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MRI-guided Focused Ultrasound Robotic system for preclinical research

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Prepared by:

Marinos Giannakou (MEDSONIC)
Theocharis Drakos (MEDSONIC)
Christakis Damianou (CUT)

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MRI-guided focused ultrasound positioning system for preclinical studies in small animals.

T. Drakos[a], M. Giannakou[a], G. Menikou[b], C. Damianou[b]

a MEDSONIC LTS, Limassol, Cyprus

b Electrical Engineering Department, Cyprus University of Technology, Cyprus,

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ABSTRACT

Background: A positioning device compatible with magnetic resonance image (MRI) utilized for preclinical studies in small animals was developed that fits in MRI scanners up to 7 T. The positioning device was designed with two computer controlled linear stages.

Materials and Methods. The positioning device was evaluated in an agar-based phantom which mimics soft tissues. Experiments with this positioning device were performed in an MRI system using the agar-based phantom. The transducer used has a diameter of 50 mm, operates with 0.5 MHz, and focuses energy at 60 mm.

Results: The functionality of the positioning device was evaluated by means of MR thermometry, demonstrating sufficient heating and accurate motion in both axes of operation.

Conclusions: The proposed system fits in MRI scanners up to 7 T. Because of the size of the positioning device, at the moment it can be used to perform preclinical studies on small animals such as mice, rats and rabbits.

Keywords: mouse, ultrasound, MRI, positioning.

INTRODUCTION

The concept of magnetic resonance guided focused ultrasound (MRgFUS), was reported in 1992 by Hynynen et al. [1]. In this first report, it was shown that focused ultrasound (FUS) can be applied inside a magnetic resonance imaging (MRI) scanner and it was demonstrated that that the contrast between necrotic tissue and normal tissue was excellent.

This interesting result motivated researchers to develop positioning devices to navigate ultrasonic transducers. The first robotic systems used hydraulic principles [2-4] (applying pressure to water in flexible tubes) in order to achieve motion. However the hydraulic robotic systems had serious accuracy problems, and as a result these were eventually abandoned.

The Israeli company Insightech (Tirat Carmel, Israel) produced the first commercial MRgFUS robotic system. The Insightec system uses piezoelectric motors to move the various motion stages. The origigal system focused on the treatment of uterine fibroids [5], and adenomyosis [6]. The Insightec system received the Food and Drug Administration (FDA) approval in 2004. The InSightec system was upgraded in the following years for other applications such as the treatment of prostate cancer [7], liver cancer [8], breast cancer [9], pain palliation of bone metastases [10], [11], and for the treatment of essential tremor [12].

Philips Healthcare (Best, the Netherlands) also joined the area of MRgFUS [13] by developing the commercial device Sonalleve. This MR guided robotic system is a 5 degree of freedom (DOF) positioning system and is integrated with the focused ultrasound transducer on the patient’s table. Sonalleve MRgFUS, received CE mark for clinical use for fibroid treatment and non-invasive palliative pain treatment of bone metastases.

Thus, the technology of MRgFUS has matured by now since commercial products are available for many applications. Therefore, there is a demand for exploring new applications in the area of MRgFUS. The new applications require the experimentation in animal models. Thus, there is a great demand for positioning devices for preclinical studies. One of the first positioning devices was reported by the team of Chopra [14] that developed an MRI-compatible three-axis robotic FUS system for small animals. Later, FUS instrument commercialize this device for use in small animals [15].

The European company MEDSONIC developed several robotic systems for animal use. One such system was developed for use in the rabbit brain [16], [17]. Another system was dedicated for MRgFUS preclinical use for prostate [18], [19] using a transrectal ultrasonic transducer. These two systems included a linear stage and an angular stage. The positioning device proposed in these two articles [4], [19] can be placed on the table of the MRI scanner.

The French company Image Guided Therapy (Pessac, France) [20] developed also an MRgFUS system for small animal experiments. Finally InnoMotion (InnoMedic GmbH, Herxheim, Germany) developed a positioning device that can be used to hold a FUS transducer. Their robotic system was originally designed for MR-guided biopsy [21] and uses five degrees of freedom (DOF) pneumatically driven stages.

The main goal in this study was to develop a positioning device that can be used for preclinical studies using MRgFUS for small animals (for example mice, rats and rabbits). The previous positioning device developed by our group [22] was also dedicated for small animals, but its size was such that it could only fit in 1.5 or 3 T MRI systems. The proposed system is reduced in size in order to fit in a 9.4 T preclinical system (bore diameter= 17 cm).

The proposed positioning device may carry a single element transducer up to a diameter of 100 mm. Based on the size of the robot and targeted animals, the maximum radius of curvature that can be used with this system is 60 mm. Due to the fact that small animals will be used there is no need for a X axis. Therefore 2 linear stages are needed (Z and Y). The advantage of using the proposed system over the phased array (electronic steering of the focus) is that the focus is steered mechanically making the system less complex and thus inexpensive. Since the size of the animals that can be used is small, it is possible to achieve trans cranial penetration in the animal with the use of a single element transducer.

MATERIALS AND METHODS

Mechanical design of the positioning device.

The positioning device includes 2 computer-controlled axes (Z and Y in MRI). Fig. 1 shows the CAD drawing of the linear axis for motion along the MRI Y axis. The Y-plate was coupled to a threaded plastic screw which was attached to the shaft of a piezoelectric motor (USR 30-S3, Shinsei Kogyo Corp., Tokyo, Japan). The rotation of this shaft converts the angular motion to linear. An encoder plastic strip was placed in the Y-axis frame and moves inside the encoder module (US Digital Corporation, Vancouver, WA 98684, USA) which is not visible in this drawing. The encoder module EM1-0-500-I (US Digital Corporation) was used for both stages. The encoder output is connected to the counter input of a data acquisition board USB 6251 (National instruments, Austin, Texas, USA). Fig.2 shows the placement of the encoder modules in one of the linear stages. Fig. 3 shows the photo of the developed Y-stage.

Compared to our previous small animal positioning device [22] the main difference was the size of the motor which is smaller in the current device (almost 50 % smaller). This enabled us to design a smaller size positioning device. The Z-axis stage was coupled to the Y-axis using a simple structure as shown in Fig 4. The principle of movement of the Z stage and its range was the same as the Y-stage. The placement of the encoder followed the same technique as the Y-stage. The transducer arm was coupled to the Z-axis plate as shown in Fig. 4. The transducer was immersed in a container which was filled with degassed water.

The transducer material was made out of P762-type piezoceramic (Ferroperm, Kvistgaard, Denmark). A backing material (epoxy) withstanding 100 ^{o}C was used as a backing material for the transducer element. The transducer's impedance was matched to 50 Ω. To reduce the transmission of high frequency harmonics, a custom made low-pass filter was used (10 MHz cut-off frequency).

The positioning device was designed using the software Microstation (V8, Bentley Systems, Inc.). The positioning device was manufactured with a 3D printer (FDM400, Stratasys, 7665 Commerce Way, Eden Prairie, Minnesota, 55344, USA) using Acrylonitrile Butadiene Styrene (ABS) material.

The positioning device can be placed on the table of any commercial MRI scanner except the 9.4 T scanner. It has a maximum height of 7 cm, a length of 40 cm, and a width of 15 cm. The motion range of the robot was 6 cm for both axes. The positioning device weights around 2.3 kg. Fig.5 shows the interior of the positioning device, and fig 6 shows the complete robotic system.

Mouse holder

To prevent motion of the mice a specially designed holder was developed. When the mouse is positioned in supine position, sideways movable holders are pushed towards the mouse preventing any mouse movement (fig. 7). Fig.8 shows the photo of the mouse as placed in the experimental setting.

Software

A user-friendly program written in C # (Visual Studio 2010 Express, Microsoft Corporation, USA) has been developed in order to control the positioning device. The software has the following functionalities: a) Communication with MRI, b) movement of the 2 axes either manually or automatically by specifying the algorithm [23], the step and the number of steps, c) MR thermometry, and d) ultrasound control (frequency, power, sonication time etc).

Electronic system

The metallic enclosure hosting the motor drivers was placed outside the MRI room. The enclosure includes a DC supply (24 V, 2 A) which drives the Shinsei motors. Wires connect the motor drivers and a data acquisition interface card (USB 6251, NI) via a connecting block. The USB 6251 interface card includes timing and digital I/O modules. The motors were driven when the ground and clockwise terminals of the motor drivers were connected to the same potential (clockwise rotation) or when the ground and anti-clockwise terminals of the motor drivers were connected to the same potential (anti-clockwise rotation).

HIFU system

The HIFU system consists of a signal generator (HP 33120A, Agilent technologies, Englewood, CO, USA), an RF amplifier (AG1012, T & C Power Conversion, Inc., Humboldt St., Rochester, NY) and a spherical transducer made from piezoelectric ceramic (Ferroperm). The transducer operates at 0.5 MHz, has focal length of 80 mm and diameter of 50 mm.

Agar-based phantom

In order to evaluate the functionality of the transducer an agar-based phantom was developed. This recipe was already used successfully in another study [24]. This phantom was used also to evaluate the effectiveness of the thermal exposure using MR thermometry. The recipe of the agar-based phantom consisted of 2 % w/v agar, 1.2 % w/v silica dioxide and 30 % v/v evaporated milk.

MR Imaging

The positioning device system was tested in a 1.5 T MR system (Signa 1.5 T, by General Electric, Fairfield, CT, USA). High-resolution MR imaging was performed to visualize the phantom/transducer setup. Thus a T2-weighted fast spin echo sequence was used with the following parameters: Repetition time (TR): 2500 ms, echo time (TE)=60 ms, slice thickness=3 mm (gap 0.3

mm), matrix=256 X 256, field of view (FOV)=16 cm, number of excitations (NEX)=3, and echo train length (ETL)=8.

For fast imaging that was used for MRI thermometry T1-weighted spoiled gradient (SPGR) was used with the following parameters: TR=50 ms, TE=2.7 ms, FOV=16 cm, matrix=256 X 256, flip angle=30^o, NEX=1.

