Project Acronym:

SOUNDPET(INTEGRATED/0918/0008)

MRI-guided Focused ultraSOUND system for cancer in PETs (dogs and cats)

Deliverable number: 1.4

Title: Communication and outreach strategy plan.

Prepared by:

Nikolas Evripidou (CUT)
Anastasia Antoniou (CUT)
Theocharis Drakos (MEDSONIC)
Christakis Damianou (CUT)

Date: 13/07/2023

Ευρωπαϊκή Ένωση
Ευρωπαϊκά Διαρθρωτικά και Επενδυτικά Ταμεία

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Table of Contents

Executive summary

Deliverable 1.4 “Communication and outreach strategy plan” is a list of all the activities related to the dissemination of the SOUNDPET project, including creation of dissemination materials for external events, presentations of the project, press releases, and the creation of social networks, flyers, newsletters and other.

The first step was to create the project’s logo. A website was next developed in line with corporate identity and regular updates were scheduled throughout the project life cycle. The project was introduced to all stakeholders with an opening event while regular communication on the project’s progress was provided throughout the project duration. The project aims and acknowledgement of partners and the RIF support were included in a brochure, as well as in project newsletters published on a biannual basis providing updates on the project’s progress. Furthermore, SOUNDPET was covered by the Focused Ultrasound Foundation and widely disseminated through social media, numerous events; locally and abroad, as well as TV appearances. Laboratory demonstrations were given to key individuals and the public. Key research outcomes were communicated to the academic community by attending numerous field-related conferences. Through these activities, we had the change to introduce our technology and create awareness of its potential commercial impact to many government executives, individuals from local and international businesses and academic institutions, investors, entrepreneurs, foreign ambassadors, and the wider public. The project outcomes and future plans were summarized in a closing event in the presence of project participants and stakeholders.

All the partners of the SOUNDPET project have contributed to the dissemination activities to relevant stakeholders. The partners regularly provided information on their dissemination activities to the dissemination manager. This overview is divided in several sections depending on the type of dissemination.

.

Logo creation

A logo was created for the SOUNDPET project (Figure 1) on July 20, 2020.

SOUNDPET
Animal therapies with focused ultrasound

Figure 1: Logo of the project.

Website

A dynamic website has been created. A dynamic website has the advantage to allow many researchers of the project with an access to upload information in the website. The language used is PHP. Data regarding the project is inserted in the relevant menu items.

The website domain is: www.soundpet.eu/.

Screenshot of the website is shown in Figure 2. Appendix 1 shows the user guide prepared for the administration of the webpage.

Figure 2: Screenshot of the main page of the website.

Another software with more advanced graphics presenting the key research activities of the Laboratory of Therapeutic Ultrasound and the SOUNDPET project has been developed. More information can be found in Appendix 1.

Facebook page

We have created a page on Facebook about the SOUNDPET project (Figure 3). In just one hour we have received 78 likes and followers and received numerous messages requesting additional information about the project.

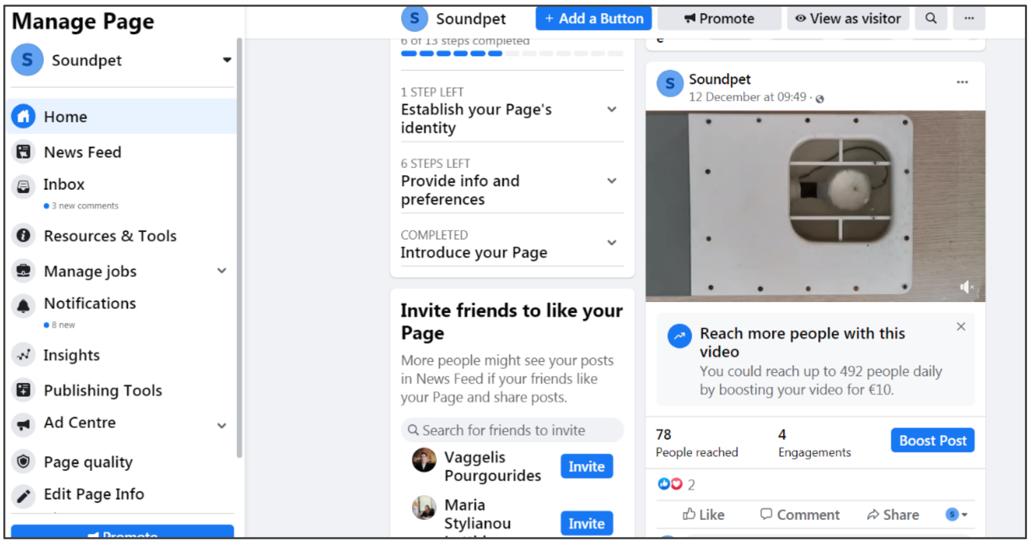


Figure 3: Screenshot of the Facebook administrator page.

Opening event

On September 30, 2020 we presented the project by inviting researchers, doctors and professionals to a virtual opening event (the invitation is shown in Figure 4).

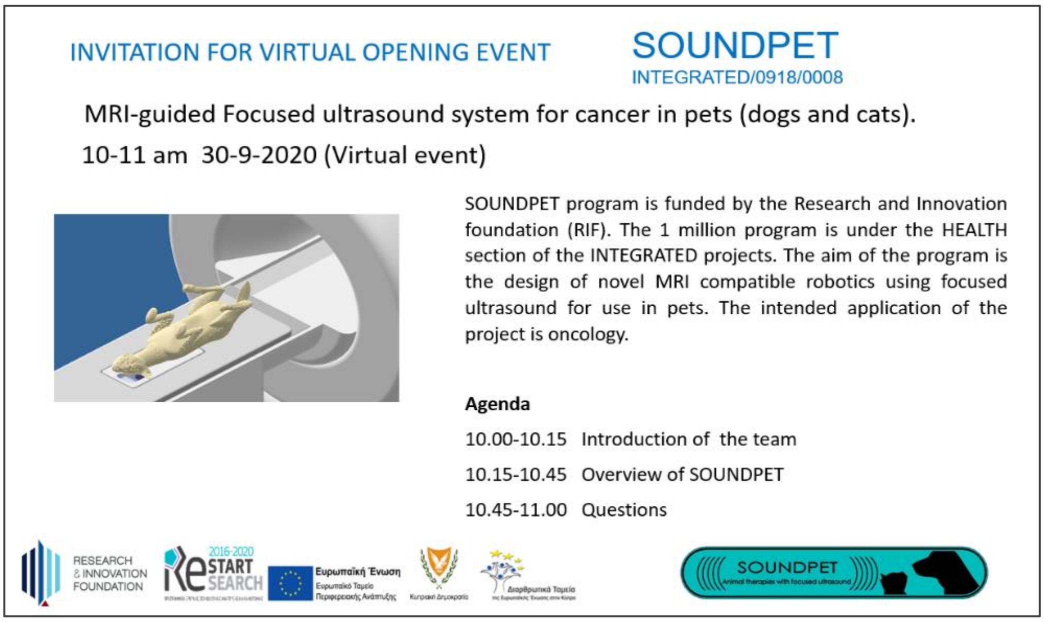


Figure 4: Invitation of the virtual opening event.

We informed the key stakeholders (researchers, health and social care professionals, policy-makers, veterinarians, purchasers and companies) and project participants about the program. A screenshot of the virtual opening event is shown in Figure 5.

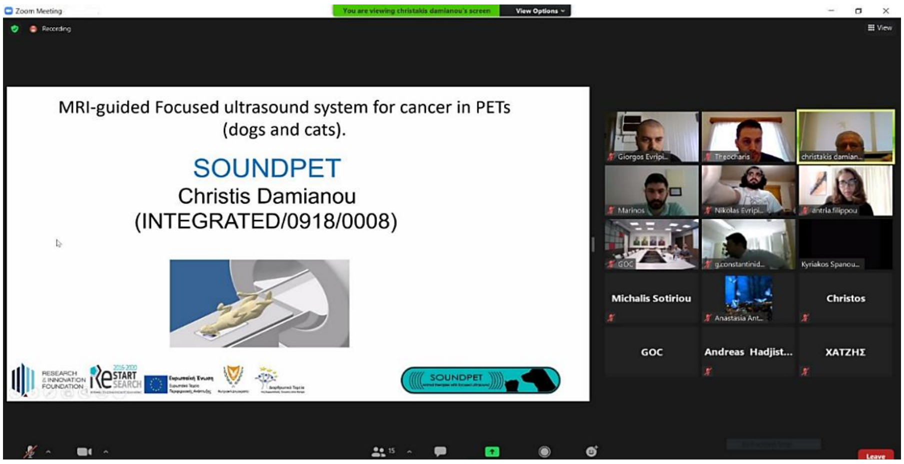


Figure 5: Screenshot taken during the virtual opening event.

Project brochure

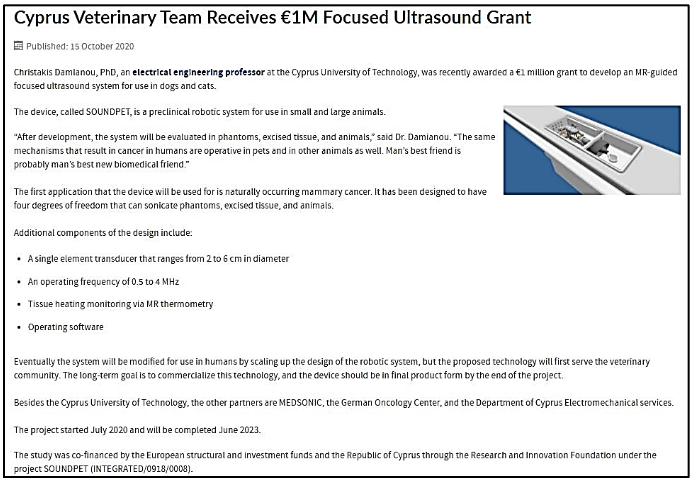
A project brochure including a summary and key research activities of the project has been produced. The brochure can be seen in Appendix 2.

Project newsletters

Project newsletters were produced providing updates on the project's progress. The newsletters can be seen in Appendix 3. In newsletter 1, the goal was to present the project, the partner organizations, and the participants. Newsletter 2 presented the four- degrees of freedom robotic device and its evaluation in terms of motion accuracy and MRI compatibility. The development of ultrasonic transducers and a medical cart was described in Newsletter 3. Information about the developed software for MRI-guided FUS therapy can be found in Newsletter 4, whereas Newsletter 5 reports key results on MRI monitoring of FUS ablation in-tissue mimicking phantoms and excised animal tissue. Finally, Newsletter 6 concerns the *in-vivo* evaluation of the SOUNDPET system initially in a rabbit thigh model and then in canine and feline patients of mammary cancer.

Focused Ultrasound Foundation post

On October 15, 2020 the project has been mentioned in the news of Focused Ultrasound Foundation. The goal of the project, the partners, the components of the design and the organizations which co-financed the project were mentioned (Figure 6).


Cyprus Veterinary Team Receives €1M Focused Ultrasound Grant

Published: 15 October 2020

Christakis Damianou, PhD, an **electrical engineering professor** at the Cyprus University of Technology, was recently awarded a €1 million grant to develop an MR-guided focused ultrasound system for use in dogs and cats.

The device, called SOUNDPET, is a preclinical robotic system for use in small and large animals.

"After development, the system will be evaluated in phantoms, excised tissue, and animals," said Dr. Damianou. "The same mechanisms that result in cancer in humans are operative in pets and in other animals as well. Man's best friend is probably man's best new biomedical friend."

The first application that the device will be used for is naturally occurring mammary cancer. It has been designed to have four degrees of freedom that can sonicate phantoms, excised tissue, and animals.

Additional components of the design include:

- A single element transducer that ranges from 2 to 6 cm in diameter
- An operating frequency of 0.5 to 4 MHz
- Tissue heating monitoring via MR thermometry
- Operating software

Eventually the system will be modified for use in humans by scaling up the design of the robotic system, but the proposed technology will first serve the veterinary community. The long-term goal is to commercialize this technology, and the device should be in final product form by the end of the project.

Besides the Cyprus University of Technology, the other partners are MEDSONIC, the German Oncology Center, and the Department of Cyprus Electromechanical services.

The project started July 2020 and will be completed June 2023.

The study was co-financed by the European structural and investment funds and the Republic of Cyprus through the Research and Innovation Foundation under the project SOUNDPET (INTEGRATED/0918/0008).

Figure 6: Post about the project in the Focused Ultrasound Foundation website.

GOC dissemination through Facebook

The project was disseminated through the partner's social media (Figure 7).

Figure 7: Posts about the project in Facebook.

Laboratory visits

Visit of the ambassador of China at the laboratory

The ambassador of China visited the laboratory and was very impressed by the SOUNDPET technology (Figure 8).

Figure 8: Photos of the laboratory visit.

Visit of US-based mentors at the Laboratory of therapeutic ultrasound on June 3rd 2022 (during their visit in Cyprus in the framework of the Cyprus Seeds Demo Day).

Three qualified mentors from the US with scientific background and experience in brining academic research to the market visited the premises of CUT (Figure 9). They were impressed by the research activities performed at the lab and offered valuable advice on how to generate impact from your research.

Figure 9: Photo during the visit of US-based mentors at the laboratory.

Visit of delegation from Hangzhou Dianzi University (HDU) on June 20th 2023

A delegation from HDU, including the rector, visited the laboratory to get a firsthand experience with the technology. The principal investigator of the project Prof. Damianou showcased the SOUNPET robotic device and accompanied software. All participants found the SOUNDPET technology and its potential impact impressive. Indicative photos are shown in Figure 10.

Figure 10: Photos during the visit of delegation from HDU at the laboratory.

Public events and presentations

Event organized by the Economic Diplomacy Department of the Ministry of Foreign Affairs and Cyprus Seeds on May 20th 2021, at Atsas Training Center and Botanic Gardens.

We had the opportunity to showcase our research in front of government executives, the Chairman and CEO of INVEST Cyprus, and an audience of 32 Foreign Ambassadors (Figure 11). The main features of our technology and its major benefits over existing therapeutic solutions were presented. By the end of the event, we received enthusiastic feedback from the audience. Key people involved in the investment sector in Cyprus showed their interest in assisting us with investment matters in the future process of commercial deployment of the technology.

