (0.81 ± 0.33 to 0.96 ± 0.40 , $p = 0.31$) and reflectivity (0.83 ± 0.37 to 0.78 ± 0.43 , $p = 0.76$) were not significantly different after exposure to stress (Simsek et al., 2018). Another study exposed mice to scopolamine (with subsequent reduced tear production) and noted loss of sensitivity via Cochet-Bonnet at 2 weeks compared to controls (2.7 ± 0.30 vs. 3.5 ± 0.40 mm, $p < 0.0001$) (Simsek et al., 2019). Interestingly, decreased corneal sensitivity has also been described in a breed of dogs that spontaneously develop ATD. In a study of West Highland White Terriers, corneal sensation was decreased in those with ATD (symptoms, Schirmer < 15 mm/min) vs. controls of the same breed [1.4 (range 0.6 – 2.3) vs. 2.2 (range 1.2 – 10.3) g/ mm^2 , $p = 0.07$] via mechanical testing (Leonard et al., 2019).

Of interest, a few studies have examined the relationship between structure (subbasal nerve attributes) and function (corneal sensitivity) in DED, the vast majority of which have reported positive relationships between nerve fiber density and corneal sensitivity. For example, the Chinese study discussed above that utilizing laser-scanning IVCN and Cochet-Bonnet on 43 subjects with ATD and 14 controls reported a positive correlation between nerve fiber density and sensitivity ($r = 0.38$, $p = 0.04$), that is, lower density correlated with lower sensitivity. Additionally, this study found that nerve fiber density ($r = -0.49$, $p = 0.01$) and corneal sensitivity ($r = -0.27$, $p = 0.02$) negatively correlated with corneal staining, that is, lower density and lower sensitivity related to higher staining (Labbé et al., 2013). A French study using laser-scanning IVCN and Cochet Bonnet on 12 subjects with ATD and 10 controls likewise reported a positive relationship between nerve fiber density and sensitivity ($r = 0.64$, $p = 0.05$) and nerve count and sensitivity ($r = 0.65$, $p = 0.04$), but not tortuosity and sensitivity ($r = 0.32$, $p > 0.05$) (Labbé et al., 2012). Further supporting these findings, a Spanish study on 10 subjects with DED and 10 controls using Belmonte reported correlations between subbasal nerve density and mechanical ($r = -0.79$; $p < 0.001$), chemical ($r = -0.80$; $p < 0.001$), and thermal cold thresholds ($r = -0.63$; $p < 0.001$); that is, lower nerve density related to lower sensitivity (Benítez-del-Castillo et al., 2007). Of note, findings studies have not been entirely uniform - the Chinese study discussed prior did not find a relationship between nerve density and sensitivity (Zhang et al., 2005).

Comprehensively analyzing human and animal data, most studies have reported decreased corneal nerve density and sensitivity in ATD, but not in evaporative DED. Among studies that examined the link between nerve density and sensitivity, most but not all reported a significant relationship between the two variables. Importantly, due to the heterogeneity between study populations and the wide variability in findings, it is difficult to apply these concepts to the individual patient in clinical practice.

C. Sjögren's-Associated Dry Eye Disease (DED).

Nerve abnormalities have also been studied in relation to Sjögren's-associated DED. The majority of studies have reported similar findings to those seen in ATD studies (e.g. lower nerve density and lower sensitivity), but an increase in tortuosity has also been reported in many studies. This is not surprising, however, because ATD is the most common DED sub-type in individuals with associated Sjögren's (Bunya et al., 2013). Exemplifying these patterns, an Italian study using laser-scanning IVCN found lower nerve counts in 35 individuals with Sjögren's DED compared to 20 controls (3.34 ± 0.76 vs. 5.10 ± 0.79 nerves/frame, $p < 0.0001$). In addition, nerve tortuosity was higher in the DED group compared to controls (2.62 ± 0.94 vs. 1.20 ± 0.70 , $p < 0.0001$) (Villani et al., 2007). In a similar manner, a Spanish study using slit-scanning IVCN reported lower nerve density (508 ± 12 vs. 769 ± 88 $\mu\text{m}/\text{mm}^2$, $p < 0.0001$) and nerve count (2.82 ± 1.16 vs. 4.64 ± 0.81 , $p < 0.0001$) in 11 individuals with Sjögren's DED compared to 21 controls. Again, an increase in tortuosity was noted in the DED vs the control group (3.18 ± 0.75 vs. 1.09 ± 0.54 , $p < 0.0001$) (del Castillo JMBt et al., 2004). However, not all studies have replicated these findings. A Chinese study using slit-scanning IVCN in 38 individuals with ATD ($n = 8$ Sjögren's, $n = 30$ without) found higher nerve counts (8.80 ± 1.30 vs. 6.30 ± 3.10 nerves/frame, $p = 0.03$) and tortuosity (3.10 ± 0.80 vs. 2.20 ± 0.90 , $p = 0.02$) in its Sjögren's group compared to 30 controls, but no significant difference in nerve density (1745.40 ± 414.70 vs. 1315.70 ± 664.70 $\mu\text{m}/\text{frame}$ [frame 340×255 μm], $p = 0.09$). (Zhang et al., 2005).

Again, similar to patterns seen in ATD studies, most Sjögren's DED studies have reported lower corneal sensitivity in subjects with disease when compared to individuals without disease. For example, a Japanese study reported lower sensitivity via Cochet Bonnet in 15 individuals with Sjögren's DED versus 26 controls (4.5 ± 1.2 vs. 5.8 ± 0.4 cm, $p < 0.01$) (Xu et al., 1996). Similarly, an Italian study found lower sensitivity in Sjögren's DED compared to controls via Cochet Bonnet (4.90 ± 0.30 vs. 5.61 ± 0.38 , $p < 0.0001$) (Villani et al., 2007). Findings are not uniform however, as one Spanish study did report similar thresholds via Cochet-Bonnet (5.3 ± 0.8 vs. 5.8 ± 0.2 cm; $p > 0.05$). (del Castillo JMBt et al., 2004).

A few studies have examined the relationships between structure and function for Sjögren's DED. Similar to ATD, a positive correlation between nerve density and sensation has been reported in current literature. In particular, one French study that used laser-scanning IVCN and Cochet Bonnet on 30 subjects with Sjögren's DED compared to 15 controls noted a positive relationship between nerve density and sensitivity, ($r = 0.54$, $p = 0.002$), that is, lower density correlated with lower sensitivity (Levy et al., 2017). Furthermore, also similar to what has been reported for ATD, lower density and sensitivity negatively affecting ocular surface health has also been reported in literature. Specifically, a Canadian study using Cochet-Bonnet on 18 individuals with Sjögren's noted that corneal staining negatively correlated with sensitivity, that is, lower sensation correlated with higher staining ($r = -0.35$, $p = 0.03$). Interestingly, this study also reported that symptom severity (via 'overall symptom severity' calculated by combining OSDI and Symptom Severity of Discomfort (SSD) scores) also negatively correlated with staining ($r = -0.43$, $p = 0.01$), suggesting a neurotrophic state (discussed below). However, independent relationships between staining and OSDI and SSD were insignificant (OSDI: $r = -0.23$, $p = 0.20$; SSD scale: $r = -0.27$, $p = 0.12$). (Adatia et al., 2005).

In summary, corneal nerve abnormalities in Sjögren's DED are near identical to those reported in subjects with ATD (e.g. the majority of studies reporting decreased density and decreased sensitivity in diseased populations). Of note, a higher tortuosity value in individuals with disease has also been reported uniformly across studies. Again, an overlap in nerve attribute values can be observed when comparing across diseased and healthy subject groups.

D. GVHD-Associated Dry Eye Disease

Studies have also described nerve abnormalities in individuals with GVHD-associated DED. Overall, findings have been nonuniform with respect to nerve density and nerve tortuosity, with most but not all

studies reporting lower nerve density/count and higher nerve tortuosity in patients with disease, a similar pattern to what has been reported for Sjögren's DED. In an American study utilizing laser-scanning IVCN, 15 individuals with GVHD had lower nerve density ($11,220 \pm 5460$ vs. $19,560 \pm 4750$ $\mu\text{m}/\text{mm}^2$, $p < 0.01$) compared to 8 controls. No differences in tortuosity were noted between the groups (2.23 ± 0.69 vs. 2.16 ± 0.43 , $p > 0.05$) (Tepelus et al., 2017a). As in ATD, other studies have used nerve count as a surrogate for density, which are difficult to compare to. Specifically, an Austrian study using laser-scanning IVCN study, 12 individuals with GVHD had lower nerve count (3.20 ± 1.80 vs. 7.70 ± 1.20 nerves/frame, $p < 0.001$) and higher tortuosity (2.8 ± 1.1 vs. 1.3 ± 0.5 , $p = 0.001$) compared to 6 controls (Steger et al., 2015). Contrasting with the above findings, a Japanese study using laser-scanning IVCN, 12 individuals with GVHD had higher nerve densities ($17,800 \pm 6170$ vs. $13,690 \pm 5080$, $p = 0.11$) than 10 controls, although the difference was not statistically significant. In this study, individuals with GVHD had higher tortuosity compared to controls (3.13 ± 0.68 vs. 2.15 ± 0.50 , $p < 0.001$). (He et al., 2017).

Compared to nerve attributes described above, values for corneal sensitivity in GVHD DED has been more uniformly reported as lower in value across studies when comparing diseased individuals to controls. An Italian study examined 20 individuals with Sjögren's DED, 19 individuals with GVHD DED, and 30 controls and found lower corneal sensitivity via Cochet-Bonnet in a combined Sjögren's and GVHD group compared to controls (5.23 ± 0.21 vs. 5.45 ± 0.16 cm, $p < 0.001$) (Giannaccare et al., 2019). Similarly, a Japanese study found lower sensitivity on Cochet Bonnet in 25 individuals with GVHD compared to 5 controls (5.50 ± 0.78 vs. 6.00 ± 0 cm; $p < 0.05$) (Wang et al., 2010). Of note, no studies have thus far examined the relationship between structural and function abnormalities in GVHD.

While fewer overall studies have evaluated subjects with GVHD DED, similar to what has been reported for subjects with Sjögren's DED, studies on GVHD DED have generally reported lower corneal nerve density/count and lower corneal sensitivity in individuals with disease compared to healthy controls. Again, these values have been reported with considerable overlap in groups across studies. Interestingly, in ATD, Sjögren's DED, and GVHD DED, the majority of studies that found divergent data (no differences or higher nerve density in disease) came from Asia, raising the question whether population-based differences may have a role in driving these data discrepancies.

3.2. Glaucoma

Corneal nerve abnormalities related to structure and function have also been examined in subjects with glaucoma. For structural deficits, IVCN studies on glaucoma have reported similar overall findings to those reported in ATD, Sjögren's, and GVHD, particularly lower nerve density/counts and higher tortuosity. An Indian study examined 25 individuals with chronic glaucoma on combination therapy (≥ 2 drops) for at least 6 months vs. 25 controls through slit-scanning IVCN found lower nerve density (6883.94 ± 1798.03 vs. $12,273.15 \pm 3516.04$ $\mu\text{m}/\text{mm}$ (Erie et al., 2009), $p = 0.001$) and nerve count (3.58 ± 0.99 vs. 5.40 ± 1.70 nerves/frame (frame = 0.16 mm^2), $p = 0.001$) in individuals with glaucoma compared to controls (Saini et al., 2017). Similar findings have been reported in individuals with congenital glaucoma - a German study used laser-scanning IVCN on 25 subjects with congenital glaucoma (treatment unspecified) and 40 controls and found that individuals with congenital glaucoma had lower nerve density (2108 ± 692 vs. 2642 ± 484 $\mu\text{m}/\text{frame}$ (frame = 0.06 mm (Erie et al., 2009)), $p = 0.003$) and count (12.30 ± 4.20 vs. 15.40 ± 3.0 nerves/frame, $p = 0.02$) compared to controls. Tortuosity, however, was not significantly different between groups (1.90 ± 0.40 vs. 1.70 ± 0.20 , $p = 0.10$). (Gatzoufas et al., 2014).

These same studies reported no difference in corneal sensitivity among their study groups, in contrast to what has been seen in subjects with ATD, Sjögren's, or GVHD. The Indian study above utilized Cochet-Bonnet and found similar sensitivity between the two groups ($4.68 \pm$

0.44 vs. 5.07 ± 0.37 cm, $p = 0.076$) (Saini et al., 2017). Similarly, the German study above also used Cochet-Bonnet and reported non-significant differences in sensitivity between groups (5.80 ± 0.20 vs. 5.80 ± 0.20 cm, $p = 0.20$). (Gatzoufas et al., 2014).

Interestingly, both individuals with acute glaucoma and individuals being treated with topical intraocular pressure (IOP) lowering medications display corneal nerve abnormalities. Exemplifying this point, an Italian study that utilized laser-scanning IVCN reported lower nerve count in 40 subjects with primary open angle glaucoma (POAG) (24 on treatment in past 2 years, 16 untreated) vs. 22 controls (2.50 ± 0.70 vs. 2.90 ± 0.90 nerves/frame, $p = 0.01$). Individuals with glaucoma also had higher tortuosity vs. controls (2.60 ± 1.0 vs. 2.00 ± 0.80 , $p = 0.01$). Notably, individuals with POAG on treatment had lower nerve count (2.30 ± 0.70 vs. 2.80 ± 0.80 nerves/frame, $p = 0.004$) and higher tortuosity (2.80 ± 1.0 vs. 2.20 ± 0.80 , $p = 0.004$) compared to untreated individuals with POAG (Ranno et al., 2011). A similar observation was noted in a sub-analysis of the Ocular Hypertension Treatment Study, which used tandem-scanning IVCN to compare 26 individuals with treated ocular hypertension vs. 21 untreated individuals. Six years from enrollment, individuals with treated ocular hypertension had lower nerve density (5643 ± 2861 vs. 9314 ± 3743 $\mu\text{m}/\text{mm}$ (Erie et al., 2009); $p = 0.01$) and count (3.80 ± 2.10 vs. 5.90 ± 2.00 nerves/frame; $p = 0.02$) compared to the untreated group (Baratz et al., 2006). Likewise, a French study using laser-scanning IVCN and Cochet Bonnet found lower nerve density ($11,765 \pm 2113$ vs. $15,956 \pm 2431$ $\mu\text{m}/\text{mm}^2$, $p = 0.01$) in 14 individuals on IOP lowering drugs for glaucoma or ocular hypertension vs. 10 controls. No differences were noted between groups with respect to tortuosity (1.83 ± 0.59 vs. 1.64 ± 0.70 , $p < 0.05$) or corneal sensitivity (5.33 ± 0.58 vs. 5.88 ± 0.22 mm, $p = 0.48$). (Labbé et al., 2012).

