A prospective, randomized, controlled trial of steroid delivery to the frontal sinus opening with a bioabsorbable steroid releasing implant vs. a bioabsorbable nasal dressing with added steroid

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## 1. PURPOSE OF THE STUDY AND BACKGROUND

### 1.1. Purpose of the study

The purpose of this study is to compare the efficacy of a bioabsorbable steroid eluting implant (Propel mini stent or Propel contour stent) vs a steroid impregnated nasal dressing (triamcinolone in Nasopore) for surgical outcomes after endoscopic frontal sinus surgery in patients with chronic rhinosinusitis with nasal polyposis.

### 1.1. Background

Chronic rhinosinusitis (CRS) is defined by persistent sinonasal symptoms (nasal obstruction, facial pressure, nasal discharge, hyposmia) lasting at least 12 weeks and by objective findings of paranasal sinus inflammation.[1] CRS with nasal polyposis (CRSwNP) represents a subset of CRS defined by the above criteria along with the presence of nasal polyps in the middle meatus and has a variety of underlying causes.[2] Overall, cases CRSwNP respond well to endoscopic sinus surgery (ESS) with improvement in quality of life, symptom scores and endoscopic appearance.[3] However, surgical treatment of the frontal sinus has been shown to be more challenging with higher rates of recurrent sinus disease. Factors associated with failure of frontal sinus ESS include advanced disease at presentation, prior ESS, inflammation or scarring in the frontal recess, middle turbinate lateralization, size of frontal sinusotomy and retained/residual frontal recess cells.[4,5,6] Given these findings, meticulous surgical planning and removal of all obstructing bony partitions and diseased mucosa within the frontal sinus is advocated.

Additionally, in an attempt to decrease frontal sinus ESS failure, many methods of improving post-operative healing such as nasal saline and/or corticosteroid irrigations, oral corticosteroids, sinus stents, and more recently steroid releasing or impregnated stents/dressings have been used.[2,7-10] Of these approaches, there are only 2 Food and Drug Administration approved steroid releasing sinus implants used at the frontal sinus opening (FSO).[11] It has been shown in a randomized controlled trial that steroid releasing sinus implants can improve both subjective and objective outcomes after endoscopic frontal sinus surgery compared to controls.[11] However, to date there has been no comparison of steroid releasing frontal sinus implants vs. other means of direct steroid delivery to the FSO after ESS, such as via a steroid impregnated dressing. Presently both stents and dressings are used routinely after ESS, but typically any one patient would get one or the other treatment for each of their sinuses.

The present study was designed to evaluate and compare the surgical outcomes of frontal sinusotomy and placement of a steroid releasing implant vs. a steroid impregnated nasal dressing within the FSO with the subject serving as their own control by receiving the stent and dressing randomly assigned to either the left or right sinus.

## 2. STUDY DESIGN

### 2.1. Overview

This is a single center, randomized & controlled trial comparing the efficacy of the Propel mini or contour stent vs. Nasopore impregnated with triamcinolone acetonide at reducing frontal sinus opening stenosis and polypoid edema after ESS in patients with CRS with polyposis. Eligible subjects who undergo standard of care bilateral frontal sinusotomy will have each frontal sinus randomly assigned to either a Propel steroid eluting stent or a Nasopore nasal dressing impregnated with 2.5 ml of triamcinolone acetonide 40 mg/ml. The specific Propel stent will be chosen based on the shape of frontal sinus opening and best fit as decided by the operating surgeon. Patients will be reassessed on approximately post-operative day 7, 14, 30, 90 days, 6 months, and 12 months at their SOC follow-up visits. On the day 14 visit, the frontal sinus Propel stent and Nasopore will be completely removed per SOC. Video will be taken of the frontal sinus opening, and assessed for scarring/adhesions, presence of polypoid edema, frontal sinus patency, need for oral steroids or other interventions. Additionally, endoscopic scoring of frontal sinus by the above measures will be evaluated by 2 independent sinus surgeon reviewers. The reviewers will also be asked to rank the two frontal sinus openings as better, same or worse, compared to the opposite side.

