

# Volume 14 - Issue 2, 2014 - Interventions

## High Intensity Focused Ultrasound's Role in Cancer Treatment

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The clinical need for local tumour control, by means of a minimally invasive approach instead of traditional invasive, risky and expensive surgical ones, represents the main reason for the very fast development of new hyper-technological branches in oncology. Invasive local treatments are very often not fully indicated because of the poor general clinical condition or the short life expectancy that may not justify any aggressive therapy. When the invasiveness of therapies is reduced, indications can often become wider, and patients who might benefit from such a nonaggressive approach will increase in number. In oncology, because the majority of patients are unable to undergo surgical resection because of the tumour sites, advanced stage of tumours, or poor general condition, novel treatment techniques, such as radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and laser-induced interstitial thermotherapy have been introduced in daily practice. Among these techniques, HIFU is the only 'nominally' non-invasive technique, and this is the main reason of the fast-growing interest in its development and evaluation for clinical use.

#### **High-Intensity Focused Ultrasound**

High-intensity focused ultrasound (HIFU) is a highly precise medical procedure, which uses focused ultrasound energy for burning and destroying the tumour tissue at depth within the body, selectively and without harming overlying and/or adjacent structures within the path of the ultrasound beam. The possibility that focused ultrasound therapy could be developed as a result of controlling local heating phenomena was introduced by Lynn et al. in the 1940s (Lynn et al. 1942), but the technique was not developed at that time because of inadequate targeting methods. The advent of more sophisticated imaging has led to a resurgence of interest in HIFU. Unlike percutaneous ablation, HIFU is completely non-invasive and can be used to reach tumour targets that are deep within the body, if there is an acoustic window for allowing for the transmission of ultrasound energy. Preliminary reports underline a reduced toxicity with HIFU ablation compared with other ablation techniques because of the non-invasive nature of the procedure. The first devices, which were never used widely in clinical practice, were transrectal probes, used predominantly to treat prostate cancer. Extracorporeal devices are significantly larger, and can be used to treat a variety of problems, most commonly intra-abdominal solid tumours. As a result, these extracorporeal devices use transducers with a longer focal length and use either US (USgHIFU) or MRI (MRgHIFU) for targeting the organ.

## **Advantages and Limitations**

Both technologies have pros and cons, relating to the specific characteristics of the two imaging modalities. US guidance may allow for realtime images, which is very helpful in the treatment of abdominal tumours located in moving organs, such as the liver, pancreas and kidneys. As the same form of energy is used both for guidance and treatment, it is usually much easier to foresee the feasibility of the treatment. However, MRI provides a much better imaging detail with a wider multiplanar view of the region where the tumour is located. Moreover, thanks to specific sequences, MRI may provide the temperature at the focal spot with the so-called 'thermal map'. In the meantime MRI cannot produce 'real-time' imaging during treatment, and moving organs still represent a big challenge both for safety and effectiveness (lack of temperature monitoring).

In order to overcome such limitations, dedicated ultrasound probes and devices are being developed for improving USgHIFU and respiratorygated techniques are under evaluation for approaching abdominal organs with MRgHIFU devices.

However, due to the aforementioned limitations, up till now liver and pancreatic tumours have been mostly, if not exclusively, approached by USgHIFU devices, with wider experience coming from authors in Asia. Bone tumours, and, more recently, brain lesions are conversely better treated with MR-based technology. Breast cancer represents a very appealing target for both the modalities and several research projects (ablation and resection) are ongoing in order to define the efficacy in terms of radicality.

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### **Challenging Tumour**

Among those several fields, pancreatic and breast tumours are now the most challenging HIFU targets in oncology:

Pancreatic Tumours: Pancreatic cancer has the worst outcomes among all malignant tumours, with a one-year survival rate of less than 10% and a median survival time of only 3-5 months. Surgical resection is considered the only option for such patients, seeking long-term survival, but no more than 20-30% of patients with pancreatic cancer are eligible for resection because of metastatic or locally advanced disease. In the meantime surgical resection is reported to have a high morbidity and re-operation rate, with a postoperative survival of around 19 months. In patients with no surgical option, their quality of life is influenced by cancer related pain. HIFU has been demonstrated to be feasible, effective and safe in those settings, both for pain and for tumour control, in patients ineligible for resection.

Breast Cancer: Over the past decades there has been a radical change in surgical treatment for breast cancer, moving towards a more conservative approach and achieving the same clinical efficacy aimed at maintaining the integrity of the woman's body.

Many papers have reported the results on HIFU treatment for breast cancer. Although the results are very encouraging and significant, the small number of cases and the non-homogeneous enrolling criteria and post histological and/or instrumental post HIFU evaluation leave enough room for further scientific speculation. The inherent advantage of HIFU in this field is the total absence of any cosmetic damage to the woman's breast and, due to the relatively superficial site of tumours, targeting and treatment are both easier and not time-consuming. It represents one of the most exciting fields of research for HIFU

Published on : Wed, 25 Jun 2014