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TITLE: Automated Ultrasound Technology to Diagnose Traumatic Retinal Detachment

PRINCIPAL INVESTIGATOR: Dr. Srikar Adhikari, M.D

CONTRACTING ORGANIZATION: University of Arizona, Tucson

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6. AUTHOR(S)

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Our objective is to develop and validate a prototype mobile AI-enabled software platform that can accurately detect sonographic signs of retinal detachment and support a regulatory filing with the Food and Drug Administration. Our goal is to make the deep-learning ultrasound algorithms commercially available for use in the clinical environment to rapidly detect retinal detachment along with the status of macula to direct appropriate therapy. We hypothesized that machine learning algorithms will be reproducible and will have accurate diagnostic capability to detect findings specific to retinal detachment and macular involvement on ultrasound images. To date, we have successfully extracted, labeled, and curated the ocular image datasets. The training dataset has been utilized to train the algorithm, with the initial focus on learning normal ocular sonographic anatomy. Our next steps will involve refining the architecture of the developed network to achieve the best fit for the distribution and validation.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRDC
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
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1. Introduction:

Title: Automated Ultrasound Technology Translation to Diagnose Traumatic Retinal Detachment

We proposed to develop artificial intelligence (AI)-enabled mobile diagnostics by training and validating a machine learning powered platform for ocular ultrasound to detect traumatic retinal detachment. Our objective is to develop and validate a prototype mobile AI-enabled software platform that can accurately detect sonographic signs of retinal detachment and support a regulatory filing with the Food and Drug Administration. Our goal is to make the deep-learning ultrasound algorithms commercially available for use in the clinical environment to rapidly detect retinal detachment along with the status of macula to direct appropriate therapy. We hypothesized that machine learning algorithms will be reproducible and will have accurate diagnostic capability to detect findings specific to retinal detachment and macular involvement on ultrasound images. To test this hypothesis, we proposed the following specific aims:

Aim 1. Develop and validate a deep-learning algorithm for the detection of retinal detachment using explicit sonographic signs of retinal detachment and implicit image content representations.

Aim 2. Develop and validate a multi-agent reinforcement-learning algorithm for discerning macular status (macula-on or macula-off) in the ocular ultrasound images with retinal detachment.

2. Keywords

Retinal detachment; vitreous detachment; macula; ocular ultrasound; artificial intelligence; deep-learning algorithm; machine learning; reinforcement-learning; convolutional neural networks

3. Accomplishments

Our major goal for this project period was to develop and validate a deep-learning algorithm for the detection of retinal detachment using explicit sonographic signs and implicit image content representations.

Major Task 1: Obtain local Institutional Review Board (IRB)/ United States Army Medical Research and Material Command (USAMRMC) Human Research Protection Office (HRPO) approval

Proposed timeline for this major task-1-2 months.

This Major Task was accomplished within the proposed timeframe.

Subtask 1: Meetings with OSU team/refine protocol

This Subtask was completed within the proposed timeframe.

Subtask 2: Submit documents for local IRB and USAMRMC HRPO review

This Subtask was completed within the proposed timeframe.

Milestones Achieved: IRB/HRPO approval

Major Task 2: Develop and validate deep learning algorithms

Proposed Timeline for this major task-4-12 Months.

Subtask 1: Phase 1-Qpath ultrasound image data access/curation/transfer

Proposed Timeline for this subtask was 1-2 months.

This Subtask was completed within the proposed timeframe.

We built a robust ocular ultrasound image dataset to be used for both Aims. **Data collection:** Qpath ultrasound image archiving database was queried for ocular ultrasound examinations performed between July 2011-June 2022, and the PI extracted images in MP4 format (separating out videos). All Protected Health Information was removed from the images. **Ground truth/reference standard:** The PI created reference standard labels at the image level. The labeling process included the following: 1) determine retinal detachment or Non- retinal detachment (normal retina or PVD) and 2) determine whether the macula is intact (macula-on vs. macula-off) in retinal detachment. All images were initially classified into two categories by the PI: retinal detachment and Non- retinal detachment. The retinal detachment images were further classified into retinal detachment with intact macula (macula-on) and retinal detachment without intact macula (macula-off). The Non- retinal detachment included images with normal retina or PVD. During data curation, the image quality was graded by the PI. Poor-quality images were excluded from the study. Subsequently the images were assigned into ***training, validation, and test datasets*** (with a ratio of 6:2:2). Images with and without retinal detachment were allocated in a ratio of 5:5 in either the training, validation, or test dataset. The image datasets were shared with the OSU research team via Buckeye Box, a secure infinite cloud storage system.

