

EDAP TMS S.A. – A World Leader in Therapeutic Ultrasound

a report by

EDAP TMS S.A.

EDAP TMS S.A., develops, produces and markets a range of technologically advanced equipment intended for non-invasive therapy, essentially designed for the treatment of urological diseases. The technologies used are based on therapeutic ultrasound, a field in which EDAP TMS is the current world leader. It is the only company manufacturing the most widely used high-intensity focused ultrasound (HIFU) device – the Ablatherm® – and one of the most widely used lithotrippers – the Sonolith. One of its subsidiaries, EDAP S.A., currently develops and markets equipment intended for the non-invasive treatment of localised prostate cancer by HIFU. Furthermore, via its subsidiary, TMS S.A., the group produces and markets equipment intended to destroy kidney stones – a procedure known as lithotripsy – via ultrasound shock waves or extra-corporeal shock wave lithotripsy (ESWL).

Ablatherm originated from the collaboration between the urology department of the Hôpital Edouard Herriot in Lyon and unit U556 of the French National Institute for Health and Medical Research (INSERM). It has been developed on an industrial scale by EDAP. Ablatherm integrated imaging is the most advanced and clinically proven choice for HIFU treatment of localised prostate cancer. HIFU treatment is shown to be a minimally invasive and effective treatment option, with a low occurrence of side-effects. Ablatherm HIFU is generally recommended for patients with localised prostate cancer (tumour stages T1–T2). These patients are those who are not candidates for surgery, who prefer an alternative option or who have failed radiotherapy treatment. The company is also developing this technology for the treatment of certain other types of tumours.

The clinical results, which have been obtained with Ablatherm over the last ten years and its adoption by the medical community, clearly position EDAP as the world leader in the treatment of prostate cancer by HIFU. Today, over 100 hospitals and clinics use this advanced technology and confirm the positive results that have been obtained up to now.

Ablatherm is supported by the results of multi-centric studies, showing its effectiveness and lower side effects, in comparison with traditional therapies.

At the end of 2004, the total number of treatments by Ablatherm HIFU was in the region of 6,600 in 63 sites. At the end of 2005, there were 9,000 treatments, carried out in 96 sites, a respective increase of 36–52%. The number of sites using Ablatherm is continuing to increase significantly, in particular, the introduction of 10 new centres since the start of 2006. This growth shows the interest in Ablatherm HIFU technology, while at the same time medical teams are familiarising themselves with, training in and guiding their patients towards this possible treatment.

Approved with the CE Mark in May 1999 after 10 years of tests and studies, Ablatherm is now used in around 100 centres worldwide and will soon have enabled nearly 10,000 patients to be treated.

The HIFU Treatment Principle

The Ablatherm HIFU device is made up of two modules, the treatment module, on which the patient is positioned and the control module, which enables the surgeon to plan and check the treatment via a computerised system. This computerised system, guides the robotic endorectal probe, which is installed on a mobile support. The ultrasound generator and the integrated ultrasound scanning equipment, or transducers, are located on the end of the probe. The probe's mobile support is an instrument with robotic movements, which enables the device to move the probe automatically and extremely precisely during the treatment, to treat the whole prostate. After a local or general anaesthetic is administered, the patient lies down on his right-hand side and stays in this position throughout the treatment. The probe is lubricated and then inserted into the rectum, via the anus. This non-invasive position enables the probe to be positioned near the prostate, which is then accessible for ultrasound treatment.

The first phase of the treatment involves an ultrasound scan of the prostate. The computerised

system will then recreate the prostate in three dimensions, to enable the surgeon to plan the treatment on-screen and to program the robot to define the area to be treated. Once the treatment has been planned, the shooting phase can begin. The robotic probe will then carry out the surgeon's instructions automatically and extremely precisely – these instructions are accurate to a few millimetres. Every 10 seconds the probe generates a HIFU beam, which is used to destroy a very small part of the prostate with intense, very fast, highly localised heat. This phenomenon generates almost no pain for the patient after treatment. This elementary lesion will be followed by a number of adjacent lesions, approximately several hundred, which gradually, one after the other, enable the entire prostate to be treated. The treatment then continues, lasting between one and a half to two and a half hours depending on the volume of the prostate.

Ablatherm is Now as Effective as Reference Treatments

The treatment is based on the use of HIFU. The beams converge precisely on the targeted area, causing a very brief rise in temperature (80–90°C). The targeted tissue is then instantly and effectively destroyed, as the result of an extremely sharp area where cells undergo a coagulation necrosis. The surrounding tissue is preserved, showing a radical difference compared with treatment using ionising rays, which destroy a great deal more of the tissue.