When examining the relationship between structure and function in individuals with glaucoma, the majority of studies have reported no significant relationship between nerve density and sensitivity. Instead, there has been more uniform reports of a significant negative relationship between nerve tortuosity and sensitivity. For example, in the French study above, corneal sensitivity was not significantly related to nerve density ($r = -0.33$, $p > 0.05$) or nerve count ($r = 0.04$, $p > 0.05$). However, higher tortuosity was associated with lower sensitivity ($r = -0.62$, $p = 0.03$) (Labbé et al., 2012). Similarly, an Italian study on 84 patients with bilateral POAG or ocular hypertension and 20 healthy controls found a correlation between sensitivity (Cochet Bonnet) and nerve tortuosity ($r = -0.54$; $p < 0.05$), but not density (Martone et al., 2009). These findings have not been uniform, however, as the German study above on primary congenital glaucoma did find that sensitivity correlated with both nerve density and nerve count, although interpretation of these findings is difficult given that these relationships held true for both glaucoma ($r = 0.57$ and $r = 0.55$, $p < 0.05$) and control ($r = 0.67$ and $r = 0.56$, $p < 0.05$) groups (Gatzoufas et al., 2014).

Of note, there is biologic plausibility for topical IOP lowering medications having a negative impact on corneal nerves, and these findings have been supported by experiments done in animal models. Benzalkonium chloride (BAK), the most commonly used preservative in IOP lowering medications, has known neurotoxic effects. One mouse study applied 0.01% and 0.1% BAK to one eye daily for 7 days and used a balanced salt solution (BSS) vehicle on the contra-lateral eye as a control. After 7 days, eyes treated with BAK had decreased nerve fiber density in a dose dependent manner (0.01%: 8000 to 6000 $\mu\text{m}/\text{mm}^2$, $p < 0.05$; 0.1%: 8000 to 4000 $\mu\text{m}/\text{mm}^2$, $p < 0.005$), while controls showed no change from baseline (9000 – 9000 $\mu\text{m}/\text{mm}^2$). Corneas were then removed, stained with SMI-32 (a protein on axons), and examined via confocal microscopy. Both reversible (axonopathy) and irreversible (nerve degeneration) were noted in eyes treated with BAK compared to controls (Sarkar et al., 2012). Similar abnormalities in subbasal nerve density with BAK treatment have been reported in other animal models (Chen et al., 2013).

In summary, the findings for subjects with glaucoma diverge from

those examined for ATD, Sjögren's, and GVHD. Similar to what been reported for these three diseases, most studies on subjects with glaucoma reported that diseased individuals have lower nerve density/counts and higher tortuosity on IVCN, with both the disease and its treatment having been implicated in these findings. On the other hand, findings for glaucoma subjects diverge from DED studies with regards to sensitivity, with most studies reporting no significant differences between individuals with and without glaucoma.

3.3. Thyroid eye disease (TED)

A handful of studies have examined the abnormalities in corneal nerve structure and function in individuals TED. Findings for nerve structure abnormalities generally align with what has been reported in the above diseases, in particular glaucoma, with overall lower nerve density/count, higher nerve tortuosity, and inconsistent reports on corneal sensitivity (no difference or lower) being reported across studies. For example, in a Turkish study using laser-scanning IVCN, 40 individuals with newly diagnosed Grave's disease had lower nerve density (958 ± 394 vs. 1416 ± 744 $\mu\text{m}/\text{frame}$ [frame = 200×300 μm], $p < 0.001$), higher tortuosity (2.70 ± 0.80 vs. 1.60 ± 0.60 , $p < 0.001$), and no change in total nerve count (7.30 ± 3.10 vs. 7.30 ± 3.10 nerves/frame, $p = 1.0$) compared to 40 controls (Kocabeyoglu et al., 2015). Again, as seen with prior-discussed studies, some studies examined nerve count as a surrogate marker for density. In particular, in an Italian study which evaluated 11 active TED subjects, 15 inactive TED subjects, and 20 healthy controls via laser-scanning IVCN, lower total nerve count (3.29 ± 1.13 vs. 3.28 ± 1.21 vs. 5.04 ± 0.83 nerves/frame, $p < 0.001$ for both) and higher tortuosity (2.49 ± 0.91 vs. 2.58 ± 0.96 vs. 1.33 ± 0.64 , $p < 0.001$ for both) were seen in the TED groups compared to controls, while no significant differences were noted between active vs. inactive groups. Similar to glaucoma, differences in IVCN findings did not translate into differences in corneal sensitivity, that is, no significant differences in corneal sensitivity were noted across the three groups (Cochet-Bonnet; 5.67 ± 0.42 vs. 5.43 ± 0.82 vs. 5.85 ± 0.39 mm, $p = 0.12$) (Villani et al., 2010). Slightly diverging from this finding, a Chinese study using laser-scanning IVCN and Cochet-Bonnet also found lower nerve fiber density (12.30 ± 4.70 and 17.20 ± 6.20 vs. 28.40 ± 6.70 nerves/ mm^2 [frame = 400×400 μm], $p < 0.001$ for both) in 38 individuals with TED (14 active, 24 inactive) compared to 20 controls. However, this study instead found that corneal sensitivity was lower in the diseased population compared to controls, although this finding was only true for the inactive TED group and not the active group (5.46 ± 0.47 vs. 5.80 ± 0.32 cm, $p = 0.02$). (Wu et al., 2019).

These same studies also examined the relationships between structure, function, and symptom scores for TED. In the Italian study above, a significant inverse correlation was noted between corneal sensitivity and proptosis (value not reported; $p < 0.001$), but not with tear film parameters, suggesting that lower sensitivity is notable in individuals with more proptosis. Similar to what was reported in the discussed ATD literature, the Chinese study above found a positive correlation between nerve density and sensitivity ($r = 0.27$, $p = 0.04$) and a negative relation with nerve density and ocular symptom scores (OSDI $r = -0.60$, $p < 0.001$). Furthermore, lower density also related to more unhealthy tear film parameters (TBUT $r = 0.43$, $p = 0.001$; Schirmer $r = 0.60$, $p < 0.001$). (Wu et al., 2019).

Overall, most studies on TED reported lower nerve density/count and higher tortuosity in both active and inactive stages of disease compared to controls, without significant differences between the two disease states. Corneal sensitivity was not uniformly different between TED and controls. One study did find a significant positive link between nerve density and sensitivity, at a similar magnitude to those reported cross ATD studies (e.g. $r \sim 0.3$ for TED vs. $r \sim 0.4$ for ATD).

3.4. Neurotrophic keratitis (NK)

Neurotrophic keratitis (NK) is a clinical phenotype defined by the presence of corneal nerve abnormalities, and can occur in the setting of several disorders, including diabetes, viral infection, anesthetic abuse, neurosurgical procedures, and Sjögrens-associated DED (Sacchetti and Lambiase, 2014a). Subjects with early stage NK may experience symptoms in the form of dryness and photophobia; however, as the disease progresses, symptoms tend to regress as epithelial irregularities appear, ranging from punctate epithelial erosions to non-healing PEDs, ulceration, and perforation (Versura et al., 2018).

Studies have examined subbasal nerve structure abnormalities in individuals with NK due to a variety of etiologies. Across studies, a very uniform pattern of lower nerve density in bilateral eyes (affected more than unaffected) can be seen across studies. For example, an American study that used slit-scanning IVCN found significantly lower corneal nerve density in the affected eyes ($1400 \pm 600 \mu\text{m}/\text{mm}^2$) and contralateral unaffected eyes ($6400 \pm 700 \mu\text{m}/\text{mm}^2$) of 16 individuals with HSV keratitis compared with 15 controls ($14,100 \pm 1600 \mu\text{m}/\text{mm}^2$; all $p < 0.001$) (Moein et al., 2018). Likewise, another American study that used slit-scanning IVCN found lower nerve density (448.90 ± 409.30 vs. $2258.40 \pm 989.0 \mu\text{m}/\text{frame}$ [frame $460 \times 345 \mu\text{m}$], $p < 0.001$) and nerve count (5.20 ± 4.50 vs. 13.10 ± 3.80 nerves/frame, $p < 0.001$) in the affected eyes of 31 individuals with herpes simplex keratitis compared to 15 controls. Similar to the first study, the unaffected eye also exhibited abnormalities, including lower nerve density ($992.70 \pm 465.00 \mu\text{m}/\text{frame}$) and nerve count (7.80 ± 3.30) compared to controls ($p < 0.002$ for both) (Hamrah et al., 2010). Near-identical corneal nerve structure abnormalities have been reported in other studies examining NK due to a variety of medial conditions, including diabetic neuropathy (Rosenberg et al., 2000), neurosurgical procedures (Lambiase et al., 2013), Acanthamoeba keratitis (Müller et al., 2015a), and other studies on herpetic keratitis (Müller et al., 2015b; Hamrah et al., 2012).

Abnormalities in corneal nerve sensitivity were also examined in the above discussed studies. Overall, hypoesthesia (that is, lower sensitivity) has been uniformly reported in literature. In particular, the first American study discussed above reported lower sensation on Cochet-Bonnet in the affected eyes (2.60 ± 0 vs. 6.00 ± 0.0 cm, $p < 0.001$), but not in the contralateral eyes (5.40 ± 0.20 vs. 5.20 ± 0.20 cm, $p = 0.26$) compared to controls (Moein et al., 2018). Similarly, the second American study reported lower sensitivity in the affected eyes (3.30 ± 1.90 vs. 6.00 ± 0 cm, $p < 0.05$) with Cochet-Bonnet, while sensitivity in the contralateral eye was not assessed in this study (Hamrah et al., 2010).

Animal models support the findings of bilateral nerve dysfunction in NK after unilateral insult. A study utilizing mice demonstrated that after unilateral intraocular inoculation of live herpes virus, signs of viral infection were found on both sides of the brainstem, as well as in the contralateral eye (Streilein et al., 1997). Similarly, another mouse study compared corneal nerve anatomy in ipsilateral and contralateral eyes after unilateral surgical axotomy of the ciliary nerve, a branch of the trigeminal nerve, compared to eyes of mice that did not undergo surgery. The ipsilateral eye had lower overall nerve density on IVCN (center; $10.9 \pm 1.7 \text{ mm}/\text{mm}^2$, peripheral; $13.60 \pm 0.10 \text{ mm}/\text{mm}^2$; compared to the control eyes [center; $36.30 \pm 6.30 \text{ mm}/\text{mm}^2$, $p < 0.001$, peripheral $46.30 \pm 4.00 \text{ mm}/\text{mm}^2$, $p < 0.001$], and the contra-lateral eye from the mice with unilateral axotomy also had reduced central corneal nerve density but to a lesser degree ($77.3 \pm 6.9 \text{ mm}/\text{mm}^2$) compared to control eyes [$101.3 \pm 8.5 \text{ mm}/\text{mm}^2$, $p < 0.001$]. (Yamaguchi et al., 2013).

When examining associations between structure and function, studies have found positive correlations between corneal sensitivity and several IVCN attributes, including nerve density/count and tortuosity. The American study above reported significant connections between corneal nerve density and sensation in NK subjects ($r = 0.65$, $p < 0.0001$). In addition, herpes keratitis duration was inversely correlated

with corneal sensation ($r = -0.42$, $p = 0.02$) in affected eyes (Hamrah et al., 2010). Another American study that utilized slit-scanning IVCN and Cochet-Bonnet in 24 individuals with herpes keratitis also reported a significant correlation between nerve length (as a proxy for nerve density) and sensation ($r = 0.63$, $p < 0.001$) (Cavalcanti et al., 2018). Finally, an American study on 27 subjects with a history of herpes keratitis that used slit-scanning IVCN and Cochet-Bonnet also reported a positive relationship between sensation and nerve count ($r = 0.43$; $p < 0.0004$) and a negative relationship between sensation and nerve tortuosity ($r = -0.32$; $p < 0.02$), while nerve density was not assessed in this study (Hamrah et al., 2013).

In summary, human and animal studies have uniformly reported lower nerve density/count and lower sensitivity in eyes with NK, irrespective of underlying cause. Interestingly, studies reported involvement of both the affected and non-affected eye in diseased individuals after unilateral insult. When examining correlations between structure and function, positive relationships between nerve attributes and sensitivity have been reported at a strength of relationship higher in magnitude ($r \sim 0.65$) than those reported in ATD studies ($r \sim 0.4$).

4. Systemic diseases associated with nerve abnormalities

4.1. Migraine

Only a few studies have examined abnormalities in corneal nerve structure and function in individuals with migraine (Farhangi et al., 2020). Compared to previously described illnesses, results from nerve structure studies in particular have been much more non-uniform. For example, an American study using laser-scanning IVCN found lower nerve density (48.40 ± 23.50 vs. 71.00 ± 15.00 nerves/ mm^2 [frame = $300 \times 300 \mu\text{m}$], $p < 0.001$) in 19 individuals with migraine compared to 30 controls (Kinard et al., 2015). An Indian study using laser-scanning IVCN further separated individuals with migraine into those with and without photophobia during the interictal period (period between migraine episodes). After statistical analysis, individuals with migraine and concomitant photophobia ($n = 36$) had lower nerve lengths than individuals with migraine alone ($n = 24$) and controls ($n = 24$) (14.76 ± 3.98 vs. 18.13 ± 3.33 vs. $17.26 \pm 4.29 \text{ mm}/\text{mm}^2$; $p = 0.01$), however no difference in nerve density was found across the 3 groups ($24,690 \pm 8120$ vs. $28,640 \pm 6890$ vs. $24,280 \pm 6660 \mu\text{m}/\text{mm}$ (Erie et al., 2009), $p = 0.13$) (Shetty et al., 2018). Further diverging from these results, a Chinese study on 10 subjects with migraine and 10 controls using laser-scanning IVCN reported higher nerve density (36.3 ± 7.29 vs. 30.5 ± 6.19 fibers/ mm (Erie et al., 2009), $p = 0.10$) and nerve length (25.0 ± 2.65 vs. $22.3 \pm 2.41 \text{ mm}/\text{mm}^2$, $p = 0.05$) in the migraine group, although the relationships were not statistically significant (Shen et al., 2019). This study in particular has similar findings to the previously described Chinese study on subjects with ATD, raising the question on whether population based differences are driving these divergent findings (Zhang et al., 2005).

