Project Acronym:
FUSVET (SEED/1221/0080)

Focused Ultrasound System for veterinary chemotherapeutic applications for oncology

Deliverable number: 2.2

Title: Presentation at a scientific conference

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Cyprus_tomorrow RECOVERY AND RESILIENCE PLAN

Republic of Cyprus

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The FUSVET project is funded by the Recovery and Resilience Facility of the NextGenerationEU instrument, through the Research and Innovation Foundation (RIF) of Cyprus.

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Executive summary

This deliverable presents the Conference papers that were presented during the 2nd reporting period of the FUSVET project. The papers addressed the development of Magnetic Resonance Imaging (MRI) tissue mimicking tumor phantoms, the performance evaluation of the FUSVET system in phantoms and *ex-vivo* porcine tissue, as well as the treatment of various tumors in pets by FUS-induced coagulative necrosis.

Table 1 provides details on each paper, including its title and presentation format (oral or poster), and the conference where it was presented. The relevant oral and poster presentations given can be found in the Appendix in the same order as in Table 1.

Table 1: List of conference papers presented during the 2nd reporting period of the FUSVET project.

#	Title	Conference	Date	Type	Online/ In-person
1	T1 and T2 values of an agar-based phantom with inclusion of tumour	*10th International Conference on Biomedical and Bioinformatics Engineering* (ICBBE 2023) Kyoto, Japan.	9-12 November 2023	Oral presentation	In person
2	Veterinary ablation system using MRI guided focused ultrasound	*10th International Conference on Biomedical and Bioinformatics Engineering* (ICBBE 2023) Kyoto, Japan.	9-12 November 2023	Oral presentation	In person
3	Veterinary Oncology using MRI guided Focused Ultrasound	*6th International Conference on BioMedical Technology* (ICBMT 2024) Ho Chi Minh, Vietnam.	23-25 February 2024	Oral presentation	In person
4	Robotic device for MRI guided focused ultrasound for veterinary oncology	*6th International Conference on Intelligent Medicine and Image Processing* (IMIP 2024) Bali, Indonesia	26-29 April 2024	Poster presentation	In person
5	Focused ultrasound tumor bearing phantom	*6th International Conference on Intelligent Medicine and Image Processing* (IMIP 2024) Bali, Indonesia	26-29 April 2024	Poster presentation	In person
6	Canine and feline tumor ablation field trial with a FUS ablation system	*23rd Annual International Symposium on Therapeutic Ultrasound* (ISTU 2024) Taipei, Taiwan	19-22 September 2024	Poster presentation	In person

Submitted abstracts

1. **10th International Conference on Biomedical and Bioinformatics Engineering (ICBBE 2023), Kyoto, Japan.**

T1 and T2 values of an Agar-based phantom with inclusion of tumour

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Abstract— In this paper, an agar-based mimicking material which includes a tumour was developed. The phantom can be used to evaluate the temperature produced by a focused ultrasound transducer. The tumour model was made out of water, agar (6 % w/v) and 4 % w/v silica. In the tissue surrounding the tumour no silica was used. The slight difference in silica content between tumour and surrounding tissue resulted in excellent contrast between tumour and tissue in Magnetic Resonance Imaging (MRI). Based on coronal images showing the transducer and tumour/tissue it was possible to precisely move the focused ultrasound beam within the phantom using an MR compatible positioning device. MR temperature was detected within the tumour and outside the tumour. T1 and T2 values were measured in a 3 T MRI. Due to the inclusion of silica in the tumour the absorption was increased within the tumour, and therefore, higher temperatures were measured in the tumour. Temperature across a plane parallel to the beam showed some deflection of the beam in areas of tumour curvature. This is an excellent tumour model that can be used to evaluate the physics of focused ultrasound. The results are currently being compared to an ongoing in vivo trial.

Key words: Ultrasound, MRI, veterinary

2. <u>10th International Conference on Biomedical and Bioinformatics Engineering (ICBBE 2023), Kyoto, Japan.</u>

Veterinary ablation system using MRI guided focused ultrasound

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Abstract— In this paper Focused Ultrasound (FUS) technology was used for veterinary oncology applications. This modality is an additional tool beyond traditional approaches. In this study we investigated the ability of FUS to precisely ablate hypothetical targets mimicking canine and feline tumours. Agar based targets were ablated with a Magnetic Resonance guided FUS (MRgFUS) robotic system featuring a single element spherically focused transducer of 2.7 MHz. The robotic system includes 3 linear cartesian axes and two manual axes. The MRgFUS system was capable of producing well-defined overlapping lesions in the mimicking tumours. The tumour mimicking phantom was imaged using 3T MRI. This technology has potential as a therapeutic solution for veterinary cancer. Although the device is MRI compatible, it can be used also outside the MRI setting using ultrasonic imaging. The next step is to apply this technology in animals and in humans.

Key words: Ultrasound, MRI, veterinary

3. **International Conference on BioMedical Technology (ICBMT 2024), Ho Chi Minh, Vietnam.**

Veterinary oncology using MRI guided focused ultrasound

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ABSTRACT

This paper focuses on the evaluation of a Focused Ultrasound MRI- guided robotic positioning device for veterinary oncology. The system was developed to be compatible with MRI using 3D printed technology. The positioning device includes MR compatible piezoelectric motors and encoders. The positioning device includes a single element spherically focused MRI compatible transducer. The system is portable and can be easily transferred into the veterinary clinics. The system was evaluated initially in phantoms, then freshly excised pork tissue and then in 8 pets (dogs and cats). This technology has potential as a therapeutic solution for veterinary cancer in pets.

KEYWORDS: MRI, ultrasound, positioning device, dogs, cats

ACKNOWLEDGMENTS: The study was co-funded by the European Structural & Investment Funds (ESIF) and the Republic of Cyprus through the Research and Innovation Foundation (RIF) under the project FUSVET (SEED/1221/0080).

4. **International Conference on Intelligent Medicine and Image Processing (IMIP 2024), Bali, Indonesia.**

Robotic device for MRI guided focused ultrasound for veterinary oncology

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Abstract— This paper presents a robotic device for Focused Ultrasound (FUS) technology for the treatment of veterinary cancer using an MRI compatible robotic system with 3 cartesian axes and one angular axis. The robotic device includes a single element spherically focused transducer operating at around 2.7 MHZ. The system was evaluated initially in agar-based phantoms and freshly excised tissue. The software of the system communicates with Siemens MRI scanner using the Access-I modules. Using the proton frequency shift equation temperature, thermal dose and thermal necrosis can be estimated from the phase images of gradient pulse sequences. Using deep learning techniques, it is possible for the user to be provided with the optimum ultrasonic protocol and navigation scheme. The positioning device is now under evaluation in cats and dogs with cancer. This technology has potential as a therapeutic solution for veterinary cancer.

Key words: MRI, ultrasound, robotic, veterinary, oncology.

ACKNOWLEDGMENTS: The study was co-funded by the European Structural & Investment Funds (ESIF) and the Republic of Cyprus through the Research and Innovation Foundation (RIF) under the project FUSVET (SEED/1221/0080).

5. **International Conference on Intelligent Medicine and Image Processing (IMIP 2024), Bali, Indonesia.**

Focused Ultrasound Tumor bearing Phantom

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Abstract— The current study proposes an agar-based tissue mimicking phantom with embedded tumor mimic that can be used for evaluating the heating abilities of Focused Ultrasound (FUS) transducers. The background material mimicking normal tissue was made of agar and water, whereas the tumor mimic was differentiated by including proper concentration of silicon dioxide. This difference in the silicon dioxide content resulted in excellent contrast between the tumor and surrounding normal tissue in Magnetic Resonance Imaging (MRI). High power sonications were performed within the phantom using a single element transducer as integrated in an MRI compatible positioning device under MR thermometry guidance in a 3 T MRI scanner. Based on coronal images showing the experimental setup, it was possible to move the FUS beam within the phantom precisely. MR temperature monitoring within and outside of the tumor simulator revealed higher heat accumulation within the tumor mimic owing to the inclusion of silicon dioxide, which increased its ultrasonic absorption. Temperature maps acquired in a plane parallel to the beam revealed beam deflection at the tumor boundaries. Overall, the developed tumor phantom model was proven to be a cost-effective and ergonomic tool for MRI-guided FUS studies.

Key words: agar-based phantom, focused ultrasound, MR thermometry, tumor mimic.

ACKNOWLEDGMENTS: The study was co-funded by the European Structural & Investment Funds (ESIF) and the Republic of Cyprus through the Research and Innovation Foundation (RIF) under the project FUSVET (SEED/1221/0080).

6. **International Symposium on Therapeutic Ultrasound (ISTU 2024), Taipei, Taiwan.**

Canine and feline tumor ablation field trial with a FUS ablation system

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Preferred Presentation Type:
In-Person Poster Presentation

Abstract Topic:
Immunotherapy, Oncology, Combination Therapy

Abstract Title:
Canine and feline tumor ablation field trial with a FUS ablation system

Objectives:

Herein, Focused Ultrasound (FUS) ablation was utilised for treating spontaneous tumors in dogs and cats, employing a custom-made Magnetic Resonance-compatible FUS robotic system.

Methods:

The system utilizes a single-element, spherically focused transducer operating at 2.6 MHz to non-invasively deliver high intensity ultrasonic energy to the tumor site. The efficacy of this

technology was assessed through a trial involving 12 dogs and cats. All treatment procedures were performed successfully prior to tumor excision by the referring veterinarian.

Results:

Histological examination of excised tumors revealed evidence of thermal necrosis on the H&E-stained slides, visualized as well-defined regions of destroyed cell architecture. Overall, the FUS system demonstrated precise targeting capabilities, enabling partial ablation of tumors at various anatomical locations in veterinary patients. Notably, the system's portability facilitated its seamless integration into veterinary clinics.

Conclusions:

The study outcomes revealed promising therapeutic potential, suggesting that the developed technology could provide a viable avenue for non-invasive therapeutic interventions in veterinary oncology.

Acknowledgements:

The study was funded by the European Structural & Investment Funds& the Republic of Cyprus through the Research and Innovation Foundation (FUSVET (SEED/1221/0080).

Appendix: Oral and Poster Presentations

2023 10TH INTERNATIONAL CONFERENCE ON BIOMEDICAL AND BIOINFORMATICS ENGINEERING

November 9-12, 2023, Suzaku Campus, Ritsumeikan University, Kyoto, Japan

T1 AND T2 VALUES OF AN AGAR-BASED PHANTOM WITH INCLUSION OF TUMOUR

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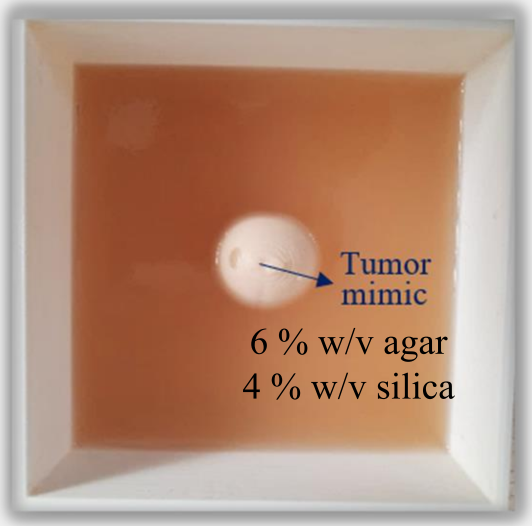
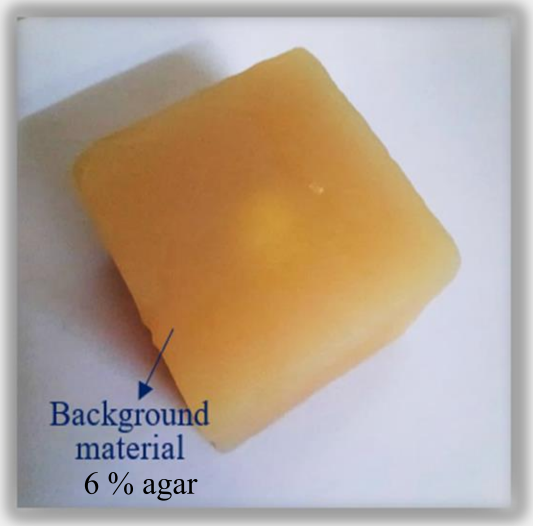
**Corresponding author*

PHANTOM DEVELOPMENT

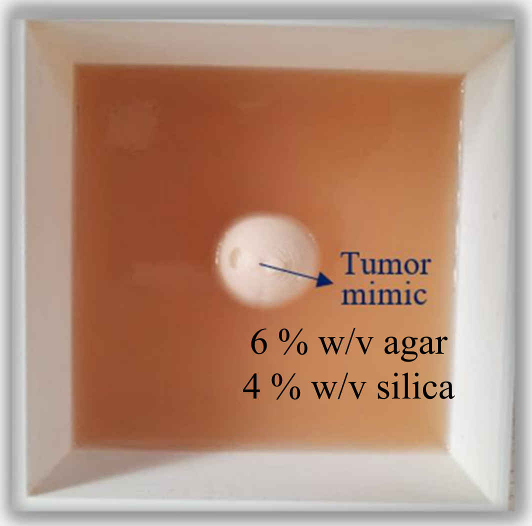
An agar-based mimicking material which includes a tumour was developed. The phantom can be used to evaluate the temperature produced by a focused ultrasound (FUS) transducer. The tumour model was made out of water, agar (6 % w/v) and 4 % w/v silica. In the tissue surrounding the tumour no silica was used.

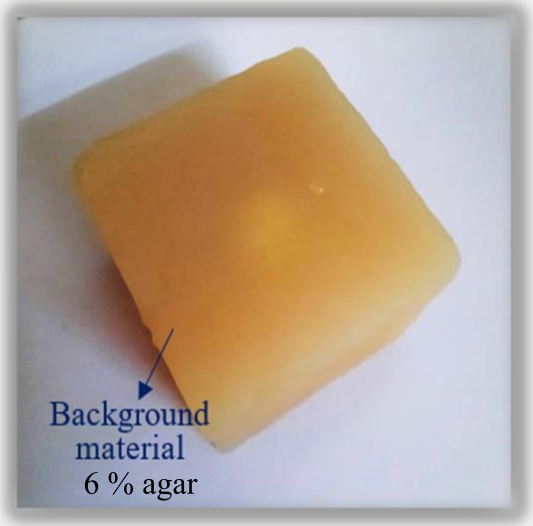




PHANTOM EVALUATION

- The T1 and T2 relaxation times of the phantom were measured in a 3T Magnetic Resonance Imaging (MRI) scanner; Magnetom Vida, Siemens Healthineers.
- FUS sonications were performed in the phantom using an MR compatible positioning device to examine its response to thermal heating using MR thermometry.



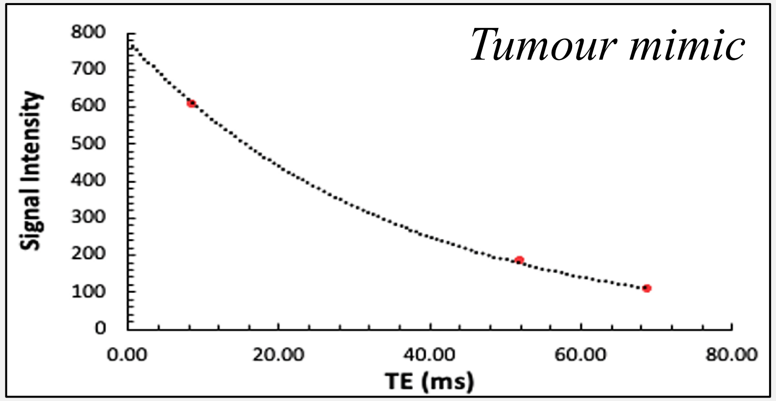


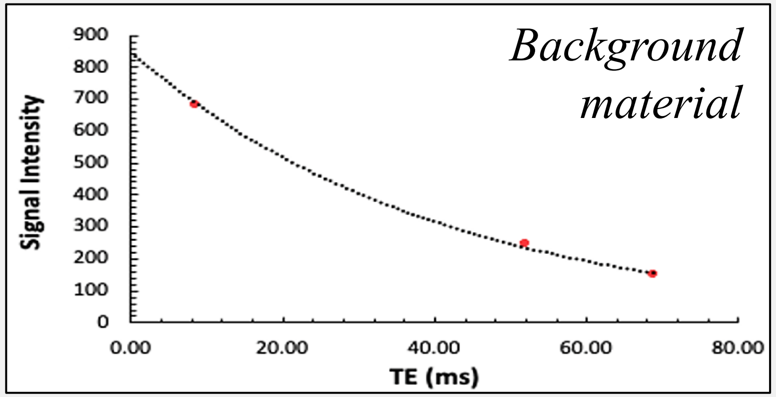
T1 AND T2 MAPPING

- The slight difference in silica content between tumour and surrounding tissue resulted in excellent contrast between tumour and tissue in MRI.
- The tumour mimic showed lower relaxation times owing to the addition of silica.

Material	T1 (ms)	T2 (ms)
Tumour mimic	2099.2	35.7
Background material	2135.8	40.0

***T2 mapping**: T2-W TSE sequence with varying TE values of 8 to 69 ms (TR = 250 ms, FA = 180º, FOV = 260 × 260 x 10 mm^3, matrix size =128 × 128, NEX = 2, ETL = 12).*
***T1 mapping**: Gradient Echo (GRE) sequence with varying FA values of 3 to 15º (TR = 15 ms, TE = 1.93 ms, FOV = 250 x 250 x 5 mm^3, matrix size = 256 x 256, NEX = 1, ETL = 1).*

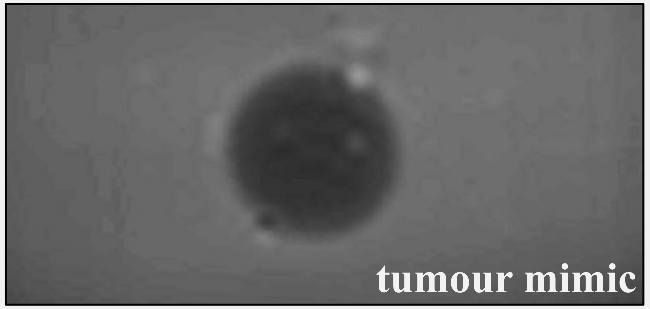




Signal intensities measured from T2-W Turbo Spin Echo (TSE) images using varied Echo time (TE) values for T2 mapping.

MRI-BASED FUS NAVIGATION

Based on coronal images showing the transducer and tumour/tissue it was possible to precisely move the focused ultrasound beam within the phantom using the MR compatible positioning device. MR temperature was detected within the tumour and outside the tumour.



