Project Acronym:
FUSROBOT (ENTERPRISES/0618/0016)

MRI-guided Focused Ultrasound Robotic system for preclinical research.

Deliverable number: 2.3

Title: Presentation at a scientific conference

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Date: 21/12/2020
Submitted Abstract:

MRI-guided Focused Ultrasound Robotic System for Preclinical Use

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Abstract—Magnetic resonance-guided focused ultrasound (MRgFUS) has been demonstrated as a promising treatment modality. A robotic device with 4 degrees of freedom intended for preclinical applications of MRgFUS has been developed. It employs a 1.1 MHz transducer, and thus it is suitable for percutaneous ablation of deep tissue, drug delivery, and blood brain barrier opening. The performance of the device in terms of MR-compatibility, positioning accuracy, and reliability was evaluated in agar-based phantoms, excised tissue, and in vivo thigh tissue of rabbit models in both laboratory and MR environments. The average positioning error was measured utilizing a specially designed structure with an integrated digital caliper and found to be 0.11 mm. Its functionality in terms of temperature evolution during high intensity focused ultrasound exposures was demonstrated utilizing MR thermometry. Well-defined cigar-shaped lesions arranged in discrete and overlapping patterns were produced successfully. Accordingly, in vivo experiments resulted in local coagulative necrosis without destructing healthy intervening tissues. Overall, the device maintains high standards of animal welfare. It can be safely operated inside the scanner of any commercial MR imaging system up to 7 T to treat small animals. In the future, the device could be scaled up to manage abdominal cancer in humans.

Key words: MRgFUS, preclinical, rabbit ablation, robotic system

Acknowledgements
The work was funded by the Research Promotion Foundation of Cyprus under the project FUSROBOT (ENTERPRISES/0618/0016).
MRI-guided Focused Ultrasound Robotic System For Preclinical Use

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INTRODUCTION

- A **Magnetic Resonance guided Focused ultrasound (MRgFUS)** robotic device has been developed.

- Preclinical use on excised tissue, phantoms and small animals (mice, rats, cats, rabbits and small dogs).

- Motion in 4 PC-controlled axes.

- The device can fit in the table of any commercial MRI scanner up to 7 T.

Figure 1: Animal configuration on robotic device.
4-DOF ROBOTIC DEVICE

- 3D printed (FDM 400, Stratasys, Minnesota, USA) with Acrylonitrile Butadiene Styrene (ABS).

- Motion in 3 linear (X,Y,Z) and 1 angular (Θ) axes.

- Motion actuated by piezoelectric motors (USR30-S3N, Shinsei, Tokyo, Japan).

- Motion control achieved with optical encoders (US Digital Corporation).

- Dimensions: 57 cm (L) x 21 cm (W) x 11.5 cm (H).

Figure 2: CAD drawing of the robotic device A) external and B) internal view.
FUS TRANSDUCER

- Simulations of power field and heating effects of beam performed to find optimal transducer characteristics.

- Two transducers manufactured with piezoceramic material in ABS holder.

- **Non-magnetic materials** for operation inside MRI.

- Frequency: **1.1 MHz** for deep targets (Radius of curvature: 100 mm, Diameter: 50 mm).

- Frequency: **2.58 MHz** for shallow targets (Radius of curvature: 61 mm, Diameter: 38 mm).

Figure 3: Photo of the manufactured transducer.
SYSTEM EVALUATION
MRI COMPATIBILITY OF TRANSDUCER

- Assessed using FSPGR sequence in a 1.5 T MR system (Signa, General Electric, Fairfield, CT, USA) using a GPFLEX coil (USA instruments, Cleveland, OH, USA).
- Measurement of the SNR in a phantom (6 % w/v agar and 30 % v/v evaporated milk).
- SNR measured for different activation conditions of transducer and amplifier.
- SNR drop during activation proves transducer and amplifier compatibility.

Figure 4: SNR using TI-SPGR sequence measured for various activation conditions.
SYSTEM EVALUATION
MRI COMPATIBILITY OF THE ROBOTIC DEVICE

- Assessed using T2-FRFSE, FSPGR and EPI sequences in a 1.5 T MR system (Signa, General Electric, Fairfield, CT, USA) using a GPFLEX coil (USA instruments, Cleveland, OH, USA).
- Measurement of the SNR in an MR quality phantom.
- SNR measured for different activation conditions and sequences.
- T2-FRFSE resulted in largest drop in SNR.

Figure 5: SNR for three MR imaging protocols for various activation conditions of robot.
SYSTEM EVALUATION

MOTION ACCURACY OF THE ROBOTIC SYSTEM

- Use of special structures designed for securely mounting the digital calipers on the motion stages.
- Motion commands through specially designed software.
- Forward and reverse movement of the robotic device in X, Y, and Z axes in 1 mm, 5 mm, and 10 mm steps.
- Clockwise (CW) and counterclockwise (CCW) rotation by 1°, 5°, and 10°.

Figure 6: CAD design of the experimental set-up for evaluation of accuracy.
SYSTEM EVALUATION

MOTION ACCURACY OF THE ROBOTIC SYSTEM

- Distance measured with caliper compared with distance set in software.
- Motion in linear axes resulted in a greatest error of 0.1 mm.
- Smaller errors in larger distance steps.
- Typical speed of motion in Y axis (3.0 mm/s) almost double than X axis (1.6 mm/s).
- Typical speed of motion in Z axis (7.8 mm/s) almost five times higher than X axis (1.6 mm/s).
- Typical angular speed: 40°/s.