Very few studies have examined corneal sensitivity in migraine. A Turkish study using Cochet-Bonnet during the interictal period reported a slightly higher corneal sensitivity in 58 individuals with migraine compared to 30 controls (5.40 vs. 5.30 cm, $p = 0.05$) (Aykut et al., 2018a). Unfortunately, no study has examined structure and function concomitantly in migraine, and thus, potential connections between sensitivity and IVCN measures have yet to be assessed.

To conclude, inconsistent IVCN measures have been reported in individuals with migraines, and only one study examined corneal sensitivity, which reported hyperesthesia. Subjects with migraine and photophobia may have more abnormal subbasal nerve attributes than those with migraine alone, but this is difficult to interpret given conflicting IVCN findings across studies. However, biologic plausibility exists, as migraine pathogenesis has been connected to trigeminal nerve activity in animal and human studies, particularly through descriptions of trigeminal involvement in photophobia, a common feature of

migraine (Nosedá and Burstein, 2011; Digre and Brennan, 2012).

4.2. Fibromyalgia (FM)

Abnormalities in corneal nerve structure and function have also been described in subjects with fibromyalgia (FM). For nerve structure, all examined studies have uniformly described lower nerve density/count in diseased individuals. A Turkish study using laser-scanning IVCN found decreased nerve density (1563 ± 620 vs. 2545 ± 973 $\mu\text{m}/\text{frame}$ [frame = 450×340 μm], $p < 0.001$) and count (5.00 ± 1.80 vs. 10.30 ± 2.10 nerves/frame, $p < 0.001$) in 34 individuals with FM compared to 42 controls (Erkan Turan et al., 2018). A Mexican study using slit-scanning IVCN also found decreased subbasal nerve density (85 ± 29 vs. 107 ± 26 nerves/ mm^2 [frame = 340×255 μm], $p = 0.02$) in 17 females with FM compared to 17 controls (Ramírez et al., 2015). Similar findings regarding lower nerve density in FM have been reported across other studies (Oudejans et al., 2016; Hussain et al., 2012).

In comparison to structural abnormalities, discrepant findings have been described for sensitivity. The Turkish study above noted no difference in sensation between groups via Cochet Bonnet (0.4 g/ mm^2 in both groups, $p = 1.0$)⁸³, however, both groups felt the filament when fully extracted, and thus comparison of sensitivity was difficult. On the other hand, another Turkish study using Cochet-Bonnet reported higher sensitivity in 3 of 5 corneal points measured in 36 subjects with FM compared to 39 controls [central (6.00 vs. 5.50 cm, $p = 0.03$), superior (5.75 vs. 5.00 cm, $p = 0.005$), inferior (5.39 vs. 4.60 cm, $p < 0.001$), temporal (5.50 vs. 5.39 cm, $p = 0.28$), nasal (5.44 vs. 5.37 cm $p = 0.52$)] (Aykut et al., 2018b). To add to this discrepancy, a Spanish study of 20 individuals with FM and 18 controls utilizing Belmonte reported hypoesthesia in FM compared to control, specifically to chemical ($31.16\% \pm 2.04\%$ CO₂ vs $15.72\% \pm 0.67\%$ CO₂), heat (1.87 ± 0.11 °C vs 0.99 ± 0.05 °C), and cold (-2.53 ± 0.11 °C vs -0.76 ± 0.05 °C, $p < 0.001$ each) stimuli. No differences were noted in mechanical thresholds (123.00 ± 8.00 vs. 107.80 ± 4.40 mL/min, $p = 0.28$). Of note, a potential confounder affecting these results is that the majority (18/20) of individuals with fibromyalgia reported concomitant dry eye symptoms, and thus many of these examined subjects may have had underlying ATD (Gallar et al., 2009).

Like with migraine, very few studies have examined relationships between structure and function in FM. In fact, only one study has examined the relationship between nerve abnormalities and sensitivity, which reported a relationship that was inverse in nature, unlike studies on subjects with DED and NK which reported relationships that were positive in nature. In particular, an American study examining 19 subjects with FM and 19 controls found that nerve length correlated negatively with sensation via Cochet Bonnet ($r = -0.33$, $p = 0.04$), however, comparisons to other studies are difficult as nerve length is not an identical proxy to nerve density. Further reported in this study, nerve length also negatively correlated with symptoms via OSDI ($r = -0.35$, $p = 0.03$), indicating that higher sensitivity related to lower nerve length. Symptoms via OSDI was also found to positively correlate with tortuosity ($r = 0.41$, $p = 0.009$) and negatively correlate with nerve count ($r = -0.41$, $p = 0.01$). Finally, scores on a questionnaire that evaluated visual function (Visual Functioning Questionnaire-25) also correlated with nerve count ($r = 0.54$, $p = 0.0005$) and tortuosity ($r = -0.36$, $p = 0.03$). Of note, relationships for VFQ-25 are opposite in direction to that of OSDI, as a higher VFQ-25 score indicates better visual functioning while a higher OSDI score indicates more severe dry eye symptoms (Hussain et al., 2012). Beyond the eye, the Turkish study described above also found that systemic pain scores (Widespread Pain Index) negatively correlated with nerve density ($r = -0.33$, $p = 0.05$), that is, subjects with lower nerve density had more severe pain in the body (Erkan Turan et al., 2018).

Overall, the few studies on FM have uniformly reported abnormalities in nerve structure (e.g. lower nerve density/count), while findings on abnormalities in corneal sensitivity have been more inconsistent.

When examining correlations between structure and function, only one negative relationship has been reported, indicating hyperesthesia related to severe structural abnormalities. This overall phenotype is more similar to that seen in migraine and opposite in direction to that seen in NK and ATD, where hypoesthesia was related to structural abnormalities.

4.3. Diabetes mellitus

Abnormalities in corneal nerve structure and function have been described extensively in subjects with diabetes. A structural hallmark for subjects with diabetes includes an elevated nerve tortuosity alongside lower nerve density, a pattern that has been uniformly reported across human and animals studies. For example, in a Turkish study using slit-scanning IVCN, decreased nerve density (39.70 ± 13.20 vs. 58.50 ± 12.40 nerves/ mm^2 [frame = 450×340 μm], $p < 0.001$) and higher tortuosity (2.49 ± 0.89 vs. 1.71 ± 0.55 , $p = 0.001$) were noted in 35 individuals with type 2 diabetes compared to 24 controls (Mocan et al., 2006). Similar findings were reported in a British study using slit-scanning IVCN, which found lower nerve fiber density (27.02 ± 1.16 vs. 40.78 ± 2.64 nerves/ mm^2 [frame = 768×576 pixels], $p < 0.001$), lower nerve length (5.71 ± 0.30 vs. 8.76 ± 0.57 mm/ mm^2 , $p < 0.001$), and higher tortuosity (25.69 ± 1.05 vs. 19.77 ± 1.35 , $p < 0.001$) in 128 individuals with type 2 diabetes compared to 26 controls (Tavakoli et al., 2011). Findings of animal models align with the above pattern of lower nerve density secondary to subbasal nerve damage with diabetes. In particular, a study utilizing leptin receptor mutant (db/db) type 2 diabetic mice found that subbasal nerve density in diabetic mice were lower than controls (27.01 ± 1.67 mm/ mm^2 vs. 58.29 ± 3.94 mm/mm (Erie et al., 2009), $p < 0.00001$). (Ueno et al., 2014).

In a similar manner, diabetes-related studies have uniformly reported lower sensitivity in diseased subjects. In a Japanese study using Cochet-Bonnet, corneal sensation was lower in 95 individuals with type 2 diabetes compared to 58 controls (4.77 ± 1.31 vs. 5.74 ± 0.53 cm, $p < 0.0001$) (Saito et al., 2003). Interestingly, this study also found that sensitivity correlated with disease severity - individuals with proliferative diabetic retinopathy had the lowest sensitivity via Cochet-Bonnet (3.83 ± 1.55 cm; $n = 20$) compared to pre-proliferative (4.23 ± 1.35 cm; $n = 11$), non-proliferative (5.00 ± 0.95 cm; $n = 23$), and no retinopathy (5.24 ± 0.95 cm; $n = 41$) (Saito et al., 2003). Near identical findings have been reported in studies utilizing Belmonte - the British study discussed above used Belmonte aesthesiometry to analyze sensitivity, and found that individuals with type 2 diabetes had higher mechanical detection thresholds (lower sensitivity) than controls (1.48 ± 0.10 vs. 0.72 ± 0.02 mbars, $p < 0.001$) (Tavakoli et al., 2011). Other studies have reported similar findings of lower overall sensitivity correlating with increasing stage of retinopathy (Rogell, 1980).

Of interest, a positive correlation with disease severity exists not only with hypoesthesia, but also with respect to IVCN-related structural abnormalities. In the Turkish study discussed above, individuals with diabetic retinopathy ($n = 13$) had significantly lower nerve density (35.30 ± 9.50 vs. 43.60 ± 12.00 nerves/ mm^2 [frame = 450×340 μm], $p < 0.001$) and higher tortuosity (3.15 ± 0.80 vs. 2.08 ± 0.67 , $p = 0.003$) compared to diabetics without retinopathy ($n = 12$) (Mocan et al., 2006). Similar findings were reported in a British study utilizing laser-scanning IVCN, which found that nerve density (13.10 ± 7.30 vs. 37.60 ± 8.20 nerves/ mm^2 [frame = 384×384 μm], $p < 0.05$) and nerve length (9.20 ± 5.70 vs. 27.30 ± 5.80 mm/ mm^2 , $p < 0.005$) were lower in a mixed group of 111 type 1 ($n = 89$) and type 2 ($n = 22$) diabetics compared to 47 matched controls. In addition, nerve fiber length was lower in individuals with severe vs. mild neuropathy (9.20 ± 5.70 vs. 17.50 ± 8.10 , mm/ mm^2 , $p < 0.05$) (Petropoulos et al., 2013). Similarly, a Taiwanese study using slit-scanning IVCN study found higher tortuosity in 14 individuals with proliferative diabetic retinopathy compared to 14 controls (75.10 ± 41.00 vs. 19.00 ± 7.50 , tortuosity coefficient, $p < 0.001$) and lower nerve density when comparing proliferative

diabetics (13.8 ± 5.7 vs. 26.5 ± 7.5 nerves/mm² [frame not specified]; $p < 0.0001$), nonproliferative diabetics ($n = 14$; 16.9 ± 6.1 vs. 26.5 ± 7.5 nerves/mm (Erie et al., 2009), $p < 0.005$), and non-retinopathic diabetics ($n = 14$; 17.5 ± 5.5 vs. 26.5 ± 7.5 nerves/mm (Erie et al., 2009), $p = 0.001$) to controls. Furthermore, a British study used laser-scanning IVCN and found lower nerve density (26.31 ± 1.19 vs. 35.42 ± 1.6 nerves/mm² [frame = 400×400 μ m], $p < 0.0001$) and nerve fiber length (47.24 ± 2.21 vs. 61.75 ± 3.02 mm/mm²), $p < 0.0001$) in 116 individuals with diabetic peripheral neuropathy vs. 22 controls subjects. Similar to data in fibromyalgia, peripheral neuropathic pain severity as measured by pain visual analogue scale (VAS) inversely correlated with nerve fiber length ($r = -0.32$, $p = 0.01$), that is, individuals with higher extremity pain levels had lower nerve fiber lengths (Kalteniece et al., 2018).

Overall, studies have uniformly described lower corneal nerve density/count and lower overall sensitivity in individuals with diabetes compared to controls. Interestingly, studies also concur on worse abnormalities with respect to both structure and function in individuals with more progressed disease severity. Of note, the phenotype described is similar to what has been reported in studies examining subjects with NK, which is not surprising given that diabetes is a common underlying etiology of NK.

5. Manifestations of corneal nerve dysfunction

Manifestations of corneal nerve dysfunction occur over a continuum, ranging from hypoesthesia and no pain with significant epitheliopathy (neurotrophic phenotype or NK) to hyperesthesia and severe pain with minimal epithelial changes (neuropathic phenotype) (Fig. 3). These different presentations of corneal nerve dysfunction generally align with varying morbidities (neurotrophic in diabetes, neuropathic in migraine and fibromyalgia), although phenotypes can overlap and co-exist, as they often do in Sjögren's associated DED (Levy et al., 2017; Vitali and Del Papa, 2015).

5.1. Chronic pain

One commonly observed symptom of corneal nerve dysfunction is ocular surface pain. Chronic ocular surface pain is often described using words such as “dryness”, “burning”, “aching”, and “tenderness”, to name a few (Kalangara et al., 2017). Pain can occur spontaneously or be triggered by wind and light (the ocular equivalents of hyperalgesia and allodynia, respectively) (Galor et al., 2015). We have found that some descriptors (burning, photophobia, wind sensitivity) are suggestive of underlying nerve dysfunction (Galor et al., 2018). Besides these descriptors, pain out of proportion to ocular surface findings and persistence of symptoms despite treatment aimed at improving ocular surface health are other clues that can suggest potential nerve dysfunction as a

cause of pain.

Animal studies on ocular pain are challenging to interpret. However, animal models of induced peripheral nerve injuries (e.g. saphenous nerve and sciatic nerve) have demonstrated direct relationships between nerve damage and systemic pain, providing support for a similar relationship between corneal nerve injury and ocular pain (Attal et al., 1994; McLachlan et al., 1993).

