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IRBM 29 (2008) 326–336

IRBM

Brief communication

Ultrasound hyperthermia control system for deep-seated tumours: Ex vivo study of excised tumours, modeling of thermal profile and future nanoengineering aspects

Système de contrôle par ultrasons d'hyperthermie de tumeurs profondes : étude ex vivo de tumeurs explantées, modélisation du profil thermique et aspects de nano-ingénierie

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Received 14 March 2007; accepted 19 March 2008
Available online 9 July 2008

Abstract

Hyperthermia is a technique of raising the temperature locally to treat say tumours. There are several hyperthermia modalities like radio frequency (RF), microwave, and ultrasound. RF and microwave hyperthermia are good for superficial treatment while ultrasound is good for the therapeutic treatment of deep-seated tumours, with the ability of easy focussing. Focussed ultrasound system developed for deep-seated tumours, say in the complex brain tissue, is studied here. Nanotechnological approach is presented here for different control mechanisms for the control of ultrasound intensity, focussing beam, thermal profile of temperature distribution in the tissue and dosage control levels. Ex vivo study of excised tumours, like breast tumours, bone tumours and other such samples, with the present system is also presented. Physical and biological effects on the human health are discussed.

Résumé

L'hyperthermie est une technique d'augmentation de la température locale pour le traitement des tumeurs. Il existe plusieurs méthodes pour obtenir une hyperthermie : la radio fréquence (RF), les micro-ondes et les ultrasons. Si l'hyperthermie par RF ou par micro-ondes donne de bons résultats dans le cas de traitements superficiels les ultrasons sont plus appropriés pour le traitement de tumeurs profondes et offrent une facilité de focalisation du traitement. L'étude porte sur le système de traitement ultrasons focalisé pour les tumeurs profondes, comme celles de tissus cérébraux. L'approche nanotechnologique des différents contrôles du système sont présentés : ultrasons, focalisation, profil thermique et distribution dans les tissus, niveaux du contrôle et dosage. Une étude ex vivo de différentes tumeurs explantées – tumeur de cancer du sein, tumeurs osseuses et autres, par le système ultrasons est également présentée. Les effets physiques et biologiques sur la santé humaine sont discutés.

Keywords: Hyperthermia; Ultrasound; Nanoengineering; Modeling; Tumour

Mots clés : Hyperthermie ; Ultrasons ; Efficacité clinique ; Nano-ingénierie ; Tumeurs ; Modélisation

1. Introduction

As the cancer is a recognised global problem, there is an urgent need for a better noninvasive and nonsurgical technique for cancer diagnosis and treatment. Generally, imaging techniques are used for the diagnosis and chemotherapy and cobalt

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doi:10.1016/j.rbmret.2008.03.007

therapy etc. are used for the treatment of the cancer, but these techniques have their limitations, and hence hyperthermia has come into use in the recent past. The hyperthermia modality is mainly based on focussing of heat energy within the cancerous cell or in the tumour. There are other local hyperthermia techniques like radiofrequency and microwave, but focal ultrasound, with a focussing mechanism, has been found to be more suitable for better penetration depth with better intensity in the focal zone. In this technique, ultrasound beams are focussed to concentrate the total energy at a desired target, say the area of tumour.

The tumours when deep-seated in the brain are very dangerous and serious. The surgery is only the possible treatment if taken up in time. In most of the cases, the patient is not able to recover. However, if the patient recovers, some abnormality is developed. Focussed ultrasound modality has been tried recently and is found effective [1–10]. Ultrasonic vibrations are orderly oscillatory motions generated by an external source. A typical source (transducer) is a crystal driven electrically to vibrate, and placed in contact with outside surface of the medium. As soon as the surface particles move, the net force on their neighboring particles alters, so that they also begin to move. In this way, mechanical vibrations pass very quickly through the material. Thus, both vibrational and therapeutic effects are used for the diagnostic and therapeutic applications in medical field.

