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Magnetic resonance-guided focused ultrasound surgery (MRgFUS): Ablation of liver tissue in a porcine model

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Abstract

Background: Liver surgery is technically demanding and is considered a major procedure with relatively high morbidity rates. Magnetic resonance-guided focused ultrasound surgery (MRgFUS) uses focused ultrasonic energy to create a heat coagulation lesion, which can be achieved in a totally controlled, very accurate manner (<1 mm). The aim of this study was to evaluate the safety and accuracy of non-invasive focal ablation of liver tissue achieved by consecutive MRgFUS sonications.
Materials and methods: Six MRgFUS procedures were performed in five pigs under general anesthesia, with the ExAblate 2000 system (InSightec, Israel). Real-time imaging and temperature mapping (Signa Twinspeed 1.5T, GEHC, USA) enabled the immediate evaluation of the results of each sonication. Different foci were chosen within the liver. These mock lesions were ablated by several sonications, each of them performed during 20–30 s of apnea. Between sonications, the pigs were normally ventilated. The pigs were sacrificed 3–21 days after the procedure and their livers were examined.
Results: The MRgFUS created complete tissue destruction of mock lesions in different areas of the pig's liver. The lesion sizes in each animal varied according to the number of sonications used and the extent of overlap between adjacent sonications. The lesion ranged in size from 1.5 cm × 1.5 cm × 2.0 cm to 5.5 cm × 4.5 cm × 2.0 cm. There was no morbidity.
Conclusions: MRgFUS under general anesthesia is a safe, completely non-invasive technology for the ablation of liver tissue. Liver tissue can be ablated in a very accurate manner, based on the pre-treatment planning on the MR images. The MR imaging characteristics, including real-time temperature mapping, enable real-time control of every step of the ablation process. Mechanical ventilation with intermittent periods of apnea is a technique that overcomes the problem of the respiratory movements of the liver.

Keywords: Liver ablation; Magnetic resonance-guided focused ultrasound surgery; Animal experiment

1. Introduction

Liver tumors, benign or malignant, primary or secondary, are among the most common tumors in human beings. Surgical removal is very often the only chance for cure. Only a small percentage of such tumors is operable. Major liver surgery is technically demanding and is considered a very complicated procedure with high morbidity rates [1]. The evolution of liver surgery during the last few decades, from non-anatomical and imprecise resections, which are associated with very high rates of morbidity and mortality, to a well-understood, accurate, anatomical procedure with acceptably low rates of complications, represents a major development in the surgical practice of the 20th century [2]. Minimally invasive ablative technologies, such as ethanol injection, microwave, laser ablation, radiofrequency, and cryoablation, are being used primarily as adjuvant palliative procedures. These technologies are, however, imprecise and suffer

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from a lack of real-time control of their efficacy [3–9]. The ablation of liver tumors by a non-real-time controlled, ultrasound-guided, focused ultrasound has been reported recently [10]. The integration of focused ultrasound and magnetic resonance imaging has resulted in a new method of non-invasive surgery. By using this integrated delivery system, the surgeon can correctly localize tumors, optimally deliver acoustic energy ("sonicate"), monitor energy deposition in real-time, and accurately control the deposited thermal dose within the entire volume of the tumor. It has been claimed that this novel technology represents a potential revolution not only in liver surgery but also in many other surgical fields [11,12]. However, to allow safe and effective treatment of the liver with magnetic resonance-guided focused ultrasound surgery (MRgFUS), one has to overcome the problem of respiratory movement of the liver during energy delivery. Otherwise, energy is not delivered to a focused region, and the magnetic resonance (MR) system is unable to provide quality thermal imaging.

The aim of this study was to evaluate the safety and accuracy of the MRgFUS for the focal ablation of liver tissue, in a totally non-invasive manner, using general anesthesia with intermittent short periods of apnea.