A few studies have examined relationships between structural nerve abnormalities and ocular symptoms including chronic pain, with different relationships found with respect to different underlying diseases. Many of these studies evaluated relationships between nerve parameters and the OSDI. The OSDI is comprised of 12 questions regarding various eye symptoms (pain and visual disturbances), triggers (sensitivity to light and wind), and activity of daily living implications (Schiffman et al., 2000). Some studies specifically focus on relationships between nerve parameters and pain symptoms, while others compare nerve parameters to total severity scores. The latter results are more difficult to interpret as total OSDI scores can be driven by pain, visual disturbance, or both. With these caveats in mind, an American study used laser-scanning IVCN found a strong negative correlation between nerve density and OSDI ($r = -0.92$, $p < 0.001$) in 44 eyes with Sjögren's DED, 44 with non-Sjögren's DED, and 10 controls, implying more severe ocular symptoms in individuals with lower densities (Tepelus et al., 2017b). In contrast, an Indian study that used laser-scanning IVCN in 52 individuals with evaporative DED compared to 43 controls did not find significant relationships between nerve density ($r = 0.10$, $p = 0.33$) and fiber length ($r = 0.15$, $p = 0.13$) with OSDI-discomfort scores (Shetty et al., 2016). Several other studies examined relationships between nerve density and total OSDI score in various DED sub-types including post-keratectomy DED ($r = -0.46$, $p < 0.05$)¹⁰⁴, glaucoma therapy ($r = -0.82$, $p < 0.05$)⁵³, and TED ($r = -0.60$, $p < 0.001$)⁶² with negative relationships of various magnitudes throughout. Furthermore, in individuals with fibromyalgia, OSDI scores negatively correlated with nerve count ($r = -0.41$, $p = 0.01$) and positively with tortuosity ($r = 0.41$, $p = 0.01$) (Hussain et al., 2012). Overall, the majority of studies support a negative relationship between IVCN nerve density/count and patient-reported symptoms, that is, decreased nerve density associated with more severe symptoms.

Studies have also examined relationships between ocular symptoms and corneal sensitivity, with results again varying by underlying disease type. Discrepancies have also been found within diseases, most notably in DED. For example, some studies in DED have not found relationships between sensitivity and OSDI. A Chinese study using laser-scanning IVCN on 43 subjects with ATD (irritation, TBUT <10, Schirmer < 5 mm) and 14 controls noted lower sensitivity in the DED group (5.79 ± 0.34 vs. 5.98 ± 0.04 , $p = 0.01$) and insignificant correlations between sensitivity (Cochet-Bonnet) and symptom and signs of DED (OSDI: $r = 0.13$, $p = 0.42$; TBUT: $r = 0.04$, $p = 0.82$; Schirmer's: $r = 0.04$, $p = 0.82$)

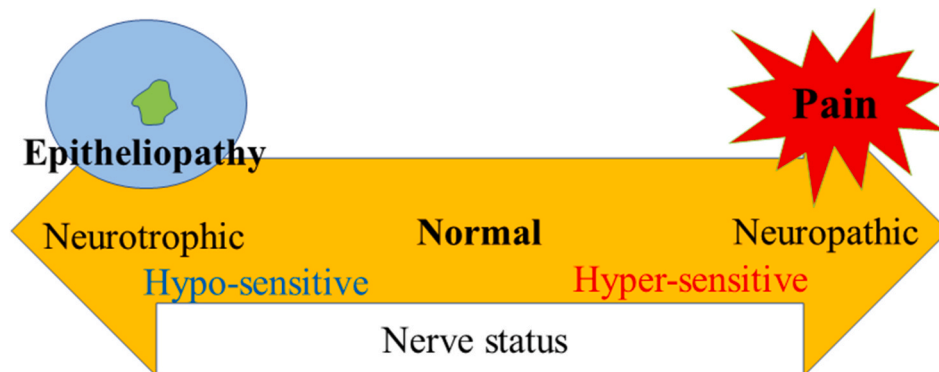


Fig. 3. Manifestations of corneal nerve dysfunction generally occur on a continuum ranging from hypoesthesia and significant epitheliopathy (neurotrophic phenotype) to hyperesthesia and pain but with minimal epithelial changes (neuropathic phenotype), although these phenotypes can co-exist in the same individual.

(Labbé et al., 2013). Similar findings were reported in another Chinese study of 54 patients with ATD (irritation, TBUT <10, Schirmer < 5 mm) vs. 32 controls. Mean sensitivity was lower in DED (5.74 ± 0.41 vs. 5.98 ± 0.07 , $p = 0.002$) but relationships between mean sensitivity (Cochet-Bonnet) and symptoms were insignificant (OSDI: $r = -0.14$, $p = 0.21$) (Liang et al., 2016). Other studies have found significant relationships between sensitivity and symptoms. A French study that used Cochet-Bonnet in subjects with post-keratectomy DED reported a significant inverse relationship between sensitivity and OSDI ($r = -0.65$, $p < 0.01$) with insignificant relationships with TBUT ($r = 0.01$, $p > 0.05$) and Schirmer's ($r = -0.15$, $p > 0.05$) (Denoyer et al., 2015). An American study using Belmonte noted negative correlations between detection and pain thresholds and symptoms (dryness and pain) in 129 subjects with DED symptoms (Dry Eye Questionnaire score ≥ 6) (Chalmers et al., 2010). While the relationships were significant based on the number of participants, the magnitude of the relationship was weak and similar to that of the Chinese studies (OSDI: $r = -0.18$, $p = 0.04$ and $r = -0.20$, $p = 0.03$ for detection and pain thresholds respectively; Neuropathic Pain Symptom Inventory modified for the Eye (NPSI-E) (Farhangi et al., 2019): $r = -0.23$, $p = 0.01$ and $r = -0.21$, $p = 0.02$). Similar to other studies, other tear parameters, including Schirmer values, did not correlate with sensitivity ($r = 0.02$, $p = 0.82$ and $r = 0.90$, $p = 0.34$) (Spierer et al., 2016). Overall, in DED, most studies have found weak ($r < 0.3$) correlations between corneal sensitivity and symptoms, with both positive and negative relationships reported. Of note, a stronger relationship was found in a study on Sjögren's associated DED. In particular, a Finnish study utilizing Cochet Bonnet on 20 patients with Sjögren's and 10 healthy controls reported a moderate negative relationship between corneal sensitivity and OSDI ($r = -0.46$, $p < 0.01$), that is, progressive hypoesthesia related to more severe symptoms (Tuisku et al., 2008).

Compared to DED, studies on other diseases have examined these relationships to a much lesser extent. A Turkish study using Cochet Bonnet in 36 subjects with fibromyalgia found positive correlations between central, superior, inferior, temporal, and nasal corneal sensitivity and OSDI ($r = 0.44$, $p = 0.01$; $r = 0.43$, $p = 0.01$; $r = 0.34$, $p = 0.04$; $r = 0.38$, $p = 0.02$; $r = 0.47$, $p = 0.004$, respectively) compared to 39 controls (Aykut et al., 2018b). That is, higher sensitivity on Cochet Bonnet translated into more severe symptoms. On the other hand, studies examining TED (Villani et al., 2010), diabetes (DeMill et al., 2016), and glaucoma/ocular hypertension (Van Went et al., 2011) did not find any significant associations between sensitivity and clinical measures, including OSDI, TBUT, and Schirmer's.

In summary, ocular surface pain is one of many manifestations of corneal nerve dysfunction. Studies have found more robust relationships between IVCM-related structural abnormalities and symptom severity (of which pain is one component) in comparison to studies relating corneal sensitivity to symptom severity, which have been less consistent overall. Importantly, heterogeneity in disease phenotypes may underlie some of the discrepancies.

5.2. Persistent epithelial defects (PEDs)

Epitheliopathy is another manifestation of corneal nerve dysfunction, often seen in individuals with decreased sensation and without pain (Fig. 4). The corneal epithelium is a barrier composed of a tightly linked network of cells acting as a first line of defense for the eye. Corneal nerves play an important role in maintaining a healthy epithelium, particularly in aiding re-epithelialization after injury. The importance of corneal nerves in wound healing was demonstrated in a rabbit study that used capsaicin (an exogenous ligand for polymodal receptors) to induce release and subsequent depletion of neuropeptides (e.g. substance P, neurokinin A, etc.) stored within corneal sensory nerve terminals (Hua et al., 1986). After 3 weeks of treatment, an epithelial defect was made centrally, and eyes subsequently treated with capsaicin had a significantly delayed time to epithelial defect resolution than contralateral eyes treated with vehicle (42.6 ± 4.0 vs. 34.0 ± 1.1 h; $p < 0.05$) (Gallar et al., 1990). Besides this, studies also suggest that epithelial cells act as surrogate Schwann cells for corneal nerves, with identical responses to axonal injury (including Ca^{2+} influx, axonal retraction, toll-like receptor expression, MMP9 activation, macrophage recruitment, and staggered axon outgrowths) (Stepp et al., 2017). Overall, these findings highlight a significant connection between the corneal epithelium and subbasal nerve plexus.

Due to dysfunction in epithelium maintenance, individuals with abnormal corneal nerve function are at increased risk for NK epitheliopathy, which can range from chronic punctate epithelial erosions to a non-healing epithelial defect that leads to ulceration and perforation. One grading scale of NK severity is the Mackie classification, with stage 1 defined as punctate epithelial erosions, stage 2 as persistent epithelial defects (PED) (failure to heal within 2 weeks), and stage 3 as corneal ulceration and perforation (Sacchetti and Lambiase, 2014b). An Italian study utilized laser-scanning IVCM and Cochet-Bonnet in 45 individuals with NK from a variety of etiologies and reported that IVCM and sensitivity findings correlated with NK grade, including nerve density (Grade 3: $0.33 \pm 0.37 \mu\text{m}/\text{mm}$ (Erie et al., 2009), Grade 2: $3.11 \pm 0.39 \mu\text{m}/\text{mm}$ (Erie et al., 2009), Grade 1: nerve density of $10.06 \pm 0.51 \mu\text{m}/\text{mm}^2$), nerve count (Grade 1: 1.8 ± 0.79 per mm (Erie et al., 2009), Grade 2: 0.7 ± 0.8 per mm², Grade 3: 1 ± 0.4 per mm²), and corneal sensitivity (Grade 1: 1.5 ± 0.6 cm, Grade 2: 1.53 ± 0.6 cm, Grade 3: 0.44 ± 1 cm). (Mastropasqua et al., 2019).

In summary, individuals with corneal nerve abnormalities are at higher risk of developing epithelial abnormalities, including PEDs. This is particularly the case for subjects with underlying diseases such as diabetes and viral herpes NK, which especially predispose for epithelial dysfunction due to severe corneal nerve damage. Underlining this relationship, current literature suggest that epithelial defect severity positively correlates with degree of corneal nerve abnormalities.

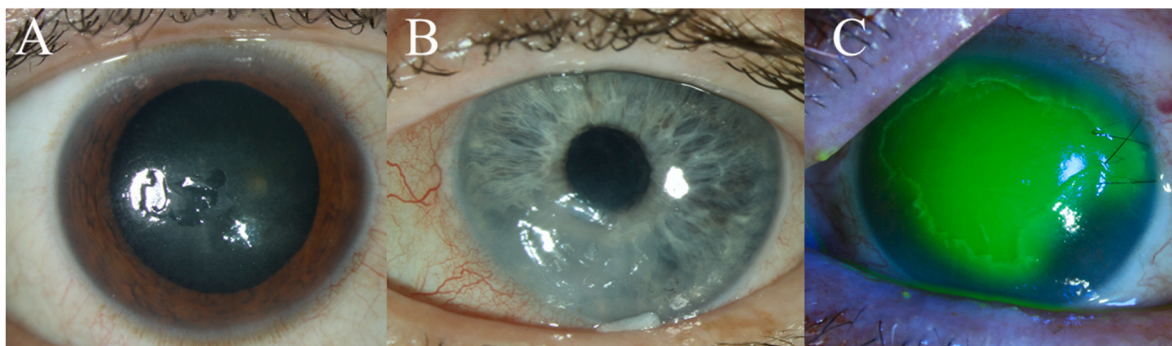


Fig. 4. Persistent Epithelial Defects (PED) following A.) stroke, B.) herpes zoster ophthalmicus, and C.) cataract surgery associated with diabetes mellitus.

6. Treatment of corneal nerve dysfunction

6.1. Treatment of chronic pain

The management of ocular pain depends on the underlying etiology of pain. An important first step in approaching subjects is a comprehensive evaluation to look for sources of pain. In general, pain is split into two broad categories, nociceptive and neuropathic pain, although these types of pain can co-exist in an individual. Nociceptive pain is defined as “pain that arises from actual or threatened damage to non-neural tissue” and is due to the activation of nociceptor pathways, while neuropathic pain is defined as “pain caused by a lesion or disease of the somatosensory nervous system.” (IASP terminology, 2019) Nociceptive sources of ocular surface pain can include anatomic abnormalities (e.g. of the eyelid, conjunctivae, and/or cornea) or an unhealthy tear film with unstable osmolarity and inflammation. In general, the treatment workup for chronic ocular surface pain begins with treatment of nociceptive sources of pain (Mehra et al., 2020). If pain persists despite treatment, or if individuals display specific symptoms (e.g. burning, wind and light sensitivity) or co-morbidities (migraine, fibromyalgia, pain post refractive surgery) suggestive of nervous damage, neuropathic pain should be considered instead (Jacobs, 2017).

Treatment modalities of nociceptive pain includes artificial tears and topical anti-inflammatories, to name a few. Numerous studies have evaluated the efficacy of such treatment modalities for controlling nociceptive pain. For example, a Turkish study treated individuals with Sjögren's with 0.05% cyclosporine ($n = 36$) or saline ($n = 20$). Individuals treated with cyclosporine reported improved discomfort after 1-month compared to controls, including pain (24–10 vs. 17 to 16, $p = 0.01$), light sensitivity (23–9 vs. 17 to 16, $p = 0.001$), and burning (23–15 vs. 18 to 18, $p = 0.001$) (Deveci and Kobak, 2014). Similar findings were reported in a large-scale American randomized controlled trial (RCT) evaluating cyclosporine use in subjects with DED (Sall et al., 2000). Of note, not all subjects with nociceptive pain respond to anti-inflammatory treatments. In fact, baseline nerve metrics has been found to predict response to treatment – an American study used laser-scanning IVCN to evaluate corneal nerves in 60 individuals with meibomian gland dysfunction-associated DED (OSDI >22, corneal staining ≥ 4 , and diagnosis of MGD) treated with loteprednol 0.5%. Loteprednol improved DE symptoms (SANDE questionnaire) only in those with near-normal ≥ 16.84 mm/mm², $n = 29$) but not in those with low baseline corneal nerve fiber length (<16.84 mm/mm², $n = 25$) (60.10 ± 17.40 to 50.0 ± 22.70 , $p = 0.04$ vs. 55.90 ± 22.80 to 59.40 ± 17.10 , $p = 0.43$). (Kheirkhah et al., 2015).