T2-W TSE images *(TR = 2500 ms, TE = 52 ms, FA =180°, ETL =12, FOV = 260 x 260 x 10 mm^3, matrix size = 128 x 128, and NEX = 2).*

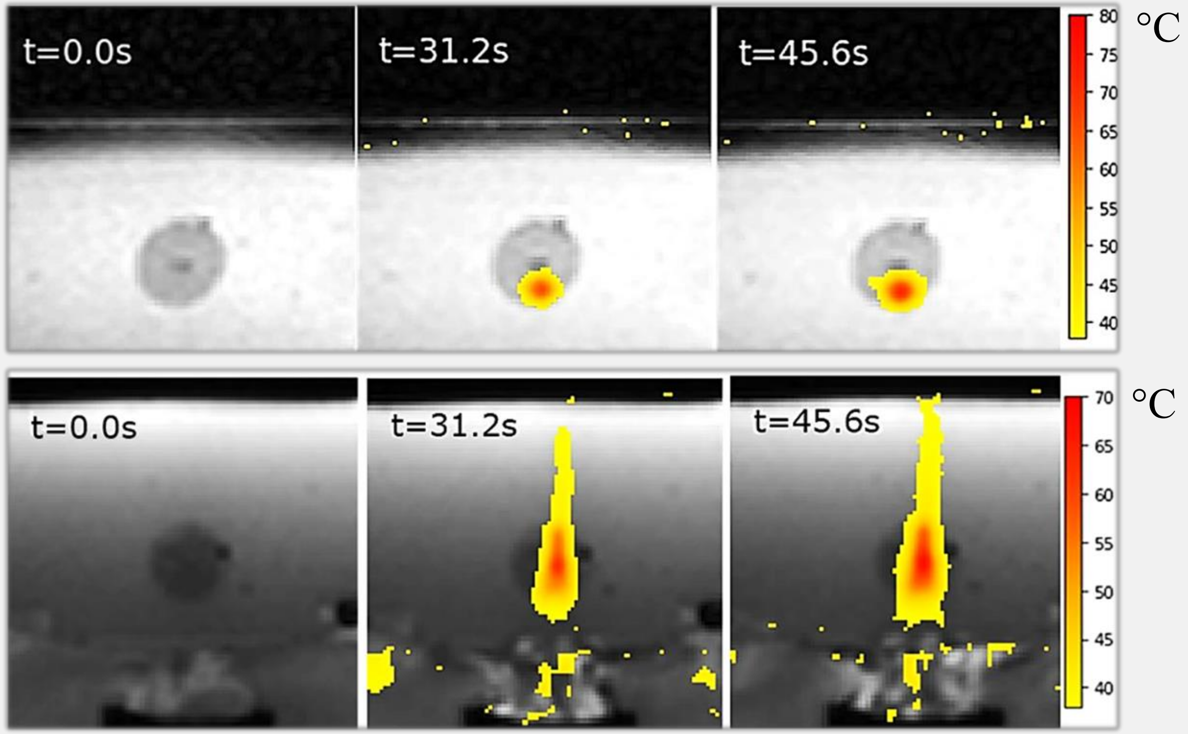
SONICATION WITHIN THE PHANTOM

ICBBE 2023

Indicative thermal maps acquired during sonication within the tumour mimic:

Coronal maps

Axial maps

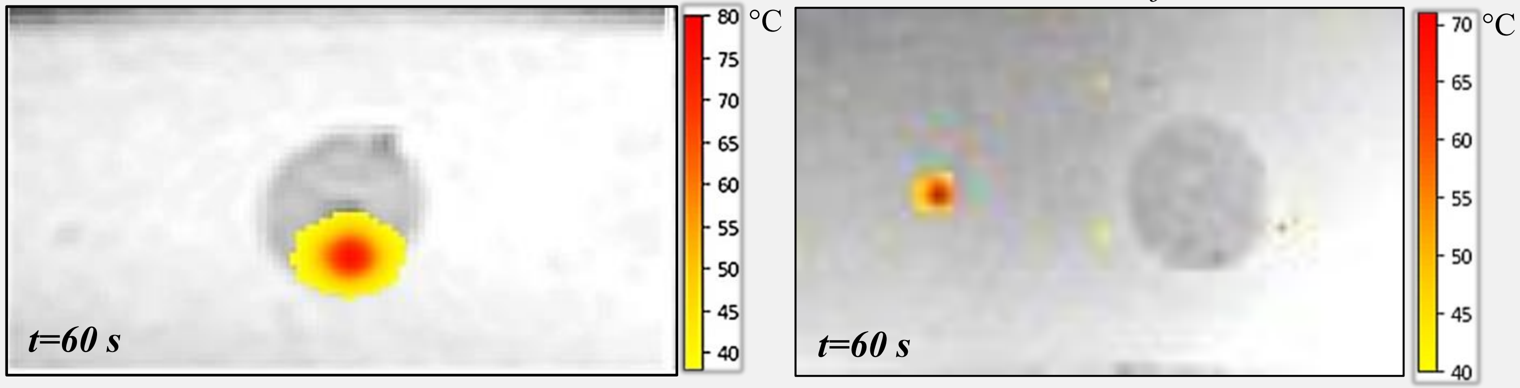


SONICATION WITHIN THE PHANTOM

Indicative thermal maps acquired during sonication within and outside of the tumour mimic:

- A maximum temperature of **65 ºC** was recorded **outside of the tumour** using acoustic power of 60 W for 60 s.
- A higher temperature of **75ºC** was reached **within the tumour** (baseline of 37ºC).

Sonication within the tumour *Sonication outside of the tumour*



Thermal coronal maps *acquired at the end of sonication (60 W acoustic power, 60-s duration, 35-mm focal depth) extracted from FLASH images (TR=25 ms, TE=10 ms, FOV = 280×280x3 mm^3, NEX = 1, FA = 30^o, ETL = 1, matrix = 96 x 96).*

CONCLUSIONS

ICBBE 2023

Due to the inclusion of silica in the tumour the absorption was increased within the tumour, and therefore, higher temperatures were measured in the tumour. Temperature across a plane parallel to the beam showed some deflection of the beam in areas of tumour curvature.

This is an excellent tumour model that can be used to evaluate the physics of the FUS technology. The results are currently being compared to an ongoing in vivo trial.

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2016-2020 RESTART RESEARCH

ΠΡΟΓΡΑΜΜΑΤΑ ΕΡΕΥΝΑΣ, ΤΕΧΝΟΛΟΓΙΚΗΣ ΑΝΑΠΤΥΞΗΣ ΚΑΙ ΚΑΙΝΟΤΟΜΙΑΣ

Κυπριακή Δημοκρατία

Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης

Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

FUSVET (SEED/1221/0080)

ACKNOWLEDGEMENTS

Thank you for your attention!

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VETERINARY ABLATION SYSTEM USING MRI GUIDED FOCUSED ULTRASOUND

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European Union
European Structural and Investment Funds

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Structural Funds of the European Union in Cyprus

OUTLINE

- ❑ Development of an MRI-guided focused ultrasound (MRgFUS) robotic system for veterinary cancer applications.
- ❑ Robotic system has 5 degrees of freedom (DOF).
- ❑ The robotic system navigates a compact single element transducer.
- ❑ System is compatible with all conventional MRI scanners.
- ❑ Development of software for controlling the system.
- ❑ Development of modern medical cart to assemble system components.
- ❑ Evaluation of the system in phantoms, and excised tissue.

HARDWARE DESIGN – **5 DOF ROBOTIC SYSTEM**

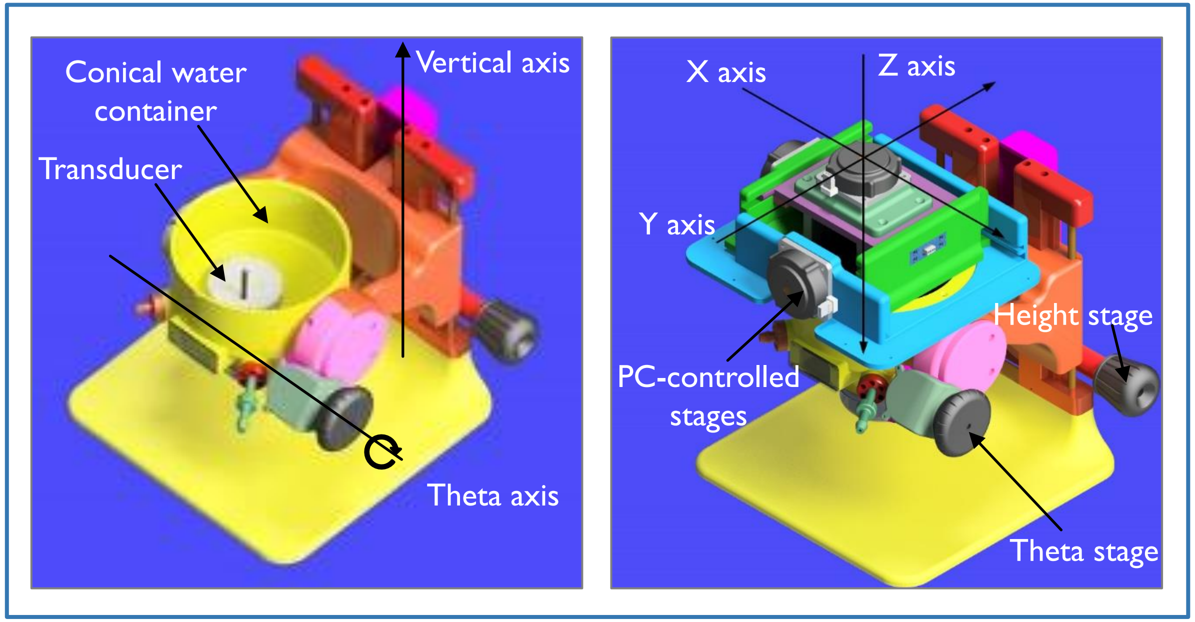
Prototype

- Developed for veterinary FUS cancer applications.

Mechanical design

- Motion in 3 PC-controlled (X, Y, and Z) & 2-manually controlled (Height, and Theta) axes.
- Transducer integrated in conical water container.
- PC-controlled axes linearly move the transducer in:
  - Vertical (Z), &
  - Horizontal (X, and Y) stages.
- Manual stages manipulate water container:
  - Height stage: linear motion along vertical axis.
  - Theta stage: rotational motion around X-axis.

CAD drawings of the robotic system



HARDWARE DESIGN – **5 DOF ROBOTIC SYSTEM**

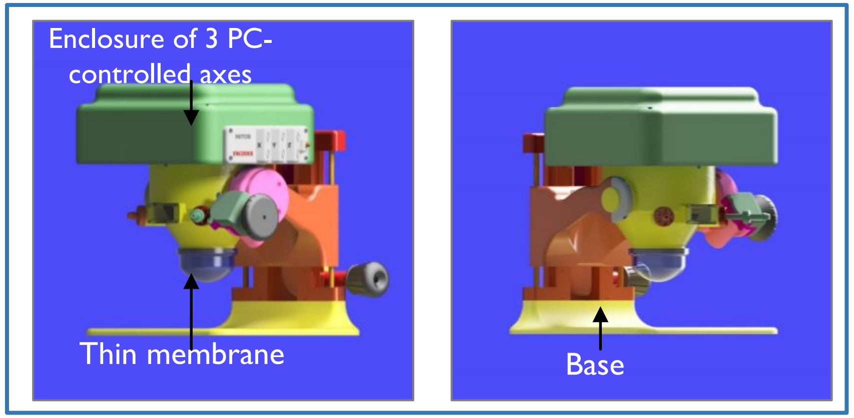
Mechanical design

- ❑ PC-controlled motion:
  - ❑ Actuated by piezoelectric motors (USR60-S3N, Shinsei, Tokyo, Japan).
  - ❑ Controlled with optical encoders (EM1-0-500-I, US Digital Corporation, Tokyo, Japan).
- ❑ PC-controlled stages housed in enclosures.
- ❑ Water container sealed with silicone bellow and thin membrane.
  - ⇒ Isolate mechanisms from water.

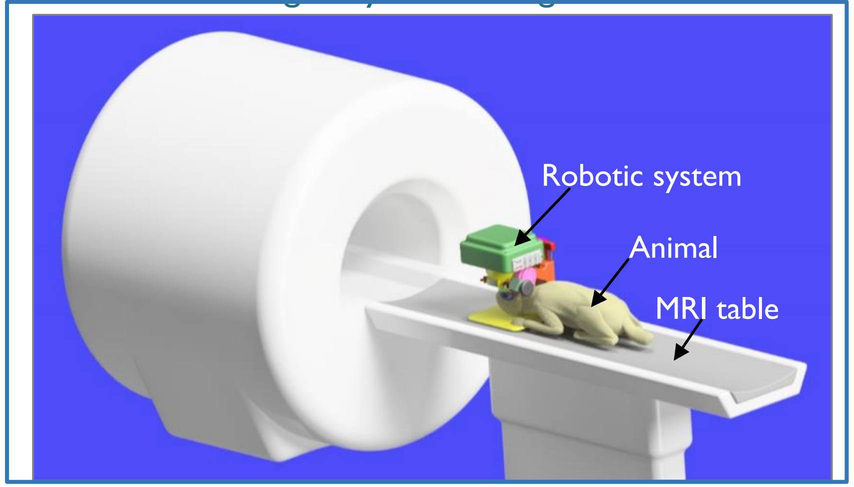
Manufacturing

- ❑ Designed using Inventor (Autodesk, USA, California).
- ❑ 3D-printed (F270, Stratasys, Minnesota, USA) using polylactic acid (PLA) thermoplastic.
- ❑ Accommodated on table of all MRI scanners for top to bottom treatment.

CAD drawings of the robotic system



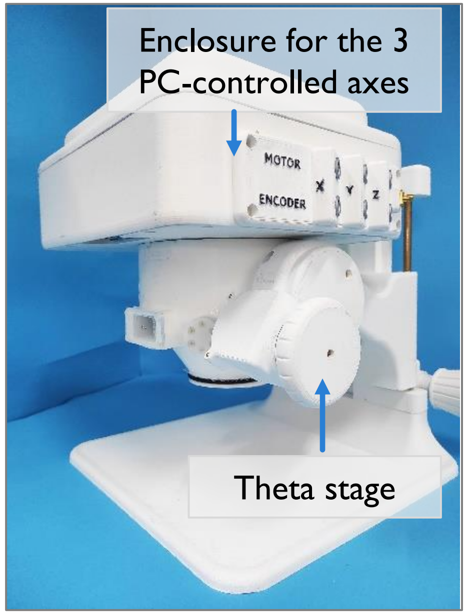
CAD drawing of system configuration in MRI



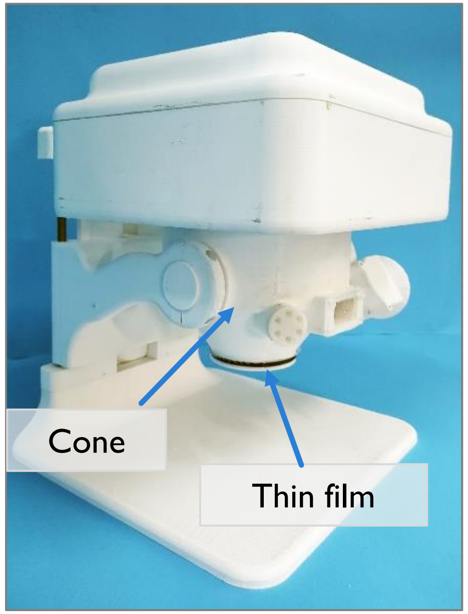
HARDWARE DESIGN – **5 DOF ROBOTIC SYSTEM (VERSION 1)**

Photos of manufactured device

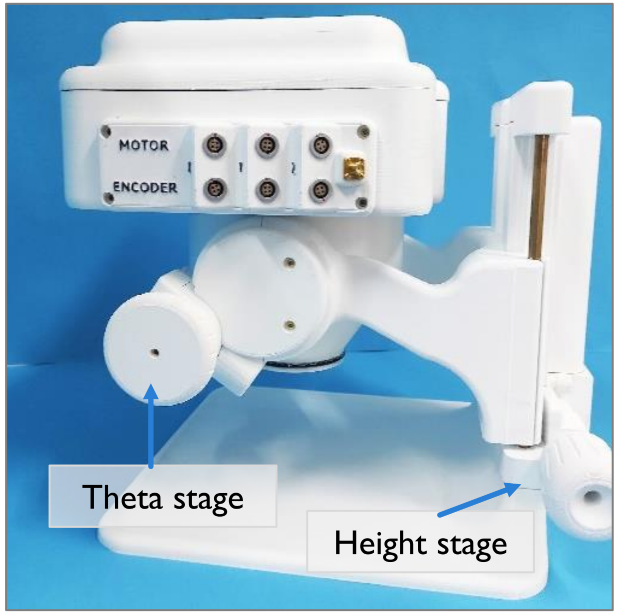
Front Right-side view



Front Left-side view



Right view

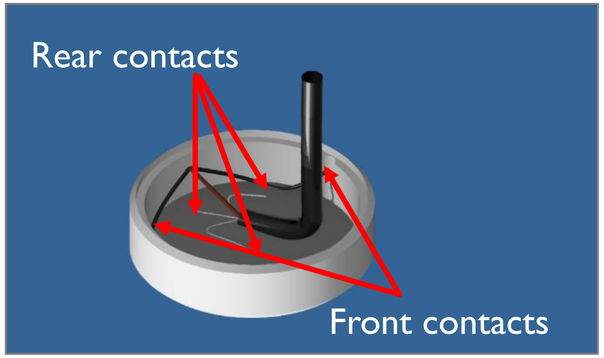


Front view

HARDWARE DESIGN – **ULTRASONIC TRANSDUCER MANUFACTURING**

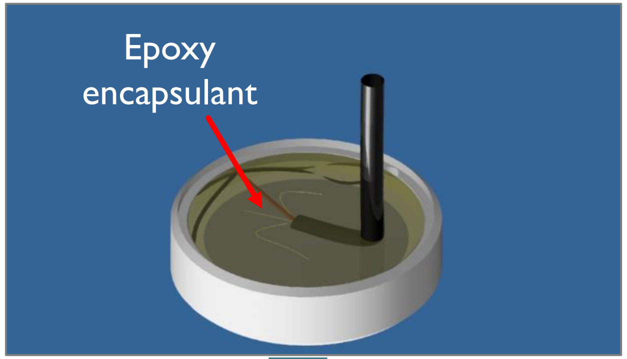
Electric circuit creation

- Conductive surfaces connected to cable.



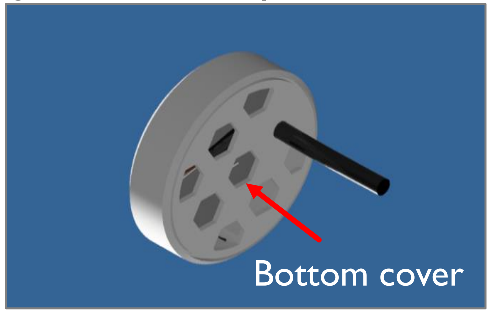
Electrical isolation

- Housing filled with epoxy.



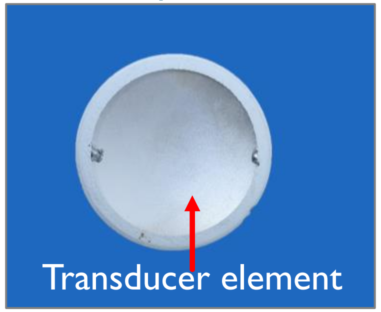
Transducer cooling

- Housing sealed with perforated cover.

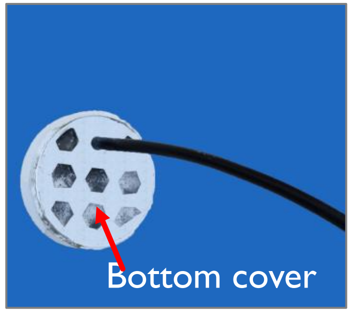


Manufactured transducer

Top view



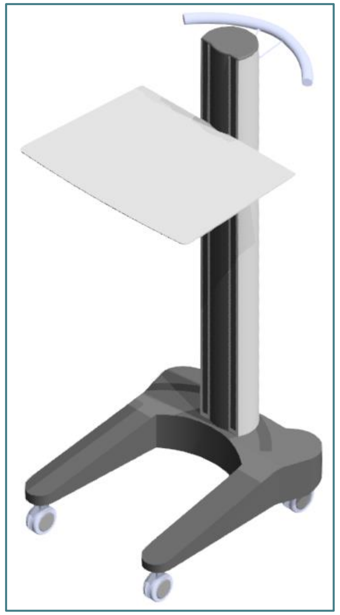
Bottom view



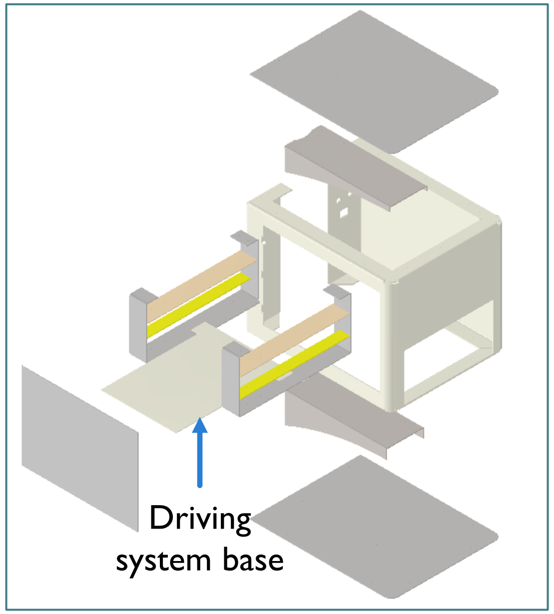
HARDWARE DESIGN – **MEDICAL CART**

- ❑ Hosts all electronic devices.
- ❑ Developed using commercial cart base:
  - ❑ Metal enclosures incorporated.
    - ❑ Designed based on component’s specifications.

