Original Article

MR-guided focused ultrasound application for moving target tumor ablation in abdominal area: coil selection

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Senay Mihcin[1], Cesare Gagliardo[2], Patrizia Toia[2], Andrew Dennison[1], Jan Strehlow[3] and Andreas Melzer[1]

Abstract

Background: Magnetic Resonance Imaging (MRI)-guided Focused Ultrasound Surgery (MRgFUS) is a non-invasive thermal ablation method utilizing high-intensity focused ultrasound (HI-FU) energy for tissue ablation under MRI with real-time thermal mapping. Ablating to a dynamic target as in the liver is very challenging, requiring approval. A novel quality-assured liver tumor ablation system has been proposed for clinics. The paper reports the evaluation of conventional and new MR-receiving coils.

Purpose: To evaluate the suitability of MR coils as part of the MRgFUS treatment system for liver, while simulating breathing motion in pre-clinical settings.

Material and Methods: The novel software communicates with the MR scanner and the transducer. To monitor the temperature via proton resonance frequency (PRF) methodology echo planar imaging (EPI) sequence was used while the algorithms of static, static and dynamic tracking were tested with sonications of 100 W for 30 s on tissue-mimicking phantoms. Different coil sets were used to assess the performance of the system for fitness for dynamic thermometry. Finally, in vivo experiments were performed over a porcine model.

Results: Single-loop four-channel Duoflex and Gem coils provided adequate signal-to-noise ratio and contrast with consistent thermal readings. Body array coils showed severe loss of signal in dynamic cases since the integration of tracking algorithm causes low efficiency.

Conclusion: Body array coils are unsuitable for MRgFUS of the liver due to signal loss. The dedicated coil set with a single loop around the FUS transducer combined with four-channel arrays might be the best option for liver treatment using dynamic MRgFUS applications.

Keywords

Coils, magnetic resonance thermometry, tracking, echo planar imaging, magnetic resonance-guided focused-ultrasound surgery, CE marking, validation, verification

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Introduction

Treatment of hepatocellular carcinomas is very stage dependent. Surgical resection is the gold standard solution only for stage 0 disease (PST 0, Child-Pugh score A, with small nodules) in clinical practice (1). However, surgical resection of tumors has the associated risk of liver failure, due to the insufficient volume of liver tissue after surgery. Out of 5 million cases of liver cancer in the world, only 15%–30% are suitable for surgery (2). Hence, minimally invasive technologies are in demand for clinical applications. Magnetic

[1]IMSaT, Division of Imaging and Technology School of Medicine. University of Dundee, Dundee, UK
[2]Section of Radiological Sciences, Department of Biomedicine, Neuroscience and Advanced Diagnostics, University of Palermo, Palermo, Italy
[3]Fraunhofer Institute for Medical Image Computing MEVIS, Bremen, Germany

Corresponding author:
Senay Mihcin, Mechanical Engineering Department, Engineering Faculty, Izmir Institute of Technology, Urla, Izmir, Turkey.
Email: senaymihcin@iyte.edu.tr

resonance-guided focused ultrasound systems (MRgFUS/MRHiFU) have been CE (Conformité Européene) marked, and Food and Drug Administration (FDA) approved for the treatment of uterine fibroids, treatment of pain for bone metastasis, and a few functional neurological disorders so far (3–6).

Currently, the use of MRgFUS in clinical settings is at a pilot trial level in oncological units (3–6). The technology allows only for treatment in apnea. While the liver is maximally pushed out of the rib cage margin by a ventilator, under general anesthesia, sonicating a stationary tumor location in the lower liver segments (Fig. 1). The application is limited to the right lower lobe of the liver. Due to restrictions in positioning the ultrasound (US) beam and the tumor, the prolonged treatment time has inhibited the clinical translation. Only a very limited number of patients could benefit from this method (5).

