CONSENT TO PARTICIPATE IN A RESEARCH STUDY

TITLE: Prospective Evaluation of CyberKnife® as Monotherapy or Boost Stereotactic Body Radiotherapy for Intermediate or High Risk Localized Prostate Cancer: An Observational Study

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SPONSOR: Advocate Lutheran General Health Partners Endowment

PURPOSE OF THE STUDY

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

This study has been reviewed, approved and will be monitored according to federal law by the Institutional Review Board (IRB) of Advocate Health Care, 3075 Highland Parkway, Downers Grove, IL 60515. An IRB is a group of people, independent of the study sponsor and investigators, whose role is the review and oversight of research studies to ensure the safety and rights of participants.

You are being invited to take part in this study because you have prostate cancer. This study is a clinical evaluation of a highly focused radiation treatment for prostate tumors using the CyberKnife® system (manufactured by Accuray Incorporated, Sunnyvale). The CyberKnife® system has been approved by the US Food & Drug Administration (FDA).

If you choose to participate in this study you will receive the same routine medical care as recommended by your doctor. This study is designed to systematically gather information regarding the treatment process, side effects, and outcomes, so as to further document this treatment options for people with prostate cancer. If you decide to participate in this evaluation, you will need to meet a number of requirements before your doctors determine that this treatment is appropriate for you. The purpose of this evaluation is to look at the effect this treatment will have on your tumor and your quality of life at various times for five (5) years after your treatment.

The purpose of this study is to document the effects of CyberKnife® radiosurgery in patients with prostate cancer and to evaluate the effects of the therapy on subjects' quality of life over a 5 year period. The CyberKnife® system is a radiation machine that precisely focuses large doses of x-rays on the tumor. The system permits a greater concentration of the x-rays onto the tumor than conventional therapies so as to minimize radiation damage to the nearby normal tissue. Based on the characteristics and extent of your particular cancer your doctor will determine whether Intensity

Modulated Radiation Therapy (IMRT) will also be used in conjunction with the Cyberknife® system. Your doctor will discuss the alternative therapies available for your care.

All therapies to be employed within this study are FDA approved for the treatment of prostate cancer; this study does not employ investigational or experimental treatments. The purpose of the study is to collect data on your course of care, your outcomes and the impact of the treatments on your quality of life. The same course of care would be recommended by your doctor whether or not you choose to participate in this study.

Possible benefits of the Cyberknife® focused radiation treatment that have been observed in some patients are that the higher doses of radiation permitted by the tightly focused radiation beam may be more damaging to the tumor and, therefore, lengthen the time to tumor progression and improve the prognosis. The focused radiation is also less damaging to surrounding tissue and thereby minimizes side effects. The Cyberknife® therapy requires 4 – 7 visits and is given on an out-patient basis.

Advocate Lutheran General Hospital, Advocate Illinois Masonic Medical Center and Advocate Good Shepherd Hospital are expecting to enroll up to 150 subjects in this study.

PROCEDURES

Before you begin the study

You will need to have the following exams, tests or procedures to determine if you qualify for the study. These exams, tests or procedures are part of regular cancer care and are necessary 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.

- History and physical exam
- Prostate Specific Antigen (PSA)
- Blood tests (including a test to confirm your kidneys are working properly)
- Prostate biopsy within the last 12 months that shows that you have prostate cancer
- Digital Rectal Exam (DRE) to determine if the cancer can be felt.

Before Treatment Begins

You will be asked to complete 3 questionnaires. These questionnaires will ask you multiple choice questions about your bowel, bladder and sexual function. They will also ask you some general questions about your mood, activity and energy levels, and general health. The questionnaires are: American Urological Association (AUA) symptom index and Expanded Prostate Cancer Index Composite (EPIC-26), as well as a sexual function questionnaire the Sexual Health Inventory for Men (SHIM). These questionnaires will take approximately 20 minutes to complete.

