

Ultrasound & Therapy

by EDAP TMS



Information on therapeutic ultrasound in the urology practice

ESWL

Extracorporeal Shockwave Lithotripsy

www.edap-tms.com

Editorial

Sonolith® i-sys receives FDA clearance



Sonolith® i-sys, the latest high-end integrated lithotripter from EDAP TMS, received 510(k) clearance from FDA (Food and Drug Administration) on August 2009, 2 years after its initial launch in Europe.

This made the sale of the first unit in the United States to a mobile lithotripsy service possible, allowing US patients to receive treatments from one of the best ranked lithotripters in the rest of the world. With its unique and patented Electroconductive Technology generating the highest pressured shockwave of all lithotripters in the market, its high capacity and ease of use, the Sonolith® i-sys is the perfect system for US patients. It can adapt to a wide range of conditions, from kidney stones to lower-ureteric stones, from pediatric to bariatric patients. The main characteristics of this system show its adequacy to the patient needs :

The Sonolith® i-sys was launched in Europe first in July 2007 and is now in operation in hospitals in 16 countries on 5 continents.

- Fully **Robotized** and Motorized **Isocentric** movements of X-Ray C-Arm, Ultrasound and Shock Wave Generator
- **Simultaneous** use and display of both Ultrasound and X-Ray imaging
- **Stone Locking System:** Automated stone localization via a unique Touch Screen user's Interface
- Patented **Automatic Ultrasound Positioning System**
- Unique and Patented Electroconductive Technology for the most **effective** results reported in the literature.



- 1 Electroconductive Shockwave Generator**
 - Exclusive and patented Electroconductive technology
 - Unique Automatic Pressure Regulator
 - Patient dry coupling with silicone membrane
 - Motorized and instrumented isocentric movements around F2 from 49 to 0°/ vertical.
 - Power control from 0 to 100% in 1% steps
 - Opening angle of the shockwaves: 80°
 - Penetration depth capacity : 170mm
 - Positive acoustic pressure: max.1290bars
 - Variable focal volume according to the pressure
- 2 Dual ESWL / Endo-uro Table**
 - Dual ESWL / Endo-uro Table
 - 4 motorized axes (longitudinal, transversal, vertical and Trendelenburg)
 - Patient height 6'6" max.
 - Patient weight: 450lbs max.
- 3 Isocentric Ultrasound imaging**
 - Automatic Ultrasound Positioning System
 - Direct contact between probe and patient.
 - Dynamic F2 display
 - Instrumented motorized isocentric movements:
 - 30° (+/- 15°) rotation patient length
 - 49° (0° / -49°) rotation patient transverse
 - 90° (0° / -90°) rotation around probe axis
 - Linear from 30-185mm/F2 in 2 modes (30-130mm and 85-185mm)
 - B-K UltraSound System
- 4 Isocentric X-Ray imaging**
 - Motorized C-arm with double isocentric rotations:
 - +/- 23° patients length,
 - -10° / +27° patients transverse
 - 15 kW generator
 - 3 000 rpm rotating anode
 - 0.3mm and 0.6mm focal spots
 - 12" Image Intensifier (9" optional)
 - Fluoro, pulsed, low-dose or snap shot modes
 - 1k x 1k camera
- 5 TouchScreen user interface**
 - Dual live imaging (X-Ray and U/S)
- 6 X-Ray Imaging Display**
 - Dedicated to high-resolution X-Ray Imaging

In 2009, EDAP TMS celebrates 30 years of success in developing and marketing innovative minimally-invasive therapies for urology.

Everyday EDAP TMS is focused on delivering technologies that guarantee positive and reproducible outcomes with low side effects and preserved quality of life. This leadership is based on its close basic science cooperation with Inserm (the French Institute of Medical Research), and clinical cooperation with University Hospitals. This second issue of Ultrasound & Therapy newsletter highlights the phase III FDA trial for Ablatherm® HIFU treatment of prostate cancer with an update on the trial progress and Dr. Gill's interview. The clinical experience section emphasizes the latest Ablatherm® HIFU European results for radical treatment with 7 year follow-up outside of the US showing excellent biochemical survival rates. The ESWL section features the latest lithotripter available in the US: the Sonolith® i-sys with exclusive technologies uncovered.

