High Intensity Focused Ultrasound for Prostate Cancer

Patient Information

Exploring a Minimally Invasive Prostate Cancer Therapy

Sonablate® HIFU

The Choice for HIFU Worldwide

A Patient's Guide to Prostate Cancer and Sonablate® HIFU

Contents

Important Information about this Medical Device

The Sonablate® 500 is being studied in clinical trials for use in the treatment of prostate cancer in the United States and is not approved for use by the U.S. Food and Drug Administration. HIFU with the Sonablate® 500 is available for use for the treatment of prostate cancer in Canada, Argentina, the Dominican Republic, the Bahamas and Mexico.

The content of the brochure is provided for general information purposes only and is not intended to replace sound professional medical advice and care. All decisions regarding patient care should be made with a qualified healthcare provider.

Prostate Cancer

Prostate cancer is the most common non-skin cancer in men and the third leading cause of male cancer deaths. Typically, prostate cancer is very slow growing, but sometimes the disease can grow and spread quickly. Even with the latest research, it is extremely difficult for doctors to know which men have a slow growing cancer and which have a cancer that will spread rapidly.

What are the Symptoms of Prostate Cancer?

The early stages of prostate cancer generally show few symptoms. When a tumor becomes more advanced, patients may experience

- A weak urinary stream
- Inability to urinate
- Interruption of urinary stream
- Frequent urination (especially at night)
- Pain or burning during urination
- Blood in urine

Who's at Risk for Prostate Cancer?

- Men over the age of 40
- Known risk factors include age, race and family history
- African-American men have a higher incidence of prostate cancer than Caucasian or Asian men in the U.S.

Many physicians, as well as the American Cancer Society, recommend that all men over the age of 50 have a prostate-specific antigen (PSA) test regularly.

Prostate Cancer Treatments

Traditional Treatments for Prostate Cancer

There are numerous treatment options for prostate cancer. Each treatment has benefits and drawbacks. Together, patients and their physicians need to weigh all the factors as they search for the best treatment option.

Treatment Advantages/Disadvantages

Hormone Therapy

Advantages	Disadvantages
Excellent means of dealing with complications and pain of metastatic cancer	Not curative
Therapy can easily be stopped; allowing return of normal hormone production	Frequent Side Effects: loss of libido & potency - loss of muscle & bone strength - flushing, breast swelling & anemia
May prolong survival of patients with extensive prostate cancer	Only works for a limited time that is variable
Easily administered (surgery/drugs)	Can be very expensive
	1 - 3 month recovery period

Radical Prostatectomy

Advantages	Disadvantages
Prostate removed	Surgery can take 2-8 hours depending on type of surgery (open, laparoscopic, robotic)
Cancer potentially removed	Requires hospital stay
Long history of use	Risks associated with procedure include: blood loss - infection, leaks - fistulae - mortality
Results easy to monitor with post-operative PSA tests	Side effects of radical prostatectomy include: high risk of impotence - chance of incontinence - risk of urinary stricture
Failures can be followed with radiation if necessary	1 - 3 month recovery period

Cryotherapy

Advantages	Disadvantages
Little blood loss	Potential side effects may include: high degree of impotence with full gland ablation - incontinence - rectal injury
Minimally invasive	Temporary soreness
Shorter recovery time than surgery	No long term data on "nerve sparing therapy"

Radiation Therapy

Advantages	Disadvantages
No prolonged hospitalization is required	Treatment program is prolonged (may require more than 30 sessions of radiation over 4 to 6 weeks)
Less risk associated with radiation than with surgery	Side effects of radiation include: impotence - urinary frequency & urgency - rectal bleeding - proctitis (inflammation of the lower rectum) - may decrease energy levels
Outcomes relatively predictable	Seed migration (with brachytherapy)
	Risks of complications from anesthesia
	Prostate is not removed (possibility of tumor regrowth)
	Surgical retreatments carry a high degree of risk for severe complications

