

Randomized Trial Comparing Anchorsure® Suture Anchoring System and the Capiro™ Slim Suture Capturing Device for Sacrospinous Ligament Suspension.

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ABSTRACT

Sacrospinous ligament fixation is a common method of repairing apical support for pelvic organ prolapse but it currently suffers from a high rate of postoperative buttock and posterior thigh pain. Rates of buttock and thigh pain 6 weeks after sacrospinous ligament fixation with the widely used Capiro™ Slim device (Boston Scientific) are about 15-16% with immediate postoperative pain occurring in 55-84% of patients. Our study is a randomized controlled single-blind study with the primary goal of investigating if there is an improvement in the rate of buttock and posterior thigh pain 1 day, 1 week, and 6 weeks after sacrospinous ligament fixation with a new device, the Anchorsure® Suture Anchoring System (Neomedic) compared to the widely utilized Capiro™ Slim (Boston Scientific) device. We will enroll 60 patients who are planned to undergo sacrospinous ligament fixation for treatment of pelvic organ prolapse. The patients will be randomized into two study groups; one will have sacrospinous ligament fixation using the Capiro™ Slim device and the other with the Anchorsure® device. The patient's pain will be recorded via numerical rating scales (NRS), a validated pain evaluation tool. The study is powered to detect a 2.5 point difference in pain between the two groups, a value that has been shown in studies to be clinically significant to patients. Secondary outcomes of surgeon satisfaction and efficiency with the devices will be assessed via surgeon questionnaires. The demonstration of a significant decrease in postoperative buttock or thigh pain, improved surgeon efficiency, or decreased operative time with the use of the Anchorsure device will demonstrate an advantage of the suture anchoring devices over suture capture devices and will fuel the need for a larger efficacy study for the Anchorsure device. Demonstration of improved safety and/or improved surgical outcomes could ultimately change the standard in sacrospinous ligament fixation surgical technique.

BACKGROUND AND SIGNIFICANCE

Pelvic organ prolapse (POP) describes the loss of anatomic support of the vagina where women present with a vaginal bulge with or without associated bladder, bowel or sexual complaints. The lifetime risk of undergoing surgery for female pelvic organ prolapse is estimated at 19%.¹ One of the most common approaches to repair of apical vaginal prolapse is suspension of the vaginal apex or cervix to the **sacrospinous ligament** using suture material, a technique that avoids entry into the peritoneal cavity.

The current standard practice is to use a self-capturing suture delivery systems like the **Capiro™ Slim Suture Capturing Device**. This procedure is associated with a significant risk of **postoperative buttock and posterior thigh pain**.^{2,3} Such pain can arise from entrapment of the pudendal or sciatic nerves given their close anatomic proximity to the sacrospinous ligament suture fixation (Figure 1) or from entrapment of the levator ani nerve that runs along the surface of the

coccygeus muscle.⁴ Immediate postoperative buttock and posterior thigh pain with the Capiro™ device has been reported in 55-84% of patients with persistent pain at 6 weeks postoperatively in 15-16%.^{4,2}

The use of an anchor-based system into the sacrospinous ligament, as opposed to a suture-based system, could theoretically reduce the risks of suture entrapment particularly of the levator ani nerve thereby reducing the high rate of postoperative buttock and thigh pain. Anchor-based pelvic organ prolapse repair systems have been studied and utilized domestically and internationally for mesh-based prolapse repair kits. However, there is currently little evidence about the rates of postoperative buttock and posterior thigh pain from anchor-based fixation to the sacrospinous ligament for native tissue vaginal repair.

The **Anchorsure®** (Figure 2 and Figure 3) is a new FDA-approved sacrospinous ligament fixation device that deploys a permanent anchor directly into the ligament and requires high pull-out force for extraction. The device is a Class II surgical device that was FDA approved via a 510(k) premarket notification in 2012. Its approval was based on the FDA approved device Surelift® (Neomedic). Surelift® uses the same anchoring system as Anchorsure but is attached to vaginal mesh as opposed to Anchorsure which is designed to attach to suture material. Surelift® is used widely and has been studied in abstracts⁵⁻⁹ and a published study¹⁰ confirming safety and surgical efficacy. Abstracts on the use of Anchorsure have additionally been published indicating safety and efficacy of use.^{11,12} A summary of the available data for the Capiro Slim™, Surelift®, and Anchorsure® devices is listed in Appendix 1.