Figure 11: Photos of the event organized by Cyprus Seeds at Atsas Center, Nicosia.

Event organized by the Cyprus Cancer Research Network on July 8th 2021, at the University for Cyprus.

The goal of this event was to bring together groups that focus on research in cancer so that they can form a research network. In this event, SOUNDPET was presented. There was a lot of interest for collaboration. Dr Damianou presented SOUNDPET. Figure 12 shows the program of the event.

Figure 12: Photo of the program of the event organized by the Cyprus Cancer Research Network.

Event organized by Cyprus Seeds on October 18th 2021, at Eurobank, Nicosia.

Anastasia Antoniou presented the projects of CUT including SOUNDPET in front of various stakeholders (investors, doctors, TTO, government officials), as well as the VC fund Manager Zachariah George (Figure 13).

Figure 13: Photos of the event organized by Cyprus Seeds at Eurobank, Nicosia.

Annual Integrative Ultrasound Meeting 2022 (AIUM), 12-16 March 2022, in San Diego, CA, USA.

Two oral presentations of key research results of the SOUNDPET project were given at this conference (Figure 14). We also had the chance to meet and introduce our technology to key individuals from top ultrasound companies.

Figure 14: Photos during presenting SOUNDPET at the AIUM conference in San Diego.

Startup Investment Forum (SIF); Three-day exhibition organized by the MIT Enterprise Forum (MITEF) Saudi Arabia between 21-23 February 2022, in Madinah, Saudi Arabia.

In this event, we had the chance to present our technology to local investors and participants from local and international start-up companies. We were also provided a booth and had the chance to explain the technology to many visitors (Figure 15). In the booth we had a laptop showing a video demonstration of SOUNDPET.

Figure 15: Photos of the SIF event in Madinah, Saudi Arabia.

"Cypriot Academia INNOVATING" Event organized by Cyprus Seeds and the A.G. Leventis Foundation on April 28th 2022, at the Science Museum, in London, England.

In this event, we had the change to introduce our technology and create awareness of the potential impact of its commercial deployment to many London-based business-people and entrepreneurs (Figure 16).

Figure 16: Photos during presenting at the Cyprus Seeds event in London, England.

Open event organized between German Oncology Center and Cyprus University of Technology in September 2022.

In this event, local and German organizations presented their work in the area of medical imaging and Oncology. Presenters were from the University of Freiburg, University of Dresden, University of Cyprus, Cyprus University of Technology and Theramir. The event attracted 45 researchers from Germany and Cyprus. In the event, SOUNDPET was presented by the PhD. candidate Anastasia Antoniou (Photos are shown in Figure 17).

Figure 17: Photos from the event organized between CUT and German Oncology Center (LINAC's affiliation)

Cyprus Seeds Innovation Showcase 2022 organized by Cyprus Seeds on June 1st 2022, at the Cyprus Institute, in Nicosia, Cyprus.

We were provided a booth and had the chance to explain our technology to many visitors. Our booth included demonstration material and brochures about the treatment planning/monitoring software we have developed. During the event, we presented our technology (Figure 18) and were approached by a lot of business- people, entrepreneurs, and startup consultants who were interested to learn more about the technology.

Figure 18: Photos during presenting at the Cyprus Seeds Innovation Showcase in Nicosia, Cyprus, and screenshot of the live streaming on YouTube (bottom right).

Cancer Research and Innovation Centre (CARIC) Workshop

In this event, presentations were performed by the German Oncology Centre and CUT. SOUNDPET was presented by the PhD. candidate Antria Filippou. Photos from this event are shown in Figure 19.

Figure 19: Photos from the presentation at the CARIC workshop.

Poster presentation in the Interventional MRI conference in Germany.

Christakis Damianou and Anastasia Antoniou (CUT) presented an article produced during SOUNDPET entitled “Challenges regarding MR compatibility of an MRGFUS robotic system” at the *13th Interventional MRI symposium* that took place between 14 – 15 October 2022 in Leipzig, Germany (Figure 20).

Figure 20: Photos from the poster presentation (Leipzig, Germany).

Poster presentation at the UltraCon Annual Meeting in USA.

Christakis Damianou (CUT) presented an article produced during SOUNDPET entitled “Focused Ultrasound Phantom With Inclusion Of Tumour” at *UltraCon Annual Meeting 2023*, which took place between 25-29 March 2023 in Orlando, Florida, USA (Figure 21).

Figure 21: Photos from the poster presentation (Orlando, Florida, USA).

Another article produced during SOUNDPET entitled “Focused Ultrasound Ablation Of Canine Mammary Cancer” was presented by Anastasia Antoniou (CUT) at *UltraCon Annual Meeting 2023* (Figure 22).

Figure 22: Photos from the poster presentation (Orlando, Florida, USA).

Poster presentation at the 6th International Caparica Conference on Ultrasonic-based applications from analysis to synthesis (ULTRASONICS 2023) in Portugal.

The *6th International Caparica Conference on Ultrasonic-based applications from analysis to synthesis* took place between 26–29 June 2023 in Caparica, Portugal. Prof. Christakis Damianou (CUT) presented a paper produced during SOUNDPET entitled “MR thermometry for a multipurpose phantom for focused ultrasound.” Another paper entitled “Opening of the Blood-brain barrier using focused ultrasound with simultaneous delivery of anti-Aβ antibodies in a 5XFAD amyloid beta mouse model” was presented by the PhD candidate Anastasia Antoniou (CUT). Figure 23 shows sample photos from the conference.

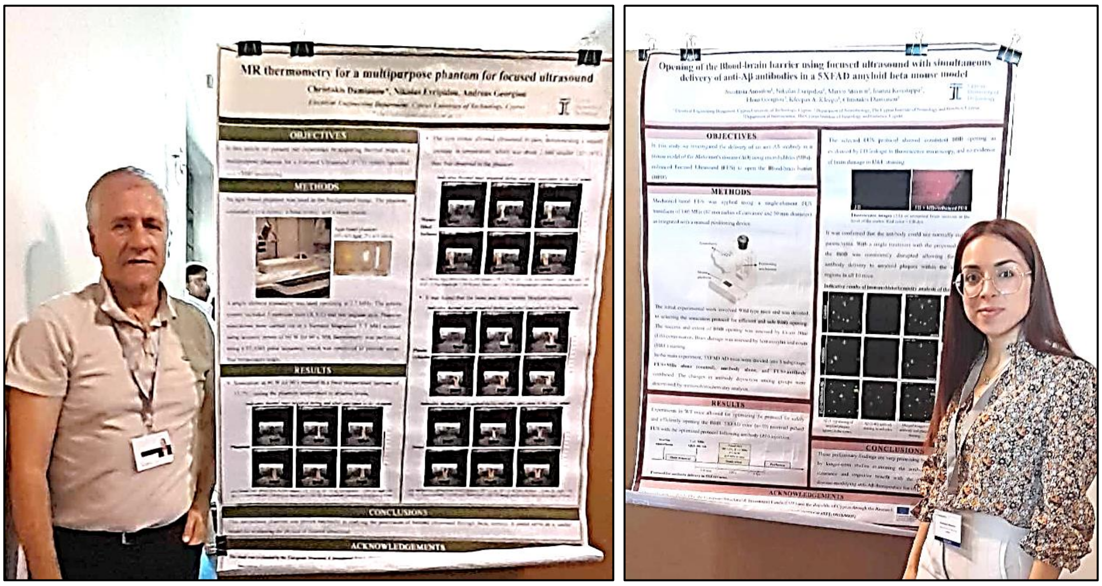


Figure 23: Photos from the poster presentations.

Training of the project's veterinarian

The veterinarian of the project (Kyriakos Spanoudes) was trained for the system and software. His feedback was valuable for designing the final version of the software (Figure 24).

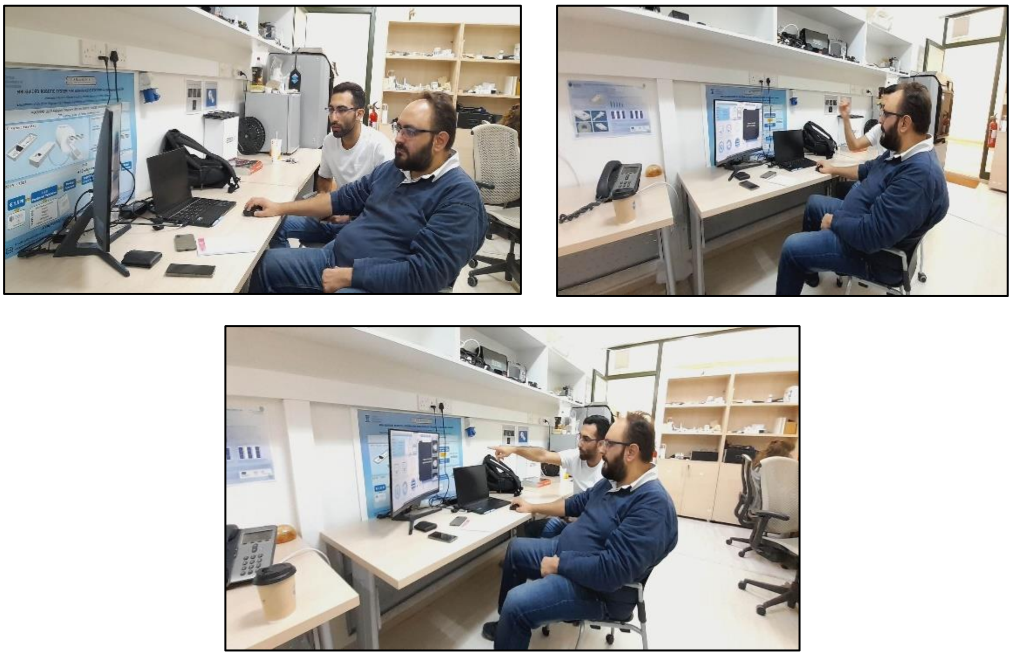


Figure 24: Training of the veterinarian from the software developer (Andreas Georgiou).

Demonstration to the public

The project and the laboratory of therapeutic ultrasound were presented to the general public in several occasions. Our technology (robotic systems and industrial 3D printers) was demonstrated (see typical photo in figure 25).

Figure 25: Presentations to the general public.

Magazine article

The project was presented by GOC (LINAC's affiliation) in a magazine article (27-4-2021). An article was written in a magazine (boussias health) presenting the main projects of GOC (Figure 26). One of the projects presented was SOUNDPET.

Figure 26: Pages of the magazine where the project was presented.

Social media

The project was disseminated through LinkedIn as well (Indicative example in Figure 27).

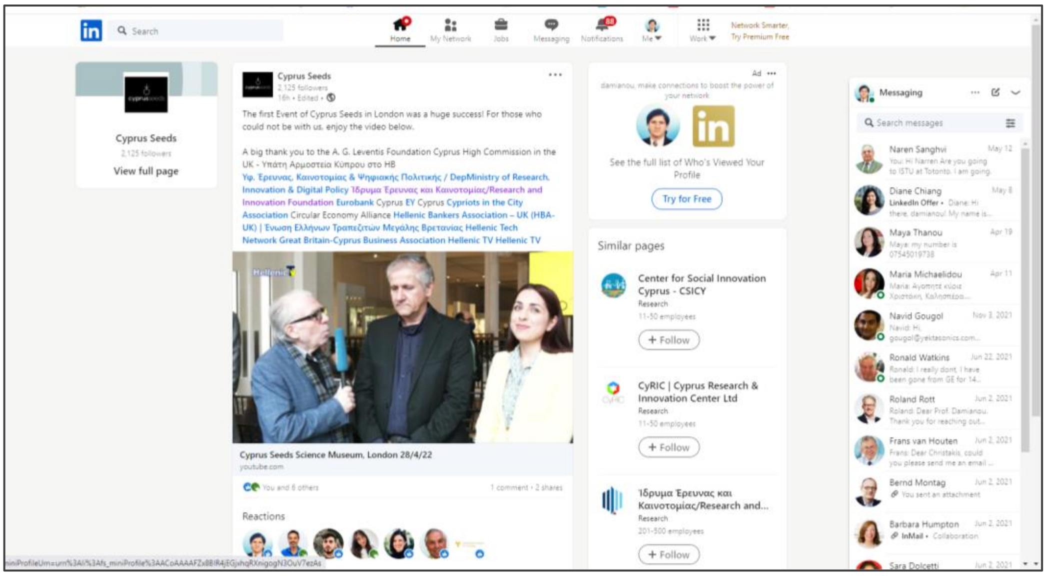


Figure 27: Project dissemination through LinkedIn.

Focused ultrasound foundation coverage

Two of our articles submitted in *AIUM 2022* were highlighted in the Focused ultrasound foundation website (Figure 28).

Meeting Report: American Institute of Ultrasound in Medicine (AIUM) 2022 Annual Meeting

Published: 11 May 2022

Key Points

- The annual AIUM meeting was held March 12-16, in San Diego, CA.
- Two scientific sessions featured recent focused ultrasound research.

The annual integrative ultrasound meeting of the **American Institute of Ultrasound in Medicine (AIUM)** was held March 12-16, 2022, in San Diego, CA. The two scientific sessions that featured focused ultrasound presentations were titled "Therapeutic Ultrasound," and "Therapeutic Applications in Cardiovascular Medicine: Mechanisms and Instrumentation."

The Foundation's Research Director for Applied Physics, Frédéric Padilla, PhD, attended the meeting.

"The Focused Ultrasound Foundation and AIUM have developed an incredible partnership for promoting and supporting the field," said Dr. Padilla. "We are happy to work with AIUM to support this multidisciplinary medical association and its multiple activities beyond the annual meeting, including workshops, webinars, and standard-setting work groups."

The focused ultrasound–based sessions and presentations are outlined below:

Therapeutic Ultrasound Scientific Session
Tuesday, March 15, 2022, 5:30 – 7:00 PM
This session was moderated by Yusef Sayeed, MD, MPH, MEng, DABPM, FAIUM, Physician with United States Air Force.

