

AWARD NUMBER: W81XWH-18-1-0702

TITLE: Using Emotional Expression as a Novel Indicator of Functional Outcomes and Facial Rehabilitation Following Face Transplantation via Software-Based Video Analysis

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REPORT DATE: October 2019

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE October 2019		2. REPORT TYPE Annual		3. DATES COVERED 09/15/2018 to 09/14/2019	
4. TITLE AND SUBTITLE Using Emotional Expression as a Novel Indicator of Functional Outcomes and Facial Rehabilitation Following Face Transplantation via Software-Based Video Analysis				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-18-1-0702	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S)				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Brigham and Women's Hospital 75 Francis St Boston MA 02115				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 Face transplantation (FT) outcomes have traditionally been defined by improvement of motor and sensory function. However, FT recipients seek to reintegrate into society, where ability to express emotions is integral to success. The ability to generate identifiable emotional expressions has not been yet successfully used as a quantitative outcome assessment in FT. Human observers use information from different areas of the face to successfully recognize expressed emotion. To the best of our knowledge, there is currently no established method to objectively assess expressed emotion the way human observers do in FT. Additionally, detection of immune rejection still poses challenges in the early stages after FT, and especially for visually impaired patients. There exists an unmet need for non-invasive, high-precision assessment of visual changes related to immune rejection of facial allografts. Aim 1: Quantitatively assess the ability to form identifiable facial emotional expression as a functional outcome of face transplantation. Aim 2: Develop					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			Unclassified

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. Introduction

Many individuals lose parts of their faces, their limbs or their abdomen in traumatic incidents such as active combat, burns, gunshot wounds, violent attacks, and motor vehicle accidents, amongst others. People with these types of traumatic injuries have decreased quality of life and are often disabled. Although they may receive the best of the available conventional reconstruction therapies, they continue to suffer from chronic pain, psychological distress, social isolation, and limitations in their ability to perform daily activities such as bathing, dressing, ambulating, and eating without substantial help.

Face transplantation is a viable reconstructive option for patients with severe facial deformity showing promising long-term results in improving functionality and quality of life. Outcome measures of face transplantation have traditionally assessed the recovery of vital functions (ability to breathe, eat, and speak) and independent functions (motor movement, protective and discriminative sensation); as well as the procedure's functional psychological impact on quality of life and mental health. Measuring the restoration of these functions is necessary to determine the value of face transplantation to the individual patient, but their recovery alone is not sufficient to achieve or explain societal reintegration after face transplant.

Non-verbal communication via facial emotional expression – a social function of the face – has evolved under the pressures of interacting in a social environment. Six specific emotional expressions – happiness, sadness, anger, surprise, fear, and disgust – are recognized across cultures and are the focus of social psychology research. Despite high relevance, limited quantitative data is available on restoration of facial emotional expression after face transplantation. Existing evidence comes from methods such as facial surface electromyography, a sensitive measure but one that requires painstaking placement of several electrodes on the skin; and appearance-based facial feature extraction, which is similar to facial recognition technology but requires significant data processing that limits reproducibility. These methods are obtrusive and prone to human instrumentation error. Their clinical implementation would be time-consuming and bind patients to laboratory settings, which could impact medical adherence over time. The need to find a less obtrusive and more reliable method for evaluating emotional expression as an outcome measure of face transplantation remains.

Software-based video analysis, a merger of facial recognition technology and deep learning, has proven capable of assessing facial motor movement functions after face transplantation. Our objective is to recognize emotional expression as a novel indicator of functional outcomes and rehabilitation following face transplantation via objective, non-invasive, and non-obtrusive software-based video analysis. We will complete a retrospective, matched-cohort study using 6 face transplant recipients and 6 healthy subjects. Noldus video-analysis software will be used to detect emotional expression of all subjects. Imaging data will be used to quantitatively assess the ability to form identifiable facial emotional expression as a functional outcome of face transplantation. Images and videos taken of 8 face transplant recipients during rejection episodes will be shared with Noldus to develop the software further for clinical monitoring of facial allograft rejection. We believe this video-analysis software can provide useful clinical information and aid rehabilitation after face transplantation.

