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Technical notes

Quantitative evaluation of internal marks made using MRgFUS as seen on MRI, CT, US, and digital color images – A pilot study

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ABSTRACT

This pilot study compared the detectability of internal thermal marks produced with MRI-guided focused ultrasound (MRgFUS) on MRI, computed tomography (CT), ultrasonography (US), and color images from digital scanning. Internal marks made using MRgFUS could potentially guide surgical, biopsy or radiotherapy procedures. New Zealand White rabbits ($n = 6$) thigh muscle were marked using a Philips MRgFUS system. Before and after sonications, rabbits were imaged using T_1- and T_2-weighted MRI. Then rabbits were sacrificed and imaging was performed using CT and US. After surgical excision specimens were scanned for color conspicuity analysis. Images were read by a radiologist and quantitative analysis of signal intensity was calculated for marks and normal muscle. Of a total of 19 excised marks, approximately 79%, 63%, and 62% were visible on MRI, CT, and US, respectively. The average maximum temperature elevation in the marks during MRgFUS was 39.7 ± 10.1 °C, and average dose diameter (i.e., the diameter of the area that achieved a thermal dose greater than 240 cumulative equivalent minutes at 43 °C) of the mark at the focal plane was 7.3 ± 2.1 mm. On MRI the average normalized signal intensities were significantly higher in marks compared to normal muscle ($p < 0.05$). On CT, the marked regions were approximately 10 HU lower than normal muscle ($p < 0.05$). The results demonstrate that MRgFUS can be used to create internal marks that are visible on MRI, CT and US.

Introduction

Localized marking techniques are often used to guide radiotherapy in cancer treatments. Radiotherapy positioning can be checked prior to treatment using computed tomography (CT), but only if there are identifiable features in the images, such as bony anatomy, biopsy clips or other implants [1]. The utility of bony anatomy is limited when the targeted regions are highly deformable (e.g. in the breast), or can be moved due to changes in nearby anatomy (e.g. bladder filling impacting prostate position). Internal implants using gold or tantalum seeds for guiding radiotherapy have shown promising results, but come with limitations because they require invasive surgical placement [2,3] and may move after placement. Therefore, an internal fiducial, placed non-invasively under MRI guidance, would be beneficial for patients undergoing radiotherapy.

In addition to guiding radiotherapy, localized marking techniques are also used to guide surgical procedures. Current preoperative localization marking techniques include guide wire locators, radioactive injections and charcoal suspensions. Notably, all these techniques are invasive. Wire localization is performed under image guidance to mark a lesion so that greater accuracy can be achieved during lumpectomy. Radioactive occult lesion localization involves injecting technetium (Tc-99m) labeled serum albumin particles into the center of the lesion and then using a gamma camera probe to detect the lesion for removal [4]. Mathieu et al. proposed using a charcoal suspension for tumor marking and demonstrated its use in both breast and colon cancer [5]. The various marking techniques for breast cancer have risen out of a need to map deformable anatomical regions during cancer treatment. These previous results suggest that magnetic resonance

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guided focused ultrasound (MRgFUS) could play an important role in guiding surgery, and because it is non-invasive and potentially more accurate – could have advantages relative to existing methods.

MRgFUS provides excellent anatomic resolution for treatment planning and online feedback of temperature elevation during the treatment. It is commonly used for ablative procedures [6–9], but can also be used for internal marking [8]. Schmitz et al. demonstrated the utility of high intensity focused ultrasound 'tattoos' in an *ex vivo* model as a guide for surgical excision [10], as compared to guidewire locators. Yang et al. [11] evaluated the appearance of thermal lesions under CT and ultrasound in rabbit liver. MRI detection of marks made using other methods such as RF ablation [12] and laser-ablation [13] have also been demonstrated.

In this research, we use a multi-modality approach to detect marks made with MRgFUS *in vivo* in rabbit thigh muscles and quantitatively evaluate thermal lesions observed on MRI, CT, US, and on a digitized photograph. The purpose of this study was to assess these internal thermal marks for their conspicuity on multiple imaging modalities, to demonstrate their potential utility for guiding radiation therapy, biopsy or surgery in the future.

Materials and methods

Animals

All procedures were carried out with approval from and in accordance with our Institutional Animal Care and Use Committee. A total of six New Zealand White rabbits were used in this study. Animals were anaesthetized prior to experimental studies and anesthesia was maintained during imaging with 1.5–3% isoflurane. The respiration rate and heart rate were monitored at all times using standard MR-compatible devices. Both rabbit thighs were clipped to remove as much hair as possible and a depilatory cream (Avon Products Inc, New York, NY, USA) was applied to remove the remaining fine undercoat. The thigh to be marked was submerged in an in-house built degassed water bath (diameter = 18 cm), that sat within the acoustic window of the focused ultrasound (FUS) tabletop (diameter = 25 cm) and was coupled to the membrane using degassed water.