MR thermometry

The temperature during the thermal ablation was estimated using the proton resonance frequency shift equation which is described in great detail in Menikou and Damianou [25]. The equation relates the measured phase with the temperature elevation (ΔT). This relationship is given by:

$$\Delta T = \frac{\varphi(T) - \varphi(T_0)}{\gamma \alpha B_0 TE}$$

where φ(T) and φ(T_0) are the phases at a starting and final temperature T and T_0 respectively, γ is the gyromagnetic ratio, α is the PRF change coefficient, B_0 is the magnetic field strength and TE is the echo time. The SPGR pulse sequence was used to extract the MRI thermometry maps.

RESULTS

Fig. 9 shows the accuracy test performed for one of the linear axis (Y). On the horizontal axis the intended step in mm is presented which varied from 1 to 10 mm (n=20). On the vertical axis the measured distance is shown in mm. Note that the distance moved (red line) is slightly bigger than the expected distance (average difference was 0.04 mm at 1 mm step and for the 10 mm step the average difference in distance was 0.1 mm). The other axis (Z) revealed similar differences in accuracy.

The next series of figures were performed in the MRI setting. Fig. 10 shows a T2-W FSE MR image of the transducer of the positioning device and of the agar phantom that was used to produce MR thermometry. No MRI compatibility evaluation was performed since the same motors and encoders were used in previous studies of our group [27-29]. Note the excellent contrast between water, agar-based phantom and transducer. The images did not reveal any air spaces between the water and agar phantom interface. The image coil was placed around the agar-based phantom.

Fig. 11 shows MR thermometry map in a coronal plane at different time intervals (every 12 s) using acoustical power of 20 W for 60 s. Fig. 12 shows the corresponding MR thermometry map in a sagittal plane with the same time intervals. This figure demonstrates the growth of the thermal beam (highlighted with an arrow) of the proposed transducer.

Fig. 13 shows MR thermometry map in a coronal plane demonstrating the motion of one of the linear stages of the positioning devices. The acoustical power used was 20 W for 60 s. The intended spatial step was 10 mm. The average distance measured using MR thermometry was 9.95 mm with a standard deviation of 0.2 mm (n=12).

DISCUSSION

An MRgFUS positioning device was developed for use with small animals (mice, rats and rabbits) which can fit in commercial MRI scanners up to 7 T. The motion accuracy of the positioning device was tested using MR thermometry by using 10 mm steps. The measured distance was compared with the intended distance resulting to excellent spatial accuracy. The tests were performed in a custom-made agar/silica/evaporated milk gel phantom.

The positioning device can move the in two dimensions with a good spatial accuracy and therefore multiple heating spots along a desired grid can be delivered. The MRI compatibility of the system enables simultaneous imaging and motion due to the use of miniature piezoceramic motors and MR compatible optical encoders.

The range of motion of the system 6 cm (Z and y axis) is enough for the small animal proposed. The design of this robot can be scaled up so that it can be applied in humans. It can be extended to over 15 cm in both axes and therefore utilized for 1.5 or 3 T MRI scanners. The positioning device is 7 cm in height. With improved design, this can be lowered even further. Therefore, this system can be easily converted into a commercial product for use in humans for the abdominal area (liver, kidney, and pancreas) or fibroids, or breast. The expansion to a human positioning device will require the addition of one computer-controlled linear axis and one computer-controlled two angular axes.

The MR thermometry shown in Fig. 10 and 11 demonstrated the heating capabilities of the low-frequency transducer using the PRF method. This type of transducer is suitable for transcranial ablation of mice [30]. Extensive evaluation is required in the future in small animal experiments (mice, rats and rabbits) for other applications.

Because of the use of MR compatible encoders, the positional error of the linear stage is in the order of 0.1 mm. These errors are by far better than the requirements needed for oncological interventions. Therefore, our intention is to develop new applications for MR compatible positioning devices for focused ultrasound surgery. As mentioned elsewhere the ultimate goal is to add additional axes (one linear and two angular) in order to use it in the clinical setting with improved manoeuvrability. The key advantages of the proposed positioning device is the low cost and simplicity, but yet functional and accurate device.

The main innovation of this device is that its size is small compared to the available devices. Currently, the only device to perform this [20] uses phased arrays which moves the beam electronically. The proposed system uses single element transducer, which makes the system simple and affordable and yet as effective as the other available systems. In our opinion for experimental work in small animals, the use of a positioning device with two axes and the use of a single element transducer are sufficient.

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Ευρωπαϊκή Ένωση
Ευρωπαϊκά Διαρθρωτικά
και Επενδυτικά Ταμεία

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία
της Ευρωπαϊκής Ένωσης στην Κύπρο

Conflict of interest statement

T. Drakos declares no conflict of interest.

M. Yiannakou declares no conflict of interest.

G. Menikou declares no conflict of interest.

C. Damianou declares no conflict of interest.

Statement that all human and animal studies have been approved and performed in accordance with ethical standards.

Not applicable

Informed consent

Not applicable

List of figure captions

Fig. 1 CAD drawing of the linear axis for motion along the MRI Y axis.

Fig.2 Placement of the encoder modules in one of the linear stages.

Fig. 3 Photo of the developed Y-stage.

Fig 4 Coupling of the two linear stages (Z-axis stage and Y-axis stage). The transducer arm was coupled to the Z-axis plate.

Fig.5 Interior of the positioning device,

Fig 6 Complete robotic system showing both linear axes.

Fig.7 CAD drawing of the mouse holder.

Fig.8 Photo of the mouse holder.

Fig. 9 Measured linear step vs. intended step in mm for the Y-axis).

Fig. 10 T2-W FSE MR image the transducer of the positioning device and of the agar phantom that was used to produce MR thermometry.

Fig. 11 MR thermometry map in a coronal plane at different time intervals (every 12 s) using acoustical power of 20 W for 60 s.

Fig. 12 MR thermometry map in an sagittal plane at different time intervals (every 12 s) using acoustical power of 20 W for 60 s.

Fig. 13 MR thermometry map in a coronal plane demonstrating the motion of one of the linear stages of the positioning devices. The acoustical power used was 20 W for 60 s.

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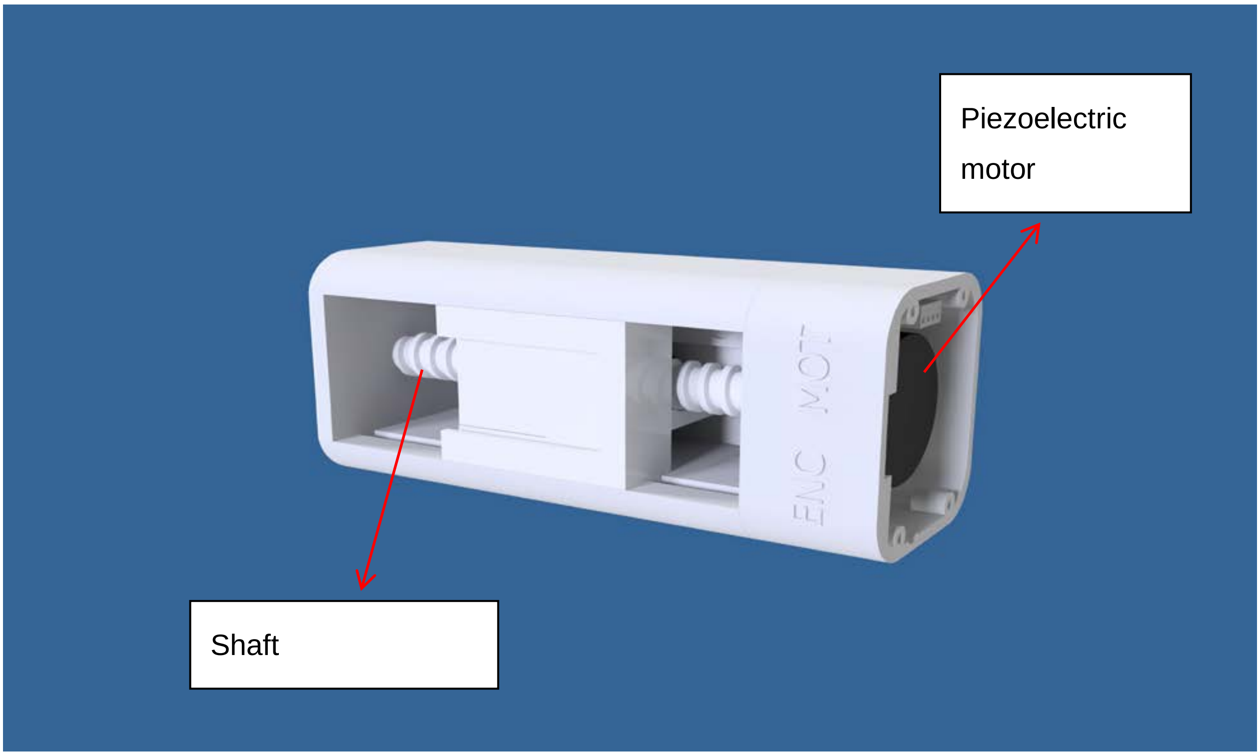