MR-guided ablation of a moving target using free-breathing motion is a novel treatment system that has been designed to be tested with the intention of clinical use. The novel system is configured to execute sonication using a free-breathing motion without any anesthesia or contrast agents. Motion-tracking algorithms detect the motion of the liver using magnetic resonance imaging (MRI) (7,8). Active beam steering of the FUS phased array transducer allows the sonication of the targeted tumor area. Without tracking and beam steering, there is risk of ablation of healthy liver tissue (Fig. 2a). Via beam steering and tracking, acoustic energy is delivered almost exclusively to the target to achieve the desired level of temperature increase (Fig. 2b). The trans-coastal beam steering methodology prevents sonication of the ribs (Fig. 2c and 2d) (7,8). The skin burn problem due to sound reflection from the ribs during sonication is reduced so that correct dosimetry can be applied only to the tumor area. The regions which are normally covered under the ribcage during the free-breathing motion can be reached, enabling for wider range targets in the liver. Since the treatment can continue during free breathing, the full treatment time is reduced. The transducer is totally external to the skin surface; hence the system is fully non-invasive. In PRF thermometry, the sensitivity to the temperature change is lower when using clinical scanners (3-T) compared to the ultra-high field strength scanners (9). However, using a 1.5-T scanner, temperature changes can be measured with a good accuracy in phantoms and homogeneous tissue with 0.6°C and 1.5°C, respectively (10).

This novel motion-compensated FUS technique is designed for continuous sonication under the free-breathing motion. However, since the system delivers energy to the patient for ablation, the system's control software is classified as a class 3/C: high risk where serious injury or death could be possible based on the international standard IEC 62304. Currently, the control software has gone through a thorough design documentation and testing in silico (4,7,8,11,12) as well as in pre-clinical settings for validation with the aim of obtaining CE (Conformité Européene) marking for liver treatment at a component feature level. The treatment parameters were defined with specifications to evaluate energy delivery, sonication duration, temperature, and positional accuracy (11,12). The test protocols demonstrated that the software met the required specifications for safe use for power delivery and sonication duration (11,12).

The system requires the best set of MR coils arranged in optimum configuration to minimize the interference of the dedicated liver transducer in the MR scanner and to provide highest possible contrasts and signal-to-noise ratio (SNR). Standard MR coils (GE eight-channel body and cardiac arrays) are used for static MRgFUS treatment. As there were no dedicated MR coils available to use during sonication under the free-breathing motion for motion compensated MRgFUS treatment liver, we developed a single loop coil together with MR instruments (Minetoka,

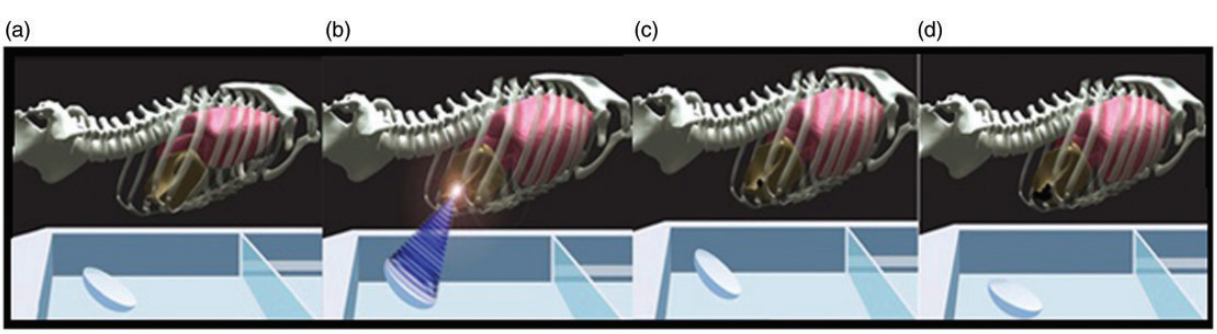

Fig. 1. (a) Liver inside the ribcage during inhale posture of the lungs; (b) liver maximum pushed out during exhale, only possible position to sonicate; (c) first ablated liver with coagulated tumor area; (d) liver with multiple number of sonication's to ablate the tumor fully (© Fraunhofer. MEVIS, Bremen, Germany).

MN, USA) that fits around the transducer to be combined with one or two four-channel 24×24 cm coil paddles. The aim of the present study was to evaluate the use of clinically approved set of coils to apply MRgFUS treatment over abdominal organs under a free-breathing motion through simulating a one-dimensional breathing motion first in vitro and then in vivo, based on the results of in vitro studies for optimum outcome.

Material and Methods

The experiments were planned in two sections: in vitro, over tissue-mimicking phantoms; and in vivo, animal experiments based on the evaluated results of the in vitro part.

Moreover, for usability and positioning of the coils with the transducers over human subjects, ethics committee permission was obtained. This was tested over three healthy volunteers as demonstrated in Fig. 3.

