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3aBAb3. Non-invasive toroidal high intensity focused ultrasound transducer for increasing the coagulated volume in depth

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A device composed of 32 elements (78 mm2 each) arranged on a toroidal transducer (operating frequency: 2.5 MHz) was developed to increase the coagulated volume. To date, our previous work on toroidal transducers used the outer envelope of a torus as a reference surface. Here, the transducer geometry was based on the interior part of a torus. This produces a focus that is ring-shaped but the ultrasound beams also intersect between the principal focal ring and the transducer surface to form a secondary focal zone, which contributes to increase the size of the lesion. The radius of curvature was 70 mm with a diameter of 67 mm. A 7.5 MHz ultrasound imaging probe was placed in the centre of the device. Twenty ablations were produced in vitro by using electronic beam steering, each ablation was created in 55 seconds. The average depth of intervening tissues (skin-fat-muscle) was 11±1 mm and the average depth of liver tissues that have been spared was 21±4 mm. No significant temperature rise in intervening tissues was measured (maximal temperature: 41°C). The dimensions of these ablations were an average diameter of 10±1 mm and an average depth of 27±3 mm.

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INTRODUCTION

In recent years, a number of clinical studies have demonstrated that High Intensity Focused Ultrasound (HIFU) is feasible for treatment of malignant tissues in several organs such as, for example, the prostate, liver and breast\textsuperscript{1-3}. Ultrasound waves can be focused at a given point. The high energy levels carried in a HIFU beam can therefore be delivered with precision to a small volume, while sparing surrounding tissues. The focused energy, after being absorbed by the tissues for only a few seconds, can generate irreversible tissue necrosis in the target region. Although HIFU therapy is effective in destroying tissues noninvasively with shorter recovery times and lower side-effects than invasive surgical techniques\textsuperscript{4}, it still suffers from a relatively long treatment time for ablation of large tissue volumes due to the small focal zone\textsuperscript{5}. Several techniques have been developed to decrease the treatment time of noninvasive ultrasound therapy. One of them is the use of toroidal transducers. The principal interest is the possibility to treat large volumes of soft tissues in a short period of time (ablation of 5-7 cm\textsuperscript{3} in 40 seconds).

A first toroidal-shaped HIFU device, developed for the treatment of liver metastases during surgery, has been described to be used as a tool for assisting liver resection. It was previously shown that this HIFU prototype allowed the creation of large HIFU lesions in the liver and that accurate visualization of the ablated zones is feasible \textit{in vivo} using ultrasound imaging\textsuperscript{6,7}. Currently, this device is tested clinically for the treatment of liver metastases. The selected approach for the first evaluation of this toroidal HIFU treatment is surgical laparotomy. This approach makes it possible to reach all of the regions of the liver without penetrating the hepatic capsule. Furthermore, such an intraoperative approach enables the protection of the surrounding organs and eliminates the risk of secondary lesions\textsuperscript{8}. Here we report \textit{in vitro} results obtained using a second version of this toroidal transducer. Unlike the previous prototype, the transducer is developed based on the interior volume of a torus. The aim is to verify whether the use of this geometry combined with electronic beam steering is capable of creating large volumes of ablations in depth in soft tissues without damages in intervening tissues (skin-fat-muscle).

MATERIAL

A spindle torus is generated by the rotation of a circle around an axis of revolution with a distance between the axis and the center of the circle lower than the radius of the circle. After rotation, the volume obtained is composed of two envelopes that can be used to create a toroidal transducer. To date, our previous work on toroidal transducers used the outer envelope as a reference surface. In this work a transducer geometry based on the interior part of a torus has been developed. Unlike previous toroidal transducers, this geometry creates a second focal zone between the transducer and the ring-shaped focal plane. The operating frequency was 2.5 MHz. The radius of curvature was 70 mm with a diameter of 67 mm. An ultrasound imaging probe was placed in a central circular opening of 26 mm in diameter. The transducer was also divided into 32 rings of 78 mm\textsuperscript{2} each.

The driving equipment has been already described (N’Djin et al. 2011). Briefly, thirty-two channels of a 50-channel pattern generator (PG1050 Acute, Hsin Chuang City, Taiwan) generated 32 TTL signals at working frequency (3 MHz). Thirty-two power amplifiers (AHF 855, ADECE, Artannes, France) converted the TTL signals into amplified sine waves, which were required to drive the 32 elements of the transducer. The gain of each amplifier was adjusted using digital-analog output cards. Inside each amplifier, a directional coupler generated two voltages that were directly proportional to the direct and reflected electrical power. The 32 voltages were captured by analog digital input cards and registered on the hard disk of a Pentium 4 PC, which controlled both the input-output cards and the pattern generator. The phase between the channels can be adjusted with a resolution of 1.4 degrees, in order to make it possible to change the diameter and depth of the focus to maximize dimensions of the HIFU ablations.

