STUDY TITLE:

A Randomized Controlled Trial of Tegaderm vs. EyeGard for Eye Protection During Anesthesia

STUDY SPONSOR:

Department of Anesthesiology and Perioperative Medicine, Tufts Medical Center

PRINCIPAL INVESTIGATOR

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Tufts Health Sciences IRB Protocol Template
Template Revised: 08/16/2016

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1. Study Schema

Enrollment	Randomization	Arm 1	159 patients	Tegaderm™ on R eye, EyeGard® on L eye
		Arm 2	159 patients	Tegaderm™ on L eye, EyeGard® on R eye

2. Introduction

2.1 Background and Rationale

In the 1980s, taping eyes shut during anesthesia became a common practice due to the recognition of corneal abrasions as a risk of anesthesia (1). However, there is no single accepted practice of how to protect the eyes during anesthesia, and a variety of different tapes and techniques have been adopted in different institutions.

While the risk of corneal abrasion significantly decreases with the use of eye tape, patients may occasionally experience eyelid irritation from the adhesive. While the eyelid irritation is generally limited to mild erythema that resolves on its own within a day or two of receiving anesthesia, the irritation may affect patient satisfaction (2).

At Tufts Medical Center, a variety of adhesive tapes are used to shut the eyes during anesthesia, including 3M™ Tegaderm™ and the Sharn Anesthesia EyeGard®, with no preference for one or the other. While all of these products decrease the risk of corneal abrasion, none of these products have been shown to be superior to the others in terms of eyelid irritation. According to Sharn Anesthesia, "The [EyeGard®] adhesive is light enough to reduce damage to the outer eye" (3). However, there is no scientific evidence to support this claim. All we know is that the EyeGard is coated with a medical grade, pressure-sensitive acrylic adhesive and that there are no phthalates, it is latex free and silicone free.

The purpose of this study is to compare the rate of eyelid erythema after anesthesia with the use of Tegaderm™ vs. the EyeGard®. Our hypothesis is that there will be a difference in the rate of erythema between the two groups.

- Is there an active control group?

  ☐ **Yes** ☑ **No**

2.2 Risks to Subjects

The risk of having Tegaderm™ or the EyeGard® placed on the eyelids is the development of skin irritation (e.g. erythema) that lasts for 1-2 days postoperatively. Given that eyelids are always shut with adhesive tape when patients undergo anesthesia, patients are already accepting these risks as part of the anesthetic. Our study does not pose any additional risks beyond those associated with getting anesthesia. The purpose of this study is to determine if one of the eye tapes results in a lower risk of skin irritation than the other.

Another risk of participating in the study is loss of confidentiality. In order to minimize that risk, all paperwork will be stored in a secure location. Furthermore, all electronic data will be held in a Tufts Medical Center provided, password protected, encrypted, Box.com storage account, which is compliant with institutional policies regarding HIPAA and the IT department.

2.3 Potential Benefits to Subjects

This study will not directly benefit participants. However, future patients undergoing anesthesia may benefit from an improved understanding of the potential erythema that may result from protective tape.

2.4 Alternatives

The alternative is not participating in the study.

3 Objectives

This objective of this study is to compare the effects of Tegaderm™ vs. EyeGard® on the eyelids during anesthesia.

- Primary Outcome:
  - The proportion of eyelids with erythema at the end of surgery after removal of Tegaderm™ vs. EyeGard®

- Secondary Outcomes:
  - Patient Satisfaction
  - Rate of Corneal Abrasions

4 Enrollment and Withdrawal

4.1 Inclusion Criteria

- Age ≥ 18
- Surgeries scheduled for anesthesia of any duration

4.2 Exclusion Criteria

- Any patient that does not consent
- Any patient who has:
  - Pre-existing eyelid erythema or other eyelid trauma
  - Eyelid piercings
- Any surgery on the head, brain, neck, teeth, mouth, eyes or face
- Surgery in the prone position
- Patients <18 years old

4.3 Withdrawal of Subjects

All subjects will be included in the primary analysis as dictated by the theory of intention to treat analysis. Patients who decide to withdraw prematurely will be withdrawn and provided the standard of care at Tufts Medical Center.