Treatment Options Comparison

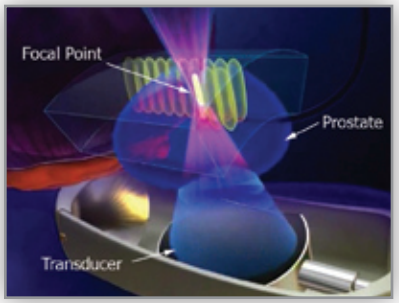
Treatment	Description	Selected Risks*	Expected Recovery	Selected Outcomes
High Intensity Focused Ultrasound (HIFU) as approved and used outside the U.S.	Minimally invasive use of intersecting, precision-focused ultrasound waves to ablate diseased tissue	In approved countries • Incontinence : 2-3% • Impotence: 20-30%	Temporary catheter worn for approximately 4 weeks; resume normal lifestyle almost immediately	• 94% biochemical disease-free survival rate at 4 years • 87% negative biopsy rate at 6 months
Cryotherapy	Minimally invasive procedure using controlled freeze and thaw cycles to destroy cancerous cells	• Incontinence: 4 – 27% • Impotence: 40 – 100%	2-3 hour procedure with possible overnight stay; return to normal activities within a few days	• 78% biochemical disease free survival at 1 year; 60% at 5 – 7 years • 88% negative biopsy rate at 5 years
Radical Prostatectomy	Major surgery to remove prostate; can be open retropubic, laparoscopic or robotic	• Incontinence: 4 – 34% • Impotence: 51 – 80%	2-3 day hospital stay; catheter for 2-3 weeks for open surgery; shorter hospitalization and fewer postoperative complications for robotic procedures	• 85 – 91% biochemical disease-free survival at 2 years • 68 – 72% biochemical disease-free survival at 10 years
External Beam Radiation	6 to 8 week treatment, beaming radiation through healthy tissues	• Incontinence: 4 – 7% • Impotence: 41 – 62 % • Bowel problems more common than with other treatments	Five treatments per week for 6 to 8 weeks; up to 2 months fatigue after full course of treatment	• 78% survival rate at 5 years • 55 – 65% biochemical disease-free survival at 5 years; 49% at 10 years
Internal Radiation Seeds (Brachytherapy)	Minimally invasive implants of radiation seeds in the prostate	• Incontinence: 3 – 18% • Impotence: 44 – 58%	1-2 hour procedure with possible overnight stay; return to normal activities within a few days	85 – 91% biochemical disease-free survival at 10– 12 years

Data presented are for clinically localized, low-risk primary prostate cancer, generally defined as PSA ≤10 ng/mL, Gleason score ≤6, clinical stage T1 or T2a.

Chart was researched and compiled by Synteract, a third party CRO. The information provided in the chart may not include all potential risk, recovery and outcome information.

For a complete list of general references for all treatment modalities see page 22

High Intensity Focused Ultrasound (HIFU)



A Minimally Invasive Way to Treat Prostate Cancer

High Intensity Focused Ultrasound, or HIFU, is a therapy that destroys tissue with rapid heat elevation- which essentially "cooks" the tissue. Ultrasound energy, or sound waves, is focused at a specific location and at that "focal point," the temperature raises to almost 90 degrees Celsius in a matter of seconds. Any tissue at the "focal point" is destroyed; however, any tissue outside of the focal point remains unharmed.

HIFU has produced oncological results, in studies performed outside the United States, that are broadly comparable to standard therapies and HIFU is a minimally invasive prostate cancer therapy that does not use ionizing radiation[1], which can be potentially harmful.

Advantages of HIFU	Disadvantages of HIFU
• No blood loss • Quick recovery • Non surgical • Radiation free • An outpatient procedure	• No long term (20-30 years) outcome data • Potential risk of impotence • Potential risk of incontinence

See page 16 for Risks and Potential Side effects.

[1] Illing, R., Chapman, A. The clinical applications of high intensity focused ultrasound in the prostate. Int. J. Hyperthermia, March 2007; 23(2):183-191.

Sonablate® HIFU

The Sonablate® 500 is a ***minimally invasive*** medical device developed by Focus Surgery, Inc. (Indianapolis, IN), that uses HIFU to treat prostate cancer and benign prostatic hyperplasia (BPH). The Sonablate® 500 may be an appropriate treatment for the thousands of men who will be diagnosed with the disease.

Features of the Sonablate® 500

The Sonablate® 500 is the **only** HIFU device for prostate cancer that

- Ensures patient comfort during procedure,
- Allows physician the flexibility to treat large prostates (up to 50 grams) with no TURP,
- Incorporates 3D imaging for enhanced prostate visualization of irregularities and for ease of treatment planning by physician and;
- Allows the physician to plan therapy using real-time ultrasound images of the prostate.

Precise and Controlled

The Sonablate® obtains real-time ultrasound images of the prostate and surrounding areas. From these images, the doctor plans where the ultrasound energy will be delivered. The Sonablate® software allows the physician to precisely define the treatment zones in order to destroy the entire gland.