The **primary aim** of this study is to conduct a prospective randomized trial of this new anchor-based system versus our current suture-capture-based fixation systems to compare the rates of postoperative buttock and posterior thigh pain. This is important because decreased buttock and posterior thigh pain can reduce patient suffering and potentially reduce postop narcotic use. Our **secondary aims** are to compare intraoperative complications, general postoperative pelvic pain and post-hospitalization opioid use as well as surgeon satisfaction and surgical efficiency with the device. The demonstration of a significant decrease in postoperative buttock or thigh pain, improved surgeon efficiency, or decreased operative time with the use of the Anchorsure device will demonstrate an advantage of the suture anchoring devices over suture capture devices and will fuel the need for a larger efficacy study for the Anchorsure device. Demonstration of improved safety and/or improved surgical outcomes could ultimately change the standard in sacrospinous ligament fixation surgical technique.

Figure 1. Pelvic anatomy demonstrating the neurovascular structures near the sacrospinous ligament.⁴

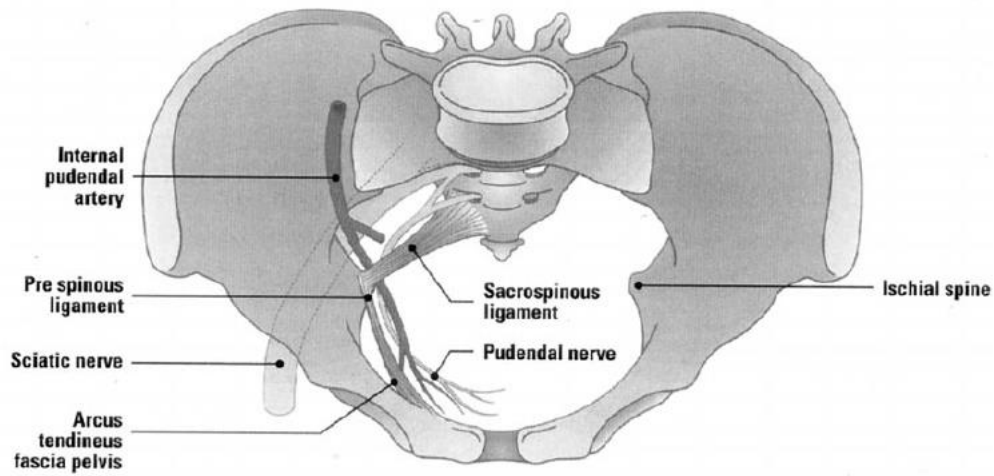


Figure 2. Anchorsure® System¹³

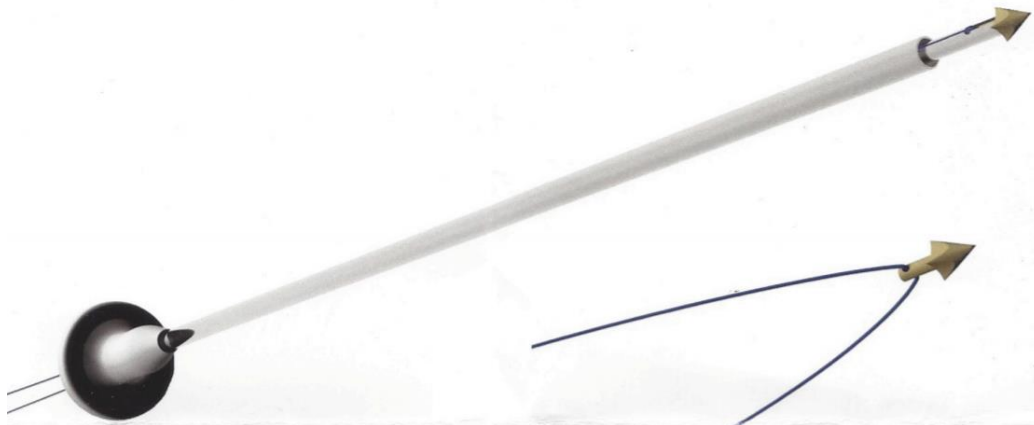
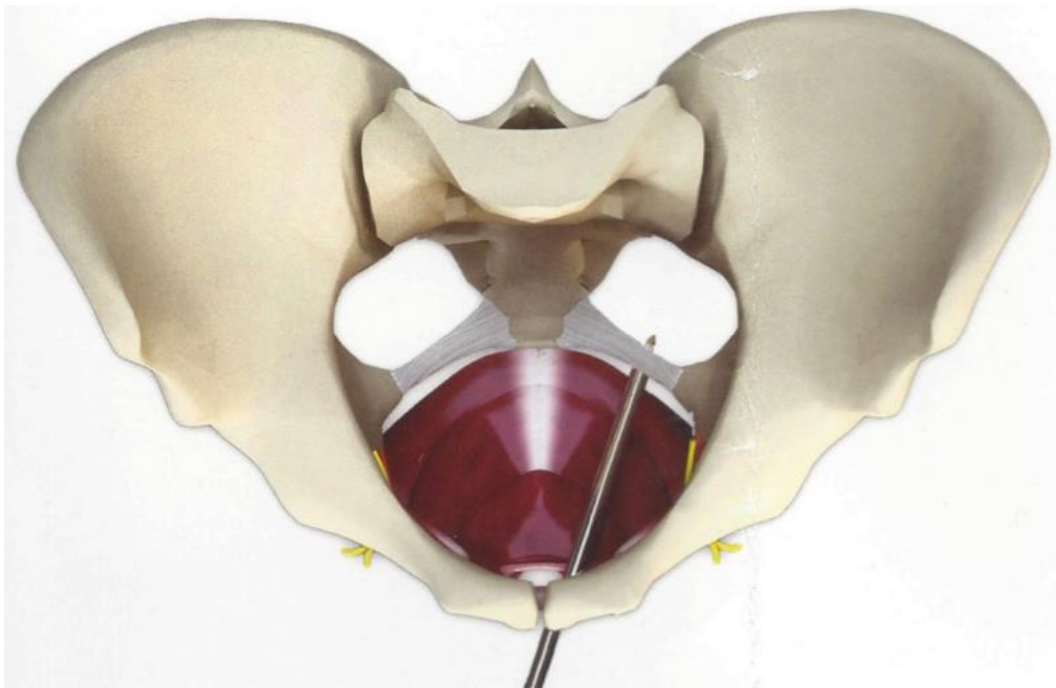


Figure 3. Anchorsure® System application to sacrospinous ligament¹³



STUDY OBJECTIVES

Hypothesis 1: Anchorsure® System will reduce postoperative buttock and posterior thigh pain at 1 day, 1 week, and 6 weeks following sacrospinous ligament fixation compared to the Capio™ Slim Suture Capturing Device

Specific Aim 1:

