NCT number: NCT05366842

Study title: Assessment of clinical outcomes post application of StravixPL for robotic prostatectomy

Date of the study protocol: 7/03/2023

Johns Hopkins Medicine - eIRB Protocol (eForm A)

Assessment of clinical outcomes post application of StravixPL for robotic prostatectomy

****

7/03/2023

1. Abstract

Erectile dysfunction is common in patients undergoing radical prostatectomy for prostate cancer and is thought to result from disruption of normal blood and nerve supply to the penis. There have been significant advances in surgical technique, including nerve sparing prostatectomy, as well as post prostatectomy penile rehabilitation, which have improved erectile recovery after surgery. Clinical use of growth factors and anti-inflammatory substances for prostate neurovascular bundle regrowth have emerged as a new technique to further enhance recovery of potency and potentially continence after prostate surgery. Patel et al. studied outcomes after placement of a dehydrated chorionic allograft membrane on neurovascular bundles during prostatectomy and reported that 65.5% of patients with moderate to high preoperative sexual function had return to potency at 8 weeks vs. 51.7% of patients with standard care[1]. The mean time to recovery was 1.34 months[1]. Johnson et al. compared viable to nonviable dehydrated placenta for chronic wounds and showed superior outcomes with viable tissue[2].

Surgical implantation of Stravix (Smith and Nephew. Columbia, MD), a lyopreserved placental tissue (LPT) is now FDA approved and has been used extensively in wound care. The use is expanding and more recently, LPT has been used in the management of diabetic foot ulcers, acute and chronic surgical wounds, various fistulas and even as a nerve wrap on the common peroneal nerve (Rodriguez, Foot and Ankle, 2017)[3].

We intend to study whether placement of LPT over the spared neurovascular bundles during nerve-sparing prostatectomy will improve return to potency and/or continence after radical prostatectomy for prostate cancer. This research could provide a potentially meaningful advancement in quality of life outcomes for patients undergoing radical prostatectomy for prostate cancer.

2. Study Procedures

This is a single center, randomized; singe blinded, two-arm trial comparing the effects of direct placement of LPT over the spared neurovascular bundles vs. standard care (no placement of tissue) on erectile recovery and quality of life in patients undergoing bilateral nerve sparing radical prostatectomy for prostate cancer.

VCUT for Erectile Recovery During Bilateral Nerve Sparing RRP Protocol											
	Consult	Baseline Eval	Surgical Day	Post Op Day 1	2 weeks Post Op	1 Month Post Op	3 months Post Op	6 months Post Op	9 months Po	12 months Post Op	18 Months Post Op
Informed Consent	x										
Medical Clearance		x									
IIEF		x				x	x	x	x	x	x
QEQ		x				x	x	x	x	x	x
EPIC, SF12, AUA SI		x				x	x	x	x	x	x
Randomization		x									
Rx (PDE5i)						x					
AE Monitoring			x	x	x	x	x	x	x	x	x
PSA Monitoring							x			x	

The sample size will be 10 patients randomized to each study arm (20 patients total). Study procedures will involve screening and informed consent after initial consultation, baseline evaluation including medical clearance and completion of validated questionnaires, and randomization.

In order to minimize the need for research-only in-person visits, telemedicine visits may be substituted for in person clinical trial visits or portions of clinical trial visits where determined to be appropriate and where determined by the investigator not to increase the participant's risks. Prior to initiating telemedicine for study visits the study team will explain to the participant, what a telemedicine visit entails and confirm that the study participant is in agreement and able to proceed with this method. Telemedicine acknowledgement will be obtained in accordance with the Guidance for Use of Telemedicine in Research. In the event telemedicine is not deemed feasible, the study visit will proceed as an in-person visit. Telemedicine visits will be conducted using HIPAA compliant method approved by the Health System and within licensing restrictions

Assessment tools will consist of the following questionnaires, *which will be administered online using a REDCap site hosted by the Data Informatics Services Core within the Johns Hopkins Biostatistics Center or via mail per patient preference*: IIEF questionnaire, the Quality of Erection Questionnaire (QEQ), and the version of the Expanded Prostate Cancer Index Composite (EPIC) that combines the Short Form Health Survey (SF-12) and AUA Symptom Index (AUA-SI). Standard practice associated with surgery, blood transfusion and postoperative laboratory testing will be performed. Operating room time, estimated blood loss, surgical margin status and length of hospital stay will be recorded. Patients will be prescribed a phosphodiesterase type 5 inhibitor (sildenafil, tadalafil or vardenafil) at 1 month following surgery to be used as conventional "on-demand" therapy. Adverse event monitoring will be performed. PSA monitoring is recommended at 3 and 12 months with the definition for biochemical recurrence set as a PSA of 0.2ng/mL (rising from an undetectable level after surgery).

3. Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Male sex 40 to 70 years of age with localized prostate cancer (clinical stage less than or equal to T2a, Gleason grade less than or equal to 3+4=7, including 4+3=7 (Gleason 8 will be excluded), PSA less than or equal to 20 ng/mL)
2. Scheduled to undergo curative radical prostatectomy applying bilateral nerve-sparing procedure
3. Intact pre-surgical erectile function (International Index of Erectile Function [IIEF]-5 / Sexual Health Inventory for Men (SHIM) score greater than or equal to 18)
4. Willingness to attempt intercourse at least 5 times per month following surgery.
5. Has a sexual partner of at least 6 months with current sexual activity (within the past 4 weeks)

Exclusion criteria:
1. Known penile deformity or a history of Peyronie's disease
2. Pre or postoperative androgen therapy
3. Pre or postoperative radiation therapy
4. History of high or low blood pressure that is not controlled
5. Taking nitrates medications
6. History of heart problems such as angina, heart failure, irregular heartbeats, or myocardial infarction
7. History of drug or alcohol abuse
8. Current smoker has a 20 pack/year history of cigarette smoking
9. History of acute or chronic depression
10. History of liver problems or kidney problems
11. History of retinitis pigmentosa or severe vision loss, including a condition called NAION
12. History of spinal trauma or surgery to the brain or spinal cord
13. Other contraindications to the use of PDE 5 inhibitors
14. History of known sensitivities to any of the following reagents used for processing, disinfection, and storage, which may remain on the product:

• ***Lyopreservation Solution***: 18.9% w/v Trehalose in Dulbecco's Phosphate Buffered Saline
• ***Disinfection Solution*****:** 0.5% v/v Gentamicin Sulfate, 0.1% v/v Vancomycin reconstituted in Water for Injection (WFI), 1% v/v Amphotericin B, 98.4% Dulbecco's Modified Eagle's Medium (DMEM)
• ***Processing Solution:*** DMEM, Dulbecco's Phosphate Buffered Saline (dPBS), 11% Anticoagulant Citrate Dextrose Solution in Saline, Formula A (ACD-A), 1.7% w/v Trehalose in Dulbecco's Phosphate Buffered Saline

4. Drugs/Substances/Devices

a. The rationale for choosing the drug or substance dose or for choosing the device to be used.

Stravix (Smith and Nephew. Columbia, MD) is a Lyopreservation placental tissue that is FDA approved for homologous use as a wound cover or surgical wrap. There are no known contraindications to the use of Stravix. The product is available for use at Johns Hopkins and has been used by the pediatric urology department in the management of rectovaginal fistula[4] it has also been used by the colorectal surgery department. Novel clinical use of growth factors and anti-inflammatory substances for prostatic neurovascular bundle regeneration has been shown with the use of a dehydrated human chorion membrane[1]. Chronic wound studies have shown viable chorionic tissue, such as Stravix, to be superior to non-viable dehydrated chorionic tissue[2]. We plan to prospectively study surgical placement of Stravix directly to neurovascular bundles and assess for improvement in erectile recovery as well as quality of life after radical prostatectomy for prostate cancer.

5. Study Statistics

The primary outcome variable is the patient's score on the IIEF questionnaire (erectile function domain) at 1,3, 6, 9, 12 and 18 months post-surgery. Comparison of changes in initial IIEF score will be evaluated to determine treatment efficacy. We anticipate a gradual increase in baseline IIEF score over the course of the study. The secondary outcome variables will be the patient's scores on the QEQ, combined EPIC/SF-12/AUASI questionnaires, other domains of the IIEF questionnaire. For statistical analysis based on ANOVA, the sample size is powered for a power of 80% with one-sided alpha of 0.05 showing a sample size of 23 patients in each arm is necessary to detect an expected difference of 5 points in IIEF scores (i.e. 20 vs. 15) at 6 months post-surgery. Therefore, the study is planned to enroll 30 patients in each arm. This sample size will accommodate dropout rate during follow-up.