On the other hand, for suspected neuropathic pain, treatment is based on the location of nerve dysfunction. Peripheral neuropathic pain is defined as “pain caused by a lesion or disease of the peripheral somatosensory nervous system”, as is seen when individuals have corneal nerve abnormalities. One way to evaluate for the presence of corneal nerve abnormalities is by examining their appearance on IVCN. However, many studies have found that anatomy does not necessarily correlate with nerve function. Another commonly used test to evaluate for peripheral pain is the proparacaine challenge. In this test, individuals are asked to rate their ocular pain before and after a drop of topical anesthetic is placed in the eye. If pain completely resolves after anesthetic placement, this suggests that the pain is either due to nociceptive or peripheral nerve abnormalities. Persistent pain after placement of a topical anesthetic suggests a central or non-ocular component to pain. Of note, corneal nerve sensitivity tests the function of the entire pathway and cannot be used to separate peripheral and central nerve function.

For cases of peripheral neuropathic pain, or pain that partially responds to a topical anesthetic, local therapies may be considered, such as autologous serum tears (AST). A case series of 51 American subjects with systemic autoimmune diseases and DED (defined using OSDI, corneal fluorescein staining, and history of failed previous DED therapy; defining values not provided) treated with 20–50% AST for a mean of

14.3 ± 11.7 months reported improvement in OSDI symptom scores (baseline 62 ± 24.2 to final visit 47 ± 22.3 , $p = 0.03$) in 85.1% of individuals, with a third of the subjects (34.6%) noting complete resolution of ocular discomfort and 14.9% reporting no benefit (Ali et al., 2018). Another American study evaluated pain and subbasal density (laser-scanning IVCN) before and after AST (mean 3.8 ± 0.5 month, range 1–8) in 16 individuals with corneal neuropathic pain (defining characteristics not included). Pain severity decreased (9.10 ± 0.20 (range 8–10) to 3.10 ± 0.30 (range 0–4), $p < 0.0001$) and nerve count increased (10.50 ± 1.40 to 15.10 ± 1.60 nerves/frame, $p < 0.0001$) with AST treatment (Aggarwal et al., 2015).

In individuals with a suspected central component of pain (e.g. persistent pain after anesthesia, such as in co-morbid fibromyalgia or migraine), therapies to consider include $\alpha_2\gamma$ ligands (gabapentin and pregabalin), selective serotonin-norepinephrine reuptake inhibitors (e.g. duloxetine), and tricyclic antidepressants (e.g. nortriptyline). In an American retrospective case series of 8 subjects with suspected neuropathic ocular pain (pain out of proportion to clinical findings, poor response to topical therapies), gabapentin (starting dose of 300 mg daily and escalation to 600–900 TID) and pregabalin (starting dose of 75 mg daily and escalation to 150 mg BID) led to complete ocular pain relief in 2 subjects (NRS = 0 on a 0–10 scale), significant pain improvements in 3 subjects (NRS ≤ 2), and slight but noticeable improvement in 1 subject (NRS = 10 to 7), while 2 subjects reported no improvements in pain (Small et al., 2020). In this same study, the two subjects who noted complete pain relief were also on concomitant duloxetine (20 mg starting dose with escalation to 60 mg daily based on effect). While no studies have examined duloxetine as a treatment modality for chronic ocular pain, studies have demonstrated its efficacy in peripheral neuropathic pain due to diabetes. In particular, in a multicenter RCT, 348 type 1 or 2 diabetics received duloxetine 60 mg once daily, duloxetine 60 mg twice daily, or placebo for 12 weeks ($n = 116$ each). Individuals randomized to duloxetine more frequently reported a 30% reduction in pain at 12 weeks (0–10 scale, 24 h recall: daily 68%, twice daily 64%, placebo 43%) (Raskin et al., 2005). Finally, tricyclic antidepressants such as nortriptyline have also been evaluated for use in controlling chronic ocular pain. In particular, a retrospective British study on 25 individuals diagnosed with neuropathic corneal pain who were treated with nortriptyline (10–25 mg starting dose escalated to 100 mg daily based on effect and tolerance) had lower pain scores at 4 weeks post-vs. pre-treatment (via NRS; 3.8 ± 2.4 vs. 6.4 ± 2.2 ; $p < 0.0001$), with overall pain improvement reported in 84% of subjects ($n = 21$), including 28% with >50% improvement ($n = 7$), 40% with 25–50% improvement ($n = 10$), and 32% with <25% improvement ($n = 8$). (Ozmen et al., 2019).

Adjuvant therapies have also been used to treat chronic ocular pain, including transcutaneous electrical nerve stimulation (TENS), botulinum toxin therapy, and emotional therapy. One study evaluating the efficacy of TENS (which consists of delivering an electrical stimulus at the level of the peripheral trigeminal nerves) found that an in-office 30 min session improved ocular pain in an open-label fashion in 14 individuals with chronic ocular surface pain. Overall, mean pain intensity was reduced 5 min post-vs. pre-treatment (0–10 NRS: right eye 4.5 ± 3.2 to 1.9 ± 2.5 , $p = 0.01$; left eye 4.5 ± 3.4 to 2.0 ± 2.4 , $p = 0.01$) (Sivanesan et al., 2018). This therapy can be incorporated into the long term treatment of chronic ocular pain, as demonstrated by persistent use (mean 6.6 ± 3.6 months) in 10 individuals with chronic ocular surface pain from a variety of etiologies. Overall, pain scores decreased post-vs. pre-treatment by 27% (5.6 vs. 7.6; $p = 0.02$) (Zayan et al., 2020). Botulinum toxin type A (BoNT-A) has also been investigated as a treatment for chronic ocular surface pain (Venkateswaran et al., 2019). In a study of 62 individuals with migraine treated with BoNT-A (100–150 units every 3 months), BoNT-A had positive effects on migraine pain and photophobia (3.4 ± 2.5 vs. 4.9 ± 3.0 ; $p < 0.001$) 6 weeks post-vs. pre-treatment (Diel et al., 2019a). This effect was found to be independent of tear film volume (Diel et al., 2019b). Finally, given the close

association of ocular pain and psychological dysfunction (Galor et al., 2013; Patel et al., 2019), treatment in the form of cognitive-behavioral therapy (CBT) can be considered in individuals suffering from chronic ocular pain. While no studies have examined the use of CBT for treating ocular pain specifically, studies have demonstrated that CBT is a viable treatment adjuvant for other pain conditions, such as low back pain. Exemplifying this point, a British RCT separated 598 adults with low-back pain into CBT ($n = 399$) and control groups ($n = 199$). Individuals in the CBT had greater improvements in pain level compared to controls at 12 months, measured via Von Korff pain scale (range 0–100%; mean decrease in pain scale of 13.8% vs. 5.4%; $p < 0.0001$). (Lamb et al., 2010).

Besides the treatments listed above, several compounds have been examined for their therapeutic potential in neuropathic pain, including melatonin analogs (Dubocovich and Markowska, 2005), cibinetide (Culver et al., 2017), and vitamin B12, Julian et al., 2020 although these compounds have not specifically been tested for ocular pain. Other novel therapies have been evaluated for use in ocular pain in pre-clinical animal studies, including TRPV1 agonists, TRPV1 antagonists, and cannabinoid agonists. Medications that bind to and activate the TRPV1 (transient receptor potential cation channel) calcium channel, such as the agonist resiniferatoxin (RTX), induce an analgesic effect indirectly by maintaining TRPV1 in an open state, allowing sustained influx of calcium resulting in calcium-induced cytotoxicity and nerve ablation (Venkatachalam and Montell, 2007). One animal study examined the effects of RTX in controlling ocular pain after capsaicin challenge (50 μ L 0.02% CAP) in a rat model and found that pain in the form of eye wipe count was reduced in a dose-dependent manner in RTX-treated mice. Specifically, the difference in mean eye wipe counts between RTX-treated eyes and contralateral untreated eyes became significant at doses $\geq 1 \mu$ g (Bates et al., 2010). Importantly, antagonistic compounds that bind and block the TRPV1 receptor also induce analgesia by preventing nociceptive function directly, and animal studies have shown success with controlling ocular pain with use of such compounds (Gavva et al., 2005; Bereiter et al., 2018; Chen et al., 2014). Cannabinoids, like TRPV1 agonists and antagonists, have also been evaluated for controlling ocular pain in animal models. In a rat model of chemical cauterization, combination treatment of cannabinoid receptor 1 (CB1) synthetic agonists led to reduced pain measured as number of eye wipes after capsaicin challenge. Specifically, treatment with either combination agonist lead to decreased eye wipes (18 ± 4 and 14 ± 6 respectively) compared to mice in the vehicle-treated group (30 ± 5 , $p < 0.001$ and $p < 0.0001$ respectively; $n = 8$). (Thapa et al., 2020).

Overall, a wide range of treatments are available to treat ocular surface pain which should be tailored to the clinical examination findings and co-morbidities of the individual subject. Topical therapies can be considered in cases of nociceptive or peripheral neuropathic pain. Oral and adjuvant therapies can be considered in cases of central neuropathic ocular pain. Several novel therapies are being evaluated in the preclinical stage, some of which may add to the list of accepted therapeutic modalities in the future after further study.

6.2. Treatment of Persistent epithelial defects (PEDs)

As discussed above, Grade 2 NK manifests as a PED (Tsubota et al., 1999). If untreated, the natural history of NK associated PED is ulceration and perforation. Therapies for advanced NK thus aim to quickly heal the PED in order to avoid permanent corneal scarring. When treating a PED, it is important to address the underlying condition along with improving ocular surface health; for example, varicella zoster associated PEDs may need to be treated with anti-viral therapy. Given the propensity to progress to corneal scarring, thinning, and potential perforation, it is important to quickly move up the treatment ladder if conservative measures (e.g. artificial tears and bandage contact lens) fail to heal a PED.

Several therapies have been studied in this regard. Matrix

metalloproteinase inhibitors (e.g. doxycycline) are often added for their potential anti-inflammatory and anti-melting properties. For example, an American retrospective study examined the effect of doxycycline in 7 subjects with refractory recurrent corneal erosions. Individuals were treated with oral doxycycline (50 mg, twice daily, for 2 months) and topical corticosteroid (either methylprednisolone 1%, prednisolone acetate 1%, or fluoromethalone 0.1%; three times a day, for 2–3 weeks), and all PEDs healed within 2–10 days. Fortunately, visual acuity in 4 subjects improved to 20/20, and no recurrent PEDs were observed during a mean follow-up period of 21.9 months (Dursun et al., 2001). Supporting this study, a rabbit study of bilateral alkali burns (via 1 N sodium hydroxide for 30s in an 11-mm circular plastic well) found that treatment with oral doxycycline (5 mg/kg daily) for 14 days led to enhanced re-epithelialization compared to the rabbits left untreated (area of PED at 14 days 7.1% vs. 50.0%, $p = 0.002$). (Perry et al., 1993).

Autologous serum tears (AST) are frequently used in cases of refractory PEDs (Pan et al., 2017). An American study treated 25 subjects with refractory PEDs (mean duration 13.9 weeks) with AST 50% drops and found complete resolution in 23 subjects within 22.4 days of treatment (median 14 days). The defect in the remaining 2 subjects decreased, but tarsorrhaphy was required for complete resolution. In support for early initiation of therapy, time to PED resolution was longer in individuals with long standing PEDs prior to AST initiation ($r = 0.68$, $p = 0.001$) (Jeng and Dupps, 2009). A British study evaluated autologous finger-prick treatment as an alternative to AST in 10 individuals with refractory PEDs (average baseline diameter of 2.04 mm). In this small study, PEDs healed in 6 subjects and persisted but were reduced by half in 1 subject over a 28 day period; 3 subjects were lost to follow up (Balal et al., 2020). In rabbits, AST led to faster epithelial healing after superficial keratectomy (using a corneal trephine of 8-mm diameter, up to a depth of 0.3 mm, to remove epithelial) in comparison to controls treated with artificial tears (mean time to healing - 4 vs 8 days; $p = 0.001$). (Akyol-Salman, 2006).

Amniotic membrane transplant (AMT) is another option in the treatment of PEDs (Shaheen et al., 2014). In a German prospective study, 11 subjects with PEDs underwent amniotic membrane transplantation (AMT) and were followed post-operatively for 1 year. Total resolution within 4 weeks was noted in 9 of 11 subjects, and the effects persisted for 1 year. The 2 unresolved cases continued experiencing recurrent epithelial defects secondary to severe neurotrophic keratitis (Kruse et al., 1999). Similarly, a British study examined outcomes in 10 subjects with varying PED severity. Four of 5 subjects with PED alone and 0 of 2 with PEDs and stromal involvement healed with AMT, emphasizing the need to intervene early in these cases (Azuara-Blanco et al., 1999). Animal studies support these human observations. A rat study of herpes keratitis reported that AMT in eyes with ulceration promoted more rapid epithelialization compared to untreated controls. In the AMT group, ulcers healed within 2 days in all mice, which was significantly different than the control group which showed continued progression for all ulcers and perforation in 3/16 eyes ($p < 0.001$). (Heiligenhaus et al., 2001).

In locations where access to AST and AMT are limited, tarsorrhaphy is another option for treating PEDs. In a review of 77 subjects who underwent tarsorrhaphy for PED (24 temporary and 53 permanent) (mean age 68.3 ± 1.9 years, range 4–95 years, 46.8% men), complete resolution of the defect was noted in 70 eyes (90.9%) (Cosar et al., 2001). An Indian study compared tarsorrhaphy to pressure patching in 36 subjects with post-keratopathy PEDs and found better outcomes with lateral tarsorrhaphy (time to epithelial healing 7.61 ± 0.91 days vs. 12.6 ± 1.61 days, $p < 0.05$). (Panda et al., 1999).

