Role of High Intensity Focused Ultrasound in Treatment of Solid Tumors

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List of Abbreviations

Abbreviation	Meaning
CT	Computed tomography
FDA	Food and Drug Adminstration
FUS	Focused ultrasound
GnRH	Gonadotropin- releasing hormone
HCC	Hepatocellular carcinoma
HIFU	High intensity focused ultrasound
MDCT	Multi detector Computed tomography
MI	Mechanical index
MRgFUS	Magnetic resonance–guided focused ultrasound
MRI	Magnetic resonance imaging
PEI	Percutaneous ethanol injection
PET	Positron Emission Tomography
RF	Radio-frequency
RFA	Radiofrequency ablation
SPGR	Spoiled gradient-recalled echo sequence
TACE	Transcatheter arterial chemoembolization
TRUS	Transrectal ultrasound
UAE	Uterine artery embolization
URFs	Urethrorectal fistulas
US	Ultrasound
USgFUS	Ultrasound guided focused ultrasound
WI	Weighted image

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Introduction:

One of the medical field's aspirations is to provide patients with minimally invasive therapy. With such therapy, infection and blood loss is minimized, procedure and recovery time is shortened, and procedures can be offered on an outpatient basis ***(Chan et al., 2004)***.

For many decades open surgery remained the only way available for local control of body tumors. In order to decrease the patients' morbidity and mortality several image guided minimally invasive procedures have been adopted. High intensity focused ultrasound (HIFU) is an extracorporeal non invasive method for tumor ablation **(*Shehata, 2012).***

In comparison to traditional cancer treatment methods (i.e., open surgery, radiotherapy or chemotherapy) and other physical methods for tissue ablation (i.e., laser, microwave or radio-frequency [RF]), HIFU ablation has the advantages of noninvasiveness, precise focusing and deeper penetration without exposing patients to ionizing radiation. Substantial evidence suggests that the risk of metastasis is not increased after HIFU treatment, and fewer treatment related complications have been observed ***(Zhou et al., 2011).***

HIFU has the potential to provide the clinician with another truly noninvasive, targeted treatment option. Its scope is not, however, limited to the direct treatment of cancers. It may also be used in a palliative setting for relief of chronic pain of malignant origin, for haemostasis, or even for the treatment of cardiac conduction or congenital anomalies ***(Kennedy et al., 2003).***

HIFU is capable of inducing coagulative necrosis in tissues by delivering acoustic energy to a precise focal point within the body, but without skin incision or harming adjacent structures in the path of the acoustic beam. Lynn first introduced this technique in the 1940s, and results written in Fry et al. have indicated that HIFU might be used in clinical practice. However, this technique was not developed at that time because of inadequate targeting methods. With the development of diagnostic imaging, this technique had gradually received more international attention in the 1990s. In the last decade, HIFU was used for the treatment of both benign and malignant solid tumors. Recently, clinical results have indicated that HIFU can be safely used to ablate tumors close to major blood vessels (***Jiang et al., 2013).***

HIFU is a promising modality to treat tumors in a complete, non invasive fashion where image guidance and therapy control can be achieved by magnetic resonance imaging (MRI) or diagnostic ultrasound (US). In the last 10 years, the feasibility and the safety of HIFU have been tested in a growing number of clinical studies on several benign and malignant tumors of the prostate, breast, uterus, liver, kidney, pancreas, bone and brain. For certain indications this new treatment principle is on its verge to become a serious alternative or adjunct to the standard treatment options of surgery, radiotherapy, gene therapy and chemotherapy in oncology. In addition to the now clinically available thermal ablation, in the future, focused ultrasound (FUS) at much lower intensities may have the potential to become a major instrument to mediate drug and gene delivery for localized cancer treatment (***Al-Bataineh et al., 2012***).