Clinically, hyperthermia has emphatically antitumour effects in patients in whom all conventional modes of therapy had failed. Thus, hyperthermia is likely to emerge as a primary mode of cancer therapy, as important as surgery, radiation or drugs. There is good evidence that tumours exhibit slightly greater heat sensitivity than normal tissues. Tumours, specifically those that are large, can be characterized by an inadequate blood supply and thus have a marginal supply of nutrients and oxygen. When heated to hyperthermia temperature, their cellular metabolic processes are accelerated increasing the nutritional and oxygen requirements that cannot be met by their deficient blood supply. These cells, therefore, cannot recover from hyperthermia induced damage and do not reproduce, thus leading to the arrest of tumour growth on the death of these cells, the tumour shrinks by attrition. Although tumours exhibit a greater sensitivity to heat damage than normal tissue, but the difference is rather small. Furthermore, even a small difference in heat dose produces a large difference in cell killing. This fact underscores the crucial need for developing sophisticated hyperthermia system that generates precisely controllable heat, which can be restricted to the tumour so that the risk of damage to surrounding tissue is minimized.

1.1. Plane hyperthermia

Hyperthermia is thus a technique of raising the temperature locally to treat say tumours and other such diseases. There are several hyperthermia modalities like radio frequency (RF), microwave, and ultrasound. RF and microwave hyperthermia are good for superficial treatment while ultrasound is good for the therapeutic treatment of deep-seated tumours, with the ability of easy focussing [1–4]. In normal tissues, blood vessels open up, (dilate) when heat is applied, dissipating the heat and cooling down the cell environment. Unlike healthy cells, a tumour is a tightly packed group of cells, and circulation is restricted and sluggish. When heat is applied to the tumour, vital nutrients and oxygen are cut off from the tumour cells. This results in a collapse of the tumour's vascular system and destruction of the cancer cells [5–8]. Hyperthermia is a low and smooth temperature elevation, with long exposure times. An overview of therapeutic applications of high intensity ultrasound for thermal ablation of tumours is given here.

As an example, multi-thermocouple temperature monitoring of hyperthermia is feasible because the temperature profile in tissue is smooth after a long exposure time. Similar approach to HIFU in clinics looks unreasonable.

1.2. Focussed ultrasound

Focussed ultrasound holds promise in a large number of therapeutic applications. It has long been known that High-Intensity Focussed Ultrasound (HIFU) can kill tissue through coagulative necrosis. Thus, HIFU, is short sonication in seconds with sharply delineated focal spot. However, it is only in recent years that practical clinical applications are becoming possible, with the development of high-power ultrasound arrays and noninvasive monitoring methods. In the last decade, HIFU has been adapted and used to treat localized prostate cancer. Early results demonstrated that prostate HIFU is efficient to obtain local control for low- and intermediate-risk localized prostate cancer; however, long-term follow-up is still needed to estimate the efficacy of prostate HIFU in terms of specific cancer mortality. This makes HIFU a viable alternative in patients not candidate for radical therapy [9–14]. Clinical hyperthermia can be divided into: superficial, interstitial, whole-body and deep-body hyperthermia. Nonablative deep heating in the human trunk is a precondition for novel very promising methods of cancer treatment, such as heat-guided modalities of drug targeting and gene expression [15–42]. Further, a noninvasive monitoring of temperature (and other physiological parameters) in a patient under thermotherapy (due to ultrasound or otherwise) is required [43–56]. Some of the studies suggest that extracorporeal high-intensity focussed ultrasound (HIFU) might have potential as a noninvasive method of tumour ablation [57–59].

High-intensity focussed ultrasound (HIFU) has been shown capable of selective tissue destruction in humans, with promise as a tool for ablation of tumours, although one practical problem is reflection of sound at gas or bony interfaces within the body. A water-filled cylindrical metal tube has been evaluated as a waveguide for HIFU, since such a general technique might be useful for ablation of otherwise inaccessible tumours in the body. Our studies indicate that such a waveguide is capable of propagating HIFU from a piezoelectric source, with resultant heating of tissue specimens to greater than 80 °C, causing focal tissue destruction [60–64].

Focussed ultrasound system developed for deep-seated tumours, say in the complex brain tissue, is studied here. Nanotechnological approach is presented here for different control mechanisms for the control of ultrasound intensity, focusing