- Feasibility of Therapeutic Ultrasound Application in Topical Scleral Delivery of Avastin, by Hanaa Almogbil from George Washington University
- Ultrasound-Enhanced Transcorneal Drug Delivery for Fungal Keratitis by Claire M. Allison, from George Washington University
- Agar/Wood-powder Phantom Mimicking Breast Tissue in Magnetic Resonance guided Focused Ultrasound Applications by Christakis Damianou from Cyprus University of Technology
- Robotic Device for Preclinical and Veterinary Trials of Magnetic Resonance Guided Focused Ultrasound by Christakis Damianou from Cyprus University of Technology

Figure 28: Screenshot from the website of Focused ultrasound foundation.

TV appearances

RIK1

The work of the project's coordinator (C. Damianou) and researcher Anastasia Antoniou was highlighted by the national TV channel RIK (Figure 29).

Figure 29: Screenshot from the TV appearance.

Hellenic TV

The coordinator (C. Damianou) and researcher Anastasia Antoniou were highlighted by the UK channel Hellenic TV (Figure 30).

Figure 30: Screenshot from the TV appearance.

Conference papers

1) T. Drakos, M. Giannakou, G. Menikou, G. Constantinides, C. Damianou, "Characterization of an agar/wood powder soft tissue-mimicking material for MRgFUS therapies". 12th Annual Scientific Symposium, Ultrahigh Field Magnetic Resonance: Clinical Needs, Research Promises and Technical Solutions, Berlin, Germany, 2-3 September 2021.

2) M. Giannakou, T. Drakos, N. Evripidou, G. Evripidou, A. Antoniou, C. Damianou, "MRI-guided Focused Ultrasound Robotic System for Preclinical Use of Small and Large Animals". 20th Annual International Symposium for Therapeutic Ultrasound (ISTU 2021), HICO, Gyeongju, Korea, 6-9 June 2021. **Oral Presentation.** Virtual Attendance due to Covid-19 pandemic.

3) M. Giannakou, N. Evripidou, A. Antoniou, C. Damianou, "Robotic Device for MRgFUS applications in veterinary medicine". *2021 International Conference on Medical Imaging Science and Technology (MIST 2021)*, Virtual Conference, 1-3 December 2021, **Oral Presentation**.

4) M. Giannakou, N. Evripidou, A. Antoniou, C. Damianou, "MRI compatible robotic device for FUS therapy of canine and feline mammary tumours". *2021 VI International Scientific Conference – INDUSTRY 4.0*, Borovets, Bulgaria, 8-11 December 2021, **Oral Presentation** (in person attendance).

5) M. Giannakou, N. Evripidou, A. Antoniou, C Damianou, "Robotic device for veterinary applications of MRgFUS". *2021 VI International Scientific Conference – INDUSTRY 4.0,* Borovets, Bulgaria, 8-11 December 2021, **Poster Presentation (i**n person attendance**)**.

6) M. Giannakou, N. Evripidou, A. Antoniou, C. Damianou, "Robotic device for preclinical and veterinary trials of magnetic resonance guided focused ultrasound", *Annual Integrative Ultrasound Meeting 2022 (AIUM),* San Diego, CA, USA, 12-16 March 2022, **Oral Presentation** (in person attendance).

7) C. Damianou, A. Filippou, M. Giannakou, N. Evripidou, "Agar/Wood-powder Phantom Mimicking Breast Tissue in Magnetic Resonance guided Focused Ultrasound Applications", *Annual Integrative Ultrasound Meeting 2022 (AIUM)*, San Diego, CA, USA, 12-16 March 2022, **Oral Presentation** (in person attendance.).

8) A. Georgiou, N. Evripidou, A. Antonioua, I. Demetriadesa, C. Messios, C. Damianou, "Algorithm for path planning in MRgFUS therapy", *21st Annual International Symposium for Therapeutic Ultrasound (ISTU 2022),* Toronto, Canada, USA, 07-10 June 2022, **Poster Presentation (**in person attendance**)**.

9) A. Filippou, M. Giannakou, N. Evripidou, A. Antoniou, C. Damianou, "Agar/Wood-powder Breast Phantom for Focused Ultrasound Applications", *21st Annual International Symposium for Therapeutic Ultrasound (ISTU 2022),* Toronto, Canada, USA, 07-10 June 2022, **Poster Presentation (**in person attendance**)**.

10) M. Giannakou, N. Evripidou, A. Antoniou, C Damianou, "Robotic Device For Preclinical and Veterinary Trials Of Focused Ultrasound", *21st Annual International Symposium for Therapeutic Ultrasound (ISTU 2022),* Toronto, Canada, USA, 07-10 June 2022, **Poster Presentation** (in person attendance**)**.

11) A. Antoniou, M. Giannakou, C. Damianou, "Two simple 3D printed robotic systems for opening the blood brain barrier of small animals", *8th International symposium on Focused ultrasound,* Bethesda, USA, 23-25 October 2022, **Oral Presentation**.

12) A. Antoniou, N. Evripidou, C. Damianou, "Challenges regarding MR compatibility of an MRGFUS robotic system" *13th Interventional MRI Symposium,* Leipzig, Germany, 14-15 October 2022, **Poster Presentation** (in person attendance).

13) A. Antoniou, N. Evripidou, C. Damianou, "Focused Ultrasound Ablation Of Canine Mammary Cancer", *UltraCon Annual Meeting 2023*, Orlando, Florida, USA, 25-29 March 2023, **Poster Presentation** (in person attendance).

14) C. Damianou, A. Antoniou, N. Evripidou, "Focused Ultrasound Phantom With Inclusion Of Tumour", *UltraCon Annual Meeting 2023*, Orlando, Florida, USA, 25-29 March 2023, **Poster Presentation** (in person attendance).

15) C. Damianou, K. Spanoudes, "MRI guided focused ultrasound system for veterinary oncology", *12th Veterinary Forum on companion animal medicine*, Thessaloniki, Greece, 01-02 April 2023, **Poster presentation** (in person attendance).

16) C. Damianou, K. Spanoudes, "T1 and T2 values of an Agar-based phantom with inclusion of tumour", *12th Veterinary Forum on companion animal medicine*, Thessaloniki, Greece, 01-02 April 2023, **Poster presentation** (in person attendance).

17) A. Antoniou, N. Evripidou, K. Spanoudes, and C. Damianou, "Treatment of cancer with focused Ultrasound in cats and dogs", *The 22nd Annual International Symposium on Therapeutic Ultrasound (ISTU),* Lyon, France, 17-20 April 2023, **Poster presentation** (in person attendance).

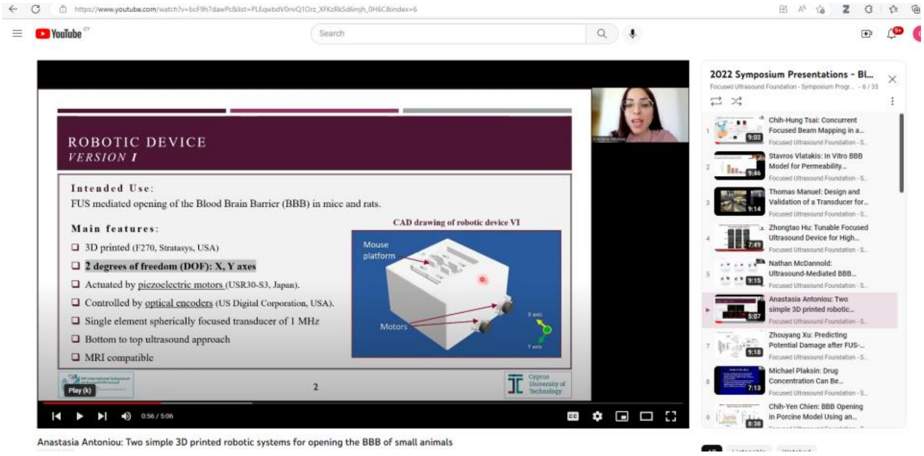
18) N. Evripidou, A. Antoniou, and C. Damianou, "Ultrasound and MRI guided focused ultrasound system for veterinary applications", *The 29th annual international conference of the Australian sonographers association*, Brisbane, Australia, 26-28 May 2023, **Oral presentation** (in person attendance).

19) C. Damianou, N. Evripidou, and A Georgiou, "MR thermometry for a multipurpose phantom for focused ultrasound", *6th International Caparica Conference on Ultrasonic-based applications from analysis to synthesis,* Caparica, Portugal, 26–29 June 2023, **Poster Presentation** (in person attendance).

20) A. Antoniou, N. Evripidou, M. Stavrou, I. Kousiappa, E. Georgiou, K. A. Kleopa, and C. Damianou, "Opening of the Blood-brain barrier using focused ultrasound with simultaneous delivery of anti-Aβ antibodies in a 5XFAD amyloid beta mouse model", *6th International Caparica Conference on Ultrasonic-based applications from analysis to synthesis,* Caparica, Portugal, 26–29 June 2023, **Poster Presentation** (in person attendance).

<u>Video available on YouTube</u>:

https://www.youtube.com/watch?v=bcF9h7dawPc&list=PLEqwbdV0nvQ1Orz_XFKzRkSd6mjh_0H6C&index=6



Journal papers

<u>Published or accepted</u>:

1. T. Drakos, M. Giannakou, G. Menikou, G. Constantinides, and C. Damianou, "Characterization of a soft tissue-mimicking agar/wood powder material for MRgFUS applications," *Ultrasonics*, 113:106357, 2021, doi: 10.1016/j.ultras.2021.106357.
2. A. Antoniou, T. Drakos, M. Giannakou, N. Evripidou, L. Georgiou, T. Christodoulou, N. Panayiotou, C. Ioannides, N. Zamboglou, and C. Damianou, "Simple methods to test the accuracy of MRgFUS robotic systems," *International Journal of Medical Robotics and Computer Assisted Surgery*, 17(4): e2287, 2021, doi: 10.1002/rcs.2287doi: 10.1002/rcs.2287.
3. A. Antoniou, C. Damianou, "MR relaxation properties of tissue-mimicking phantoms (Review)," *Ultrasonics*, 119, 2022, doi: 10.1016/j.ultras.2021.106600.
4. A. Antoniou, L. Georgiou, T. Christodoulou, N. Panayiotou, C. Ioannides, N. Zamboglou, and C. Damianou, "MR relaxation times of agar-based tissue mimicking phantoms," *Journal of Applied Clinical Medical Physics*, 23(5), 2022, doi:10.1002/acm2.13533.
5. A. Antoniou, M. Giannakou, N. Evripidou, S. Stratis, S. Pichardo, and C. Damianou "Robotic system for top to bottom MRgFUS therapy of multiple cancer types," *International Journal of Medical Robotics and Computer Assisted Surgery*, 18(2): e2364, 2022, doi: 10.1002/rcs.2364.
6. A. Antoniou, A. Georgiou, N. Evripidou, and C. Damianou, "Full coverage path planning algorithm for MRgFUS therapy," *International Journal of Medical Robotics and Computer Assisted Surgery*, 18: e2389, 2022, doi: 10.1002/rcs.2389.
7. A. Filippou, C. Damianou, "Ultrasonic attenuation of canine mammary tumours," *Ultrasonics*, 125, 2022, doi: 10.1016/j.ultras.2022.106798.
8. M. Giannakou, A. Antoniou, and C. Damianou, "Preclinical robotic device for magnetic resonance imaging guided focussed ultrasound," *International Journal of Medical Robotics and Computer Assisted Surgery*, 19(1): e2466, 2023, doi: 10.1002/rcs.2466.
9. A. Antoniou, L. Georgiou, N. Evripidou, C. Ioannides, and C. Damianou, "Challenges regarding MR compatibility of an MRgFUS robotic system, *Journal of Magnetic Resonance*," 344:107317, 2022, doi: 10.1016/j.jmr.2022.107317.
10. A. Antoniou, C. Damianou, "Simple, inexpensive, and ergonomic phantom for quality assurance control of MRI guided Focused Ultrasound systems," *Journal of Ultrasound*, 26(2):401-408, 2023, doi: 10.1007/s40477-022-00740-w.
11. A. Filippou, I. Louca, and C. Damianou, "Characterization of a fat tissue mimicking material for high intensity focused ultrasound applications" *Journal of Ultrasound*, 26(2):505-515, 2023, doi: 10.1007/s40477-022-00746-4.
12. A. Antoniou**,** M. Giannakou, E. Georgiou, K. Kleopa, and C. Damianou, "Robotic device for transcranial FUS applications in small animal models", *International Journal of Medical Robotics and Computer Assisted Surgery*, 2022, doi: 10.1002/rcs.2447.
13. A. Antoniou, A. Nikolaou, A. Georgiou, N. Evripidou, and C. Damianou, "Development of an US, MRI, and CT imaging compatible realistic mouse phantom for thermal ablation and focused ultrasound evaluation," *Ultrasonics*, 131, 2023, doi: 10.1016/j.ultras.2023.106955.

14. A. Antoniou, K. Spanoudes, and C. Damianou, "Treatment of mammary cancer with Focused Ultrasound: A pilot study in canine and feline patients," *Ultrasonics*, 132, 2023, doi: 10.1016/j.ultras.2023.106974.
15. A. Antoniou, N. Evripidou, L. Georgiou, A. Chrysanthou, C. Ioannides, and C. Damianou, "Tumor phantom model for MRI guided Focused Ultrasound ablation studies," *Medical Physics*, 2023, doi: 10.1002/mp.16480.
16. A. Antoniou, C. Damianou, "Feasibility of ultrasonic heating through skull phantom using single-element transducer," *Journal of Medical Ultrasound*, Accepted: 31/03/2023.
17. A. Antoniou, M. Stavrou, N. Evripidou, E. Georgiou, I. Kousiappa, A. Koupparis, S. S. Papacostas, K. A. Kleopa, and C. Damianou, "FUS-mediated Blood-brain barrier disruption for delivering anti-Aβ antibodies in 5XFAD Alzheimer's disease mice," *Journal of Ultrasound*, Accepted: 28/06/2023.
18. A. Antoniou, N. Evripidou, and C. Damianou, "Focused ultrasound heating in brain tissue/skull phantoms with 1-MHz single-element transducer," *Journal of Ultrasound*, Accepted: 09/07/2023.
19. P. Sofokleous and C Damianou, "High Quality Agar and Polyacrylamide Tumour Mimicking Phantom Models for MR-guided Focused Ultrasound Applications," *Journal of Medical Ultrasound*, Accepted: 13/07/2023.