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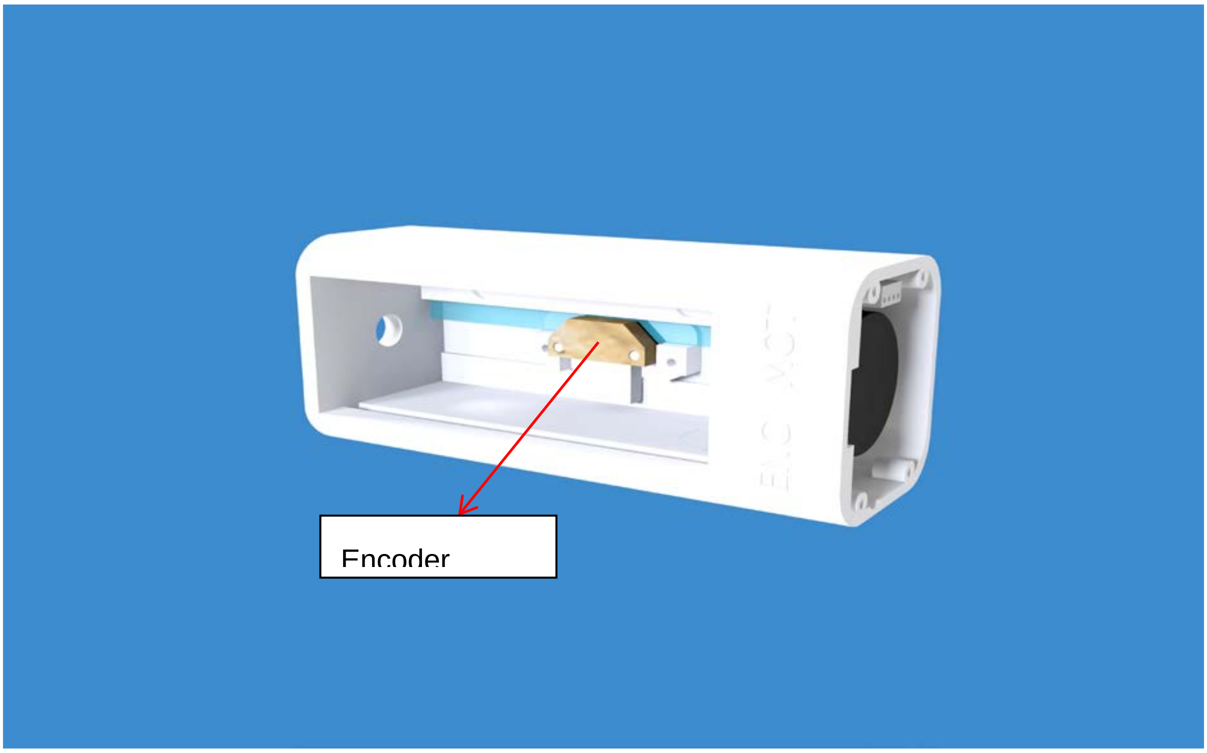


Fig. 2

Fig. 3

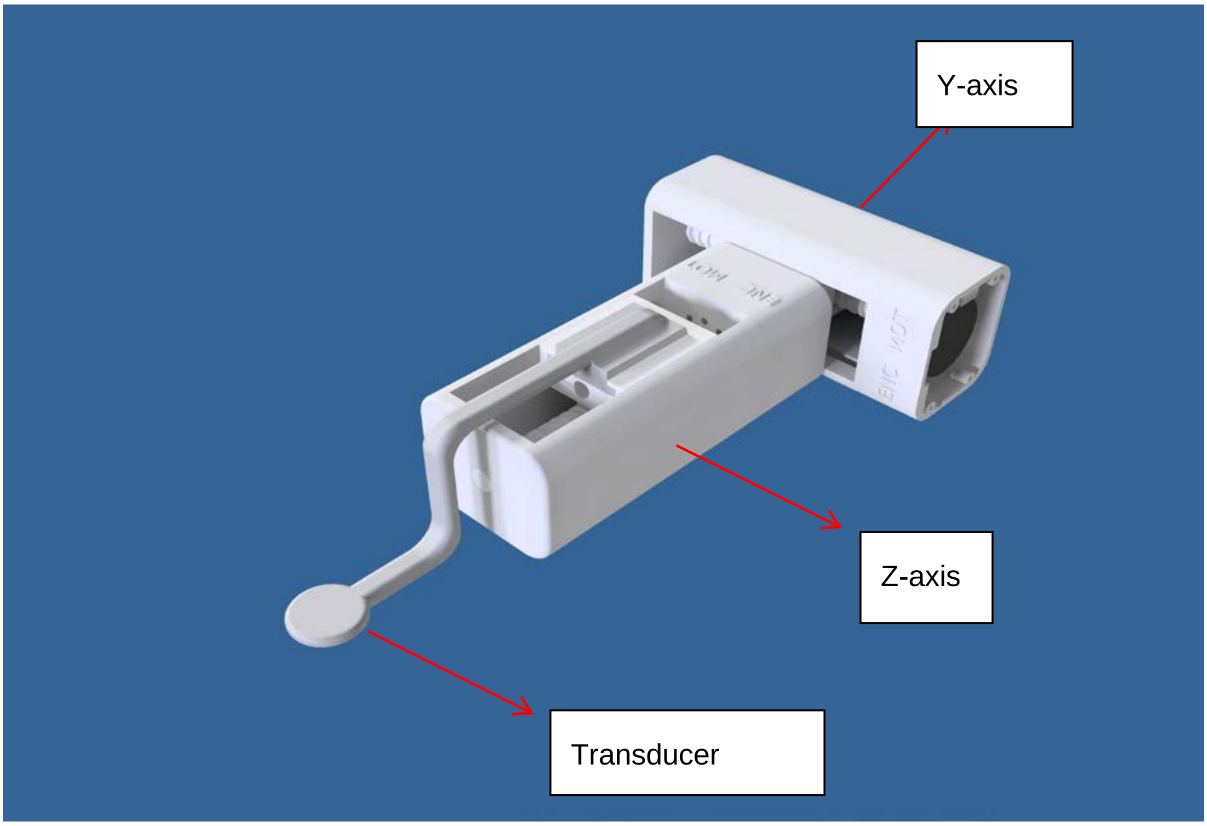


Fig. 4

Fig 5

Fig. 6

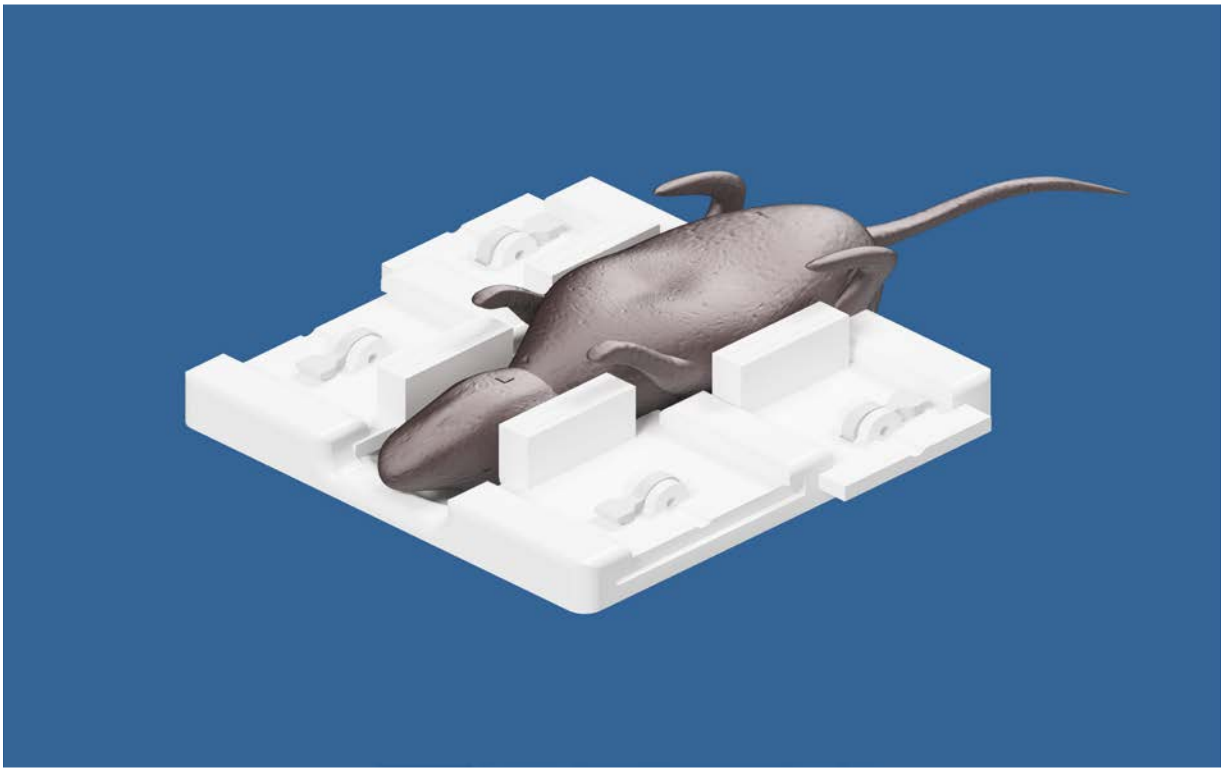


Fig 7

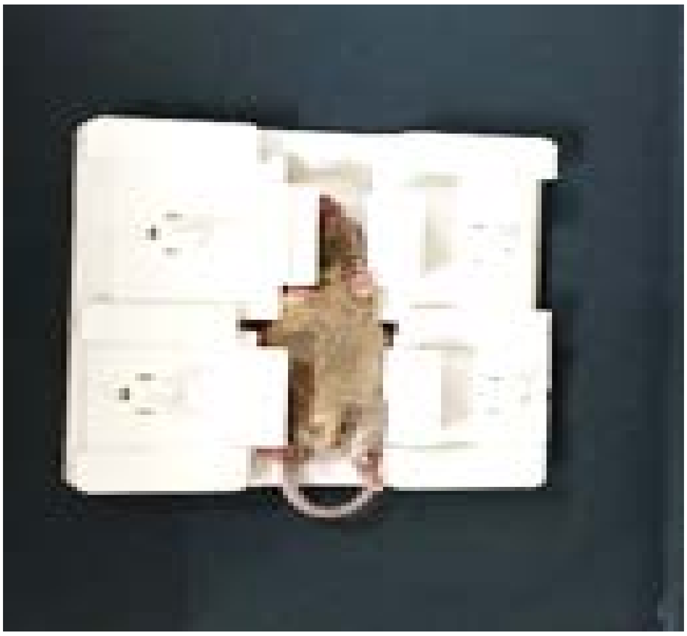
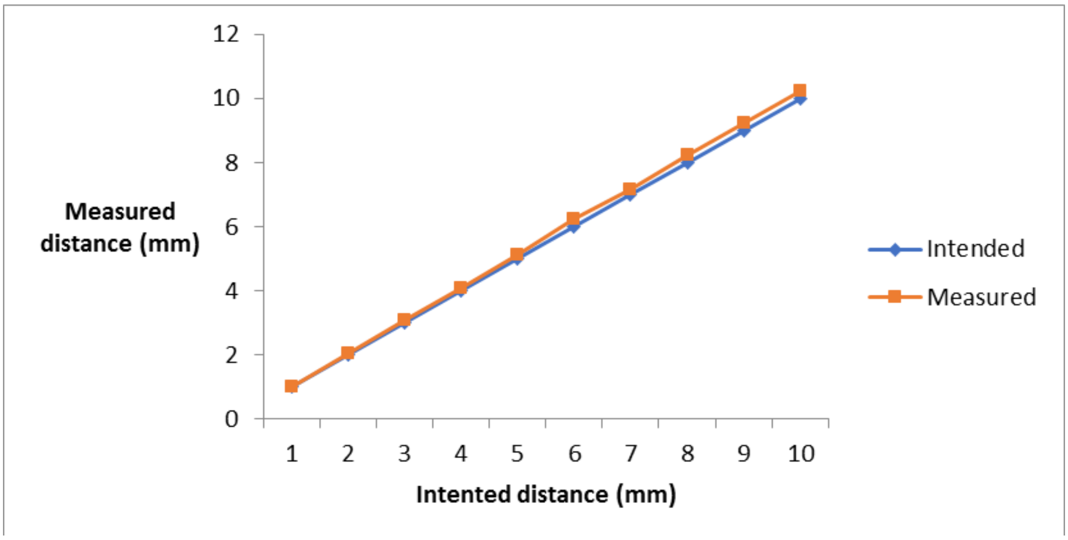