Subtask 2: Phase 2-training and tuning of algorithm

80% of this subtask is completed.

<u>Training strategy</u>:

Machine learning algorithms typically demand vast datasets, sometimes involving millions of samples, for effective training in their designated tasks. However, when access to extensive data is limited, an alternative approach lies in refining the training strategy itself. In the medical domain, where large datasets are often scarce, we leveraged our available dataset by adopting a training approach reminiscent of how expert physicians train residents (physicians in training) to diagnose retinal detachment. A resident's conventional training entails grasping the anatomical intricacies and geometric cues of a normal eye to discern between normal and abnormal cases. Our machine learning algorithm followed a similar trajectory. For each ultrasound instance, the training goals mirrored the medical trainee's objectives: focusing on the relevant eye portion contributing to accurate diagnosis and utilizing geometrical/anatomical cues. This approach extends to our ML pipeline. A case in point is locating the macula, a critical eye organ, which significantly bolsters precise retinal detachment diagnosis that requires immediate intervention. Our initial training strategy dictates that the machine learning algorithm learns to encode normal eye anatomy from instances of such cases exclusively. After the "encoder" learns the core representation of a normal eye, a discriminator algorithm is trained using the rest of the dataset. This further classifies cases into Normal, Retinal Detachment, and Posterior Vitreous Detachment categories.

Machine learning:

To address the retinal detachment issue, our lab has crafted a machine learning algorithm comprising a crucial encoder network coupled with a subsequent discriminator/classifier component. In essence, the encoder functions by characterizing an ultrasound instance and producing features that encapsulate the anatomical attributes. Subsequently, the discriminator leverages this enriched knowledge to group similar cases within the same category. This is achieved by congregating comparable instances within a shared 'embedding space' while simultaneously pushing dissimilar cases apart. The schematic representation of our ML architecture is depicted in the figure below.

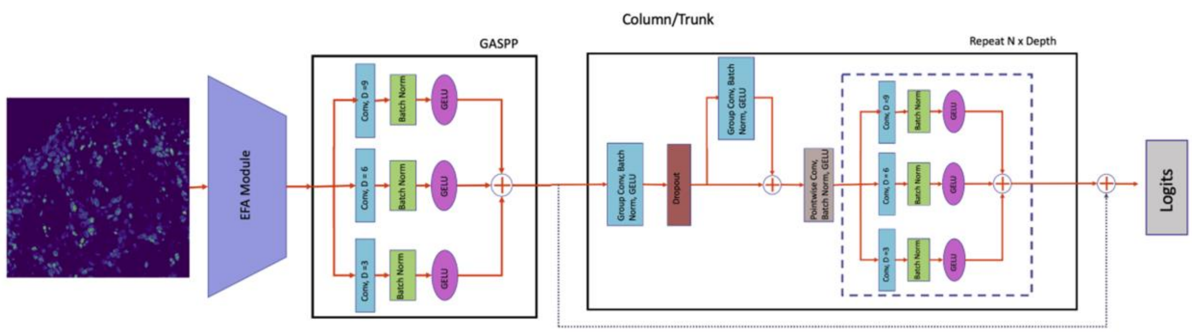

Figure. The architecture of our proposed ML. It contains three major sub modules. Early feature extraction module, Group Atrous Pyramid Pooling module and Column/Trunk module.

When it comes to developing machine learning algorithms within the medical domain, certain precautions become imperative. Most machine learning methods operate optimally when trained on large-scale datasets initially. These methods typically encompass intricate solutions tailored for extensive data. However, given the scarcity of our ultrasound dataset, a paramount concern while formulating our proposed ML algorithm is the necessity to curtail model complexity significantly. This reduction is pursued without compromising the ability to interpret intricate ocular ultrasound instances effectively. We achieved this goal by focusing on the training strategy and consolidating the detection of anatomical and geometrical cues within our proposed ML framework.

