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# Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

**Protocol Number: H-45549**
Status: Approved
Initial Submit Date: 7/17/2019
Approval Period: 3/18/2022 - 3/17/2023

## Section Aa: Title & PI

### A1. Main Title

NEWLY-DESIGNED VAGINAL STENT TO IMPROVE TISSUE HEALING FOR GIRLS AND WOMEN WITH CONGENITAL AND REPRODUCTIVE ANOMALIE

### A2. Principal Investigator

| | | | |
|---|---|---|---|
| Name: | JULIE HAKIM | Phone: | (832) 826-7464 |
| Id: | 185416 | Fax: | |
| Department: | OB-GYN: ADMINISTRATIVE | Email: | jhakim@bcm.edu |
| Center: | | Mail Stn: | BCM610 |

### A3. Administrative Contact

| | | | |
|---|---|---|---|
| Name: | JENNIFER MCCRACKEN | Phone: | 832-824-5833 |
| Id: | 201048 | Fax: | |
| | | Email: | mccracke@bcm.edu |
| | | Mail Stn: | BCM610 |

### A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

## Section Ab: General Information

### A4. Co-Investigators

| | | | |
|---|---|---|---|
| Name: | JENNIFER DIETRICH | Phone: | 832-826-7464 |
| Id: | 130087 | Fax: | 832-832-9349 |
| Department: | OB-GYN: GYNECOLOGY | Email: | jedietri@bcm.edu |
| Center: | | Mail Stn: | BCM610 |

| | | | |
|---|---|---|---|
| Name: | ANTHONY COSTALES | Phone: | 832 8267466 |
| Id: | 208504 | Fax: | |
| Department: | OB-GYN: GYNECOLOGIC ONCOLOGY | Email: | costales@bcm.edu |
| Center: | | Mail Stn: | 122609 |

Name: DALLESE JONES
Id: 232479
Department: OB-GYN: ADMINISTRATIVE
Center:
Phone:
Fax:
Email: 232479@bcm.edu
Mail Stn:

Name: KENESHIA LANE
Id: 232877
Department: OB-GYN: ADMINISTRATIVE
Center:
Phone:
Fax:
Email: 232877@bcm.edu
Mail Stn:

Name: GISELE CALDERON
Id: 233562
Department: OB-GYN: GYNECOLOGY
Center:
Phone: 832-824-5833
Fax:
Email: 233562@bcm.edu
Mail Stn:

Name: LINDA ALPUING RADILLA
Id: 238014
Department: OB-GYN: ADMINISTRATIVE
Center:
Phone:
Fax:
Email: u238014@bcm.edu
Mail Stn:

### A5. Funding Source:

Organization: NATIONAL INSTITUTES OF HEALTH (NIH)

### A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine
HCHD: Harris County Hospital District Ben Taub
TCH: Texas Children's Hospital
Texas Children's Hospital- Women's Pavilion

### A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

### A7. Research Category:

### A8. Therapeutic Intent

Does this trial have therapeutic intent?
Yes

### A9. ClinicalTrials.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
Yes

Who will be responsible for registering and maintaining the registration of this Applicable Clinical Trial?
The BCM PI will register the trial because either:

- the trial is BCM PI-initiated,
- BCM is the lead site of this multicenter trial, or,
- the industry sponsor has instructed the BCM PI to register the trial, or,

- registration of this trail is required as a term and condition of the reward by the funding agency.

ClinicalTrials.gov Identifier:
NCT04807387

## Section B: Exempt Request

### B. Exempt From IRB Review

Not Applicable

## Section C: Background Information

There is an Urgent Need for a Commercially-Available Vaginal Stents. As many as 50,000 patients per year in North America require the surgical reconstruction of a new vaginal canal [1]. The success of this procedure is dependent how well the vaginal tissues are kept from apposing one another during the post-surgical period [1]. Currently, there are no effective methods to maintain the separation of vaginal tissues vaginal reconstruction. A vaginal stent is a medical device with an inner rigid core surrounded by an inflatable balloon that is placed into the vaginal canal postoperatively such that the vaginal walls do not appose each other during the healing process. The importance of efficacious vaginal stents in the success of neo-vaginal creation in post-adolescent populations cannot be overstated; if the new vaginal canal does not maintain its patency while the tissues heal, postoperative complications may occur. The most common complication after vaginal reconstruction is restenosis and scar tissue formation, which can occur in up to 73% of patients, necessitating persistent perineal dilatation using vaginal dilators after surgery in order to maintain the caliber of the neo-vagina [2] in order to maintain the ideal vaginal structure (such as ideal length) and to avoid expensive and unpleasant surgical revisions.