More recently, recombinant human nerve growth factor (NGF) (Oxervate, Cenegermin, Dompe) has been approved for the treatment of NK-associated PEDs (Deeks and Lamb, 2020). The European REPARO study examined the safety and efficacy of 156 subjects randomized 1:1:1 to rhNGF 10 μ g/mL, 20 μ g/mL, or vehicle (6 drops per day for 8 weeks) and found improved healing in the NGF groups. At week 4, rhNGF

treated subjects showed significant reductions in lesions size compared to controls (defect <0.5 mm in 58% 20 µg/mL, 55% 10 µg/mL, and 20% vehicle). At week 8, outcomes were even better (74% vs. 75% vs. 43%, respectively). Fortunately, no recurrences were noted in >96% of individuals up to 56 weeks (Bonini et al., 2018). Similar results were found in a multicenter trial in the USA of 48 subjects with NK randomized to Cenegermin 20 µg/mL or vehicle eye drops (6 drops daily for 8 weeks). Cenegermin-treated subjects showed significant reductions in lesion size and disease progression in comparison to controls (defect <0.5 mm in 69.6% vs. 29.2%). Of the 16 subjects treated with Cenegermin who achieved a defect <0.5 mm, 2 (12.5%) underwent re-treatment for recurrence. The epithelium healed in both subjects after re-treatment without recurrence through the end of follow-up (24 weeks). All individuals who failed vehicle (n = 13) received open-label Cenegermin and 9 (69.2%) met the primary outcome of less than 0.5 mm of lesion staining. Of these subjects, 4 of 9 (44.4%) experienced recurrence. Three were re-treated, and two achieved closure of the epithelial defect (Pflugfelder et al., 2020). Of note, a major drawback of Cenegermin treatment is the large cost associated with treatment (Sheha et al., 2019).

Corneal neurotization is another treatment modality for NK-induced PEDs, although it is generally reserved for individuals with severe NK, such as those seen in individuals post-neurosurgical procedures. Neurotization is a surgical procedure that reinnervates tissue by redirecting sensory innervation from one area of the body to another. In regards to the cornea, this involves harvesting a section of a sural nerve from the lower extremity and conjoining it with a functional branch of the trigeminal or auricular nerve (Fung et al., 2018; Kolseth et al., 2020). A retrospective analysis evaluated outcomes in 23 adult subjects with severe NK and reported markedly diminished sensitivity (median disease duration 11.8 months) in those who underwent neurotization. Sensation overall improved via Cochet Bonnet (median time point 11.3 months post-operative, range 6–20 months; 1.6 cm–3.6 cm, $p = 0.03$), and full sensation returned to 2 subjects post-operatively (5 months, mean 5.5 cm vs. 12 months, 6.0 cm). In addition, 4 of 6 subjects with PEDs had complete healing without subsequent treatment; one subject required surgical intervention with corneal transplant, AMT, and tarsorrhaphy at postoperative month 8 for complications of fungal keratitis, and the second subject required AMT at postoperative month 1 for recurrent PED. (Kim et al., 2020) Similarly, another American review of 6 subjects with NK (mean disease duration 7.00 ± 8.56 years) found improved average corneal sensation post-vs. pre-surgery (0.20 ± 0.45 cm to 2.78 ± 2.26 cm, $p < 0.02$) via Cochet-Bonnet over several years of follow-up (16.3 ± 2.42 years). Throughout follow-up, the individual with grade 3 NK reverted to grade 1 NK after surgery and maintained this phenotype for 18 years (Terzis et al., 2009). Overall, this surgical approach is a viable option in severe NK cases that are refractory to medical therapy.

In summary, several treatments are available for PEDs. First line therapies include lubrication, contact lens use, and doxycycline but these treatments should be escalated to AST or AMT if the PED fails to resolve. In areas without access to AST and AMT, surgical tarsorrhaphy can be used and is often helpful in refractory or severe cases. Recently, topical rhNGF has become available in some countries and has shown great success in treating NK associated PEDs. Neurotization can be considered in severe cases that are not amenable to medical therapy.

7. Conclusion

Corneal IVCN enables high quality visualization and quantification of the cellular and neural attributes in both health and disease states. Corneal sensitivity can be used to evaluate sensation in the corneal nerve pathway. Through application of IVCN and sensitivity measurement with instruments like the Cochet Bonnet and Belmonte aesthesiometers, numerous studies have categorized structural and functional abnormalities in individuals with ocular and systemic disorders, with some discrepancies across studies. Furthermore, IVCN density values have a

wide range with overlap across studies and between diseases states and controls. Regardless of etiology, manifestations of corneal nerve dysfunction include chronic ocular pain on one end of the spectrum (i.e. neuropathic pain) and PEDs on the other end (i.e. neurotrophic keratitis), although both processes can occur in the same individual, such as in Sjögren's. Treatment modalities for these manifestations of dysfunction vary, but individuals with refractory conditions should be immediately treated and closely followed given potential risks for further damage to the subbasal nerve system and corneal epithelium.

In closing, this review summarized current views on the physiology of corneal nerves and pathologic changes seen in ocular and systemic disorders. Furthermore, findings of studies that have examined the microscopic changes in subbasal nerve attributes and/or functional change related to corneal sensitivity were grouped and compared across disease states. With this, our review adds to the existing literature in its attempt to categorize diseases into phenotypic patterns based on exam findings, which we hope may guide clinicians.

↑ = higher value in disease vs. controls; ↓ = lower value in disease vs. controls; – = nonsignificant difference in values across groups; /= two disease groups compared to controls.

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References

- Adatia, F., Michaeli-Cohen, A., Naor, J., Caffery, B., Bookman, A., Slomovic, A., 2005. Correlation between corneal sensitivity, subjective dry eye symptoms and corneal staining in Sjögren's syndrome. *Can. J. Ophthalmol.* 39, 767–771.
- Aggarwal, S., Kheirkhah, A., Cavalcanti, B.M., et al., 2015. Autologous serum tears for treatment of photolodysnia in patients with corneal neuropathy: efficacy and evaluation with in vivo confocal microscopy. *Ocul. Surf.* 13 (3), 250–262.
- Akyol-Salman, I., 2006. Effects of autologous serum eye drops on corneal wound healing after superficial keratectomy in rabbits. *Cornea* (10), 25.
- Alhatem, A., Cavalcanti, B., Hamrah, P., 2012. Vivo confocal microscopy in dry eye disease and related conditions. *Semin. Ophthalmol.* 27 (5–6), 138–148.
- Ali, T.K., Gibbons, A., Cartes, C., et al., 2018. Use of autologous serum tears for the treatment of ocular surface disease from patients with systemic autoimmune diseases. *Am. J. Ophthalmol.* 189, 65–70.
- Attal, N., Filiatreau, G., Perrot, S., Jazat, F., Di Giamberardino, L., Guilbaud, G., 1994. Behavioural pain-related disorders and contribution of the saphenous nerve in crush and chronic constriction injury of the rat sciatic nerve. *Pain* 59 (2), 301–312.
- Aykut, V., Elbay, A., Esen, F., Kocaman, G., 2018a. Savran elibol E, oguz H. Patterns of altered corneal sensation in patients with chronic migraine. *Eye Contact Lens* 44.
- Aykut, V., Elbay, A., Çigdem Uçar, I., et al., 2018b. Corneal sensitivity and subjective complaints of ocular pain in patients with fibromyalgia. *Eye* 32 (4), 763–767.
- Azuara-Blanco, A., Pillai, C.T., Dua, H.S., 1999. Amniotic membrane transplantation for ocular surface reconstruction. *Br. J. Ophthalmol.* 83 (4), 399.
- Balal, S., Nitiapapand, R., Hassan, A., et al., 2020. Finger-prick autologous blood in the treatment of persistent corneal epithelial defects. *Cornea* (5), 39.
- Baratz, K.H., Nau, C.B., Winter, E.J., et al., 2006. Effects of glaucoma medications on corneal endothelium, keratocytes, and subbasal nerves among participants in the ocular hypertension treatment study. *Cornea* (9), 25.
- Bates, B.D., Mitchell, K., Keller, J.M., et al., 2010. Prolonged analgesic response of cornea to topical resiniferatoxin, a potent TRPV1 agonist. *Pain* 149 (3), 522–528.
- Belmonte, C., Gallar, J., Lopez-Briones, L.G., Pozo, M.A., 1994. Polymodality in Nociceptive Neurons: Experimental Models of Chemotransduction. In: *Cellular Mechanisms of Sensory Processing*, pp. 87–117. Berlin, Heidelberg.
- Benítez-del-Castillo, J.M., Acosta, M.C., Wassfi, M.A., et al., 2007. Relation between corneal innervation with confocal microscopy and corneal sensitivity with noncontact esthesiometry in patients with dry eye. *Invest. Ophthalmol. Vis. Sci.* 48 (1), 173–181.
- Bereiter, D.A., Rahman, M., Thompson, R., Stephenson, P., Saito, H., 2018. TRPV1 and TRPM8 channels and nocifensive behavior in a rat model for dry eye. *Invest. Ophthalmol. Vis. Sci.* 59 (8), 3739–3746.