Jeff Howell
VP Sales & Marketing USA

Interview with an EDAP Medical Monitor

Inderbir S. Gill, MD, MCh

Chairman and Professor, Department of Urology - Executive Director, USC Institute of Urology
- Associate Dean (Clinical Innovation) - Keck School of Medicine - University of Southern California, Los Angeles, CA



You are best known for innovations in laparoscopic and robotic oncologic surgery – what is it that intrigued you about HIFU for prostate cancer?

For the carefully selected patient with organ-confined prostate cancer, the concept of non-invasive ablation is powerful. It is important to emphasize the words "carefully selected patient"; not every

patient will be a candidate, with only approximately 20% of patients with organ-confined cancer qualifying for HIFU, at least at this point, until more data are available. What intrigues me about HIFU is that it presents the possibility of delivering ablative energy non-invasively to the prostate in a controlled, reproducible manner. Further, HIFU has considerable potential as a

modality for focal treatment for prostate cancer. This is in addition to its already established role as a whole gland ablation modality in Europe.

The European experience in HIFU is extensive with a very wide indication of patients being treated. What indication most interested you?

Already data are available from select European centers attesting to its efficacy in achieving PSA nadirs in the 0.1 ng/ml range within 2-4 weeks of treatment. It was shown at the WCE in Munich that patients who achieve such a nadir can expect a durable biochemical response and low positive biopsy rates. The indication that most interests me is the use of HIFU for patients with a low-risk prostate cancer who are uncomfortable with watchful waiting.

What do you foresee the most significant indication for HIFU in the United States 5 years from now?

There are two ways to look at

this. If there are no breakthroughs in diagnostic imaging, HIFU will likely be used similarly to how it is used in Europe today: as a middle ground between observation and intervention for patients who desire therapy but are not comfortable with surgery or radiation. However, if indeed there are breakthroughs in diagnostic imaging and it becomes possible to image cancer within the prostate HIFU appears to be the ideal tool for targeted focal ablation. Of course, the main stumbling block for focal ablation is the well recognized multi-focality and heterogeneity of prostate cancer. Nevertheless, focal therapy has the potential to open exciting new possibilities for research and clinical applications. Over the years, many patients in my own practice have asked me why the entire prostate needs to be removed - why not just the cancer? From a patient's standpoint, make no mistake about it - the concept of "male lumpectomy" is a powerful one.

Next page ... ▼

How can you participate in the ENLIGHT Trial?

Patients who are interested and meet the basic inclusion criteria can be prescreened by a member of ENLIGHT's patient advocacy group by calling:

1-800-300-7275
or visiting
www.pcaresearch.com

The eligibility criteria include but are not limited to:

- Previously untreated low risk prostate cancer (PSA ≤ 10, Stage ≤ T2a, Gleason ≤ 6)
- Prostate volume ≤ 40 cc with anterior posterior height ≤ 25 mm

enlight

Continued ...

Inderbir S. Gill, MD, MCh

However, it is our responsibility to make sure the field of focal ablation is developed in a scientifically responsible and rigorous manner.

Why is the ENLIGHT clinical trial important?

With many men currently seeking HIFU treatment outside of the United States, there is an urgent need for solid, reliable American data. The ENLIGHT trial represents the first serious effort to study the results of

HIFU in the USA. With the European data taking the lead, if similar data can be generated within the US regarding efficacy and reproducibility across 12 different centers, that will be a powerful confirmation and a powerful statement. FDA approval is contingent upon these data. Ultimately, I feel that the ENLIGHT trial represents an excellent opportunity to add important data to the emerging field of HIFU for prostate cancer.

Enlight

Ablatherm® HIFU clinical trial in the US

Dr. John Rewcastle, Medical Director of EDAP TMS

Enlight is the IDE study sponsored by EDAP TMS and is taking place at a dozen clinics in North America. Two new centers have recently been added which are Triangle Urologic Group in Pittsburgh, Pennsylvania and New York Methodist Hospital in Brooklyn, New York.