Figure 7: Measured distance versus intended distance for the X axis forward motion.
MRI EVALUATION OF THE THERMAL HEATING OF THE TRANSDUCER
MR THERMOMETRY

Uses the proton resonance frequency shift equation:

\[ \Delta T = \frac{\phi(T) - \phi(T_0)}{\gamma \alpha B_0 T E} \]

Colour-coded temperature maps:

Figure 8: Typical MR thermometry maps acquired during ablation.
MRI EVALUATION OF THE THERMAL HEATING OF THE TRANSDUCER IN TISSUE MIMICKING PHANTOM

- Development of a tissue-mimicking phantom (6 % w/v agar and 30 % v/v evaporated milk).
- Placement of transducer and phantom inside MRI scanner.
- Beam targeting confirmed using MR thermometry.
- Recorded temperature change of 24.83 °C using 2.58 MHz at 6.4 W for 60 s.

Figure 9: T2-W FSE image (axial plane) of the experimental set up.

Figure 10: Thermal map recorded for 2.58 MHz on A) coronal and B) axial plane.
MRI EVALUATION OF THE THERMAL HEATING OF THE TRANSDUCER IN EXCISED PORCINE TISSUE

- **Use of high energies for lesion formation**

- 1.1 MHz transducer created 44 mm long cigar shaped lesion at 63 W for 30 s.

- Maximum temperature elevation at transducer surface of 7 °C.

Figure 11: Thermal map recorded on axial plane during sonication.

Figure 12: A) MR image of the formed lesion (axial plane) and B) Photo after dissection.
EX VIVO EVALUATION OF THE SYSTEM

- Robotic movement of the transducer in grid patterns.
- Discrete and overlapping lesions in porcine tissue.

Figure 13: Experimental set up for ex vivo ablation.
EX VIVO EVALUATION OF THE SYSTEM

- 1.1 MHz transducer

Discrete cigar shaped lesions
- 59 W for 15 s
- 2 x 4 grid (5 mm step)

Overlapping lesions
- 59 W for 10 s
- 3 x 6 grid (3 mm step)

- 67 W for 10 s
- 3 x 6 grid (3 mm step)

Figure 14: Dissected tissue with lesions formed in plane parallel to the beam for several sonication parameters.
**IN VIVO EVALUATION OF THE SYSTEM**

- All experiments were approved by the authorities of the Veterinary Services, Ministry of Agriculture (CY/EXP/PR L7/2019).
- **Thigh ablation** in **20 rabbits** in vivo.
- Robotic movement of the transducer in **grid patterns**.
- **Real-time MR thermometry** monitoring.
- High resolution images of the ablated area.

Figure 15: Animal positioning in the laboratory setting.
IN VIVO EVALUATION OF THE SYSTEM
MRI SETTING

- Placement of rabbit above the transducer in high resolution MR images.

- **Real-time MR thermometry** during in vivo ablation.
- Sufficient heating was confirmed.

2.58 MHz transducer
27 W for 60 s
Temperature change of 40 °C (at 60 s)

Figure 16: T2-weighted Fast Recovery Fast Spin Echo (T2-FRFSFSE) axial image of the transducer and rabbit.

Figure 17: Thermal maps obtained in sagittal plane using Echo-planar imaging (EPI).
IN VIVO EVALUATION OF THE SYSTEM
MRI SETTING

- High resolution MR images during in vivo ablation in a grid.
- 2.58 MHz transducer
- 27 W for 60 s
- 3x3 grid pattern (5 mm step)
- Lesion formation was confirmed.

Figure 18: Series of T2-FRFSE coronal images of the ablation pattern.

Figure 19: T2-FRFSE axial image with fat suppression of the ablated area.

Figure 20: Capture of the dissected tissue.
**IN VIVO EVALUATION OF THE SYSTEM**

- **2.58 MHz**
  - discrete tadpole shaped lesions.
  - Sonications at 15.6 W for 30 s
  - 3-point grid (10 mm step, 10 mm focal depth)

- **overlapping lesions.**
  - Sonications at 29.9 W for 30 s
  - 3 x 3 grid (4 mm step, 10 mm focal depth)

![Figure 21: Formed lesions A) in a plane perpendicular to the beam, B) in a parallel plane (after dissection).](image1)

![Figure 22: Formed lesions A) in a plane perpendicular to the beam, B) in a parallel plane (after dissection).](image2)
IN VIVO EVALUATION OF THE SYSTEM

- **1.1 MHz**
- **overlapping lesions.**
- **Sonications at 74 W for 8 s**
- **32-point grid (3 mm step, 20 mm focal depth)**
- **15 mm of unaffected tissue, followed by lesion of 20 mm length.**

Figure 23: Formed lesions A) in a plane perpendicular to the beam (absence of lesion), B) in a plane parallel to the beam (arrow) after dissection.
SUMMARY

- Development of a **4-DOF robotic device** for preclinical use of MRgFUS.
- The positioning device is **MR compatible** and maintains **high accuracy of motion**.
- **Efficient performance** evidenced by evaluation of the system in agar phantoms, excised pork tissue, and rabbits.
- The system maintains **high standards of animal welfare**.
- Its simple design makes it **portable** and **cost-effective**.
- It can be **used in any MRI** up to 7 T.
- Size modification for **future use in humans** for treating abdominal cancer.

Figure 24: A) Animal configuration on robotic device, B) Photo of the robotic device.
Acknowledgements

FUNDED BY:

PROTOCOL NUMBER: ENTERPRISES/0618/0016

PARTNERS:

Cyprus University of Technology