To conduct a prospective, randomized, single-blind trial of sacrospinous ligament fixation of the cervix or vaginal apex using Anchorsure® system versus the Capio™ Slim device in women with \geq Stage II pelvic organ prolapse who are undergoing native tissue vaginal repair. The **primary outcome** will be the level of postoperative pain using a 10-point numerical rating scale (NRS) on postoperative day 1, week 1, and 6 weeks postoperatively for pain that is localized to the posterior thigh or buttocks on the side(s) that the sacrospinous fixation was performed. The difference in mean pain ratings will be at least 2.5 on the 10-point NRS.

Hypothesis 2: Surgeon satisfaction, surgical efficiency, intraoperative complications, objective surgical success, symptomatic success, opioid use within the first week postoperatively following hospitalization, and overall postoperative pelvic pain will be similar for both devices.

Specific Aim 2:

The **secondary outcomes** will compare overall surgeon satisfaction with the 2 devices using a 5-point Likert rating scale and surgical efficiency measured in minutes from the start of the use of the surgical device until the surgeon is satisfied with the application of all sacrospinous sutures (does not require the sutures to be tied down). Intraoperative complication related to sacrospinous ligament suspension will be recorded including the need for suture or anchor replacement, hemorrhage that requires additional surgical interventions or blood transfusion, and equipment malfunction. General postoperative pelvic pain will be assessed at postoperative day 1, week 1, and 6 weeks along with buttock and posterior thigh pain via NRS questionnaires. Objective apical repair anatomical success will be assessed at the 6 week postoperative visit via a POP-Q examination with Stage II or greater indicating anatomical failure. Symptomatic surgical success will be evaluated by statistically significant increases or decreases in the responses to the PFDI-20 and PFIQ-7 questionnaires at the 6 week postoperative visit compared to preoperative values.