4.4 Recruitment and Retention

4.4.1 Local Recruitment Methods

All faculty and staff in the Department of Anesthesiology and Perioperative Medicine at Tufts Medical Center will be informed about the study at one of the departmental meetings (see "Departmental Meeting Script"). Once the patients arrive to the pre-operative area, the co-investigator, Katelyn Ward, will meet with the patients and discuss the study with them further. If they agree to participate, informed consent will be obtained.

4.4.2 Study-Wide Recruitment Methods

Is this a multicenter study where subjects will be recruited by methods not under the control of the local Tufts site (e.g., call centers, national advertisements)?

☐ **Yes** ☑ **No**

4.4.3 Payment

Will subjects receive money, gifts, or any other incentive for participating in this study?

☐ **Yes** ☑ **No**

4.4.4 Reimbursement

Will subjects be reimbursed for their expenses, such as travel, parking, meals, or any other study related costs?

☐ **Yes** ☑ **No**

5 Study Design

5.1 Study Timelines

- Study subjects will be participating in the study for a total of 2 days.
- On day 1, study subjects will enroll in the study and undergo anesthesia with application of Tegaderm™ and EyeGard® on the eyelids. Once surgery is complete, the Tegaderm™ and EyeGard® will be removed and photograph will be taken. This will conclude participation in the study on day 1
- On day 2, study subjects will be approached by the co-investigator, Katelyn Ward, and will be given a patient satisfaction survey. Completion of the survey will conclude study subject participation in the study.
- We anticipate that we will be able to enroll 5 subjects per day during weekdays. Given that we plan to recruit 159 study subjects, it will take approximately 2 months to enroll all the study subjects.
- The estimated date for primary analyses will be October-December 2018.

5.2 Procedures

- Is there a placebo control arm?

☐ **Yes** ☑ **No**

We will perform a prospective, double-blind, randomized controlled trial. Participants will be approached by the co-investigator, Katelyn Ward, on the day of the surgery. The research study will be explained and potential participants will be given an informed consent form to read. After the participant has had adequate time to read through the informed consent form, think about the risks and benefits, and ask questions, he or she will be asked to sign the form if he or she wishes to participate in the study. The informed consent form will then be stored in the principal investigator's locked office. Once a study subject is enrolled, the anesthesia provider, surgical provider, as well as the nurse will be informed that this parturient is part of the study. The co-investigator, Katelyn Ward, will then gather baseline patient demographic and clinical data.

Photographs will be taken using a digital camera at an angle parallel to the eyes (such that the camera is facing the patient directly), at a distance of 6 inches from the eyes to the lens of the camera, and will be done in the operating room with all room lights on. The photographs will be taken and cropped in such a way that both eyelids are visible but no other facial features will be recognizable. As such, photographs will not be identifiable. A disposable paper ruler will be used to determine camera distance and then placed on the patient's forehead during photography as a marker of size.

Upon entry into the operating room and prior to induction of anesthesia and prior to administering oxygen, the co-investigator, Katelyn Ward, will ask the study subject to close his or her eyes. The co-investigator will then take a photograph of the eyelids as a baseline assessment. Afterwards, anesthesia will be induced according to standard of care at Tufts Medical Center. Once the anesthesia provider establishes mask ventilation, the co-investigator, Katelyn Ward, will apply the EyeGard® on one eye and the Tegaderm™ on the other eye according to the

randomization schema. The exact time of application will be documented. At the end of the surgery, the co-investigator, Katelyn Ward, will remove the EyeGard® and Tegaderm™. She will then take another photograph of the eyelids and document the time.

On post-op day 1, the co-investigator, Katelyn Ward, will administer a patient satisfaction survey. Once the survey is collected, the subject's participation in the study will cease.

All photographs will be uploaded to a hospital-provided Box.com account. Photograph files will be named in the following format: "001pre.xxx" or "001post.xxx," such that the "001" portion indicates study subject number, and the "pre" or "post" indicates when the photograph was taken ("pre" indicates that the photograph was taken prior to application of the EyeGard®/Tegaderm™, post indicates that the photograph was taken after removal of the EyeGard®/Tegaderm™). The "xxx" indicates the file format in which the photograph is saved.