### 2.2. Rationale for Study Design

Steroid impregnated bioabsorbable implants can reduce scarring and inflammation post-operatively in the ethmoid cavity. Recent studies have also shown that an FDA approved bioabsorbable steroid releasing implant placed in the frontal sinus after endoscopic sinus surgery can improve surgical outcomes. However, no study to date has compared different methods of steroid delivery to the frontal sinus after endoscopic sinus surgery. Our study will add to the limited data in the literature regarding the efficacy of steroid eluting implants placed in the frontal sinus opening after endoscopic sinus surgery and provide a direct comparison of two established steroid delivery methods. Patients will serve as their own control in order to provide a direct comparison between both steroid delivery systems while limiting bias from interpatient variability.

## 3. CHARACTERISTICS OF THE RESEARCH POPULATION

### 3.1. Subject Characteristics

a) **Number of Subjects:** We plan to enroll 30 total subjects (60 frontal sinusotomies total): each patient will have undergone bilateral frontal sinusotomy

b) **Gender and Age of Subjects:** Subjects 18 years of age and older will be included in the study. There will be no gender restrictions.

c) **Racial and Ethnic Origin:** There will be no restriction based on race or ethnicity.

### 3.2. Inclusion and Exclusion Criteria

1) **Inclusion Criteria:**
   a) Adults aged 18 and older
   b) Diagnosis of chronic rhinosinusitis with nasal polyps based on the American Academy of Otolaryngology–Head and Neck Surgery guidelines
   c) Patient scheduled for bilateral endoscopic sinus surgery with evidence of bilateral frontal sinus disease based on Computed Tomography (Lund-Mackay score greater than or equal to 1).
   d) At the time of surgery bilateral frontal sinusotomy of type Draf 2a or 2b was performed using the same technique on both sides.
   e) Bilateral endoscopic sinus surgery performed successfully without complication
   f) Frontal sinus opening diameter greater than 4.0 mm achieved (4 mm olive tipped suction easily passed into frontal sinus)

2) **Exclusion Criteria:**
   a) Any patient who had frontal sinus surgery for tumor
   b) Allergy to mometesone and/or triamcinolone
   c) Frontal sinusotomy type Draf 1 or Draf 3 performed
   d) One or both frontal sinus openings not amenable to implant placement
   e) Patients with chronic oral steroid dependent conditions
   f) Invasive fungal sinusitis
   g) Immune deficiency

   Pregnancy precludes elective endoscopic sinus surgery due to the risks of general anesthesia. Consequently pregnant women will not be included in this study.

### 3.3. Discussion of Subject Population

Patients enrolled in the study have been diagnosed with chronic rhinosinusitis with nasal polyps and deemed appropriate for surgical intervention. A complete pre-surgical work up and discussion regarding the treatment options including observation, continued medical treatment and surgical intervention will be offered as is standard for any patient with this condition. After discussion of the risks and benefits of surgery vs medical therapeutic options some patients will choose surgery and they will be offered participation in the study.

The ESS surgical procedure typically has a 1% complication rate and approximately 5% frontal sinusotomy failure rate at the time of surgery (inclusion criteria e-f). Thus by ensuring subjects meet inclusion criteria a) through d) and that none of the exclusion criteria apply prior to enrollment, we would have a very low rate of screen failure, where an enrolled subject does not ultimately meet inclusion criteria e) and f).

## 4. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT

### 4.1. Method of Subject Identification and Recruitment

Patients will be recruited from the clinical practice of the principal investigator. Preferentially subjects will be approached by an ENT resident (listed as study personnel) for consent to mitigate the potential coercion of having their surgeon inquire on their willingness to participate. However logistics may dictate that the PI or SC are the only people available and they may also obtain consent.

### 4.2. Process of Consent

If eligible, patients will be approached by an approved study team member to discuss the study prior to their surgery date, typically in person after they have chosen to proceed with sinus surgery. In a private room, candidate subjects will be assured that their decision to participate or not to participate will not affect the medical care that they can expect. If they are interested in participation, they may take the consent form home or they may provide consent at that time. When ready to consent, the teach-back method will be used to ensure that the subject understands their participation in the study.

The person obtaining consent will pass the form to the SC. Consent will be documented by the SC in a consent log in REDCap and signed forms will be stored in the Otolaryngology Department Research Office.

