

Ultrasound & Therapy

by EDAP TMS

Information on therapeutic ultrasound in the urology practice

Program



Annual Meeting
29 May - 3 June 2010
San Francisco, CA

Do not miss out the AUA Annual Meeting!
EDAP TMS booth # 1938

Ablatherm® HIFU abstracts presented

- **Hormone resistant prostate cancer treated by robotic high intensive ultrasound.** *Christian Chaussy et al.*
- **Outcomes of HIFU for prostate cancer in 880 consecutive patients.** *Sebastien Crouzet et al.*
- **HIFU following failed radiation therapy: biochemical survival of Ablatherm registry.** *John F.Ward et al.*
- **Correlation of different PSA-Nadir cut offs and biochemical failure after high-intensity focussed ultrasound (HIFU) of prostate cancer based on the Stuttgart failure criteria – analysis from the @-registry.** *Roman Ganzer et al.*

ESWL Sonolith® abstracts presented

- **Emergency shockwave lithotripsy for ureteric calculi is superior to elective shockwave lithotripsy following stent placement: results from a matched-pair analysis.** *Simon Phipps et al.*
- **The effect of different delivery rate on shockwave lithotripsy treatment outcome, renal injury and pain tolerance.** *Anthony Lo et al.*



Ablatherm® HIFU



Sonolith® i-sys

Ablatherm® HIFU and Sonolith® i-sys devices will be displayed on booth

NEW!
Latest FDA
approved lithotripter
presented at AUA 2010

Sonolith®
i-sys



Sonolith® i-sys
Integrated ESWL

- ▶ Patented Electroconductive Technology **UNIQUE**
- ▶ Fully Robotized Movements **UNIQUE**
- ▶ Simultaneous Dual Imaging **UNIQUE**
- ▶ Cranio-Caudal & Orbital X-ray Projections **UNIQUE**
- ▶ Stone Locking System **UNIQUE**



Editorial

Before the annual AUA meeting in San Francisco, we want to share some fresh information on HIFU and ESWL.

This new issue of Ultrasound & Therapy newsletter highlights the unequalled fragmentation performance of the EDAP TMS patented electroconductive shockwave technology for ESWL. Our latest FDA approved lithotripter uses this technology for extremely high clinical efficacy. On the HIFU side, we are informing you of our completion of recruitment for phase III FDA approved lithotripter uses this technology for prostate cancer; patient follow-up is now at the heart of the trial. Professor Van Velthoven shares his pioneering European experience on focal HIFU treatment, one of the most promising evolution axes for prostate cancer. Both Ablatherm® HIFU and Sonolith® technologies are highlighted in the AUA's scientific program. Please feel free to stop by the booth for more in-depth information.

Jeff Howell
VP Sales & Marketing USA

HIFU expert interview

Ablatherm® HIFU is not yet FDA approved

Three year experience on focal treatment with Ablatherm® HIFU

Roland Van Velthoven, MD, PhD
Institut Jules Bordet, Brussels (Belgium)



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Can you introduce your hospital, Institut Jules Bordet?

Institut Jules Bordet is the integrated oncological hospital in Brussels. It is organized on the model of Memorial Sloane-Kettering of New York and the

urology unit is celebrating its 20th anniversary in 2010. We treat all genito urinary cancers as well as side effects associated with or resulting from cancer treatment.

What is your experience of HIFU?

We started HIFU in 2001 with the the first generation (Maxis) protocol for total treatment of prostate with localized stage T1-2 cancer. In 2006, we upgraded our Ablatherm® HIFU device with Integrated Imaging whereby the treatment and imaging components are combined into a single probe. We also apply the specific protocol for EBRT failure and in 10 years, around 150 patients benefited from this approach.

Why start a focal treatment protocol with HIFU in 2007?