You will also have a physical examination and a procedure to place 4 small gold seeds into the prostate. This procedure is commonly done in patients receiving standard external beam radiation for prostate cancer and is not an experimental procedure. These markers will be used to determine the location of the prostate during the CyberKnife® treatment. An ultrasound probe is placed into the rectum and needles containing the metal seeds are guided into the prostate and then the seeds are deposited. You will need to clean out your rectum and take antibiotics the day of the seed

placement. You may also have a SpaceOAR hydrogel placed. It remains in place for 3 months during radiation treatment and is then absorbed and leaves the body in your urine, leaving nothing behind. This will be determined between you and your treating physician.

SpaceOAR hydrogel is an option for men who undergo radiation treatment for prostate cancer and is approved by the FDA. It acts as a spacer providing space between the rectum and the prostatewith the intent to reduce the radiation dose delivered to the anterior rectum. It is injected into place prior to the start of radiation treatment. Patients may be awake or asleep under general anesthesia for the procedure. SpaceOAR hydrogel is minimally invasive, remains stable during radiation therapy and then is gradually absorbed by the body after radiation therapy has been completed.

More information can be located at the following website: https://www.spaceoar.com/

Within 5-10 days after placement of the gold seeds, you will be asked to have a planning CT scan of the pelvis. This is a regular CT scan and is standard procedure for patients receiving external beam irradiation. The images obtained during the scan will be used to plan the CyberKnife® treatments. You will also have an MRI scan of the pelvis, unless medically contraindicated (for example if you have a pacemaker) which will be used for treatment planning purposes.

During Treatment

Intermediate risk patients will be treated with either:

- CyberKnife® boost followed by IMRT; or,
- CyberKnife® SBRT alone.

High risk patients will be treated with CyberKnife® boost followed by IMRT.

Both intermediate and high-risk patients may be recommended to undergo androgen deprivation therapy (ADT) per current standards of care. ADT is a hormone therapy that reduces the amount of naturally occurring male hormones available to support the cancer cells. The duration and type of treatment and possible side effects will be discussed with you by your doctor.

CyberKnife® treatment will usually be started a few days after the CT scan of the pelvis. Your course of radiation will consist of 3 to 5 separate CyberKnife® treatments usually delivered over consecutive weekdays (maximum 7 days), with at least 12 hours between any two fractions. Each treatment session will take approximately 1.5 - 2.5 hours. You will lie on the treatment table and breathe normally while you receive your radiation treatment.

All high-risk patients and some intermediate risk patients (as determined by the characteristics of your cancer) will follow the CyberKnife® treatments with 25 sessions of IMRT administered weekdays over 5 weeks. Each IMRT session will require approximately 20 minutes.

After Completion of Treatment

When you are finished with your radiation therapy, you will continue to follow-up with your doctor for regular exams, tests or procedures that are a standard part of regular cancer care. You will be followed for 5 years after the treatments.

Timing	What you do
1 month	• Follow-up appointment with radiation oncologist • Complete: AUA, EPIC 26 and SHIM questionnaires
3 months	• A physical examination, including a digital rectal exam (DRE) • Prostate Specific Antigen (PSA) • Complete AUA, EPIC 26 and SHIM questionnaires
Every 6 months the first 3 years, then every 12 months until year 5	• A physical examination, including a digital rectal exam (DRE) • Prostate Specific Antigen (PSA) • Complete: AUA, EPIC 26 and SHIM questionnaires

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for 5 years. During that time, you may receive CyberKnife® treatment for 4 - 7 days. After you are finished with treatment, the study doctor will ask you to visit the office. At some of these visits you will be asked to complete questionnaires about your bowel, bladder and sexual functioning and your quality of life.

If it is suspected your tumor is growing or if there are concerns about disease progression based on your PSA exams, a prostate needle biopsy of the tumor may be performed. After you complete your study therapy, your study doctor will ask you to visit the office for follow- up exams (as described above) for 5 years from the time you joined the study. We would like to keep track of your health during that time. Keeping in touch with you and checking on your condition helps us to look at the long-term effects of the study therapy.

RISKS

You may have side effects while on the study. These possible side effects are the same whether or not you choose to participate in the study. While on study you will be watched carefully for any side effects. However, doctors may not know all the side effects of the treatment. Side effects may be mild or very serious, long lasting, or may never go away. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop radiation therapy. You should talk to your study doctor about any side effects that you have while taking part in the study.

The administration of radiation therapy itself is painless and the only discomfort is expected to be from having to lie very still during the treatment.