Fig. 8


12
10
8
6
4
2
0
Measured distance (mm)
1
2
3
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5
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9
10
Intented distance (mm)
Intended
Measured

Fig. 9

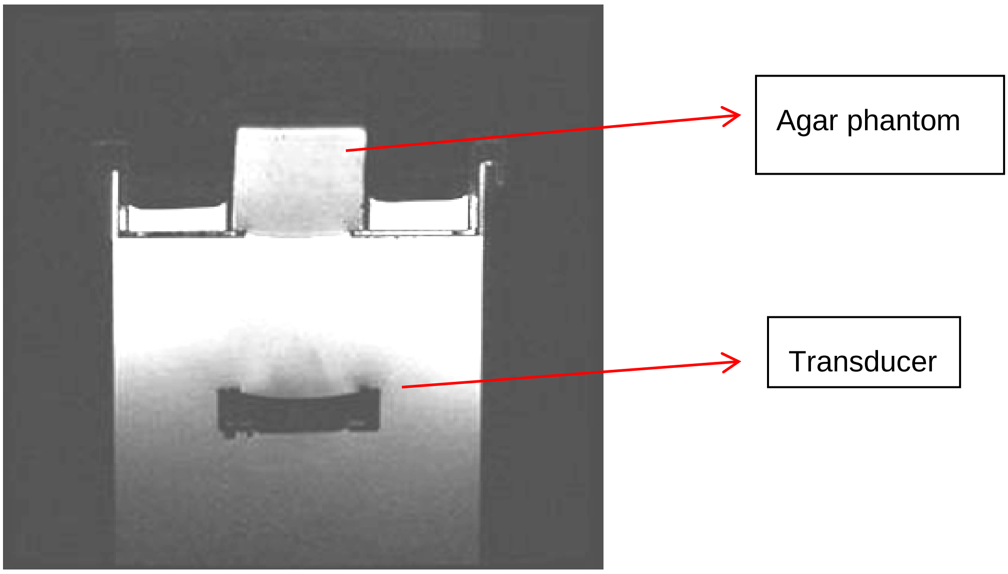
Agar phantom
Transducer

Fig. 10

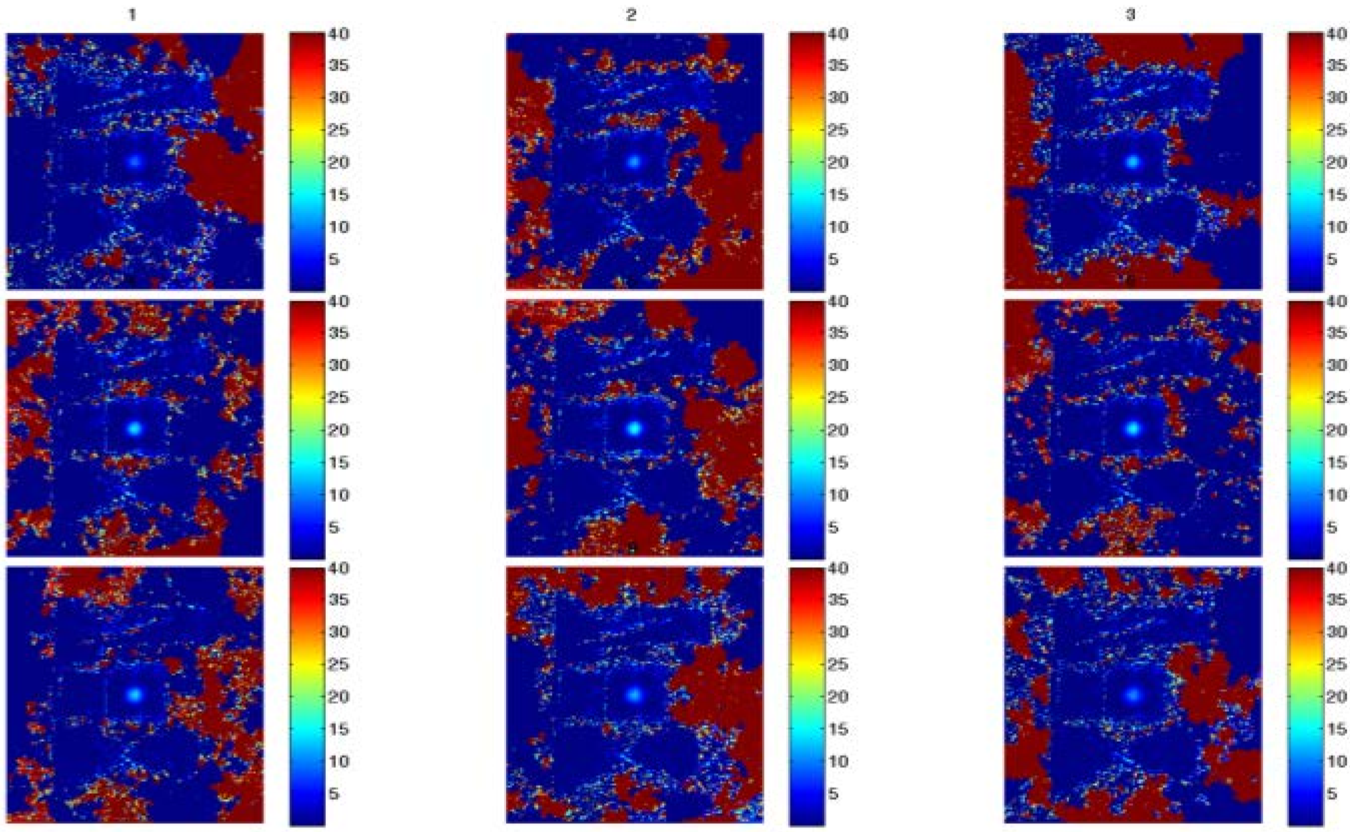

Fig. 11

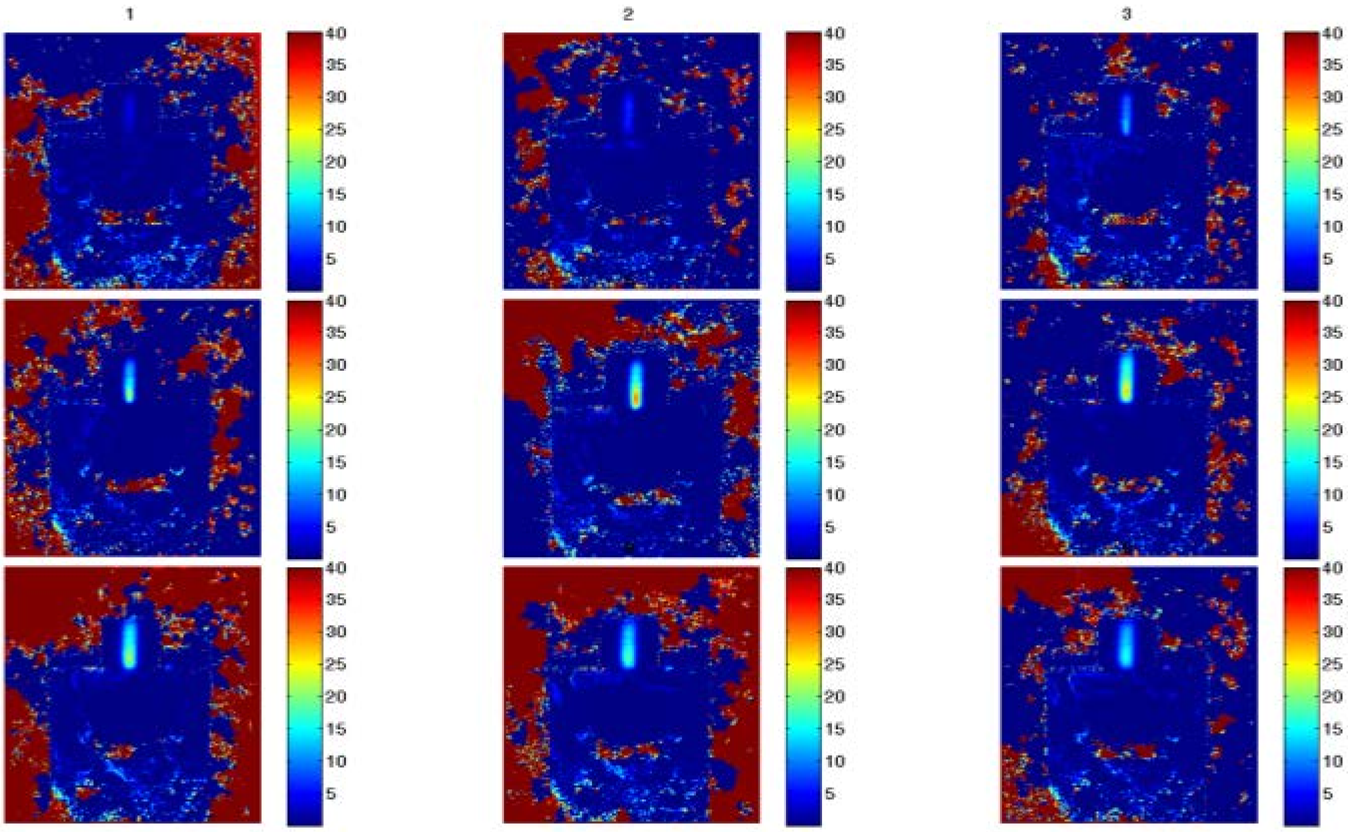

Figure 12

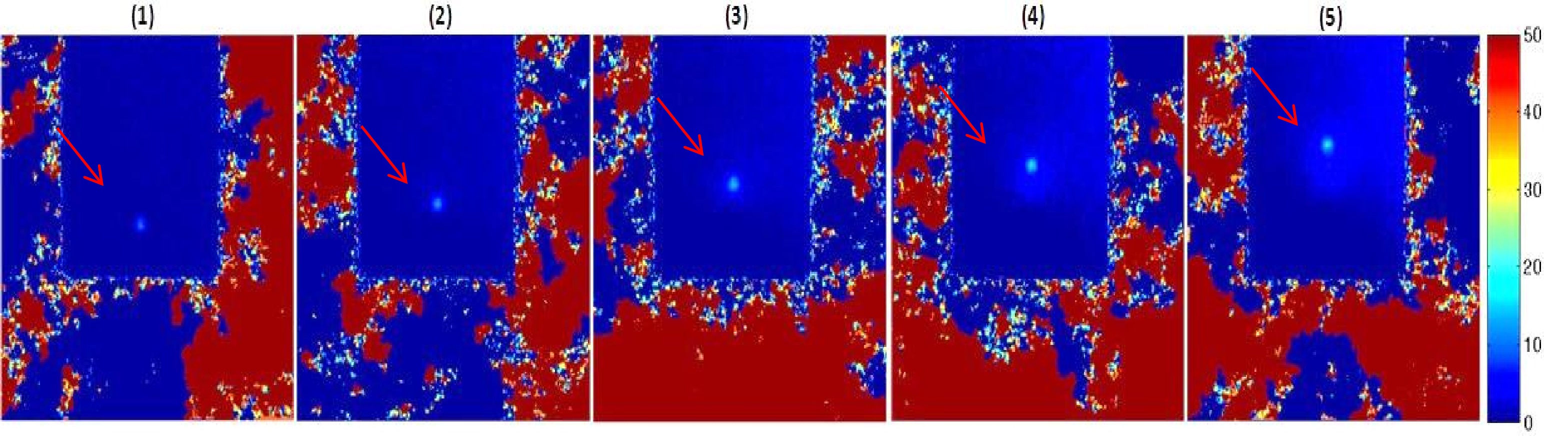

Fig. 13

MRI-guided focused ultrasound robotic system with subject placed in prone position.

C. Damianou[a], M. Giannakou[a], G. Menikou[b], L. Ioannou[c],

a Electrical Engineering Department, Cyprus University of Technology, Cyprus,

aMedical physics division, Nicosia General Hospital, Nicosia, Cyprus

c Radiology department, Ygia Polyclinic, Limassol, Cyprus,

ABSTRACT

In this article a medical robotic system that performs MRgFUS ablation is presented. The main innovation of this robotic system is that all the actuators are placed outside the water container. The transducer is immersed in water via an arm which is attached to the angular stage. The system includes 3 linear and one angular stage. The system was tested in the MRI environment and was proved to be MR compatible. The accuracy of the system was tested, and it was found that spatial steps of 0.2 mm can be safely and reliably achieved. With this robotic system it is possible to access many organs that ultrasound penetrates with the patient placed in prone position.

KEYWORDS: ultrasound, MRI, robotic, medical

INTRODUCTION

The first focused ultrasound surgery (FUS) system was built in 1940 [1] and the general technology existed in an experimental setting for over 50 years. FUS can be focused on a targeted point to cause a rise in temperature between 60-80 ℃. This can result in thermal tissue coagulation necrosis.

Each sonication heats only a small focal target, so multiple sonications, must be used to ablate an entire target area [1]. Due to the propagation mechanism of ultrasound, this technique should be performed with caution near nerves, bone, and rectum.

This technology has been employed in the nineties for prostate interventions. The FUS devices available for prostate cancer therapy are: Ablatherm (EDAP TMS SA, Vaulx-en-Velin, France) [3]and Sonablate (Focus Surgery Inc., Indianapolis, IN, USA, now called SONACARE) [5].

Recently, magnetic resonance FUS (MRgFUS) has been introduced due to a better ability to plan and monitor treatments in real-time [6]. This technique is approved by the Food and Drug Administration (FDA) for fibroid ablation. The InSightec systems have been deployed very fast in the last decade in other applications such as the treatment of prostate cancer [7], breast cancer [8], liver [9] and for pain palliation of bone metastases [10]. Recently, Insightech developed a transcranial MRgFUS system which eliminates non-invasively essential tremor [11]. This application is becoming a primary choice of treatement and establishes FUS as a safe, effective and non-invasive surgery. Therefore, the number of research institutions involved in the area of MRgFUS is growing rapidly. There is an unmet need for research institutions for affordable and functional preclinical robotic systems in order to explore new applications in MRgFUS.

There is an evolution of preclinical systems in the last decade, which is somehow slow. Chopra et al 2009 [12] developed an MRI three-axis positioning system that delivers focused ultrasound in small animals for high-throughput preclinical drug delivery studies.

Another company that developed an MRgFUS system for small animal experiments is the French company Image Guided Therapy (Pessac, France) [13]. Image guided therapy uses phased arrays to move the focus and therefore, this technology is more expensive than the other existing technologies.

Another positioning device is the fully MR-compatible robotic assistance system InnoMotion (InnoMedic GmbH, Herxheim, Germany) which was originally designed for MR-guided interventions with needles [14]. This system has five pneumatically driven degrees of freedom and can be moved over a wide range within the bore of the magnet. The robotic system was combined with a fixed-focus ultrasound transducer. The size of this system is large, thus the price of this system is high. The Canadian company FUS instruments [15] developed a 2-axis positioning device, with all moving parts immersed in water. This is a quite successful company regarding commercialization of MRgFUS preclinical systems.