## 5. METHODS AND STUDY PROCEDURES

Screening may take place at the initial presentation to the principal investigator or a pre-operative visit up to 90 days prior to a planned Operative procedure. As part of their standard of care pre-surgical work-up subjects will provide a complete medical and sinonasal history and a complete head and neck exam including bilateral rigid nasal endoscopy will be performed. Pictures from this standard endoscopy will be taken of the frontal recess or frontal sinus opening if possible. Patients will also have had a CT sinus scan performed pre-operatively for surgical planning and intra-operative image guidance. Subjects will consent to this medical information being released to the study, which will be abstracted when the subject completes the study. If any patients do not have evidence of bilateral frontal sinus disease based on CT results (Lund-Mackay $\geq 1$), they will be screen-failed prior to surgery and will not be randomized.

Pre-operatively patients may receive oral steroids and/or antibiotics as deemed medically necessary. Each patient will receive the indicated sinus surgery based on their exam and symptoms, and in no way will be influenced by their decision to decline or enroll in the study. For treatment, the patients will undergo bilateral endoscopic sinus surgery which will include bilateral frontal sinusotomy of Draf 2a or 2b type as previously described in the literature. At the conclusion of the procedure, if the patient still meets all inclusion criteria, one frontal sinus will be randomly assigned using the envelop method to receive a bioabsorbable steroid releasing implant and the other frontal sinus will receive a bioabsorbable nasal dressing impregnated with steroid. Patients will taper their pre-operative oral steroids from 40 mg daily to 10 mg daily and continue use until their first post-operative visit and then stop. Post-operative antibiotics will be prescribed as deemed medically necessary. Patients will be encouraged to irrigate their sinus twice daily with a high volume (240 ml bottle) of normal saline solution. Patients will be allowed to continue nasal steroid sprays and/or orally inhaled sprays for control of asthma. The patient

will have standard post-operative visits at approximately 1 week, 2 weeks, 30 days, 90 days, 6 months and 12 months. On post-operative day 14 the first endoscopic evaluation of the frontal sinus opening after implant removal will be performed. Video is routinely recorded and this will be copied for the study, edited to remove any identifying features of the subjects, for review and scoring by qualified independent reviewers. If at any of the post-operative visits oral steroids, antibiotics or in-office procedures is deemed medically necessary this will be allowed and recorded as part of the study results. Subjects' participation will conclude at the 12 month visit.

Schedule of Activities (R Research/SOC Standard of Care)

| Visit | 0 (Screening) | Operative Visit | FUV 1 | FUV 2 | FUV 3 | FUV 4 | FUV 5 | FUV 6 |
|---|---|---|---|---|---|---|---|---|
| Visit timing | Up to 90 days pre-operative | Day 0 | 1 week post op (+/-3 days) | 2 weeks (+/-5 days) | 1 month (28 to 56 days post op) | 3 months (+/-14 days) | 6 months (+/-21 days) | 12 months (+/-21 days) |
| Obtain informed consent/confirm eligibility (R) | X | | | | | | | |
| Medical and sinonasal history evaluated (SOC) | X | | | | | | | |
| Bilateral endoscopic sinus surgery (SOC) | | X | | | | | | |
| Confirm eligibility/ Randomize treatment (R) | | X | | | | | | |
| Placement of frontal sinus opening treatments (SOC) | | X | | | | | | |
| Obtain validated SOC sinonasal symptom and quality of life questionnaires (SOC) | X | | X | X | X | X | X | X |
| Complete ENT and sinonasal exam including rigid endoscopy (SOC) | X | | X | X | X | X | X | X |
| Rigid endoscopy with documentation (SOC) | X | X | X | X | X | X | X | X |
| Abstraction from endoscopy record on frontal sinus opening scarring, polypoid edema, | | | | X | X | X | X | X |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| overall condition for data analysis and external review (R) | | | | | | | | |
| Adverse event review (R) | | | X | X | X | X | X | X |

## 5.1. **Efficacy Assessments**

Efficacy will be determined by comparing the right and left frontal sinus opening after removal of the stent and dressing on POD 14, and then around day 30, 90, 6 month and 12 months. The frontal sinus opening will be assessed with a rigid endoscope, using 30, 45 and/or 70 degree scopes as necessary. Our primary efficacy outcome will be a grade assigned by 2 blinded, independent sinus surgeon experts as: better, worse or same, comparing overall appearance of the study subject's frontal sinus openings after implant removal.