***Submitted* (under review):**

1. A. Filippou, N. Evripidou, A. Georgiou, L. Georgiou, A. Chrysanthou, C. Ioannides, and C. Damianou, "MR thermometry of Focused Ultrasound (FUS) using a preclinical FUS robotic system at 3 T," *Physica Medica* (1st revision submitted: 22/05/2023).
2. A. Filippou, N. Evripidou, A. Georgiou, A Nikolaou, and C. Damianou, "Estimation of PRF coefficient in agar based phantoms," *Ultrasonics*, (Submitted: 03/01/2023).
3. A. Filippou, A. Georgiou, A. Nikolaou, N. Evripidou, and C. Damianou, "Advanced software for MRgFUS treatment planning," *Computer Methods and Programs in Biomedicine* (1st revision submitted: 03/07/2023).
4. A. Antoniou, N. Evripidou, A. Nikolaou, A. Georgiou, M. Giannakou, A. Chrysanthou, L. Georgiou, C. Ioannides, and C. Damianou, "MRI monitoring of thermal lesions produced by focused ultrasound," *Medical Physics* (Submitted: 01/05/2023).
5. N. Evripidou, A. Antoniou, L. Georgiou, C. Ioannides, and C. Damianou, "MRI compatibility testing of commercial HIFU transducers," *Physica Medica* (Submitted: 03/07/2023).
6. N. Evripidou, A. Antoniou, G. Lazarou, L. Georgiou, A. Chrysanthou, C. Ioannides, and C. Damianou, "Workflow of a preclinical robotic MRI-guided FUS body system." *Physica Medica* (Submitted: 05/07/2023).

To be submitted after pattern application is filed

Robotic device for Magnetic Resonance Imaging guided Focused Ultrasound treatment of abdominal targets , *Medical Robotics and Computer Assisted Surgery*.

Appendix 1

Administrator Tool

Website I

Website main page

The website domain is: www.soundpet.eu/. Screenshot of the website is shown in Figure 1. In the main page, a summary of the project, a CAD design of the robotic device and a video of the motion are included.

Figure 8: Main page of the SOUNDPET project website.

Log-In

The researchers with access can add information regarding the project from the following link http://www.soundpet.eu/administrator.php as shown in Figure 2.

Figure 2: Log-In Page.

Administrator - Options

There is a list with available options to add information as shown in Figure 3.

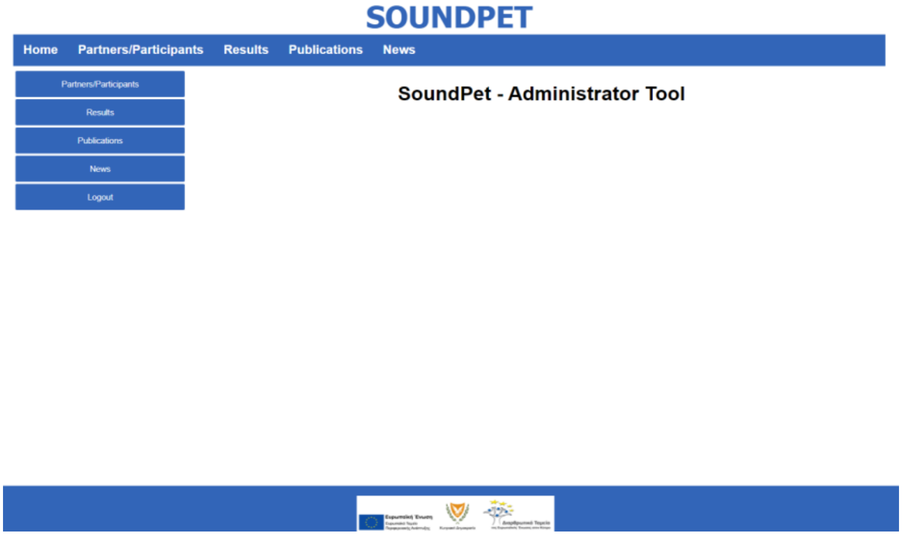


Figure 3: List of administrator options.

The administrator of the website has the following options (listed at the left-hand site of the website):

-
- **Partners/Participants**: List of partners and participants to add new/edit/delete partners,
- **Results:** List of results and option to add new/edit/delete results,
- **Publications:** List of publications and option to add new/edit/delete publications,
- **News:** List of news and option to add new/edit/delete news, and
- **Logout** from the administrator tool.

Add/Edit Media icons (in all entities/options) are available to add or delete media files related to the partners section (Figure 4).

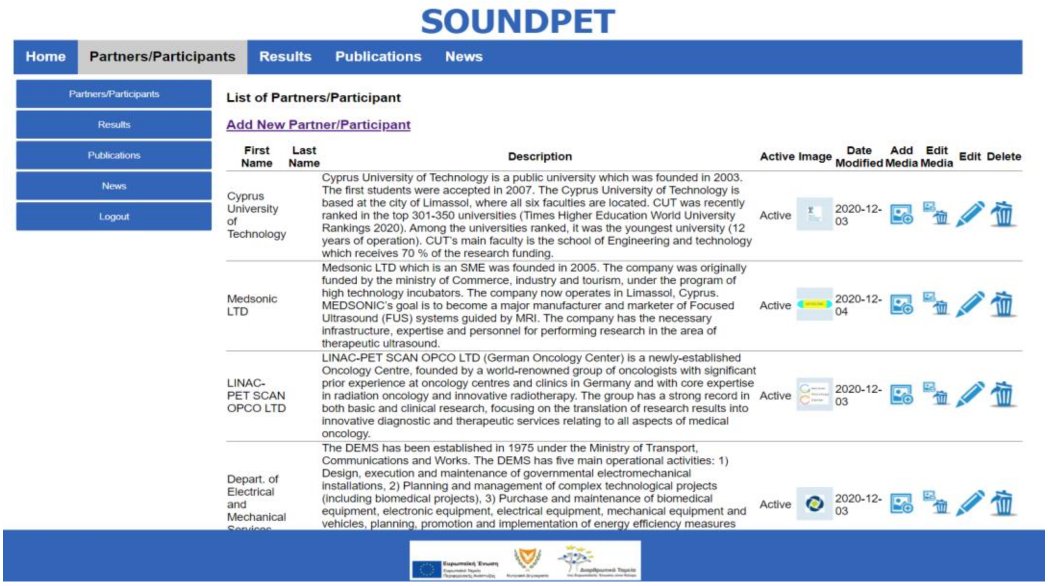


Figure 4: List of Partners.

Figure 5 shows how the user can edit partners and any other entity of the website. Sort order number used by the system to sort the products on the main page in ascending order.

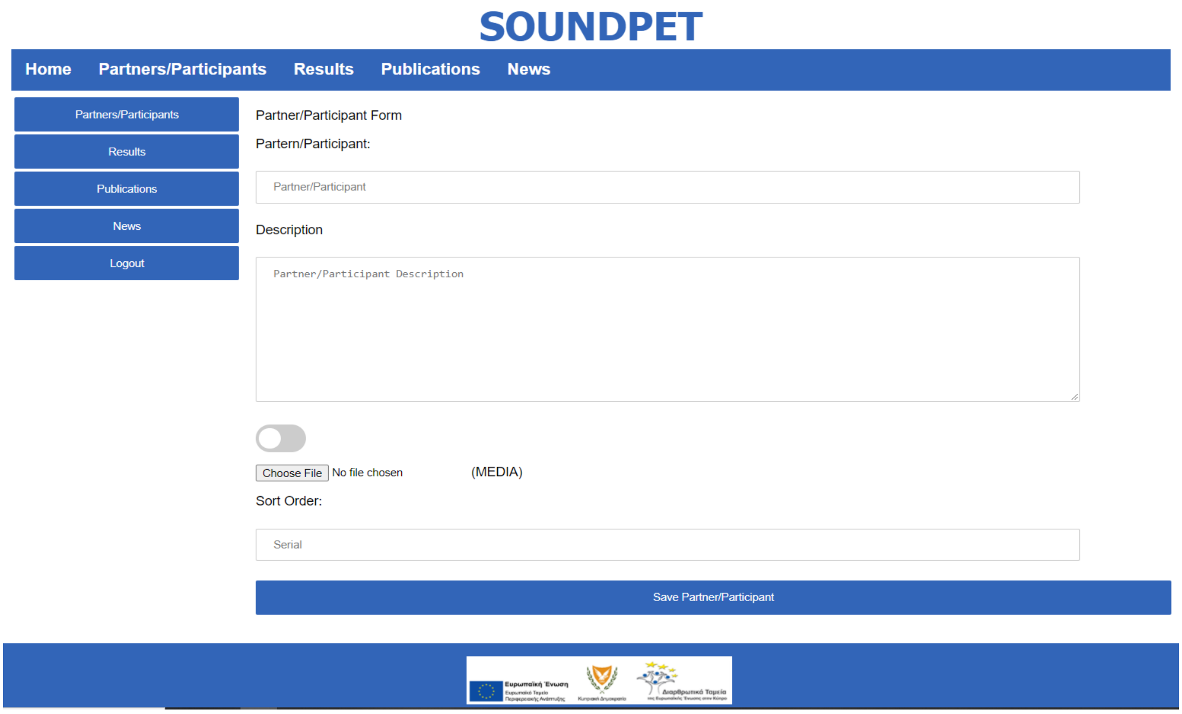


Figure 5: Partners edit page.

Figure 6 shows a list of results. Here the user can add/edit/delete a result or add results.

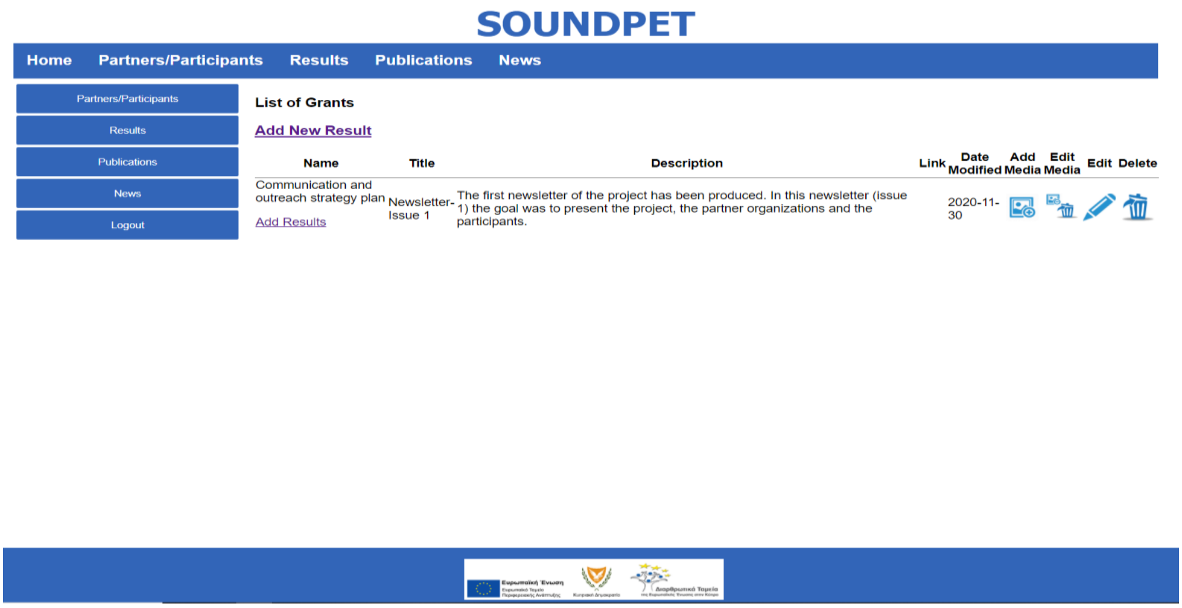


Figure 6: List of results.

In Figure 7 the user can add results in pdf format.

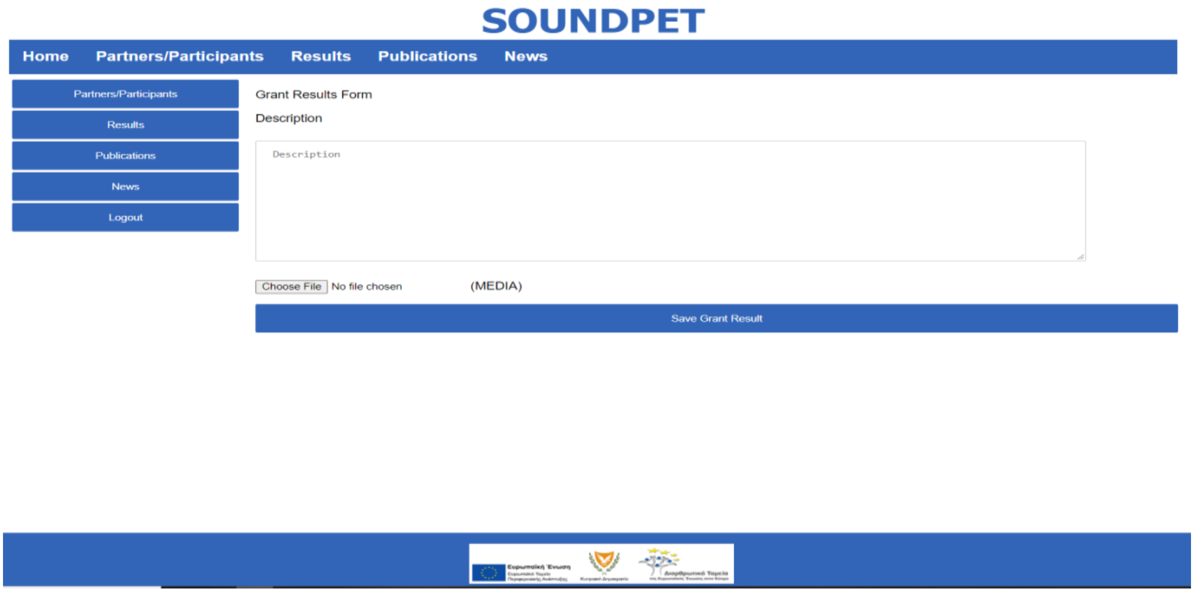


Figure 7: Results add page.