The biopsy and placement of the gold markers may cause some discomfort as these procedures require the use of small needles inserted into the prostate. Discomfort from these procedures will be minimized by the use of local numbing medications (anesthetics) and you may receive intravenous injection of small doses of medications to make you drowsy (sedatives). It is likely that a patient undergoing this procedure may experience discomfort from placement of the needles and minor bleeding because of injury to small blood vessels in the path of the needle. The majority of cases do not require treatment and the bleeding resolves spontaneously. Other possible side effects, which are rare, include infection requiring antibiotic treatment and significant bleeding requiring transfusion and/or surgery.

Risks and side effects related with External Radiation Therapy:

Likely 20% or More	Less Likely 20% or less	Rare but Serious 3% or Less
▪ Temporary fatigue ▪ Temporary frequent or loose stools ▪ Temporary urinary frequency, irritation, or reduced stream ▪ Reduction in ejaculate volume	▪ Temporary redness, tanning, or hair loss of skin in the treatment area ▪ Permanent urinary "bother", e.g. need to urinate urgently or frequently ▪ Leakage of small amounts of urine, which could require wearing pads in underwear ▪ Impotence	▪ Rectal bleeding ▪ Urinary obstruction which could require catheter placement ▪ Urethral scarring, which could impair urine stream, and could require surgery to repair ▪ Permanent inability to control urine, which could require a catheter, penile clamp, or surgery to repair ▪ Urinary bleeding
	▪ Pain with ejaculation, or change in the sensation of orgasm	▪ Prostate, bladder, urethra, or rectal pain ▪ Rectal or urethral ulceration, or fistula, which could result in colostomy and/or ileostomy

SpaceOAR Hydrogel RISKS
What Are The Risks?
SpaceOAR is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer and in creating this space it is the intent of SpaceOAR hydrogel to reduce the radiation dose delivered to the anterior rectum. The SpaceOAR hydrogel is composed of biodegradable material and maintains space for the entire course of prostate radiotherapy treatment. It is completely absorbed by the patient's body over time.

Clinical data comparing patients with and without SpaceOAR hydrogel demonstrated the benefits of SpaceOAR hydrogel to include reduction of rectal toxicity resulting in improved bowel function, improvements in urinary function, and a higher likelihood to maintain sexual function.

Potential complications associated with SpaceOAR hydrogel include but are not limited to pain associated with SpaceOAR hydrogel injection; pain or discomfort associated with SpaceOAR hydrogel, needle penetration of the bladder, prostate, rectal wall, rectum, or urethra; injection of SpaceOAR hydrogel into the bladder, prostate, rectal wall, rectum, or urethra; local inflammatory reactions; infection; injection of air, fluid or SpaceOAR hydrogel intravascularly; urinary retention; rectal mucosal damage, ulcers, necrosis; bleeding; constipation; and rectal urgency.

BLOOD DRAWING RISKS
There may be bruising, bleeding or inflammation at the sites where blood samples are taken. Care will be taken to avoid these complications.

If the possibility of side effects makes you too uncomfortable, you are encouraged to contact the study doctor as soon as possible.

BENEFITS

There is no guarantee of direct benefits from participating in this research study. Taking part in this study may or may not make your health better.

The information which is obtained from this clinical evaluation will be used to see how helpful this treatment is to patients with prostate cancer and to look at the effect this treatment has on your quality of life over time. This information could help future cancer patients.

ALTERNATIVE THERAPY

Your other choices may include:

- Watchful waiting: a program of close follow-up delaying definitive treatment of your cancer
- Surgery: surgical removal of the prostate
- Brachytherapy: the placement of a radioactive source into the prostate
- External Beam Radiation: the use of a machine to deliver radiation to the prostate
- CyberKnife radiation therapy as described above but without participating in the study
- Hormonal Therapy: the use of hormones to lower or block the male hormone testosterone, to suppress prostate cancer growth
- Cryotherapy: freezing of the prostate

Please talk with your doctor about your choices before you decide if you will take part in this study.

COSTS

You and/or your health insurance plan will be responsible for the entire cost of treating your cancer in this study, including the cost of managing any side effects of therapy, and subsequent evaluation.

