PHASE II TRIAL OF VAGINAL CUFF BRACHYTHERAPY FOLLOWED BY ADJUVANT CHEMOTHERAPY WITH CARBOPLATIN AND DOSE DENSE PACLITAXEL IN PATIENTS WITH HIGH-RISK ENDOMETRIAL CANCER

Informed Consent Form Version 2.0 Dated 1/27/2017

NCT#03189446

Consent Form
Stephenson Cancer Center
OU Medical Center
University of Oklahoma Health Sciences Center (OUHSC)

PHASE II TRIAL OF VAGINAL CUFF BRACHYTHERAPY FOLLOWED BY ADJUVANT CHEMOTHERAPY WITH CARBOPLATIN AND DOSE DENSE PACLITAXEL IN PATIENTS WITH HIGH-RISK ENDOMETRIAL CANCER

Principal Investigator: Lisa Landrum, MD

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only patients who choose to take part in them. Please take your time to make your decision. Discuss this with your family and friends. You can also discuss it with your health care team. If you have questions, you can ask your study doctor for more explanation.

Why Have I Been Asked To Participate In This Study?

You are being asked to take part in this trial/study because you have been diagnosed with a high-risk early stage endometrial cancer. Even though the cancer appears to be confined to the uterus (Stage I or II), there are additional risk factors which make the likelihood of the cancer coming back (recurrence) more common. You are being asked to participate in a research study to determine if the risk of the cancer coming back can be reduced by the treatments used in this study.

Why Is This Study Being Done?

The purpose of this study is to evaluate the ability of radiation administered to the upper part of the vagina (vaginal cuff brachytherapy) combined with three cycles of chemotherapy to reduce the chance that your cancer recurs. The standard treatment would include radiation to the vagina or entire pelvis. The addition of chemotherapy to the standard of care treatment might be effective in preventing recurrences outside the pelvis. The study will evaluate the effects both good and/or bad that result with additional treatment. This study is designed to compare recurrence, survival, side effects, and differences in where the cancer may recur in patients who receive this treatment to patients who previously received treatment using different therapy.

What is the Status of the Drugs (Devices or Procedures) involved in this study?

Carboplatin and paclitaxel are approved by the US Food and Drug Administration for use as chemotherapeutic agents.

The Vaginal Cuff Brachytherapy device is approved by the US Food and Drug Administration.

How Many People Will Take Part In The Study?

About 50 people will take part in this study, all at this location.

What Will Happen If I Take Part In This Research Study?

Before you begin the study

Endometrial cancer is commonly treated with surgery. You must have already had surgery including hysterectomy (removal of the uterus) prior to being considered eligible for this study. The surgery may also include removal of the ovaries, and removal of pelvic and para-aortic lymph nodes. Following your surgery, your doctor has identified you to have factors related to the cancer which place you at a greater risk for the cancer returning.

Prior to being treated in this study you will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- ***Physical examination, including pelvic examination***
- ***Blood tests to evaluate blood counts, and kidney and liver function (2-3 tablespoons of blood drawn from a vein in your arm)***
- ***Chest x-ray***
- ***CT scan abdomen/pelvis if you did not have did not have a bilateral pelvic and para-aortic lymphadenectomy***

During the study

If the exams, tests and procedures show that you can be treated in the study, and you choose to take part, then you will receive radiation therapy to the upper portion of the vagina. Following radiation therapy, three cycles of chemotherapy will be given. You will need the following tests and procedures. They are part of regular cancer care**.**

- ***Blood tests to monitor effects of radiation therapy and chemotherapy and to evaluate blood counts, and kidney and liver function (2-3 tablespoons of blood drawn from a vein in your arm)***

You will need these tests and procedures that are either being tested in this study or being done to see how the study is affecting your body.

