Study Protocol Title: Prospective randomized trial of Stratafix vs. Vicryl on operating room time and wound closure time in Total Knee Arthroplasty

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Regulatory Sponsor:

This study is an Investigator Initiated research trial. Each study site will be considered its own regulatory sponsor and is responsible for internal data monitoring and any study reporting required by ClinicalTrials.gov.

Introduction:

Total knee arthroplasty is an effective orthopedic procedure to improve function, correct gait, and alleviate symptoms of late-stage arthritis in patients who have failed non-operative management. With constant introduction of various techniques for wound closure, assessment of closure times and outcomes will be a topic of marked importance.

The STRATAFIX (Ethicon, Johnson and Johnson, Somerville, New Jersey) Knotless Tissue Control suture device is a barbed suture that uses anchor technology to securely engage with the soft tissues while also eliminating the need for knots. The anchors, or barbs, are pressed out of the device core or formed within the core in a geometric pattern and arranged in a tapered manner to allow the device to pass through tissue in the direction toward the needle during closure. These knotless tissue control devices are deployed using a continuous technique, which we anticipate to be faster and more cost-effective than interrupted suturing.

Background and Significance/Preliminary Studies:

Preclinical and biomechanical studies have demonstrated efficacy in cosmetic skin and deep tissue closures.[1], [2] In addition, barbed sutures have been shown to provide water-tight closure and wound strength comparable to or superior to closure with conventional sutures. Many comparative studies have been published contrasting barbed sutures to conventional closure techniques in multiple surgical fields. [3], [4]

Various studies have evaluated the outcomes of different barbed suture devices, however there are no reports assessing the length of closure times using STRATAFIX (Ethicon, Johnson and Johnson, Somerville, New Jersey) Knotless Tissue Control Devices during deep closure in total hip arthroplasty. Stephens et al. [5] performed a prospective randomized study of 500 total knee arthroplasty patients who received either barbed suture (250) or conventional sutures (250) for deep closure of the surgical wound. The mean operating time was significantly shorter in the barbed group as compared to conventional group (64.3 vs 68.1 minutes, $p=<0.001$). In a study of 80 TKA (61 barbed, 19 conventional deep sutures) and 54 THA patients (37 barbed, 17 conventional deep sutures), Smith et al. [6] found significantly shorter closure time in the barbed suture group (16.78 vs. 26.5 minutes, $p<0.001$). One study reports one the use of Stratafix suture for intracorporeal suturing in myomectomy. Giampaolino et al. [7] performed a prospective randomized study on 47 patients and evaluated the mean operative time for laparoscopic posterior myomectomy using Stratafix or conventional suture for intracorporeal suturing. There was a significant decrease in mean operative time associated with use of Stratafix suture as compared to conventional suture (66.3 vs 73 minutes, $p=0.005$).

This prospective randomized single-center study will examine the outcomes, mainly closure time, of deep closure during total knee arthroplasty using the STRATAFIX Symmetric PDS Plus (Ethicon, Johnson and Johnson, Somerville, New Jersey) barbed suture compared to interrupted VICRYL suture (Ethicon, Johnson and Johnson, Somerville, New Jersey).

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Study Design:

In this prospective study examining the deep closure during total knee arthroplasty, active subjects will receive the STRATAFIX Symmetric PDS Plus (Ethicon, Johnson and Johnson, Somerville, New Jersey) suture while the control subjects will receive interrupted VICRYL suture (Ethicon, Johnson and Johnson, Somerville, New Jersey). Superficial closure will be the standard of care for both groups.

The purpose of this study is to compare end points (see below):

- **The primary endpoint** of the study will be closure time and operative time.
- **Secondary endpoints** will examine: wound complications, costs comparison between the two techniques.

Post-operatively, patients will be assessed at clinic visits at 6 weeks and 3 months. At these time points, we will assess **(Table 1):**

Table 1.

REQUIRED STUDIES	**Pre-Op**	**Intra-operative**	**6 week post-op**	**3 month post-op**
Informed Consent	x			
Length of surgery time		x		
Length of closure time		x		
Amount of suture material used		x		
Surgeon experience level		x		
Wound complications			x	x

Methods

- A prospective randomized pilot study

Sample

- 60 subjects for a pilot study

Inclusion Criteria:

1. Males and females, between the ages of 18 to 80 years at the time of signing the informed consent document.
2. Understand and voluntarily sign an informed consent document prior to any study-related assessments/procedures are conducted.
3. Able to adhere to the study visit schedule and other protocol requirements.

4. Able to fluently speak and understand the local language
5. If female, is non-pregnant (negative pregnancy test results at the baseline/randomization visit) and non-lactating.
6. End-stage osteoarthritis patients planning to undergo primary total knee arthroplasty
7. BMI less than 40 kg/m2

Exclusion Criteria:

1. BMI greater than or equal to 40 kg/m2.
2. History of known bleeding disorder.
3. History of medical co-morbidity that may result in poor wound healing (i.e. diabetes mellitus, peripheral vascular disease).
4. Patients <18 or >80 years of age.
5. Patients who are prisoners.
6. Mentally unable to sign informed consent.
7. Has an uncontrolled illness that, in the opinion of the investigator, is likely to cause the patient to be withdrawn from the trial or would otherwise interfere with interpreting the results of the study.