The idea of a lighter approach for localized prostate cancers is conditioned by the simultaneous presence of 3 clinical ele-

ments specific to prostate cancer: first, the notion of an "index" lesion responsible for the evolution of the disease and therefore of its prognostic. The second element is the improvement of positive prostate biopsy localization by a systematic ultrasound-guided biopsy protocol under local anesthesia. The last element is the concordance of biopsy results and those obtained with endoprostatic lesion images obtained by the combination of different sequences of high resolution MRI. Today, cross-checking this information enables to only treat the hemi-prostate.

Are there preliminary results available for focal treatment?

Over a period of 3 years, 25 patients with a mean age of 70 were treated using a unilateral "zonal" approach. The residual prostate is regularly evaluated according to active surveillance criteria. The follow-up of PSA marker from the PSA Nadir

obtained 3 months after treatment enables to make a decision for potential control biopsies. Three patients out of the 25 underwent biopsies with this approach, all of them being negative. One patient showed a fast evolution of the cancer, most likely a consequence of under-graded disease. One patient was lost to follow-up. All patients treated have normal urinary continence and patients without initial erectile dysfunction maintain an unchanged function.

How do you see the future of this focal treatment protocol?

The future of this approach is based on a broader validation of these encouraging results through prospective studies. The major interest of the focal treatment protocol is the local control of the disease and more specifically of the main lesion while sparing the patient the morbidity of unnecessary treatments such as surgery, radiation therapy or hormone therapy.

The direct financial impact on public health expenses in the mid and long-term could be reduced if focal treatment were to be widely validated.



Ablatherm® HIFU device

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 22,000 treatments have been performed outside of the US to date.

Enlight

Ablatherm® HIFU is not yet FDA approved

Ablatherm® HIFU clinical trial in the US

John Rewcastle,
Medical Director of EDAP TMS

The treatment phase of the Enlightenment trial is now past; we are in the follow-up phase awaiting all patients to reach the primary 2 year endpoint.

This will occur in May 2012 and the data will be analyzed and submitted to the FDA for review and possible approval. Data generated from patients treated with HIFU outside of the US will be submitted as supporting information. At EAU 2010 in Barcelona there were several important presentations regarding HIFU and here we review two that are especially relevant. A multi-institutional and multinational study using the @-Registry to collect data from patients treated with HIFU as a primary therapy for prostate cancer without any previous prostate cancer intervention, including hormone therapy, was reported by Dr. Andreas Blana of Fürth, Germany. There were 367 patients followed for an aver-

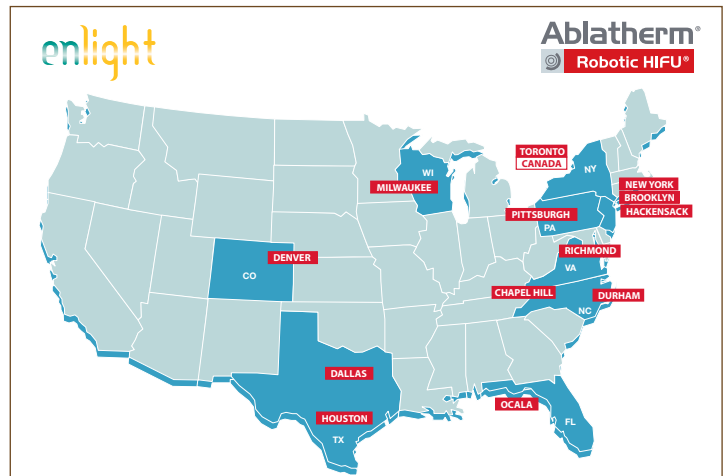
age of 36.6 ± 24.6 months. Negative biopsy rates and biochemical survivals were observed according to the Phoenix and Stuttgart definitions as summarized in the table. Also of important relevance to the ENLIGHT trial was a study presented by Dr. Roman Ganzer from Regensburg, Germany also emanating from the @-Registry. He looked at the correlation of PSA nadir of 803