The novel software is installed on a dedicated workstation interacting with an MR scanner (GE Signa HDxt 1.5T, GE Medical System, Milwaukee, WI, USA) in real time to collect images, and plan and monitor the treatment. The motion compensated FUS works in a loop that starts with the acquisition of monitoring data. In the next stage, the imaging data are processed to extract the relevant information, e.g. temperatures or motion data. In the final stage of the loop, the results of the image analysis are displayed to the clinician and/or used to control therapeutic devices automatically. To enable an efficient intervention, our treatment aims at compensating the respiration-induced motion continuously and in real time. The system latency was calculated as 409 ms previously (12), for compensation to take place to predict the state of the patient at the time of therapy sonication.

The CE marked transducer of the ExAblate 2100 (InSightec Ltd., Tirat Carmel, Israel), Conformal Bone System (CBS), was utilized in this study. The transducer is driven by the software to execute the real-time ablations. For liver imaging, three-dimensional (3D) fast imaging employing steady-state acquisition (FIESTA), in the sagittal and coronal

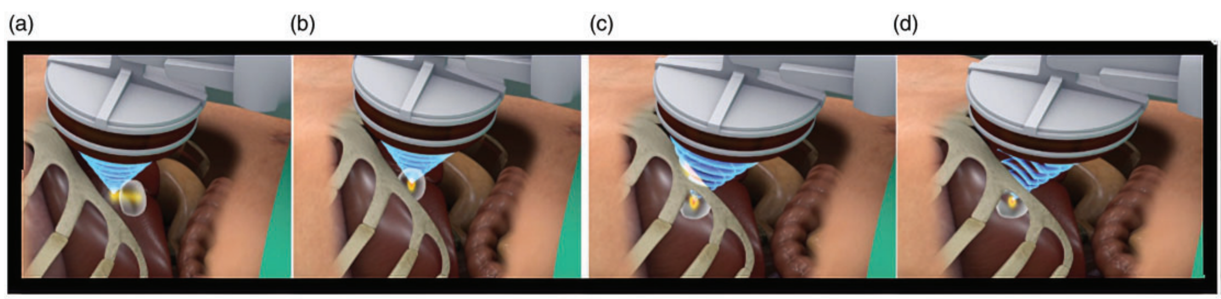

Fig. 2. (a) Sonication under the free-breathing motion without beam steering demonstrating sonicating to a healthy tissue; (b) sonication under controlled beam steering during the free-breathing motion; (c) sonication through ribcage resulting in undesired sonication of ribs and not efficient delivery of energy into the tumor area; (d) sonication by trans-costal beam steering by switching off selected elements of the transducer to avoid direct sonication to the ribcage.

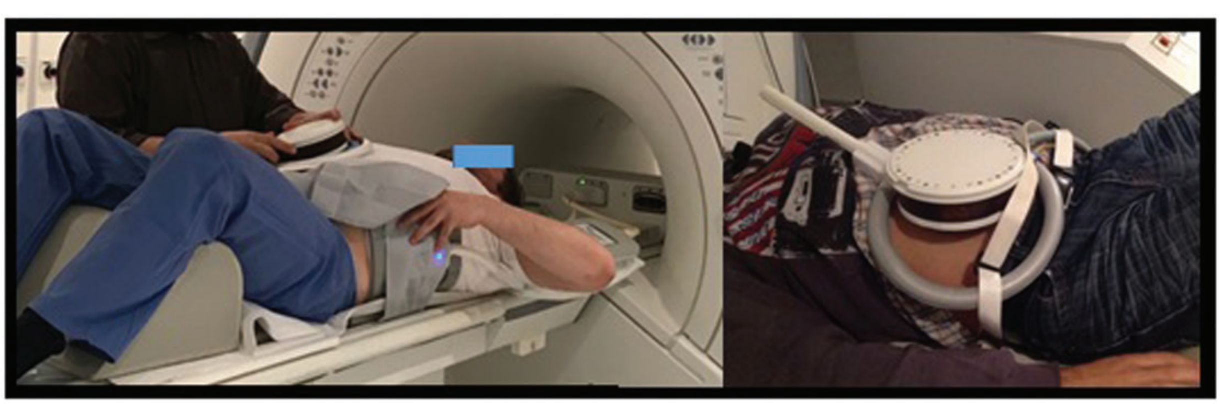

Fig. 3. The new single loop coil fitting around the focused ultrasound transducer. It can be combined with one or two 24×24 cm four-channel arrays.