- Bessou, P., Perl, E.R., 1969. Response of cutaneous sensory units with unmyelinated fibers to noxious stimuli. *J. Neurophysiol.* 32 (6), 1025–1043.
- Bonini, S., Lambiase, A., Rama, P., et al., 2018. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis. *Ophthalmology*. 125 (9), 1332–1343.
- Bourcier, T., Acosta, M.C., Borderie, V., et al., 2005. Decreased corneal sensitivity in patients with dry eye. *Invest. Ophthalmol. Vis. Sci.* 46 (7), 2341–2345.
- Bunya, V.Y., Langelier, N., Chen, S., Pistilli, M., Vivino, F.B., Massaro-Giordano, G., 2013. Tear osmolarity in Sjögren syndrome. *Cornea* 32 (7), 922–927.
- Cavalcanti, B.M., Cruzat, A., Sahin, A., Pavan-Langston, D., Samayoa, E., Hamrah, P., 2018. In vivo confocal microscopy detects bilateral changes of corneal immune cells and nerves in unilateral herpes zoster ophthalmicus. *Ocul. Surf.* 16 (1), 101–111.
- Chalmers, R.L., Begley, C.G., Caffery, B., 2010. Validation of the 5-Item Dry Eye Questionnaire (DEQ-5): discrimination across self-assessed severity and aqueous tear deficient dry eye diagnoses. *Contact Lens Anterior Eye* 33 (2), 55–60.
- Chao, C., Stapleton, F., Badarudin, E., Golebiowski, B., 2015. Ocular surface sensitivity repeatability with cochet-bonnet esthesiometer. *Optom. Vis. Sci.* (2), 92.
- Chen, W., Zhang, Z., Hu, J., et al., 2013. Changes in rabbit corneal innervation induced by the topical application of benzalkonium chloride. *Cornea* 32.
- Chen, X., Sun, W., Gianaris, N.G., et al., 2014. Furanocoumarins are a novel class of modulators for the transient receptor potential vanilloid type 1 (TRPV1) channel. *J. Biol. Chem.* 289 (14), 9600–9610.
- Choi, E.Y., 2015. Kim T-i, seo KY, kim EK, lee HKJJoTKOS. Corneal Microstructural Changes in Non-Sjögren Dry Eye Using Confocal Microscopy: Clinical Correlation 56, 680–686.
- Cortina, M., He, J., Li, N., Bazan, N., Bazan, H., 2011. Recovery of corneal sensitivity, calcitonin gene-related peptide-positive nerves, and increased wound healing induced by pigment epithelial-derived factor plus docosahexaenoic acid after experimental surgery. *Arch. Ophthalmol.* 130, 76–83.
- Cosar, C.B., Cohen, E.J., Rapuano, C.J., et al., 2001. Tarsorrhaphy: clinical experience from a cornea practice. *Cornea* (8), 20.
- Craig, J.P., Nichols, K.K., Akpek, E.K., et al., 2017. TFOS DEWS II definition and classification report. *Ocul. Surf.* 15 (3), 276–283.
- Culver, D.A., Dahan, A., Bajorunas, D., et al., 2017. Cibinetide improves corneal nerve fiber abundance in patients with sarcoidosis-associated small nerve fiber loss and neuropathic pain. *Invest. Ophthalmol. Vis. Sci.* (6), 58. BIO52-BIO60.
- Deeks, E.D., Lamb, Y.N., 2020. Cenegeerin: a review in neurotrophic keratitis. *Drugs* 80 (5), 489–494.
- del Castillo JMBt, Wasfy MAS., Fernandez, C., Garcia-Sanchez, J., 2004. An in vivo confocal masked study on corneal epithelium and subbasal nerves in patients with dry eye. *Invest. Ophthalmol. Vis. Sci.* 45 (9), 3030–3035.
- DeMill, D.L., Hussain, M., Pop-Busui, R., Shtein, R.M., 2016. Ocular surface disease in patients with diabetic peripheral neuropathy. *Br. J. Ophthalmol.* 100 (7), 924.
- Denoyer, A., Landman, E., Trinh, L., Faure, J.-F., Auclin, F., Baudouin, C., 2015. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. *Ophthalmology*. 122 (4), 669–676.
- Deveci, H., Kobak, S., 2014. The efficacy of topical 0.05 % cyclosporine A in patients with dry eye disease associated with Sjögren's syndrome. *Int. Ophthalmol.* 34 (5), 1043–1048.
- Diel, R.J., Hwang, J., Kroeger, Z.A., et al., 2019a. Photophobia and sensations of dryness in patients with migraine occur independent of baseline tear volume and improve following botulinum toxin A injections. *Br. J. Ophthalmol.* 103 (8), 1024.
- Diel, R.J., Hwang, J., Kroeger, Z.A., et al., 2019b. Photophobia and sensations of dryness in patients with migraine occur independent of baseline tear volume and improve following botulinum toxin A injections. *Br. J. Ophthalmol.* 103 (8), 1024–1029.
- Digre, K.B., Brennan, K.C., 2012. Shedding light on photophobia. *J. Neuro Ophthalmol.* 32 (1), 68–81.
- Dubocovich, M.L., Markowska, M., 2005. Functional MT1 and MT2 melatonin receptors in mammals. *Endocrine* 27 (2), 101–110.
- Dursun, D., Kim, M.C., Solomon, A., Pflugfelder, S.C., 2001. Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids. *Am. J. Ophthalmol.* 132 (1), 8–13.
- Erie, J.C., McLaren, J.W., Hodge, D.O., Bourne, W.M., 2005. The effect of age on the corneal subbasal nerve plexus. *Cornea* (6), 24.
- Erie, J.C., McLaren, J.W., Patel, S.V., 2009. Confocal microscopy in ophthalmology. *Am. J. Ophthalmol.* 148 (5), 639–646.
- Erkan Turan, K., Kocabeyoglu, S., Unal-Cevik, I., Bezci, F., Akinci, A., Irkeç, M., 2018. Ocular surface alterations in the context of corneal in vivo confocal microscopic characteristics in patients with fibromyalgia. *Cornea* (2), 37.
- Farhangi, M., Feuer, W., Galor, A., et al., 2019. Modification of the neuropathic pain symptom inventory for use in eye pain (NPSI-eye). *Pain* 160 (7), 1541–1550.
- Farhangi, M., Diel, R.J., Buse, D.C., et al., 2020. Individuals with migraine have a different dry eye symptom profile than individuals without migraine. *Br. J. Ophthalmol.* 104 (2), 260–264.
- Fung, S.S.M., Catapano, J., Elbaz, U., Zuker, R.M., Borschel, G.H., Ali, A., 2018. Vivo confocal microscopy reveals corneal reinnervation after treatment of neurotrophic keratopathy with corneal neurotization. *Cornea* (1), 37.
- Gallar, J., Pozo, M.A., Rebollo, I., Belmonte, C., 1990. Effects of capsaicin on corneal wound healing. *Invest. Ophthalmol. Vis. Sci.* 31 (10), 1968–1974.
- Gallar, J., Morales, C., Freire, V., Acosta, M.C., Belmonte, C., Duran, J.A., 2009. Decreased Corneal Sensitivity, Production, Tear, 2009. In fibromyalgia. *Invest. Ophthalmol. Vis. Sci.* 50 (9), 4129–4134.
- Galor, A., Feuer, W., Lee, D.J., Florez, H., Venincasa, V.D., Perez, V.L., 2013. Ocular surface parameters in older male veterans. *Invest. Ophthalmol. Vis. Sci.* 54 (2), 1426–1433.
- Galor, A., Zlotcavitch, L., Walter, S.D., et al., 2015. Dry eye symptom severity and persistence are associated with symptoms of neuropathic pain. *Br. J. Ophthalmol.* 99 (5), 665–668.
- Galor, A., Moein, H.R., Lee, C., et al., 2018. Neuropathic pain and dry eye. *Ocul. Surf.* 16 (1), 31–44.
- Gatziofias, Z., Labiris, G., Hafezi, F., et al., 2014. Corneal sensitivity and morphology of the corneal subbasal nerve plexus in primary congenital glaucoma. *Eye* 28 (4), 466–471.
- Gavva, N.R., Tamir, R., Qu, Y., et al., 2005. AMG 9810 [(E)-3-(4-t-butylphenyl)-N-(2,3-dihydrobenzo[b][1,4] dioxin-6-yl)acrylamide], a novel vanilloid receptor 1 (TRPV1) antagonist with antihyperalgesic properties. *J. Pharmacol. Exp. Therapeut.* 313 (1), 474.
- Giannaccare, G., Pellegrini, M., Sebastiani, S., Moscardelli, F., Versura, P., Campos, E.C., 2019. In vivo confocal microscopy morphometric analysis of corneal subbasal nerve plexus in dry eye disease using newly developed fully automated system. *Graefes Arch. Clin. Exp. Ophthalmol.* 257 (3), 583–589.
- Golebiowski, B., Papas, E., Stapleton, F., 2011. Assessing the sensory function of the ocular surface: implications of use of a non-contact air jet aesthesiometer versus the Cochet-Bonnet aesthesiometer. *Exp. Eye Res.* 92 (5), 408–413.
- Hamrah, P., Cruzat, A., Dastjerdi, M.H., et al., 2010. Corneal sensation and subbasal nerve alterations in patients with herpes simplex keratitis: an in vivo confocal microscopy study. *Ophthalmology*. 117 (10), 1930–1936.
- Hamrah, P., Sahin, A., Dastjerdi, M.H., et al., 2012. Cellular changes of the corneal epithelium and stroma in herpes simplex keratitis: an in vivo confocal microscopy study. *Ophthalmology*. 119 (9), 1791–1797.
- Hamrah, P., Cruzat, A., Dastjerdi, M.H., et al., 2013. Unilateral herpes zoster ophthalmicus results in bilateral corneal nerve alteration: an in vivo confocal microscopy study. *Ophthalmology*. 120 (1), 40–47.
- He, J., Ogawa, Y., Mukai, S., et al., 2017. Vivo confocal microscopy evaluation of ocular surface with graft-versus-host disease-related dry eye disease. *Sci. Rep.* 7 (1), 10720.
- Heiligenhaus, A., Bauer, D., Meller, D., Steuhl, K.-P., Tseng, S.C.G., 2001. Improvement of HSV-1 necrotizing keratitis with amniotic membrane transplantation. *Invest. Ophthalmol. Vis. Sci.* 42 (9), 1969–1974.
- Hua, X.Y., Saria, A., Gamse, R., Theodorsson-Norheim, E., Brodin, E., Lundberg, J.M., 1986. Capsaicin induced release of multiple tachykinins (substance P, neurokinin A and eledoisin-like material) from Guinea-pig spinal cord and ureter. *Neuroscience* 19 (1), 313–319.
- Hussain, M., Raval, N., Hamid, M., Williams, D.A., Clauw, D.J., Shtein, R.M., 2012. Vivo corneal confocal microscopy and clinical correlations in fibromyalgia. *Invest. Ophthalmol. Vis. Sci.* 53 (14), 85.
- IASP terminology, January 2019. Accessed. <http://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698>.
- Jacobs, D.S., 2017. Diagnosis and treatment of ocular pain: the ophthalmologist's perspective. *Current Ophthalmology Reports*. 5 (4), 271–275.
- Jalbert, I., Stapleton, F., Papas, E., Sweeney, D.F., Coroneo, M., 2003. In vivo confocal microscopy of the human cornea. *Br. J. Ophthalmol.* 87 (2), 225.
- Jeng, B.H., Dupps Jr., W.J., 2009. Autologous serum 50% eyedrops in the treatment of persistent corneal epithelial defects. *Cornea* (10), 28.
- Julian, T., Syeed, R., Glasgow, N., Angelopoulou, E., Zis, P.J.N., 2020. B12 as a Treatment for Peripheral Neuropathic Pain: Syst. Rev. 12.
- Kalagara, J.P., Galor, A., Levitt, R.C., et al., 2017. Characteristics of ocular pain complaints in patients with idiopathic dry eye symptoms. *Eye Contact Lens* 43 (3), 192–198.
- Kalteniece, A., Ferdousi, M., Petropoulos, I., et al., 2018. Greater corneal nerve loss at the inferior whorl is related to the presence of diabetic neuropathy and painful diabetic neuropathy. *Sci. Rep.* 8 (1), 3283.
- Khamar, P., Nair, A.P., Shetty, R., et al., 2019. Dysregulated tear fluid nociception-associated factors, corneal dendritic cell density, and vitamin D levels in evaporative dry eye. *Invest. Ophthalmol. Vis. Sci.* 60 (7), 2532–2542.
- Kheirkhah, A., Dohlman, T.H., Amparo, F., et al., 2015. Effects of corneal nerve density on the response to treatment in dry eye disease. *Ophthalmology*. 122 (4), 662–668.
- Kinard, K.L., Smith, A.G., Singleton, J.R., et al., 2015. Chronic migraine is associated with reduced corneal nerve fiber density and symptoms of dry eye. *Headache J. Head Face Pain* 55 (4), 543–549.
- Kloosterboer, A., Dermer, H.L., Galor, A., 2019. Diagnostic tests in dry eye. *Expt Rev. Ophthalmol.* 14 (4–5), 237–246.
- Kocabeyoglu, S., Mocan, M.C., Cevik, Y., Irkeç, M., Ocular Surface Alterations, In Vivo Confocal, 2015. Microscopic features of corneas in patients with newly diagnosed graves' disease. *Cornea* (7), 34.
- Kolseth, C.M., Charlson, E.S., Kossler, A.L., 2020. Corneal neurotization: a surgical treatment for neurotrophic keratopathy. *J. Neuro Ophthalmol.* (2), 40.
- Kruse, F.E., Rohrschneider, K., Völcker, H.E., 1999. Multilayer amniotic membrane transplantation for reconstruction of deep corneal ulcers. *Ophthalmology*. 106 (8), 1504–1511.
- Labbé, A., Alalwani, H., Van Went, C., Brasnu, E., Georgescu, D., Baudouin, C., 2012. The relationship between subbasal nerve morphology and corneal sensation in ocular surface disease. *Invest. Ophthalmol. Vis. Sci.* 53 (8), 4926–4931.
- Labbé, A., Liang, Q., Wang, Z., et al., 2013. Corneal nerve structure and function in patients with non-sjögren dry eye: clinical correlations. *Invest. Ophthalmol. Vis. Sci.* 54 (8), 5144–5150.
- Lamb, S.E., Hansen, Z., Lall, R., et al., 2010. Group cognitive behavioural treatment for low-back pain in primary care: a randomised controlled trial and cost-effectiveness analysis. *The Lancet*. 375 (9718), 916–923.
- Lambiase, A., Sacchetti, M., Mastropasqua, A., Bonini, S., 2013. Corneal changes in neurosurgically induced neurotrophic keratitis. *JAMA Ophthalmology*. 131 (12), 1547–1553.