Additionally, the frontal sinus opening will also be graded on an adhesion/scarring scale, a polypoid edema scale, size in mm of the opening as measured by a visual analog scale/comparison to 4 mm suction, and visualization of the roof of the frontal sinus.

## 5.2. **Safety Assessments**

As standard of care for evaluation and management of any CRS patient who has failed medical treatment and is considering surgical treatment, patients will provide information on their general medical and specific rhinologic health. They typically receive a thorough ENT and rhinology focused physical exam. A CT sinus scan will be obtained on all patients as part of standard of care for image guidance during surgery and this will be reviewed in order to confirm inclusion and exclusion criteria prior to surgery. Appropriate SOC surgical screening lab tests as necessary will be reviewed to rule out metabolic, endocrine, inflammatory, autoimmune, and hematologic issues.

For safety assessment, the initial standard of care CRS workup and prior treatments will be documented when the subject enters the study. At each study visit after subjects have undergone a surgical intervention, subjects will be asked about changes to medical and rhinologic health, and in particular if they have had bleeding, eye swelling, change in vision, headaches, nasal discharge or other symptoms since surgery or their last visit.

## 5.3. **Costs to the Subject**

Standard costs of office visits, office procedures and surgery will be billed to the subject's insurance. Subjects would be expected to pay standard copayments for office visits and costs incurred through their insurance as described above. These costs could be identical to that which would have been incurred if a subject had not enrolled or withdrawn from the study depending on the patient's insurance. The bioabsorbable steroid eluting implant, if not covered or only partially covered by insurance, may end up costing more than the steroid impregnated nasal dressing. Both randomized dressing materials are currently used as part of standard of care in the

setting of frontal sinus surgery of Draf 2a and 2b types, and costs for both methods of packing/steroid delivery are subject to insurance variability and hence cost to the patients. This would be true of study and non-study patients.

### 5.4. Payment for Participation

Subjects will not be paid for participating.

### 5.5. Return of Individual Research Results

Individual research results will not be provided back to subjects.

## 6. SUBJECT WITHDRAWALS

Subjects will be advised in the written informed consent forms that they have the right to withdraw from the study at any time without prejudice. Subjects will be withdrawn from the research without their consent by the investigator if they no longer qualify for the inclusion/exclusion criteria, are non-compliant (miss required scheduled study visits precluding analysis), or if the investigator determines that it is in the best interest of the subject. There are no additional study activities requiring completion prior to subject withdrawal from the study. Subjects withdrawn from the study will not be replaced.

## 7. STUDY DEVICES

### 7.1. Bioabsorbable steroid releasing sinus implant: Propel mini stent ©
### 7.2. Bioabsorbable steroid releasing sinus implant: Propel contour stent ©

The PI will select which stent to use based on the shape of the post-surgical sinus opening. That is, in some cases the straight mini stent is a better fit, while in others the contour stent better matches the shape of the opening.

### 7.3. Bioabsorbable nasal dressing impregnated with 2.5 ml of Triamcinolone Acetonide 40 mg/ml: Nasopore ©

The Propel mini/contour stent and the Nasopore nasal dressing with triamcinolone acetonide are commercially available products and approved for use in the nasal sinuses after sinus surgery (see appendix 1-4). It is within standard practice to use these implants after sinus surgery in an attempt to improve mucosal healing and prevent scarring and/or stenosis.

### 7.4. Subject Enrollment/Randomization

Subjects will be enrolled on the basis of the inclusion and exclusion criteria and signed informed consent. Subjects will be randomized using the envelope method to have either the Bioabsorbable steroid releasing stent placed or Nasopore soaked with 2.5 ml of triamcinolone acetonide 40 mg/ml placed in the left frontal sinus opening. The right frontal sinus opening will

have the other device placed. Patients will serve as their own comparison group and as such there will be a 1:1 ratio of frontal sinus openings treated with each method.