The Box.com folder containing the photographs will be shared with the dermatologists who will evaluate the degree of erythema. The dermatologists will be asked to evaluate the erythema based on the following tape-associated skin index grading scale,:

Erythema assessment:
0 - no visible erythema
1 - mild erythema
2 - moderate erythema
3 - severe erythema

Each dermatologist will be given a "Dermatologist Evaluation Sheet" which will list all of the photographs that are to be evaluated. He or she will independently evaluate each photograph.

Once all dermatological evaluations of the photographs are complete, the results will be compared. Should there be inconsistency in the Grade rating, the majority (two out of three) will be counted.

If the EyeGard® and/or Tegaderm™ fall off prior to the end of surgery, a photograph will be taken at that time and the time duration noted. Afterwards, a new tape will be re-applied.

5.3 Evaluations

Will you perform any laboratory tests for this study?

☐ **Yes** ☑ **No**

5.4 Collection and Storage of Human Biological Specimens (Tissue Banking)

Will biological specimens be stored for **future, unspecified**, research?

☐ **Yes** ☑ **No**

6 Ethics and Protection of Human Subjects

6.1 Informed Consent Process

Will subjects be required to provide informed consent?

☑ **Yes** ☐ **No**

- The informed consent will take place in the pre-operative area in the patient's individual holding bed, the same location where surgical and anesthesia consent is performed as well.
- The patient will have one hour before the start of the procedure to make a decision regarding enrollment.
- The consent will be obtained in person and documented in writing according to SOP: Informed Consent Process for Research (HRP-090)

- Non-English speakers will be enrolled using interpreters and IRB approved Short Forms per the IRB's Short Form policy

6.2 Waiver or Alteration of Consent Process

- Is a waiver or alteration of the consent process being requested for this study?
  ☐ **Yes** ☑ **No**
- Is a waiver of the consent process being requested for parents for research involving children?
  ☐ **Yes** ☑ **No**
- Is a waiver of the consent process for planned emergency research being requested?
  ☐ **Yes** ☑ **No**

6.3 Confidentiality

In order to maintain confidentiality, the following measures will be taken:

- All study related materials will be stored in a secure location. The consent forms and other paper forms (e.g. data collection sheet) will be stored in the principal investigator's locked office. All digital files (e.g. excel forms, photography) will be stored on a Tufts Medical Center provided, password protected, encrypted, Box storage account, which is compliant with institutional policies regarding HIPAA and the IT department.
- The principal investigator and co-investigators will have exclusive access to the forms.
- Records will be stored for 7 years after the study is closed with the IRB, as per IRB policy.
- A certificate of confidentiality will not be obtained.

6.4 Provisions to Protect the Privacy Interests of Subjects

Subjects will be assured that their contact with any member of the research team is optional, and that the information they share will be strictly confidential.

6.5 Provisions to Monitor the Study to Ensure the Safety of Subjects

- This study does not pose any additional safety risks beyond those associated with the application of protective tape over the patient's eyelids that occurs during standard surgical procedures. These risks include injury to the eyelid such as mild to severe erythema, edema, and abrasion. Patient safety is a top priority. If at any time a patient's safety is threatened during that patient's participation in this study, for example in the event that a patient has an allergic reaction to the tape or perhaps an unrelated surgical complication necessitates the removal of the tape, the tape will be removed and the patient will not complete his/her participation in the study.
- No Data and Safety Monitoring Board will be used in this study.

6.6 Compensation for Research-Related Injury

Does the research involve greater than minimal risk to subjects?

☐ **Yes** ☑ **No**

6.7 Economic Burden to Subjects

Does the research involve any costs to subjects?

☐ **Yes** ☑ **No**

6.10 Vulnerable Populations

Will pregnant women be enrolled?

☐ **Yes** ☑ **No**

Will the research involve neonates of uncertain viability or non-viable neonates?

☐ **Yes** ☑ **No**

Will subjects who are not yet adults (neonates, children, teenagers) be enrolled?

☐ **Yes** ☑ **No**

Will minors who are:

i) married, widowed, divorced; or
ii) the parent of a child; or
iii) a member of any of the armed forces; or
iv) pregnant or believes herself to be pregnant; or
v) living separate and apart from his/her parent or legal guardian, and is managing his/her own financial affairs

be approached for study participation for either themselves or their child?