Unlike radiation, HIFU is non-ionizing so it can be repeated, if necessary, without damaging healthy tissue. This means that HIFU may also be used as a salvage technique if other prostate cancer treatments fail.

The Sonablate® is the only HIFU device for prostate cancer that does not require a transurethral resection of the prostate (TURP), an invasive, surgical procedure, prior to treatment in order to achieve effective results.

▲ Sonablate® 500 with Sonachill™

Comparison of Features offered by HIFU Devices

HIFU Device for Prostate Disease	Sonablate®500	Ablatherm®
Prostate Size Requirement	Can treat prostates up to 50cc without invasive surgery prior to HIFU	Requires a transurethral resection of the prostate (TURP) for prostates larger than 24cc
Patient Comfort	The probe is positioned by the physician for optimal outcomes and comfort	A larger diameter probe is fixed on the treatment table and not directly controlled by the physician
Imaging	Real-time images and reference images give immediate feedback to physician during HIFU Physician can view the prostate in 3D	No 3D imaging available Not able to view prostate from multiple angles
Planning	Customized planning for each patient by physician Blood flow around nerves is identified with color overlay in real-time to aid in treatment planning	Three pre-set power levels Physician cannot adjust power levels beyond the three pre-set levels for treatment
Treatment	During HIFU with the Sonablate®, physician can adjust energy levels between 0-40W depending on visual changes seen during treatment Reference images are provided during the procedure to help the physician monitor the progress of the procedure	There are no reference images to allow the physician to note a change in the prostate during HIFU HIFU is delivered according to pre-defined power levels depending upon primary, salvage or repeat HIFU treatments
Patient Safety	Active cooling system circulates chilled water through the probe during the procedure to ensure patient safety	Relies on external motion detection and refrigerated gel to keep temperatures low

Your HIFU Treatment

Who is a Candidate for HIFU with the Sonablate® 500?

Sonablate® HIFU may be effective for men who have early stage, localized prostate cancer that has not spread or metastasized outside the prostate. It is recommended that you discuss your individual medical records and history with a physician in order to confirm whether or not you are a candidate for Sonablate® HIFU.

Sonablate® HIFU may also be an effective therapy for recurrent prostate cancer when patients may not have any other treatment options. Many patients, who have had primary therapy for prostate cancer, experience a rise in PSA years later and discover that the cancer is back. These patients may be candidates for the Sonablate® HIFU treatment as well.

The Sonablate® HIFU Procedure

Before HIFU Patients are given two enemas two hours prior to the procedure. It is very important that the patient does not move during Sonablate® HIFU thus patients are given an epidural (spinal) anesthesia and light intravenous sedation.

During HIFU There is no pain during treatment. A small probe inserted into the rectum emits ultrasound waves directly to the prostatic tissue. During the procedure, the Sonablate® 500 delivers real-time images of the prostate and the surrounding area giving the physician immediate and detailed feedback. Treatment time varies, but generally lasts one to four hours, depending on the size of the prostate.

After HIFU Immediately after Sonablate® HIFU patients typically spend one to two hours recovering at the treatment facility and then are discharged. The doctor will prescribe medications, but most patients do not experience any pain after the procedure. A catheter is inserted for two to four weeks to ensure the bladder empties properly. Patients should have their PSA checked three months after the procedure.

Effectiveness of the Sonablate® HIFU

HIFU has been studied extensively in Japan and Europe. Studies and presentations from outside the United States report that HIFU is a technique broadly comparable to standard therapies for the treatment for prostate cancer.[2] A Japanese 3-year study of HIFU in patients who had a pre-HIFU PSA <10, had a biochemical disease free rate of 94%.[3]

Potential Side Effects and Complications

All treatments for prostate cancer carry some risk for potential side effects and complications. Side effects include frequency, urgency, mild discomfort or discharge in urinary stream. Studies performed outside the US report that less common side effects (these may be more severe) may also include urinary stricture, retention, incontinence, impotence and rectal fistula. As with any medical procedure, all potential side effects and complications should be discussed with a physician before undergoing therapy. For a complete list of all possible risks associated with HIFU please refer to www.InternationalHIFU.com.

[2] Illing, R., Chapman, A. The clinical applications of high intensity focused ultrasound in the prostate. Int. J. Hyperthermia, March 2007 23(2):183-191.