## 8. RISK/BENEFIT ASSESSMENT

### 8.1. Potential Risks

- Invasion of subject privacy
- NB The risks of ESS are identical to non-study subjects who received similar procedures
- Theoretical risk of misplacing the stent and piercing the sinus bone.

### 8.2. Protection Against Risks

Privacy will be protected by minimizing the number people with access to the subject's identifying data, which will be stored in REDCap, making use of its built-in privacy protections. All study personnel will have training in human subject protections.
The risk of misplacing the stent is mitigated by direct imaging of the frontal sinus as the stent is being inserted and by the surgical skill of the surgeon.

### 8.3. Potential Benefits to Subjects

There is no anticipated benefit to the subject of participating since both stent and dressing treatments are presumed to be equally efficacious.

### 8.4. Alternatives to Participation

The alternatives to participation in the study include no medical or surgical treatment, continued medical therapy, or standard surgical therapy as deemed clinically indicated by the principal investigator or other treating physician.

## 9. CONFIDENTIALIATY OF DATA AND INFORMATION STORAGE

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from the subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for the use of their PHI

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

We will exercise the following practices to maintain confidentiality of data and protecting against unauthorized disclosure:

- not downloading identifying information from REDCap except subject ID number (i.e., keep any identifying information separately from any research data)
- locking up research files while they are unsupervised
- using screensavers
- shredding excess copies of paper documents
- protections for codes that link patients to their data
- electronic and physical security of data storage devices and networks
- security measures to protect storage and transmission of electronic data

Quality of life and other questionnaires are routinely acquired for patients during their SOC visits. They are then scanned into the electronic medical record and shredded. Data from these will be abstracted by approved study staff into a REDCap eCRF.

Endoscopic video and images are routinely acquired for frontal sinus patients. The PI transports these from the Clinic to the Medical Center in an AES-256 encrypted hard drive that is unlocked by his thumb print and loaded into DScope, which is hosted on a URMC password-protected server, where they are identified by patient name. The PI and ENT residents have routine access to this video. Video for the study will be edited from this raw footage, first to remove any brief images of the subject e.g. if the scope is moved quickly between nostrils in one take of video. Next it will be edited to standard segments for review and identified with the subject number, side, and time point.

## 10. RESEARCH INFORMATION IN MEDICAL RECORDS

Study participation will be indicated in the medical record.

## 11. DATA ANALYSIS AND MONITORING

### 11.1. **Data & Safety Monitoring Plan**

**I. Overview**

A. This is a single center, prospective, observational, minimal risk study performed with a cohort of adult subjects undergoing frontal sinus surgery. Subjects will have SOC surgery and at the end of surgery each nostril will get a dressing or stent that provides mechanical support and also exudes a steroid to aid wound healing. Presently either dressing or stent is typically used in both sinuses at the surgeon's discretion, and this trial will put one of each in each sinus (left/right at random) to compare with each subject as their own control, whether there are noticeable differences in wound healing due to either treatment, during the post-operative course. Subjects will be followed for up to 12 months post-surgery.

B. Adherence statement. The Data and Safety Monitoring Plan (DSMP) outlined below for this study will adhere to the protocol approved by the University of Rochester Research Subjects Review Board (RSRB).

**II. Adverse Events**

A. Adverse event assessment
   a. This is a minimal risk study and there is a risk of loss of privacy and of misplacement of the stent.
   b. Risk to privacy will be determined by whether identifying subject data had been released. This will be assessed annually.
   c. Misplaced stent will be determined by whether the stent is correctly in the sinus when it is removed at the post-operative visit when it would normally be extracted.

B. Adverse event reporting
   a. Every adverse event that is reported to either the PI or study staff by the subject or other medical staff caring for the subject and which meets the above criteria, or which otherwise merit documentation in the judgement of the PI, will be documented with a description of the event along with a determination by the PI of severity and relatedness to study participation.
   b. Adverse events will be reported annually to the RSRB as part of their Continuing Review of the study.

**III. Safety Review Plan and Monitoring**

A. Justification of sample size

The sample size is justified below in section 11.2

B. Safety and study progress reviews

The principal investigator will review adverse events as they occur and annually will review and report to the RSRB on study progress including recruitment and protocol adherence. This annual report will include a list and summary of adverse events, a statement of whether adverse event rates are consistent with pre-study assumptions, a summary of recruitment, and reason for withdrawals.

