

HIFU for the Treatment of Prostate Cancer with the Sonablate® 500 System

General information: High-Intensity Focused Ultrasound (HIFU) is ultrasound energy that is sharply focused to converge at a selected distance from the transducer elements. The curvature of the transducer determines the distance to the focal length. Although the intensity of the ultrasound is relatively low at the face of the transducer (30 Watts), the site intensity at the focal zone can reach levels greater than 2,000W/cm². This is a sufficient intensity to raise the tissue temperature in the focal zone to 70-100°C in less than one second, thereby making it a perfect energy for noninvasive therapy – which is real time image-guided.

The Sonablate® 500 HIFU-system offers a revolutionary state-of-the-art technology which makes the usage of HIFU for the treatment of prostate cancer more precise, safe, and effective.

The system consists of 3 components: the console (size 120x85x35 cm, weight approx. 100 kg) with a flat monitor, the so-called chiller, a cooling device (size about 35x35x40cm) mounted on a pole with wheels, and the transrectal probe together with an articulated arm which fits the rails of any standard or-table thus making it very flexible for positioning but keeping it stable during the treatment..

The setting: The treatment requires a "normal-sized" room of about min. 12-15 m² with standard electrical outlet and a standard but stable or- or examination-table. It does not require OR settings as it does not require a sterile environment. Office or endo examination settings are just fine. Concerning staffing it needs the certified urologist to run the treatment and an assistant to support him.

Patient indication, selection - the treatment is indicated for T1/T2 localized prostate cancer patients (primary and recurrent/after radical and radiation) with PSA <20. The criteria are the same as for brachytherapy. Best results are achieved with a PSA<10 and Gleason<7.

Patient exclusion criteria are: Prostates larger than 40gr and/or maximum distance rectal wall - anterior pole more than 4cm; patients with large, intra-prostatic stones or calcifications (if they cause significant shadowing); patients with previous rectal wall surgery or hemorrhoids; patients with latex allergy reactions (probe sheath material is latex)

Patient preparation - Detailed, comprehensive patient education is the most important tool for success and patient satisfaction. Prior to the procedure (1 day) the volume of the prostate and mainly the distance rectal wall/anterior pole is precisely measured and the patient receives 2 times enema to cleanse the bowl carefully

For **the treatment** the patient is placed in a lithotomy position. The treatment is performed under spinal or sacral (epidural) anesthesia. but depending on how restless the patient is a general anesthesia could be recommendable. After insertion of the transrectal probe, the prostate is visualized and the probe is positioned in a way to best cover the prostate. As most prostates will hardly be completely covered by the cone of the emitted energy the gland will be segmented. The following graph shows a standard regimen for this segmentation:



The respective treatment areas for each segment are defined according to the shape of the individual prostate and one segment after the other is treated.

During the treatment, the transducer fires and moves inside the housing of the probe under computer-controlled real-time visualization until the entire pre-determined volume has been treated. Each time it fires a rice-corn shaped lesion of necrotized tissue is created. All lesions overlap slightly thus destroying the tissue of the total gland without leaving any untreated tissue behind. In average a standard treatment lasts about 3-4 hours depending on size and shape of the prostate. At the end of the treatment a transurethral catheter is placed as the heat destruction creates a significant edema. This catheter stays in place for about 10-14 days. As in most cases the treatment is performed as out-patient procedure the patients will have to stay for about 2 more hours but this is fully depending on the decision of the anesthetist. The following day the patient will return for examination.

The following overview shows a **comparison** of HIFU with other modalities for prostate cancer treatments:

Table 1: Efficacy comparison published 5-year biochemical disease free rate following radical prostatectomy (RP), cryoablation (CRYO), Brachytherapy (Brachy), 3-D conformal radiation therapy (3D-CRT), external beam radiation therapy (XRT) and HIFU

	RP	CRYO	Brachy	3D-CRT	XRT	HIFU
Low	76-98%	60-92%	78-89%	76-87%	81-86%	70.1-71.4%
Moderate	60-76%	61-89%	66-82%	51-58%	26-60%	

Table 2: Negative biopsy results observed following radiation therapy, cryoablation and HIFU