planes (product PSD), is used (TR = 600 ms, TE = 1 ms, matrix = 192 × 192, flip angle [FA] = 40°). The planning imaging requires the calibration scan with 3D FIESTA, in the sagittal and coronal planes (TE = 1.3 ms, FA = 60°). Next, treatment-planning data are entered via a keyboard, consisting of sonication location, sonication duration, and sonication power information, for the control software. MR thermometry information based on proton-resonance frequency (PRF) is obtained by the use of single-shot echo planar imaging (EPI) with partial parallel imaging (GE's array spatial sensitivity-encoding technique [ASSET]) with the following imaging parameters: TR = 145 ms; TE min full = 38.2 ms; matrix = 96 × 96; frequency field of view (FOV) = 28 cm; phase FOV = 1.0; slice thickness = 3 mm; delay after each acquisition = 0.1 s; ASSET = 1; ramp sampling = on; maximum monitoring time (512 phases per location with interleaved phase acquisition order) = 125 s.

In the present study, thermal readings were used to evaluate the ablations. These readings were assessed under three different conditions: first, sonicating to a static target with no tracking option; second, to a static target with tracking algorithm enabled; and, finally, on dynamic targets with tracking algorithm activated. In addition to this, a code was written in MATLAB to calculate the SNRs and peak SNR by calculating the difference in signal intensity between the region of interest (ROI) and the background image.

In vitro phantom tests

A novel phantom, providing both temperature information and detecting a sufficient number of landmarks for the tracking algorithm, was developed. For measuring thermometry and observing coagulation procedure, the middle part of the phantom consisted of polyacrylamide (PAA) egg white material surrounded by 2% agar and samphire to replicate the vein structure of liver. EPI was used during sonication to provide real-time thermometry information using a 1.5-T GE Scanner.

Four different sets of coils were selected during the in vitro experiments: cardiac coils (8 Channel, GE Signa, WI, USA), interventional DuoFlex coils (single loop and 2 × 4 channel arrays, MR Instruments, MN, USA), Gem Flex coils (8 channel, NeoCoil, WI, USA), and torso coils (8 Channel, GE Signa, WI, USA). The proposed coils could be aligned in different orientations during the application of the surgery. These are grouped as coils which are positioned: group A = parallel to the axis of the FUS path; and group B = perpendicular to the axis of FUS path (Fig. 4). Due to their orientation during sonication, interventional Duoflex coils (single loop and 2 × 4 channel arrays, MR Instruments, MN, USA) and Gem Flex coils (8 channel, NeoCoil, WI, USA) are classified in group A. Torso coils and cardiac coils (8 Channel, GE Signa, WI, USA) fall into group B as they are positioned perpendicular to the FUS path.

To monitor thermometry, 100 W of sonication power for 30 s was applied. This procedure was repeated three times for each coil sets by giving 30-min breaks for the cool-down process.

To simulate the breathing motion, a phantom set-up was moved within a 20–30-mm range by using the INNOMOTION Robotic arm (IBSmm, Brno, Czech Republic) (13). A special phantom holder was designed to provide the linear motion with the robotic arm while sonicating using the transducer of CBS. The phantom was placed on a custom-made phantom holder. The distance between the coils was designed to be 127 cm. The experiment set-up is as shown in Fig. 5 for the coil sets in group A.

For the coil sets in group B, the motion was provided using an air ventilator mechanism to push (inhale) and pull (exhale) the phantom to be able to perform the scan. An air ventilator was programmed to inhale for 2 s, then exhale 4 s. The flow rate was set as 0.75 L/s at 1 atm. The air ventilator inflated the air balloon (inhale phase) which pushes the phantom block, then the water balloon produces a returning spring force at ventilator (exhale phase), simulating respiratory motion at controllable rates. Below the eight-channel torso coils (GE, Signa, WI, USA), configuration B is assembled with the respiratory motion simulator model (Fig. 6). The difference between the robotic arm and air ventilator mechanism is their capacity to allow for parallel and vertical positioning of the coils with respect to the sonication path in one-dimensional breathing activity simulation.