**IV. Informed Consent**

Consent is discussed in section 4.2 above.

**V. Data Quality and Management**

A. Data collection forms will be completed during and after study visits and transcribed to the REDCap database within a week of the study visit. The PI will review all data collection forms and REDCap on a monthly basis.

B. The REDCap database is cloud based and backed up by the University of Rochester. It logs data entry and modification and so provides an audit trail if necessary. It also allows compliance of data types during data entry and has other quality control tools to allow the PI to assess the completeness and accuracy of data entry.

**VI. Confidentiality**

Confidentiality is addressed in section 9, above.

11.2. **Sample Size Determination**

Sample size is based on a non-inferiority design. Based on historical data it can be estimated that frontal sinusotomy will have a patency (success) rate of 85%. Given the lack of any known evidence to the contrary, we will assume that both the Propel mini/contour stent and the Nasopore impregnated with 2.5 mls of Kenalog 40 mg/ml placed in the FSO after ESS will result in a patency rate of 85%. Given that all prior clinical trials investigating local delivery of steroid to the FSO have utilized the Propel mini or contour stent, this will serve as our "standard therapy" group. Using an $\alpha = 0.05$, Power= 80%, and a minimum significant difference ($\delta$) of 25%, 28 patients (56 total frontal sinus interventions) will be enrolled to be 80% sure that the upper limit of a one-sided 95% confidence interval will exclude a difference in favor of the "standard therapy" group of more than 25%. The ESS surgical procedure typically has a 1% complication rate and frontal sinusotomy failure rate of approximately 5%. Thus by ensuring subjects meet inclusion criteria a) through d) and that none of the exclusion criteria apply prior to enrollment, we would have a very low rate of screen failure, where an enrolled subject does not ultimately meet inclusion criteria e) and f). Hence enrolling 30 subjects should be sufficient to reach our statistical needs.

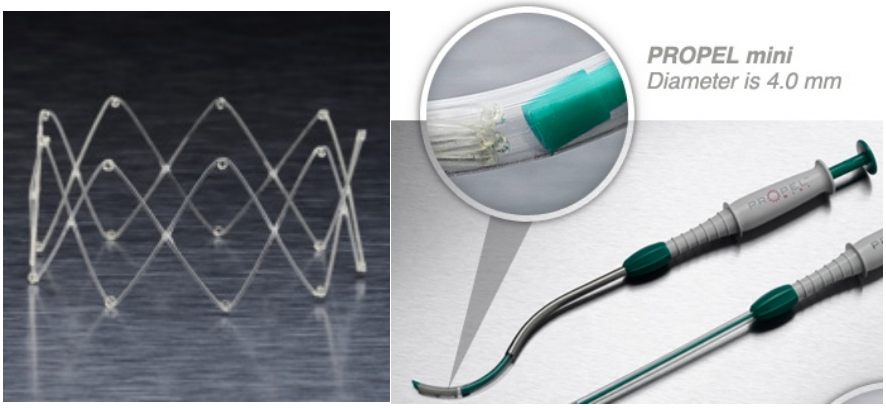
11.3. **Planned Statistical Analysis:**

**Primary outcome measure:** Grading by a blinded independent sinus expert as to whether the the propel sinus stent frontal sinusotomy side is better, worse or the same.

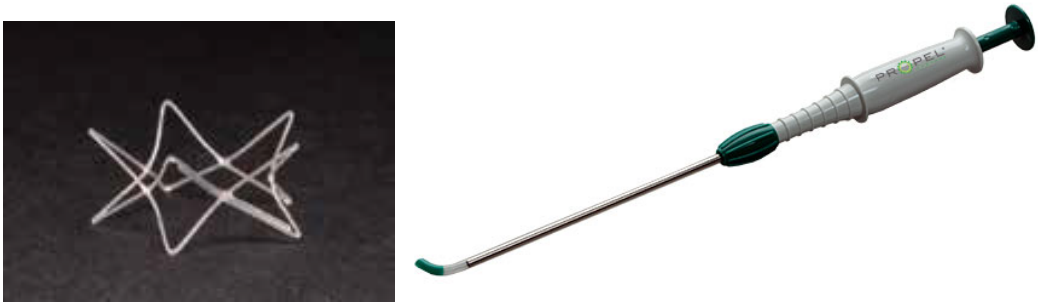
**Secondary outcome measures:**

1. Mucosal/polypoid edema
2. Adhesion/scarring
3. Size of frontal sinus opening
4. Visualization of the frontal sinus roof
5. Need for post-operative oral steroids
6. Need for post-operative interventions beyond normal debridement