Because HIFU does not require an internal applicator, there is no risk for puncture-related bleeding or needle track dissemination of malignant cells, and it is effective even when the tumor is poorly perfused (as opposed to electroconductive treatments that require a relatively uniformly hydrated treatment volume) ***(Ward, 2011).***

Aim of the work:

To review updates on High Intensity Focused Ultrasound as a non-invasive, non-ionizing modality for treatment of a variety of solid tumors.

Principles of High Intensity Focused Ultrasound:

Sound is vibration. In physics, the term “ultrasound” applies to all acoustic energy (longitudinal, mechanical wave) with a frequency above the audible range of human hearing: between about 20 and 20,000 Hz. Sounds with frequencies higher than this range are termed ultrasound. Planar ultrasound waves deposit clinically insignificant energy as they travel through tissues ***(Ward, 2011).***

All medical applications of ultrasound make use of the piezoelectric effect **(Fig. 1 A, B).** The piezoelectric effect is a reversible process in which certain solid materials (notably crystals and some ceramics) will have internal generation of a mechanical force when an electrical charge is applied (converse piezoelectric effect). These materials will also exhibit the direct piezoelectric effect, namely the generation of an electrical charge when a mechanical force is applied. When a series of electrical pulses (i.e., an alternating electrical current) is passed through a piezoelectric crystal, mechanical waves are created that propagate away from the crystal. As the waves pass across an interface of different tissues, the speed of the wave propagation will change. Each time the speed of sound changes, i.e., different tissue density, some of it will be reflected, or echoed, back to the crystal, and some will continue propagating forward. When an echo returns, it vibrates the crystal, creating an electric current that can be analyzed and processed to construct an image. Typical diagnostic US has a single crystal that rapidly alternates between transmission and listening modes. Diagnostic sonographic scanners typically operate in the frequency range of 2 to 18 MHz, the choice of frequency being a trade-off between spatial resolution of the image and imaging depth: lower frequencies produce less resolution but image deeper into the body ***(Ward, 2011).***

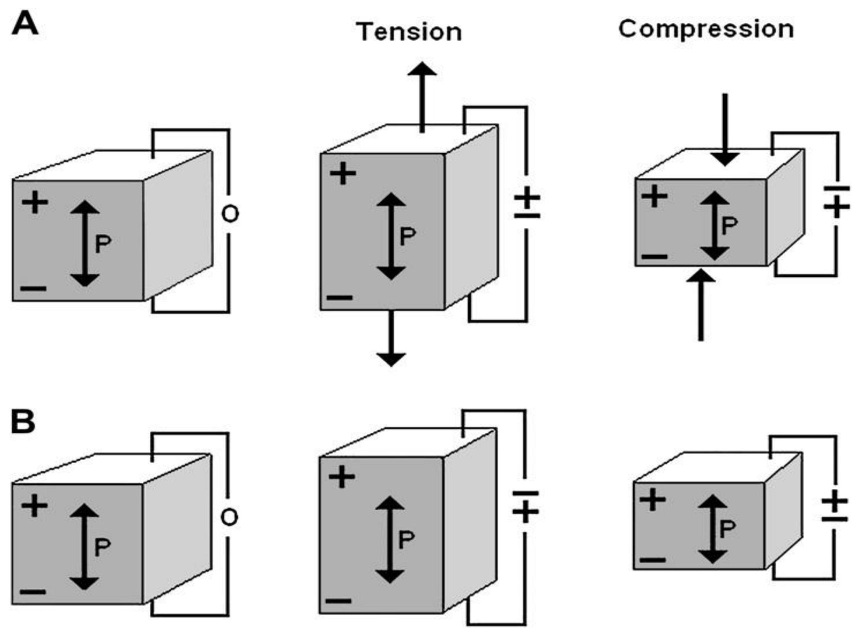

Fig. 1: (A) Direct piezoelectric effect: Certain single crystal materials when mechanically strained, or when the crystal is deformed by the application of an external stress, will generate an electric charge on the surface of the crystal. When the direction of the strain reverses, the polarity of the electric charge is reversed. (B) Converse