In vivo animal tests

To evaluate the safety and the technical efficacy of generating predefined necrotic lesions in the healthy animal liver, a swine model was utilized. The ongoing animal trial (swine model) makes use of supine positioning (feet first) and a coil set-up as in human trials. A set of DuoFlex coils was used for liver imaging, procedure planning, and thermal monitoring. The DuoFlex (four channels, 24 × 247 cm) was placed on the right side of the animal and the single loop coil (one channel, 237 cm) concentrically around transducer, that is positioned on the animal's abdomen. Anatomical pre-procedural imaging included a fast 3D fast spoiled gradient echo sequence (Liver Acquisition with Volume Acquisition, LAVA Sequence details; Fig. 9) that was repeated after the administration of i.v. contrast medium at the end of

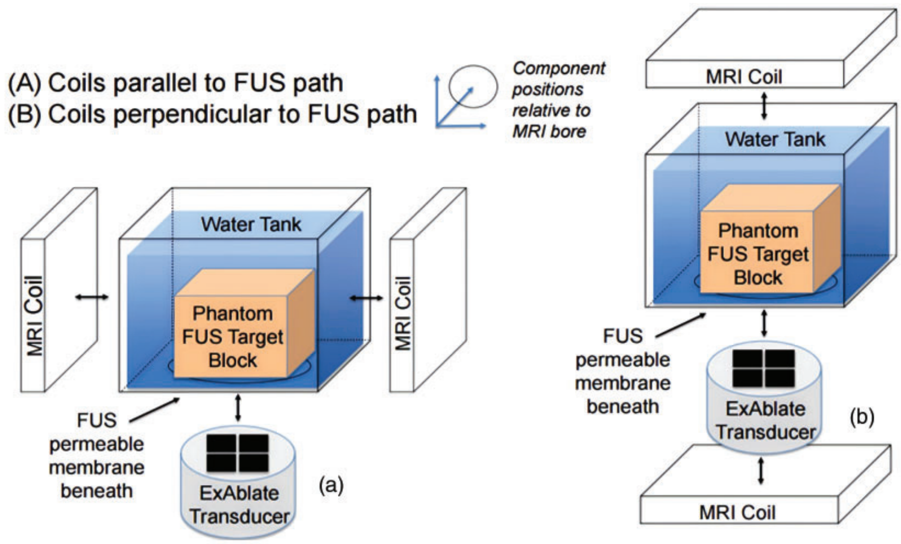

Fig. 4. Classification of MR coils during MRgFUS according to their orientation during the application of MRgFUS: (a) in parallel configuration to the axis of the beam; or (b) in perpendicular configuration to the axis of the beam. MRgFUS, magnetic resonance imaging-guided focused ultrasound surgery.

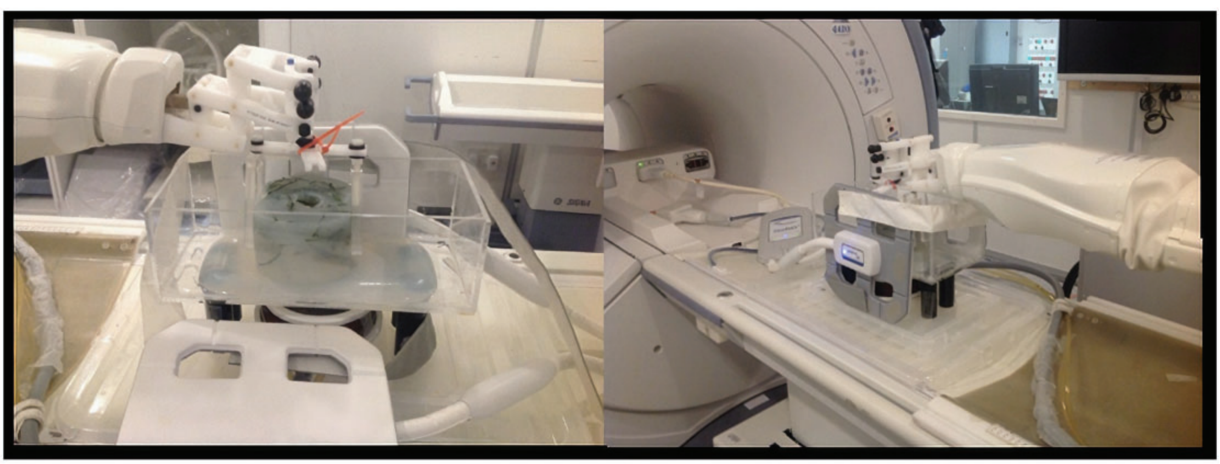

Fig. 5. Experiment set-up showing the phantom which includes vein mimicking samphire structure on the left image inside the custom-made phantom holder, and the robotic arm while using four-channel DuoFlex coil arrays (© IMSaT, Dundee, Scotland, UK).

the MRgFUS experimental procedure for liver lesion identification.