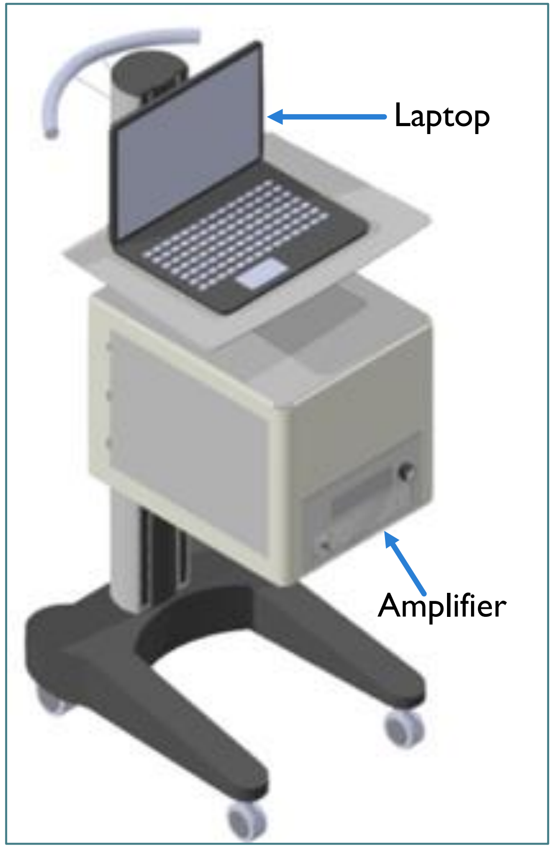
Ergonomic design



CAD model of cart base



CAD model of metal cart enclosures



CAD model of assembled medical cart

HARDWARE DESIGN – **MEDICAL CART**

Medical cart photos

Front view

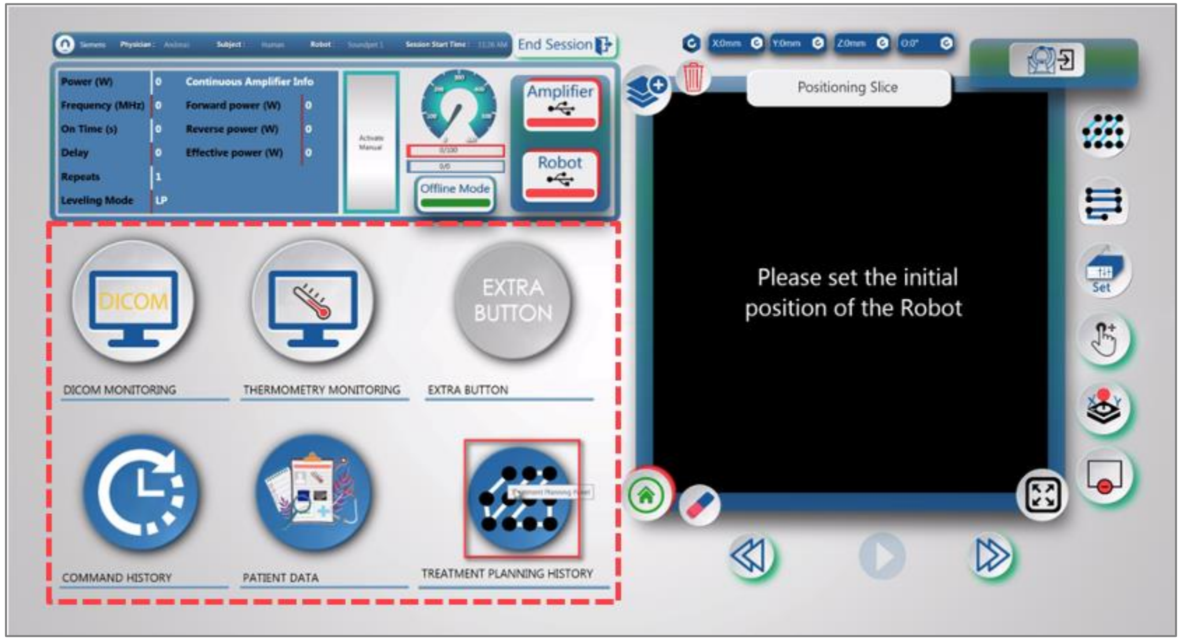
Side view

Rear view

HARDWARE DESIGN – **SOFTWARE DEVELOPMENT**

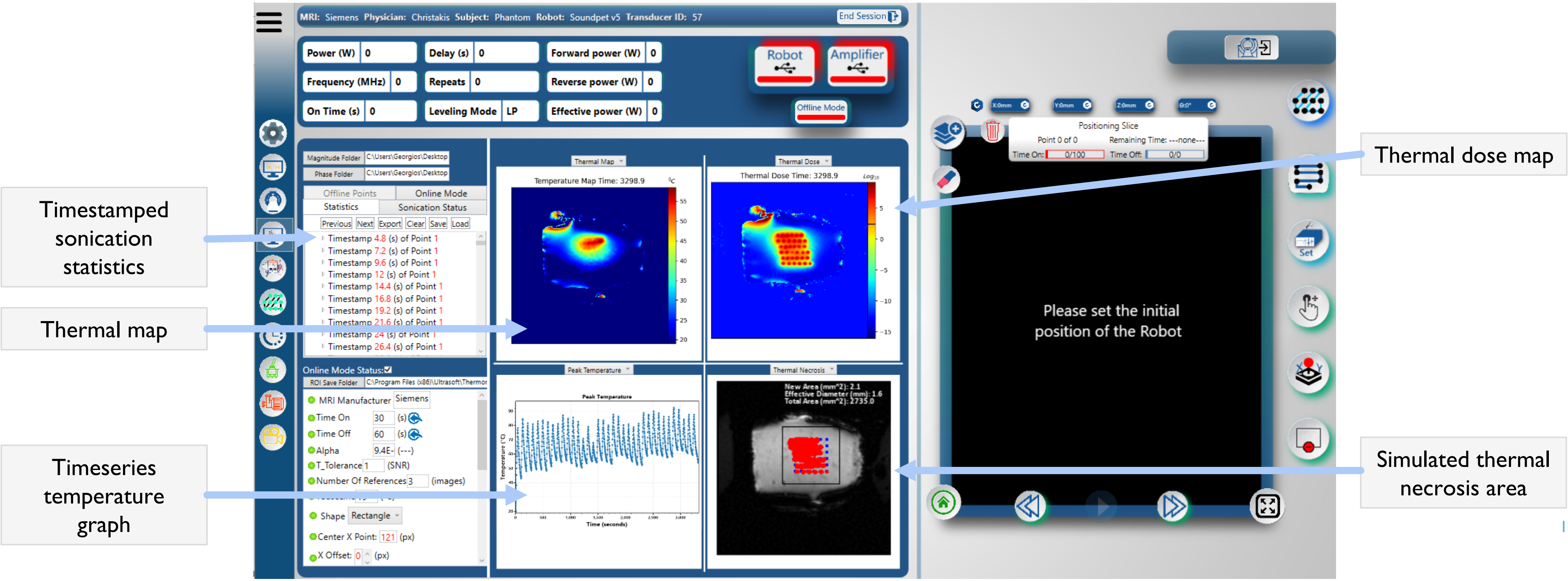
- ❑ Software developed in C# to control:
  - ❑ Robotic system motion
  - ❑ Ultrasonic transducer energy delivery
  - ❑ MRI scanner
    - ❑ Integrates tools for treatment planning and monitoring.
- ❑ Previous software platform improved and optimized:
  - ❑ Tools developed enabling easier treatment planning
  - ❑ Commands incorporated for remote MRI control
  - ❑ Tools developed offering improved treatment monitoring
  - ❑ User interface redesigned:
    - ❑ Functionality buttons integrated in toolbar ⇒ Easy interchange between functionalities.

Screenshot of main window of previous software platform



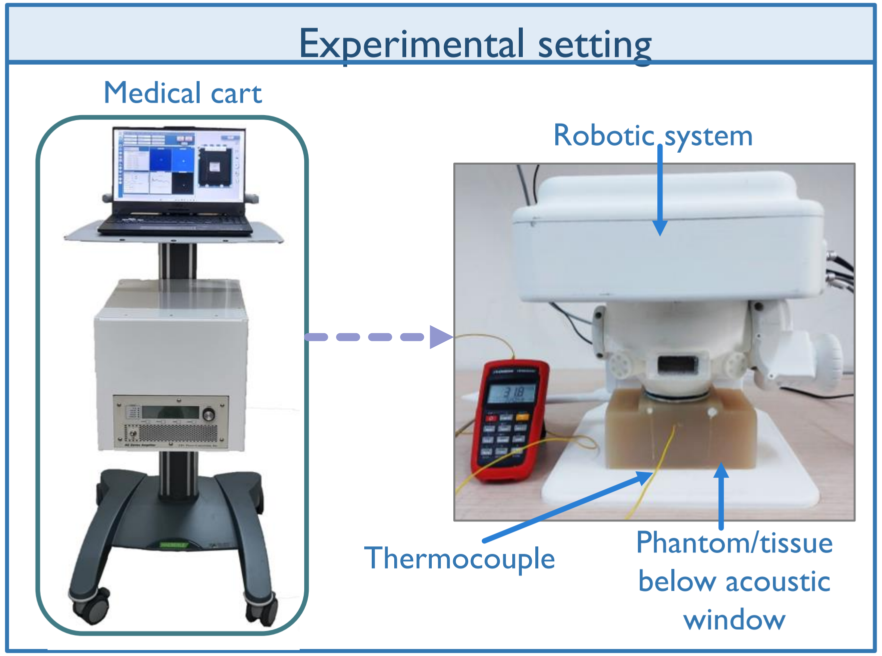
SOFTWARE DEVELOPMENT– **MR THERMOMETRY MONITORING PANEL**

- Thermometry data displayed next to treatment planning window.

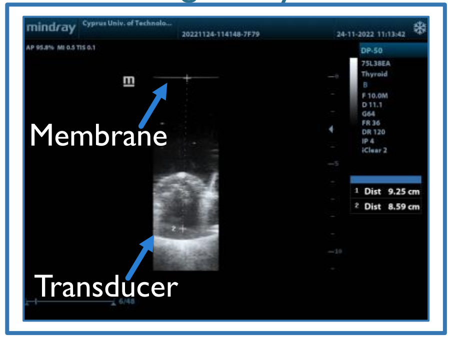


LABORATORY EXPERIMENTS – **TEMPERATURE INCREASE IN PHANTOM/TISSUE**

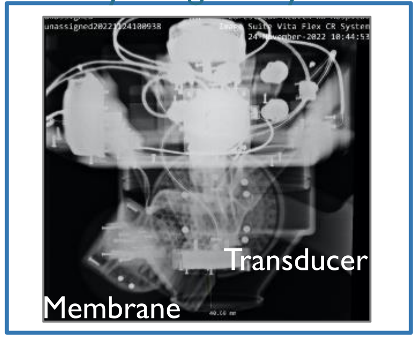
- Sonications executed on:
  - Agar-based phantoms (6 % w/v agar), &
  - Freshly excised pork tissue.
- Ultrasound (US) (DP-50, Mindray, Shenzhen, China) and X-ray (IMS001, Shenzhen Browiner Tech, Shenzhen, China) images of system acquired:
  - Determine transducer/membrane distance.
  - Set focal depth of sonications.
- Varied acoustical power (30-60 W) applied for 60 s to evaluate effect on temperature increase.



US image of system



X-ray image of system

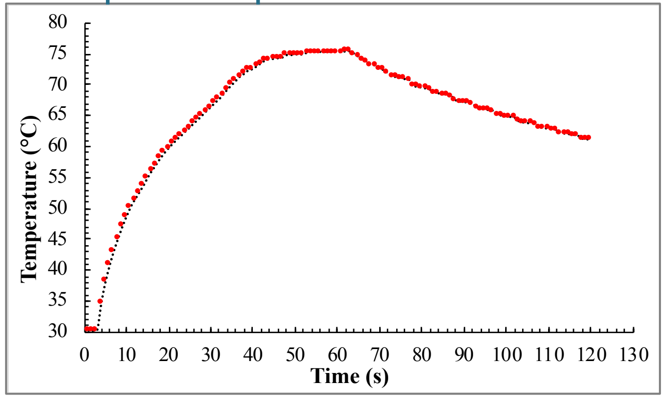


LABORATORY EXPERIMENTS – **TEMPERATURE INCREASE IN PHANTOM/TISSUE**

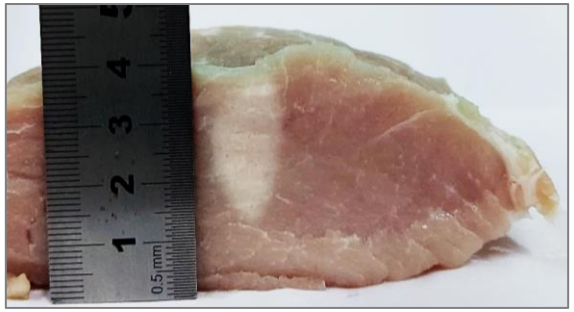
- In both phantom & excised tissue:
  - Increased ablative temperatures were induced at higher acoustical power.
- In excised tissue:
  - Temperature increase of 45.1 °C recorded with applied power of 45 W.
  - Lesions successfully inflicted at each applied power.
    - Increased lesion dimensions evidenced at higher applied acoustic energy.

⇒ Thermal heating capabilities of transducer validated.

Temperature profile in excised tissue



Inflicted lesions plane parallel to the beam



30 W for 60 s

60 W for 60 s

FUSVET vet ex machina Cyprus University of Technology

LABORATORY EXPERIMENTS – **EXCISED TISSUE GRID ABLATIONS**

- ❑ Grid ablations executed on excised pork tissue.
- ❑ Acoustical power of 45 W applied for 20 s.
- ❑ Robotic motion commanded along varied grid sizes:
  - ❑ Grid size progressively increased investigating system's ability in ablating large tissue areas.
  - ❑ 2×2 and 3×3 grid patterns used.
- ❑ Overlapping lesions were inflicted with a 7 mm step.

Overlapping lesions

Plane perpendicular to beam

Plane parallel to beam

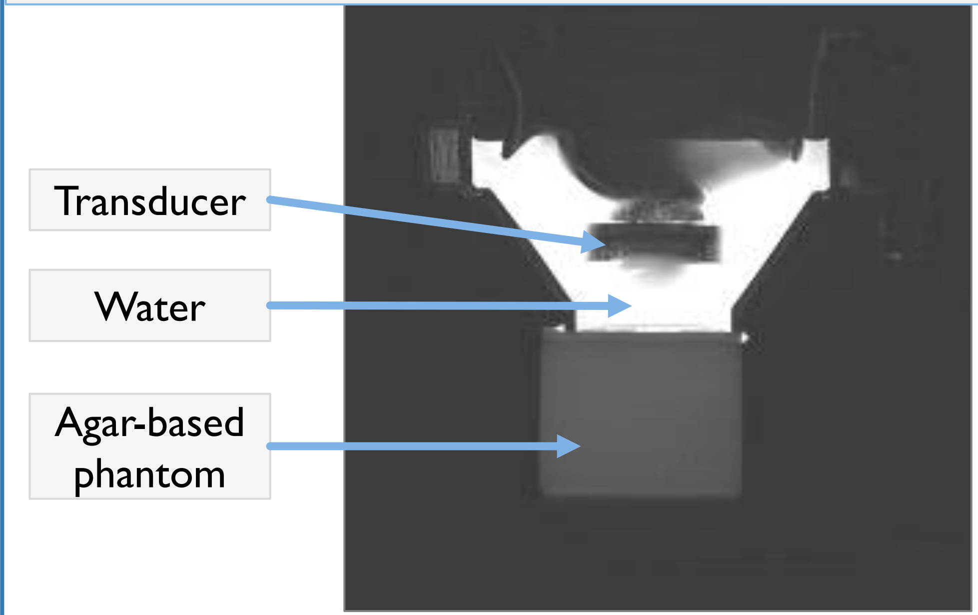
45 W for 20 s
3×3 grid, 7 mm step

MRI EXPERIMENTS – **ACOUSTIC COUPLING**

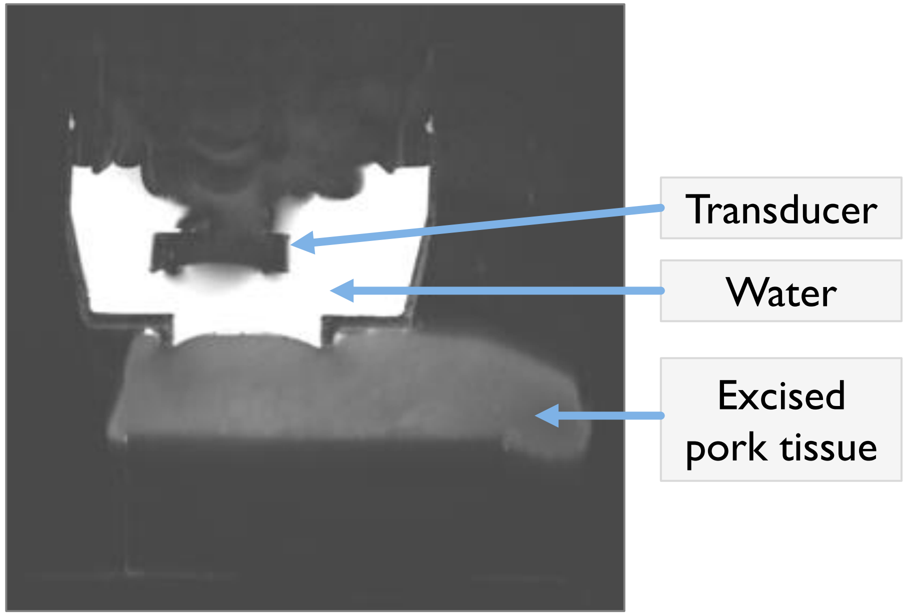
- Experimental setting scanned before experiments with T2-W FSE.

T2-W FSE images of experimental setting

Agar phantom



Excised pork tissue

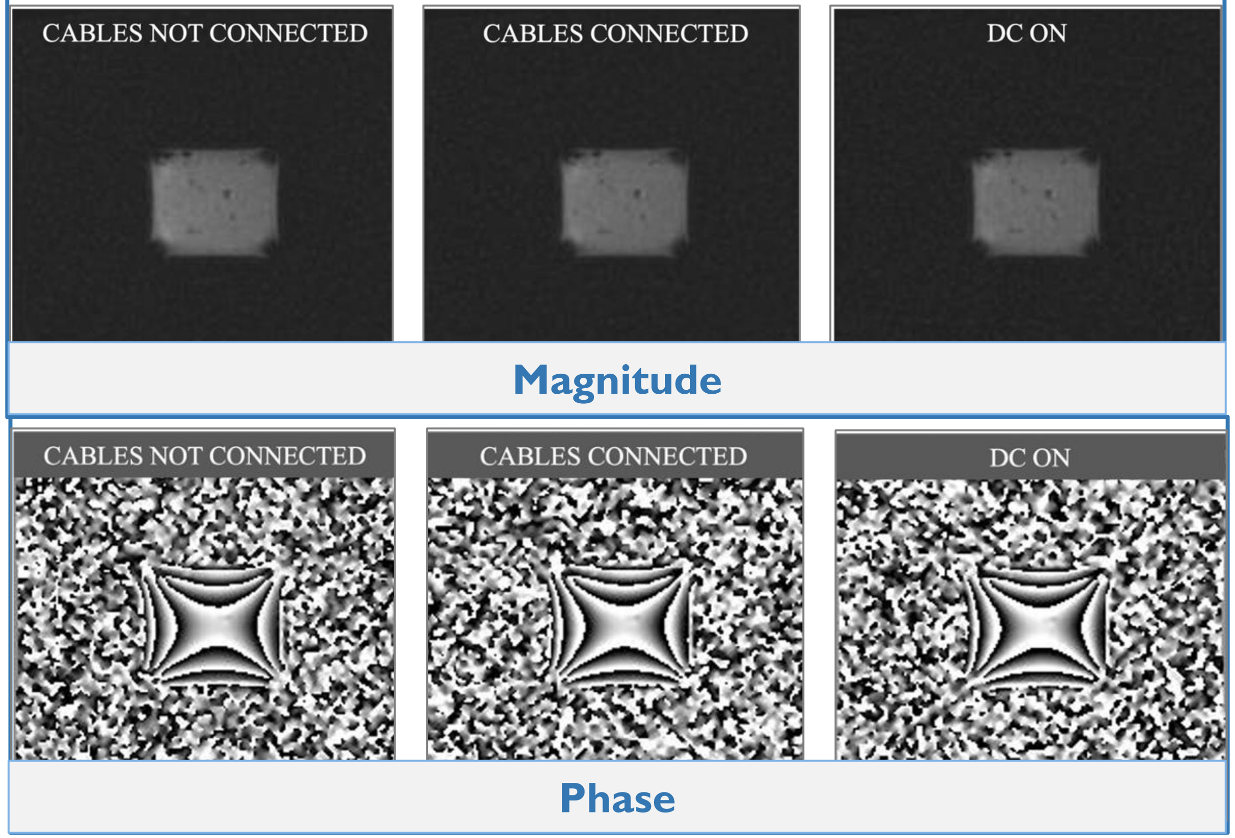


⇒ Excellent acoustic coupling between robotic system and phantom/tissue evidenced.