Screening and Recruitment: Informed Consent

Informed consent will be obtained by one of the study coordinators/co-investigators during a clinical visit prior to procedure in the privacy of an examination room or an office. Patients will be informed about the study and inquired about their interest to participate. A consent document will be given and key parts of the research study will be explained in lay-terms to the patient to ensure full understanding. Any questions regarding the research study will be answered at that time. It will be emphasized that participation is voluntary. Those patients who are willing to participate will be asked to sign the consent document along with the consenting researcher. A signed copy of the consent document will be handed to the patient while another copy is kept in their study file.

In the event that an approach prior to the day of surgery is not feasible, same day of procedure consenting will be attempted. Patients will be contacted by telephone (see phone script), and those interested in participating in the study will be informed about what is involved, the follow-up visit, and that participation in the study is strictly voluntary, and will not affect the scheduling of their upcoming surgery. If the patient is interested in participating, the patient can be either mailed or emailed a copy of the informed consent form, and then arrangements will be

made to complete the informed consent process prior to the patient being taken back into the preoperative area on the day of surgery. The patient will be asked to come to the hospital on the day of surgery earlier than the time they were told to arrive by surgical scheduling in order to make sure there will be adequate time to discuss the study, including what is involved, risks, benefits, and alternatives. We do not believe that an eventual approach on the same day of procedure would represent an added stress for the patient or delay the start of the procedure. Similar to obtaining informed consent prior to the day of procedure, the process will occur in a private setting with ample time to discuss the study's implications, risks, benefits, and alternatives. No procedures or tests will be conducted on the screening visit after consenting the patient.

Randomization procedures:

Patients will be randomized to either arm of the study as follows: sealed envelopes in a random order will be used to place study participants in either the barbed suture arm or in the traditional suture arm of the study. Patients will be randomized in a one to one ratio. At the commencement of each arthroplasty, a random envelope will be drawn which dictated the type of suture to be used, thus blinding the patients to the type of suture they received.

Research Procedure:

A medial parapatellar approach will be performed. All closures will be performed in 3 layers, with the knee in approximately 90° of flexion to minimize potential imbrication of the capsule. For the traditional closure (control group), the arthrotomy (deep layer) is repaired using number 1 Vicryl followed by closure of the intermediate layer with a 2-0 Vicryl and a subcutaneous layer with a 2-0 Monocryl followed by steri-strips and adhesive.

For the active arm of the study, wound closure will be performed similarly in 3 layers with the use of barbed equivalents at every layer: STRATAFIX symmetric PDS Plus #1 will be used to close the capsule (See Table 2). The subcutaneous layer will be then closed with simple interrupted knots using number 2-0 braided absorbable sutures (Vicryl), followed by closure of the subcutaneous layer using a number 2-0 monofilament absorbable suture with inverted interrupted knots (Monocryl, Ethicon; Johnson & Johnson) followed by the use of steri-strips and adhesive (See table 2).

Closure with the bidirectional barbed suture involves starting at the midpoint of the wound and proceeded simultaneously both proximally and distally to the ends. At the ends of the wounds, the suture is backstitched at this subcuticular level (2-3 throws) toward the midpoint for

further reinforcement before bringing the needle out through the skin; the suture is then cut flush with the skin tissue at its free end. With each throw, the leading end of the suture is pulled with only enough tension to engage the barbs with the surrounding tissue, thereby locking the wound edges into approximation. As with the traditional closure and in concordance with our routine protocol, barbed closures were finished with skin steri-strips and adhesive.

Table 2: Suture Type for Closure Following Total Knee Arthroplasty.		
Layer	Control Group	Active Group
Capsule	Vicryl #1 (J947H#1)	STRATAFIX (SXPP1A04#1)
Subcutaneous	Vicryl 2-0 (J945H 2-0)	Vicryl 2-0 (J945H 2-0)
Subcuticular	Monocryl 4-0 (Y496H)	Monocryl 4-0 (Y496H)
Skin	Steri-strips, glue (Standard of care)	Steri-strips, glue (Standard of care)

Patient Protection:

All data collection sheets will be de-identified. All patients will be assigned a study ID. All data collected will be entered into Excel sheet and stored on Cleveland Clinic secure computers. Only members of the study team (listed on the IRB application) will have access to protected health information of patients included in this study.

Safety Monitoring Plan

Procedural safety will be documented in this study through patient and surgeon reported adverse events. AEs will be documented for all cases in this study. An Unanticipated Problem involving risks to participants or others is any event that (1) is unforeseen, (2) caused harm or placed a person at increased risk of harm, and (3) is related to the research procedures.