Our next step will focus on refining the architecture of the developed network to achieve the best fit for the distribution. Our approach involves implementing a hierarchical learning process, ensuring that each stage of instructing the machine learning pipeline about the eye's anatomy builds upon the foundation laid by the preceding steps.

Subtask 3: Phase 3-testing of algorithm/data analysis

This subtask will be accomplished once the tuning of the algorithm is completed. We anticipate completing this subtask in the next 3-4 months.

Major Task 2: Develop and validate a multi-agent reinforcement-learning algorithm for discerning macular status (macula-on or macula-off)

Proposed Timeline for this task is 12-20 months

Subtask 1: Phase 1-ultrasound image data curation/transfer

Proposed Timeline for this task is 12-14 months.

This Subtask was completed ahead of the proposed timeframe.

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

Nothing to Report.

How were the results disseminated to communities of interest?

Nothing to Report.

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

-Complete the training and tuning of algorithm followed by testing of algorithm/data analysis in the next 3-4 months (by December 2023)

-Scaling up the algorithm to detect Macular status followed by testing of algorithm/data analysis at the end of 9 months (by May 2024)

-Data analysis and dissemination by August 2024

4. Impact

Nothing to Report.

5. Changes/Problems

Nothing to Report.

6. **Products**

Nothing to Report.

7. Participants & Other Collaborating Organizations

- **What individuals have worked on the project?**

Name:	Srikar Adhikari
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	*https://orcid.org/0000-0003-3196-1851*
Nearest person	2

month worked:	
Contribution to Project:	*Dr. Adhikari assumed comprehensive administration and project oversight roles. He managed the IRB submission, implemented the study protocol, facilitated data collection, and diligently monitored study progress. He created reference standard labels at the image level. His responsibilities extended to the extraction, review, classification, and categorization of ocular ultrasound images from the extensive database. Leveraging his expertise, he played a pivotal role in the development of machine learning ocular ultrasound algorithms.*
Funding Support:	N/A

Name:	Alper Yilmaz
Project Role:	Subaward PI
Researcher Identifier (e.g. ORCID ID):	https://scholar.google.com/citations?user=MeQC1XYAAAAJ&hl=en Alper Yilmaz Professor, The Ohio State University - Cited by 13,138 - Biomimetic Navigation - Deep learning - Computer Vision - Photogrammetry scholar.google.com
Nearest person month worked:	1
Contribution to Project:	*Dr. Yilmaz mentored the Graduate Research Associate, co-designed neural network model and worked with PI on data curation and protocol.*
Funding Support:	N/A

Name:	Pouyan Boreshnavard
Project Role:	Graduate Research Associate
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	6
Contribution to Project:	*Pouyan designed, coded the neural network model, and generated the training scheme.*
Funding Support:	N/A

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

- **Srikar Adhikari**-New Active support:
  Grant ID: 1R21EB030677-01A1
  Automated Sonographic Detection of Pulmonary Embolism Using Machine Learning Algorithm
  Supporting Agency: NIBIB
  Role: PI
  Effort: 1.89 person months

- **Elaine Situ-LaCasse**-New Active support:
  Grant ID: 1R21EB030677-01A1
  Automated Sonographic Detection of Pulmonary Embolism Using Machine Learning Algorithm
  Supporting Agency: NIBIB
  Role: Co-I
  Effort: 0.52 person months

- **Adrienne Yarnish**-New Active support:
  Grant ID: 1R21EB030677-01A1
  Automated Sonographic Detection of Pulmonary Embolism Using Machine Learning Algorithm
  Supporting Agency: NIBIB
  Role: Co-I
  Effort: 0.52 person months

- **Josie Acuna**-New Active support:
  Grant ID: 1R21EB030677-01A1
  Automated Sonographic Detection of Pulmonary Embolism Using Machine Learning Algorithm
  Supporting Agency: NIBIB
  Role: Co-I
  Effort: 0.52 person months

