Informed Consent

A Randomized, Non-Inferiority Study of a Hydrogel Packing System Compared to Standard of Care Packing During Image-Guided High-Dose Rate Brachytherapy Boost for Cervical Cancer

Version Date: 24 January 2022

NCT04499521

Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

Medical Record # _____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a copy of this form.

Who is funding this study?

This study is being funded by BrachyFoam, LLC, who has received funding from the National Cancer Institute of the National Institutes of Health to conduct this study. BrachyFoam, LLC, the manufacturer of the BrachyGel Vaginal Hydrogel Packing system (BrachyGel VHPS,) is providing the device (BrachyGel VHPS) used in this study.

Key Information About This Research Study

Principal Investigator:	Kara Romano, MD
Funding Source:	National Cancer Institute of the National Institutes of Health
Device Manufacturer:	BrachyFoam, LLC

You are being asked to take part in a research study. You do not have to take part in this study. You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers or others before you make a decision.

What problem is this study trying to solve?

As part of vaginal brachytherapy, the organs that do not need to receive radiation (unrelated organs) are moved out of the way of the radiation with a "packing system". The usual low cost and available standard of care packing systems to move these unrelated organs out of the way can sometimes be uncomfortable, may not move all of the unrelated organs all the way out of the radiation's path, and rely on the doctor to place them correctly.

This study is trying to find out whether a new, low cost packing system ("BrachyGel VHPS") is at least as good as standard options at keeping the unrelated organs away from radiation, and to better understand the safety and patient discomfort of BrachyGel VHPS. This is the first use of this device in humans. Studies with this device in the laboratory have demonstrated that the device may be relatively safe and compatible for use in humans. The precise level of safety and ability to keep unrelated organs away from the path of the radiation is unknown.

You are being asked to take part in this study because you are planning to undergo brachytherapy for cervical cancer.

Why would you want to take part in this study?
You might like to take part in this study because, based on laboratory studies and the review of the FDA, the BrachyGel VHPS approach is expected to be safe, more comfortable than existing options and move nearby organs "at risk" (ie. bladder and rectum) away from the high dose radiation at least as well as existing options.

Why would you NOT want to take part in this study?
You might not want to take part in this study because BrachyGel VHPS is considered experimental and has not been approved by the FDA. BrachyGel VHPS has not been tried in humans before and it is not known how safe, comfortable, and well it keeps the unrelated organs away from the path of the radiation.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form.
If you take part in this study you will:

- Out of a total of 5 treatments of brachytherapy, receive 3 treatments with a standard packing option (the same way it would be done if you were not participating in the study) for keeping unrelated organs away from the path of radiation and 2 treatments with BrachyGel VHPS to keep your unrelated organs away from radiation. The order you receive the standard packing or BrachyGel VHPS packing will be determined by the study.
- Answer a couple of questions about your experience after each of the 2nd through 5th treatments of brachytherapy
- Have a physical exam and answer questions about your medical history and performance status before starting brachytherapy (during the treatment 1 visit), if it has been more than 30 days since your last physical exam. A physical exam will also be done about a month after finishing brachytherapy at the follow up visit.
- Information will be recorded from your medical records. This information includes your medical history, demographics, performance status, current medications, and results of any imaging studies or labs you may have had related to the cervical cancer.

What is the difference between being in this study and getting usual care?
If you take part in this study, the following things will be done differently than if you do not take part in this study.

- If you participate in this study, you will receive brachytherapy at the same doses of radiation to the related organs, but you would receive 3 treatments with a standard packing option and 2 treatments with BrachyGel VHPS. You will be randomized to either use BrachyGel VHPS at the 2nd and 4th treatments of brachytherapy, or at the 3rd and 5th treatments.

What other treatments may I receive if I decide to not take part in this study?
The following alternative treatments are available to you if you decide not take part in this study:

- You may use a standard packing option (and not BrachyGel VHPS) at every treatment of brachytherapy. This may include gauze packing or a rectal retractor (as will be used in this study, depending on what is standard where you are being treated), or balloon packing and this may be given over 4-6 treatments.

Up to 47 cancer patients will be in this study at UVA. Up to 57 cancer patients will be in this study at all places.

Is there a possible conflict of interest?

When a person or an organization has a financial or other interest large enough to seem as if it could affect their judgment, it is called a conflict of interest. Members of this study team have a conflict of interest with this study which is explained below.