The procedure planning was performed using 3D FIESTA in the sagittal and coronal planes (product PSD; TR = 600 ms, TE = 1 ms, matrix = 192 × 192, FA = 40°). The planning imaging requires the calibration scan with 3D FIESTA in the sagittal and coronal planes (TE = 1.3 ms, FA = 60°) and related multiplanar reconstructions (MPRs) that enabled the expected anatomical details along the entire path of the HI-FU beam for procedure guidance. Thermal monitoring was based on two-dimensional EPI imaging (TR = 145 ms, TE min full = 38.2 ms, matrix = 96 × 96, frequency FOV = 287 cm, phase FOV = 1.0, slice thickness = 3 mm, delay after each acquisition = 0.1 s, ASSET = 1, ramp sampling = on, maximum monitoring time [512 phases per location with interleaved phase acquisition order] 125 s), which allowed a proper spatial, contrast, and temporal resolution for procedure monitoring.

Results

During the in vitro executions, thermometry readings from the images were collected in Excel spreadsheets

Fig. 6. (a) Experiment set-up showing the phantom which includes vein mimicking samphire structure on the left image inside the custom-made phantom holder, including a water balloon and air bag, which is connected to the air ventilator to push the phantom to simulate the breathing motion. (b, c) Images of the 8 Channel Torso Coils including the CBS transducer inside the assemble for sonication side and orthogonal views, respectively (© IMSaT, Dundee, Scotland, UK).

Table 1. Coil sets and collected temperature values (in °C) in in vitro experiments.

	Experiment conditions		
Coil sets	Static mode	Static with tracking algorithm	Dynamic with tracking algorithm
Torso (GE, USA)	8.4 ± 1.0	7.7 ± 0.5	2.6 ± 0.3
DuoFlex Coil (MR Instruments, USA)	15.6 ± 0.3	13.4 ± 0.6	15 ± 0.2
Gem Flex (NeoCoils, USA)	16.5 ± 0.4	15 ± 0.5	15.4 ± 0.3
Cardiac Coils (GE, USA)	16.3 ± 0.3	15.6 ± 0.4	15.4 ± 0.2

Values are given as mean ± SD.

for each scan completed with each coil set. Mean and SD values were calculated as shown in Table 1.

The results show that the readings from the scans of torso coils demonstrate very low temperature values when compared to other coil sets. Fig. 7 shows a reading collected while scanning with torso coils. The first image is a reading collected while in static mode, the second reading is collected in static mode but with the tracking algorithm on. The final reading is completed when there is a motion induced by air pump, simulating a breathing motion with the tracking algorithm on. The difference in static readings and the dynamic reading show that Torso (GE, USA) coils result in low thermometry readings even if the thermal values are high. The remaining coil sets produced similar and consistent temperature ranges.

The SNR depends on the field strength, coils, and the subject under investigation in the MR image. In our experiments, field strength was 1.5 T for MRgFUS applications. RF transmitter and receiver coils, available as a part of clinically available MR systems, were assessed for SNR in vitro. SNR values were calculated for each coil sets using the code written in MATLAB and listed in below (Table 2). Since SNR values are sensitive to the distance between the coils in in vitro experiments, this distance was kept constant (17.57 cm) by using a custom-made phantom holder during the experiments.

Discussion

To apply MRgFUS for the liver, a novel system is required. For this, the system controller has been validated. The coils and the FUS transducer are the subcomponents of the system. For correct dosimetry and safe monitoring of the system, coil sets play a crucial role. It is very important to test and provide evidence of which coil sets and their spatial orientations are the best for correct monitoring and dosimetry for the safety of the patients. For this reason, available coil sets were investigated in connection with their alignment to the FUS transducer. The thermometry monitoring results show that it is best to avoid Torso (GE, USA) coil sets for the treatment of liver tumors via MRgFUS. The other three coil sets produce comparable results with each other. Cardiac coil (8 Channel, GE, USA), Gem Flex coil (NeoCoils, USA), and DuoFlex coil sets (MR Instruments, USA) were evaluated to be suitable. It has been noted that with the tracking algorithm enabled in static mode, there is a drop in the efficiency. However, this is part of another investigation that is not within the scope of this paper.