Website II

Another website featuring significantly enhanced graphics and design was developed. The website domain is: https://theralabcut.org/. A screenshot of the website's home page is shown in Figure 8. As can be seen from this Figure, in the main page, the core research activities of the Therapeutic Ultrasound laboratory are briefly described. Figures of the developed MRgFUS software and typical lesion created on excised tissue by FUS ablation with the SOUNDPET system are also shown.

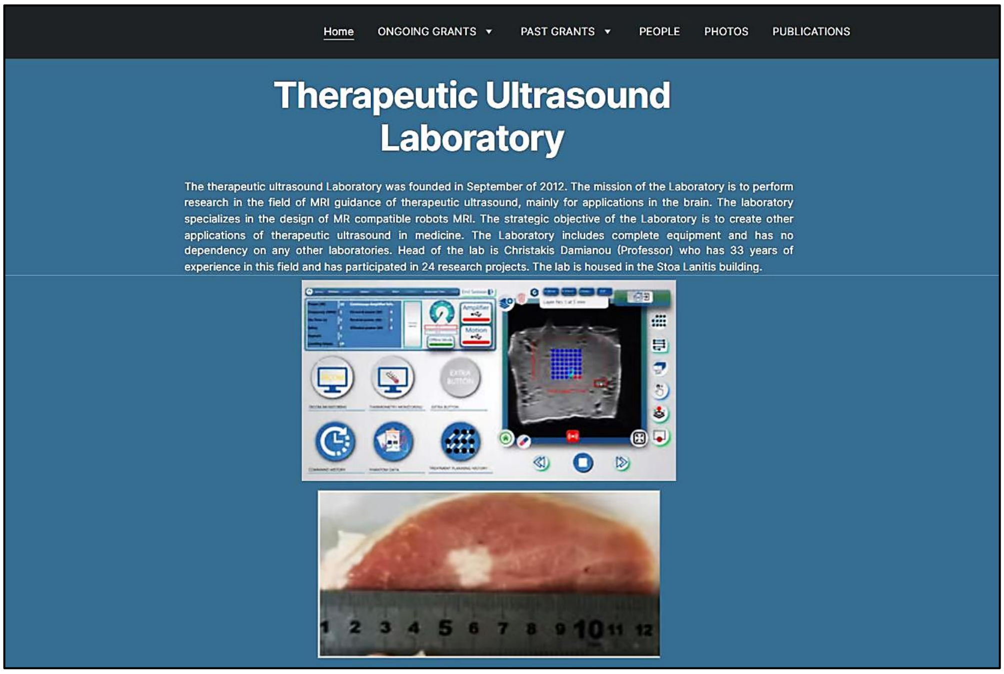


Figure 8: Website home page.

The main website page further includes a dedicated section at the bottom, from where the website visitors can contact us for further inquiries and information. The relevant section can be seen in Figure 9.

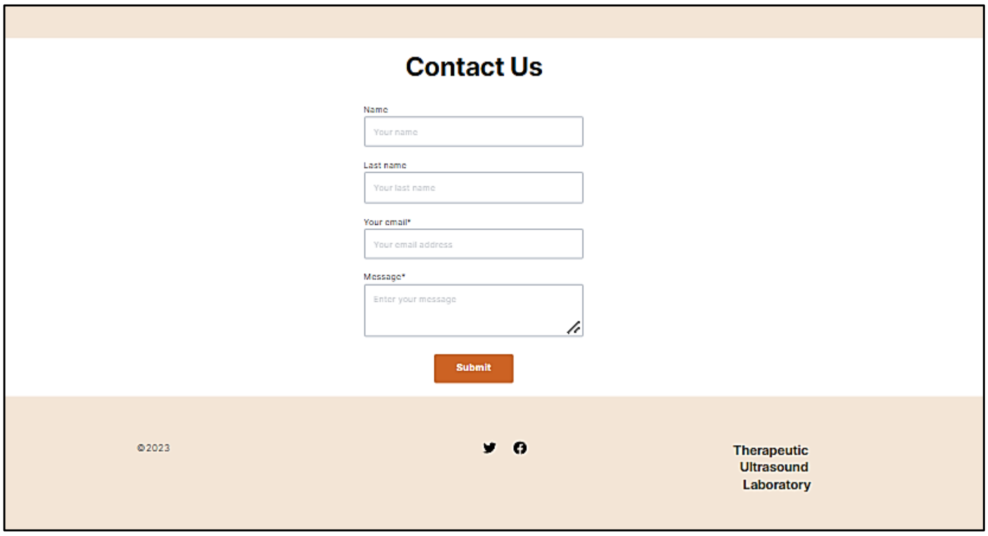


Figure 9: Website home page – Contact section.

The user can find detailed information about the SOUNPET project via the *Ongoing grants* button at the menu bar on the top. The relevant page includes the project summary and a demonstration video of the SOUNDPET system, as shown in Figure 10.

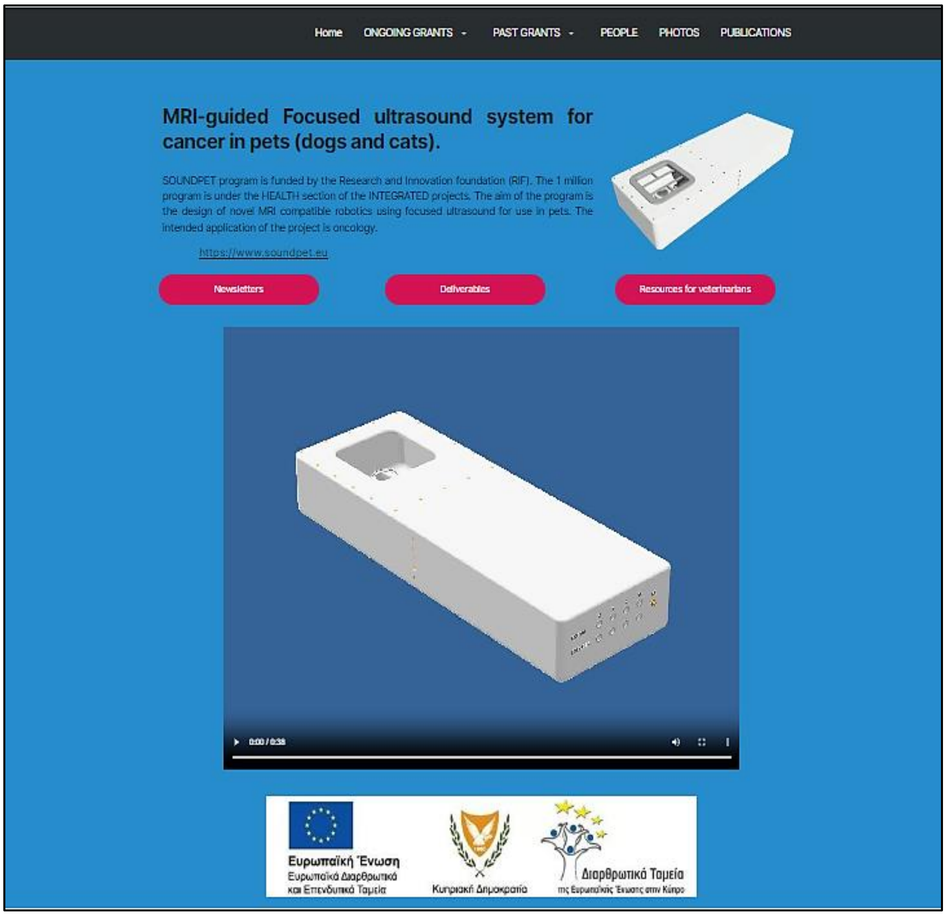


Figure 10: SOUNDPET page.

Through this page the user can also access the project's Newsletters and Deliverables through the relevant buttons. Figure 11 shows the *Deliverables* page, and Figure 12 the *Newsletters* page. The user can easily download a specific Newsletter/Deliverable by simply pressing the corresponding button.

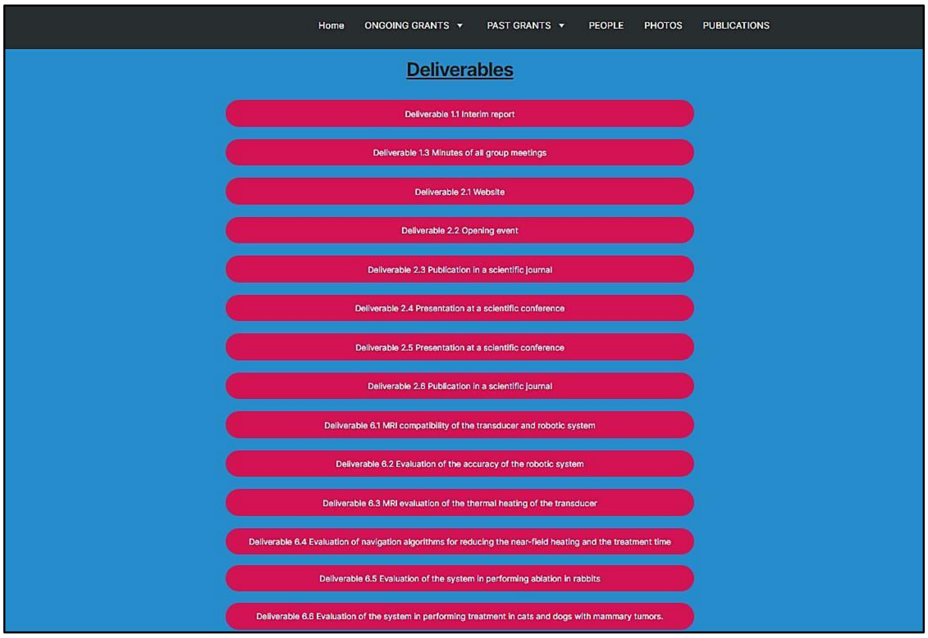


Figure 11: Page with list of SOUNDPET deliverables.

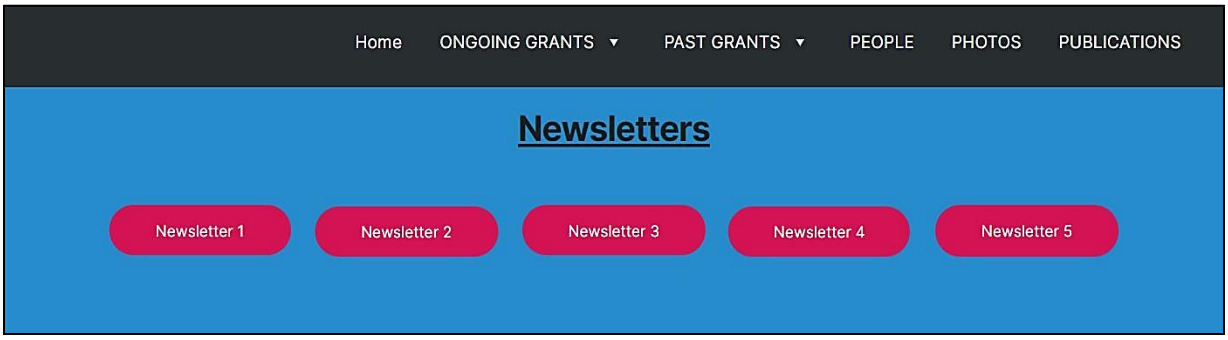


Figure 12: Page with list of SOUNDPET newsletters.

Appendix 2

Brochure

SOUNDPET

MRI-guided Focused ultraSOUND system for cancer in PETs (dogs and cats)

The SOUNDPET (INTEGRATED/0918/0008) project started in July 2020 and will be completed in June 2023. The study was co-financed by the European structural and investment funds (ESIF) and the Republic of Cyprus through the Research and Innovation Foundation (RIF).

Project Summary

SOUNDPET's main goal was the development of an MRI-guided focused ultrasound (MRgFUS) robotic system for preclinical applications in small and large animals.

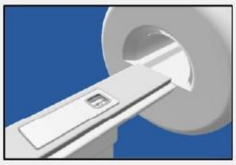
A four degrees of freedom robotic system intended for sonicating phantoms, excised tissue and animals of all sizes using MRgFUS was developed. The robotic device can be either integrated inside or attached to the MRI bed, enabling treatment of patients placed in the prone and supine positions, respectively. The device comprises a positioning mechanism dedicated to navigating the ultrasonic source in three linear and angular axes. Two transducers (1 and 2.5 MHz) were manufactured so that good ultrasonic focusing is achieved over a large depth, thus targeting both shallow and deep tissue accurately. Beneficially, tissue heating can be monitored precisely using MR thermometry. A user friendly software allows controlling the system by sending commands to an in-house electronic driving system. MRI compatibility and highly accurate motion were demonstrated through extensive experimentation. Discrete and overlapping lesions were formed in phantoms and excised tissue successfully. The final product will be applied in dogs and cats with naturally occurring mammary cancer. Since the same mechanisms that result in cancer in humans are also operative in pets, veterinary applications may contribute to enhance human medicine.

Partners

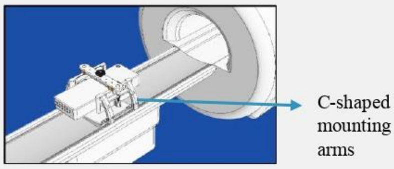
1

Hardware

The device can be integrated in the MRI bed for a bottom to top ultrasonic delivery to a subject placed in the **prone position**.

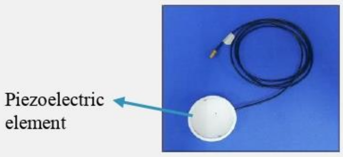


The device can be attached to the MRI bed for a top to bottom ultrasonic delivery to a subject placed in the **supine position**.