A study carried out between 1995 and 2000 on 402 patients in six European hospitals showed a disappearance of cancerous tissue in over 87% of patients treated first of all. The follow-up of patients treated at the Hôpital Edouard Herriot in Lyon has enabled the establishment to gain a cure rate of 85% in patients who had a favourable prognosis before treatment, with no recurrence within five years.

Ablatherm also provides hope for men whose cancer has come back after radiotherapy, for whom it appears as the most effective recovery treatment, with local control of the tumour observed in 84% of patients.

Unlike radiotherapy, brachytherapy and surgery, Ablatherm may also be repeated if necessary and may be associated with other treatments.

Today, treatment by Ablatherm is offered as a priority to patients who are not suitable for radical surgery, either because of their age or because of associated illnesses which make surgery too much of a risk. The long-term results – over 15 years – are not yet available and mean that younger patients must be given transparent information in this area.

Currently, there are seven hospitals in France equipped with a permanent machine but recent mobile Ablatherm device solutions have allowed many centres to access this kind of treatment, without having to buy the machine. In France, over 30 sites may, therefore, perform the treatment.

European Association of Urology (EAU) 2006 Congress Outcomes

Conference response from the urological community has already been exceptionally strong, clearly supporting Ablatherm HIFU as a therapy of great interest, for mainstream use on patients with localised prostate cancer.

Dr Francois-Joseph Murat of Edouard Herriot University Hospital, presented details of Ablatherm HIFU results when used as salvage therapy, following external beam radiation therapy failure. He looked at more than 150 patients between 1995 and 2006. He found that patients fail radiotherapy treatment of localised prostate cancer at rates of up to 50% and have few current treatment choices, all with significant side-effects. Almost all patients are offered palliative care options – designed to reduce symptoms and slowing disease progression but not stopping the cancer – rather than curative solutions such as, surgery or cryotherapy. Both are difficult to use in these cases and present substantial complications, making them often undesirable.

Dr Murat's study demonstrated that Ablatherm HIFU provided a 76.5% negative biopsy rate and a prostate-specific antigen (PSA) back to normal in local tumour control, with low-level side effects, especially when compared with alternate therapy side-effect rates. Control of the cancer was highly correlated to the pre-radiation cancer risk level, with those patients at earlier stages showing the best outcomes. The results also demonstrated that specific post-radiation failure protocols, introduced for Ablatherm HIFU in 2002, reduced the occurrence of fistulas to zero and lowered the occurrence of incontinence to below surgery and cryotherapy incidence rates. This confirms Ablatherm HIFU as a preferable choice for both limiting side effects and treating the cancer itself, as compared with other options with lower success rates and higher side effect occurrences.

Dr Stefan Thüroff presented a discussion on efficacy, results and safety covering 10 years of experience, based on treatments at the University Hospital of Munich in Harlaching, Germany. The 10-year experience with Ablatherm HIFU in Europe clearly demonstrates the clinical, technical and safety strengths compared to other treatments. In 2006, Ablatherm HIFU is now

fully accepted as a treatment for localised prostate cancer, offering a minimally invasive solution for patients with localised prostate cancer who cannot undergo surgery or have failed radiotherapy. Over the past 10 years, EDAP has been fully dedicated to enhancing Ablatherm HIFU, bringing average treatment times now to 95 minutes, following the introduction of the advanced imaging head. In addition, the company introduced nerve-sparing applications that can preserve potency in up to 85% of patients electing this option. A review of the first indication patient data, including patients treated in 1996, shows incontinence in less than 2% of patients and preservation of potency in 45% of patients electing complete prostate treatment rather than nerve-sparing choices. These findings compare very well with, or better than, traditional care options. Dr Thüroff's presentation reiterates negative biopsy rates from 79.4% in locally advanced prostate cancer to 93.7% in localised low to medium risk prostate cancer cases.

Dr Gail ter Haar, of the Institute for Cancer Research at the Royal Marsden NHSF Trust in

Surrey, UK, and a principal investigator of HIFU technology on a global scale, presented an outstanding review of HIFU principles and applications to date. Furthermore, he presented a summation of HIFU technology marketed today among which, the Ablatherm is a leading choice. Specifically, the Ablatherm HIFU addresses the localised prostate cancer market with its best-in-class integrated imaging, industry-leading safety features and efficient treatment. Dr ter Haar's presentation concluded that HIFU is becoming a choice in future therapies based on significant benefits, including its minimally invasive profile, repeatability, flexibility and efficacy. ■

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