Appendix 1 – Images- Propel mini stent

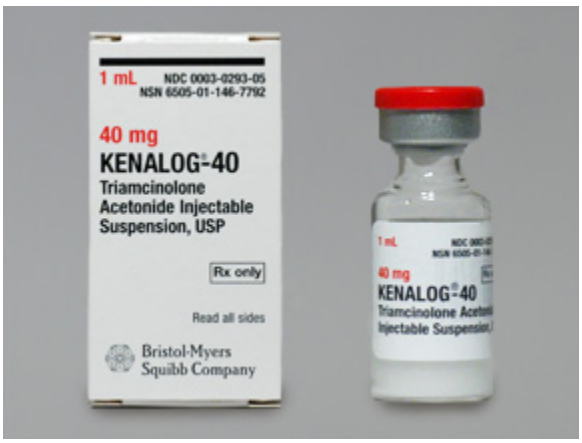


Appendix 2- Images- Propel contour stent

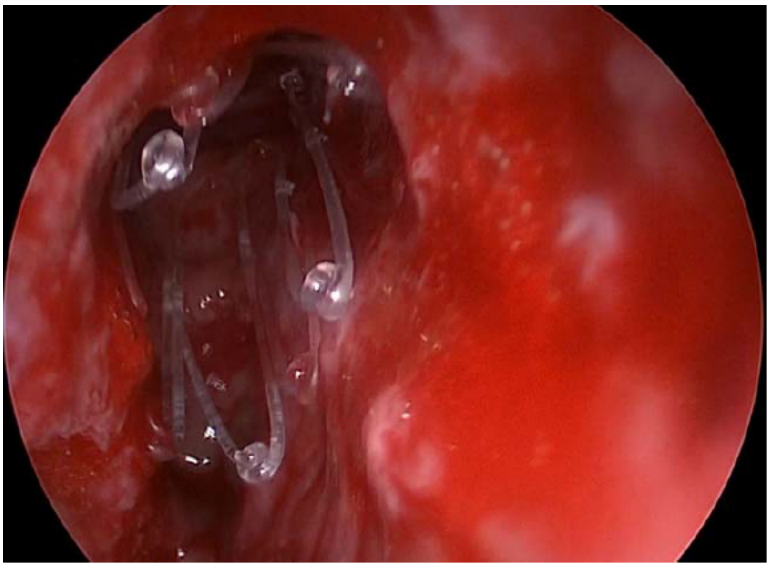


Appendix 3 – Images- Nasopore

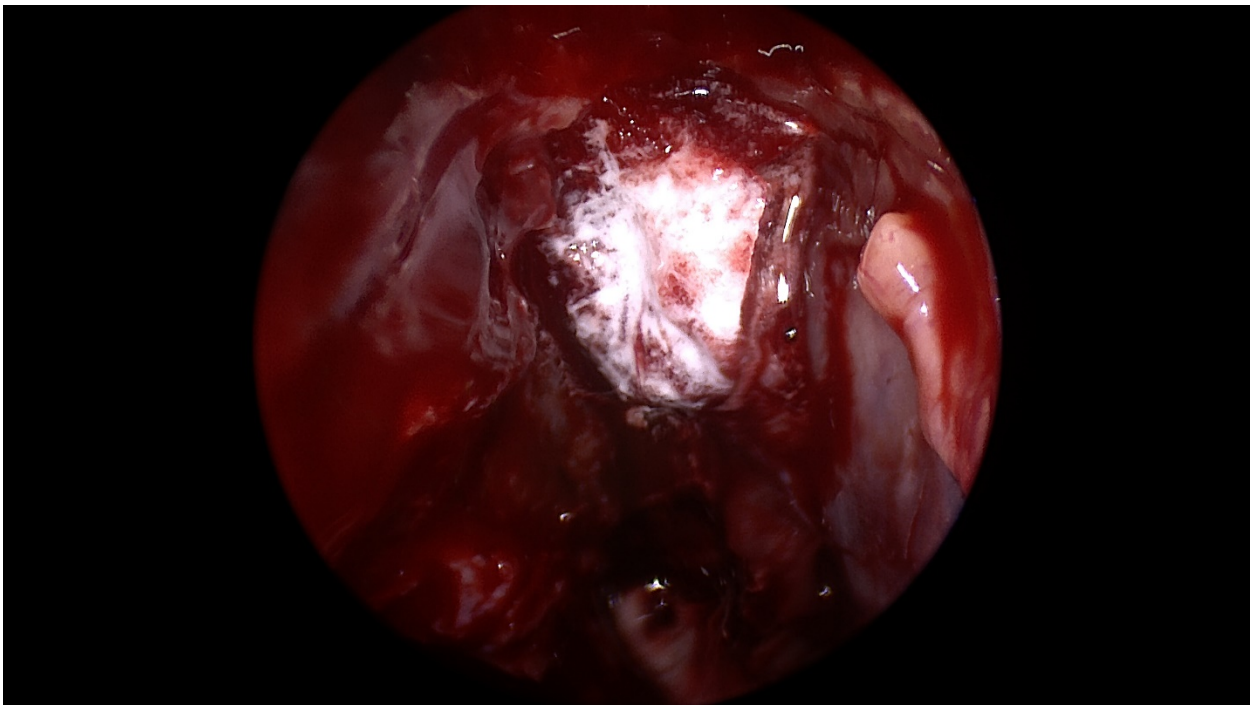
Appendix 3- images [triamcinolone acetonide 40 mg/ml (Kenalog 40)]



Appendix 4 – images of implant within frontal sinus opening as described by protocol



B) **Nasopore impregnated with 2.5 mls of Kenalog within the frontal sinus opening after endoscopic sinus surgery**



References:


1) Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg 2015; 152: S1–S39
2) Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on Rhinosinusitis and nasal polyposis. Rhinology 2012; 50: 1-298.
3) Ragab SM, Lund VJ, Scadding G, et al. Impact of chronic rhinosinusitis therapy on quality of life: a prospective randomized controlled trial. Rhinology 2010; 48:305-11
4) Chandra RK, Palmer JN, Tangsujarittha T, et al. Factors associated with failure of frontal sinusotomy in the early follow-up period. Otolaryngol Head Neck Surg. 2004; 131:514-8
5) Valdes CJ, Bogado M, Samaha M. Causes of failure in endoscopic frontal sinus surgery in chronic rhinosinusitis patients. Int Forum Allergy Rhinol. 2014; 4:502-6