  Josie Acuna-The Current Status of Gender Disparities in Emergency Ultrasound Fellowship Programs: A Survey Study-Closed

- **Alper Yilmaz**-New Active support:
  Grant ID: 1R21EB030677-01A1
  Automated Sonographic Detection of Pulmonary Embolism Using Machine Learning Algorithm
  Supporting Agency: NIBIB
  Role: subaward PI
  Effort: 0.5 person months

  Real-time tracking of gravitational field via crowdsourcing
  Supporting Agency: NGA – GEOESCON
  Role: PI
  Effort: 0.5 person months

  Tracking objects with handoff across cameras
  Supporting Agency: Immobileyes Inc. AFOSR STTR
  Role: PI
  Effort: 0 person months

  Accelerator Award for Automated Stroke Detection
  Supporting Agency: OSU Kenaan Entrepreneurship Center
  Role: PI
  Effort: 0 person months

Alper Yilmaz-STTR Phase II: Onboard compact self-contained artificially intelligent multisensory system for real-time navigation in GPS-denied or degraded Environments-Closed
IUCRC planning grant, The Ohio State University: center for accurate georeferencing of the environment (CAGE)-Closed
Context-Aware Safety Information Display for Nuclear Field Workers-Closed

- **Yong Fan**-New Active support:
  Grant ID: GRT-00000640
  Machine-learning for children with SB
  Supporting Agency: Children's Hospital of Philadelphia
  Role: Co-I
  Effort: 0.96 person months

  Grant ID: 2-R01-EB-022573-05
  Personalized Functional Network Modeling to Characterize and Predict Psychopathology in Youth
  Supporting Agency: NIBIB
  Role: Co-I
  Effort: 2.4 person months

  Grant ID: 2-R01-MH-112847-06A1
  Inter-modal Coupling Image Analytics
  Supporting Agency: NIMH
  Role: Co-I
  Effort: 0.54 person months

  Grant ID: 2-RF1-AG-054409-02
  Machine Learning and Large-scale Imaging analytics for dimensional representations of brain trajectories in aging and preclinical Alzheimer's Disease: The brain aging chart and the iSTAGING consortium
  Supporting Agency: NIA
  Role: Co-I
  Effort: 0.48 person months

  Grant ID: 1-U24-NS-130411-01
  The Neuroimaging Brain Chart Software Suite
  Supporting Agency: NINDS
  Role: Co-I
  Effort: 0.86 person months

  Grant ID: 1-R01-MH-134236-01
  Disentangling the anatomical, functional, and clinical heterogeneity of major depression, using machine learning methods
  Supporting Agency: NIMH
  Role: Co-I
  Effort: 0.96 person months

  Yong Fan-Personalized Functional Network Modeling to Characterize and Predict Psychopathology in Youth-Closed
  Predicting Weight Regain Following Weight Loss Using Physiological Measures of Appetite and Energy Expenditure-Closed
  Penn Quantitative MRI Resource for Pancreatic Cancer-Closed
  Imaging signatures of genetic mutations in glioblastoma using machine learning-Closed
  Heterogeneity of Multi-Modal Imaging Signatures of Aging, MCI, Alzheimer’s Disease via Pattern Analysis-Closed
  Center for Machine Learning in Urology-Closed

- **What other organizations were involved as partners?**
  - **Organization Name:** The Ohio State University
  - **Location of Organization:** Columbus, OH
  - **Partner's contribution to the project** *(identify one or more)*
    - **Financial support;** N/A
    - **In-kind support** *(e.g., partner makes software, computers, equipment, etc., available to project staff)*; N/A
    - **Facilities** *(e.g., project staff use the partner's facilities for project activities)*; PCVLab at OSU located at the Bolz Hall, Suite 233
    - **Collaboration** *(e.g., partner's staff work with project staff on the project)*; Sub-award-The Ohio State University. For the proposed study, Dr. Yilmaz and Pouyan contributed to ultrasound image data curation, developing ultrasound machine learning algorithms and coding the models.
    - **Personnel exchanges** *(e.g., project staff and/or partner's staff use each other's facilities, work at each other's site)*; N/A

8. Special Reporting Requirements

None

9. Appendices

None