SUBJECT SELECTION**Inclusion Criteria**

1. Female patients
2. At least 21 years of age
3. Surgical plan that includes a native tissue vaginal repair with apical support via sacrospinous ligament fixation. We will permit both hysteropexy and post-hysterectomy sacrospinous ligament suspension
4. Understanding and acceptance of the need to return for the 6 week follow-up visit
5. English speaking and able to give informed consent
6. Willing and able to complete all study questionnaires
7. Ambulatory

Exclusion Criteria

1. Prior sacrospinous ligament fixation procedure.
2. Any serious disease or chronic condition that could interfere with the study compliance
3. Inability to give informed consent
4. Pregnancy or planning pregnancy prior to the 6 week postoperative visit
5. Prior pelvic radiation
6. Incarcerated

7. Prior augmented (synthetic mesh, autologous graft, xenograft, allograft) prolapse repair
8. History of significant buttock or leg pain in the past 3 months
9. History of fibromyalgia, polymyositis, dermatomyositis, systemic lupus erythematosus, or other auto-immune myalgic conditions
10. Current regular narcotic drug therapy for any chronic pain condition
11. History of loss of motor or sensory function of the lower extremities
12. History of sacral decubitus ulcers
13. Planned concomitant levatorplasty; anal sphincteroplasty, anal fissurectomy, rectopexy, or hemorrhoidectomy

STUDY POPULATION, RECRUITMENT AND SCREENING

Study population participants will consist of women who are scheduled to undergo native tissue POP repair using apical support to the sacrospinous ligament. Women scheduled to undergo sacrospinous hysteropexy and sacrospinous suspension of the vaginal vault will be recruited at Wake Forest Baptist Medical Center.

Participants must have vaginal bulge symptoms defined by positive responses to a validated instrument, the Pelvic Floor Distress Inventory (PFDI)^{14,15}, Stage II or greater POP in any vaginal compartment as determined by the Pelvic Organ Prolapse Quantification (POPQ) system,¹⁶ a validated tool designed to assess the degree of vaginal prolapse, and an apical prolapse contribution to the patient's overall pelvic organ prolapse as deemed by the examining physician. An apical prolapse contribution is detected by either the descent of the "C" component of the POP-Q system or as the demonstration of at least partial correction of an anterior or posterior prolapse via manipulated suspension of the apex during on pelvic examination.

Study subjects will be recruited from patients who present to the Urology or Gynecology clinical sites at Wake Forest Baptist Health. Institutional review board (IRB) approval will be obtained at this site. There will additionally be advertisement of the study through print or digital media to assist in patient recruitment. All advertisements will abide by research study advertisement regulations set by Wake Forest Baptist Health.

Potential subjects will be identified by members of the Urology and Gynecology departments at Wake Forest Baptist Health. Eligible patients who agree to participate will be provided written informed consent administered by the collaborators listed on the IRB document.

PRE-INTERVENTION ASSESSMENTS

All women presenting to the participating clinical center with signs and symptoms of prolapse who have elected to undergo sacrospinous ligament suspension will be screened for their eligibility. If eligible and consenting, the following baseline data will be collected on paper forms that will then be transcribed into a secure REDCap (Research Electronic Data Capture) database:

1. Demographic data including age, race, BMI, insurance status, level of education obtained
2. Pre-operative morbidity as measured using the Charlson Comorbidity Index
3. Smoking status
4. POP-Q data
5. Need for ambulation assistance
6. History of lower extremity disease, injuries, and functionality
7. Medical and surgical history
8. Level of pre-operative pelvic pain using 10-point NRS
9. PFDI questionnaire

RANDOMIZATION AND MASKING

A computer-generated random allocation using a randomly permuted block design (10-patients per block) will be utilized. Randomization will be performed at the start of the study with study group assignments placed in sealed non-transparent envelopes. The envelopes will be numbered in order. The next envelope in numerical order will be brought to the operating room where it will be opened by a participating surgeon and another operating room staff member. Both personnel will sign the envelope to validate that proper envelope opening and interpretation were performed. The envelopes will then be collected for record keeping. This procedure will help to minimize surgeon bias as it is impossible for surgeons to be masked to the randomization. Participants and research staff will be masked during the study as much as possible, however there will be a description of the type of sacrospinous ligament fixation device used within the body of the operative note for each patient that research staff could gain access to. Intraoperative data, including any adverse event that may unmask the study coordinators, will be reported by the surgeon directly to the study administrators.