The proposed device can be applied for veterinary medicine which always lagged behind human medicine. The proposed device offers benefits of performing clinical trials (only IRB is needed) in companion animals. Our dogs and cats are exposed to the same environmental stimuli that we are, and develop many of the same diseases in a far more natural way than laboratory animals. Veterinary trials make new innovative therapies available for family pets, while simultaneously collecting data that can be used to advance human medicine.

Focused ultrasound offers several advantages over traditional treatments like surgery and radiation. It is non-invasive, which reduces the risk of infection and eliminates the need for stitches and the Elizabethan collar. Focused ultrasound can be used to ablate tissue or enhance the local delivery of therapeutic drugs. Because there is no ionizing radiation involved, treatments can be repeated if needed. Focused ultrasound has many potential applications in veterinary medicine, including but not limited to: Tumor destruction, Drug delivery (chemotherapy & immunotherapy), Pain relief for arthritis and hip dysplasia.

An MRI compatible positioning device is proposed for the treatment of pet diseases. The device features 4 DOF that is used to maneuver a single element transducer hence, it can be produced at a lower cost compared to the devices currently available. The robot includes three linear stages and one angular, this design allows the delivery of the ultrasound through multiple angles therefore, it can access multiple organs. Furthermore, it is suitable for any commercial 1,5T and 3T MRI scanner. A user-friendly software was developed that communicates with the MRI scanner, control the positioning device and the ultrasound system. In addition, the robot has small dimensions and the overall system is very compact.

MATERIALS AND METHODS

Robotic system

a) Positioning device description.

The positioning device was designed using the Microstation (V8, Bentley Systems, Inc.) CAD software. The parts were manufactured using a 3D printer (FDM400, Stratasys, 7665 Commerce Way, Eden Prairie, Minnesota, 55344, USA). The device components were made of ABS material which offers good mechanical properties thus, the positioning device is robust and reliable.

The positioning device has 4 DOF, 3 linear axis and 1 angular axis. Each axis is driven by a piezoelectric ultrasonic motor (USR60-3N, Shinsei Kogyo Corp., Tokyo, Japan). The dimensions of the device are, 64 cm in length, 25 cm in width and approximately 29 cm (when Z-axis is fully extended) in height. Due to the small dimensions of the device it can be used with any commercially available MRI scanner. The device has a motion range of 5 cm on the Z-axis, 7 cm for the X-axis, 7 cm for the Y-axis (relative to the MRI) and 180º (90º on each direction) for the Θ-axis. The weight of the positioning device is approximately 4 kg.

Fig. 1 shows the CAD representation of the robotic system. Fig. 1A and Fig. 1B shows the 3D drawings of the positioning device. Fig. 1C shows the Z-stage (MRI axis) of the positioning device, which features a jack screw mechanism for the conversion of the angular motion to linear motion. On the rear of the base the piezoelectric motor is visible which is coupled to the jack screw mechanism.

Fig. 1D shows the X-stage drawings. The X-axis moves along the Z-plate guides. The ultrasonic motor was attached to the Z-plate to transfer the motion to the X-stage. On the rear of the X-plate an optical encoder was used to ensure the accurate motion of the X-stage. Two structures were added to strengthen the X-plate, since the middle section was smaller in order to increase the motion range.

Fig. 1E shows the Y-stage which followed the same design principles with the Z-stage and the X-stage. The motor was fixed to the top of the Y-frame. On the front left side of the Y-frame an optical encoder was placed. On the front of the Y-plate a coupling was made to attach the Θ-stage (Fig. 1F). The theta stage mechanism differs from the linear stages. The motion ıs transferred through a shaft that includes a screw on the lower end. The screw is coupled to a gear that is attached to the lower arm. Using this technique, allowed the placement of the motor on the top of the Θ-stage, thus placing the ultrasonic motor far from the water container. An MR compatible ultrasonic transducer (Sonic Concepts, USA) was attached to the device using a coupling mechanism. The water was used to create an acoustical coupling between the ultrasound and the target. Fig. 2A shows the manufactured positioning device and Fig. 2B shows the positioning device as placed inside the MRI scanner.