6. Risks

Completion of the questionnaires and administration of Stravix are the only 2 procedures from this protocol that are outside of the realm of standard of care for the radical prostatectomy patient. All of the participants will be exposed to the questionnaires pre operatively and can assess whether they are willing to complete the trial, which will include 6 additional administrations of the questionnaires. If the questionnaires cause any type of discomfort or uneasiness at that time or any time during the study, the participant can decide to end their involvement with the protocol.

There are no contraindications to the use of Stravix. Smith and Nephew (Columbia, MD) reports that the product has been directly applied to spared neurovascular bundles in approximately 250 radical prostatectomies. Tissue donor screening methods are limited; therefore, certain diseases may not be detected.

The following complications of tissue transplantation may occur:[5]
• Transmission of diseases of unknown etiology;
• Transmission of known infectious agents including, but not limited to, viruses, bacteria, and fungi;
• Immune rejection of implanted Stravix®; or
• Loss of function and/or integrity of Stravix® due to resorption, fragmentation, and/or disintegration.

The occurrence of any serious adverse effects will end the patient's participation in the study and halt enrollment in the study to determine the safety of continuing the study. Each and every possible adverse effect of LPT will be investigated and treated individually to minimize the participant's discomfort. The safety of having the individual complete the study will also be assessed on an individual basis. At any time the participant can decide to terminate his participation in the study and no penalty or loss of benefits to which they are entitled.

The risks of radical prostatectomy will apply to both groups. These include but are not limited to bleeding, infection, and injury to surrounding structures. Rare complications include rectal injury requiring fecal diversion and acute blood loss anemia requiring transfusion. An ejaculation is expected. Late complications include urinary incontinence, erectile dysfunction, urethral stricture disease, and bladder neck contracture.

7. Confidentiality

Paper consent forms, enrollment check sheets, and other source or study documentation will be kept in a study binder. This binder will be stored in a locked office available only to the study team. Electronic data will be housed in a secure password protected REDCap database maintained by the Data Informatics Services Core within the Johns Hopkins Biostatistics Center. Only the study team will have access to this secure database. Of note, to maintain the protected health information of patients enrolled in this study, only the study Principal Investigator and primary coordinators will have the ability to export data containing identifying information from this master database. For the purposes of analysis, only de-identified data will be exported.

8. Benefits

The patient's conditions may improve as a result of participation in this study, specifically as related to erectile function and quality of life. However, there is no guarantee of this. The information from this research study may lead to a better treatment in the future for people with prostate cancer. The patients may not benefit from participation in this study. Their conditions may not get better or may become worse while they are in this study.

9. Payment and Remuneration

There will be no payment or remuneration for the participants in this study.

10. Costs

The cost of the Stravix will be covered by the study. There are no other anticipated costs outside of usual care. The participant's insurance, as part of routine care after radical prostatectomy, will be charged for the PDE5 inhibitor drugs such as Viagra, Cialis or Levitra. If the PDE5 inhibitor (Viagra, Cialis or Levitra) is not covered by the participants insurance, they will be responsible for the bill.

Sources

1. Patel, Vipul R., et al. "Dehydrated Human Amnion/Chorion Membrane Allograft Nerve Wrap Around the Prostatic Neurovascular Bundle Accelerates Early Return to Continence and Potency Following Robot-Assisted Radical Prostatectomy: Propensity Score–Matched Analysis." *European Urology*, vol. 67, no. 6, 2015, pp. 977–980., doi:10.1016/j.eururo.2015.01.012.

2. Johnson, Eric L., et al. "A Comparative Outcomes Analysis Evaluating Clinical Effectiveness in Two Different Human Placental Membrane Products for Wound Management." *Wound Repair and Regeneration*, vol. 25, no. 1, 2017, pp. 145–149. doi:10.1111/wrr.12503.

3. Rodriguez-Collazo, E., and Y. Tamire. "Open Surgical Implantation of a Viable Cryopreserved Placental Membrane after Decompression and Neurolysis of Common Peroneal Nerve: a Case Series." *Journal of Orthopedic Surgery and Research*, vol. 12, no. 1, Dec. 2017, doi: 10.1186/s13018-017-0587-y.

4. Taylor, Jp, and S Gearhart. "The Use of Viable Cryopreserved Placental Tissue in the Management of a Chronic Rectovaginal Fistula." *The Annals of The Royal College of Surgeons of England*, vol. 99, no. 8, 2017, doi:10.1308/rcsann.2017.0157.