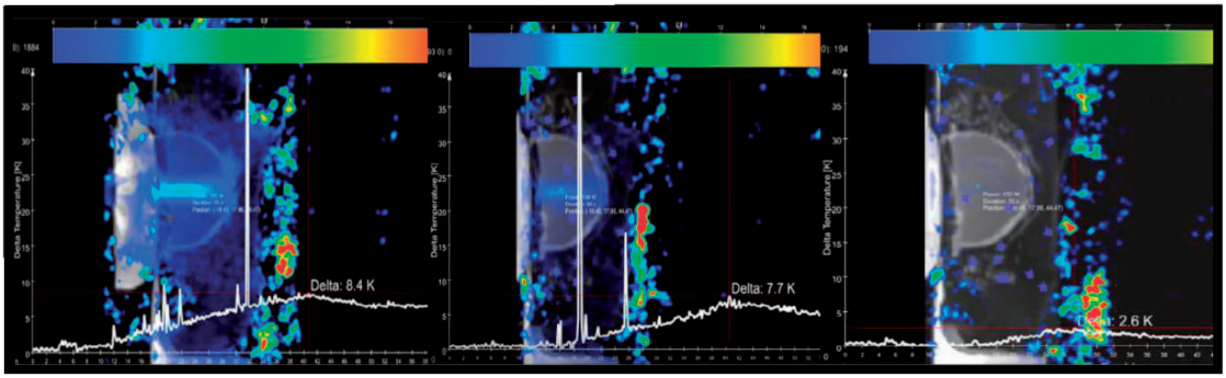

Fig. 7. Thermal images collected using Torso (GE, USA) coil sets, in static, static tracking, and dynamic tracking algorithms (© IMSaT, Dundee, Scotland, UK).

Table 2 Torso coil SNR values as calculated from the treatment monitoring images.

Coil sets	Calculated SNR values with each coil sets in vitro
Torso (GE, USA)	4.15 ± 0.6
DuoFlex Coil (MR Instruments, USA)	8.15 ± 0.4
Gem Flex (NeoCoils,USA)	7.9 ± 0.2
Cardiac Coils (GE, USA)	5.5 ± 0.3

Values are given as mean ± SD.
SNR, signal-to-noise ratio.

Field strength and SNR are directly proportional to each other. In this study, 1.5 T was the field strength, but it is expected that 3 T and 7 T scanners can provide higher SNR values. Results show that Duoflex coils showed the best SNR value at 1.5 T, which can produce better SNR values at higher field strengths such as 3 T or 7 T. However, since scanners have a fixed field strength, we prefer a better configuration and coil design which can produce more reliable images for the treatment of liver for MRgFUS applications.

Moreover, during the in vitro experiments, MR images were observed to be highly sensitive to the mechanical vibrations produced by the FUS transducer during sonication, resulting in interference with the image quality. To avoid any interference, we conclude that MR coils should not be resting on the transducer. Even if the base of the transducer (where electrical circuits are placed) is MR compatible, due to physical vibrations during the sonication, the MR images might contain noise and imagining artefacts. To avoid this problem, it is best to locate the transducer's base in the loop of the coil sets. This allows closest proximity of the coil to the target region for the best SNR. For this reason, a new set of dedicated MR coil sets seems to be the best solution for liver treatment while applying MRgFUS technique.

This coil set lies immediately around the base of the transducer fitting into the rim of the transducer to reduce the transfer of vibration and imaging artefacts. The configuration uses DuoFlex 24 cm square on one side and the MR instruments interventional 23 cm single loop around the transducer, without causing any imaging artifacts (Fig. 8).

Based on this optimum configuration, in vivo trials on animals were completed with a CE approved coil set-up but without the updated GE product key for using the single loop coil. Images from the in vivo experiments (Fig. 9) show the anatomical pre-procedural imaging, planning, and treatment imaging as described. This configuration eliminated the mechanical vibrations and provided improved image quality. The SNR value was calculated as 9.7 ± 0.2. The thermal readings were consistent with the other coil sets.