To ensure motion accuracy optical encoders was used on all the stages. Linear stages were equipped with optical encoders (EM1-0-500-I EM1, US Digital Corporation, Vancouver, WA 98684, USA) in conjunction with a polymer plastic strip (LIN-500-10-1, US Digital Corporation, Vancouver, WA 98684, USA) with resolution of 500 lines pe inch (LPI). For the angular stage an optical encoder was used (EM1-2-2500-I, US Digital Corporation, Vancouver, WA 98684, USA) in conjunction with a plastic disc (DISK-2-2500-093-IE, US Digital Corporation, Vancouver, WA 98684, USA) with a resolution of 2500 lines per 360^{o}. The encoders were connected to a data acquisition board USB-6351 (NI, Austin, USA). This robot is classified as MR conditional, according to ASTM standards, since the encoder modules and the ultrasonic transducer require electricity to operate (F2503, F2052, F2213, F2182, and F2119).

b) Software

The robotic system control software was written in C # (Visual Studio 2010 Express, Microsoft Corporation, USA). It offers a user-friendly interface and enables the user to control the robotic device motion, to activate the ultrasound amplifier and allows communication with the MRI scanner. The command history is stored, so that the user can review the previous commands if necessary. The software is automatically updating the transducer position coordinates in relation to its initial location. The software includes the option to store patient information such as, patient name, age, address health history, medical images etc. In addition, an MR compatible camera (MRC Systems GmbH, Heidelberg, Germany) can be connected to acquire images. The software can connect to the MRI scanner using the DICOM (Digital Imaging and Communication in Medicine) protocol. The connection was established by entering the appropriate parameters for the server name, application entity title, IP address, and port. The software when connected to the DICOM server can download and store study ID or series ID using the patient identification (ID). The files are downloaded in a local server and stored in the computer.

d) Robot drivers

Each ultrasonic motor is controlled by a driver that provides the appropriate sinewave signals to rotate it. A DC power supply (24 V, 6 A) is used to provide power to the drivers (D6060, Shinsei Kogyo Corp., Tokyo, Japan). The motion of the positioning device is controlled via a USB 6351 data acquisition (DAQ) interface card (National instruments, Austin, Texas, USA) which is hosted inside the electronic enclosure.

Gel phantom

A polyacrylamide gel was used (ONDA Corporation, Sunnyvale, CA, USA) for the evaluation of the system. The polyacrylamide gel is transparent and when exposed to the high temperatures it changes its colour to white. The white lesions inside the gel appear as a solid hence, it allows visual inspection of the induced lesions and confirmation of the spatial accuracy.

Additional, experiments were conducted with agar-based phantoms. The phantoms were made using 6% w/v agar, 4% w/v silica dioxide, 30% v/v evaporated milk. The evaporated milk, which is rich in fats and proteins was used to adjust the attenuation while scattering ultrasound weakly [16]. Scattering was compensated by adding to the mixture appropriate amounts of fine crystalline silica dioxide powder. The percentage of each product was adjusted to mimic the acoustic attenuation (~ 1 dB/cm-MHz) of muscle tissue as it was described by Menicou et. al. [16]. The agar gel phantoms were used to evaluate the ultrasonic protocol. By using MR thermometry, it was possible to detect the focus of the transducer and to observe the temperature elevation at the focus.

FUS system

The FUS setup is composed of a spherically focused MR compatible ultrasonic transducer (Sonic Concepts, USA) operating at a frequency of 1MHz. The transducer has a radius of curvature of 10 cm and a diameter of 4 cm. The ultrasonic transducer is operated by an RF generator (RFG 750 W, JJA, Seatlle, WA, USA) which is controlled by the software.

Experiments in gel phantoms

In order to test the functionality and repeatability of the positioning device experiments were carried out with gel phantom. The phantom was placed on the front cover of the water container, in the centre of the opening. The ultrasonic transducer was attached to the arm of the positioning device using a coupling. The transducer and the bottom surface of the phantom were immersed in the water to enable the ultrasound to reach the phantom.

MR Imaging

To assess the MR compatibility of the robotic system tests under different conditions were peerfored. The signal to noise ratio (SNR) was measured with the robot placed in a 1.5T MRI scanner (Signa, General Electric, Fairfield, CT, USA) with a GPFLEX coil (USA instruments, Cleveland, OH, USA) that enabled higher quality images of the phantom. The SNR was measured with the encoders activated and deactivated, with the presence and absence of the transducer and during activation of the transducer using a T1-weigted spoiled gradient (SPGR) sequence. The parameters used for the SPGR sequence was: Repetition time (TR)=38.5 ms, Echo time (TE)=20 ms, Field of view (FOV)=21 cm, matrix=128x128, flip angle=20^o, Number of excitations (NEX)=1.

Furthermore, the motion of the transducer was evaluated using Fast Recovery Fast Spin Echo (FRFSE) T2-weighted sequence with the following parameters: TR= 2200 ms, TE= 61.2 ms, slice thickness=15 mm, matrix=192 x 192, FOV=17 cm, NEX=1, and echo train length (ETL)= 16. The high-resolution FRFSE images were acquired between each movement. By comparing the previous MR image transducer position to the current transducer position, the repeatability and motion accuracy of the positioning device was quantified.

MR thermometry

To observe the temperature elevation during FUS sonications, MR thermometry was used in order to monitor the rate which the temperature built up. The temperature calculation was based on the phase shift proton resonance frequency shift (PRFS) phenomenon [17]. By measuring the difference in phase shift between two MR images in a pixel by pixel basis the temperature increasement was calculated.

To assess the thermometry at the focus, slices were acquired along the long axis and the short axis of the beam. This ensure the accurate detection of the peak temperature at the focus. The MR images for the thermometry were acquired using spoiled gradient echo sequence (SPGR). The images were processed by a custom-made software developed in MATLAB (MathWorks, Natick, United States). The software compares phase shifts developed during the acquisition of non-treated image (mask) and treated images. Temperature elevation was returned by the software as the maximum value in a prescribed region of interest (ROI) that was manually positioned. Temperature-color coded maps were produced by adjusting the color map (blue to red) for a range of minimum to maximum ROI temperature.

RESULTS

Fig. 3 shows results for the evaluation of motion for one of the linear axis (X). It shows the distance moved vs. intended step in mm with typical steps used during navigation of the robotic system (1to 5 mm). The test was repeated 20 times. The distance moved (red line) is very closed to the expected distance (average difference was 0.06 mm at 1 mm step and 0.2 for the 10 mm step). The other two axes (Y and Z) revealed similar differences in accuracy.

Fig. 4 shows the results for the accuracy of the angular axis. The graph shows the measured angle in degrees vs. intended angle in degrees (varied from 2 to 10 degrees with n=20). The angle moved (red line) is slightly bigger than the expected angle (average difference in degrees was 0.05^{o} at 2 degrees step and 0.1^{o} for the 10 degrees).

Fig. 5 shows the signal to noise ratio (SNR) using SPGR measured in the agar-based phantom for different component activation. The SNR was maximized when the motor, encoder and transducer were OFF (20). There was some drop in the SNR when the motor was energized and further drop in the SNR was observed when the motor was energized. The maximum decrease of SNR occurred when all components were activated (encoder, motor, and ultrasonic transducer) were energized (11).

Fig. 6 shows images using MR thermometry in a plane perpendicular to the ultrasonic propagation (coronal) at different time intervals (every 12 s) using acoustical power of 30 W for 60 s. Fig. 7 shows images using MR thermometry map in a plane parallel to the ultrasonic propagation (sagital) with the same ultrasonic exposure. This figure demonstrates the growth of the thermal beam of the transducer of the robotic-based system.

CONCLUSIONS

In this article we presented a robotic system that performs MRgFUS ablation. The main innovation of this robotic system is that the motors, encoders and moving parts are located outside the water container. The transducer is immersed in water via an arm which is attached to the angular stage. Therefore, the complexity of passing the transducer arm through water-proof mechanisms is avoided.

The system was tested in the MRI environment and was proved to be MR compatible. The accuracy of the system was tested, and it was found that spatial steps of 0.2 mm can be safely and reliably achieved.

With this robotic system it is possible to access many organs that ultrasound penetrates. With the patient placed in prone position access is possible to the breast, liver, kidney and pancreas. Access will be possible to the brain provided that a phased array replaces the single element transducer. For the brain application the patient may be positioned supine. Finally, for some cases of bone pain palliation, this system may be used.

The proposed robotic system can be easily modified so that it can be used for other applications. One example an alternative application is MRI-guided biopsy. The transducer arm can be replaced with a needle biopsy. Another application is to replace the transducer arm with a radio frequency (RF) device to perform MRI guided RF ablation. The possibilities for this system are many. Finally, the manoeuvrability of the robotic system can be enhanced further by attaching another angular stage to the system.

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Ευρωπαϊκή Ένωση
Ευρωπαϊκά Διαρθρωτικά και Επενδυτικά Ταμεία

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

FIGURE CAPTIONS

Fig. 1 3D drawings of the positioning device (A and B). C) the Z-stage (MRI axis) of the positioning device, D) X-stage, E) Y-stage, F). Θ-stage.

Fig. 2 A) Manufactured positioning device and B) positioning device as placed inside the MRI scanner.

Fig. 3 Evaluation of motion for one of the linear axis (X) showing distance moved vs. intended step in mm with typical steps used during navigation of the robotic system (1 to 5 mm). The test was repeated 20 times.

Fig. 4 Measured angle in degrees vs. intended angle in degrees (varied from 2 to 10 degrees with n=20) foe the angular stage.

Fig. 5 Signal to noise ratio (SNR) using SPGR measured in the agar-based phantom for different component activation.

Fig. 6 MR thermometry in a plane perpendicular to the ultrasonic propagation (coronal) at different time intervals (every 12 s) using acoustical power of 30 W for 60 s.

Fig. 7 MR thermometry map in a plane parallel to the ultrasonic propagation (sagital) with the same ultrasonic exposure as in fig. 6.