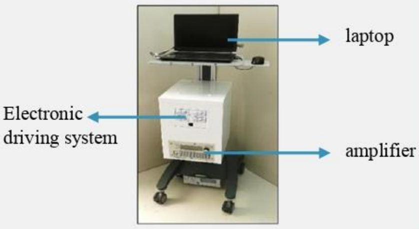


Two single element shperically focused piezoelectric transducers were manufactured based on a simulation study:

- ❖ 2.5 MHz transducer for shallow targets
- ❖ 1 MHz transducer for deeper targets



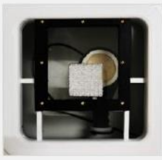
All electronic components were assempled in a modern in-house medical cart.



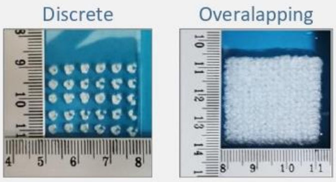
Evaluation

❖ Grid sonications on plastic films

Motion accuracy assessment by multiple ablations in a grid

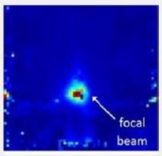


Lesions arranged in discrete and overlapping patterns depending on the ultrasonic protocol

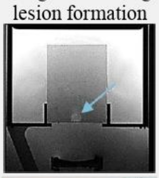


❖ High power sonication in agar/wood tissue mimicking phantom.

Heating monitored using MR Thermometry



High resolution (Proton Density) MR image confirming lesion formation



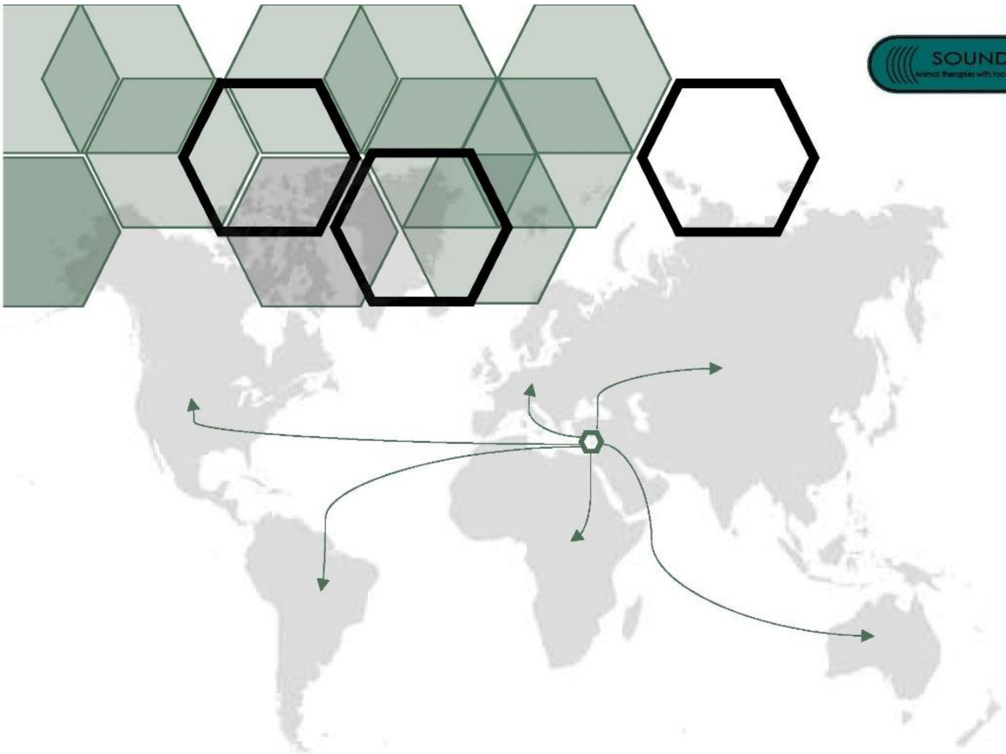
Dissected phantom with multiple discrete lesions

www.soundpet.eu

christakis.damianou@cut.ac.cy

Appendix 3

Newsletter 1



SEPTEMBER 1st, 2020

INTEGRATED/0918/0008

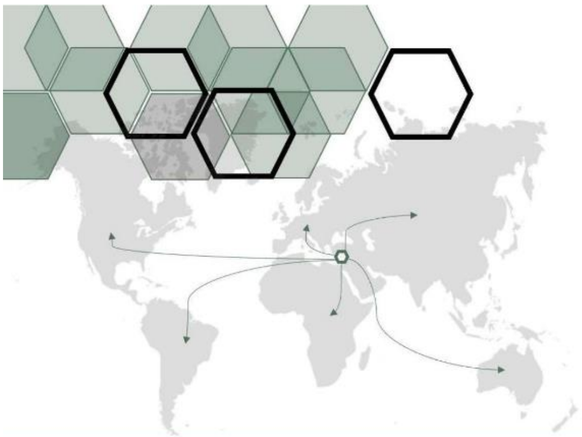
SOUNDPET NEWSLETTER

ISSUE 1

Providing with news on MRI guided Focused Ultrasound technology in the field of oncology, in the framework of the SOUNDPET project!

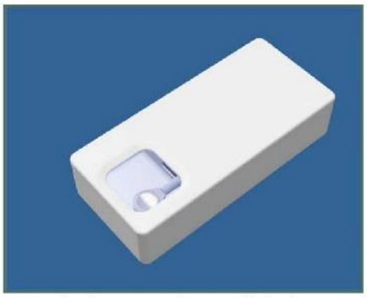
INDEX

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

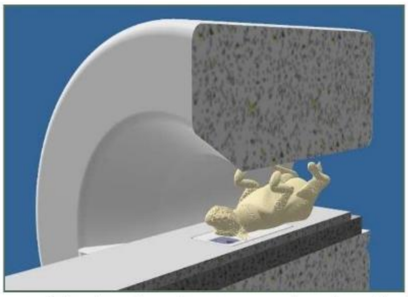


SUMMARY: THE SOUNDPET PROJECT

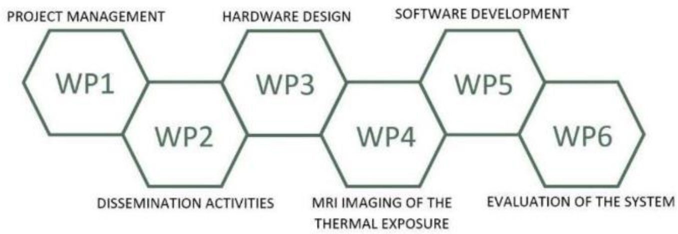
SOUNDPET (MRI-guided Focused Ultra**SOUND** system for cancer in **PET**s - dogs and cats) is a three-year project, co-funded by the European Union (through the Research & Innovation Foundation), started in July 2020 and its main goal is to develop an MRI-guided focused ultrasound (MRgFUS) robotic system for preclinical use of small and large animals. The final product will be applied in pets (dogs and cats) with naturally occurring mammary cancer. The goal is to produce a preclinical robotic system (final product) with 4 degrees of freedom (DOF) that can sonicate phantoms, excised tissue and animals using MRgFUS. The tissue heating can be accurately monitored using MR thermometry. The ultrasonic system will include a single element transducer (ranging from 20-60 mm in diameter) and will operate with a frequency ranging from 0.5 to 4 MHz. A software will be developed that will control this medical device. The system will be evaluated in phantoms, excised tissue and animals. The same mechanisms that result in cancer in humans are operative in pets and are operative in other animals **as well. Man's best friend is probably man's best new biomedical friend.** This system can be modified in the future for use in humans by scaling up the design of the robotic system. Based on the priorities of the smart specialization of Cyprus this proposal appeals to the area of Health (table II.1.6, priority B2- **'Diagnosis, prevention, risk factors, therapy')**. The proposed technology intends to serve the community of non-invasive surgery using therapeutic ultrasound and MRI guidance for veterinary applications. The long-term goal is to commercialize this technology (by the end of the project it will be in the state of final product). Since the device is applied in animals, there is no need to receive regulatory approvals (for example CE marking).



4 DOF robotic system for preclinical research.

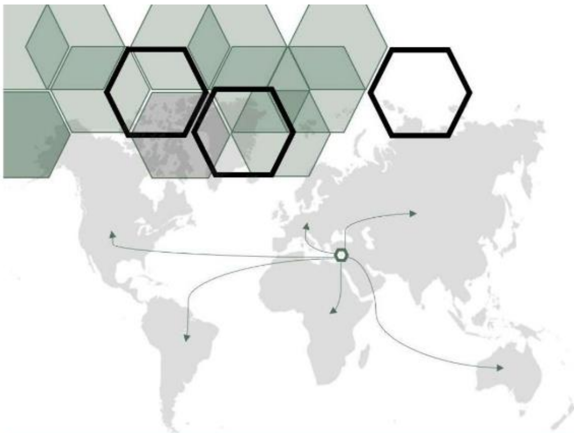


The concept of the developed system as placed on the MRI table.



Work Packages (WP) of the SOUNDPET project.

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης · Κυπριακή Δημοκρατία · Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



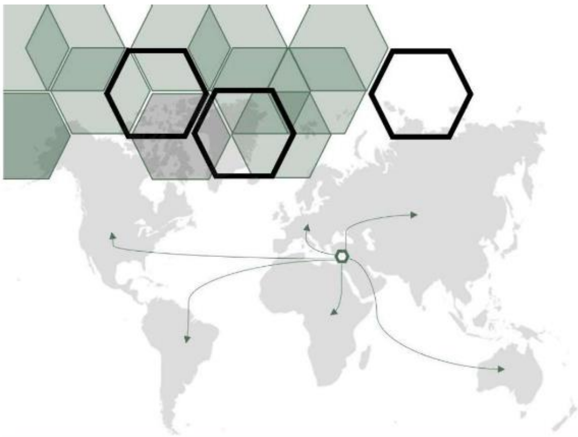
PARTNERS

MEDSONIC: MEDSONIC LTD which is an SME was founded in 2005. The company was originally funded by the ministry of Commerce, industry and tourism, under the program of high technology incubators. MEDSONIC LTD was initially hosted by the HERMIS incubator of Cyprus. The company now operates in Limassol, Cyprus. MEDSONIC's goal is to become a major manufacturer and marketer of Focused Ultrasound (FUS) systems guided by MRI. The company has the necessary infrastructure, expertise and personnel for performing research in the area of therapeutic ultrasound. So far, the company has produced a prototype FUS system for animal use that can be guided using MRI. In order to achieve this, the company has produced an MR compatible positioning device that scans an MRI compatible FUS transducer. The system is controlled by user-friendly software. The company performed extensive animal experiments, and now the goal is to convert this prototype technology into a commercial product to be applied in humans. The company will apply for clinical trials through the Cyprus Medical Device Agency.

Cyprus University of Technology (CUT): CUT is a public university which was founded in 2003. The first students were accepted in 2007. The Cyprus University of Technology is based at the city of Limassol, where all six faculties are located. CUT was recently ranked in the top 400-500 universities (Times Higher Education World University Rankings 2016). Among the universities ranked, it was the youngest university (12 years of operation). CUT's main faculty is the school of Engineering and technology which receives 70 % of the research funding. In this project CUT participates through the therapeutic ultrasound lab headed by Christakis Damianou which belongs to the Electrical engineering department. The therapeutic ultrasound lab has complete infrastructure of therapeutic ultrasound equipment. The therapeutic ultrasound lab occupies a 130 m^2 area. The laboratory is the only approved center for performing experiments in rabbits in Cyprus. CUT will undertake many research tasks for the proposed grant.

German Oncology Center: GOC is a newly-established Oncology Centre, founded by a world-renowned group of oncologists with significant prior experience at oncology centres and clinics in Germany and with core expertise in radiation oncology and innovative radiotherapy. The group has a strong record in both basic and clinical research, focusing on the translation of research results into innovative diagnostic and therapeutic services relating to all aspects of medical oncology. The Center has assembled a strong multidisciplinary care team that is well suited to adopt new methodologies and tools in precision oncology that will be the output of the proposed project. From reliable early detection investigations, to high-quality innovative radiotherapy, chemotherapy and hormone therapy, the GOC's aim is to fill an important gap in cancer-patient care in Cyprus. Moreover, the GOC has established important collaborations with both local hospitals and other hospitals in Europe, and it aspires to become an important referral center for cancer patients from all neighboring countries. Additionally, the Centre is committed to being regularly involved in research projects, conferences and other research activities that will ensure that its staff of medical professional remains constantly updated and involved with internationally innovative research. The Centre's staff roster boasts several experienced and acclaimed oncologists, each specializing in different types of cancer.

co-funded by



PARTNERS

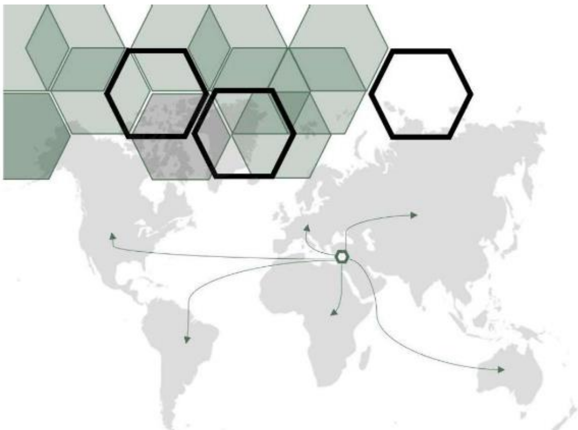
German Oncology Center: Medical services are organized into five departments: 1) the Department of Radiation Oncology 2) the Department of Nuclear Medicine, 3) the Department of Diagnostic and Interventional Radiology, 4) the Department of Medical Oncology and 5) the Department of Medical Physics and Engineering. The GOC is equipped with state-of-the-art diagnostic and therapeutic means such as MRI, CT, PET, Cyclotron, as well as with its own clinical laboratory and pharmacy. It is situated in brand new facilities overlooking the city of Limassol, and it set to become an important contributor to the delivery of world class medical care in Cyprus.