STUDY INTERVENTION

The primary intervention is sacrospinous fixation utilizing either the Anchorsure® system or the Capiro™ Slim device. Concomitant anterior and/or posterior colporrhaphy (plication of fibromuscular vaginal tissue), enterocele repairs, transvaginal hysterectomy, bilateral salpingo-oophorectomy, perineoplasty, midurethral sling procedures, or other procedures not involving the pelvis, anus, buttock, or lower extremities may be performed. Prolapse procedures will be recorded but not controlled by study protocol. Participating surgeons are all extensively experienced in sacrospinous ligament fixation. Any use of allograft, xenograft, or synthetic graft material for POP repair will not be permitted.

Access to the retroperitoneal space will be accomplished either via a circumferential pericervical, an anterior, or a posterior. The method of surgical approach will be recorded. Sharp and blunt dissection will be performed to gain access to the sacrospinous ligament(s). Surgeon discretion will determine if unilateral or bilateral fixation is performed for vaginal vault suspension but only unilateral sacrospinous ligament suspension will be permitted for hysteropexy. Surgeon discretion will determine the type and number of sutures or anchors to be placed through the sacrospinous ligament and this data will be recorded. All sutures and anchors placed into the sacrospinous ligament will be placed at least 2cm medial to the ischial spine. Suture(s) will be placed through any anchors with the choice of suture to be determined by the surgeon as this is not anticipated to interfere with any results. The suture(s) placed through anchors or the sacrospinous ligament directly will then be attached to the cervix and/or vaginal apex. Sacrospinous sutures will be tied down once all mid-vaginal repairs are completed. Transvaginal hysterectomy, bilateral salpingectomy, bilateral oophorectomy, and enterocele repair procedures will be performed prior to sacrospinous ligament fixation.

POST-INTERVENTION ASSESSMENTS

The primary study endpoints will be assessed on postoperative day 1, postoperative week 1, and postoperative week 6 via a NRS. Day 1 questionnaires will be given during morning rounds. 1 week following their procedure, patient's will be called at home to remind them to fill out the week 1 questionnaire that would have been given to them during their hospital stay. This questionnaire will be accompanied with a pre-paid and pre-addressed envelope for the patient to use or, if desired, they can bring the completed week 1 questionnaire to their week 6 follow up appointment. All patients will return to the clinic for 1-week and 6-week post-surgery follow up appointments and will fill out an NRS pain assessment (1-week and 6-week), opioid use questionnaire (1-week), PFDI questionnaire (6-week), physical examination including POP-Q (6-week), and review of any postoperative complications (1-week,6-week).

Clinical outcomes

This trial has a **primary** outcome of level of postoperative buttock or posterior thigh pain on postoperative day 1, week 1, and 6 weeks as measured using the NRS. An independent t-test will be used to compare the means of the NRS scores from the two groups. The NRS is one of the most common validated pain questionnaire modalities.^{17,18,19,20,21} A clinically significant difference will be considered 2.5 on the 10-point NRS based on a prior paper assessing buttock pain from sacrospinous ligament fixation²² and with published studies assessing clinically meaningful decreases in acute pain.^{18,17} The patient's will be given copies of the NRS questionnaire which will be collected in person on postoperative day 1, week 1, and 6 weeks postoperatively.

Secondary outcome measures will assess the degree to which the study intervention influences surgeon satisfaction, surgical efficiency, adverse events intra- and postoperatively, surgical success, symptomatic success, and the level of postoperative general pelvic pain. Surgeon satisfaction will be assessed via a 5-point rating scale (very dissatisfied, somewhat dissatisfied, neutral, satisfied, very satisfied) and treated as categorical values. Surgical efficiency will be assessed as continuous data measured as a means in minutes. Adverse events will be evaluated as dichotomous data. All adverse events will be reported by the Dindo classification system. Short-term objective surgical success will be assessed by a postoperative exam at 6 weeks and descent of the vaginal apex beyond TVL/2 will be considered surgical failure. Symptomatic success will be assessed by the PDFI-20 questionnaires to be given at 6-weeks post-operation and compared to preoperative values. The patient's will also be queried about their general pelvic pain on the same questionnaires used to assess buttock and posterior thigh pain. Oral opioid use following hospitalization until postoperation day 6 will be recorded via opioid use questions on the 1 week postoperation questionnaire. The opioid dose will be converted into morphine equivalents for data analysis. Statistical analysis will be done in collaboration with the Wake Forest Baptist Hospital CTSI Biostatistics Department. Independent t-tests will be used for all continuous data, except for the PFDI and PFIQ data that will use paired t-tests as the two samples are dependent. Chi-square tests will be used for all dichotomous and categorical data.