MR guided FUS

FUS marking experiments were performed using an integrated clinical MRgFUS platform (Sonalleve V1 1.5T, Philips Medical Systems, Vantaa, Finland). The Sonalleve system includes a 256-element phased array transducer that can be operated at 1.2 or 1.45 MHz [14]. Prior to sonication, T_2-weighted (T2W) images for localization and planning were acquired using a 3D Turbo Spin Echo (TSE) pulse sequence (TR/TE = 1000/110 ms, echo train length = 50, field of view (FOV) = 180 × 180 × 132 mm, acquisition matrix = 148 × 140 × 115, reconstructed in-plane resolution = 1.2 × 1.13 mm, slice thickness = 1.15 mm, number of excitations (NEX) = 2). Saturation bands were applied to suppress the water signal from the water bath. The target area for marking was selected within a uniform muscle region to avoid bony anatomy in the path of ultrasound propagation. A 4 mm diameter short-axis ellipsoid spot was placed using the FUS planning software. The 4 mm sonication was achieved using a geometric focal spot size ~2 mm, plus electronic steering for volumetric ablation operating at a frequency of 1.2 MHz [14].

For each rabbit, two to five sonications were planned. FUS sonications were performed in two parts. A previous study [15] demonstrated that pulsed FUS treated muscle tissue increases signal intensity in T2W MR images. Therefore, first we applied pulsed sonication to enhance the visibility of marks on MRI. A single-point 100-s pulsed sonication (80 W, 100 cycles, 50 ms pulse interval, 0.17% duty cycle, frequency 1.2 MHz) was delivered to produce mechanical force in the target region. This pulsed sonication did not cause temperature elevation, nor was it observed to cause hemorrhage. Immediately following this pulsed sonication, a 60–80 W continuous wave volumetric sonication was applied to the same location for 30 s. Six seconds prior to the sonication, a dynamic temperature monitoring sequence began, continued for the duration of the sonication, and continued to record temperature data for 60 s after the sonication ended. Dynamic temperature monitoring based on changes in proton resonance frequency [16] was performed using 2D fast field echo echo-planar imaging (EPI) (TR/TE = 38/20 ms, flip angle = 19.5°, EPI factor = 11, FOV = 200 × 200 mm, acquisition matrix = 100 × 100, reconstructed in-plane resolution = 1.25 mm, number of slices = 6, slice thickness = 7 mm, temporal resolution = 2.9 s/dynamic). Cumulative thermal doses were calculated based on the temperature data [17,18]. To avoid near field overheating, a minimum of 30 s wait time was used before marking the next spot, which was always at least 4 mm away from any other marks.

Marks observed by MRI, CT and US

To visualize the FUS marks on MRI, the same T2W imaging used in planning was repeated after all sonications. In addition, a fluid attenuated inversion recovery (FLAIR) sequence was acquired before and after marking (TR/TE = 11000/140 ms, inversion time = 2800 ms, flip angle = 90°, echo train length = 53, FOV = 230 × 230 mm, acquisition matrix = 256 × 200, in-plane resolution = 0.9 × 1.15 mm, slice thickness = 5 mm, NEX = 2).

Immediately after the MRI experiments, the rabbit was sacrificed. Sacrificed rabbits were then imaged using a clinical CT (Philips Brilliance Big Bore, Philips Healthcare, Cleveland, OH, USA) at 120 kVp, 395 mAs, contiguous 1 mm slices, typically 0.45 mm in-plane pixel size. Ultrasound imaging was performed using clinical ultrasound equipment (Acuson Sequioa, 15L8w-S, Siemens, Medical Systems, Mountain View, CA, USA). Five of the six rabbit subjects were available for US studies (due to scheduling conflicts one rabbit did not receive US).

Excision and visualization

Once all imaging was completed, dissection of the leg was performed to locate all successfully sonicated marks. Marks were excised with a margin of 5–10 mm normal muscle tissue and scanned digitally (Visioneer OneTouch 9420 USB, Visioneer, Pleasanton, CA, USA) to evaluate visual conspicuity.

For this study, conspicuity was defined using the International Commission on Illumination (CIE) $L^*u^*v^*$ color space (CIELUV) criteria, ΔE established for distinguishing color [19]. Briefly, red/green/blue color values can be converted to the LUV colorspace, and the value ΔE can be calculated describing quantitatively how well a sample color matches a reference color. A value of 0 is a perfect match, while anything less than 6 can only be distinguished by the naked eye if two colors are side by side. Previous work demonstrates that a CIELUV ΔE value of 12 can be detected in less than 5 s for a target object of the sample color on a solid reference background [20].

Image analysis

Data were processed and analyzed using either IDL (Exelis VIS, Inc., Boulder, CO, USA) or OsiriX (Pixmeo, Geneva, Switzerland). The marks seen on MRI and CT were located and contoured by a