For adult women undergoing surgery or gynecologic cancer treatments, the effects on vaginal length and quality of life are significant. About 19% of women after hysterectomy alone experience substantial vaginal length reduction and more than 100,000 women per year in the United States seek treatment for vaginal foreshortening causing dyspareunia [3,6]. After pelvic surgery and/or pelvic radiation for treatment of gynecologic cancers, up to 88% of women will develop significant vaginal stenosis with shortening, scarring with narrowing of the vagina leading to dyspareunia, tissue friability, and vaginal bleeding and pain [4,5]. Sexual dysfunction can be as high as 33% in women undergoing radiation therapy and quality of life for these women can be compromised [6]. Significant vaginal scarring may occur in 1/70 women due to dermatological diseases such as lichen sclerosis [10]. The only method to maintain the vaginal caliber postradiation is with the use of vaginal dilators after radiation treatments have concluded. Despite the vital role perineal dilation plays in restoring normal vaginal function, and in maintaining quality of life, adherence to the recommended dilation regimes is consistently low, with less than 50% of females using dilators at the recommended frequency, and as many as 75% stopping the use of the dilator within a year [11]. A vaginal stent placed after radiation treatments may maintain the vaginal caliber, reduce post-radiation fibrosis, and eliminate the need for perineal dilatation. Thus the role of vaginal stents for successful outcomes after neovaginal surgery and post-radiation is even more clear.

Post-operative difficulties with healing are even more problematic in the pediatric population, due to the simple fact that no commercially-available vaginal stent has ever existed for adolescents to prevent the need for difficult and unpleasant dilation regimes which show low patient adherence. Recent increases in malformations such as specific congenital genitourinary anomalies [12], and a societal shift towards better acceptance of male-to-female transgender surgeries have led to a surge in the number of surgeries for neo-vaginal creation in girls and young women. There are as many as 50,000 girls per year and 213,000 women per year who could benefit from postoperative treatment using newly designed vaginal stents [1,3]. Extensive scar tissue formation in the vagina, vaginal restenosis and vaginal foreshortening can have profound effects on young girls and women. As in the post-radiation population, the need for persistent dilatation post-surgery can lead to early discontinuation due to noncompliance or to significant complications including vaginal bleeding or even perforation of the vagina or bladder and fistula formation [4]. Many pediatric surgical centers quote a risk of surgical revision after vaginal reconstruction to be about 50% [5].

The availability of a vaginal stent for the pediatric and post-radiation populations offers unimaginable benefits: by reducing the need for perineal dilation, vaginal stents offer the promise of a reduction in vaginal scar tissue formation, in post-surgical and post-radiation morbidity, surgical revisions, lifelong perineal dilatation, and improvement in sexual function. Together, the improvements to the quality of life of these populations would yield physical and psychological benefits for both patients and families as well as significant health care cost savings.

Current Vaginal Stents are hand-crafted and outcomes are poor. In adolescent populations, hand-crafted, ill-fitting

vaginal stents are routinely placed via a number of procedures which can vary enormously by indication. Some inpatient procedures require stays in hospital with a tractioned vaginal stent for up to 5 days. These patients then wear a stent intermittently thereafter for up to 4 weeks depending on vaginal healing. Outpatient procedures may require use of a vaginal stent intermittently for up to two weeks. Patients are currently required to be able to remove and reinsert the vaginal stent themselves at home (usually same stent that is washed and re-used). However, due to the relative non-existence of a commercially available product, physicians are relegated to creating their own makeshift stents for their gynecology patients either using finger slots from sterile gloves and gauze, sterile cement coated in bone wax and placed in a condom, or plastic moulding. All of these are suboptimal options with resultant low patient compliance, stent egress and emergency room hospital visits for replacements, and poor patient outcomes.

Adult vaginal stents used to exist (Mentor Stent, Coloplast, Inc.), and were sold up until 2010 by Coloplast, when despite enormous benefits to patients, these devices were withdrawn due to financial and legal issues surrounding an entirely different device made by the same company. Coloplast had previously acquired Mentor's urogynecologic line that included vaginal stents, and discontinued the product after massive recalls on their breast implants due to safety issues and it was never replaced. A new company PMT corporation has recently begun selling the previous Mentor Stents with no design changes. Both the Mentor stent and makeshift devices frequently fall out, and are associated with a high numbers of complaints regarding their discomfort. Many patients require their labia sutured around the stent in order to retain it. Despite being one of the only ways to prevent the need for perineal dilation and subsequent surgical revision, difficulties with these devices lead to low patient compliance. More concerning, there has never been a vaginal stent designed for, and tested on a pediatric population. This population is left vulnerable to effects of being forced to rely on procedures such as perineal dilation for good outcomes. The need to help these patients and their physicians with a simple device that can improve both surgical outcomes and patient quality of life beyond surgery cannot be overstated. Similarly, the commercial potential for this project to lead to marketable product is significant as there is pent up demand for this product. This along with the larger commercial markets outlined in the commercialization plan, and the experience of this team in bringing novel products to market, greatly increase the chances for commercial success.