2. Key Words:

Face transplantation, facial allograft, emotional expression, rejection detection

3. Accomplishments.

Specific Aim 1 of our study was to quantitatively assess the ability to form identifiable facial emotional expression as a functional outcome of face transplantation. This involved completing sub-tasks that included: calibration and optimization of emotional expression detection for patients with face transplants, recruiting matched healthy controls for comparison, and analyzing emotional expressions of both patients with face transplants and healthy controls.

We found that all emotional expressions were able to be detected on patients with face transplant. The emotion of happiness was the most reliable expression to detect and could be restored after face transplant to a mean of 43% (range, 14% to 75%) of that of healthy controls. The study also found significant changes after post-transplant year 1 in happiness where it improved by 0.04 intensity value points each year. The software detected this improvement in happiness at a sub-clinical level which highlights the potential for this tool to be used in rehabilitation of patients with face transplants.

Completion of Specific Aim 1 occurred by July 2019. Work from this portion of the project was presented either in part or completely at a meeting of the American Society for Reconstructive Transplantation and published as an original investigation in a Journal of the American Medical Association.

Simultaneously, Specific Aim 2 of our study was being worked on to develop the software further for clinical monitoring of facial allograft rejection. This involved completing sub-tasks that included: development of a software to detect redness on face transplant allografts, validating the software, and analyzing images of patients with face transplants to determine if rejection episodes can be detected. Our collaborators were able to create a software that met our indications by September 2019.

We have proceeded to validate the software and will have more data to report back on in subsequent quarterly reports about Specific Aim 2.

4. Impact

Active combat is inflicting devastating injuries to the face with alarming incidence, resulting in facial disfigurement. Conventional reconstructive surgery is limited in its ability to restore form and function after these injuries. Considering the high incidence and devastating consequences of these complex injuries to American Service members, there is a clear need to improve their treatment outcomes. Non-verbal communication via facial expression is a vital aspect of human communication. If successful, software-based video analysis will allow clinicians to more accurately assess the outcomes of facial transplantation. Additionally, the software could be used to define and treat transplant rejection more accurately than conventional methods. This will lead

to improvements in medical outcomes, quality of life, mental health, social participation, and the American economy for transplant recipients.

5. Changes/Problems

We were unable to start the development of the rejection detector module on schedule due to both administrative and logistical setbacks. We strengthened our communication with Noldus, the collaborators, in order to clarify their position on required materials to begin development. From a logistical standpoint, we increased our dedicated time spent on working with collaborators to get back on schedule.

6. Products

Nothing to report at this time.

7. Publications, Abstracts and Presentations

- Oral presentation, “Recognizing Emotional Expression in the Face Transplant Patient”, at the American Society for Reconstructive Transplantation 6th Biennial Meeting 16-11-2018
- Scientific manuscript submitted to JAMA Network Open, an open-access academic journal:
Miguel I. Dorante, MD, MBE, Branislav Kollar, MD, Doha Obed, Valentin Haug, MD, Sebastian Fischer, MD and Bohdan Pomahac, MD. Recognizing Emotional Expression as an Outcome Measure after Face Transplant. *JAMA Network Open*. Jan 2020
DOI: 10.1001/jamanetworkopen.2019.19247

8. Inventions, Patents and Licenses

Nothing to report at this time.

9. Reportable Outcomes

For Specific Aim 1, a commercially available software, FaceReader produced by Noldus IT, was used to analyze emotional expression in patients with face transplants. Our study was the first to study its effectiveness in face transplant.

For Specific Aim 2, we collaborated with the engineers at VicarVision who designed the software in Specific Aim 1 to produce a software that could detect redness in facial allografts of patients with face transplants. The software titled, deltaR measure, is a prototype that we are still validating.

10. Other Achievements

Nothing to report at this time.

11. Participant and other collaborating organizations

Our collaboration with Noldus remains in place and active.

12. Special Reporting Requirements

None.

13. Appendices

None.