Risk Group	Biochemical Survival (Phoenix : nadir+2)	Biochemical Survival (Stuttgart : nadir+1.2)	Negative Biopsy Rate
All patients	82 %	71 %	89 %
Low	86 %	79 %	91 %
Moderate	80 %	64 %	80 %
High	75 %	65 %	76 %

patients treated with HIFU and the long term biochemical control. The median follow-up of the patients in the study was 5.9 years. The outcomes reaffirmed previously reported single center observations that the nadir, which occurs within the first 6 months of treatment, has a highly significant correlation with treatment

failure. A PSA-nadir of ≤0.2 ng/ml, 0.21–0.5 ng/ml, 0.51–1 ng/ml and >1 ng/ml was reached by 53.3%, 16.1%, 11.2% and 19.4% of patients, respectively. Treatment success rates during follow-up were 84.6%, 66.7%, 52.4% and 42.6%, respectively for the 4 groups (p<0.001). The actuarial biochemical disease free survival rate at 5 years were 84%, 64%, 40% and 30% for the 4 groups (p<0.001). By the time the data set from the patients treated in the ENLIGHT trial matures published data from the European experience will mount and will likely include ten year outcomes. This will be important to solidify the potential and role of HIFU in the management of localized prostate cancer.

Blana et al, Total HIFU as a primary therapy for localized prostate cancer: outcomes from the @-Registry database; Ganzer et al, Correlation of PSA-nadir and biochemical failure after High-Intensity Focused Ultrasound (HIFU) of localized prostate cancer based on the Stuttgart failure criteria-analysis from the @-Registry; Both presented at the EAU 25th Anniversary Congress in Barcelona, Spain (April 16-20, 2010).



Sites participating in the Enlightenment trial

- Duke University, Durham, NC
- Virginia Urology, Richmond, VA
- Florida Foundation for Health Research, Ocala FL
- Triangle Urology, Pittsburgh, PA
- University of Colorado, Denver, CO
- 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

More information about Enlightenment clinical study ?

For patients: www.pcaresearch.com/ www.clinicaltrials.gov
For physicians: Contact our Medical Director, Dr John Rewcastle jrewcastle@edap-tms.com

ESWL

Extracorporeal Shockwave Lithotripsy

Electroconductive vs. Electromagnetic

In-vitro fragmentation comparison of electroconductive (EDAP TMS) and electromagnetic technologies

Véronique Boubllil, MD, Hôpital Edouard Herriot, Lyon (France)



Introduction

Lyon Public Hospitals (HCL) purchased a new lithotripter one year ago: the Sonolith® i-sys. In order to make an educated decision, this system was evaluated for several weeks at Edouard Herriot Hospital in Lyon in parallel with the lithotripter in use for more than 5 years.

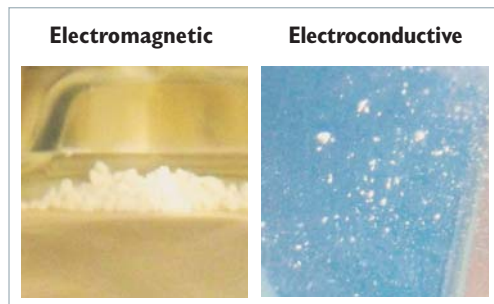
A quick literature review showed that the electroconductive technology patented by EDAP TMS showed a better Stone Free Rate at 2 months (81,5% vs. 76,5% for electrohydraulic technology and 74% electromagnetic technology), and at 3 months for ureteric

technology and 45 to 65% for piezoelectric technology³. Therefore, it was decided to conduct in-vitro tests in order to objectively show the fragmentation quality of the new electroconductive lithotripter compared to the lithotripter in use for 5 years using electromagnetic technology.