A Predicate Device for Stents in Pediatrics. We have assembled a unique team of engineers, commercialization experts, and clinicians, representing the first group, to our knowledge, to design a vaginal stent system that addresses the anatomic needs of the pediatric patients, and could be expanded to use in a much larger post-gynecologic cancer patient population. Members of our team, as well as those of our outside advisory board of pediatric gynecology and gynecologic oncology experts have strong confidence in the potential of our device to eliminate post-surgical stricture, facilitate physician procedures, and reduce early discontinuation in patients. Our work supporting this premise will be presented at the 2021 North American Society for Pediatric Adolescent Gynecology (NASPAG) Annual Clinical Meeting, and published in their conference literature. Our group, at this time, is on the cusp of improving outcomes for tens of thousands of girls every year undergoing vaginal surgery and those women undergoing radiation treatments. Now is the time to move this project forward and optimize the stent design and complete steps required for commercialization so it can reach patient populations as soon as possible, reducing the need for dilation and / or surgical revision in females who have undergone neovaginal surgery or radiation treatments.

(Works cited and copy of NIH grant submission are attached in Section S.)

## Section D: Purpose and Objectives

This proposal seeks to develop a production-ready novel vaginal stent specifically designed to improve postsurgical outcomes with regard to restenosis for girls who have undergone neo-vaginal creation and for women who have undergone pelvic surgery or radiation due to gynecologic cancer treatment. In our Phase I project we designed, built, and tested multiple configurations of our stent design, performed bench-top testing in anatomical models and excised porcine tissue using our stent prototypes, and evaluated the performance of the vaginal stent prototypes in vivo in a porcine animal model. In this Phase II project, we will refine the current device into a final clinically-ready format, test usability factors in a population of healthy volunteers, and finally evaluate its use in a broad cohort of our target clinical populations. The end result of this effort will be a new clinical instrument specifically designed for maintenance of the vaginal caliber after surgery and/or pelvic radiation.

Specific Aim I: Finalize design for a clinical-ready version of our vaginal stent system and perform preliminary verification and validation testing.

1a: Optimize the stent design. Biotex engineers will integrate our current prototype designs into two different inflatable configurations which cover desired diameters and length ranges. Efficacy of our vaginal stent is shown by its retention in the vaginal canal for 2 weeks. We will work closely with clinical collaborators to refine our stent designs as well as insertion and retrieval tools with the goal to finalize stent materials, size ranges, and factors which will improve patient compliance with stent use.

1b: Completion of product testing required for FDA submission and commercialization. Vital steps towards enabling product distribution include performing required validation activities (biocompatibility, sterilization, packaging,

performance testing) for FDA 510(k) submission. After finalization of stent designs, product development engineers will develop protocols under design controls, manage production of final units, and execute required testing.

Specific Aim II: Examine the acceptance and success of our novel vaginal stent in healthy (non- clinical) subjects. Accruing clinical samples large enough for both development and testing can be prohibitive due to the low numbers of adolescent patients at any one institution requiring neovaginal surgery. In addition, clinical samples a can be heterogenous on key variables which may relate to the success of our stent, such as age,maturity, or comorbid conditions. Therefore, we will conduct aim 2 in a non-clinical population.

2: Quantify key factors to better understand stent efficacy. In 20 non-clinical volunteers, we will associate factors such as design, pull-out forces, comfort, and inflation/ deflation / retrieval ergonomics with stent retention.

Specific Aim III: Evaluate the success of our vaginal stent in a broad cohort of clinical subjects. After establishing the regulatory (aim 1), practical (aims 1 and 2) and patient factors (aim 2), we will use this information to inform the protocol of our pseudo-clinical trial in aim 3.

3a: Demonstrate vaginal stent retention in the vaginal canal for two weeks in a clinical population. In 10 post-surgical patients and 10 post-radiation adult women, the efficacy of our novel vaginal stent will be demonstrated both through lack of egress and through patient compliance to using the device.

3b: Demonstrate that retention of our novel vaginal stent in the vaginal canal is superior to that of existing makeshift / handmade vaginal stents.

By leveraging the unique medical database available at our institutions (Texas Children's Hospital and Baylor College of Medicine), we will demonstrate success of our new vaginal stent by comparing the number of vaginal stents still in place at a 2-week post-surgical follow-up in neovaginal surgery.

## Section E: Protocol Risks/Subjects

### E1. Risk Category

Category 2: Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects.

### E2. Subjects

Gender:
Female

Age:
Adolescent (13-17 yrs), Adult (18-64 yrs)

Ethnicity:
All Ethnicities

Primary Language:
English, Spanish

Groups to be recruited will include:
Both patients and healthy, non-patient, normals

Which if any of the following vulnerable populations will be recruited as subjects?
Children

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

Informed consent will be obtained by trained research personnel. An initial screening interview via phone will be held, followed by an invitation to speak with a study coordinator (plus interpreter if needed). The study risks and procedures will be fully explained, eligibility assessed, and the participants' rights enumerated (including the right to withdraw at any time). Potential participants will be given time to answer questions. For subjects under age 18, parental consent and adolescent assent will be obtained prior to participation. Subject confidentiality will be maintained at all times; phone calls and in-person recruitment will be held in private rooms. All patient information will be kept on a secure, HIPAA-compliant electronic server or in a locked file cabinet when not in use.