Department of Electrical and Mechanical Services (DEMS): The DEMS has been established in 1975 under the Ministry of Transport, Communications and Works. The DEMS has five main operational activities: 1) Design, execution and maintenance of governmental electromechanical installations, 2) planning and management of complex technological projects (including biomedical projects), 3) purchase and maintenance of biomedical equipment, electronic equipment, electrical equipment, mechanical equipment and vehicles, planning, promotion and implementation of energy efficiency measures and energy management of the governmental buildings, and 5) Competent Authority for implementing the EU legislation for the electromagnetic compatibility of equipment (EMC directive), the low voltage directive (LVD) and the safety of many types mechanical equipment and for implementing non-harmonizing legislation. The DEMS actively participates in research programs. In 2015 the DEMS has completed the project ENERGEIN in co-operation with the Department of Public Works and the Energy Service in the context of the Cross-**border Cooperation Programme "Greece**-Cyprus 2007-**2013". Currently the** DEMS participates in the project iHeERO with the Cyprus University of Technology in the context of the CEF Transport Competitive Program, the Internal market budget JA2015-EMCLVD for LED Floodlights and the Joint Market Surveillance Action 2015 (JA2015) for Consumer Products of the Consumer Programme for 2014-2020.

TEAM MEMBERS

Christakis Damianou (CUT-Project Coordinator) received a B.Sc., M.Sc., and Ph.D. from the University of Arizona in Electrical engineering in 1988, 1990 and 1993 respectively. His research interests include MRI guided therapeutic ultrasound and MRI compatible robotics. Between 1988 and 1993, during his master and doctoral studies he worked as a research assistant in the department of radiation oncology at the University of Arizona. Between 1993 and 1994 he worked as postdoctoral fellow in the department of radiology at Harvard University in Massachusetts. Between 1994 and 1995 he worked as a research scientist in the department of biophysics at Indiana University. He is currently professor at Cyprus University of Technology (CUT) at the Electrical engineering, computer engineering and Informatics department. So far Dr. Damianou was involved in 34 research programs, having the coordination of 11 of them. The acronyms of the main programs that he participated are: ULTRASOUND I, ULTRASOUND II, SONOTHERM, ODISEAME, NETTLE, TROY, N2L, SONOMRI, BRAINSONIC, SONOSTROKE, PROFUS and ULTRASTROKE. He received so far 2 infrastructure grants from the research promotion foundation. Based on **his research activities 130 publications were published and 3 book chapters. He is the inventor of the patent: 'MRI pos**itioning **system for ultrasound brain surgery' (WO/2007/082495). Another patent was issued by European patent office (**'Multi-**purpose robotic system for MRI guided focused ultrasound treatment')**. In 2015 Dr. Damianou created at CUT a master program in Biomedical engineer. Currently 6 Ph.D. students are working under the supervision of Dr. Damianou. So far 4 Ph.D. students have graduated under his supervision.

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



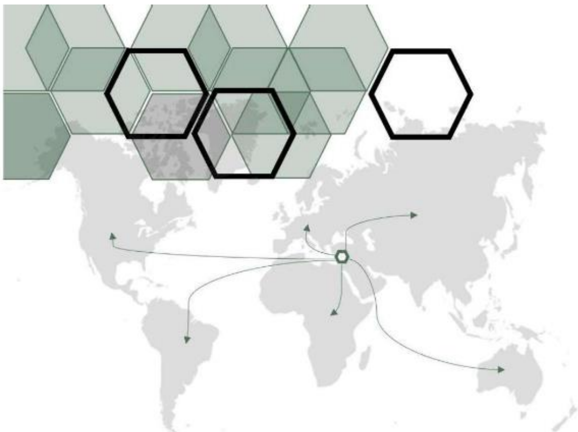
TEAM MEMBERS

Georgios Constantinides (CUT) has more than a decade of experience in the field of nanoscale materials characterization and composite/contact mechanics modelling. During his PhD and Post-Doctorate positions at the Massachusetts Institute of Technology (MIT) he has been trained on various nanomechanical tools and exposed to a variety of materials systems ranging from metals and ceramics to polymers, biomaterials and composites. He is currently an Assistant Professor in the Department of Mechanical Engineering and Materials Science and Engineering at CUT and a founding member of the Research Unit for Nanostructured Materials Systems (http://www.cut.ac.cy/runms/). In 2009 he established the Nano/Micro Mechanics of Materials Lab (http://cutnanolab.weebly.com/) which develops experimental and computational techniques for small scale mechanical testing and modelling. Apart from contributing his experience on material characterization he will also help on materials engineering and optimization. He is the author/co-author of 2 book chapters and >30 Journal publications (>1600 citations, h-index: 14, Scopus). He serves regularly as a reviewer on more than 25 Journals and has participated in various US, EU and national (CY) projects with total funding in excess of €5M.

Marinos Yiannakou (MEDSONIC) graduated from University of Cyprus in 2012 with the degree of Electrical Engineering. He received his Ph.D. at Cyprus University of Technology in 2017. His Ph.D. dissertation was related to an MRI guided FUS robotic system for brain surgery. He did his Ph.D. work under the supervision of C.Damianou. He worked as a teaching assistant under the guidance of Dr. C. Damianou, teaching medical imaging courses. He has published so far 12 peer-reviewed scientific papers, 16 conference papers, and one patent ('Multi-purpose robotic system for MRI guided focused ultrasound treatment'). His main interest is design of MRI compatible robots and transducer design. He has participated so far as a researcher in 3 research grants related to therapeutic ultrasound. He currently the CEO of MEDSONIC and main designer of MRgFUS robotic systems. His main research interest is focused ultrasound, MRI imaging, robotic design and design of ultrasonic phantoms.

Nikolaos Zamboglou (GOC) was born and raised in Limassol, Cyprus, and in 1967 he moved to Germany for his studies. He was awarded a degree in Physics from RWTH Aachen in 1974, and in 1977 he obtained his PhD in Physics at the University of Düsseldorf. He completed his degree in Medicine in 1984, and his PhD in Medicine in 1989, both at the University of Essen. From 1986 to 1992, Prof. Zamboglou held the post of Consultant of Radiation Oncology at the University of Düsseldorf. He subsequently assumed his appointment as Director and Professor of the Department of Radiation Oncology at Clinikum Offenbach, at the Academic Hospital of Wolfgang Goethe University, Frankfurt, where he remained until 2016. Prof. Zamboglou also is appointed as Adjunct Research Professor at the Technical University of Athens since 1993. He is elected as corresponding member of the Academy of Athens in 2010. Most notably, he was President of the German Society of Radiation Oncology between 2005 and 2007, and in 2012 was declared an Honorary Member of the Austrian Radiation Oncology Society. Finally, in 2015 he was honoured with the Alfred-Breit Award of the German Society of Radiation Oncology (the highest society award). Since 2016, Prof. Zamboglou has been acting as Medical Director of the German Oncology Centre.

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



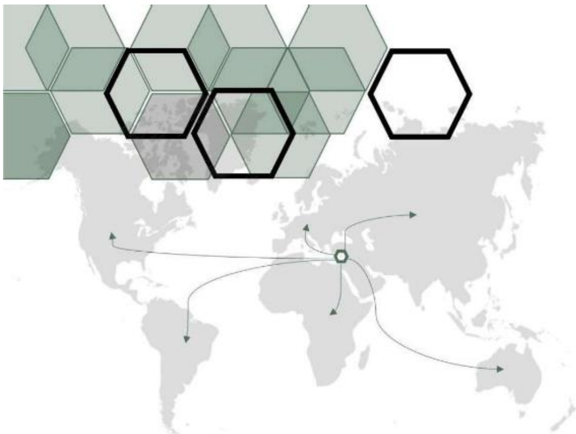
TEAM MEMBERS

Nikolaos Zamboglou (GOC) awards: 1991 Hans Langendorff Price of the Medical Society for Radiation Protection, Germany, 1998 Price of the German Society for Senology, 2001 Richard-Mertens Price for Innovative Research, 2002 Price of the German Society for Surgery , 2003 Price of the German Society for Medical Technology, 2009 Corresponding Member of the **Academy of Athens, 2009 Honorary Member of the Medical Society of Limassol, Cyprus, 2010 "Strebel Medal for Brachytherapy" of the German, Austrian and Swiss Societies for Radiation Oncology, 2011 Honorary Member** of the Austrian Society of Radiation Oncology, 2014 Alfred Breit Price of the German Society for Radiation Oncology, 2017 Honorary Doctorate awarded by Cyprus University of Technology.

Kleanthis Ioannides (GOC) has a medical degree from University of Vienna since 1996. He obtained specialization in radiology from university of Athens in 2002. He received specialization in Magnetic Resonance Imaging between 2002 and 2004 from the University of Athens. He is the director of interventional radiology department at GOC. He published several papers in the area of MRI. His main research interest is MRI imaging of the thermal effects of ultrasound.

Georgios Anagnostopoulos (GOC) is the Head of the Medical Physics Department at the German Oncology Center, Limassol. He was awarded a degree in Physics from the University of Athens, Greece in 1997. He then moved to Germany for his postgraduate studies at the University of Heidelberg and his practical training as a Medical Physicist at Klinikum Offenbach, and in 2001 he obtained his MSc Degree as well as his working license as a Medical Physicist in Germany. He was appointed as a full time Medical Physicist in the Klinikum Offenbach and at the same time he started his PhD studies at the University of Heidelberg in 2002, which he completed in 2006 by receiving the PhD Degree in Physics. From 2001 to 2007, Dr Anagnostopoulos held the post of Medical Physicist at Klinikum Offenbach and subsequently assumed his appointment as Medical Physicist at the Metropolitan Hospital, in Athens, Greece, where he remained until 2012. He then started working for NZ Medical Ltd. and in association with the Central Clinic of Athens and the Athens Medical Centre in the field of Interventional Radiation Oncology (Brachytherapy) as clinical Medical Physicist as well as research and development fellow with Pi-Medical Ltd., Greece, participating in the evaluation section of the CEIROS project. During that time, he also worked in the field of Monte Carlo dose calculations and the development of radiobiological applications in the field of Radiation Therapy. In June 2017, Dr. Anagnostopoulos was appointed as Head of the Medical Physics Department of the German Oncolo**gy Center in Limassol. He is a member of the Cypriot, the Greek and the German Association of Medical Physicists, an** author of scientific papers published in the journals of Medical Physics, Physics in Medicine and Biology, Brachytherapy and in the Journal of Radiation Oncology Biology and Physics and he is reviewer for the journal of Medical Physics. He has also **made contributions in the book 'The Physics of modern Brachytherapy for Oncology' (Taylor and Francis, CRC Press).**

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



TEAM MEMBERS

Konstantinos Ferentinos (GOC) was born in Ioannina Greece, where he studied Medicine. He was awarded the degree in Medicine in 2007. He was resident in the Department of Radiation Oncology at the Klinikum Offenbach in Germany under the supervision of the renowned oncologist Prof. Zamboglou. His main areas of interest were the Interventional Radiotherapy and the novel radiation techniques. He was responsible for the Stereotactic Radiotherapy in his department. In 2012 he obtained the PhD in Medicine at the Goethe University Frankfurt. From 2013 to 2015 he worked as consultant at the Klinikum Offenbach and since 2016 as a senior consultant in the Department of Interventional Radiotherapy at the Iatriko Kentro Hospital in Athens. He is the head of the Department of Radiation Oncology at the German Oncology Center in Limassol.

Leonidas Georgiou (GOC) graduated from the University of Manchester (2010-2014), with a PhD in Pharmacokinetic Imaging, in a collaboration with AstraZeneca, to explore the potential of magnetic resonance imaging techniques in drug-drug interactions. In 2010, Dr Leonidas Georgiou graduated from the University of Manchester with MSc Physics and Computing in Medicine and Biology and a BSc (Hons) in Physics. His work experience includes work placement in AstraZeneca for in vitro test systems and quantification techniques (LC-MS/MS, fluorescence analysis) (2010-2014), software developer within the quantitative biomedical imaging laboratory team of the University of Manchester (2014-2015) and a research fellow in the Division of Biomedical Imaging in the University of Leeds (2015-2017), with a focus on MRI techniques for monitoring treatment effects. His research area is focused on exploiting non-invasive MRI techniques for quantitative insights into pathophysiology using novel approaches in the field, such as quantitative dynamic contrast-enhanced MRI and diffusion weighted imaging with authored articles in the field. Since then he has been employed by the German Oncology centre as a medical physicist with a wide area of responsibilities both in the Radiotherapy and Radiology department.