MRI EXPERIMENTS – **MRI COMPATIBILITY**

- ❑ Agar phantom (6 % w/v agar, 4 % w/v silica) scanned with FLASH sequence.
- ❑ FLASH images acquired for different activation conditions of:
  - ❑ Robotic system, &
  - ❑ Transducer.
- ❑ For each activation configuration:
  - ❑ SNR measured on magnitude FLASH images.
  - ❑ Signal intensity (SI) measured on phase FLASH images.

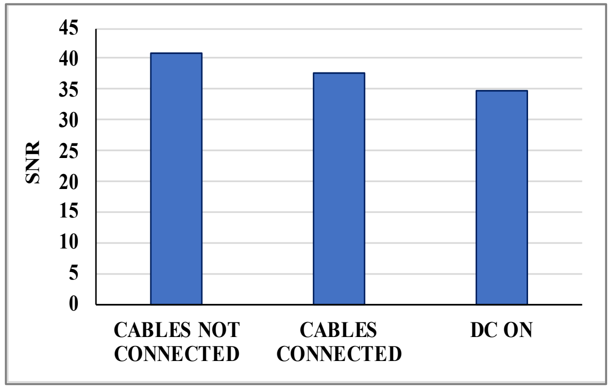
FLASH images acquired at various activation states of the robotic system



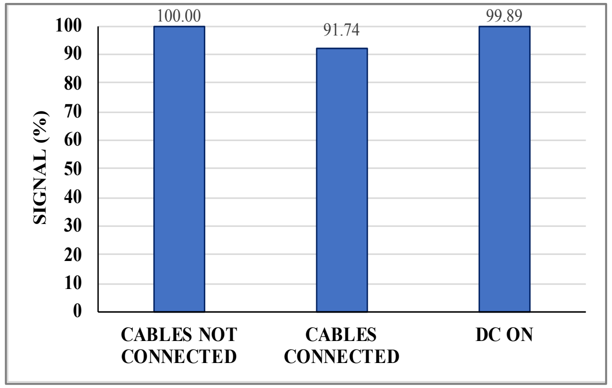
MRI EXPERIMENTS – **MRI COMPATIBILITY OF ROBOTIC SYSTEM**

- No artifacts were visible on FLASH images acquired at the various activation states.
- Magnitude FLASH images:
  - SNR minorly decreased:
    - Upon connection of motion cables, &
    - Electronic driving system activation.
- Phase FLASH images:
  - Small SI reductions observed between the different configurations.

Measured SNR from magnitude FLASH images at differect robotic system activations



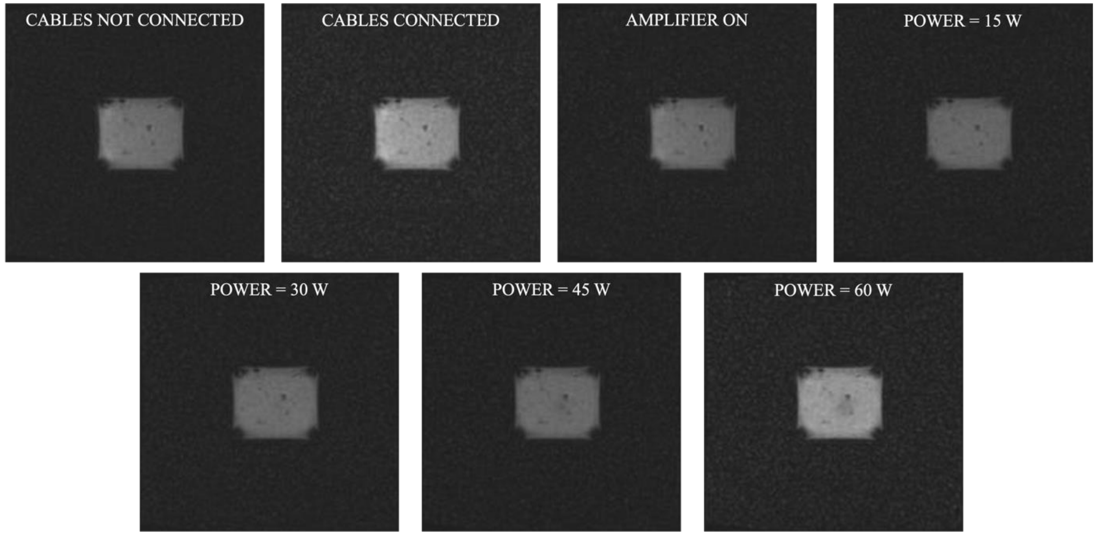
Measured SI from phase FLASH images at differect robotic system activations



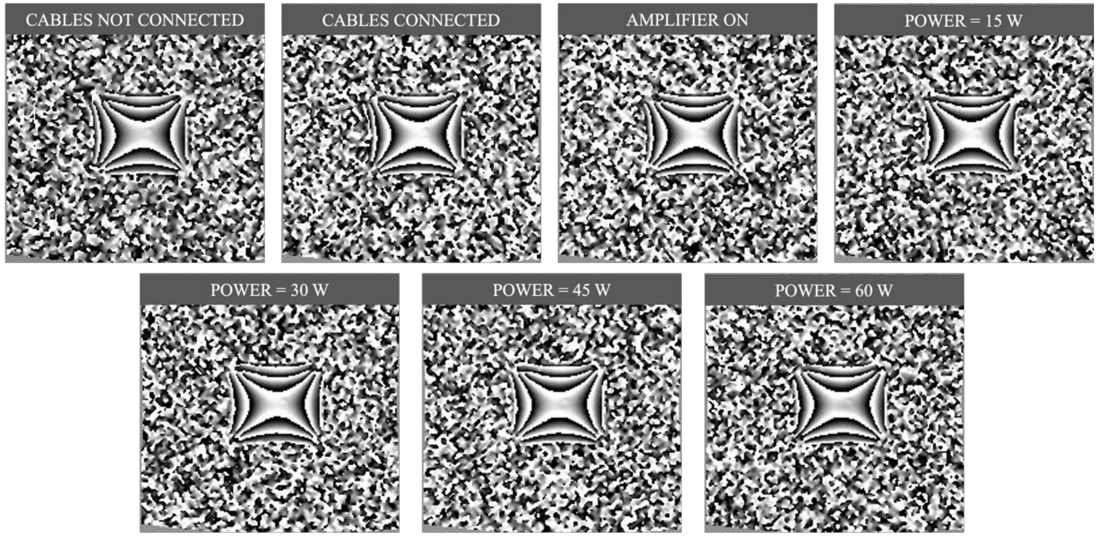
MRI EXPERIMENTS – **MRI COMPATIBILITY OF TRANSDUCER (VISUAL RESULTS)**

FLASH images acquired at various activation states of the transducer

Magnitude



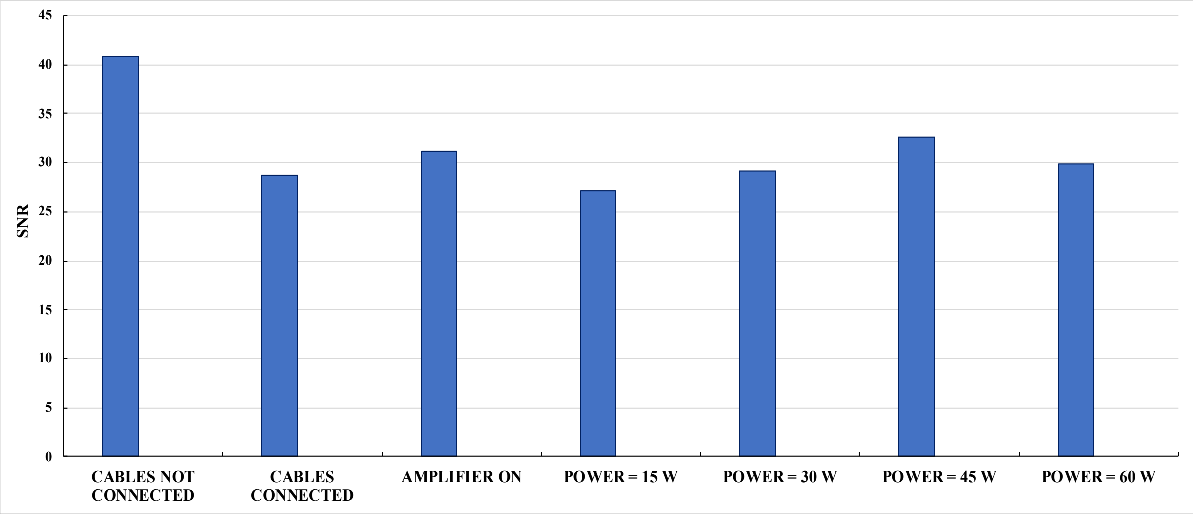
Phase



⇒ **Minimal impact on image quality.**

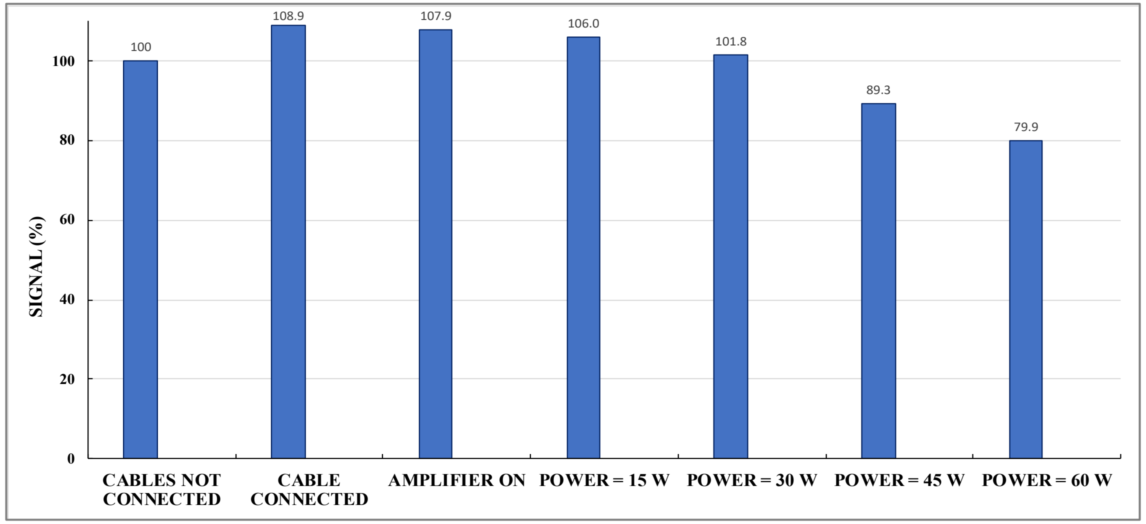
MRI EXPERIMENTS –**MRI COMPATIBILITY OF TRANSDUCER (SNR & SI RESULTS)**

- Magnitude FLASH images:
  - Small SNR reductions from reference observed for the various configurations.
  - SNR variations observed during transducer activation at acoustic power of 15-60 W.



Measured SNR from magnitude FLASH images at differect transducer activations

- Phase FLASH images:
  - SI variations existed between the various activation states.
  - Higher SI reductions evident during transducer activation at increased acoustic power.



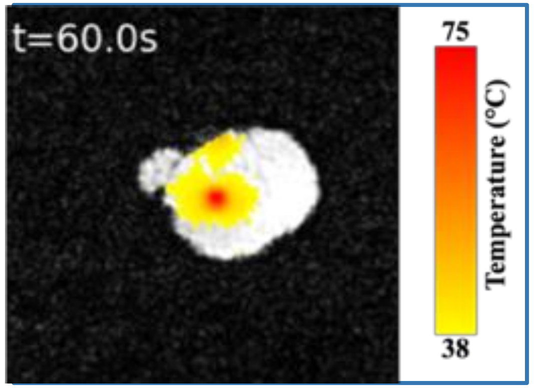
Measured SI from phase FLASH images at differect transducer activations

MRI EXPERIMENTS–**THERMAL HEATING EVALUATION WITH MR THERMOMETRY**

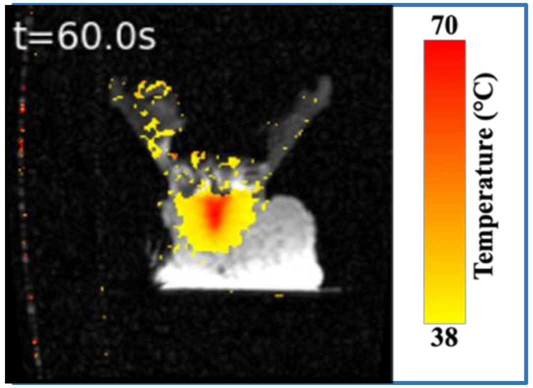
- Sonications were executed evaluating MR thermometry monitoring.
- Varied power of 15-60 W applied for 30-60 s.
- Sonications executed on phantom & tissue.
  - Scanned with FLASH sequence in coronal & axial planes.
- Thermal heating clearly visible on coronal and axial thermal maps.
- Higher temperatures recorded in coronal thermal maps.
- Ablative level temperatures generated in tissue.
  - Lesion formation evidenced with T2-W FSE images.

60 W for 30 s

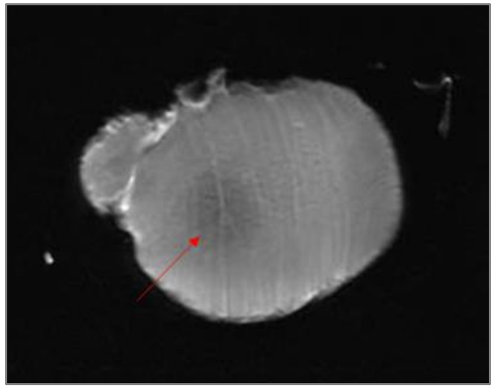
Coronal thermal map of tissue



Axial thermal map of tissue



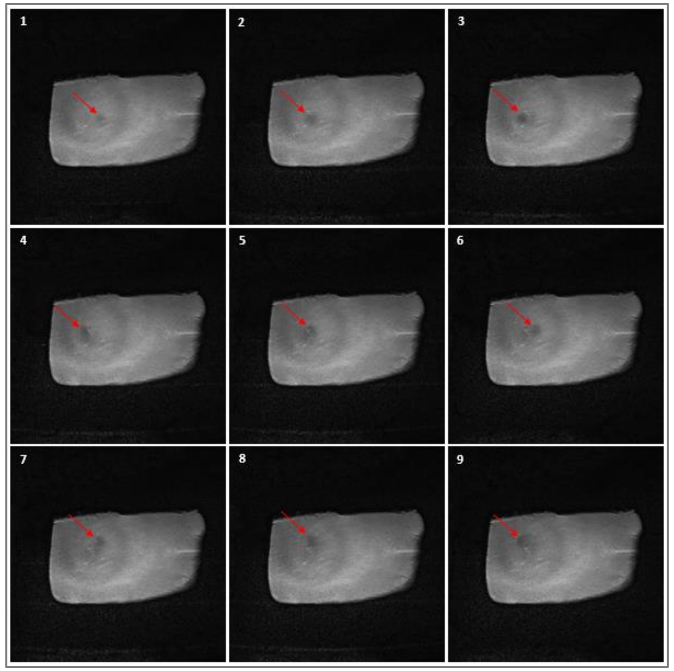
T2-W FSE image of inflicted lesion



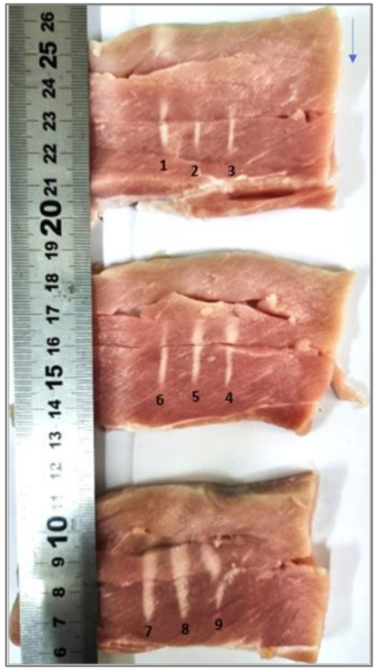
MRI EXPERIMENTS – **LESION DETECTION (MONITORING FORMATION)**

- ❑ A 3×3 grid operation with 7 mm step executed on excised tissue.
- ❑ Acoustic power of 60 W applied for 20 s.
- ❑ T2-W FSE images acquired during grid operation assessing lesion formation.
- ❑ Inflicted lesions clearly visible on T2-W FSE images.
- ❑ Discrete lesion formation evidenced with tissue slicing.
    - ❑ Equally spaced lesions ⇒ Robotic motion accuracy.
    - ❑ Similar dimensions ⇒ Constant acoustic energy delivery.

T2-W FSE images of inflicted lesion



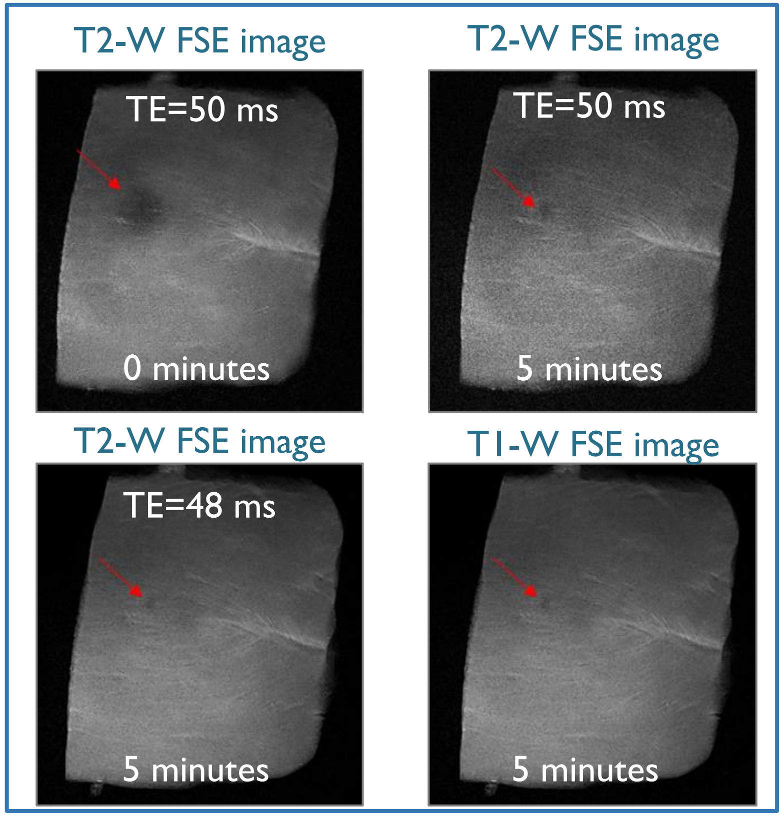
Inflicted lesions



MRI EXPERIMENTS – **OPTIMAL LESION DETECTION**

- Sonications executed on excised tissue.
- Acoustic power of 75 W applied for 60 s.
- Tissue lesions imaged using T2-W FSE sequence with varied TE:
  - 48 ms &
  - 50 ms

  At 0-5 minutes post-sonications.
- And T1-W FSE sequence.
- T2-W & T1-W FSE images visually assessed for optimal contrast between lesion and surrounding tissue.