Study	Tx	n	Pretreatment PSA (ng/ml)	Gleason	Clinical T Stage	Median follow-up	% negative biopsy
Stock et al. 1996	Brachy	97	75% < 20	82% < 7	T1-T2	18 mos	74%
Ragde et al. 1997	Brachy	126	78.7% < 10; median 5.0	2-6	T1-T2	7 yrs	80% ^b
Ragde et al. 1998	Brachy	152	Median 11.0	91% < 8	98% < T3	10 yr	85%
Zelevsky et al. 1998	3D-CRT	743	Median 15	81 < 8	T1-T3	> 30 mos	52%
Dinges et al. 1998	XRT	82	Median 14.0		T2-T3	24 mos	73%
Crook et al. 1998	XRT	102			T1-T3	40 mos	67% ^a
Babaian et al. 1995	XRT	31	70% > 10		T1-T3	51 mos	29%
Laverdiere et al 1997	XRT	120	Median 11.2	24.3% >6	T1-T3	24 mos	38%
Ljung et al. 1995	XRT	55		35% > 6	T1-T3	6.8 yrs	33%
Long et al. 2001	CRYO	975	33% > 10	14.4% 2-5 74% 6-7	75% < T3	2 yrs	82%
Bahn et al. 2002	CRYO	590	24.5% > 10	58.4% >6	T1-T4	5.72 yrs	87%
Donnelly et al. 2002	CRYO	76	38 % > 10	56 % > 6	T1-T3	5.1 yrs	85%
Gelet et al. 2001	HIFU	102	Mean 8.38		T1-T2	19 mos	75%
Gelet et al. 2003	HIFU	137	Mean 8.8		T1-T2	33 mos	81%
Turloff et al. 2003	HIFU	402	Mean 10.9	13% 2-4 77.5% 5-7	T1-T2	22 mos	87.2%
Blana et al. 2004	HIFU	146	Mean 7.6	5 ± 1.2	T1-T2, N0,M0	22 mos	93.4%
Uchida et al. 2002	HIFU	33	Mean 10.97	29% 2-4 66% 5-7	T1b-T2	13.2 mos	100%
Uchida et al. 2004	HIFU	214	Mean 16.1	21% 2-4 71% 5-7 8% 8-10	T1c-T2b	20.6 mos	95%

3D-CRT, three-dimensional conformal radiation therapy; brachy, brachytherapy; TCAP, targeted cryoablation of the prostate; XRT, external beam radiation therapy

a 15% indeterminate

b 13% indeterminate

Table 3. Morbidities observed following radical prostatectomy, radiation therapy, cryoablation and HIFU

	Impotence	Incontinence (any pt, any pad)	Rectal injury			
			Urgency	Bleeding	Diarrhea	Fistula
Prostatectomy	51-96%	7-52%	6-16%	1-3%	6-19%	
Radiation	50-61%	0-15%	19-17%	13-17%	12-42%	
Cryo	82-100%	1.3-5.4%				<0.5%
HIFU	28-100%	0-23%				< 0.5 – 7.5%

Source: High Intensity Focused Ultrasound for Prostate Cancer: Clinical Results and Technological Evolution

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As there is more than one system on the market that do principally the same by destroying prostate tissue with HIFU please note some technical differences:

- The Sonablate[®]500-system has one single confocal transducer for imaging and therapy ("firing") which is proven in his reliability over years and guarantees excellent accuracy for targeting and therapy and not an integrated imaging crystal;
- the transducer is "sandwich-sided" focusing the energy with one side at 3cm deep with the other side at 4cm deep into the tissue which allows a very precise targeting especially in the dorsal parts of the gland close to the rectal wall;
- a 2-D AND a 3-D volume imaging mode for precise treatment planning;
- it treats with a frequency of 4 MHz (B-mode imaging with 3-8 MHz) which delivers a bit shorter but significantly more precisely shaped lesions thus allowing to treat very close to critical areas (in the apex up to the sphincter e.g.) without risking to do any harm;
- Reflectivity Index Measurement (*RIM*[™]) for continuous real-time rectal wall monitoring, automatic temperature control, and continuous measurement of rectal wall distance to avoid damage of the rectum;
- reference images taken before the treatment and stored to compare with real-time treatment images for enhanced safety;
- a flexibly controlled power output interface to adopt the power intensity to special given tissue situations (e.g. radiological pretreated prostates) thus making the treatment a real surgeon-controlled interactive process;
- an articulated probe arm that fits all standard or-tables and allows an easy and very flexible positioning of the probe while stabilizing it during the actual treatment;
- finally the treatment in lithotomy position, which makes a special treatment-table unnecessary and enabled the development of a compact and mobile, slim space-saving device.

With the Sonablate[®]500-system a TURP prior to the HIFU-treatment is not recommended.

Benefits of the Sonablate[®]500-system are: truly non-invasive, safe and physician controlled, effective, adaptable to physician's and patient's therapeutic goals, repeatable, no therapeutic impasse (alternative options still open post Sonablate[®]500 therapy).