POWER CALCULATION:

This study is a head to head two sample comparative study. The null hypothesis is that there is no difference in the prevalence of immediate postoperative new buttock or posterior thigh pain with the use of the Anchorsure® System compared to the Capio™ Slim device for sacrospinous ligament fixation. In prior published study by Ferrando et al the mean postoperative day 1 buttock or posterior thigh pain had a greater standard deviation (2.7-2.9) compared to week

1 and week 6 data. Therefore for our power calculation used an expected standard deviation of 2.9 to provide confidence in our power of assessing the difference in pain scores across all three timepoints.²² A decrease in in-hospital postoperative buttock or posterior thigh pain prevalence of 2.5 on a 10-point scale was chosen as clinically significant and is consistent with published data.^{22,18,17} Using a standard deviation of 2.9 and a difference in pain scores of 2.5 setting the level of significance, 21 patients are required in each group to provide a power of at least 80% to reject the null hypothesis (H0) that the Anchorsure® System does not lead to significantly less postoperative buttock and posterior thigh pain than does the Capiro™ Slim Device in favor of the alternate hypothesis that the Anchorsure® System leads to significantly less postoperative pain than the Capiro™ Slim Device using a two-sample normal approximation test of means with a two-sided 5% significance level. Assuming a 15% loss to follow-up or drop-out rate for the duration of the study, the total enrollment goal is 48 patients (24 in each group). The null hypothesis will be declared rejected if the mean of immediate postoperative buttock and posterior thigh pain with use of the Anchorsure® device is less from the mean with the use of the Capiro™ Slim device with a p-value of 0.05 or less. The power calculations and their adjustment from the original study goal of 60 recruited patients (using 90% power and a standard deviation of 3) were confirmed with the Wake Forest Baptist Hospital CTSI Biostatistics Department.

CALENDAR OF EVENTS

Form / Intervention	Preop Clinic	Intra-operatively	Day 1	Week 1	Week 6
Informed Consent	X				
Study Inclusion Form	X				
Preop Baseline Data Form with Charlson Comorbidity Index and POP-Q	X				
PFDI-20 and PFIQ-7 Forms	X				X
NRS Pain Questionnaires	X		X	X	X
Oral Opioid Use Questionnaire				X	
Randomization		X			
Adverse events		X	X	X	X
Surgeon Questionnaire		X			
Gift Card Disbursement and Gift Card Confirmation Form					X
Completion of Study Form					X

DATA COLLECTION & MANAGEMENT

Data collection will occur in the clinic and in the hospital at each encounter outlined in the Calendar of Events. All study data will be recorded on data collection sheets and will be transcribed into REDCap. Any discrepancies between progress notes and supporting source documents such as physician's notes should be explained in the progress notes. Any changes made to original written entries in progress notes should be crossed through with a single line, initialed, and dated by the person making the correction to not obscure the original entry. Any changes made to original electronic entries in progress notes should be implemented in an electronic note addendum that is signed and dated by the person making the correction to not obscure the original entry.

Data will be entered by study staff into a REDCap database (described in detail in the "STUDY SUBJECT PROTECTION" section of this protocol) that will be stored on a secure server by the data coordinating center. Study data source documentation and progress notes will be monitored by the data coordinating center as outlined in the "STUDY MONITORING AND DOCUMENTATION" section. Data collected from visits should be entered into REDCap within 5 business days. Any queries to data entered into REDCap should be addressed within 5 business days. The study coordinators will regularly check REDCap for queries.

The study site will maintain all essential study documents in original format and source documentation that support the data collected on study participants in compliance with ICH/GCP guidelines. Documents must be retained until at least 2 years have elapsed since the formal discontinuation of the clinical investigation. The study site will be responsible to ensure that these essential documents are retained and are not accidentally damaged or destroyed prior to the required elapsed time.