**Please note** The Spanish forms -consent form, recruitment flyers, questionnaires- are being translated as of 2/2/21.

We will attach these forms when translation is complete.

### E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

### E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

### E5. Children

Will children be enrolled in the research?

Yes

## Section F: Design/Procedure

### F1. Design

Select one category that most adequately describes your research:

k) Device, Phase II, Single Center

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.

This is a non-randomized clinical trial of healthy and patient cohorts, females ages 13-64 years will be recruited into different groups. 20 healthy participants (ages between 13-64 years) will be recruited initially to try wearing 2 stents separately for 24 hours each, provide feedback, then wear the preferred stent for 2 weeks. Subsequently, 20 patient participants, 10 post-surgical adolescent patients and 10 post-radiation adult patients, will be recruited to wear the stent for 2 or 4 weeks, respectively. Neither healthy nor patient participant will be randomized. (Procedure details in section F2.) A control cohort will not be recruited; rather, within-group outcomes will be measured. The adolescent versus adult female patient outcomes will also be compared.

Physician participants will be asked to complete a post-stent questionnaire which will evaluate the level of difficulty with stent insertion and removal.

Inclusion Criteria:

Healthy volunteers: (a) female between 13-64 years of age, (b) not currently pregnant, (c) if under age 18, parents must be able to give informed consent and volunteer must give informed assent, (d) ability to understand the requirements of the study and abide by the restrictions, (e) ability to travel to Houston for study evaluations, (f) ability to understand English or Spanish to a grade 5 level, (g) no history of prior vaginal surgery or radiation.

Patient volunteers: (a) adolescent female patients, ages 13-18 undergoing vaginal reconstructive surgery at high risk for vaginal fibrosis including those with transverse vaginal septa, vaginal atresia, or post-radiation, (b) adult female patients undergoing vaginal brachytherapy for cancer at high risk of vaginal fibrosis, (c) not currently pregnant, (d) ability to give informed consent (If patient is under age 18, must be able to give informed assent with parent consent), (e) ability to understand the requirements of the study and abide by the restrictions, (f) ability to travel to Houston for study evaluations, (g) ability to understand English or Spanish to a grade 5 level.

Physician volunteers: Physicians who oversee the patient volunteers and deploy the current vaginal stent post surgery/post radiation will be asked to complete a Physician Post-Stent Questionnaire (attached to Section S).

Exclusion Criteria:

All volunteers: (a) Non-English or Spanish language (b) pregnant patients (c) women with BMI >45 (d) women with prior vaginal surgeries (e) women with comorbid conditions such as diabetic neuropathy or other conditions limiting use of hands for stent removal, vaginismus, urinary retention, bacterial or fungal infections, allergies to stent material such as silicone, seizure disorder. (f) in healthy participants only: any pain with sexual intercourse or tampon insertion. in post-surgical and post-radiation participants: pain >5 on a 10 pt Likert Scale with sexual intercourse or tampon insertion

### F2. Procedure

This study has 3 phases. Phase 1: 20 healthy volunteers to determine the better of 2 stents, based on highest retention and comfort. Phase 2: the same 20 healthy volunteers will wear the stent for 2 weeks to evaluate retention and comfort. Phase 3: 20 patient volunteers (adolescent females after surgery and adult females after radiation treatment) will evaluate stent on same criteria. During all phases, the option of obtaining vaginal pressure measurements will be available. For pressure measurements, a pressure gauge will be attached to the end of the stent, outside of the vagina, and the pressure between the stent and vagina will be measured as the participant lies, stands, squats, walks around the clinical room, and intentionally exerts downward pressure in the vaginal cavity. The pressure will be measured for 1 minute during each activity, after which the pressure gauge will be removed.

Phase 1: 20 Healthy volunteers will be recruited through flyers placed at hospitals, research institutions, and device accelerators within TMC, the study recruitment pages of BCM website, and through the electronic BCM and TCH newsletters. Social media will be used to promote the study with a direct link to the BCM recruitment page. All comments and replies will be disable and no PHI will be obtained or discussed via social media. (See Section S). Following an initial screening call with research personnel, eligible participants will be invited to TCH for orientation and to obtain consent by a study coordinator (interpreter if needed). Participants will then undergo a urine pregnancy test, vaginal assessment via visual exam, speculum, or colposcopy to assess vaginal mucosa and a vaginal swab to rule out presence of bacterial or fungal infections. Physicians will complete the Vaginal Assessment Form (VAF). Participants will complete a Pre-Stent Questionnaire to establish any vaginal baselines that may effect stent performance and a trained clinician will insert one of two stents. Instructions will be reiterated to the participant. After 24 hours, the participant will return to the clinic and the clinician will remove the stent. A vaginal exam and culture will be performed to ensure the tissue is intact and the participant did not experience any unexpected adverse events (AE). The participant will complete a Phase I Questionnaire and the clinician will complete VAF. The participant will return 24 hours later for a vaginal exam and culture, the clinician will insert the second stent, and the patient instructions will be reiterated. The participant will wear the second stent for 24 hours, return to clinic for removal, exam, and culture and both clinician and participant will complete the same questionnaires.

