

## Ongoing data show high-intensity focused ultrasound's promise in low-risk prostate cancer

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**Vail, CO**—High-intensity focused ultrasound (HIFU), while still years away from clinical use in the United States, shows promise as a first-line treatment for low-risk prostate cancer, a leading researcher of the therapy reported at the International Prostate Cancer Update here.

"This is the best minimally invasive treatment I have ever seen for low-grade, low-stage prostate cancer," said Cary N. Robertson, MD, associate professor urology at Duke University Medical Center, Durham, NC. "It offers good local control, which satisfies the goal of any definitive treatment, with minimal side effects compared to other options currently available. It's also a procedure that is relatively easy to learn."



Cary N.  
Robertson, MD

Developed in France and the United States over the past 10 years, HIFU is not yet FDA approved, although that has not stopped some U.S. patients from receiving the treatment outside the country (see, "Medical tourists' receive HIFU treatment abroad,").

Data from a multicenter retrospective study suggest that HIFU offers long-term cancer control in men with low- or intermediate-risk localized prostate cancer (*Eur Urol* 2008; 53:1194-201). The study included 140 men with PSA <15.0 ng/mL and Gleason score <7 who underwent treatment between 1997 and 2001. After a 6-year follow-up, 86.4% of patients had negative prostate biopsies and the median PSA nadir was 0.16 ng/mL (range, 0-0.91 ng/mL). Biochemical disease-free survival rates were 77% at 5 years and 69% at 7 years, and actuarial disease-free survival rates were 66% and 59% at 5 and 7 years, respectively.

Another European study included 227 men with T1-2 localized prostate cancer, PSA  $\leq$ 15.0 ng/mL, and Gleason score  $\leq$ 7, prostate volume  $\leq$ 40 cc, and no previous radical treatment for prostate cancer who underwent HIFU (*Eur Urol* 2007; 51:381-7). At mean post-treatment follow-up of 12 to 121 months, 86% of the men had negative control biopsies and a median nadir PSA of 0.10 ng/mL. The actuarial 5-year disease-free survival rate was 66%. Treatment-related adverse events included incontinence (1%-6%), recto-urethral fistula (0%-0.5%), and erectile dysfunction (10%-50%).

The HIFU procedure uses focused ultrasound to ablate tissue inside the prostate. While the patient is under local or general anesthesia, a lubricated probe is inserted into the rectum. An initial ultrasound of the prostate is performed to create a three-dimensional image that can be visualized on a computer screen. After the surgeon defines the target volume, the computer is programmed and the robotic probe carries out the treatment plan automatically.

During treatment, tissue effects are visible during each focal burn, Dr. Robertson explained. Rectal cooling is provided by a cooling solution around the probe and adjacent to the rectal wall, while computer software monitors the rectal wall thickness to ensure safety. The entire treatment lasts approximately 2 hours, depending on the volume of the prostate. After treatment, urinary retention is almost universally experienced, and a catheter is placed for 7 to 14 days. Pain can be managed with nonsteroidal anti-inflammatory drugs.

Dr. Robertson said that about 15% of patients with localized prostate cancer are good candidates for HIFU treatment.

"The ideal patient is a man with a small gland—less than 25-cc volume prostate—who has low-volume disease," he said.

### Multiple benefits

"There are multiple benefits with HIFU," he added. "It offers imaging and treatment with quick tissue destruction. It's bloodless, precise, and accurate, and it can be performed on an outpatient basis in a non-sterile environment. Another benefit is that it can be used as radiation failure salvage therapy."

Potential side effects are thickening and scarring of the rectal wall and transient thickening and scarring around the prostate. Collateral damage may occur in the adjacent rectum, bladder, urethral sphincter, and neurovascular bundles. Reported impotence rates vary from 10% to 50%. Since there is no cooling catheter in the urethra and the urethra does undergo ablation, there can be a small contracture to the urethral channel.

"There is about a 10% incidence of stricture formation," Dr. Robertson said. "The strictures are sloughing tissue and soft strictures that eventually disappear. Long-term incidence of strictures is pretty low. The other obvious toxicity is, if too much heat is delivered to the rectal wall, then eventually that could result in a fistula."

Dr. Robertson is a principal investigator for a phase III clinical trial of the Ablatherm HIFU device made by EDAP TMS, for which he serves as a paid consultant. That trial is currently enrolling patients in the United States.

While only time will tell about the long-term effectiveness of this procedure, Dr. Robertson says that, thus far, he has been impressed by his patients' experience with the treatment.

"After the procedure, patients don't seem to notice much change in their daily life," he said. "Most patients don't even take pain pills. I called two of my patients 4 days after treatment, and they were both back at work with their catheters in place. I'm looking forward to seeing the data from ongoing long-term clinical studies when it matures."

### 'Medical tourists' receive HIFU treatment abroad

While HIFU is not FDA approved for use in the United States, that hasn't discouraged some physicians from sending their prostate cancer patients to Mexico, Germany, or other countries for the treatment, and from receiving financial compensation in return.

According to an article in *The New York Times* (Jan. 18, 2008), US HIFU, based in Charlotte, NC, is recruiting American physicians to be trained in performing the procedure at sites outside of the United States. The company sponsors "offshore treatment weekends" in such places as Puerto Vallarta, Mexico, for physicians and their patients with prostate cancer. In return, the physicians receive financial compensation ranging from \$5,000 to \$7,500 per

procedure, the *Times* reported. The patient can pay \$25,000 to \$30,000 for a treatment that is not usually reimbursed by insurance companies.

The practice of "medical tourism," as it pertains to HIFU, has met with criticism by some urologists who say that the practice raises questions about the influence of financial motives on medical decisions. Amanda Willis, a US HIFU vice president, defended the company's policies and patients' freedom of choice.

"Men with prostate cancer also have the right, and should have the right, to choose their medical treatment and to choose where to have it," Willis said. "We know of no law that prohibits U.S. patients from either learning about or seeking medical treatments outside of the U.S. We believe that to prohibit doctors from learning about or using new medical therapies that are available in other countries would be unethical.

"US HIFU does not pay any physician to make patient referrals," she added. "Nor are physicians paid to be trained or compensated for travel. We believe that all of the physicians who have provided HIFU medical services have acted in accordance with all applicable codes of professional ethics and always in the best interests of their patients."

Cary N. Robertson, MD, a Duke University urologist and principal investigator for the Ablatherm (EDAP TMS), a competing HIFU device currently recruiting patients for clinical trials in the United States, called the practice unethical.

"We're still learning about this technology, and we don't really know how it compares to standard treatment yet," Dr. Robertson said. "For a technology that is emerging and showing promise, I personally feel that it should only be available through a rigorous clinical trial."

US HIFU recently announced that it received conditional written approval from the FDA to begin a pivotal trial for the treatment of recurrent prostate cancer with its Sonablate 500 in men who have failed external beam radiation therapy.