⇛

- **For optimal lesion detection:**
  - T2-W FSE sequence &
  - TE =50 ms

ACKNOWLEDGEMENTS

The project was funded by the Research and Innovation Foundation of Cyprus. The robotic device used for the purposes of the study was developed under the project FUSVET (SEED/1221/0080).

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https://theralabcut.org/

ICBMT 2024
2024 6th International Conference on BioMedical Technology
(ICBMT 2024)
February 23-25, 2024, Ho Chi Minh, Vietnam

VETERINARY ONCOLOGY USING MRI GUIDED FOCUSED ULTRASOUND

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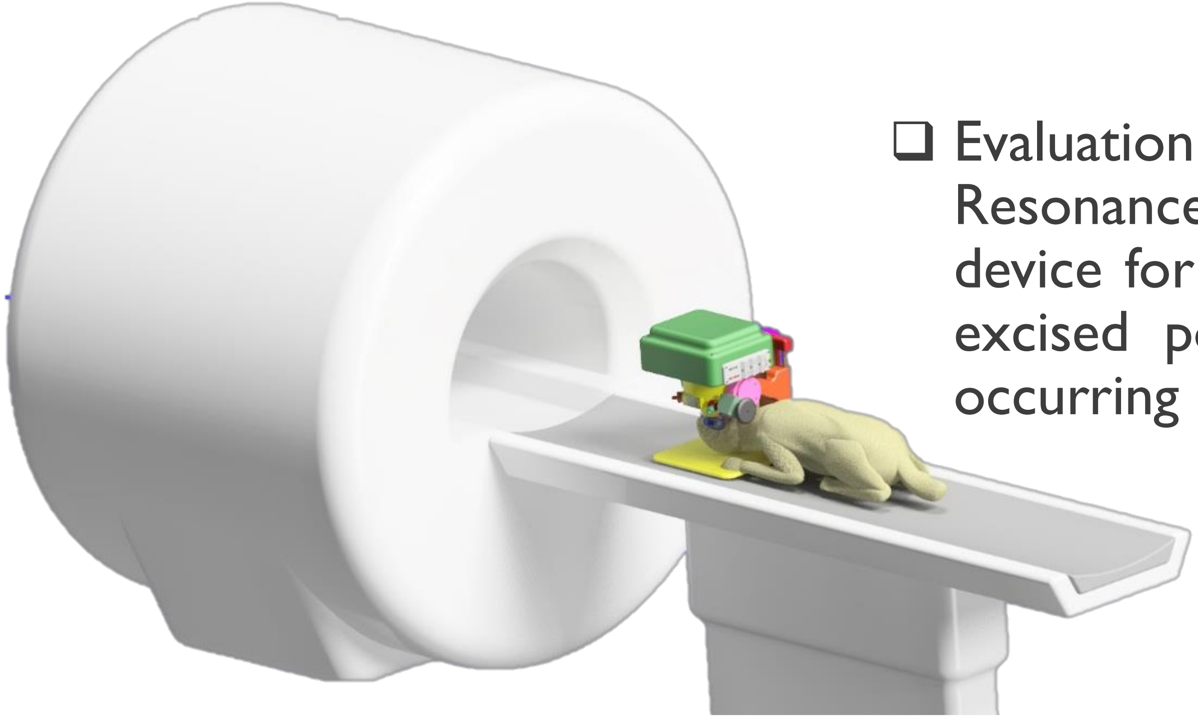
PURPOSE



- Evaluation of a Focused Ultrasound (FUS) Magnetic Resonance Imaging (MRI) - guided robotic positioning device for veterinary oncology in phantoms and freshly excised pork tissue, and then in pets with naturally occurring cancer.

5 DOF ROBOTIC SYSTEM

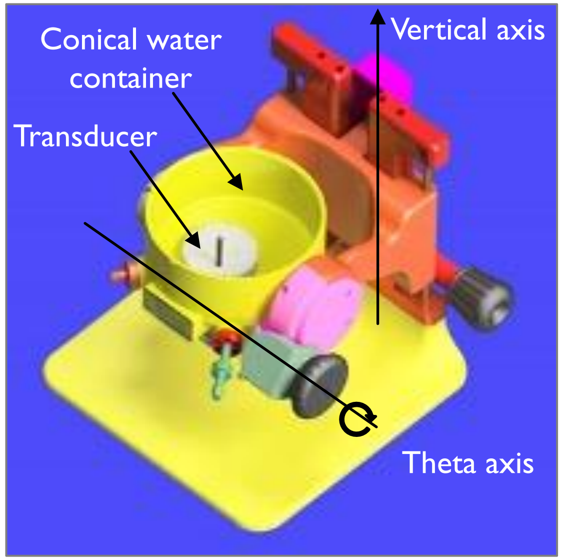
Prototype

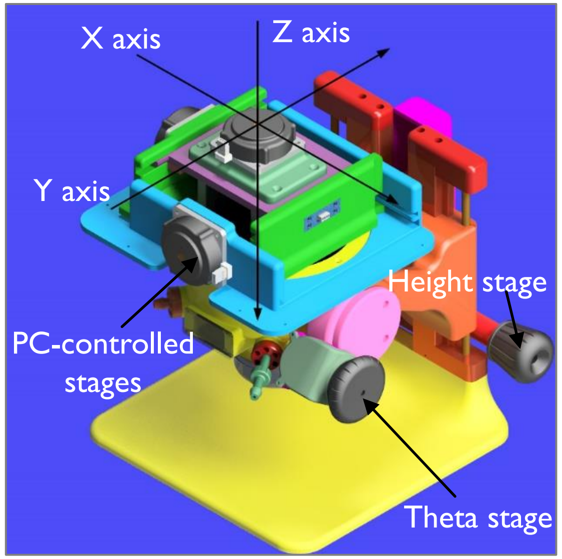
- Developed for veterinary FUS cancer applications.

Mechanical design

- Motion in 3 PC-controlled & 2-manually controlled axes.
- Transducer integrated in conical water container.
- PC-controlled axes linearly move the transducer in:
  - Vertical (Z) & Horizontal (X, and Y) stages.
- Manual stages manipulate water container:
  - Height stage: linear motion along vertical axis.
  - Theta stage: rotational motion around X-axis.

CAD drawings of the robotic system





5 DOF ROBOTIC SYSTEM

Mechanical design

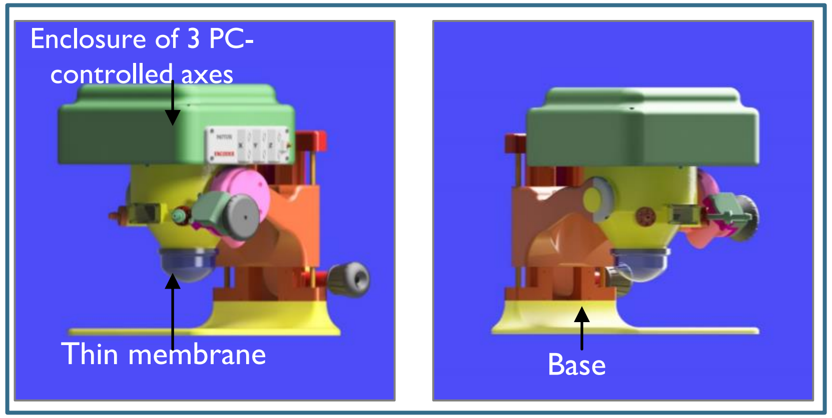
- ❑ PC-controlled motion:
  - ❑ Actuated by piezoelectric motors (USR60-S3N, Shinsei, Tokyo, Japan).
  - ❑ Controlled with optical encoders (EM1-0-500-I, US Digital Corporation, Tokyo, Japan).
- ❑ Water container sealed with silicone bellow and thin membrane

  ⇒ Isolate mechanisms from water.

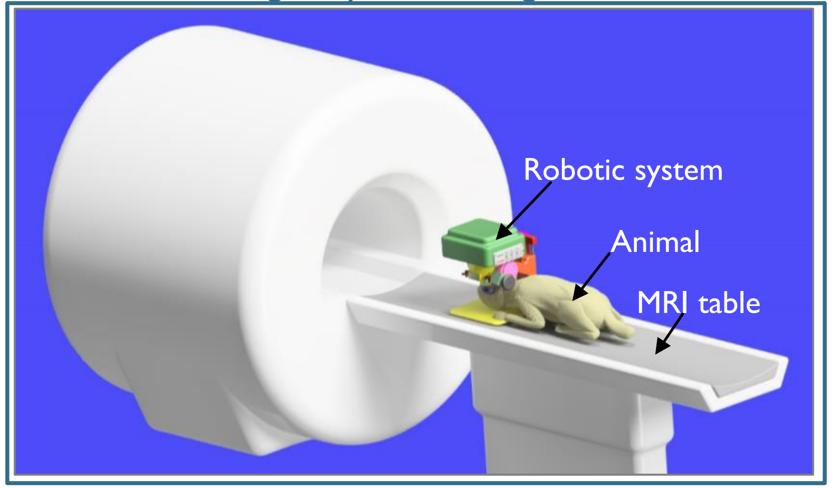
Manufacturing

- ❑ Designed using Inventor (Autodesk, USA, California).
- ❑ 3D-printed (F270, Stratasys, Minnesota, USA) using polylactic acid (PLA) thermoplastic.
- ❑ Accommodated on table of all MRI scanners for top to bottom treatment.

CAD drawings of the robotic system



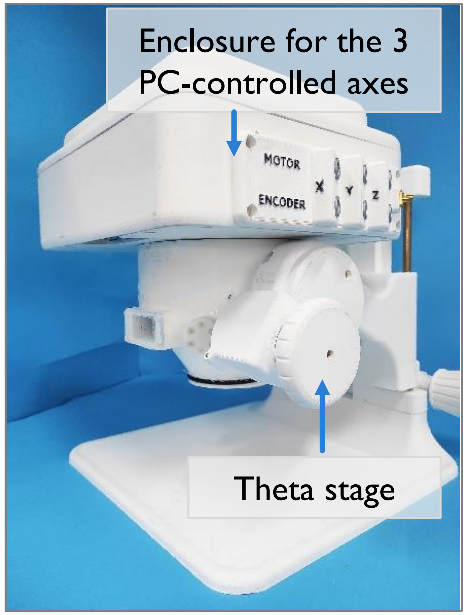
CAD drawing of system configuration in MRI



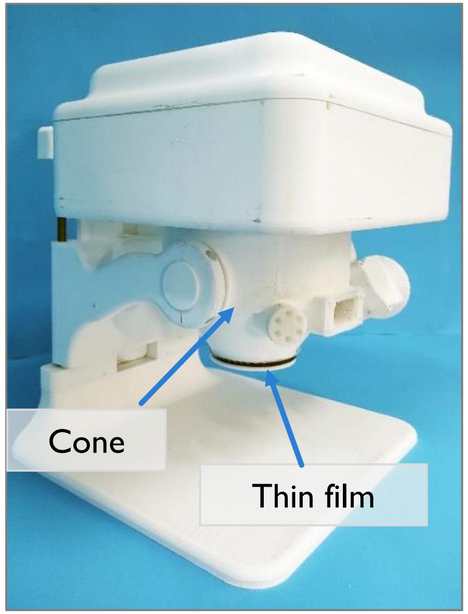
5 DOF ROBOTIC SYSTEM

Photos of manufactured device

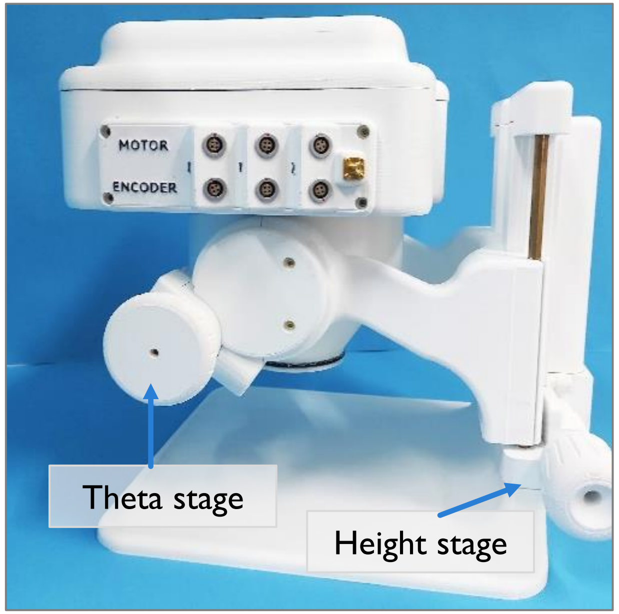
Front Right-side view



Front Left-side view



Right view

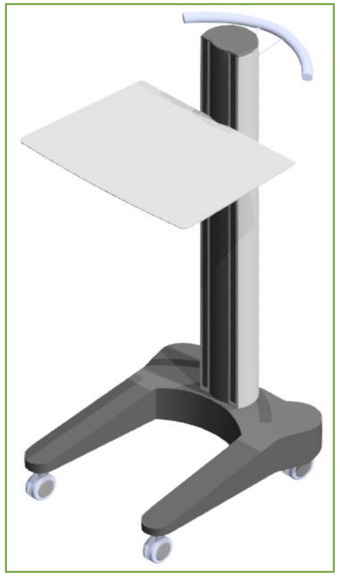


Front view

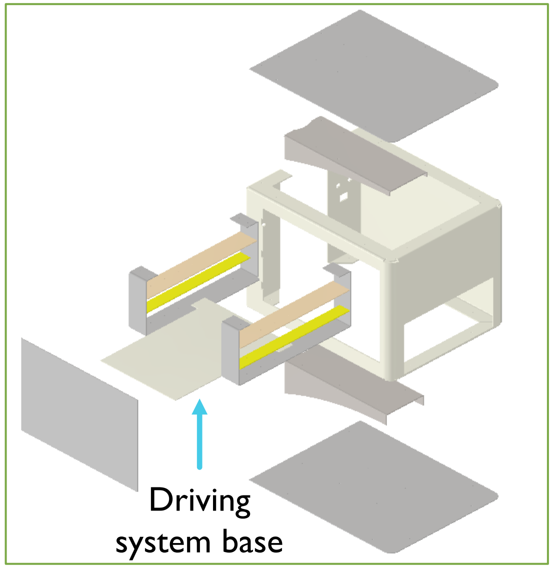
MEDICAL CART

- ❑ Hosts all electronic devices.
- ❑ Developed using commercial cart base:
  - ❑ Metal enclosures incorporated.

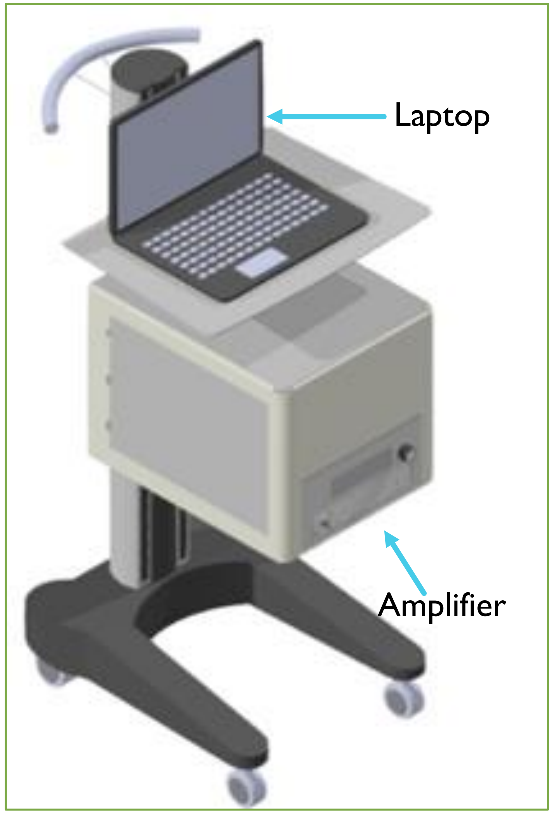
Ergonomic design



CAD model of cart base



CAD model of metal cart enclosures



CAD model of assembled medical cart

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vet ex machina

MEDICAL CART

Medical cart photos

Front view

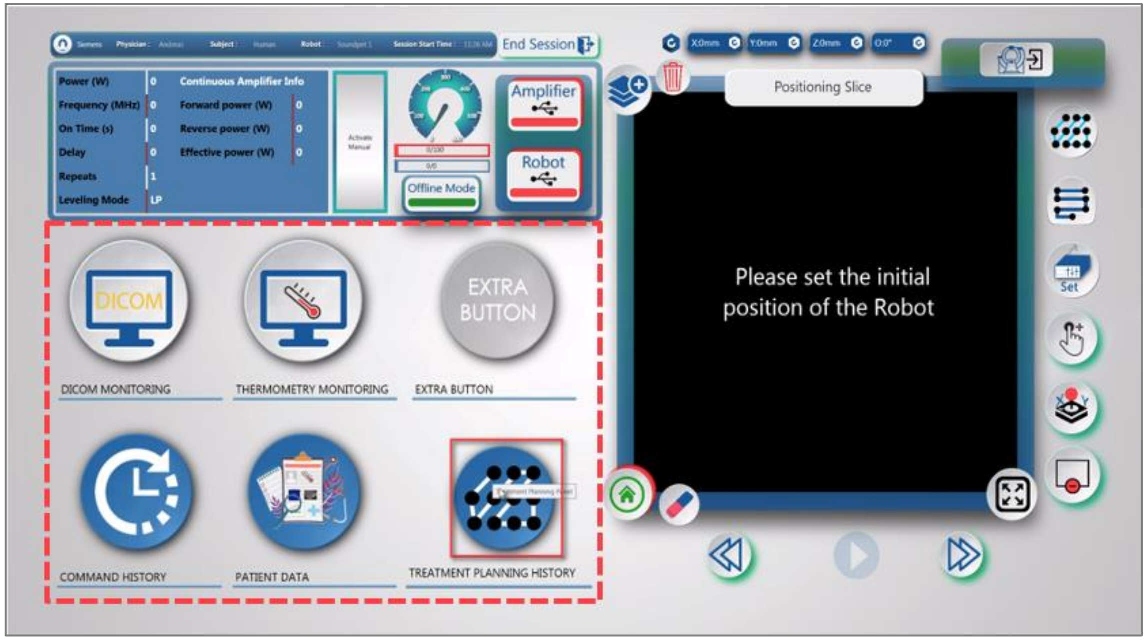
Side view

Rear view

TREATMENT PLANNING/MONITORING SOFTWARE

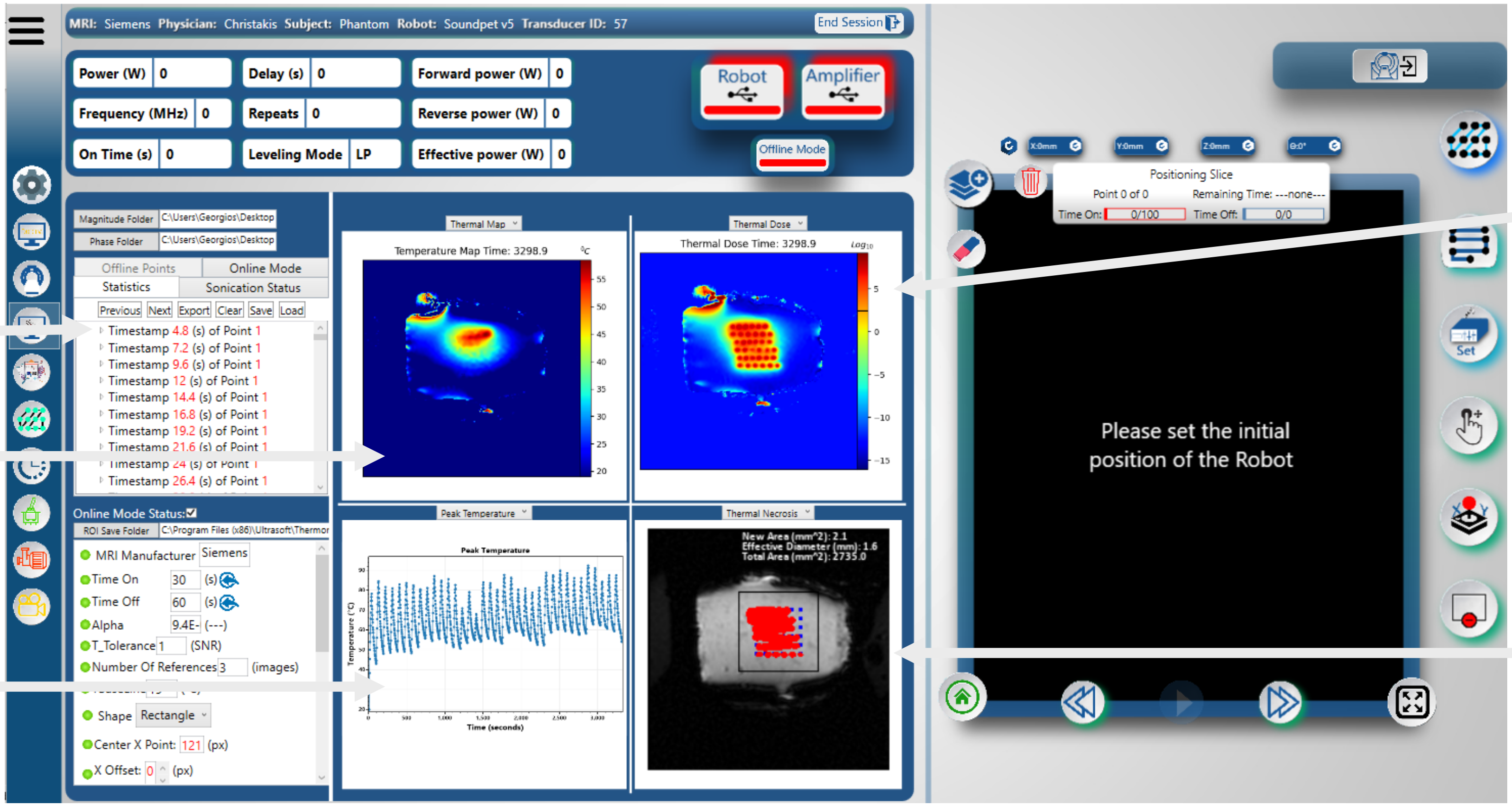
- ❑ Software developed in C# to control:
  - ❑ Robotic system motion
  - ❑ Ultrasonic transducer energy delivery
  - ❑ MRI monitoring of treatment
    - ❑ Remote MRI control
    - ❑ Integrates tools for treatment planning and monitoring.