Phase 2: Based on feedback from all participants in this healthy cohort, the stent with the highest retention and comfort/acceptability ratings will subsequently be worn by all volunteers for 2 weeks. Vaginal exam, culture, urinalysis, and pregnancy test will occur prior to stent placement. Participants will be sent a secure link to complete a daily Phase II Questionnaire. Participants in this healthy cohort will return to the clinic for a final visit after 2 weeks to have the stent removed by a clinician and have a vaginal exam and culture. The participant will complete a Phase II Questionnaire and clinician will complete VAF. One additional follow up Phase II Questionnaire one day after stent removal.

If we sense low success, or increased AEs (see section H) based on feedback from participants and clinicians, we will continue to optimize design for the vaginal stent system. The results of from healthy volunteers will help us understand factors which may alter the success rate of stent placement in our patient volunteers. We will also generate data for future studies aimed at increased adherence to vaginal stent retention, elimination of need for future vaginal dilatation, and reduction in vaginal fibrosis.

Phase 3: 20 patient participants ("patients") will subsequently be enrolled into the following groups: a) 20 adolescent female patients who will undergo reconstructive gynecologic surgery, and b) 10 adult female patients who will complete vaginal brachytherapy treatment. Patients will be recruited from the principal investigator's department adolescent patient population at TCH and in an adult gynecology oncology collaborator's patient population at Ben Taub Hospital. Flyers will be posted in general waiting areas at the Obstetrics and Gynecology clinics. Eligibility assessments and informed consent/assent will be obtained on an individual patient timeline prior to enrollment. The sterilization process for vaginal stents will occur prior to using the devices in the patient population.

a) Post-Surgical Adolescent Patients: Subjects will complete Pre-Stent Questionnaire. Prior to surgery, patients will undergo standard of care (SOC) testing including urine pregnancy and infection screening. The vaginal canal and mucosa will be assessed while in the operating room by vaginoscopy and a vaginal culture collected to rule out preoperative infection and vaginal length measurement. Vaginal surgery will be carried out per indication. A sterilized, vaginal stent will be placed postoperatively in the operating room, and instructions given to patients prior to discharge. Patients will continue to wear the vaginal stent for two weeks without removal and complete daily questionnaire on retention and comfort.

At 2 weeks post-surgery, patients will complete evaluation of the stent including tolerability, ease of use, comfort, reasons for early discontinuation, as well as any vaginal symptoms such as pain, bleeding or other AE. They will then be reassessed in the operating room (SOC) for stent removal, vaginal length measurement, vaginal culture, urinalysis, evaluation of the vaginal mucosa via vaginoscopy to assess for adhesions, granulation tissue, stricture, and remaining septal tissue. Physicians will complete the VAF.

Subsequent Visits: Patient participants will be re-evaluated at 4 and 6 weeks and 3, 6, and 12 months postop in the clinic. This visit frequency is considered SOC for adolescents who are postop from vaginal reconstructive surgery. Measured outcomes will include possible pain, bleeding, painful intercourse at 3 months postop, difficulty with tampon insertion, menstrual fluid retention, need for vaginal dilators. A physical exam will also be completed including a single digit vaginal exam to evaluate stricture, granulation tissue and adhesions. Patients may also be asked to demonstrate

placement of the vaginal stent (used as a corollary to adequate and maintained vaginal caliber).

b) Adult Females, Post-Radiation: Post-radiation vaginal fibrosis occurs more slowly than post-surgical fibrosis and these women do not have post-surgical wounds, so we expect the adult post-radiation patient population to be able to wear the vaginal stent continuously for two weeks and then for an additional 2 weeks. Following consent adult patients undergoing vaginal brachytherapy treatments, will complete Pre-Stent Questionnaire and the vaginal stent will be placed by Dr. Anthony Costales or another co-investigator physician at the conclusion of their final brachytherapy treatment. Prior to stent placement, the vaginal canal and mucosa will be assessed by speculum exam, vaginal culture, urine pregnancy test, and urinalysis will be obtained and the physician will complete the VAF. Instructions will be given to the patients prior to discharge. If the participant is at a high risk for tissue erosion, per physician discretion, she will be prescribed a topical vaginal estrogen (e.g. Premarin cream or Repagyn hyaluronic acid gel). It is SOC to prescribe vaginal estrogen to current patients with vaginal stents or pessaries who are at higher risk for tissue erosion (e.g. post-menopausal patients); thus, use of the cream or gel in the current study is not experimental. Participants will be sent a secure link to complete a daily questionnaire on retention and comfort.