STUDY MONITORING AND DOCUMENTATION**Study Monitoring**

The Principal Investigator will monitor the study and assess the need for amendments as the study progresses. If a protocol revision is necessary for reasons including but not limited to the rights, safety, or welfare of participants, or scientific integrity of the data, an amendment is required. IRB or equivalent approvals of the revised protocol—and if necessary, revised informed consent—must be obtained prior to implementation.

Data Monitoring

Semi-annual data verification will be conducted by Dr. Plair to verify that data entry into REDCap is accurate, and to assess compliance with the study protocol requirements. Study data will be source verified for roughly 25% of the overall data collection efforts.

Protocol Deviations

Protocol deviations must be documented on the protocol deviation CRF provided by the study investigators, logged in the study site protocol deviation log, and entered into REDCap.

Deviations will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective and preventative actions (including notification, personnel re-training, or discontinuation) will be put into place by the principal investigator.

Study staff must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. Study staff shall notify the PI and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency, and those deviations which affect the scientific integrity of the clinical investigation. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred. All deviations from the investigational plan, with the reason for the deviation and the date of occurrence, must be documented and reported to the Data Coordinating Center.

REPORTING ADVERSE EVENTS

Adverse events (AEs) will be recorded and reported according to the criteria and timeline below.

All AEs must be recorded on the AE CRF supplied by the study coordinator, entered into the site AE log, and then entered into REDCap. Each AE will be sequentially numbered according to patient. For example, patient 008's first AE would be 008.01. The principal investigator will determine the relationship of the AE to the operative procedures, the relationship of the AE to the device, along with the severity of each reportable AEs. All complications will be adjudicated by a Co-Investigator assigning DINDO scores. The adjudicating Co-Investigator will also determine if the complications are more likely to be related to the overall surgery, sacrospinous ligament fixation surgery or both. Complications that are deemed not related to the surgery will be excluded (such as, a carpal tunnel

syndrome exacerbation at 6 weeks post-operation).

Severe AEs (SAEs) must be reviewed by the PI within two business days.

TABLE 1. Classification of Surgical Complications DINDO Grade Definition

Grade 1	Any deviation from the normal postoperative course without the need for pharmacologic treatment. Allowed therapeutic interventions are: drugs as antiemetics, antipyretics, analgesics, physiotherapy
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
Grade III IIIA IIIB	Requiring surgical, endoscopic or radiological intervention - Intervention not under general anesthesia - Intervention under general anesthesia
Grade IV IVA IVB	Life-threatening complication (including CNS complications)* requiring IC/ICU management - Single organ dysfunction (including dialysis) - Multi-organ dysfunction
Grade V	Death

Reportable AEs include those determined to be related to the operative procedures or the device as listed below:

Intraoperative complications attributable to sacrospinous ligament fixation:

- Pelvic hemorrhage
- Buttock pain or posterior thigh pain on a side with a sacrospinous ligament fixation
- Lower extremity impaired sensation on a side with a sacrospinous ligament fixation
- New neurologic conditions in the lower extremity on a side with a sacrospinous ligament fixation
- Rectal or bladder injury during dissection or placement of sacrospinous ligament sutures
- Avulsion/loss of bullet on Capio™ device

Postoperative complications:

- Infection requiring antibiotics

- Cardiac or myocardial infarction
- New neurologic conditions
- New pulmonary conditions
- Pelvic abscess
- Blood transfusion
- Venous thromboembolism
- Hospital readmissions
- Emergency room evaluations
- Unplanned clinic visit
- Leg pain or difficulty ambulating on a side of the body without a sacrospinous ligament fixation
- Pelvic fistulas involving the vagina, bladder, or bowels
- Reoperations including repeat prolapse surgery

Please note that underlying diseases are not reportable as AEs unless there is an increase of severity or frequency during the course of the study that is directly attributable to the surgical intervention. If an AE has not resolved at the time of AE Form completion, the form will be saved as incomplete in REDCap until resolved. Once the AE is resolved, the AE form will be updated, saved as complete, and entered into REDCap.

