Concept of biological focal field and its importance in tissue resection with high intensity focused ultrasound.

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Abstract: In this research the shape and size of necrosed tissue volume produced by HIFU with 1.6 MHz focused transducer were carefully checked and compared in pigs. This volume was generated by a single exposure. It was showed that with the same therapeutic parameters, HIFU could selectively necrose one region of liver in pigs. However, its shape and size differed between in vitro and in vivo. These changes implied that the necrosed tissue volume in vivo depended upon not only HIFU conditions, but also the function state, blood perfusion, function, and movement of target tissue. In contrast with physical focal region, necrosed tissue volume in vivo could also be termed the biological focal field of HIFU. Theoretically, it more resembled the living tissue damaged by HIFU. In order to avoid side effects, it is important to set up the data about biological focal fields of different organs in tissue resection with HIFU.

INTRODUCTION

Many studies showed that in vitro the size and shape of the necrosed tissue volume generated by high intensity focused ultrasound (HIFU) were dependent upon the transducer size and radius of curvature, operating frequency, input power, pulse duration, and delay time between each pulse. The tissue necrosis was a result of the transient hyperthermal and cavitation effects caused by HIFU. However, some biological characteristics of the living tissues in vivo, such as functional state, blood perfusion, movement of target tissue, may potentially affect the necrosis volume of in vivo target tissues. Yet studies of a similar kind are rarely reported. Intended to explore the concept of biological field and its importance in tissue resection with HIFU, with the same physical parameters used, this study compared in vitro and in vivo necroses tissues in volume difference, morphological change, and other characteristics.

MATERIALS AND METHODS

HIFU Therapeutic Unit This unit was composed of 5 parts: ultrasound diagnostic and positioning device, transducers combined of a diagnostic and a therapy transducer, movement controlling device, and a therapeutic bed attached with a degassed water tank. Computer controlled, the unit is capable of moving in X, Y, Z directions and automatically positioning and treating target tissues. The therapy transducer was developed on the basis of lens focussing theory with a focal volume of 1.1 mm × 1.1 mm × 4 mm, a frequency of 1.6 MHz, a focal length of 120 mm, and an output acoustical power of 4920 W/cm².

Pig liver in vitro Fresh miniswine liver was chosen and preserved in normal saline. The volume and shape of the necrosed region was observed after HIFU sonication.

Miniswine After 12 hours of starvation, depilation, degasification, and deroisinaton were performed on upper abdomen skin after 28 pigs received intra-abdominal anesthesia with 3% pentobarbital sodium (30 mg/kg). Using B-mode ultrasound to diagnose the HIFU sonicated tissue of the swine's left liver lobe under the xiphoid, the correlation between localization or the depth size of ablative lesions receiving hyperthermia treatment and the adjacent tissues was determined.

HIFU sonication After these preliminary preparations, the fresh pig liver or miniswine was placed in the
degassed water tank attached to the therapeutic bed. The diagnostic scanner was then switched on and the target region was predetermined. With a computer guiding the three dimensional movement system, the focal volume of the therapy transducer was shifted onto the target tissue. Simultaneously, the therapy transducer was started, and single exposures of HIFU were applied. Sonication duration was 5s, 10s, 15s, 20s, and 25s respectively.

RESULTS

Pig liver in vitro  Pale coagulated necrosis emerged in target tissues after HIFU treatment. Without altering any other physical parameters, necrosis volume in the target region was found to be increasing with the lengthening of sonication time in each exposure.

Miniswine in vivo  The damaged area of liver tissues in the target region of HIFU was found to be made up of three parts: the central area of pale acute coagulating necrosis, a ring of blood congestion on the outer edge, and the intervening area of subacute necrosis. Necrosed volume was also increased with lengthening of sonication in each exposure. The necrosis volume of pig liver in vivo was comparatively smaller than that of pig liver in vitro.

DISCUSSION

It has been verified by most studies that lesion volume caused by HIFU is dependent upon operating frequency, power, pulse duration, delay time between two pulses, and the degree of heat diffusion within tissues. With the focused transducer and frequency fixed, increase of input power and lengthening of pulse duration may result in increase of the volume of tissue necrosis. Through heat conduction pulses of long duration produce larger volume of tissue necrosis. But the longer the sonication lasts, the more thermally sensitive tissues become. Therefore, special attention must be paid to the damage on adjacent tissues, which is caused by prolonged sonication. It follows that the increase of acoustical power, reducing of focal region, and shortening of single pulse duration is crucial in ensuring the safety of HIFU treatment. As different biological tissues vary in thermal sensitivity and sonicated organs and tissues also differ in physiological movement, a uniform standard of lesion volume produced by HIFU in certain tissues is both necessary and significant in clinical application of focused ultrasound surgery.

It was revealed through this study that using the same physical parameters, the increase of pulse duration led to extension of the necrosis volume of liver within the treated region. Because the lesion volume directly reflects changes in histology, structure, and lesion that are caused by thermal effect, we termed it the biological focal field. Theoretically, physical focal region is the basis for biological focal field. Under certain circumstances, physical focal region is completely identical to biological focal field.

Given the same fixed physical parameters, differences were revealed through this study. They were epitomized in two ways: ①Tissue necrosis volumes vary, with that of the in vitro strongly exceeding that of in vivo, ②Histological and morphological features of liver tissue necrosis also differ in vitro liver lesion region was largely one of homogenous coagulating necrosis while that of in vivo consisted of acute necrosis, subacute necrosis, and an area of congestion. These differences indicated that in vivo tissue functional state, blood perfusion, and target tissue movements were the major factors effecting changes in biological focal field. Concerning the correlation between the biological focal field and the physical focal region, three instances were observed: ①Biological focal field equals the physical focal region of HIFU. ②Biological focal field is smaller than the physical focal region of HIFU. ③Biological focal field exceeds the physical focal region. As volume of this biological focal field was of determining influence over effectiveness and safety of HIFU as a therapy, top concern should be given to it. It naturally follows that precise control and checking of the culminating temperature elevation induced by consecutive pulse could exercise far-reaching impact over the quantitative study and clinical use of HIFU as a therapy for malignant tumors.

1072