Evaluation at 2 and 4 weeks: Patients will be examined in clinic by a physician co-investigator at 2 weeks post-stent placement. At the time of assessment, patients will complete evaluation surveys on the vaginal stent as well vaginal symptoms such as pain or bleeding. The vaginal stent will be removed and the vaginal cavity will be assessed by a physician for any adhesions, granulation tissue, stricture, fibrosis, necrosis by speculum exam and vaginal culture. Vaginal length will be measured. Physicians will also rate ease of stent removal and complete VAF for each patient. Any patient-reported symptoms will be documented. At 2 weeks, if no AEs are reported, vaginal stent will be replaced by a physician for an additional two weeks of use. If AEs are reported, clinical decisions regarding continued use of stent will be made. Participants will be sent a secure link to complete a daily survey. If no AE seen in first three patients, clinician may determine two week follow up is not necessary and patients can wear stent for four weeks continuously.

Subsequent Visits: Adult patients will be re-evaluated 3, 6, and 12 months as SOC. Patients will complete questionnaires regarding vaginal symptoms at each clinical visit as described above for adolescents. Physicians will complete the VAF regarding ease of instruction, placement, improvement over standard of care, overall utility for the stent system, and any complications. Outcomes will include pain, bleeding, painful intercourse at 3 months postop, difficulty with tampon insertion, menstrual fluid retention, and need for vaginal dilators. A physical exam will also be completed including a single digit vaginal exam to evaluate stricture, granulation tissue and adhesions. Patients may be be asked to demonstrate placement of the vaginal stent (used as a corollary to adequate and maintained vaginal caliber).

AE monitoring: Participants will be informed about the potential for AEs at the screening call, first clinic visit, and at the visit for insertion of subsequent stents. Participants will be asked to report all AEs via a study phone line. A Data Safety Monitoring Board consisting of an independent investigator recruited from BCM clinical faculty will take responsibility for ensuring that all AEs are reported to the IRB at BCM, in accordance with their standard procedures. In the event of a severe AE (infection, bleeding, mucosal reaction, or inability to carry out Activities of Daily Living), the Board member and representatives from the BCM IRB will meet and discuss mitigation plans and plans for the study future. We anticipate that stopping criteria will include severe AEs in 20% of subjects. Data Safety Monitoring Plan is attached to Section S. Materials- Each vaginal stent system will be individually packaged. Healthy females will receive devices that are sanitary (akin to the cleanliness of a tampon) that have been swabbed with alcohol or other compatible solutions. Devices prepared for the patient population will undergo a 66-hour, costly sterilization process due to the vulnerability of the vaginal tissue after surgery and radiation treatment. The stent size most appropriate to the patients' age and approximate vaginal canal dimensions will be selected. Testing will be monitored by a physician at all stages of the project. All stents will be discarded after single use.

Participant feedback - Participants will be given questionnaires, via RedCap, with questions related to baseline vaginal metrics, stent comfort (during insertion, wear, removal), retention, ability to carry out normal Activities of Daily Living, and any AEs. At all points of instruction during clinic visits, patients will be given ample time to ask questions and voice concerns. A research coordinator or clinician will be available via phone for patient questions.

## Section G: Sample Size/Data Analysis

### G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 40 Worldwide: 40

Please indicate why you chose the sample size proposed:

As a feasibility study, the low recruitment numbers will be used to evaluate the design concept with respect to functionality, comfort and any unforeseen safety issues (beyond those which were accounted for in earlier stages of the product design). The current participants will guide additional device refinements.

### G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

Exploratory analyses of 20 healthy community participants: We code the stent as successful if, after 2 weeks, it has been retained in the vaginal canal. We will tentatively explore predictors of success using binomial logistic regression models, with a log-link estimator, which specify success (retained / not retained) as the outcome and participant group (under 18/over 18), and presence of bacterial / fungal infection at baseline and followup as three separate models. We will also run exploratory binomial logistic regression models, as above, with comfort, acceptability, ability to carry out normal Activities of Daily Living (ADLs), and number of AEs as outcomes, and participant group as the predictor. To maximize power, and recognize the exploratory nature of these analyses, we will not correct for multiple testing.

Analyses of 20 clinical patient participants: Initial analyses will compare the two patient groups on baseline characteristics (vaginal cavity assessments by physicians and patient and physician questionnaires) using two sample t-tests, specifying patient group as the predictor. T-tests were selected for the robust to non-normal distributions with small sample sizes, and their suitability to small sample sizes as low as four per group (ref: york.ac.uk/depts/maths /histstat/student.pdf). Our main analyses will examine whether the stent was successful in our population (ie. examining whether the proportion of retained stents was significantly different from zero). A one-sample t-test will be run, with success (returned at 2 weeks coded as 1, not retained coded as 0) as the independent variable. Significance will be set at P<.05.