☐ **Yes** ☑ **No**

Will wards of the state and/or children at risk of becoming wards of the state be enrolled (this includes foster children or any child that is in state custody)?

☐ **Yes** ☑ **No**

Will cognitively impaired adults (adults with impaired-decision making capacity) or adults who may lose the capacity to consent be enrolled?

☐ **Yes** ☑ **No**

Will prisoners be enrolled?

☐ **Yes** ☑ **No**

Will students and/or employees be enrolled in this research?

☐ **Yes** ☑ **No**

7 Adverse Event Monitoring

7.1 Definitions

The study does not carry a higher risk of adverse events than typically expected from the use of tape over the eyelids during surgical procedures. Possible adverse events may include allergic reaction to the tape and abrasion caused by tape removal.

Adverse event: An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal physical exam or laboratory finding, symptom, or disease, temporally associated with a subject's participation in the research.

Serious adverse reaction: a serious medical occurrence associated with the use of Tegaderm™, or EyeGard® such as life-threatening allergic reaction.

Unanticipated problems: any incident, experience, or outcome that meets **all** of the following criteria: unexpected; related or possibly related to participation in the research; and suggests that the research places subjects at a greater risk of harm than was previously known or recognized.

7.2 Reporting Procedures

Patients are routinely monitored for development of adverse events as part of their anesthetic care. This occurs on a continuous basis from the moment the anesthetic is administered until the moment the patient is

discharged home. A computerized system exists which alerts clinicians to the development of some adverse effects, and is recorded in the medical record. The co-investigator, Ms. Ward, will be alerted in these situations and all adverse events will be forwarded to the principal investigator. Clinicians are alerted to events immediately as they occur. Clinical staff are trained to deal with such events. The co-investigator, Ms. Ward, will be responsible for contacting the principal investigator to report the occurrence of adverse events. The principal investigator will then complete any necessary safety forms, include the Anesthesia Department's Quality Assurance form. The events will be reported within 24 hours to the QI director and the Chairman of the department, and to the IRB within 5 days.

7.3 Reportable New Information

Reportable new information will be reported to the IRB per the Tufts Health Sciences IRB's "Reportable New Information policy". The PI will submit any updated information that may affect the conduct of this study or subject safety, rights, welfare or willingness to take part in the research.

8 Statistical Considerations

8.1 Study Endpoints

Primary endpoint: immediately upon removal of Tegaderm™ and EyeGard®
Secondary endpoint: post-operative day 1 when patient satisfaction data is acquired

8.2 Statistical Analysis

We will convert our Grading Scale into a binary variable where 0 indicates no erythema and 1 indicates any erythema. The difference in erythema between Tegaderm™ vs. EyeGard® will be compared using the McNemar test.

Secondary outcomes:

1. Aggregate patient satisfaction score, is on a Likert scale from 015. The mean for each group (Tegaderm™ vs. EyeGard®) will be calculated and then the difference between the two groups will be determined using Student's *t*-test.
2. Corneal abrasion rate

8.3 Number of Subjects

A previous study by Zeng et al. found that the rate of any level of eyelid erythema when using 3M Medipore is 50% while when using 3M Kind Removal Silicone Tape is 33%. We will assume that the rate of erythema with 3M Tegaderm may be similar to that of 3M Medipore and the rate of erythema with EyeGard may be similar to that of 3M Kind Removal Silicone Tape. Given that we are doing a study of matched pairs of subjects (the same study subject will undergo both treatments, one on each eye), the McNemar test is most appropriate. In order to detect a difference in erythema rates with an alpha of 0.05 and 80% power, G*Power determined that the total sample size needs to be 288 eyes, which is 144 patients. In order to account for a 10% attrition rate, we will plan on recruiting 159 study subjects.

8.4 Data Management

The data to be collected will be divided into two general groups: (1) Paper forms, such as the consent forms and data collection sheets, will be stored in the principal investigator's locked office. (2) Digital form, such as the data collection excel spreadsheet which includes the following variables: Subject ID, R and L eye tape assignments, length of surgery, R and L eye pre-op photo numbers, R and L eye pre-op scores (from three dermatologists), R and L eye post-op photo numbers, R and L eye post-op scores (from three dermatologists), final erythema score (post minus pre), patient satisfaction with R eyelid condition, patient satisfaction with L eye condition, and additional notes, will be stored on a Tufts Medical Center provided, password protected, encrypted, Box storage account, which is compliant with institutional policies regarding HIPAA and the IT department. (3) All photos will also be stored on Box.com.