Some health plans will not pay these costs for people taking part in studies. You should check with your insurance carrier to find out what they will pay for. Taking part in this study may or may not cost your insurance plan more than the cost of regular cancer treatment. You will be responsible for paying any deductibles, coinsurance, and co-payments as required under the terms of your insurance plan(s). Ask the study staff for help in determining your insurance coverage. Your doctor will discuss these with you.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at:http://cancer.gov/clinicaltrials/understanding/insurancecoverage

You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

COMPENSATION

You will not be paid for taking part in this study. The study doctors will not be paid for your participation in this study.

CONFIDENTIALITY

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information will not be disclosed without your written consent except as required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

During the study, your medical and personal information will be collected. This will initially be part of your medical files and will also be anonymously re-recorded in a specific case report document.

By signing this informed consent form, you authorize the recovery, access and processing of the data that will be recorded. By signing this consent, you authorize and request all health care providers who examine and/or treat you to release all medical records related to such examination and/or treatment to the Advocate Health Careat its request, for use in this protocol.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis, as required under the guidelines of the Federal Privacy Act, include research oversight groups such as the US Food and Drug Administration, the Office for Human Research Protections (OHRP) and the Advocate Health Care Institutional Review Board. These groups will be permitted to have access to information contained in your medical record, records kept prior to and related to your participation in this study, and any of the data collected, including vital records.

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 study results. You can search this web site at any time.

RESEARCH RELATED INJURY

You will get medical treatment if you are injured as a result of taking part in this study but you and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

It is important that you inform the principal investigator, Arica Hirsch, MD, or your study doctor, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him or her at 847-723-8030.

No funds have been set aside by Advocate Health Care or Radiation Oncology Consultants for injury or for any associated costs. You do not waive any of your legal rights by signing this form.

QUESTIONS

You may contact the principal investigator, Arica Hirsch, MD your study doctor or your study coordinator, at 847-723-8030 about any question or concerns you may have about this study.

For information on your rights as a study subject, you may contact the Chairman of the Institutional Review Board of Advocate Health Care at 630-929-6149.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Your participation in this study is entirely voluntary. You may choose not to participate or to discontinue your participation in the study at any time without giving a reason. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect you medical care. You can still get your medical care from our institution. However, if you decide to participate in this study, it is expected that you will comply with the study requirements. Refusal to participate or withdrawal will not result in any penalty, loss of benefits or reduction in the quality of medical care.

If you decide to withdraw from the study, no further data about your course of care or outcomes will be collected. Data that has already been collected for study purposes will be retained for use in analyses.

You are free to withdraw from this study at any time by notifying the principal investigator for this study, Arica Hirsch, MD at 847-723-8030.

It is important to tell the study doctor if you are thinking about stopping or decide to stop, so any side effects/risks from the treatment can be evaluated by your doctor. He or she will tell you how to stop safely. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing that could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he or she believes it is in the best interest for your health, if you do not follow the study rules, you need treatment not allowed in this clinical evaluation or if the study evaluation is canceled.

You will be informed of any significant new developments that may arise or if any new information becomes available during the course of this study that may affect your health or influence your continued participation.

RESEARCHER CONFLICT OF INTEREST/ DISCLOSURE STATEMENT

This study is not sponsored by a commercial manufacturer. The research is supported by a grant from the Advocate Lutheran General Health Partners Endowment. There is no financial benefit to your physician for your participation in this study.

You may ask your physician any questions you wish regarding this study. The decision whether to take part in this study is yours alone. To assist you with your decision, you may also want to consult with your personal physician, or a physician not affiliated with the study. You should have all the information you need to be comfortable with your decision.

Information about Confidentiality and HIPAA Authorization

Note: In this authorization document, "you" and "your data" refer to the subject. If you are a parent or guardian, please remember that "you" refers to the study subject.

Federal law provides additional protections of your medical records and related health information. That law is the *Health Insurance Portability and Accountability Act* (HIPAA). This study's HIPAA statement is provided below. You are providing your authorization if you sign this form and the accompanying consent or permission form to participate in the study.

Who will see my protected health information?