All analyses will be conducted in the latest version of R (version 5.1.2).

## Section H: Potential Risks/Discomforts

### H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

The participant may experience mild discomfort while using the stent. A thorough vaginal assessment will be performed by a clinician immediately after insertion to assess for any discomfort outside of normal range.

The likelihood of adverse events is small but could include bleeding, displacement of the stent such as egress, urinary retention, mucosal irritation, tearing, erosion, abscess, granulation tissue, or infection. The principal investigator will likely stop the trial for persistent displacement (>5), tearing or erosion of tissue, or abscess. The principal investigator will likely pause the trial and assess for further detail in instances of urinary retention, mucosal irritation, granulation tissue, or infection.

More severe outcomes, however unlikely, include tearing of the mucosal lining, infection, irritation, urinary retention, bleeding, or formation of granulation tissue around the stent. The most severe outcomes include vaginal tearing and formation of a fistula (abnormal connection between two structures). Symptoms of a vaginal infection may include yellow/green vaginal discharge, vaginal pain, fevers, or abdominal pain. Symptoms of urinary retention may include inability to empty the bladder or pelvic pain. Symptoms of vaginal tearing or granulation tissue formation in the vagina may include unexpected vaginal bleeding or vaginal pain. Symptoms of a vaginal fistula may include passage of urine or feces from the vaginal cavity as well as fevers or pelvic and vaginal pain. These outcomes are highly unlikely and we do not expect them to occur. Please reference attachment "Adverse Event Grading Chart".

A clinician or study nurse will be available at all times via phone for additional participant questions or concerns.

### H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

Yes

NOTE: The answer to the questions in H2 requires the completion of the form: 'Section H – Data and Safety Monitoring Plan' as an attachment in Section S.

### H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

## Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

There are no direct benefits from participating as a healthy volunteer. Clinical patients may benefit from a reduced likelihood of restenosis, additional surgeries, and scarring.

Describe potential benefit(s) to society of the planned work.

Benefits to society include improved post-surgical outcomes for females after pelvic surgery or radiation due to gynecologic cancer treatment. Increased comfort and effectiveness will increase adherence to wearing the stent, which will reduce the likelihood of restenosis, perineal dilation, surgical revision, and scarring. Sexual function is likely to improve. Overall, the improvements to quality of life will yield physical and psychological benefits for both patients and families, as well as significant health care cost savings.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

Due to the unforeseen likelihood of experiencing an adverse event, compared to the potential to permanently improve the quality of life in young women after gynecologic revisions and gynecologic cancer populations, the anticipated benefits outweigh potential risks.

## Section J: Consent Procedures

### J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

No

### J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

Yes

Explain how the research involves no more than minimal risk to the participants, and the specifics demonstrating that the research does not involve procedures for which written consent is normally required outside of the research context.

The waiver for written documentation of consent applies to physicians who will complete a vaginal assessment form. The form includes a cover letter (attached to Section S), indicating that completing any portion of the survey evidences their desire to participate in the study. Participating poses no more than minimal risk and will not affect their employment status in any way. Physician participant names will not be disclosed to anyone outside of the research team. Their responses will be kept confidential and reported only in aggregate, de-identified form.

### J2. Consent Procedures

Who will recruit subjects for this study?

PI
PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Potential participants will be recruited through flyers placed at hospitals, research institutions, and device accelerators within the Texas Medical Center, via the study recruitment pages of the BCM website, and through the electronic BCM and TCH newsletters. Flyers will also be sent to BCM graduate students, post docs, and medical students through list respective list servs. (See flyers in Section S.) Additional flyers may be placed on local college campuses. No individual will be allowed to participate that is or may be graded or trained by any co-investigator. Interested participants will be invited to speak to a study coordinator (plus an interpreter if needed). (However, no Spanish speaking individuals will be consented in the research until all applicable English documents - informed consent form, flyers, questionnaires- are translated into Spanish and submitted to the IRB via an amendment.) Interested participants will be provided a copy of the current informed consent document either via email or in the clinic prior to consenting in order to allow adequate time to review before the first appointment.

The meeting with the study coordinator will be held in a private room within the TCH Clinical Research Center or Pavilion for Women or Ben Taub Hospital. At that time, the study risks and procedures will be fully explained, eligibility assessed, and the participant's rights (including the right to withdraw at any time) enumerated. Eligibility will be determined by the inclusion and exclusion criteria described in Section F1. The study coordinator will review the criteria

with interested participants to determine eligibility. If eligible, the study coordinator will review the consent form and reiterate items related to study objectives, procedures, risks, benefits, compensation, and participant rights. Adequate time will be given for any questions the potential participant may have. The potential participant will have the option of signing the consent form at that time, declining participation, or returning at a later date to provide consent.