- ***CA 125 blood test (1 tablespoon of blood from a vein)***
- ***Chest x-ray, cat scans, MRI's, or ultrasounds will only be done if your doctor needs them to evaluate problems***

Study Chart

You will receive carboplatin every 3 weeks and paclitaxel every week in this study. This 3-week period of time is called a cycle. The cycle will be repeated 3 times. Each cycle is numbered in order. The chart below shows what will happen to you during treatment and future treatment cycles as explained previously. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

Day	**What you do Revise to include new schedule for chemo**
Within 6 weeks	• Start vaginal radiation therapy

of your hysterectomy	
Within 7 days before starting chemotherapy (within 8 weeks from your surgery)	• Return to your doctor's office for an examination • Get routine blood tests.
Day 1	• Chemotherapy treatment carboplatin and paclitaxel • You will receive medications to prevent nausea and possible allergic reactions to the chemotherapy
Day 8	• Get routine blood tests. • Paclitaxel chemotherapy treatment
Day 15	• Get routine blood tests. • Paclitaxel chemotherapy treatment
Day 15-21	• Return to your doctor's office for examination and to make sure you are tolerating the treatments well • Get routine blood tests.
Day 22	• Next cycle of treatment. This schedule will be repeated for 3 cycles.

How Long Will I Be in the Study?
You will be asked to take radiation therapy to the upper vagina until an appropriate dose of radiation is delivered. The radiation therapy will start within 6 weeks after your hysterectomy.

In general, there are 2 techniques for vaginal radiation therapy. One requires 3 outpatient treatments spaced over about 2 weeks. The other requires 1-2 treatments given in the hospital which require a 1-2 day stay in the hospital. Your doctor will discuss which method is best for you and why. Following completion of radiation therapy, you will start chemotherapy. In general, chemotherapy may start shortly after the radiation therapy is completed, and within 8 weeks from your hysterectomy. The chemotherapy will last for 9 weeks (3 cycles, given every 3 weeks).

After you are finished with all of the treatments the study doctor will ask you to visit the office for follow-up exams at least every 3 months for the first 2 years, then every 6 months for the next 3 years, then yearly thereafter. We would like to keep track of your medical condition for the rest of your life. We would like to do this by calling you on the telephone once a year to see how you are doing. Keeping in touch with you and checking on your condition every year helps us look at the long-term effects of the study.

Can I Stop Being in the Study?
Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the radiation or chemotherapy can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she thinks it is best for you; if you do not follow the study rules; or if the study is stopped.

What Side Effects or Risk Can I Expect From Being in this Study?
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the carboplatin and paclitaxel. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death. You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to the **Vaginal Radiation Therapy** include those which are:
Likely (>20% of patients experience this)

- Short term (less than 1 month) vaginal and vulvar irritation/discomfort
- Short term (less than 1 month) bladder irritation/discomfort
- Short term (less than 1 month) diarrhea irritation/discomfort
- Short term (less than 1 month) rectal irritation/discomfort

Less likely but serious (>5% but < 20% experience this)

- Narrowing or shortening of the vagina
- Long term (lasting more than 3 months) vaginal, bladder, rectal irritation/discomfort
- Painful intercourse
- Urinary Tract Infection

Rare, but serious(<5% risk)

- Complete narrowing or shortening of the vagina
- Holes which develop between the rectum and/or bladder and vagina (fistula)
- Bowel Obstruction
- Malabsorption

There is a risk 0.2 % chance of getting a secondary cancer in 20 years.

Risks and side effects related to the chemotherapy include those which are:
Carboplatin:

Likely: (>20% of patients experience this)

- Low white blood cell counts - this may increase your chance of infection

- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath or fatigue
- Fatigue
- Loss of appetite and weight loss
- Diarrhea, constipation, nausea and vomiting, and abdominal pain
- Complete hair loss
- Skin rash
- Changes in taste
- Changes in electrolytes in the blood such as magnesium and potassium

Less likely, but serious: (>5% but < 20% experience this)

- Numbness or tingling in fingers or toes
- Ringing in the ears and hearing loss
- Allergic reactions
- Chills and fever with aches and pains
- Decrease in kidney or liver function
- Sores in mouth and throat (that can lead to difficulty swallowing and dehydration)
- Altered vision

Rare, but serious: (<5% experience this)

- Seizures
- Secondary cancers such as acute leukemia
- Kidney failure requiring dialysis
- Deafness
- Death

Paclitaxel (Taxol)

Likely: (>20% experience this)

- Low white blood cell counts - this may increase your chance of infection
- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath or fatigue
- Mild to severe allergic reaction which may be life-threatening with hives, wheezing and low blood pressure
- Numbness and pain of the hands and feet that sometimes worsens with additional treatment and may not disappear after the drug is stopped. This may lead to difficulty walking, buttoning clothes, etc.
- Hair loss
- Muscle weakness and muscle loss
- Muscle and joint aches