- Leonard, B.C., Stewart, K.A., Shaw, G.C., et al., 2019. Comprehensive clinical, diagnostic, and advanced imaging characterization of the ocular surface in spontaneous aqueous deficient dry eye disease in dogs. *Cornea* 38 (12), 1568–1575.
- Levy, O., Labbé, A., Borderie, V., et al., 2017. Increased corneal sub-basal nerve density in patients with Sjögren syndrome treated with topical cyclosporine A. *Clin. Exp. Ophthalmol.* 45 (5), 455–463.
- Liang, Q., Liang, H., Liu, H., Pan, Z., Baudouin, C., Labbé, A., 2016. Ocular surface epithelial thickness evaluation in dry eye patients: clinical correlations. *Journal of Ophthalmology*. 2016, 1628469.
- Lum, E., Murphy, P.J., 2018. Effects of ambient humidity on the Cochet-Bonnet aesthesiometer. *Eye* 32 (10), 1644–1651.
- Marfurt, C.F., Kingsley, R.E., Echtenkamp, S.E., 1989. Sensory and sympathetic innervation of the mammalian cornea. A retrograde tracing study. *Invest. Ophthalmol. Vis. Sci.* 30 (3), 461–472.
- Martone, G., Frezzotti, P., Tosi, G.M., et al., 2009. An in vivo confocal microscopy analysis of effects of topical antiglaucoma therapy with preservative on corneal innervation and morphology. *Am. J. Ophthalmol.* 147 (4), 725–735 e721.
- Mastropasqua, L., Nubile, M., Lanzini, M., Caliendo, R., Dua, H.S., 2019. In vivo microscopic and optical coherence tomography classification of neurotrophic keratopathy. *J. Cell. Physiol.* 234 (5), 6108–6115.
- Mazlin, V., Xiao, P., Dalimier, E., et al., 2018. In vivo high resolution human corneal imaging using full-field optical coherence tomography. *Biomed. Optic Express* 9 (2), 557–568.
- McLachlan, E.M., Jänig, W., Devor, M., Michaelis, M., 1993. Peripheral nerve injury triggers noradrenergic sprouting within dorsal root ganglia. *Nature*. 363 (6429), 543–546.
- Mehra, D., Cohen, N.K., Galor, A., 2020. Ocular surface pain: a narrative review. *Ophthalmol Ther.* 9 (3), 1–21.
- Mocan, M.C., Durukan, I., Irkeç, M., Orhan, M., 2006. Morphologic alterations of both the stromal and subbasal nerves in the corneas of patients with diabetes. *Cornea* (7), 25.
- Moein, H.-R., Kheirkhah, A., Muller, R.T., Cruzat, A.C., Pavan-Langston, D., Hamrah, P., 2018. Corneal nerve regeneration after herpes simplex keratitis: a longitudinal in vivo confocal microscopy study. *Ocul. Surf.* 16 (2), 218–225.
- Müller, L.J., Pels, L., Vrensen, G.F., 1996. Ultrastructural organization of human corneal nerves. *Invest. Ophthalmol. Vis. Sci.* 37 (4), 476–488.
- Müller, L.J., Marfurt, C.F., Kruse, F., Tervo, T.M.T., 2003. Corneal nerves: structure, contents and function. *Exp. Eye Res.* 76 (5), 521–542.
- Müller, R.T., Abedi, F., Cruzat, A., et al., 2015a. Degeneration and regeneration of subbasal corneal nerves after infectious keratitis: a longitudinal in vivo confocal microscopy study. *Ophthalmology*. 122 (11), 2200–2209.
- Müller, R.T., Pourmirzaie, R., Pavan-Langston, D., et al., 2015b. Vivo confocal microscopy demonstrates bilateral loss of endothelial cells in unilateral herpes simplex keratitis. *Invest. Ophthalmol. Vis. Sci.* 56 (8), 4899–4906.
- Murphy, P.J., Lawrenson, J.G., Patel, S., Marshall, J., 1998. Reliability of the non-contact corneal aesthesiometer and its comparison with the cochet-bonnet aesthesiometer. *Ophthalmic Physiol. Optic.* 18 (6), 532–539.
- Niederer, R.L., Perumal, D., Sherwin, T., McGhee, C.N.J., 2007. Age-related differences in the normal human cornea: a laser scanning in vivo confocal microscopy study. *Br. J. Ophthalmol.* 91 (9), 1165.
- Noseda, R., Burstein, R., 2011. Advances in understanding the mechanisms of migraine-type photophobia. *Curr. Opin. Neurol.* 24 (3), 197–202.
- Oliveira-Soto, L., Efron, N., 2001. Morphology of corneal nerves using confocal microscopy. *Cornea* (4), 20.
- Oudejans, L., He, X., Nieters, M., Dahan, A., Brines, M., van Velzen, M., 2016. Cornea nerve fiber quantification and construction of phenotypes in patients with fibromyalgia. *Sci. Rep.* 6 (1), 23573.
- Ozmen, M.C., Dieckmann, G., Rashad, R., et al., 2019. Nortriptyline is effective in ameliorating symptoms of neuropathic corneal pain. *Invest. Ophthalmol. Vis. Sci.* 60 (9), 4732.
- Pan, Q., Angelina, A., Marrone, M., Stark, W.J., Akpek, E.K., 2017. Autologous serum eye drops for dry eye. *Cochrane Database Syst. Rev.* (2).
- Panda, A., Pushker, N., Bageshwar, L.M., 1999. Lateral tarsorrhaphy: is it preferable to patching? *Cornea* 18 (3), 299–301.
- Parissi, M., Karanis, G., Randjelovic, S., et al., 2013. Standardized baseline human corneal subbasal nerve density for clinical investigations with laser-scanning in vivo confocal microscopy. *Invest. Ophthalmol. Vis. Sci.* 54 (10), 7091–7102.
- Patel, D.V., McGhee, C.N.J., 2009. In vivo confocal microscopy of human corneal nerves in health, in ocular and systemic disease, and following corneal surgery: a review. *Br. J. Ophthalmol.* 93 (7), 853.
- Patel, D.V., Tavakoli, M., Craig, J.P., Efron, N., McGhee, C.N.J., 2009. Corneal Sensitivity and Slit Scanning In Vivo Confocal Microscopy of the Subbasal Nerve Plexus of the Normal Central and Peripheral Human Cornea. *Cornea* (7), 28.
- Patel, S., Felix, E.R., Levitt, R.C., Sarantopoulos, C.D., Galor, A., 2019. Dysfunctional coping mechanisms contribute to dry eye symptoms. *J. Clin. Med.* (6), 8.
- Perry, H.D., Hodes, L.W., Seedor, J.A., Donnenfeld, E.D., McNamara, T.F., Golub, L.M., 1993. Effect of doxycycline hyclate on corneal epithelial wound healing in the rabbit alkali-burn model. Preliminary observations. *Cornea* 12 (5), 379–382.
- Petroll, W.M., Robertson, D.M., 2015. Vivo confocal microscopy of the cornea: new developments in image acquisition, reconstruction, and analysis using the HRT-rostock corneal Module. *Ocul. Surf.* 13 (3), 187–203.
- Petropoulos, I.N., Alam, U., Fadavi, H., et al., 2013. Corneal nerve loss detected with corneal confocal microscopy is symmetrical and related to the severity of diabetic polyneuropathy. *Diabetes Care* 36 (11), 3646.
- Pflugfelder, S.C., Massaro-Giordano, M., Perez, V.L., et al., 2020. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial. *Ophthalmology*. 127 (1), 14–26.
- Prasad, S., 2014. Diagnostic Neuroimaging in Neuro-ophthalmic Disorders 20 (4), 1023–1062.
- Rahman, E.Z., Lam, P.K., Chu, C.-K., Moore, Q., Pflugfelder, S.C., 2015. Corneal sensitivity in tear dysfunction and its correlation with clinical parameters and blink rate. *Am. J. Ophthalmol.* 160 (5), 858–866.
- Ramírez, M., Martínez-Martínez, L.-A., Hernández-Quintela, E., Velasco-Casapía, J., Vargas, A., Martínez-Lavín, M., 2015. Small fiber neuropathy in women with fibromyalgia. An in vivo assessment using corneal confocal bio-microscopy. *Semin. Arthritis Rheum.* 45 (2), 214–219.
- Ranno, S., Fogagnolo, P., Rossetti, L., Orzalesi, N., Nucci, P., 2011. Changes in corneal parameters at confocal microscopy in treated glaucoma patients. *Clin. Ophthalmol.* 5, 1037–1042.
- Raskin, J., Pritchett, Y.L., Wang, F., et al., 2005. A double-blind, randomized multicenter trial comparing duloxetine with placebo in the management of diabetic peripheral neuropathic pain. *Pain Med.* 6 (5), 346–356.
- Rogell, G.D., 1980. Corneal hypesthesia and retinopathy in diabetes mellitus. *Ophthalmology*. 87 (3), 229–233.
- Rosenberg, M.E., Tervo, T.M.T., Immonen, I.J., 2000. Müller LJ, grönhagen-riska C, vesaluoma MH. Corneal structure and sensitivity in type 1 diabetes mellitus. *Invest. Ophthalmol. Vis. Sci.* 41 (10), 2915–2921.
- Sacchetti, M., Lambiase, A., 2014a. Diagnosis and management of neurotrophic keratitis. *Clin. Ophthalmol.* 8, 571–579.
- Sacchetti, M., Lambiase, A., 2014b. Diagnosis and management of neurotrophic keratitis. *Clin. Ophthalmol.* 8, 571–579.
- Sade De Paiva, C., Pflugfelder, S.C., 2004. Corneal epitheliopathy of dry eye induces hyperesthesia to mechanical air jet stimulation. *Am. J. Ophthalmol.* 137 (1), 109–115.
- Saini, M., Vanathi, M., Dada, T., Agarwal, T., Dhiman, R., Khokhar, S., 2017. Ocular surface evaluation in eyes with chronic glaucoma on long term topical antiglaucoma therapy. *Int. J. Ophthalmol.* 10 (6), 931–938.
- Saito, J., Enoki, M., Hara, M., Morishige, N., 2003. Chikama T-i, nishida T. Correlation of corneal sensation, but not of basal or reflex tear secretion, with the stage of diabetic retinopathy. *Cornea* (1), 22.
- Sall, K., Stevenson, O.D., Mundorf, T.K., Reis, B.L., 2000. Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. *Reprint requests to: Linda Lewis, 575 Anton Blvd. Suite 900 Ophthalmology. 107 (4), 631–639. Costa Mesa, CA 92626.*
- Sarkar, J., Chaudhary, S., Namavari, A., et al., 2012. Corneal neurotoxicity due to topical benzalkonium chloride. *Invest. Ophthalmol. Vis. Sci.* 53 (4), 1792–1802.
- Schiffman, R.M., Christianson, M.D., Jacobsen, G., Hirsch, J.D., Reis, B.L., 2000. Reliability and validity of the ocular surface disease index. *Arch. Ophthalmol.* 118 (5), 615–621.
- Shaheen, B.S., Bakir, M., Jain, S., 2014. Corneal nerves in health and disease. *Surv. Ophthalmol.* 59 (3), 263–285.
- Sheha, H., Tighe, S., Hashem, O., Hayashida, Y., 2019. Update on cenegermin eye drops in the treatment of neurotrophic keratitis. *Clin. Ophthalmol.* 13, 1973–1980.
- Shen, F., Dong, X., Zhou, X., Yan, L., Wan, Q., 2019. Corneal subbasal nerve plexus changes in patients with episodic migraine: an in vivo confocal microscopy study. *J. Pain Res.* 12, 1489–1495.
- Shetty, R., Sethu, S., Deshmukh, R., et al., 2016. Corneal dendritic cell density is associated with subbasal nerve plexus features, ocular surface disease index, and serum vitamin D in evaporative dry eye disease. *BioMed Res. Int.* 2016, 4369750.
- Shetty, R., Deshmukh, R., Shroff, R., Dedhiya, C., Jayadev, C., 2018. Subbasal nerve plexus changes in chronic migraine. *Cornea* (1), 37.
- Simsek, C., Kojima, T., Dogru, M., Tsubota, K., 2018. Alterations of murine subbasal corneal nerves after environmental dry eye stress. *Invest. Ophthalmol. Vis. Sci.* 59 (5), 1986–1995.
- Simsek, C., Kojima, T., Nagata, T., Dogru, M., Tsubota, K., 2019. Changes in murine subbasal corneal nerves after scopolamine-induced dry eye stress exposure. *Invest. Ophthalmol. Vis. Sci.* 60 (2), 615–623.
- Sivanesan, E., Levitt, R.C., Sarantopoulos, C.D., Patin, D., Galor, A., 2018. Noninvasive electrical stimulation for the treatment of chronic ocular pain and photophobia. *Neuromodulation: Technology at the Neural Interface*. 21 (8), 727–734.
- Small, L.R., Galor, A., Felix, E.R., Horn, D.B., Levitt, R.C., Sarantopoulos, C.D., Oral Gabapentinoids, Nerve, 2020. Blocks for the treatment of chronic ocular pain. *Eye Contact Lens* (3), 46.
- Spierer, O., Felix, E.R., McClellan, A.L., et al., 2016. Corneal mechanical thresholds negatively associate with dry eye and ocular pain symptoms. *Invest. Ophthalmol. Vis. Sci.* 57 (2), 617–625.
- Stapleton, F., Tan, M.E., Papas, E.B., et al., 2004. Corneal and conjunctival sensitivity to air stimuli. *Br. J. Ophthalmol.* 88 (12), 1547.
- Steger, B., Speicher, L., Philipp, W., Bechrakis, N.E., 2015. In vivo confocal microscopic characterisation of the cornea in chronic graft-versus-host disease related severe dry eye disease. *Br. J. Ophthalmol.* 99 (2), 160.
- Steff, M.A., Tadvalkar, G., Hakh, R., Pal-Ghosh, S., 2017. Corneal epithelial cells function as surrogate Schwann cells for their sensory nerves. *Glia* 65 (6), 851–863.
- Streilein, J.W., Dana, M.R., Ksander, B.R., 1997. Immunity causing blindness: five different paths to herpes stromal keratitis. *Immunol. Today* 18 (9), 443–449.
- Tavakoli, M., Boulton, A.J.M., Efron, N., Malik, R.A., 2011. Increased Langerhan cell density and corneal nerve damage in diabetic patients: role of immune mechanisms in human diabetic neuropathy. *Contact Lens Anterior Eye* 34 (1), 7–11.
- Tepelus, T.C., Chiu, G.B., Maram, J., et al., 2017a. Corneal features in ocular graft-versus-host disease by in vivo confocal microscopy. *Graefes Arch. Clin. Exp. Ophthalmol.* 255 (12), 2389–2397.

- Tepelus, T.C., Chiu, G.B., Huang, J., et al., 2017b. Correlation between corneal innervation and inflammation evaluated with confocal microscopy and symptomatology in patients with dry eye syndromes: a preliminary study. *Graefes Arch. Clin. Exp. Ophthalmol.* 255 (9), 1771–1778.
- Terzis, J.K., Dryer, M.M., Bodner, B.I., 2009. Corneal neurotization: a novel solution to neurotrophic keratopathy. *Plast. Reconstr. Surg.* (1), 123.
- Thapa, D., Cairns, E.A., Szczesniak, A.M., et al., 2020. Ligands reduce ocular pain and inflammation. *Molecules (basel, Switzerland). Allosteric Cannabinoid Receptor 1* (2), 25. CB1.
- Tsubota, K., Goto, E., Shimmura, S., Shimazaki, J., 1999. Treatment of persistent corneal epithelial defect by autologous serum application. *Ophthalmology.* 106 (10), 1984–1989.
- Tuisku, I.S., Konttinen, Y.T., Konttinen, L.M., Tervo, T.M., 2008. Alterations in corneal sensitivity and nerve morphology in patients with primary Sjögren's syndrome. *Exp. Eye Res.* 86 (6), 879–885.
- Ueno, H., Hattori, T., Kumagai, Y., Suzuki, N., Ueno, S., Takagi, H., 2014. Alterations in the corneal nerve and stem/progenitor cells in diabetes: preventive effects of insulin-like growth factor-1 treatment. *International Journal of Endocrinology.* 2014, 312401.
- Van Went, C., Alalwani, H., Brasnu, E., et al., 2011. [Corneal sensitivity in patients treated medically for glaucoma or ocular hypertension]. *J. Fr. Ophthalmol.* 34 (10), 684–690.
- Venkatachalam, K., Montell, C., 2007. TRP channels. *Annu. Rev. Biochem.* 76 (1), 387–417.
- Venkateswaran, N., Hwang, J., Rong, A., et al., 2019. Onabotulinum toxin A improves photophobia and sensations of dryness independent of ocular surface parameters. *Invest. Ophthalmol. Vis. Sci.* 60 (9), 6757.
- Versura, P., Giannaccare, G., Pellegrini, M., Sebastiani, S., Campos, E.C., 2018. Neurotrophic keratitis: current challenges and future prospects. *Eye Brain* 10, 37–45.
- Villani, E., Galimberti, D., Viola, F., Mapelli, C., Ratiglia, R., 2007. The cornea in Sjögren's syndrome: an in vivo confocal study. *Invest. Ophthalmol. Vis. Sci.* 48 (5), 2017–2022.
- Villani, E., Viola, F., Sala, R., et al., 2010. Corneal involvement in graves' orbitopathy: an in vivo confocal study. *Invest. Ophthalmol. Vis. Sci.* 51 (9), 4574–4578.
- Villani, E., Magnani, F., Viola, F., et al., 2013. Vivo confocal evaluation of the ocular surface morpho-functional unit in dry eye. *Optom. Vis. Sci.* (6), 90.
- Vitali, C., Del Papa, N., 2015. Pain in primary Sjögren's syndrome. *Best Pract. Res. Clin. Rheumatol.* 29 (1), 63–70.
- Wang, Y., Ogawa, Y., Dogru, M., et al., 2010. Baseline profiles of ocular surface and tear dynamics after allogeneic hematopoietic stem cell transplantation in patients with or without chronic GVHD-related dry eye. *Bone Marrow Transplant.* 45 (6), 1077–1083.
- Wu, L.-Q., Mou, P., Chen, Z.-Y., et al., 2019. Altered corneal nerves in Chinese thyroid-associated ophthalmopathy patients observed by in vivo confocal microscopy. *Med. Sci. Mon. Int. Med. J. Exp. Clin. Res.* 25, 1024–1031.
- Xu, K.-P., Yagi, Y., Tsubota, K., 1996. Decrease in corneal sensitivity and change in tear function in dry eye. *Cornea* (3), 15.
- Yamaguchi, T., Turhan, A., Harris, D.L., et al., 2013. Bilateral nerve alterations in a unilateral experimental neurotrophic keratopathy model: a lateral conjunctival approach for trigeminal axotomy. *PLoS One* 8 (8), e70908.
- Yang, A.Y., Chow, J., Liu, J., Corneal Innervation, 2018. Sensation: the eye and beyond. *Yale J. Biol. Med.* 91 (1), 13–21.
- Zayan, K., Aggarwal, S., Felix, E., Levitt, R., Sarantopoulos, K., Galor, A., 2020. Transcutaneous electrical nerve stimulation for the long-term treatment of ocular pain. *Neuromodulation* 23 (6), 871–877.
- Zhang, M., Chen, J., Luo, L., Xiao, Q., Sun, M., Liu, Z., 2005. Altered corneal nerves in aqueous tear deficiency viewed by in vivo confocal microscopy. *Cornea* (7), 24.
- Kim JS, Rafailov L, Leyngold IM, 2020. Corneal neurotization for postherpetic neurotrophic keratopathy: initial experience and clinical outcomes. *Ophthalmic Plastic and Reconstructive Surgery.* Publish Ahead of Print (April 23, 2020). Doi: 10.1097/IOP.0000000000001676.