

AWARD NUMBER: W81XWH-19-1-0542

VR180058

TITLE: Intraocular Microdisplay Projection for Vision Restoration After Corneal Blindness

PRINCIPAL INVESTIGATOR: Charles Yu M.D.

CONTRACTING ORGANIZATION: Stanford University

2370 Watson Court Suite 200

Palo Alto, CA 94303

REPORT DATE: AUGUST 2021

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE AUGUST 2021		2. REPORT TYPE ANNUAL		3. DATES COVERED 1AUG2020 - 31JUL2021	
4. TITLE AND SUBTITLE Intraocular Microdisplay Projection for Vision Restoration After Corneal Blindness				5a. CONTRACT NUMBER W81XWH-19-1-0542	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Charles Yu M.D. E-Mail:				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Stanford University 2370 Watson Court Suite 200 Palo Alto, CA 94303				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT: The cornea is the front clear window into the eye through which light must pass in order for the eye to see. Because of its location at the front of the eye it is the most exposed structure to military relevant trauma such as blast, chemical, and thermal injury. About 36% of eye injuries in Operation Iraqi and Enduring Freedom involved the cornea. Future beam weapons such as infrared and UV lasers, and microwaves will be primarily absorbed by the cornea when hitting the eye. When the cornea is injured and blood vessels grow onto the cornea, there is currently no effective treatment because corneal transplantation (replacing the cornea with a cornea from a deceased donor) does not work in this situation due to high risk of rejection. Plastic buttons placed into the cornea have been performed but these are exposed to the external environment and are at high risk of infection and other complications such as falling out. In addition to disease, there are thousands of patients who suffer corneal injuries in work related accidents. Due to the industrial nature of many ocular chemical and thermal burns, corneal injury disproportionately affects those in the prime of their life. Lastly, 12.7 million people around the world are unable to obtain corneas for transplantation due to a shortage of donors. Building on the most recent developments in state-of-the-art high-resolution small display technology we have created a tiny projector (like a movie projector) that can be implanted into the eye (intraocular) of these patients. The device can wirelessly receive video data and power from a camera and processor positioned upon the frame of a pair of glasses. A lens focuses the image onto the retina. This in effect will place a miniature movie projector inside the eye, so that the patient will be able to see a projected image even with a completely scarred cornea or even if the eyes are closed. This design is superior to currently used devices because it is completely covered and not exposed to infection and it does not require cornea tissue to be collected from donors. The risks of our implant are that it may become dislocated or there may be leakage of liquid around the cable. Both of these can be fixed with further surgery. We have demonstrated prototypes of this device and discussed our published findings that this is a feasible technology. In this study we propose to test this type of device in animals.					
15. SUBJECT TERMS NONE LISTED					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	15	19b. TELEPHONE NUMBER (include area code)

TABLE OF CONTENTS

Page

1. Introduction
2. Keywords
3. Accomplishments
4. Impact
5. Changes/Problems
6. Products
7. Participants & Other Collaborating Organizations
8. Special Reporting Requirements
9. Appendices

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

This project seeks to build and test 15 intraocular projection devices, then perform their implantation and observe their function in living rabbits. This device is the basis of a new way of treating corneal blindness and is free from the limitations of traditional methods. It also forms the basis of possible vision enhancing technology with military applications. Successful demonstration in rabbits validates the technology.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Cornea, blindness, display, transplant, vision, wireless, projection, LED, LCD, keratoprosthesis

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Year 2 of this project is implantation of implants in live rabbits. It is covered by

Specific Aim 2

Major Task 1: In vivo Animal trial

Subtask 1: Surgical implantation of device into 15 animals (Done in three batches of 5)	Months 13-31	Dr. Yu
Mile Stone 3: implantation of 5 animals	Month 13	Dr. Yu
Mile Stone 4: implantation of 10 animals	Month 19	Dr. Yu
Mile Stone 5: implantation of 15 animals	Month 25	Dr. Yu
Subtask 2: Weekly examination and monthly VEP vision testing	Months 13-31	Dr. Yu Dr. Palanker

We have now completed implantation of 9 animals with weekly examination and testing, with 6 surgeries remaining. We are slightly behind timeline due to adjusting design of implant arms for better results after results from the first 3 animals, but remain on schedule to catch up within 1-2 quarters.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

In this second year of the project:

- 1) Major activities were implantation of animals and observing them during the trial
- 2) Specific activities: rabbit surgeries and projector implantation 9 animals.
- 3) Significant results: are successful implantation of 9 animals thus far with limited complications (1 case iris synechia and 1 case transient bleeding due to haptic contact). Also, we were able to improve the sensitivity of our VEP tracing with placement of skull screws and obtain the required signals.
- 4) Other accomplishments: we were able to complete and publish two papers (see below)

Figures demonstrating work this year are below.

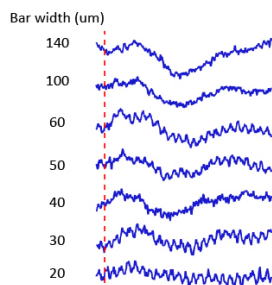
Implanted Rabbit (Rabbit 2)



Vision Testing



Vision Electrophysiologic Tracing (VEP via skull mounted wires)



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

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

We submitted an abstract for presentation at the MHSRS, which was held online only due to the pandemic yet again.

We published two papers, see below

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

If this is the final report, state “Nothing to Report.”

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We will complete implantation and analysis of rabbit vision and eyes.

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

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

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

- 5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:*

Nothing to report

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

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

To improve stability of implant we adjusted design of implant arms which resulted in a few months delay, but we are on schedule to catch up.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Delay in rabbit surgery has pushed more of the costs to next project year, we are currently under budget due to fewer total animals per diem costs. However, this will be balanced by higher than budgeted per diem costs during year 3.

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

None

Significant changes in use of biohazards and/or select agents

None

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

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

Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume; year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Temperature elevation in the human eye due to intraocular projection prosthesis device *J.*

Thermal Sci. Eng. Appl. Gongal, D., Thakur, S., Panse, A., Stark, J., Yu, C. Q., Foster, C. D. 2021 PUBLISHED, YES acknowledgement of federal support.

Axisymmetric Thermal Finite Element Analysis of Effects of Intraocular Projector in the Human Eye

American Journal of Undergraduate Research Stark, J. A., Foster, C. D., Yu, C. 2021; 17 (4) PUBLISHED, YES acknowledgement of federal support.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

None

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Yu CQ. A Computer Inside the Eye to Restore Vision After Corneal Injury. MHSRS 2021

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

<https://yulab-stanford.github.io/people/> - github lab website for PI

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

None

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

None

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*

- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

None

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Name: Elton Ho

Project Role: Post Doc

Research ID: n/a

Person months worked – 3.91 calendar months

Contribution to Project: rabbit vision testing

Name: Victoria Fan

Project Role: Research Assistant

Research ID: n/a

Person months worked – 0.20 calendar months

Contribution to Project: rabbit care and photography

Name: Daniel Palanker

Research Role: Co Investigator

Research ID: 2-0480-3025 ORCID

Person Months worked – 1.20 calendar months

Contribution to Project: advising on rabbit electrophysiology

Name: Charles Yu

Research Role: PI

Research ID: 1-8095-2930 ORCID

Person Months worked – 3.00 calendar months

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

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

None

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*
- *Other.*

None

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.*

9. **APPENDICES:** *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*