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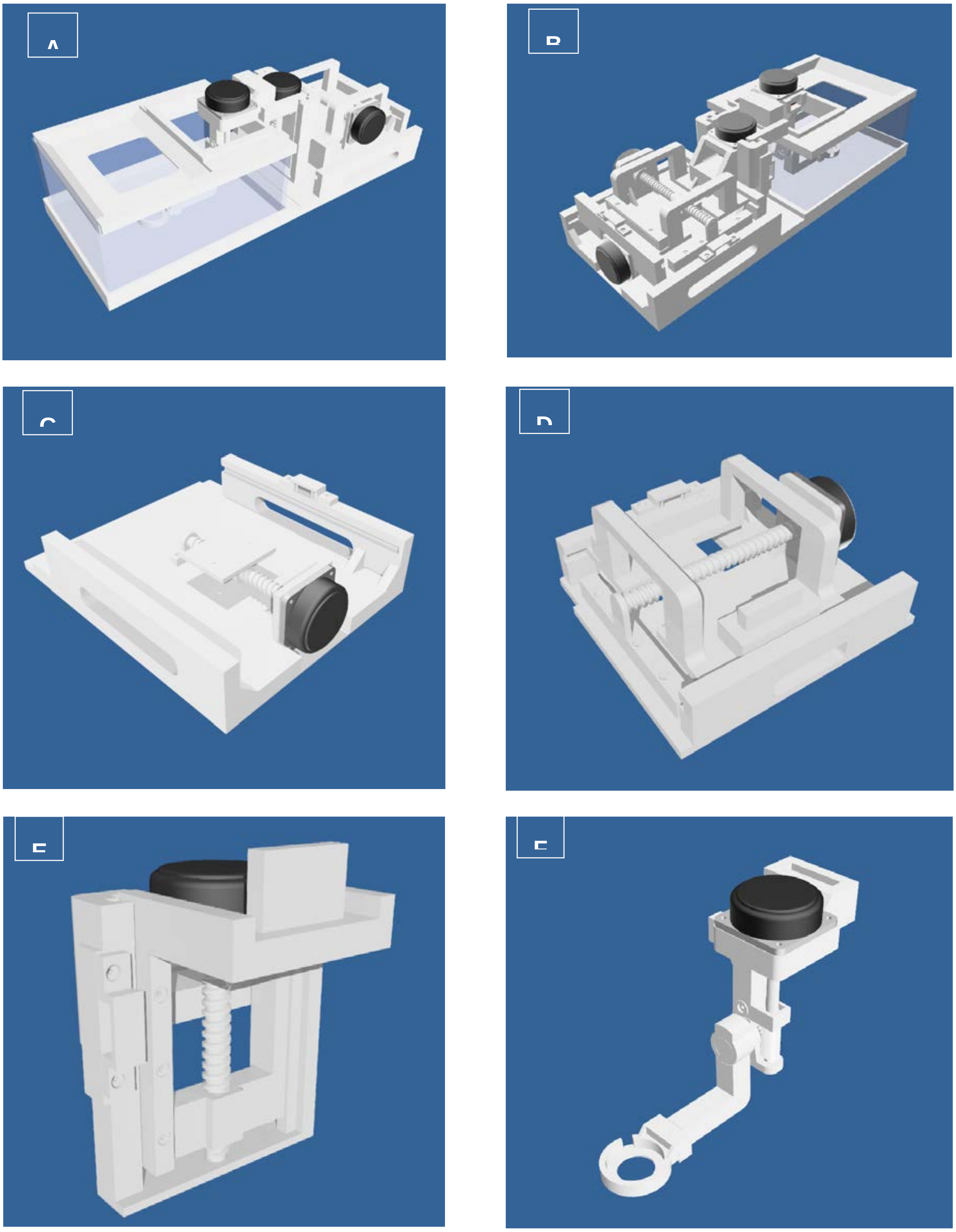


Fig. 1

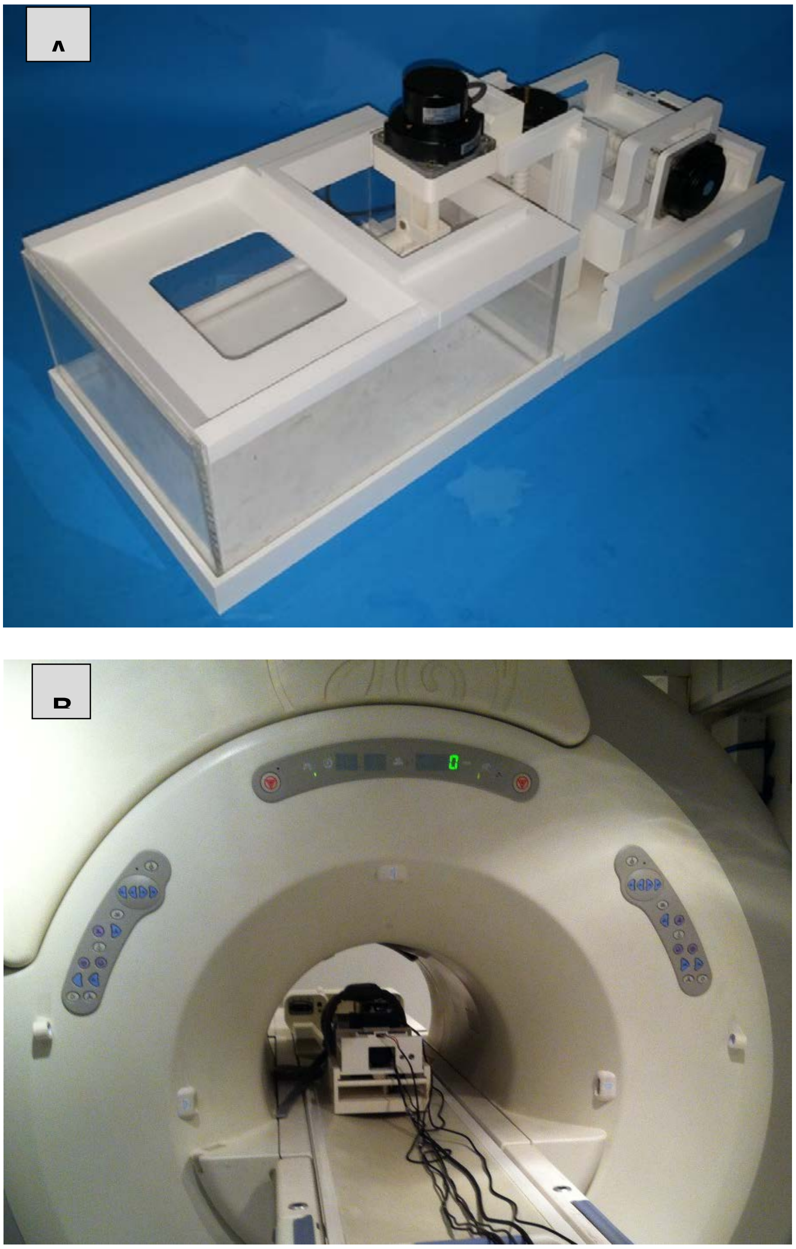
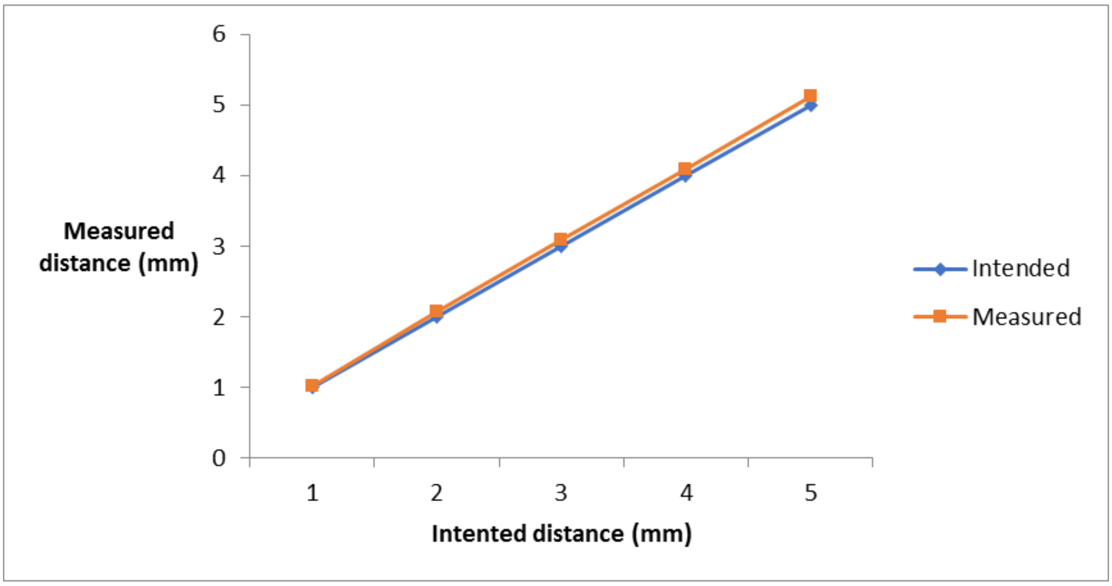


Fig. 2



6
5
4
3
2
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Measured distance (mm)
1
2
3
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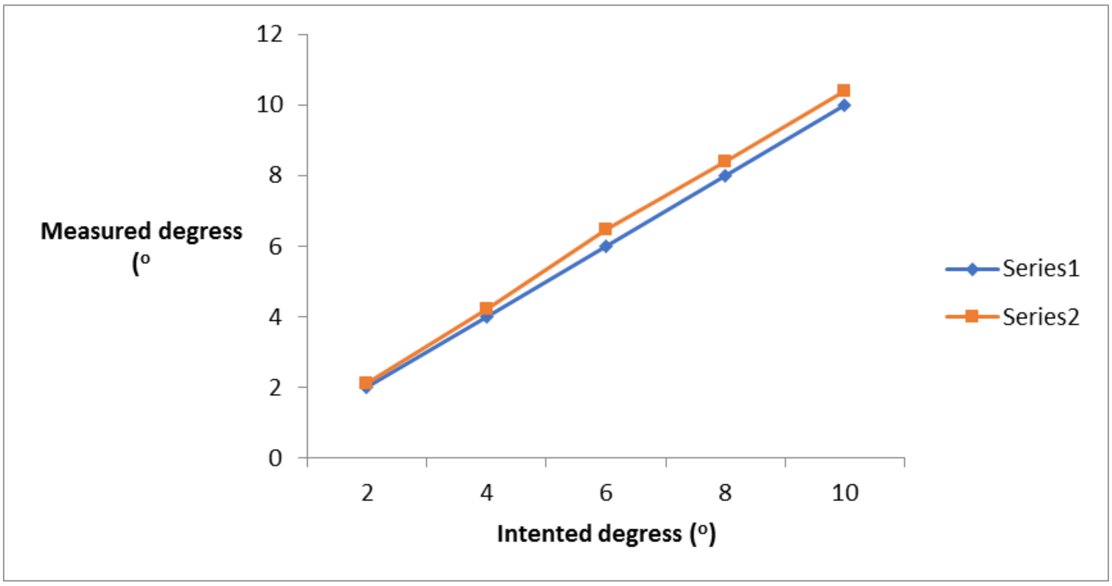
5
Intented distance (mm)
Intended
Measured

