

High intensity focused ultrasounds

The use of focused ultrasound for therapeutic purposes has been known since the beginning of this century, but only in the last two decades it has been observed a concrete development of advanced imaging techniques that made their clinical utilize possible, such as the high intensity focused ultrasounds (HIFU) systems in combination with diagnostic ultrasounds (USgFUS) or magnetic resonance imaging (MRgFUS).

To date, if the FDA-approved clinical use is still limited to a few areas, such as the ablation of uterine fibroids and prostatic cancer plus the bone metastases pain palliative treatment, in terms of scientific research, a great ferment is related to the optimization of protocols and methods to maximise the use of this technology in the field of solid tumours ablation and the treatments of neurodegenerative diseases, pain and vascular problems.

Furthermore, since the modulation of physical parameters generates a multiplicity of thermal and non-thermal effects having disparate biological implications, multiple areas of researches are on-going worldwide on drug delivery, blood barrier opening, hyperthermia and cell sensitization to radiation treatments. In this sense, the beam intensity modulating renders the use of US an adjuvant therapy in combination to traditional surgery, radiation or chemotherapy treatments.

This special issue has the purpose to describe the current state of art and the future scenario of MRgFUS treatments and the other therapeutic methods in development. It consists of three sections.

The first one is dedicated to the use of ablative techniques for the treatment of oncological and neurological diseases, with the direct comments of specialists who describe their direct experiences. In detail, this section includes: (I) the report of C. Ticca group from Niguarda Cà Granda Hospital (Milan, Italy), who discusses the aspects demonstrating the effectiveness of uterine fibroids ablation by MRgFUS treatment; (II) the report of F. Zaccagna team and their experience at the Umberto I Hospital (Rome, Italy) on advantages and limitations of MRgFUS technique for pancreas and liver cancer treatment, two carcinomas still characterized by low survival rates and poor prognosis; (III) the report of F. Arrigoni group from San Salvatore Hospital (L' Aquila, Italy), who describes the technical aspects of MRgFUS bone treatment, the indications for a proper patient selection and the main applications in the field of musculoskeletal MRgFUS; (IV) the report of E. Martin team from the Kantonsspital (Zurich, Switzerland), who describes the amazing experience of treating neurological diseases, such as chronic pain, essential tremor, Parkinson's disease, glioblastoma or brain metastases, by using a transcranial MRgFUS system.

The second section describes the main physical and engineering research fields moving toward the improvement of protocols and technologies for the HIFU clinical and research uses. This section includes: (I) the work of Sinden D. and Ter Haar G. (Sutton, UK), which describe the dosimetry aspects and fundamental requirements for a proper ultrasound dose delivery in the context of a required treatment; (II) the work of C. Militello group (Cefalù, Italy), who describes the areas of engineering development for the enhancement of automatic image segmentation methods, the real time temperature monitoring and methods for motion compensation; (III) the work of F. Vicari and G. Russo (Cefalù, Italy), which describes protocols of daily quality assurance for *in vitro* experiments, needed to obtain experimental repeatability of results among research groups.

Finally, the third session is dedicated to the biological research fields, aiming to identify new therapeutic strategies supporting conventional therapies. This section includes: (I) the work of Cammarata FP and Forte GI (Cefalù, Italy), who describe, in a systematic way, all the biological effects obtainable by modulating physical ultrasound parameters and their implications for therapeutic purposes; (II) the work of Aubry JF group (Paris, France), which offers a summary of *in vivo* ultrasound-based strategies, to deliver drug payloads into tumor environments, to permeabilize vessel walls and membranes, and to *in situ* activate drugs and genes; (III) the work of G. Borasi (Bologna, Italy), who suggests the use of combined US and radiation therapies as a new sensitizing strategy improving the success of radiotherapy protocols, with the implication of using lower and less toxic radio-therapeutic doses.

Overall, this special issue provides to the reader an overview of the use of focused ultrasound for therapeutic purposes, highlighting both the present uses, and especially the future ones, resulting in new therapeutic horizons for personalized medicine.

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