Dr. Timothy Showalter, the medical monitor for this study, is also the chief executive officer and founder of Brachyfoam, the manufacturer of the BrachyGel Vaginal Hydrogel Packing System (VHPS) used in this study. He serves as a resource for study design and planning, but will not enroll patients, or supervise any students or trainees involved in research on this project. He will administer about half of the treatments of brachytherapy at the University of Virginia, but he will not be involved with the analysis of the study results.

As the owner of the patent of BrachyGel VHPS, the University of Virginia may make money if this study has good results.

How long will this study take?

Your participation in this study will require 7 study visits over 6 – 15 weeks.

What will happen if you are in the study?

Your participation in this study will require assessments that would be done whether or not you are on the study (listed below as procedures for "clinical care"). Other tests that are just for the study are listed as being for "research" in the sections below.

SCREENING (visit will last about 1 hour)

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate.

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- Your medical history and medication list will be reviewed.
- A physical exam will be performed.
- You will be asked questions about your ability to complete daily activities and how you are feeling. This is called "performance status."

If these tests show you are eligible, you will return to the clinic within 6 weeks to begin study treatment.

RANDOMIZATION

You will be randomly assigned (like the flip of a coin) to 1 of 2 study treatment groups. The only difference between the two groups is the timing of the 2 treatments of BrachyGel VHPS. BrachyGel will either be used during treatments 2 and 4 or during treatments 3 and 5. You have an equal chance of being assigned to any one of the groups. Neither you nor your doctor can choose which group you are assigned. You will be told to which group you have been assigned.

GROUP A: Participants in Group A will receive standard of care packing during treatments 1, 2 and 4 of brachytherapy and BrachyGel VHPS during treatments 3 and 5.

GROUP B: Participants in Group B will receive standard of care packing during treatments 1, 3 and 5 of brachytherapy and BrachyGel VHPS during treatments 2 and 4.

Each brachytherapy visit will last two to three hours, including medications, applicator placement, and treatment planning and delivery**.**

STUDY TREATMENT

The following will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- You will have a physical exam before starting brachytherapy (during the treatment 1 visit), if it has been more than 30 days since your last physical exam. A physical exam will also be done about a month after finishing brachytherapy at the follow up visit.

- Your medical history will be reviewed, if it has been more than 30 days since your last screening visit.
- Your medication list will be reviewed.
- If it has been more than 30 days since the screening visit, you will be asked questions about your ability to complete daily activities and how you are feeling. This is called "performance status." This will be repeated about a month after finishing brachytherapy at the follow up visit.
- Standard Packing administration: After the placement of the standard brachytherapy applicators ("tandem & ovoid" or "tandem & ring"), the standard vaginal packing (gauze or rectal retractor) is placed in the vagina. This will occur during the 3 procedures where standard of care packing will be used.
- You will be asked about any side effects you may be having.
- Your medications will be reviewed during and after brachytherapy.

The following will be performed and recorded for research purposes:

- Brachygel Packing administration: After placement of the standard brachytherapy applicators ("tandem & ovoid" or "tandem & ring"), the BrachGel vaginal packing system is placed in the vagina. During the 2 procedures where BrachyGel is used as packing, a clear bag is placed next to the applicators and filled with a liquid that thickens and forms a gel to move the nearby organs (bladder and rectum) away from the path of the radiation. After the procedure, the gel is made soft by injecting water into the bag and the entire device is completely removed from your body.
- You will be asked a few questions for research after treatments 2-5 of brachytherapy. These questions will be about your experience and discomfort level during the preparation for brachytherapy and during brachytherapy (if you are awake during the procedure). This will take about 2-3 minutes. Your physician (the one that does the brachytherapy procedure) and the person that helps with designing the path of the radiation (the physicist) will also be asked to complete questionnaires about their experience with each method for protecting the unrelated organs.

FOLLOWUP 30 days after last Brachytherapy Treatment (visit will last about 1 hour)

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- A physical exam will be performed.
- You will be asked questions about your ability to complete daily activities and how you are feeling. This is called "performance status."
- You will be asked about any side effects you may be having.

Study Schedule

	Screening	Treatment #1	Treatment #2	Treatment #3	Treatment #4	Treatment #5	30 day Follow up after #5
Informed Consent	x						
Review study eligibility	x						
Medical History	x	x[1]					
Physical Exam	x	x[1]					x
Randomization			x (before)				
Performance status	x	x[1]					x
Review medications related to pain			x	x	x	x	
Assess side effects			x	x	x	x	x
Brachytherapy[3]		x	x	x	x	x	
Complete short questionnaire[2]			x	x	x	x	

[1] These assessments are not required at this time-point if they were done within 30 days of treatment 1.