8.5 Randomization

Will subjects be randomized?

☑ **Yes** ☐ **No**

In order to randomly allocate study subjects to one of three arms entirely by chance, we will use the on-line randomization tool "Research Randomizer Version 4.0, www.randomizer.org," which is a computer-based "random number generators," the numbers are generated by use of a complex algorithm (seeded by the computer's clock) that gives the appearance of randomness. This tool has been studied and validated as an adequate randomization tool, to generate a randomization list. Allocation concealment will be maintained by preparing sequentially numbered, sealed, opaque envelopes, which will contain the randomization assignment consistent with the generated randomization list.

The following strategies will be implemented in order to ensure blinding:

(a) When a subject enrolls in the study, the co-investigator, Ms. Ward, will open the envelope with randomization number inside. Ms. Ward will be the one to apply and remove the tapes. Once the tapes are removed, a second set of photographs will be taken. The dermatologists who will be in charge of determining the primary outcome (erythema score) will not be present during any part of the procedure.

(b) The photos will only be linked to the experimental variable (tape type) by the data collection spreadsheet that is only accessible to the principal investigator, Dr. Drzymalski, and the co-investigator, Ms. Ward. After data collection for the study is complete, the photos will be presented to the dermatologists independently in a blinded manner.

(c) Each dermatologist's grading will subsequently be recorded in the data collection spreadsheet by the co-investigator. Therefore, the dermatologist will have no opportunity to determine the type of tape used at any point during the study.

(d) Study subjects will not be informed of which tape is assigned to which eyes, and the tape will be applied and removed while the patient is under anesthesia. Therefore, the patient will be blind to the type of tape used throughout the course of the study, including when he/she is reporting his/her satisfaction with post-operative eyelid condition.

9 Drugs or Devices

Will the research involve drugs?

☐ **Yes** ☑ **No**

Will the research involve devices?

☐ **Yes** ☑ **No**

10 Study Administration

10.1 Setting

Tufts Medical Center will be the sole research site. Tegaderm™ and EyeGard® tapes will be administered in the operating room per routine clinical care. Patients will then be followed in the recovery room until post-operative day 1.

10.2 Registration

The co-investigator, Ms. Ward, will ensure the eligibility of subjects and obtain their informed consent before implementing any study related interventions.

10.3 Resources Available

The research team is composed of the following members:

- Principle investigator: Dan Drzymalski, MD, Assistant Professor of Anesthesiology
    - Dr. Drzymalski is responsible for the preparation, design, conduct, and administration of the study.
- Co-investigator: Katelyn Ward, Tufts Medical School M1
    - Responsible for writing the study's protocol under the principle investigator's guidance, obtaining the informed consent, performing the study intervention, managing data collection, and data analysis.

Tufts Medical Center facilities provide medical resources that might be needed by study subjects. The average number of operating procedures that fall under our inclusion criteria is approximately 10 per day, which makes it possible to enroll the total number of study subjects within a two-month period.

10.4 IRB Review

An appropriate IRB registered with the OHRP, will review and approve this study. Any amendments to the protocol or informed consent documents will be reviewed and approved by the IRB prior to use, unless required to eliminate an apparent immediate hazard to subjects.

10.5 Multi-Site Research

Is this a multi-site study where Tufts is the sponsor, primary grant recipient, or coordinating site?:

☐ **Yes** ☑ **No**

10.6 Community-Based Participatory Research

Will this study involve community-based participatory research?

☐ **Yes** ☑ **No**

10.7 Sharing Results with Subjects

Will results (overall study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) be shared with subjects or others (e.g., the subject's primary care physician or the subject's treating physician)?

☐ **Yes** ☑ **No**

11 References

1. Cucchiara RF, Black S (1988). Corneal Abrasion during Anesthesia and Surgery. *Anesthesiology*. **12**(69): 978-979.
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3. "Why Do We Tape Patient's Eyes during Surgery?" *Eyegard Eye Protection*, Sharn Anesthesia, www.sharn.com/eye-protection/a/Eyegard/.