Adverse Event Definitions

Adverse Event: any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including abnormal laboratory finding) in subjects, whether or not related to the operative procedures

Serious Adverse Event: an adverse event that:

- Led to death
- Led to serious deterioration in the health of the subject that either resulted in
 - a life-threatening illness or injury
 - a permanent impairment of a body structure or a body function
 - in-subject or prolonged hospitalization of existing hospitalization
 - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
- Led to fetal distress, fetal death or a congenital abnormality or birth defect

Relationship of AE to Operative Procedures:

- Unrelated: No evidence that the timing of the AE has a relationship to the operative procedures performed.
- Possibly Related: The AE has a timely relationship to the operative procedures performed, however a potential alternative etiology may be responsible for the AE.
- Probably Related: The AE has a timely relationship to the operative procedures performed and the causative relationship can clearly be established. No potential alternative etiology is apparent.

Relationship of AE to Device:

- Unrelated: No evidence that the timing of the AE has a relationship to the device placement.
- Possibly Related: The AE has a timely relationship to the device placement, however a potential alternative etiology may be responsible for the AE.
- Probably Related: The AE has a timely relationship to the device placement performed and the causative relationship can clearly be established. No potential alternative etiology is apparent.

STUDY SUBJECT PROTECTION

Protection of each subject's personal health information will be a priority in this study. One master Excel file containing subject personal information including name and medical record number will be kept in a password-protected file, on a designated protected research drive on a password-protected computer in a locked office at the study institution. In that file, each subject will be assigned a subject identification number that will be used for the purposes of data collection in order to de-identify subjects.

All paper forms used for data collection will be kept in a research cabinet dedicated to this project, which will be locked at all times, in a locked office at Wake Forest Baptist Health. All forms will contain de-identified information when sent to the Data Monitoring Safety Board. Identification numbers will correspond to the subjects listed in the master excel file.

All study data will be transferred and managed electronically using REDCap. Each subject will be entered into REDCap using the assigned identification number from the master excel file. REDCap is a secure, web-based application designed to support data capture for research studies, providing user-friendly web-based case report forms, real-time data entry validation, audit trails, and a de-identified data export mechanism to common statistical packages. The

system was developed by a multi-institutional consortium that was initiated at Vanderbilt University and includes Wake Forest Baptist Health. The database is hosted within the Clinical and Translational Research Unit at Wake Forest and is managed by the Quantitative Health Sciences Department. The system is protected by a login and Secure Sockets Layers (SSL) encryption. Data collection is customized for each study based on a study-specific data dictionary defined by the research team with guidance from the REDCap administrator in Quantitative Health Sciences at Wake Forest.

AUTHORSHIP

For the primary paper, Dr. Plair will serve as first author and Dr. Matthews as senior author. All study investigators and personnel will be listed as co-authors and the list of authorship will depend on subject enrollment.

All investigators will have equal access to the primary data set for secondary analyses. For any secondary analyses, Dr. Matthews will serve as the senior author and only those members of the group involved in the secondary analysis will be listed as authors on any subsequent papers.

Appendix 1. Current knowledge of the discussed sacrospinous ligament fixation devices

Timeframe		Pain Type	Device Type		
			<i>Capio Slim</i> ^{2,3,22}	<i>Anchorsure attached to suture</i> ¹²	<i>Surelift</i> ^{5,6,9,10} or <i>Anchorsure attached to mesh</i> ¹¹
Intraop		Surgical Time	SSLF only - 6.9 min	Whole procedure – 86 min*	Whole procedure – 56 min +/- 12 min
Day 1		Gluteal or buttock pain	55.4 - 90.2%	NR	NR
		Blood Transfusion	0/44	NR	0.6% (2/300)*‡
		Hematoma**	UR	NR	5% (1/20)*; 2.6% (8/300)*‡
Week 1		Gluteal or buttock pain	63.2%	NR	NR
Week 4-6		Gluteal or buttock pain	15.3-26.9%	NR	NR
		Pain intervention	2.1% (5/242)	NR	NR
Other		Gluteal or buttock pain	NR	15.4% (2/13) [anytime up until 5 months]*	NR
		Pelvic pain	NR	NR	11.6% [36mo]*; 0.3% (1/300) [unspecified time]*
		Success %***	92-95% [17months]	92.3% (12/13) [5 months]*	77-92.4% [36mo]*; 80-94% (48-51/54) [unspecified time]*; 89.7% (26/29) [3yr]*
		Suture/Anchor Removal	2.3% (1/44) [17 months]	NR	1.95% (1/49) [unspecified time]

* Based on abstract data

** Criteria not well described

*** Surelift and Anchorsure with mesh success for any placement, anterior or posterior

‡ Anchorsure used with custom mesh implants

NR – Not Reported

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