6) DeConde AS, Smith TL. Outcomes After Frontal Sinus Surgery: An Evidence-Based Review. Otolaryngol Clin North Am. 2016; 49:1019-33
7) Rowe-Jones JM, Medcalf M, Durham SR, et al. Functional endoscopic sinus surger y : 5 year follow up and results of a prospective, randomised, stratified, double-blind, placebo controlled study of postoperative fluticasone propionate aqueous nasal spray. Rhinology. 2005; 43:2-10.
8) Wright ED, Agrawal S. Impact of perioperative systemic steroids on surgical outcomes in patients with chronic rhinosinusitis with polyposis: evaluation with the novel Perioperative Sinus Endoscopy (POSE) scoring system. The Laryngoscope. 2007;117(11 Pt 2 Suppl 115):1-28.

9) Huang Z, Hwang P, Sun Y. Steroid-eluting sinus stents for improving symptoms in chronic rhinosinusitis patients undergoing functional endoscopic sinus surgery. Cochrane Database of Systematic Reviews. 2015; 6: 1-21.
10) Cote DJ, Wright ED. Triamcinolone-impregnated nasal dressing following endoscopic sinus surgery: A randomized, double-blind, placebo-controlled Study. Laryngoscope. 2010; 120:1269-73
11) Smith TL, Singh A, Luong A, et al. Randomized controlled trial of a bioabsorbable steroid releasing implant in the frontal sinus opening. Laryngoscope. 2016; 126:2659-2664.