Are foreign language consent forms required for this protocol?
Yes

Which of the following ways will you document informed consent in languages other than English?
A full-length informed consent document

### J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?
No

### J4. Children

Will children be enrolled in the research?
Yes

### J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

### J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
No

### J7. Prisoners

Will Prisoners be enrolled in the research?
No

## Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
Yes

Specific information concerning alcohol abuse:
No

Specific information concerning drug abuse:
No

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
Yes

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
No

Identifiable biospecimens
No

Other:
No

At what institution will the physical research data be kept?
Records will be kept in a secure area at in locked credenzas or investigator offices at Texas Children's Hospital and Baylor College of Medicine. Minimal physical research data will be collected.

How will such physical research data be secured?
Data will be accessed, used, disclosed, and/or extracted and kept in a locked cabinet in or adjacent to investigator offices at Texas Children's Hospital and Baylor College of Medicine. The records will be located in personnel-restricted floors and accessible only to research personnel.

At what institution will the electronic research data be kept?
Electronic research data will be maintained by secure, institutional server or using a secured, cloud-based services at all times. Research personnel will store all research-related data in a secure manner.

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):
Yes

Such electronic research data will be secured via Other:
No

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?
No

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.
N/A

Will you obtain a Certificate of Confidentiality for this study?
No

Please further discuss any potential confidentiality issues related to this study.
N/A

## Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.
The cost of the device and any service that is strictly research related (i.e. stent insertion, removal, study questionnaires) and outside of the normal standard of care for post-surgical or post radiation treatment will be covered by the research study. However, any clinic fees, procedures, or labs done as part of standard of care (i.e. as part of normal, post-surgical or post-treatment clinical follow-up) will not be covered by the research study. Services provided as part of standard of care will be billed to the subject's insurance.

All direct costs associated with the healthy volunteers participation will be covered by the study.

Services outside of standard of care for each patient participant group include the following:

1. Adolescent patients: - pre-operative urine analysis and vaginal culture in operating room - at 2 weeks postoperative evaluation: vaginal culture in operating room at stent removal

2. Radiation patients: - Prior to stent placement: physician vaginal assessment exam, vaginal culture, urine analysis, pregnancy test, vaginal length measurement - Evaluation at 2 weeks post stent placement: physician vaginal examination, vaginal length measurement, vaginal culture

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

600

Distribution Plan:

Healthy participants will be compensated fairly for their time and parking. Healthy participants will be compensated $250 for the first phase of the study (5 clinic visits, including orientation, vaginal exam/labs, insertion/removal of 2 separate stents which will be worn for 24 hrs each, questionnaires), and $350 for the second phase of the study (3 clinic visits, vaginal exam/labs, and wearing 1 stent for 2 weeks, daily questionnaires). They will incur no cost to themselves or their insurance for participation. Vaginal exams, device, and lab fees will be paid for by the research study.

Healthy participants will be issued a ClinCard Prepaid Mastercard at the time of consent. Compensation amounts will be distributed electronically to the participant's ClinCard number upon completing clinic visits and/or surveys.The participant will be notified via email or text when the card is reloaded with additional funds.

Patient participants will not receive monetary compensation.

## Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

## Section N: Sample Collection

### SAMPLE: Urine

What is the purpose of the sample collection?

To determine pre-stent infection and pregnancy. This is standard of care for pre-operative adolescent patients.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.

Is there the possibility that cell lines will be developed with this sample?No

Sample will be obtained from:

Pathology

Will the sample be stripped of identifiers?

No

**If sample will be released outside the hospital:**

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?

no

Will sample material be sold or transferred to any third parties? Will the information be de-identified?

no

**If sample will be banked for future use:**

Where will the sample be banked and for how long?

sample will not be banked

Does the banking institution have an approved policy for the distribution of samples?

**If the entire sample will NOT be used during the course of this research study:**

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?

Remaining sample will be discarded appropriately

Will samples be made available to the research subject (or his/her medical doctor) for other testing?

No

**If a subject withdraws from the study:**

Will subject have the option to get the remaining portion of their sample back?

No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?

Remaining sample will be discarded appropriately

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?

Data from the sample will not be deleted as long as subject remains on study.

Will study data or test results be recorded in the subject's medical records?

Yes

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?

Yes, subject will be notified of results and instructed to contact primary care physician if needed.

Please identify all third parties, including the subject's physician, to receive the test results.

## Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)

No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?

No

### O1. Current Drugs

Is this study placebo-controlled?

No

Will the research involve a radioactive drug?

No

## Section P: Device Studies

Does this research study involve the use of ANY device?

Yes

Device 1: vaginal stent

## Section Q: Consent Form(s)

Vaginal Stent Study in Healthy Participants

Vaginal stent to improve post-surgical outcomes and gynecologic cancer treatment

## Section R: Advertisements

None