Less likely, but potentially serious: (>5% but <20% experience this

- A slowing of the heart rate (a slow pulse is not harmful; however if you should develop any other irregularities in heart rate during treatment, an EKG and other tests may be required.)
- Irregular heartbeats
- Heart attack
- Nausea and/or vomiting
- Diarrhea
- Sores in the mouth or throat (that can lead to difficulty swallowing and dehydration)
- Fatigue
- Lightheadedness
- Headaches
- Kidney damage
- An increase in triglycerides (a blood lipid) levels which could increase risk of hardening of the arteries
- Liver damage
- Confusion; mood changes
- Skin tissue damage if some of the drug leaks from the vein while it is being given
- Changes in taste
- Irritation and swelling of the skin in an area previously treated with radiation therapy
- Rash
- Inflammation of the colon, pancreas or lungs
- Blurred vision or other changes in eyesight such as sensation of flashing lights or spots

Rare, but serious: (<5% experience this)

- Liver failure
- Swelling of the brain
- Seizures
- Death

Are There Benefits to Taking Part in the Study?

Taking part in this study may or may not make your health better. While doctors hope combining vaginal radiation therapy with chemotherapy will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about radiation and chemotherapy as a treatment for endometrial cancer. This information could help future cancer patients.

What Other Choices Do I Have If I Do Not Take Part in this Study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study

- Pelvic radiation without chemotherapy
- Getting no treatment

Talk to your doctor about your choices before you decide if you will take part in this study.

What About Confidentiality?
Efforts will be made to keep your personal information confidential. You will not be identifiable by name or description in any reports or publications about this study. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. You will be asked to sign a separate authorization form for use or sharing of your protected health information.

There are organizations outside the OUHSC that may inspect and/or copy your research records for quality assurance and data analysis. These organizations include the US Food & Drug Administration, and other regulatory agencies. The Department of Ob/Gyn , the OUHSC Human Research Participant Program office, the OUHSC Institutional Review Board, and the OUHSC Office of Compliance may also inspect and/or copy your research records for these purposes.

What Are the Costs of Taking Part in this Study?
You and/or your health plan/ insurance company will need to pay for all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Both chemotherapy drugs used in this study are commercially available and are not provided for being in the study.

What if I am Injured or Become Ill While Participating in this Study? In the case of injury or illness resulting from this study, emergency medical treatment is available. No funds have been set aside by The University of Oklahoma Health Sciences Center, OU Medical Center or Stephenson Cancer Center to compensate you in the event of injury.

What Are My Rights As a Participant?
Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. If you agree to take part and then decide against it, you can withdraw for any reason; however, at certain times during the treatment, it may be harmful for you to withdraw, so please be sure to discuss leaving the study with the study doctor (Principal Investigator) or your regular physician. Refusal to participate or leaving the study will not result in any penalty or loss of benefits that you are otherwise entitled.

We will tell you about any significant new findings that develop during the course of the research that may affect your health, welfare or willingness to stay in this study.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study has completely finished and you consent to this temporary restriction.

Whom Do I Call If I have Questions or Problems?
If you have questions, concerns, or complaints about the study or have a research-related injury, contact the Principal Investigator, Dr. Lisa Landrum, at (405) 271-8707.

For questions about your rights as a research subject, contact the OUHSC Director, Human Research Participant Protection Program at (405)271-2045.

If you cannot reach the Principal Investigator or wish to speak to someone other than the Principal Investigator, contact the OUHSC Director, Office of Human Research Participant Protection at (405)271-2045.

Signature:

By signing this form, you are agreeing to participate in this research study under the conditions described. You have not given up any of your legal rights or released any individual or entity from liability for negligence. You have been given an opportunity to ask questions. You will be given a copy of this consent document.

I agree to participate in this study:

_____	_____	_____
PARTICIPANT SIGNATURE (age ≥18) (*Or Legally Authorized Representative)*	Printed Name	Date
_____	_____	_____
SIGNATURE OF PERSON OBTAINING CONSENT	Printed Name	Date

AUTHORIZATION TO USE or SHARE
HEALTH INFORMATION[1] THAT IDENTIFIES YOU FOR RESEARCH
An Informed Consent Document for Research Participation may also be required.
Form 2 must be used for research involving psychotherapy notes.