Screenshot of main window of previous software platform



TREATMENT PLANNING/MONITORING SOFTWARE - MR THERMOMETRY

- ❑ Thermometry data displayed next to treatment planning window.



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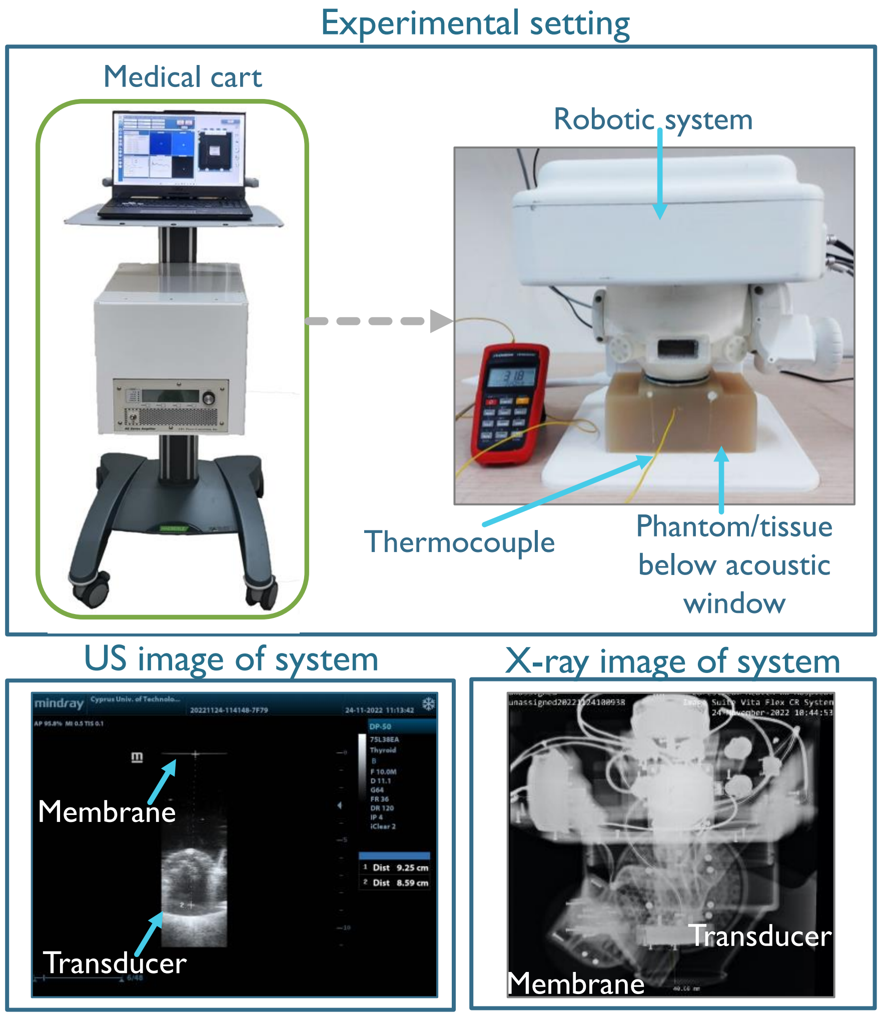

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  - ❑ Grid size progressively increased investigating system's ability in ablating large tissue areas.
  - ❑ 2×2 and 3×3 grid patterns used.
- ❑ Overlapping lesions were inflicted with a 7 mm step.

Overlapping lesions

Plane perpendicular to beam

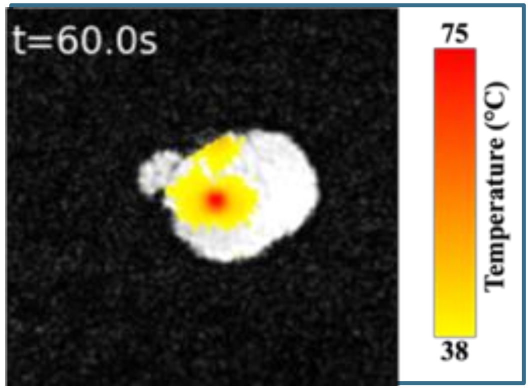
Plane parallel to beam

45 W for 20 s - 3×3 grid, 7 mm step

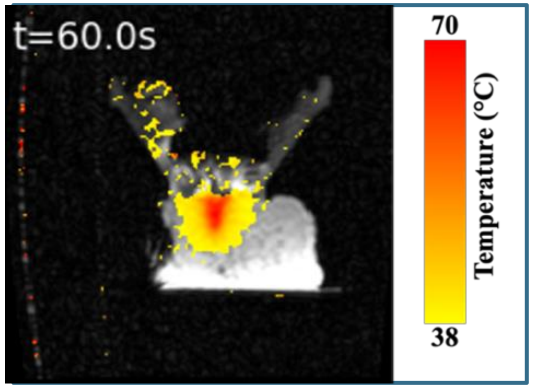
MRI EXPERIMENTS–**THERMAL HEATING UNDER MR THERMOMETRY**

- Sonications executed under MR thermometry monitoring.
- Varied power of 15-60 W applied for 30-60 s.
- Sonications executed on phantom & tissue.
- Scanned with FLASH sequence in coronal & axial planes.
- Thermal heating clearly visible on coronal and axial thermal maps.
- Ablative temperatures generated in tissue.
- Lesion formation evidenced on T2-W FSE images.

Coronal thermal map of tissue

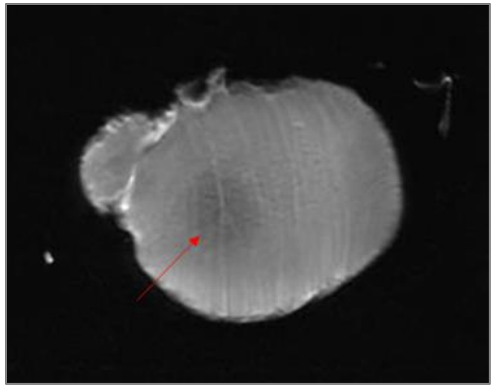


Axial thermal map of tissue



60 W for 30 s

T2-W FSE image of inflicted lesion



PET EXPERIMENTS

- Eight (8) dogs and cats with naturally occurring neoplasms recruited according to set safety criteria.
- Pet trials carried out at premises of referring veterinarians.

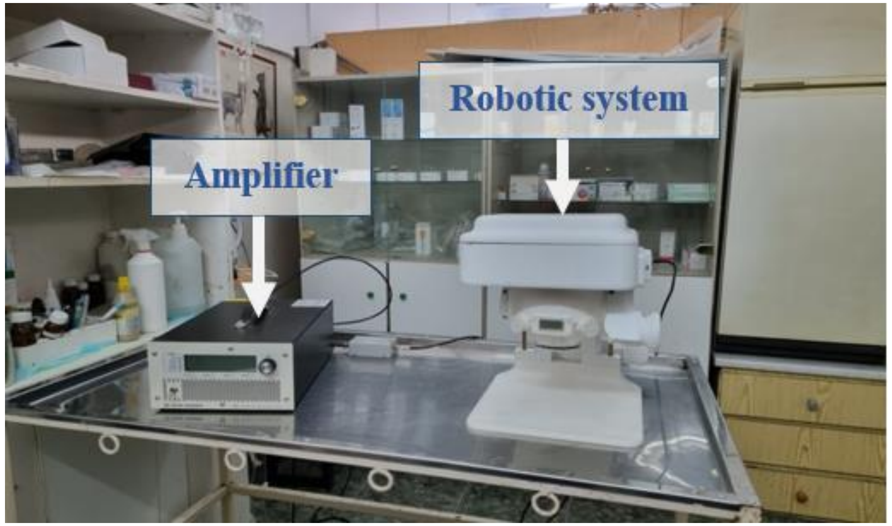
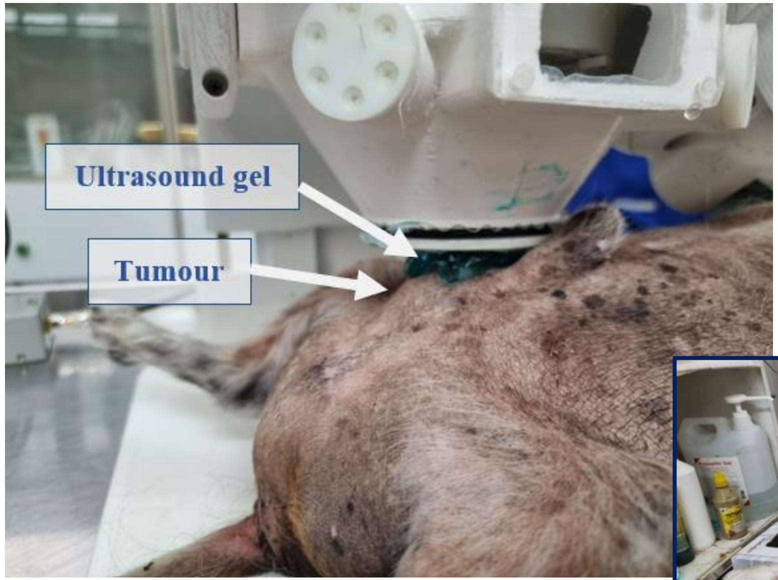


Photo of the system installed at a veterinary clinic.


Photo from veterinary trial showing the device applied on a dog.

PET EXPERIMENTS

- Veterinary patients underwent FUS ablation followed by immediate surgical resection of the tumor.
- Ablation protocol adjusted depending on the tumor size.
- Histological examination of tumors with Hematoxylin and eosin (H&E) staining.



Efficient coupling between device and tumor using US coupling gel.


Photo from veterinary trial showing the device applied on a dog.

PET EXPERIMENTS

- All pet trials performed successfully without any recorded adverse events.
- System proven capable of accurately delivering FUS to ablate different types of tumors in pets.
  - Some lesions were visible on tumor surface.

Example of thermal lesion on dog tumor after exposure at 75 W acoustic power for 30 s.

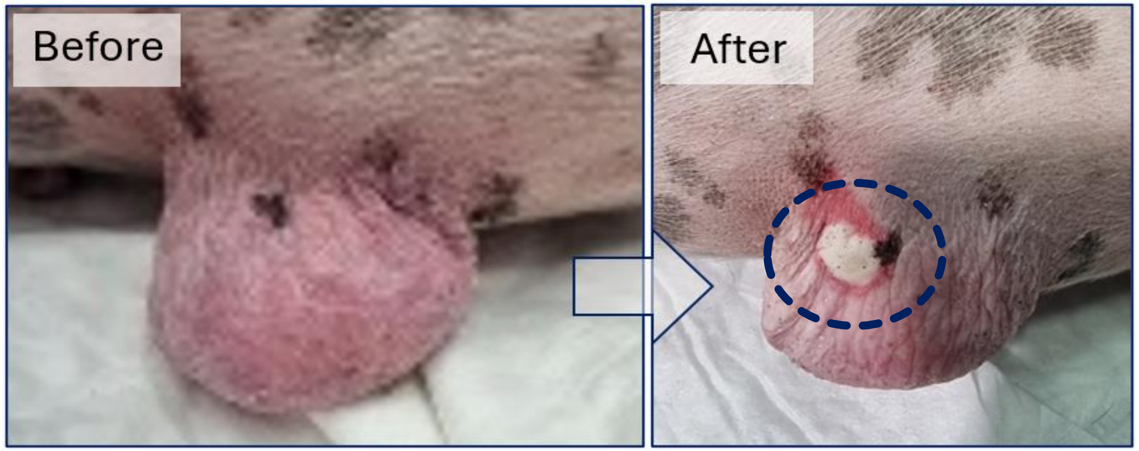


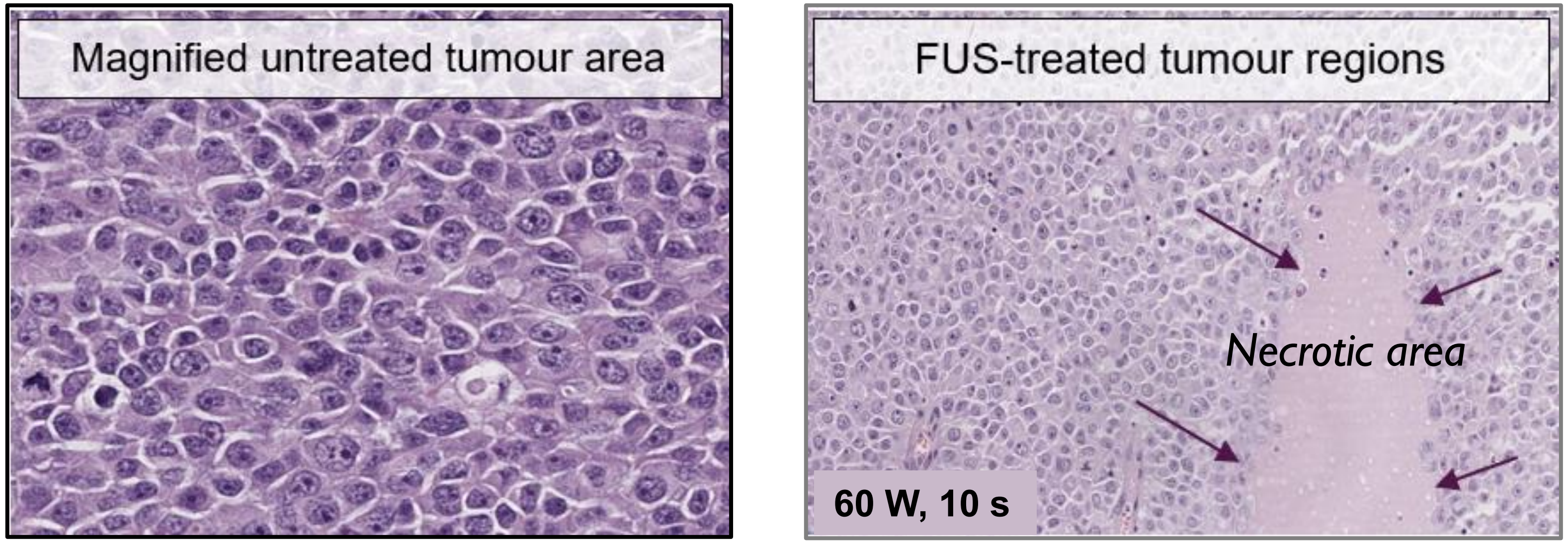
Photo of tumor before and after sonication.

Photo acquired during trial.

PET EXPERIMENTS

- System proven capable of accurately delivering FUS to ablate different types of tumors in pets.
  - Thermal necrosis observed on H&E-stained slides as well-delineated regions of disrupted cell architecture.

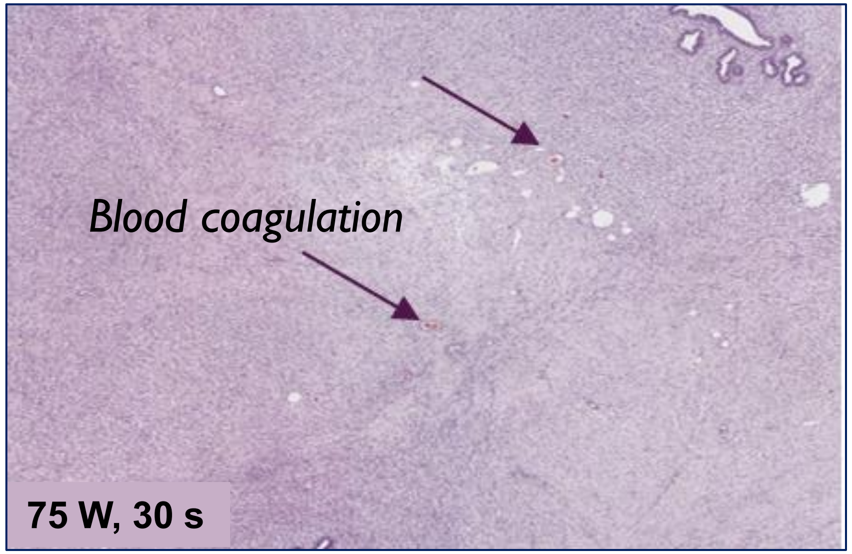
H&E slides of excised dog tumor following thermal ablation with FUS.

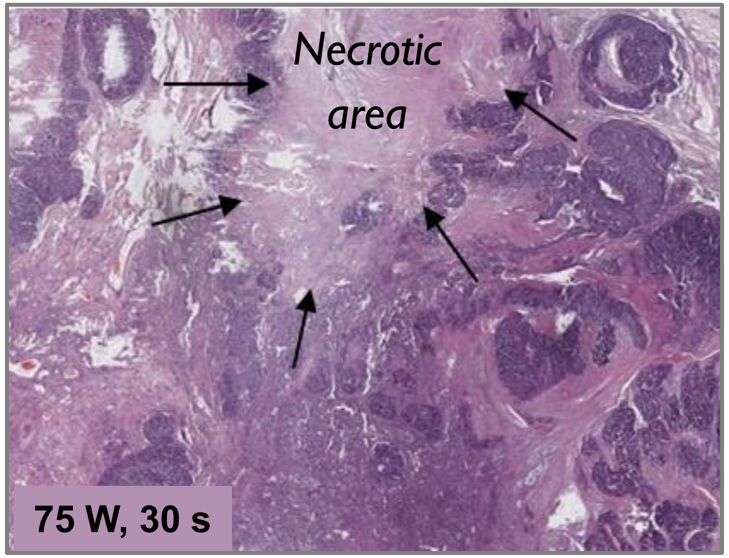


PET EXPERIMENTS

- Blood coagulation observed occasionally within the sonicated area.
- Magnification revealed a few remaining intact tumour nuclei.
- From histopathological viewpoint, the sonicated regions were deemed to be completely destroyed by FUS.

H&E slides of excised dog tumors following thermal ablation with FUS.





CONCLUSIONS

- Small to large-sized animals can be accommodated under the conical water container of the robotic system.
- Ablation of various types of tumors in pets can be achieved in a safe and efficient manner.
- The system maintains high standards of animal welfare.
- Additional research involving a larger patient cohort is necessary to fully explore the capabilities of the system.
- This technology has potential as a therapeutic solution for veterinary cancer.