Drs. Jeff Cohen and John Lyne are the investigators from Triangle Urological Group founded in 1926 and are well

known for their clinical work in prostate cryoablation. The team in Brooklyn is led by Drs. Ivan Grunburger and Edward Zoltan who both specialize in minimally invasive urologic procedures. These are two excellent sites that we are lucky to have join Enlight. This summer EDAP TMS added to its US team by hiring Karen Barrie, MA, as the Enlight Clinical Communications Manager. Karen is a licensed psychotherapist and is a veteran prostate cancer advocate with extensive experience working

with patients considering minimally invasive prostate cancer treatments. She is now working with advocacy groups, clinical sites and individual patients. Karen is now the voice at the end of the toll free line and will prescreen potential candidates for the trial and will work with all referrals to ensure they have the appropriate information for participation in the trial. She is an excellent addition to our team and a great resource for patients.

Meet EDAP TMS

HIFU

Symposium

During 3rd International Symposium on Focal Therapy & Imaging of Prostate & Kidney Cancer
February 24-27, 2010 - Fairmont Hotel - Washington, DC

Ablatherm® HIFU for PCa

Focal potential built upon a proven foundation of total gland ablation

February 25, 2010, Thursday, from 5pm to 6:15pm
Fairmont Hotel - Washington, DC

• AUA annual meeting, May 29 - June 3, San Francisco, CA

More information about Enlight clinical study ?

For patients: www.pcaresearch.com/ www.clinicaltrials.gov or please call 1-800-300-7252

For physicians: Contact our Medical Director, Dr John Rewcastle rewcastle@edap-tms.com

Sites participating in the Enlight trial enrolling patients into the HIFU arm include:

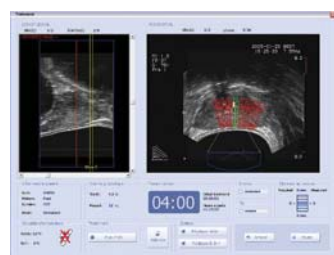
- Duke University, Durham, NC
- Virginia Urology, Richmond, VA
- Florida Foundation for Health Research, Ocala FL
- Triangle Urology, Pittsburgh, PA
- University of Colorado, Denver, CO
- University of Southern California, Los Angeles, CA
- Urology Associates of North Texas, Dallas, TX
- Hackensack UMC, Hackensack, NJ
- Memorial Sloan Kettering, New York, NY
- MD Anderson, Houston, TX
- Medical College of Wisconsin, Milwaukee, WI
- University of North Carolina, Chapel Hill, NC
- Brooklyn Urology Research Group, Brooklyn, NY
- Mc Master University, Toronto, Canada

Ablatherm® HIFU

Rectal wall monitoring

Emmanuel Blanc, Chief Technology Officer

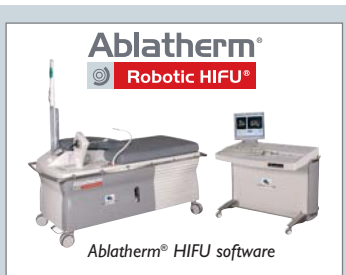
Ablatherm® HIFU is not yet FDA approved



Ablatherm® HIFU device

The Ablatherm® concept robotizes the treatment process. The surgeon plans each stage of the treatment, setting appropriate parameters, and the machine then implements the treatment in a fully-robotized process, checking all the parameters before firing each HIFU shot. As the Ablatherm® HIFU delivers focused ultrasound via an endorectal probe, monitoring the rectal wall is a crucial factor in eliminating the risk of fistulae. The rectal wall's position is detected automatically before each shot is fired. The machine will not fire the shot unless the wall's current position relative to the probe matches its position during the planning phase. The probe's position is adjusted automatically (with no need for the urologist to intervene) in order to achieve an accuracy of +/- 1 mm. If the difference in position is too large (for example if the patient has moved), the machine halts the treatment and displays a message on

screen, prompting the urologist to check the patient's position. As well as performing the advanced functions described above, the machine prevents undesirable rectal wall heating by using a liquid cooling system (containing Ablasonic® fluid) to keep the rectal wall at a temperature between 15 and 20°C. This combination of real-time rectal wall detection and constant cooling minimizes the incidence of urethra-rectal fistula, which was reported in fewer than 0.5% of cases treated with Ablatherm® HIFU since 2003.