[3] Toyaki U., Shiro B., Akira I., et al., Transrectal high-intensity focused ultrasound in the treatment of localized prostate cancer: A multicenter study.Acta Urol. Jpn. Vol. 51, No. 10, 2005.)

Frequently Asked Questions

How long has the Sonablate® 500 been in use? Where is it being used?

HIFU was originally researched in the United States almost 50 years ago. Focus Surgery, Inc., the developers of the Sonablate®, introduced the first application for prostate disease in the early 1990s. In countries where the Sonablate® is authorized or HIFU treatments are permitted, over 6,000 treatments have been done with the Sonablate®, and there are nearly 100 centers offering Sonablate® HIFU treatments.

Is it a one-time procedure or do I need multiple treatments?

In most cases, HIFU with the Sonablate® 500 is a one-time procedure that lasts approximately one to four hours, depending on the size of the prostate.

What should I expect after I have HIFU?

During the first one to two weeks after the procedure, a patient may experience very mild urinary symptoms such as frequency and/or urgency to void. In the first one to two months, a patient may pass an occasional small amount of blood, blood clots or mucus-like materials in the urine stream which is normal. A urinary catheter is inserted during the procedure and must be kept in place for two to four weeks. *See page 16 for information regarding side effects and risks.*

Is this a type of radiation like brachytherapy? Which one is a better minimally invasive procedure?

HIFU is completely radiation free. Unlike radiation, ultrasound energy is non-ionizing meaning it is less likely to harm any tissue outside of the targeted area. Although brachytherapy and HIFU are both considered minimally invasive, generally, HIFU only requires one treatment. Also the radioactive seeds that are implanted during brachytherapy remain in the prostate and could potentially cause damage to tissue around the prostate, even several years after having the procedure.

During Sonablate® HIFU is the entire prostate treated or does the doctor only treat the tumor or diseased area?

During the HIFU procedure the entire prostate gland is targeted to be ablated or destroyed.

How do I know if I am a candidate for HIFU? What are the qualifications?

If you have been diagnosed with localized prostate cancer that has not spread or metastasized outside of the gland, you may be a candidate for HIFU. It is recommended that you discuss your individual medical records and history with a physician or clinical nurse specialist in order to confirm whether or not you are a candidate for HIFU.

What happens to the urethra during HIFU? Since it runs through the center of the prostate is it destroyed during the procedure?

During HIFU, the entire prostate is ablated, including the prostatic urethra. However, the urethra is derived from a different type of tissue (bladder squamous-type epithelium) rather than prostatic tissue (glandular, fibrotic and muscular). While the urethra is an important anatomical structure, the sphincter and bladder neck are more important to maintaining the urinary function.

Is this procedure repeatable?

Yes, Sonablate® HIFU may be repeated if necessary although in most cases it is a one-time procedure. Additionally, unlike radiation, HIFU

is a clean energy source and will not prevent patients from pursuing other types of salvage therapy in the event of a recurrence.

How long will I have to stay in the hospital?

Sonablate® HIFU is an outpatient procedure and does not normally require an overnight hospital stay. The procedure usually takes one to four hours and recovery time lasts two to three hours. After recovery, the patient is discharged.

Where is the procedure available?

There are International HIFU Centers in Canada, Mexico, Costa Rica, the Bahamas, Argentina, South Africa, and the Dominican Republic. To learn more about these locations and scheduling a procedure, call 1-888-874-4384.

Why can't I have it done in the United States?

The Sonablate 500® is not approved for use in the U.S. The Sonablate 500® remains investigational in the U.S. and is being studied for the treatment of prostate cancer in clinical trials in the U.S. FDA has made no decision as to the safety of efficacy of the Sonablate 500® for the treatment of prostate cancer.

May I speak with men who have already had HIFU or read comments about their experience?

You may read comments from patients online at www.InternationalHIFU.com. You may also request to speak to a HIFU patient by calling 1-888-874-4384.

What are the Benefits of Sonablate® HIFU?

- HIFU destroys cancerous tissue.
- During HIFU, patient is not exposed to any radiation.
- No hospital stay is required in most cases.
- HIFU is generally performed under local anesthesia.
- HIFU can be used to treat locally recurrent prostate cancer.
- It is repeatable, if necessary.
- Treatment is non surgical and typically lasts 1-4 hours.
- After HIFU, if needed, patients may pursue other treatment options.

*See page 16 for information regarding risks and potential side effects

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To learn more about HIFU in countries where its use is approved please call 1-888-874-4384 or visit www.InternationalHIFU.com.

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