2. Materials and methods

This study was conducted in full accordance with the regulations and approval of the local Helsinki committee for animal studies. Five female pigs, weighing 30 ± 1.2 kg, were treated under general anesthesia, as follows: i.v. fentanyl, 0.002 mg/kg/h; i.v. propofol, 2 mg/kg/h; i.v. atracurium, 0.5 mg/kg/h. The pigs were intubated and kept under controlled, positive pressure mechanical ventilation using an operating room portable ventilator (Ivent 201, Version 1.4, VersaMed Inc., 2 Blue Hill Plaza, Pearl River, NY 10965, USA), delivering a respiratory rate of 14–16 min^{-1}, an FiO_2 of 0.5, and a PEEP of 5 cmH_2O. Sonications were performed with the MRgFUS system, using a phased array transducer with 208 elements (ExAblate 2000, InSightec, Tirat Hacarmel, Israel). The areas that were defined as targets for ablation (mock tumors) by the MRgFUS were outlined on the planning screen of a coronal MR image (Signa Twinspeed 1.5T, GEHC, USA). The operator acquired a set of T1W spin echo images during apnea, using a fast spoiled gradient echo technique (FSPGR) as follows: TR = 205; TE = 1.8; flip angle = 60°; bandwidth (BW) = 15 kHz; resolution 256 × 128; field of view (FOV) = 30 cm; slice thickness of 4 mm; and slice spacing of 0 mm. Those images were used for treatment planning. The operator identified one or more regions of tissue to be treated and drew their contours. The target tissue planned for destruction was always ablated by a single layer of adjacent sonications. The ablation planning software (ExAblate 2000, Version 4.1, InSightec, Tirat Hacarmel, Israel) calculated the type and number of sonications required to completely destroy the defined region, while minimizing the total treatment time. During treatment, a small "bean-shaped" volume of focused ultrasound energy was directed into the target for 5–12 s, heating the tissue to induce thermal coagulation. Each sonication was real-time controlled by the MR scanning for anatomical accuracy and thermal efficiency. Temperature was measured using the temperature-dependent PRF shift in the fast spoiled gradient echo technique (FSPGR) as follows: TR = 27; TE = 11; flip angle = 30°; bandwidth (BW) = 5.68 kHz; NEX = 1; resolution 256 × 128; field of view (FOV) = 28 cm; and slice thickness of 3–5 mm. Slice acquisition time was 3.4 s. SNR on magnitude images was 30 with an S.D. of 1.2 on the workstation-reconstructed thermal images. Once sonication was completed at one point, the transducer was automatically moved to the next treatment point and the process was repeated until the entire target tissue had been ablated. Consecutive adjacent sonications created high temperature foci, which were detected by real-time MR thermometry. These MR images, obtained during sonication, provided a diagnostic quality image of the target tissue and a quantitative, real-time temperature map overlay to confirm the therapeutic effect of the treatment.

The mock tumors chosen as targets for ablation varied in volume and were located in different segments of the pigs' livers. In three pigs, a single region of liver parenchyma was ablated. In the other two pigs, several regions were chosen in various locations. The targets were each ablated by multiple sonications. Each lesion was created by 5–65 adjacent foci of sonication. The ablative focus of each sonication is jellybean-shaped, 0.5 cm in diameter, and 2.5 cm in length. There was a 25% overlap between adjacent sonications. Each sonication was performed during apnea. Apnea periods always began at the end of the inspiration and ranged from 22 to 30 s. Between phases of apnea, different lengths of controlled mechanical ventilation (CMV) periods were used, with a length ranging from 60 to 150 s. The pigs were monitored continuously, with evaluation of hemodynamic status and blood oxygen saturation. Arterial blood levels of gasses, pH, electrolytes, and blood counts were obtained periodically during the procedure. At the end of the ablative procedures, MR scans, including axial, sagittal, and coronal views with the administration of 2.5 cc/kg i.v. contrast agent (Dotarem, Guerbet, 95943 Roissy CdG cedex, France), were performed to evaluate the location, shape, and volume of the ablated, non-perfused areas.

In the first pig, we ablated five disparate regions, using a total of 67 sonications. In the second pig, only one region was ablated by 64 sonications. In the third pig, 18 sonications were applied on one region adjacent to the wall of the gallbladder, including the liver parenchyma in close proximity to the main trunk of the right portal vein (Figs. 1–3). The fourth pig was treated twice, the second procedure being performed 14 days after the first one. In this pig, a total of three different regions were ablated. In the second procedure on the fourth pig and on the fifth pig, we used shorter periods of sonications (reducing the period from 12 to 5 s), along with a higher level of power (330–370 W) (Table 1). Some of the ablated regions had a subcapsular margin, and others were adjacent to or included a major portal or hepatic vein. The characteristics of each treatment are summarized in Table 1.

After each procedure, the pigs were followed carefully by an experienced veterinarian staff, and daily complete blood counts, electrolyte, and liver function tests were performed. Follow-up by MR imaging was performed between 4 and 21 days after the MRgFUS procedure. Two pigs were sacrificed on the 4th