Method

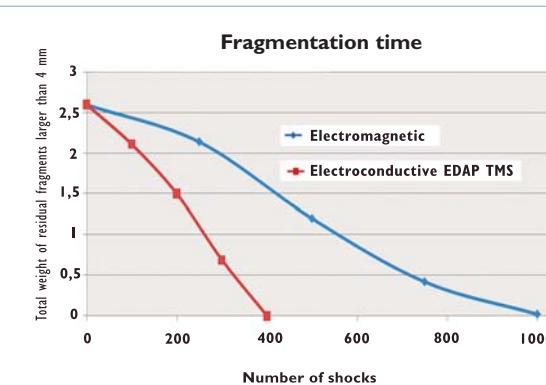
For this experience, we used a waterproof test tub filled with water and sealed with a silicone membrane in contact with the shock-wave generator membrane and we used ultrasonic gel for coupling. Inside the tub filled with water, we placed a metal basket with a 4 mm mesh containing 2 g

cylinder-shaped phantom stones (before hydration – stone composed of pure gypsum with high-grade semi-hydrate alpha). After localizing the phantom stone with the lithotripter X-ray



stones with various sizes². The same is true for retreatment rates with electroconductive technology showing the lowest retreatment rate, 14% vs. 20 to 30% for electromagnetic

C-arm, shock-waves were delivered until complete evacuation of residual fragments from the basket. The power level was set at 100% of the scale of each lithotripter and



Electromagnetic		Electroconductive EDAP TMS	
Number of shocks	Number of residual fragments larger than 4 mm	Number of shocks	Number of residual fragments larger than 4mm
0	1	0	1
250	1	100	1
500	14	200	2
750	27	300	3
1000	0	400	0

the frequency set on 2Hz. The experience was repeated on 3 phantom stones for each lithotripter. We studied 2 parameters: fragmentation time and fineness (evaluated on the number of residual fragments larger than 4 mm).

Results

Fragmentation time

The results clearly and objectively show that EDAP TMS Sonolith® i-sys with electroconductive technology fragments phantom stones faster than electromagnetic technology (427 shocks, i.e. 3 min. 34 sec. Vs. 738 shocks, i.e. 6 min. 9 sec. average, that is a 40% reduction of the fragmentation time).

Fragmentation fineness

Of note, the fragmentation process is different between electromagnetic and electroconductive technologies.

Electromagnetic fragmentation is obtained by breaking up the stone into multiple residual fragments larger than 4 mm (27 fragments larger than 4 mm observed at ¾ of the experience). Electroconductive fragmentation is obtained by erosion of the stone (only 3 fragments larger than 4mm observed at ¾ of the experience). In both cases, fragmentation is total with different numbers of shocks and fragmentation quality. This may explain the higher retreatment rate observed with electromagnetic technology compared to electroconductive.

Conclusion

Lyon Public Hospitals' choice
This test demonstrated what was sensed during lithotrippers evaluation at Edouard Herriot Hospital in Lyon. EDAP TMS Sonolith® i-sys brings a real

clinical improvement with electroconductive technology giving faster and finer fragmentation that ease spontaneous evacuation of residual fragments. These benefits therefore reduce the need for extra ESWL treatments or auxiliary procedures. Further study on animal will be necessary to confirm these first in-vitro results.

¹C. Saltutti, A. Di Benedetto et al. Extracorporeal lithotrippers: is there a new gold standard? In-vivo multifunctional comparison between 6 mobile devices. Congresso Nazionale Associazione AURO, IT, Roma, Italy, 2003. ²Pemberton R. J., D. A. TOLLEY. Comparison of a New-Generation Electroconductive Spark Lithotripter and the Compact Delta for Ureteral Calculi in a Quaternary Referral Center Journal of Endourology, vol. 20, Number 10, pp. 732-736, October 2006. ³Nomikos M. S., Sowter S. J. and Tolley D. A. Outcomes using a fourth-generation lithotripter: a new benchmark for comparison? BJU International, vol. 100, number 6, 1356-1360, December 2007

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 is FDA cleared and available for sale in the US

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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
Conception and Production - EDAP TMS
Graphic designer - Paulo Martins

Editor-in-chief
Jérôme Lavaure
Editors
Hugo Embert
Emeline Gleitz
Jérôme Lavaure
Marc Oczechowski