The Ablatherm® HIFU is the only high-intensity focused ultrasound (HIFU) device developed specifically for the treatment of prostate cancer. The Ablatherm® HIFU system, designed by EDAP TMS in conjunction with INSERM (the French National Institute for Medical Research), has been used to treat human patients since 1993. More than 20,000 treatments have been performed outside of the US to date.

European HIFU Clinical Experience

Biochemical and biopsy outcomes following Total HIFU of previously untreated prostate cancer.

C. Robertson, R Ganzer, J Ward, S. Brown, X Rebillard, A Blana

Presented at the World Congress of Endourology, October 6-10, 2009, Munich Germany.

The @-Registry is a secure online database consisting of case report forms which collect relevant de-identified pre and post treatment information for patients undergoing prostate HIFU. The registry is a multinational effort overseen by an internationally renowned advisory board all with extensive HIFU experience. Dr. Cary Robertson, the coordinating principal investigator of the Enlight trial, a US regulated study of the Ablatherm® HIFU device for the treatment of localized, low-risk prostate cancer, is a member of the @-Registry advisory board and presented outcomes of patients who underwent total prostate ablation with HIFU. High Intensity Focused Ultrasound (HIFU) is a versatile therapy for prostate cancer easily adapted to the individual patient. The extent of ablation is controlled in real time and is often intentionally less than total when nerve sparing or focal approaches are utilized. Total HIFU occurs when all prostatic tissue is ablated. Using a retrospective registry it is difficult to determine which patients underwent total HIFU.

The method used to stratify patients as those who underwent total or non-total ablation was to look at their PSA nadir. A patient with an undetectable PSA nadir (≤ 0.2 ng/ml) was considered to have undergone total HIFU. The objective of this study is to report the outcomes of patients who have undergone total HIFU without previous hormone therapy at centers participating in the @-Registry. All patients in the @-Registry were reviewed. Those included in the analysis had localized disease (T1-T2), were treated with total HIFU as evidenced by a PSA nadir ≤ 0.2 ng/ml, and had undergone no previous or concurrent intervention for prostate cancer, including radiation therapy or hormone therapy. Patients were stratified according to D'Amico's 2003 risk group definitions. Kaplan-Meier analysis was performed to determine biochemical survival with failure defined according to the Stuttgart definition of nadir+1.2 which is a new definition statistically vali-

dated to be an accurate predictor of clinical failure following total HIFU. A total of 456 patients met the inclusion criteria. The average age was 69.3 ± 6.2 years. Pre treatment PSA was 7.5 ± 5.0 ng/ml, the median Gleason sum was 6 and the median stage was T2a. Patients were followed for 46.4 ± 31.4 months (median 44.8). The percentage of patient in the low, moderate and high risk groups were 44%, 45% and 11%, respectively. Follow-up biopsies were done for 326 patients, 298 of which showed no evidence of disease (90.2%). Stratified by risk group, the negative biopsy rates were 93%, 89% and 84% for low, moderate and high risk, respectively. The median PSA nadir was 0.05 which was reached 14.7 ± 11.3 weeks after HIFU. Actuarial biochemical disease free survivals at 5 and 7 years are reported in the table below. When HIFU results in total prostatic ablation, the biochemical outcomes are similar to those of traditional therapies through 7 years.

Risk group	Biochemical Survival @ 5-years	# of Patients at risk	Biochemical Survival @ 7-years	# of patients at risk
All	86 %	167	84 %	67
Low	92 %	75	92 %	31
Moderate	81 %	70	77 %	23
High	81 %	22	75 %	13

Regulatory

HIFU

Ablatherm® HIFU is not yet FDA approved
Enlight clinical trial, in progress, more information on www.pcaresearch.com, www.clinicaltrials.gov

ESWL

Sonolith® i-sys and Sonolith® Praktis are FDA cleared and available for sale in the US

Publishers

EDAP Technomed Inc.
945 Concord Street - Framingham, MA 01701
an EDAP TMS company (Nasdaq:EDAP)
4 rue du Dauphiné - 69120 Vaulx-en-Velin - FRANCE
Tel. +33(0)4 72 15 31 50 - contact@edap-tms.com

Editor-in-chief

Jérôme Lavaure

Editors

Hugo Embert
Emeline Gleitz
Jérôme Lavaure
Marc Oczechowski

Conception and Production - EDAP TMS
Graphic designer - Paulo Martins