A sectorial ultrasound imaging probe working at a frequency of 7.5 MHz (Vermon, Tours, France) was placed in the center of the device and connected to a BK HAWK 2102 EXL scanner (B-K Medical, Herlev, Denmark) for guiding the treatment. The imaging plane was aligned with the HIFU focal zone. The HIFU probe was brought into contact with the liver using an ultrasound sterile cooling and coupling liquid (Ablasonic®, Edap-Technomed, Vaulx en Velin, France) contained in a sterile polyurethane envelope (Civco, Kaloma, Iowa, USA). Software developed in our laboratory made it possible to define the treatment zone by HIFU from a two-dimensional ultrasound image.
METHODS

Experiments were performed in 8 bovine livers purchased from a local butcher. Livers were cut into samples with dimensions matching those of a sample holder (6.5 cm × 6.5 cm). The thickness of the samples was 10 cm. Intervening tissues were composed of skin-fat-muscle taken from pigs at the butchery and were placed at the top of the liver sample. The thickness of intervening tissues was between 10 and 12 mm in order to reproduce the in vivo conditions more closely. The samples were then placed in a crystallizing dish that was filled with degassed water. The water used for all of the experiments contained between 2.5 and 3.5 mg O₂/L. The samples in the crystallizing dish were then degassed with a vacuum pump (0.7 bars for 30 min) prior to the experiment to remove any bubbles that might have formed during storage. To minimize contact with air, the sample and degassed water were both transferred into an experimental tank containing degassed water. While underwater, the sample was placed in its holder, and a thermocouple was inserted into the liver sample. The water of the tank was then heated to 37°C using a thermostat, and the liver sample was then allowed to reach 37°C (approximately 60 minutes) prior to the initiation of the experiment. The HIFU device was attached to a gantry and positioned so that the envelope just came into contact with the skin surface. The holder has a groove of 0.2 mm to cut the liver using a histologic knife. An alignment system allows the placement of the acoustic axis of the HIFU probe along the groove of the holder and therefore, enabling the cutting of the sample along a plan of symmetry. A thin thermocouple (0.1 mm in diameter) was placed in intervening tissues between the transducer and the focal zone. The ultrasound exposures were then performed using beam steering capabilities that were identified with pressure field measurements and numerical modeling. The free field acoustic power that was used was 160 watts. Total exposure time was 60 seconds for 5 focal positions. All of the samples were cut just after the HIFU exposures the dimensions of ablations were measured using a caliper.

RESULTS

In total, 10 HIFU ablations were produced with this device. Figure 7 shows a typical ablation sliced along the acoustic axis, the treated zone is homogeneous without untreated regions. The average diameters of the ablations measured in this plane were 10.3 ± 1.3 mm (8.9 – 12.7) and 26.7 ± 2.9 mm (20.0 30.3). These results are within reasonable agreement with simulation conducted prior to these experiments. The relative differences between simulations and experiments were 1 - 5 mm. When using this toroidal geometry, the ultrasound beams coming from the transducer intersect between the principal focal ring and form a secondary focal zone. This allows a significant increase of the coagulated volume. The maximal temperature in intervening tissues during treatment was 40°C. No lesions were observed in skin, fat or muscle. The average distance between the skin and the beginning of the HIFU lesion was 34.4 ± 4.9 mm. On average 20.8 ± 4.0 mm of liver tissues were spared.

Figure 1 View of gross sample of the coagulated zone in liver tissues.
DISCUSSION

The use of physical agents to achieve local tumor destruction has been of elevated interest over the last decade\textsuperscript{9, 10}. Thermal damages induced by these methods are irreversible but are generally limited to small volumes (3–4 cm in diameter)\textsuperscript{11}. Other therapeutic modalities are needed which can rapidly induce large lesions, especially for tumors in the liver which can measure up to several centimeters in diameter. HIFU is a treatment modality which presents many advantages over the above mentioned local treatments. Focused beams pass harmlessly through superficial tissue and produce sufficiently strong heating in the focal zone to coagulate cells, even at distances relatively far from the transducer\textsuperscript{12}. The focused energy, after being absorbed by tissues for only a few seconds, can induce high temperatures (typically >60 °C) and generate irreversible tissue necrosis in the target region while avoiding damage to surrounding tissue. Excellent results have been obtained both experimentally and clinically in inducing homogeneous and reproducible tumor destruction\textsuperscript{5}. This method of treatment allows for the creation of lesions with a well-defined depth and geometry (ellipsoidal region of damage: length of 8–15 mm and diameter of 1–3 mm). An array of these lesions is built up in order to destroy the entire tumor and perform conformal treatments. The main technical limitation to widespread clinical use of HIFU has been the long time required to treat tumors of several cubic centimeters. For example, HIFU thermal therapy requires significantly long treatment times for prostate cancer\textsuperscript{13} (149 min average). This fact compromises the technique for the most prominent applications, i.e., cancers where tumor may be very large (>5 cm in diameter) and where therapeutic options are limited. Previous studies have been conducted to enlarge the ablated region by using, for example, cavitation\textsuperscript{14, 15} or optimization algorithm for the focus pattern\textsuperscript{16}. However, the gain is not sufficient compared with the size of large tumors.

Using the toroidal transducer described in this study with appropriate beam steering allows the creation of large lesions in depth, without damaging intervening tissues. HIFU ablations were obtained in a short time. Because of its toroidal geometry based on the interior volume of a spindle torus, the transducer focal zone was a ring with a diameter of 30 mm and located at 70 mm in depth. Due to the geometrical characteristics of a torus, the ultrasound beams coming from the transducer intersect between the focal ring and the transducer to form a secondary focal zone, which contributes to reinforce the homogeneity of the lesion at its center. The transducer described in this study is able to produce large zones of ablation in depth without creating any damage in intervening tissues. The temperature increase in intervening tissues was very low (about +3°C). Based on these results, the potential clinical usefulness has to be further validated based on preliminary in vivo studies that will demonstrate the feasibility, efficiency and tolerance of this treatment.

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