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vet ex machina

ACKNOWLEDGEMENTS

The study was co-funded by the European Structural & Investment Funds (ESIF) and the Republic of Cyprus through the Research and Innovation Foundation (RIF) under the project FUSVET (SEED/1221/0080).

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FUSVET

ROBOTIC DEVICE FOR MRI GUIDED FOCUSED ULTRASOUND FOR VETERINARY ONCOLOGY

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OBJECTIVES

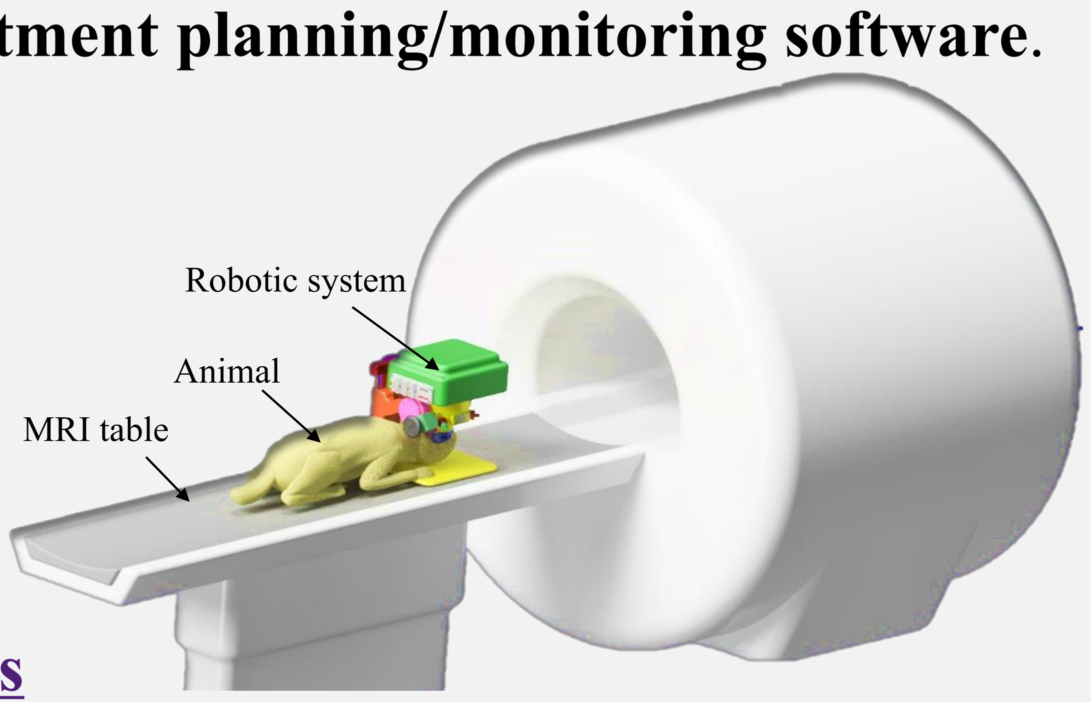
This paper presents a **robotic system** that uses **Focused Ultrasound (FUS)** technology for the treatment of **veterinary cancer** and its preliminary evaluation in phantoms and *ex-vivo* tissue.

METHODS

VETERINARY FUS ROBOTIC SYSTEM

Key components

The system includes **3 PC-controlled and 2 manually-controlled motion stages** for navigating a **single element spherically focused transducer operating at 2.7 MHZ**, relative to the region of interest. Robotic motion is actuated by piezoelectric motors (USR60-S3N, Shinsei, Japan) and controlled with optical encoders (EM1-0-500-I, US Digital Corporation, Japan). The system is **accompanied by an advanced treatment planning/monitoring software**.

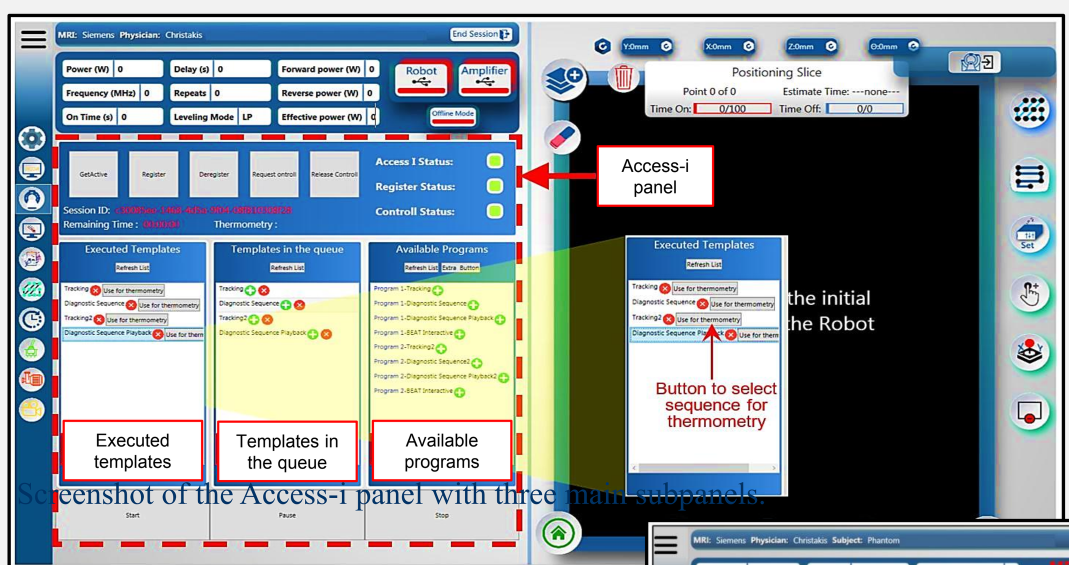


Characteristics

The robotic device was specially designed to be compact and was 3D-printed (F270, Stratasys, Minnesota, USA) using polylactic acid (PLA) thermoplastic. Non-magnetic materials were employed to achieve MRI compatibility. The device **can fit in all conventional MRI scanners for top to bottom treatment**.

TREATMENT SOFTWARE

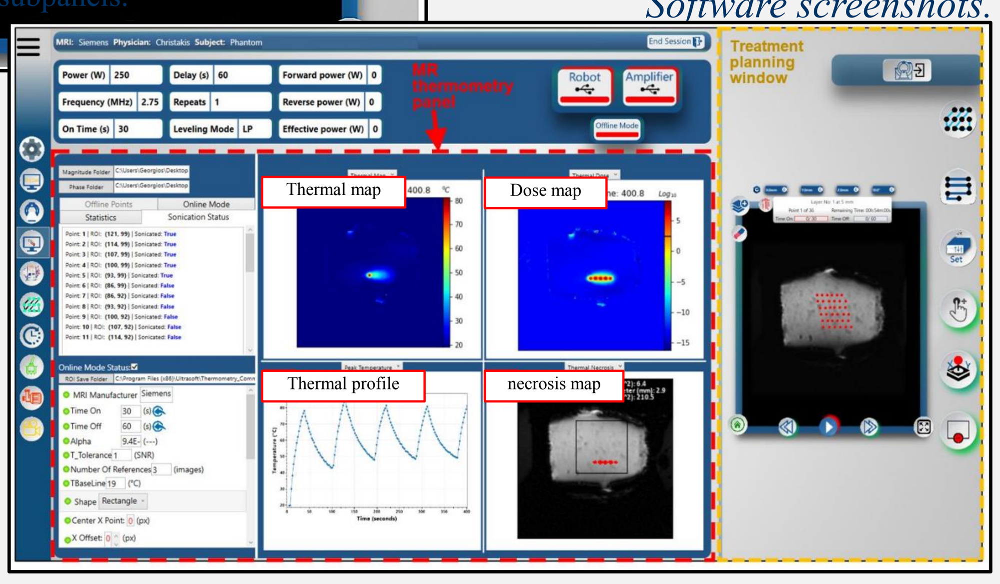
The software of the system was developed in C# and communicates with Siemens MRI scanners using the Access-I modules. Using proton-resonance frequency shift MR thermometry, the temperature, thermal dose and thermal necrosis can be estimated from the phase images of gradient pulse sequences.



Key features:

- ❑ Treatment planning
- ❑ Robotic motion control
- ❑ Ultrasonic system control
- ❑ MRI monitoring of treatment

Software screenshots.



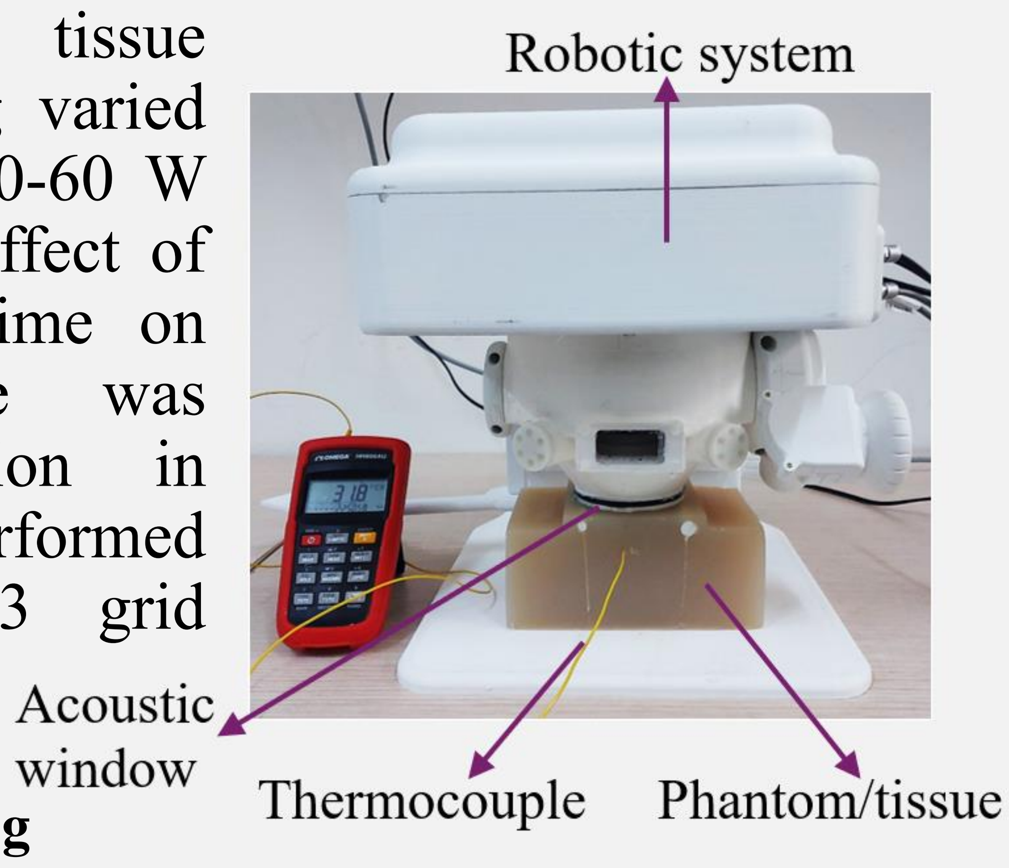
Thermometry data displayed during sonication:

- ❑ Thermal maps
- ❑ Thermal dose maps
- ❑ Timeseries temperature graph
- ❑ Thermal necrosis area overlaid on magnitude image.

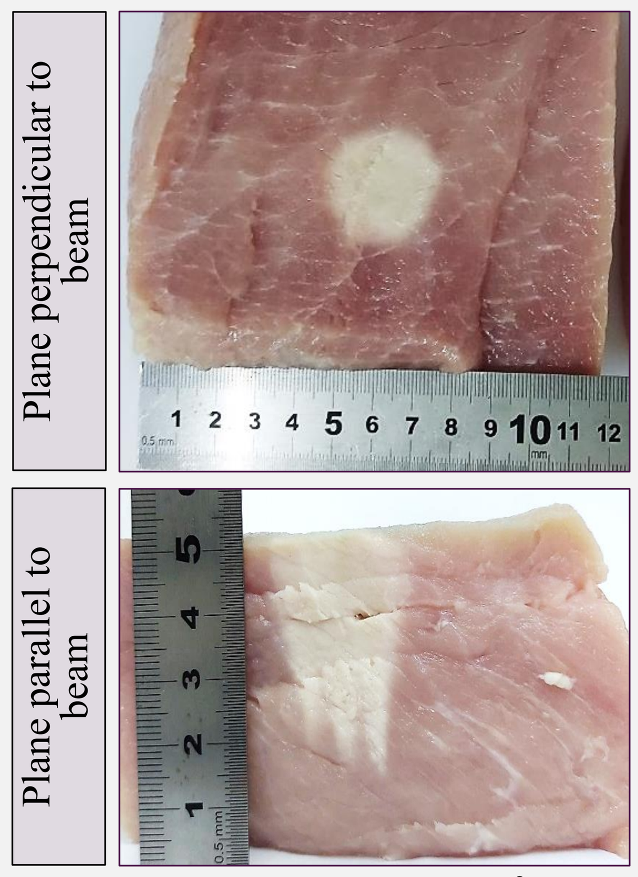
The system was evaluated by performing a series of sonications in **agar-based phantoms** (6 % w/v agar) and **freshly excised porcine tissue**.

RESULTS

Sonications in agar phantoms and excised porcine tissue were performed using varied acoustical power of 30-60 W for up to 60 s. The effect of applied power and time on temperature increase was demonstrated. Ablation in excised tissue was performed along 2×2 and 3×3 grid patterns.



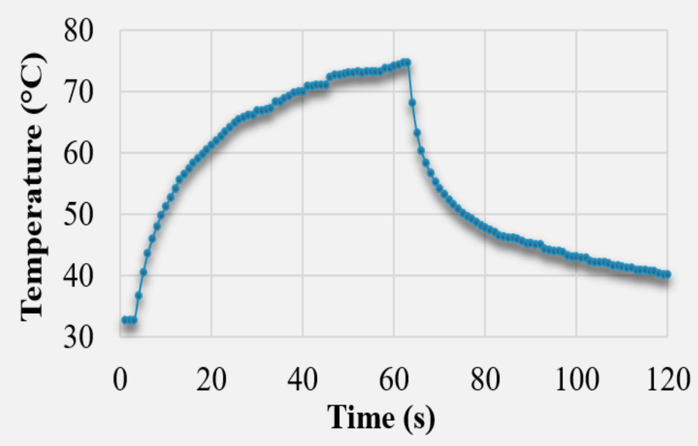
Example of overlapping lesions in excised tissue:



45 W for 20 s
3×3 grid,
7 mm step

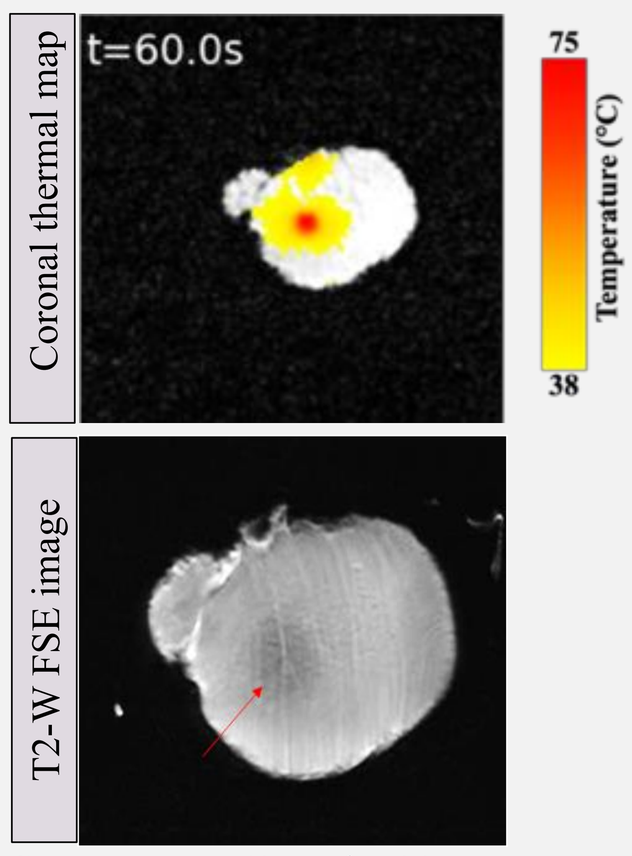
- Necrotic area of 26×28 mm^2
- length of 44 mm

Example of thermal profile during/after sonication:



Phantom sonication at 60 W for 60 s at 25 mm focal depth.

In the MRI setting, sonications were performed with varied power of 15-60 W and sonication time of 30-60 s **under MR thermometry monitoring** utilizing a FLASH sequence. The temperature evolution was visible on coronal/ axial thermal maps. Ablative temperatures were generated in tissue. Lesions were clearly visualized on post-sonication T2-W FSE images as areas of decreased intensity.



Sonication at 60 W for 30 s

CONCLUSIONS

- ❑ *Ex-vivo* functionality and heating abilities of the system demonstrated.
- ❑ Using deep learning techniques, users are provided with the optimum ultrasonic protocol and navigation scheme.
- ❑ The positioning device is now under evaluation in cats and dogs with cancer.
- ❑ This technology has **potential as a therapeutic solution for veterinary cancer**.

ACKNOWLEDGEMENTS

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FOCUSED ULTRASOUND TUMOR BEARING PHANTOM

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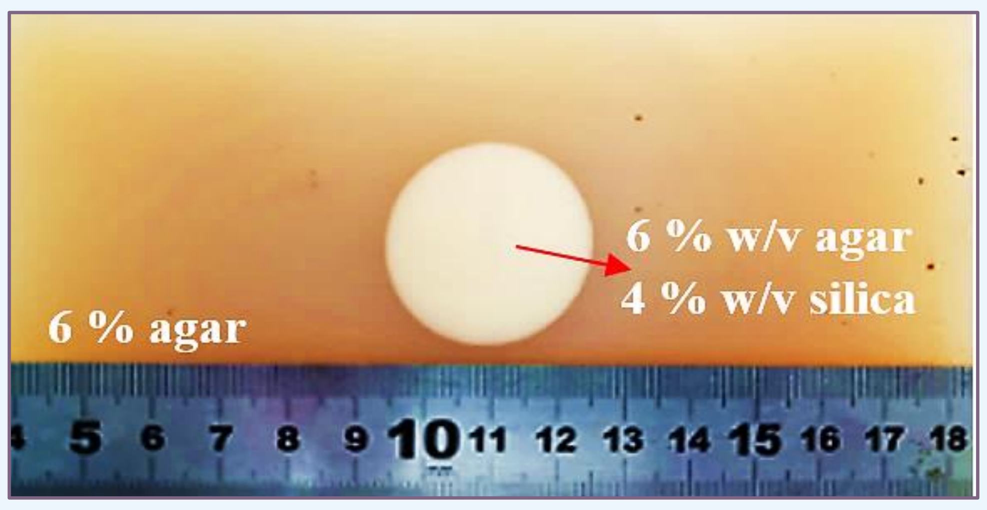
OBJECTIVES

The current study proposes an agar-based **tissue mimicking phantom with embedded tumor mimic** that can be used for evaluating the heating abilities of Focused Ultrasound (FUS) transducers.