In conclusion, in the present study, we have provided a detailed investigation on the suitability of the MR coils for the application of MRgFUS for liver treatment. The analysis shows that the distance between the channels and the target depth is a very important parameter. Not all the coils are suitable for this treatment methodology. Although Cardiac coils (8 Channel, GE, USA), Gem Flex coils (NeoCoils, USA), and DuoFlex coils (MR Coils, USA) provide reliable and comparable images and thermal readings, due to the problems such as MR interference and image artefact risks, the proposed coil system and the configuration for the liver while applying MRgFUS is observed to improve the reliability of the application as a novel system to be used in clinics, eliminating interference-related noise problems. The in vivo results with the proposed dedicated coil set demonstrated an

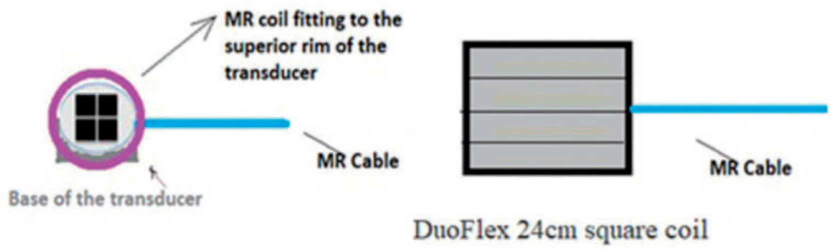

Fig. 8. Schematic view of the MR instruments interventional 23-cm single loop resting around the focused ultrasound transducer and DuoFlex 24 cm square coil system to be used in MRgFUS applications (© IMSaT, Dundee, Scotland, UK). MRgFUS, magnetic resonance imaging-guided focused ultrasound surgery.

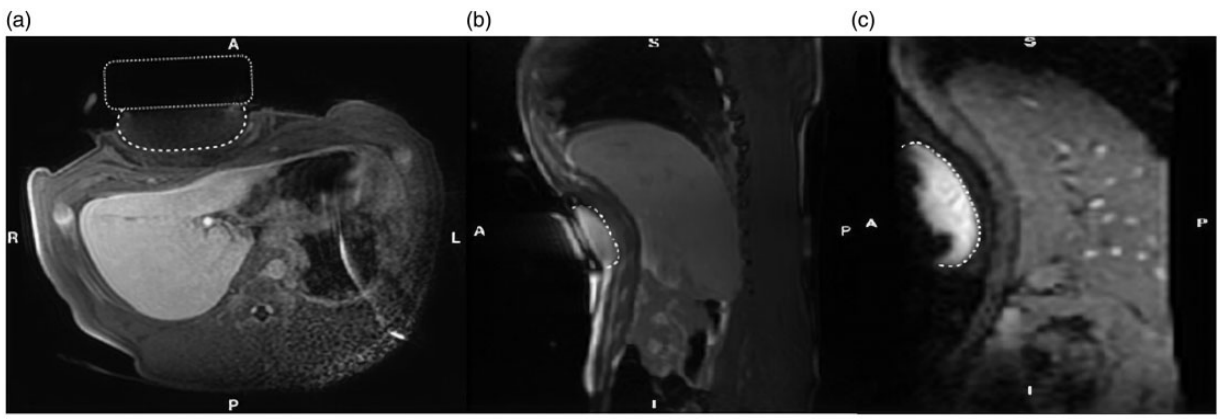

Fig. 9. (a) Animal experimental session (female swine weighing 65 kg in supine feet first position): breath-hold LAVA axial scan acquired after 2 mL/kg of gadobenate dimeglumine. The superimposed dotted square indicates the position of the HI-FU transducer while the dotted dome refers to the water filled membraned that ensure an optimal transducer-to-animal coupling. Using the optimal coil set-up (DuoFlex 24 cm square on the right flank on the right side of the animal and the 23-cm single loop on the abdomen around the transducer) the imaging quality of the region of interest is very high. (b) Animal experimental session (female swine weighing 76 kg in supine feet first position): breath-hold 3D FIESTA sagittal scan (GE 1.5-T HDx). The superimposed dotted dome refers to the transducer's water-filled membrane, enabling a very high imaging quality of the region of the liver and surrounding tissues. (c) Animal experimental session (same animal and coil set-up): EPI sagittal scan used for real-time thermal monitoring and motion compensation algorithm (© University of Palermo, Palermo, Sicily). EPI, echo planar imaging; HI-FU, high-intensity focused ultrasound.

elimination of vibrational problems, related imaging artefacts, and a high imaging quality.

Authors' note

Senay Mihcin is also affiliated with Mechanical Engineering Department, Engineering Faculty, Izmir Institute of Technology, Urla, Izmir, Turkey.

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ORCID iDs

Senay Mihcin https://orcid.org/0000-0001-5077-8927
Cesare Gagliardo https://orcid.org/0000-0003-4088-2020

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