Title of Research Project: **PHASE II TRIAL OF VAGINAL CUFF BRACHYTHERAPY FOLLOWED BY ADJUVANT CHEMOTHERAPY WITH CARBOPLATIN AND DOSE DENSE (Dd) PACLITAXEL IN PATIENTS WITH HIGH-RISK ENDOMETRIAL CANCER**

Leader of Research Team: **Lisa Landrum, MD**

Address: **Stephenson Cancer Center, 800 NE 10th Street, Oklahoma City, Oklahoma 73104**

Phone Number**: (405) 271-8707**

If you decide to sign this document, University of Oklahoma Health Sciences Center (OUHSC) researchers may use or share information that identifies you (protected health information) for their research. Protected health information will be called PHI in this document.

PHI To Be Used or Shared. Federal law requires that researchers get your permission (authorization) to use or share your PHI. If you give permission, the researchers may use or share with the people identified in this Authorization any PHI related to this research from your medical records and from any test results. Information used or shared may include all information relating to any tests, procedures, surveys, or interviews as outlined in the consent form; medical records and charts; name, address, telephone number, date of birth, race, government-issued identification numbers, and information about your response to treatments, and other medical information relating to your participation in the study.

Purposes for Using or Sharing PHI. If you give permission, the researchers may use your PHI to evaluate the ability of radiation administered to the upper part of the vagina (vaginal cuff brachytherapy) combined with three cycles of chemotherapy to reduce the chance that your cancer recurs.

Other Use and Sharing of PHI. If you give permission, the researchers may also use your PHI to develop new procedures or commercial products. They may share your PHI with other researchers, the research sponsor and its agents, the OUHSC Institutional Review Board, auditors and inspectors who check the research, and government agencies such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS), and when required by law. The researchers may also share your PHI with the department of Ob/Gyn.

[1] **Protected Health Information includes all identifiable information relating to any aspect of an individual's health whether past, present or future, created or maintained by a Covered Entity.**

Confidentiality. Although the researchers may report their findings in scientific journals or meetings, they will not identify you in their reports. The researchers will try to keep your information confidential, but confidentiality is not guaranteed. The law does not require everyone receiving the information covered by this document to keep it confidential, so they could release it to others, and federal law may no longer protect it.

YOU UNDERSTAND THAT YOUR PROTECTED HEALTH INFORMATION MAY INCLUDE INFORMATION REGARDING A COMMUNICABLE OR NONCOMMUNICABLE DISEASE.

Voluntary Choice. The choice to give OUHSC researchers permission to use or share your PHI for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for OUHSC researchers to use or share your PHI if you want to participate in the research and, if you cancel your authorization, you can no longer participate in this study.

Refusing to give permission will not affect your ability to get routine treatment or health care unrelated to this study from OUHSC.

Canceling Permission. If you give the OUHSC researchers permission to use or share your PHI, you have a right to cancel your permission whenever you want. However, canceling your permission will not apply to information that the researchers have already used, relied on, or shared or to information necessary to maintain the reliability or integrity of this research.

End of Permission. Unless you cancel it, permission for OUHSC researchers to use or share your PHI for their research will never end.

Contacting OUHSC: You may find out if your PHI has been shared, get a copy of your PHI, or cancel your permission at any time by writing to:

Privacy Official
University of Oklahoma Health Sciences Center
PO Box 26901
Oklahoma City, OK 73190

or

Privacy Board
University of Oklahoma Health Sciences Center
PO Box 26901
Oklahoma City, OK 73190

If you have questions, call: (405) 271-2511 or (405) 271-2045.

Access to Information. You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study is completely finished. You consent to this temporary restriction.

Giving Permission. By signing this form, you give OUHSC and OUHSC's researchers led by the Research Team Leader permission to share your PHI for the research project listed at the top of this form.

Patient/Participant Name (Print): _____

_____ _____
Signature of Patient-Participant Date
or Parent if Participant is a minor

Or

_____ _____
Signature of Legal Representative** Date

**If signed by a Legal Representative of the Patient-Participant, provide a description of the relationship to the Patient-Participant and the authority to act as Legal Representative:

_____
OUHSC may ask you to produce evidence of your relationship.

A signed copy of this form must be given to the Patient-Participant or the Legal Representative at the time this signed form is provided to the researcher or his representative.