Who may have access to my information:	***Purpose:***
Any sponsor, including future sponsors, of the study and anyone working on behalf of a sponsor or future sponsor	To oversee the study and make sure the information is correct.
Advocate Aurora Health consultants and employees, including IRB members.	To protect the rights and safety of subjects and make sure the study information is correct.
Organizations that regulate research (such as the FDA, Office for Human Research Protections (OHRP), or similar government agencies in the US and other countries).	To make sure applicable laws are being followed.
Organizations that grant accreditation to hospitals and research programs.	For Advocate Aurora Health to remain accredited.

By signing this form, you are authorizing access to and sharing of personally identifiable health information. This includes direct access to your medical records at Advocate Aurora Health.

Please note that the study doctor or study staff may also share personal information about you if required by law (for example, if the study doctor or study staff suspects that you are going to harm someone or yourself; reporting of communicable disease (HIV, hepatitis, tuberculosis, etc.). If you have questions about this, please ask the study doctor.

How will my information be used for this study?

This section explains who will use and share your health information if you agree to be in this study. You must authorize this use and sharing of your information by signing this form or you cannot be in the study.

The study principal investigator and study staff will collect, use, and share identifiable health information about you for the following reasons:

- to conduct this research study;
- to review the study, and to check the safety and results of the study;
- to seek government approval of an investigational study drug, vaccine, device or product if such was involved in the trial;
- to assist a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions.

Information used and shared may include:

- information from your medical records related to the research or your routine medical care;
- information collected about you during the research and any follow-up related to study visits, tests, procedures, outcomes, etc.

The collected information may contain your name, address, telephone number, health plan number, date of birth, medical record numbers, dates relating to various medical procedures, and/or other identifying information.

How will my information be kept confidential?

We will keep your personal health information as confidential as possible. Your identity will be protected as required by law and according to any policies described in the study consent form you were given. Researchers may share your information with representatives and agents of the sponsor(s) for the purposes of managing and overseeing the study. Usually the health information sent to sponsors does not directly identify participants (for example, by name or address). Instead initials and a code number are used. Some personal information, such as date of birth, will usually be included but will not be used to identify you.

Once your information leaves Advocate Aurora Health we cannot control how it is used, and the law may not require outside organizations to protect the privacy of your information.

If this study is designed so that you are intentionally not told what treatment or study intervention you are receiving (called a blinded study), you will not have access to health information in your medical record that was collected as part of this study until those who run the study determine it is no longer necessary to keep you blinded. This usually occurs after everyone in the study has completed study treatment or intervention but can sometimes last until all study data is collected and analyzed.

How do I cancel my authorization?

You can cancel your authorization to use and share your information at any time by writing a letter to the study doctor. If you cancel your authorization, you will not be able to continue in the study. If some aspects of the study were optional, you may cancel your authorization for the optional part(s) of the study and still remain in the main study.

If you cancel your authorization, no new information will be collected without your permission. The study doctor and study staff will still be able to use and share your information that has already been collected to maintain the integrity of the study.

When will my authorization expire?

The authorization to use and share your information has no end date.

If study information is used for scientific publications or educational purposes, all identifying information will be removed.

You will receive a signed and dated copy of this form for your records.

CONSENT

By signing this form, I acknowledge that this study has been explained to me, including the procedures, and potential risks and discomforts. I have read this consent form in its entirety and have spoken to the investigator or his/her representative and have had all questions answered to my satisfaction. I will receive a completed signed copy of this document. My signature indicates my agreement to voluntarily participate in this study.

________________________________ _______________
Signature of Subject Date

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Printed Name of Subject

RESEARCH REPRESENTATIVE'S STATEMENT
I have explained this research study to the subject and have answered any questions he/she had.

________________________________ _______________
Signature of Authorized Research Representative Date

_________________________________ AHC IRB #5307
Printed Name and Title of Research Representative Protocol Number

= =

A witness signature is required if the subject is illiterate or does not speak English

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WITNESS STATEMENT
I acknowledge that I witnessed the Research Representative named above discuss participation in this research study with the subject, that the subject had opportunity to ask questions about the research, and the subject agreed to participate in the research and signed to consent to that effect.

________________________________ _______________
Witness Signature Date

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Witness Name (Please print)