[2] Unless you were sedated for the procedure.

[3] Brachytherapy treatments are usually scheduled 2-7 days apart.

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety.
These responsibilities are listed below:

- You must come to each study visit.
- You must be completely truthful about your health history.
- You must follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks and side effects related to the brachytherapy procedure will be explained to you according to standard of care. Standard of care vaginal packing systems can cause discomfort while they are being placed and during brachytherapy. It is expected that brachytherapy treatments delivered with BrachyGel VHPS as the packing system will be at least as comfortable and as safe as standard of care gauze packing or rectal retractor, but it has not been used in humans before.

Known Risks of Standard of Care Packing Systems (gauze packing and rectal retractor) and Expected Risks of BrachyGel VHPS:

Likely

- Pressure in the area of the packing

Less Likely

- Discomfort in the area of the packing

Rare but serious

- Laceration or a tear in the vaginal wall

Blood Donation

If you participate in this study it may affect your ability to donate blood. If you have any questions call the organization where you donate blood and talk to one of their nurses.

Risks for women:

Being in this study might hurt your unborn baby, so you will not be able to join or stay in the study if you are pregnant. You must use an effective method of birth control during the study. You should also not get pregnant for six months after your last treatment of brachytherapy. If you have questions about birth control, please ask the study leader. If you are pregnant now, or get pregnant during the study, please tell us right away.

Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You may or may not benefit from being in this study. It is possible that the BrachyGel system will be more comfortable than the standard of care option. In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- 5 treatments of brachytherapy using standard of care packing options

If you are an employee of UVA your job will not be affected if you decide not to participate in this study. If you are a student at UVA, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will not get any money for being in this study.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance: questionnaires and BrachyGel VHPS.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required. You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for lost wages, disability, or discomfort. The sponsor will reimburse the reasonable cost of necessary and appropriate emergency and/or acute medical care for injury or illness that is determined by the principal investigator and sponsor to be directly related to the study. Injury related to the study does not include the normal progression of any disease or any underlying pre-existing medical conditions.

What happens if you leave the study early?

You can change your mind about being in the study at any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader (or the device manufacturer for this study) can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) The side effects of the treatment are too dangerous for you
c) New information shows the treatment will not work or is not safe for you
d) You do not follow your doctor's instructions
e) The device manufacturer closes the study for safety, administrative or other reasons

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

How will your personal information be shared?

The UVA researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The device manufacturer for this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- People who evaluate study results, which can include the device manufacturer, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.

- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

Information about you may be given to other researchers outside of the University of Virginia after all identifiers such as name, address, and phone number have been removed. Some of the people outside of UVA who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

A description of this clinical trial will be available on *http:// www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part of this form and return it to the researchers. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your medical records will be able to find out that you are in this study. This is done so your regular doctors will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

Your information, collected for this study, will be protected by a Certificate of Confidentiality from the federal government. If UVA receives a subpoena or court order demanding information from the study records that would identify you, we will use the Certificate to resist the demand. However, UVA will not use it in the following cases.

- You have agreed in writing to allow UVa to share the information with your employer, your insurance company for billing purposes, or someone else
- Reports to authorities where there is a danger that you may harm yourself or others, or if there is evidence of probable child or elder abuse or neglect.

In addition, the Certificate does not prevent government authorities who oversee research from reviewing this study. This Certificate does not mean that the government either approves or disapproves of this study. It just helps protect your privacy.

Please contact the Principal Investigator listed earlier in this form to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Kara Romano, MD
Emily Couric Clinical Cancer Center
1240 Lee St.
Charlottesville, VA 22903
Telephone: 434- 924-9333

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908
Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

You may also report a concern anonymously by calling the UVA Compliance Hotline phone number at 1-800-235-8700.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

If an interpreter is involved in the consent process because the potential subject does not speak English well or at all, the participant should NOT sign on the line above – leave this line blank. Instead, the participant should sign the Short Form or full consent written in the language they can understand.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study has been fully explained to the potential subject in a language they understand and have answered all their questions.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this study to a potential subject, the interpreter must sign and date the line above.

Signature of Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:
____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team. The follow up information will be collected by obtaining information from my medical records.
____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent
By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Interpreter
By signing below you confirm that the study withdrawal section has been fully explained to the subject in a language they understand and have answered all their questions.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this withdrawal section to the subject the interpreter must sign and date the line above.