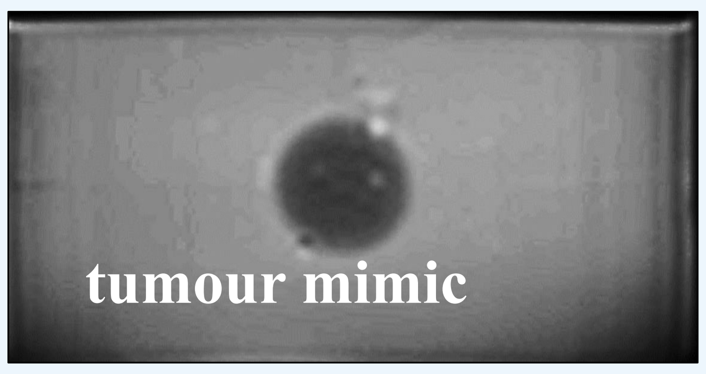
METHODS

Phantom preparation

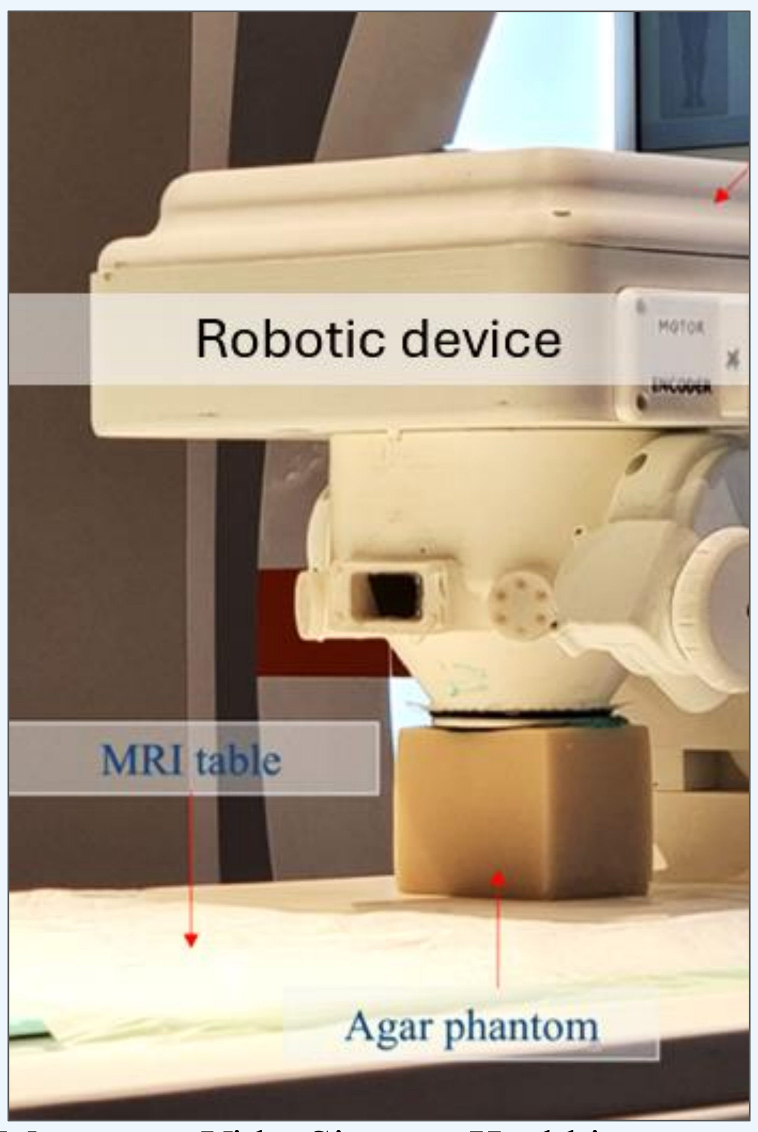
The background material mimicking normal tissue was made of agar and water, whereas the **tumor mimic was differentiated by including** proper concentration of **silicon dioxide.**



This **difference in the silicon dioxide** content resulted in **excellent contrast between the tumor and surrounding** normal tissue in Magnetic Resonance Imaging (MRI).



T2-W TSE images (TR = 2500 ms, TE = 52 ms, FA =180°, ETL =12, FOV = 260 x 260 x 10 mm^3, matrix size = 128 x 128, and NEX = 2).



Magnetom Vida, Siemens Healthineers

Phantom assessment

High power sonications were performed within the phantom using a 2.7 MHz **single element transducer** as integrated in an MRI compatible positioning device in a **3T MRI scanner.**

ACKNOWLEDGEMENTS

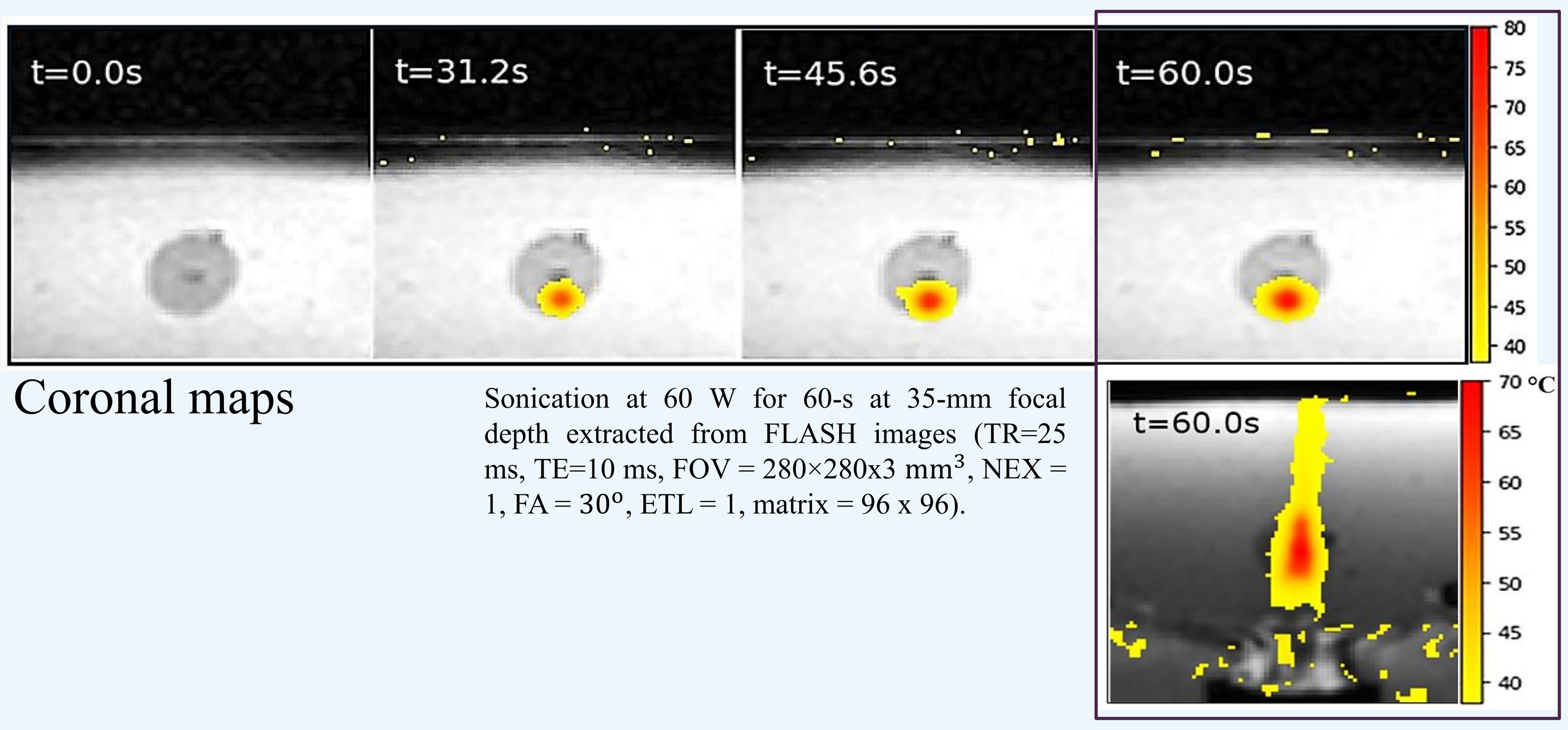
The study was co-funded by the European Structural & Investment Funds (ESIF) and the Republic of Cyprus through the Research and Innovation Foundation (RIF) under the projects **FUSVET (SEED/1221/0080)** and **SOUNDPET (INTEGRATED/0918/0008).**

RESULTS

Based on coronal images showing the experimental setup (transducer and target), it was possible to **move the FUS beam within the phantom precisely.** Sonications were performed under MR thermometry guidance.

T2-W TSE image (TR = 2500 ms, TE = 52 ms, FA =180°, ETL =12, FOV = 260 x 260 x 10 mm^3, matrix size = 128 x 128, and NEX = 2).

Indicative thermal maps during sonication within the tumour simulator:



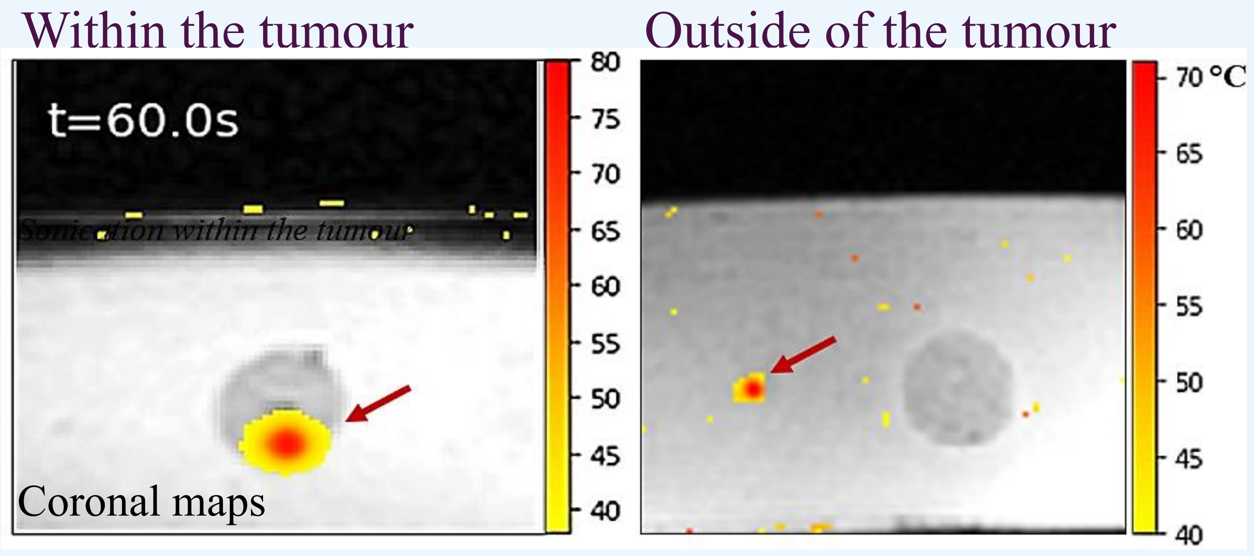
Coronal maps

Sonication at 60 W for 60-s at 35-mm focal depth extracted from FLASH images (TR=25 ms, TE=10 ms, FOV = 280×280x3 mm^3, NEX = 1, FA = 30°, ETL = 1, matrix = 96 x 96).

Axial map

MR temperature monitoring within and outside of the tumor simulator revealed **higher heat accumulation within the tumor mimic** owing to the **inclusion of silicon dioxide,** which increased its ultrasonic absorption. In addition, temperature maps acquired in a plane parallel to the beam revealed beam deflection at the tumor boundaries.

Indicative thermal maps acquired during sonication within and outside of the tumour mimic:



Extracted at the end of sonication at 60 W for 60-s from FLASH images (TR=25 ms, TE=10 ms, FOV = 280×280x3 mm^3, NEX = 1, FA = 30°, ETL = 1, matrix = 96 x 96).

Sonication at 60 W acoustic power for 60 s resulted in a maximum temperature change of **28°C** outside of the tumour. **Higher temperature** change of **38°C** was **reached within the tumour.**

CONCLUSIONS

- The silica-doped **tumor mimic** was clearly visualized as a **hypointense area** on T2-Weighted **MRI images**.
- **Addition of silica within the tumor** led to **increased ultrasonic absorption** within it during sonication, resulting in **higher temperatures**.
- Overall, the developed tumor phantom model was proven to be a **cost-effective and ergonomic tool for MRI-guided FUS studies**, especially the preliminary testing of equipment and/or therapeutic protocols.

CANINE AND FELINE TUMOR ABLATION FIELD TRIAL WITH A FUS ABLATION SYSTEM

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OBJECTIVES

Focused Ultrasound (FUS) provides an alternative non-invasive treatment for malignant tumours. Herein, FUS ablation was utilised for treating spontaneous tumors in dogs and cats, employing a custom-made Magnetic Resonance-compatible FUS robotic system.

METHODS

FUS ROBOTIC SYSTEM

The system utilized comprises a single-element, spherically focused transducer operating at 2.6 MHz to non-invasively deliver high intensity ultrasonic energy to the tumor site.

Main features

- Developed for veterinary FUS cancer applications.
- Motion in 3 PC-controlled & 2-manually controlled axes.
- Transducer integrated in conical water container.

VETERINARY TRIALS

The efficacy of this technology was assessed through a trial involving dogs and cats.

- Twelve (12) dogs and cats with naturally occurring tumors recruited based on specific safety criteria.
- Trials carried out at premises of referring veterinarians.
- Ablation protocol adjusted depending on the tumor size.
- Veterinary patients underwent FUS ablation followed by immediate surgical resection of tumor.
- Histological examination of tumors with Hematoxylin and Eosin (H&E) staining.

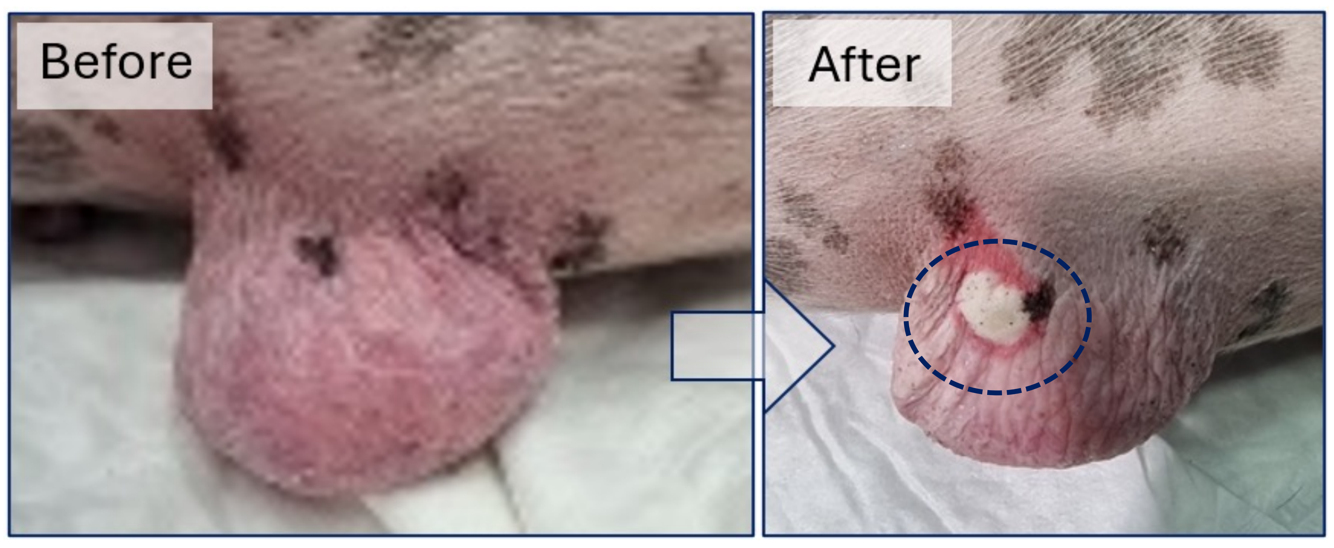
Photos from veterinary trials showing the device applied on dogs.

RESULTS

All treatment procedures were performed successfully prior to tumor excision by the referring veterinarian.

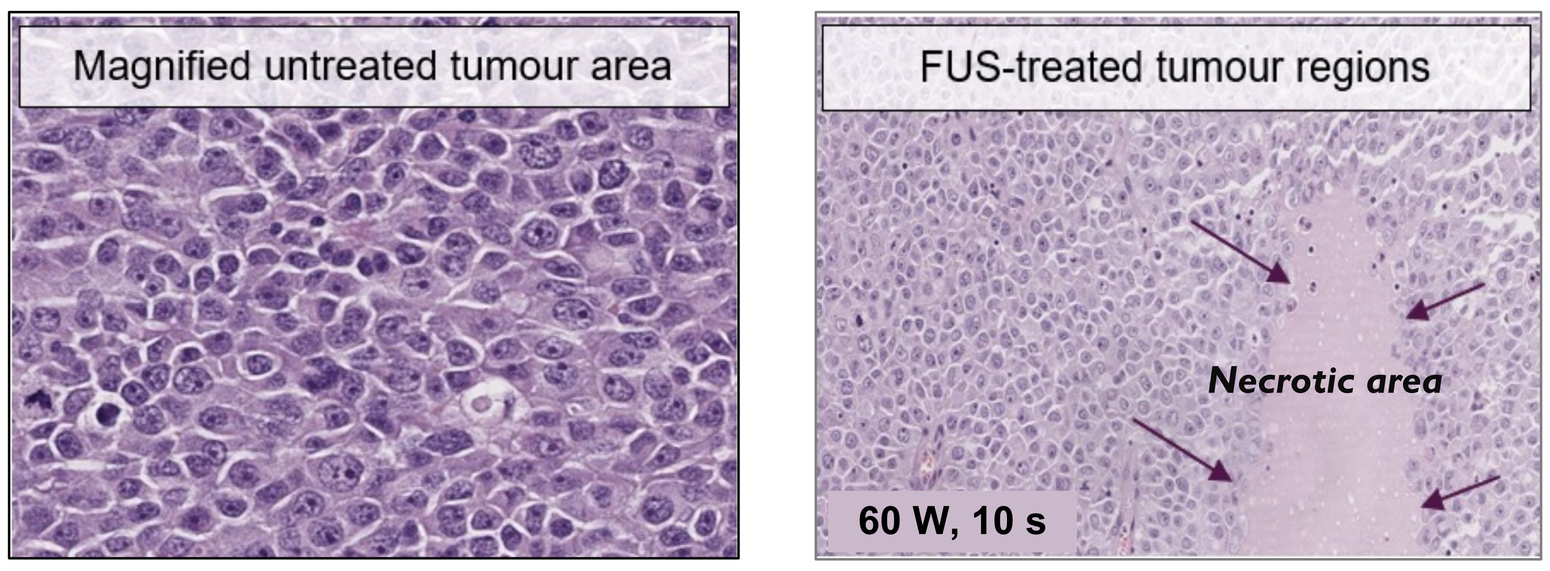
- No recorded adverse events.
- Small to large-sized animals accommodated under the conical water container of the system.
- Portability facilitated seamless system integration into veterinary clinics.

The system has proven capable of accurately delivering FUS to ablate various types of tumors in pets, with some lesions visible on the tumor surface.



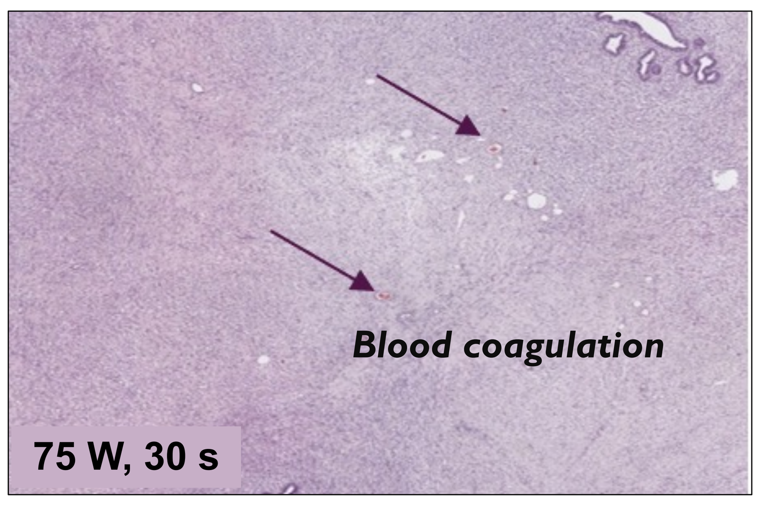
Example of thermal lesion on dog tumor after exposure at 75 W acoustic power for 30 s.

Histological examination of excised tumors revealed evidence of thermal necrosis on the H&E-stained slides, visualized as well-defined regions of destroyed cell architecture.



H&E slides of excised dog tumor following thermal ablation with FUS.

- Blood coagulation observed occasionally within the sonicated area.



- Magnification showed that only a few intact tumor nuclei remained, and from a histopathological perspective, the sonicated areas appeared to be entirely destroyed by FUS.

Overall, the FUS system demonstrated precise targeting capabilities, enabling partial ablation of tumors at various anatomical locations in veterinary patients.

CONCLUSIONS

The study outcomes revealed promising therapeutic potential, suggesting that the developed technology could provide a viable avenue for non-invasive therapeutic interventions in veterinary oncology. Additional research involving a larger patient cohort is necessary to fully explore the capabilities of the system.

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