An Adverse Event (AE) is any untoward or unfavorable medical occurrence, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptoms, or disease. Adverse events can encompass both physical and psychological harms. An Internal Adverse Event (AE) is an untoward medical occurrence, which occurs to participants in research conducted by Cleveland Clinic and/or Cleveland Clinic is the IRB of record. External Adverse Event (AE) is an untoward medical occurrence experienced by subjects enrolled at other

institutions for the same study approved at Cleveland Clinic or a different study using the same study drug/device. A Serious Adverse Event (SAE) is any adverse experience that results in any of the following outcomes:

- Death
- A life-threatening experience
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity.
- A congenital anomaly/birth defect
- Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

An Unexpected Adverse Event means any AE not previously known or included in the current Investigator's Brochure, consent form or other risk information.

Related/Possibly Related means there must be reasonable evidence to suggest the event was caused by the drug, device or investigational intervention.

1. Internal Serious Adverse Events (events that occur to participants enrolled in research being conducted by Cleveland Clinic or when Cleveland Clinic is the IRB of record) must be promptly reported to the IRB using the IRB AE Report Form within10 working days from discovery/awareness which meet any of the following criteria as assessed by the PI/Co-I:

a) Serious, Unexpected and Related/Possibly Related.

b) AE's determined to be occurring at a significantly higher frequency or severity than expected.

c) Other Unexpected AE's, regardless of severity, that changes the risk benefit ratio of the study and results in changes to the Research Protocol or Informed Consent process/document.

All Internal SAEs are also reported at continuing review using the AE Summary Log.

2. External Serious Adverse Events (events experienced by subjects enrolled at other institutions for the same study approved at Cleveland Clinic or a different study using the same study device/drug) are reportable to the IRB using the IRB AE Report Form within 10 working days from discovery/awareness when:

a. The External SAE report includes reasonable evidence as assessed by a central monitoring entity [Coordinating or Statistical Center, or a Data Safety

Monitoring Board (DSMB) or Data Monitoring Committee (DMC)] that the event is Serious, Unexpected, and Related/Possibly Related AND places the subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. This will require a change in the protocol and/or consent document.

b. External SAE reports provided by the Sponsor to the investigator indicating the event is Serious, Unexpected and Related/Possibly related but without reasonable evidence or DSMB/DMC determination of greater risk are not reportable to the IRB within the 10 day window. Without Sponsor evidence or assessment the implications of the event cannot be determined by the research team and therefore need not be reviewed. These SAE' shall be placed on the AE Summary log to be submitted at the annual continuing renewal.

3. DEATHS are to be reported to the IRB using the IRB AE Report Form according to the following guidelines:

a) Internal Death:

- Related/possibly related whether expected or unexpected– within 5 working days from discovery/awareness
- Not related and expected – at time of continuing review
- Not related and unexpected – at time of continuing review except cancer studies.
- Cancer: Not related and unexpected within 10 working days from discovery/awareness

b) External Death:

Related/possibly related and unexpected – within 5 working days from discovery/awareness not related whether expected or unexpected – at time of continuing review related/possibly related and expected – at time of continuing review

c) ALL Deaths are also reported at time of continuing review using the AE summary log.

4. Non-serious Adverse events (Internal and External) that are both Related/Possibly related and unexpected are reported on the AE Summary Log at time of continuing review to assess trends.

5. An IRB staff (a qualified, licensed practitioner assigned to this function by the IRB chair and IRB Executive Director) reviews Adverse Event Reports to determine whether they represent Unanticipated Problem Involving Risks to Participants or Others. Events that are assessed, by either the IRB Staff or Investigator, to place subjects or others at a greater risk of

harm than was previously known or recognized, or changes the risk/benefit ratio of the study, or requires a change in the protocol and/or consent document are referred to Full Board for review under Policy #70. Events that do not involve risk to Participants or Others or changes to the informed consent or protocol do not require further review. Investigators are informed of the determination and the IRB file is updated.

6. The AE Summary Log is reviewed by the IRB at the time of continuing review to identify trends in frequency and severity which may impact subject safety.

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Data Analysis:

Unless otherwise indicated, all testing of statistical significance will be two-sided, and a difference resulting in a p-value of less than or equal to 0.05 will be considered statistically significant. Also, after each analysis, General Linear Models (GLM) will be used to control for possible confounders, including BMI, gender, age and ethnicity.

References:

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[3] P. M. Parikh, S. P. Davison, and J. P. Higgins, "Barbed Suture Tenorrhaphy: An Ex Vivo Biomechanical Analysis," *Plast. Reconstr. Surg.*, vol. 124, no. 5, pp. 1551–1558, Nov. 2009.

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[5] Stephens S, Politi J, Taylor BC. Evaluation of Primary Total Knee Arthroplasty Incision Closure with the Use of Continuous Bidirectional Barbed Suture. Surg Technol Int. 2011 Dec;21:199–203.

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[7] Giampaolino P, De Rosa N, Tommaselli GA, Santangelo F, Nappi C, Sansone A, et al. Comparison of bidirectional barbed suture Stratafix and conventional suture with intracorporeal knots in laparoscopic myomectomy by office transvaginal hydrolaparoscopic follow-up: a preliminary report. Eur J Obstet Gynecol Reprod Biol. 2015 Dec;195:146–50.