Fig. 3



12
10
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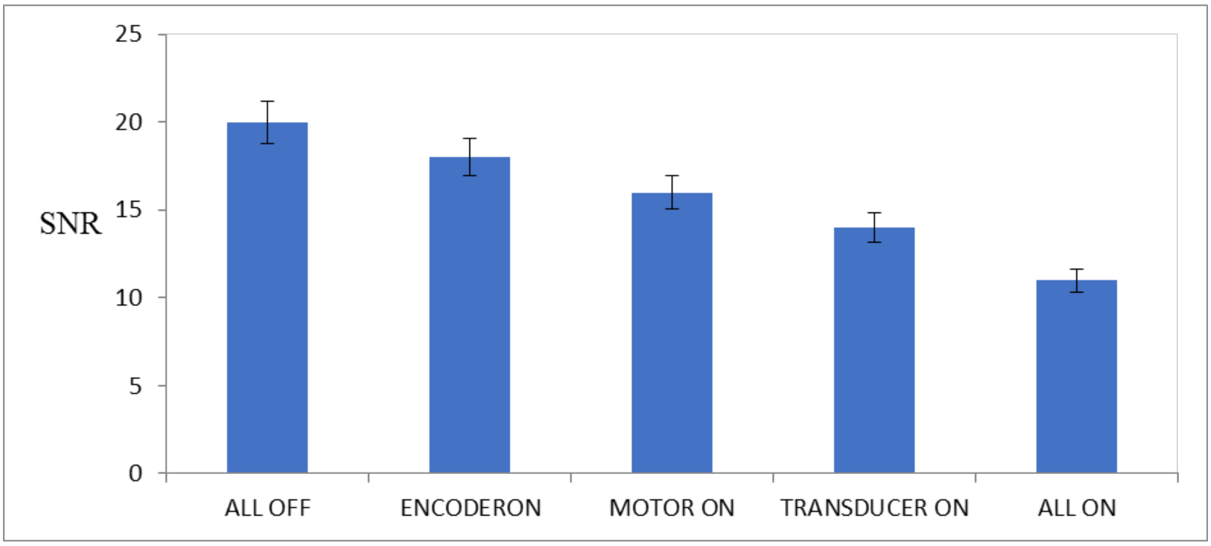
Fig. 4



SNR
25
20
15
10
5
0
ALL OFF
ENCODERON
MOTOR ON
TRANSDUCER ON
ALL ON

Fig.5

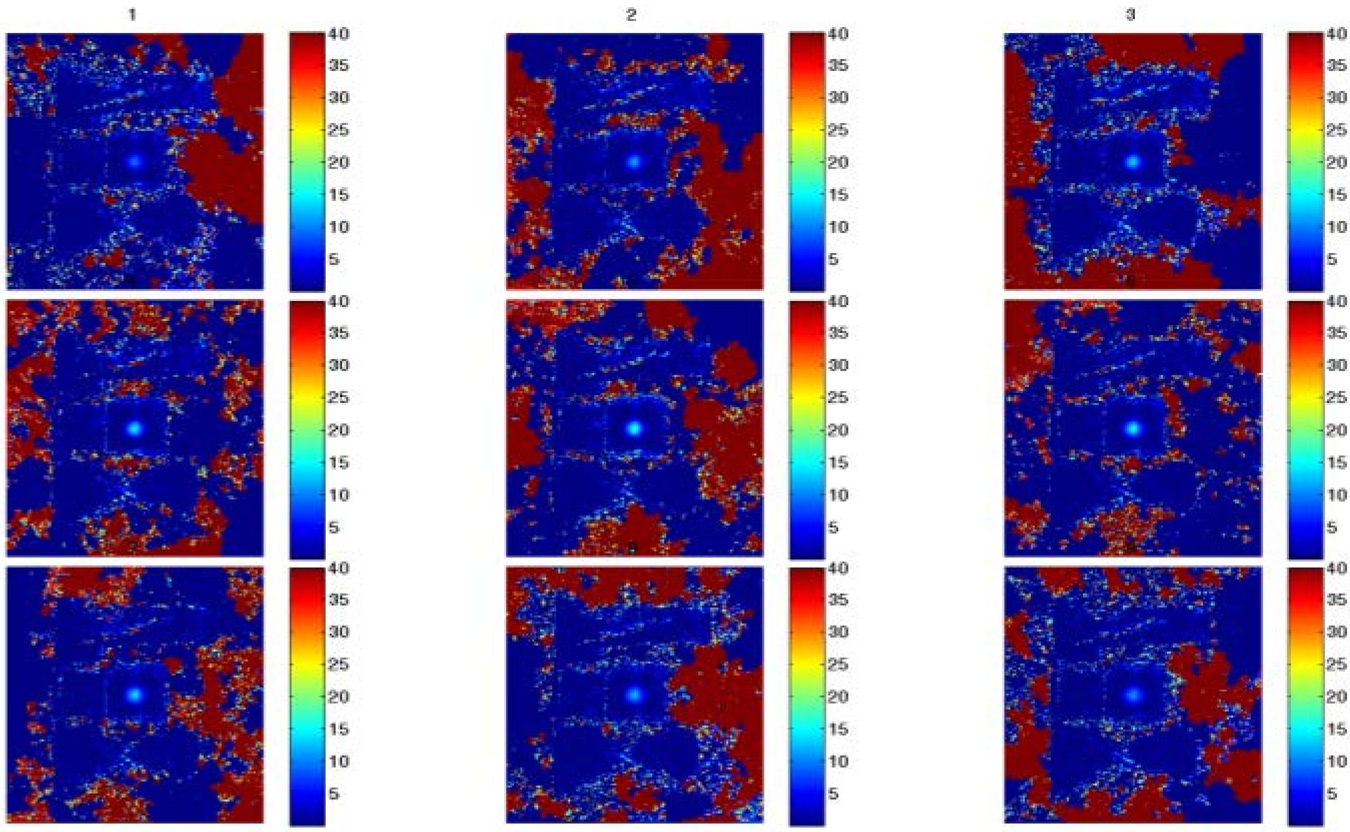


Figure 6

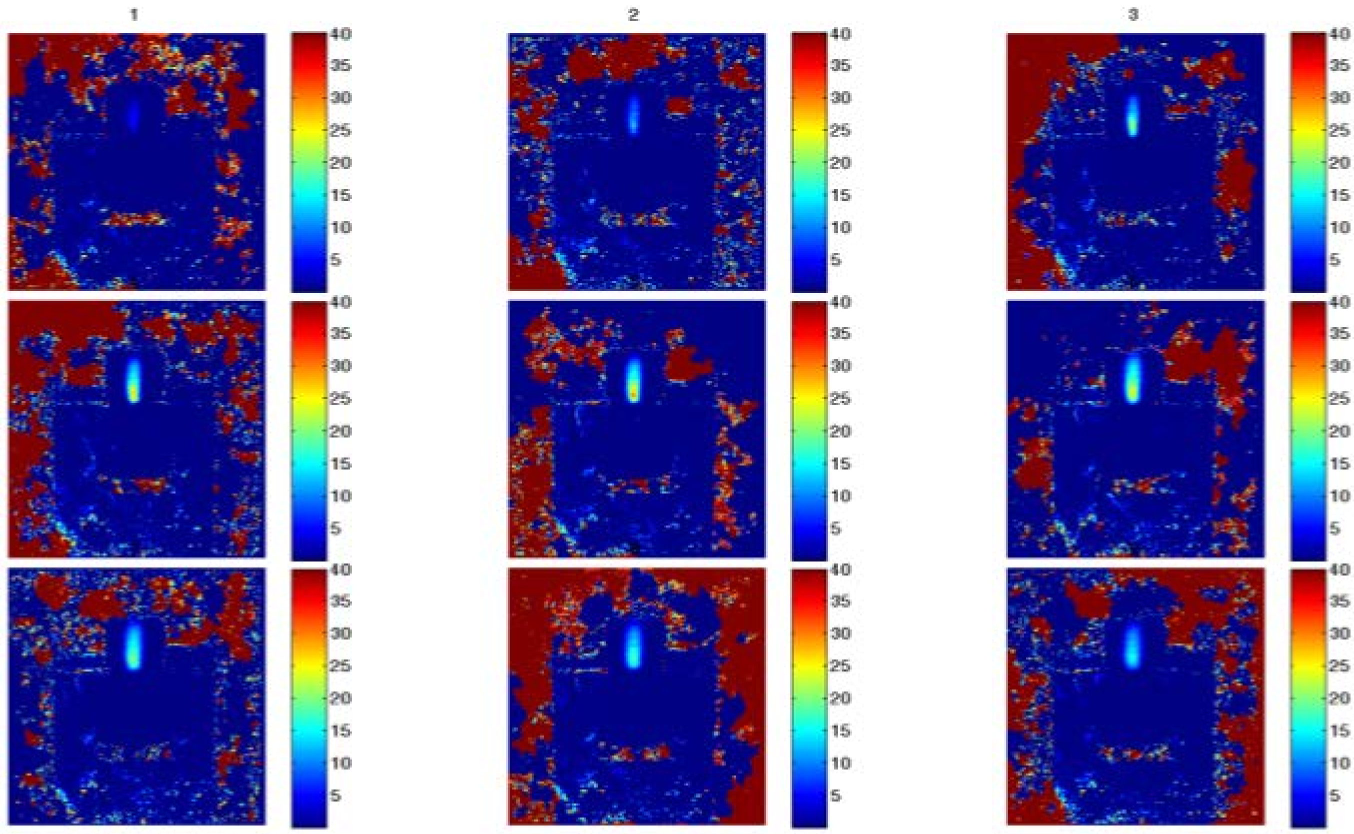


Figure 7