CONNECT WITH US

https://www.facebook.com/soundpet

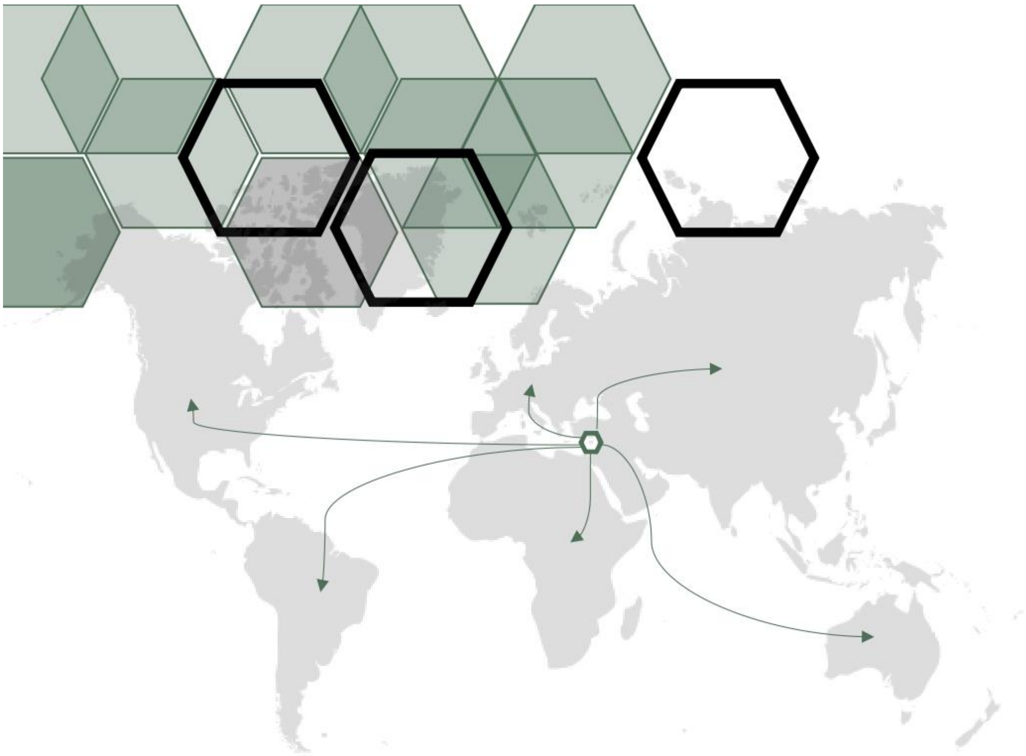
cy.linkedin.com/in/medsonic-ltd-cyprus-288286153

www.soundpet.eu

SEPTEMBER 2020

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης · Κυπριακή Δημοκρατία · Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Newsletter 2



JULY 23th, 2021

SOUNDPET
Animal therapies with focused ultrasound

INTEGRATED/0918/0008

SOUNDPET NEWSLETTER

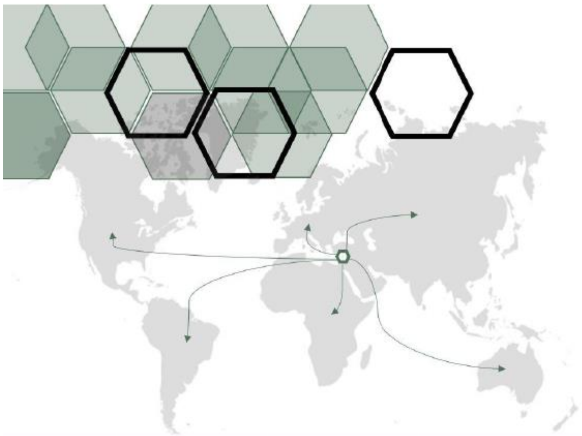
ISSUE 2

Providing with news on MRI guided Focused Ultrasound technology in the field of oncology, in the framework of the SOUNDPET project!

INDEX

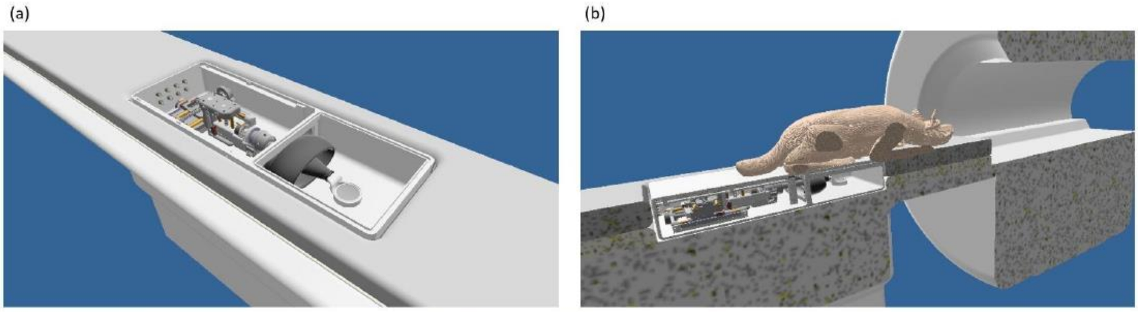
co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

SOUNDPET MRI-guided Focused ultraSOUND system for cancer in PETs (dogs and cats)

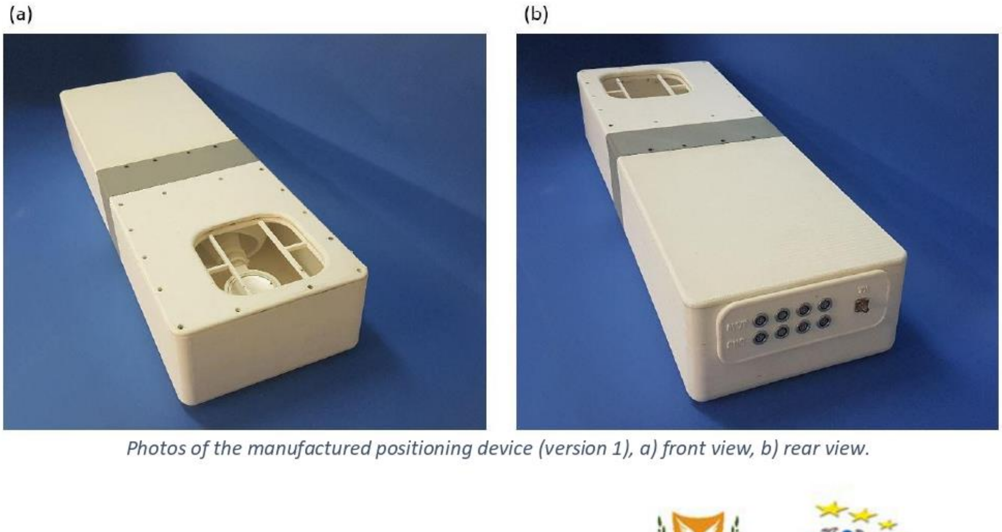


Four DOF robotic device (version 1)

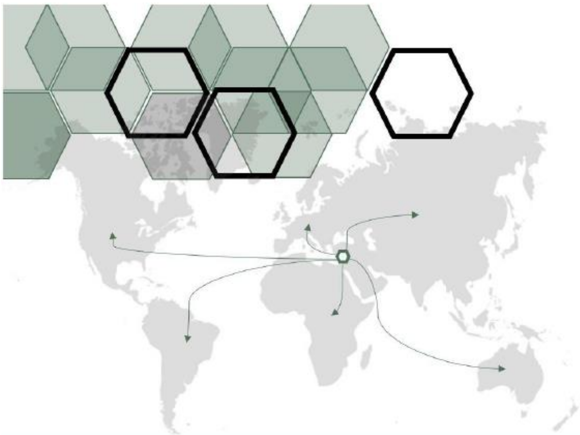
The robotic system allows navigation of the ultrasonic transducer in four stages. Specifically, the device enables linear movement 1) forward and backward (range of 55 mm), 2) left and right (range of 76 mm), and 3) up and down (range of 28 mm). An angular stage enables clockwise and counterclockwise rotation (range of 180°) of the transducer as well. The specific motion ranges were properly selected to allow access to the target organs. The linear stages are based on a jack screw principle, while the angular one uses a two-stage reduction unit which is composed of multiple gears. All four stages are actuated by small piezoelectric motors (USR30-S3, Shinsei Kogyo Corp., Tokyo, Japan) and monitored by optical encoders.



a) CAD drawing of the robotic device as placed in the MRI table, b) Cross section of the device with the dog placed in prone position.



Photos of the manufactured positioning device (version 1), a) front view, b) rear view.



Four DOF robotic device (version 2)

The second version of the robotic system incorporates larger motors (USR60-S3, Shinsei Kogyo Corp., Tokyo, Japan). The positioning device can move the transducer 60 mm in the X axis (forward and reverse), 75 mm in the Y axis (left and right), 26 mm in the Z axis (up and down) and can angulate the transducer 90° (45° left and 45° right) about the Θ-axis.

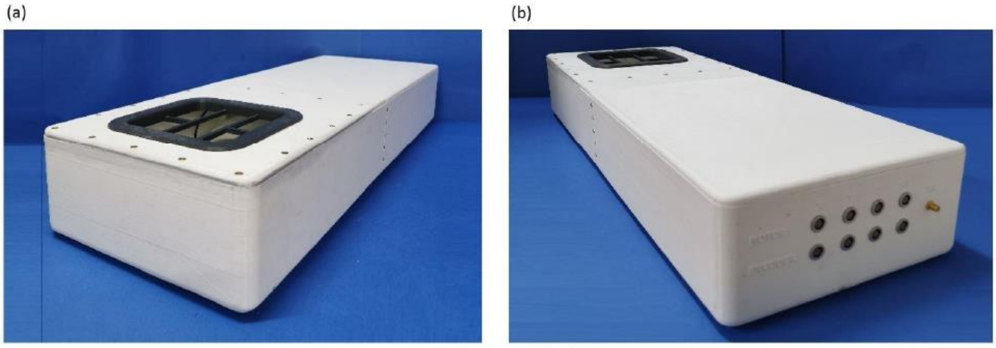
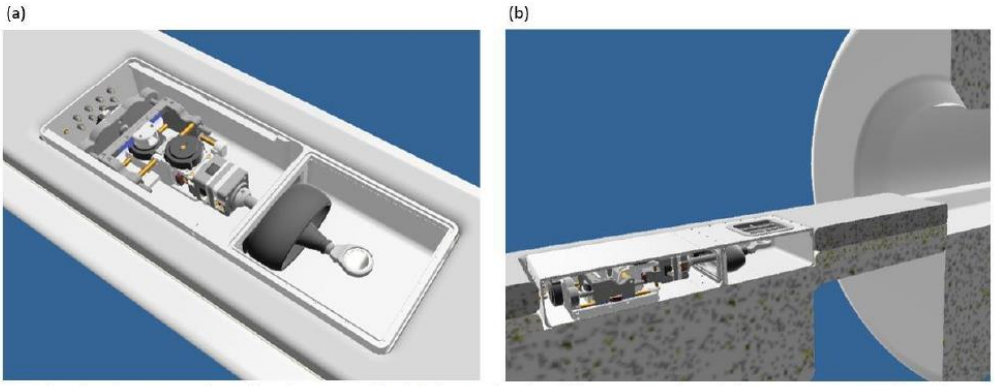


Photo of the robotic system (version 2) a) front view, b) rear view.

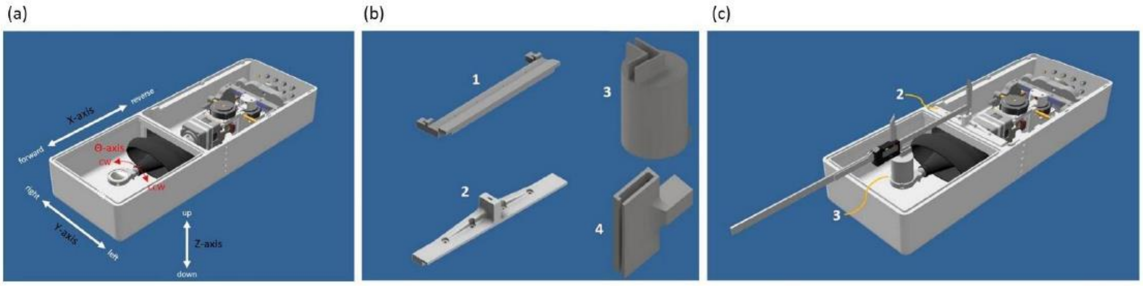


a) *Robotic system placed in the MRI with visible mechanism, b) Cross section of the MRI scanner with robot.*

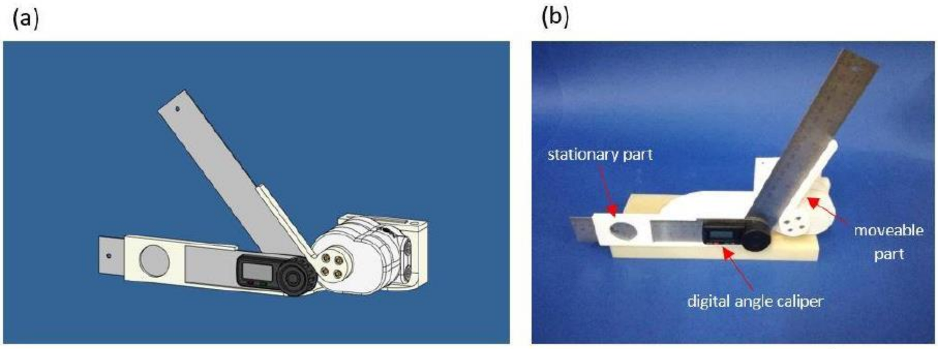
co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Motion accuracy of the robotic device

The motion accuracy of the robotic device (version 2) was assessed with three simple methods in both benchtop and MRI environments. In the first method, a digital calliper was mounted on the motion stage under evaluation with the assistance of specially designed 3D-printed parts, having its one edge fixed on a stationary part and the other on a movable part. In that way, a specific step movement of the stage resulted in an analogous increment in the calliper. The second evaluation procedure related to accuracy assessment in the MRI setting. The robotic device was sited on the MRI couch, and a plastic marker was mounted on the top of the FUS transducer so that it was visualized in MR images. The third method involved performing multiple ablations in a transparent plastic film by robotic movement of the transducer.

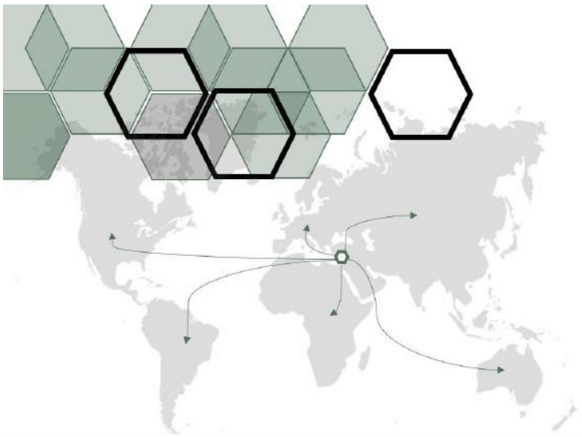


a) Computer-aided design (CAD) drawing of the 4 DOF robotic system (version 2) without the cover showing the motion axes, b) Stationary (1,2,4) and moveable (3) 3D-printed structures that were used for the X and Y axes distance measurements, c) CAD drawing of the setup that was used for the X axis motion accuracy estimation.



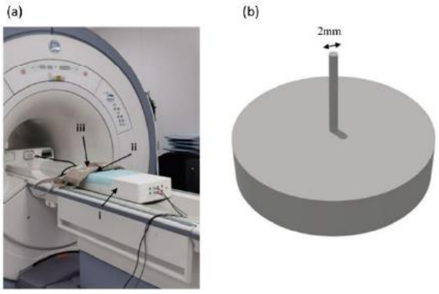
Experimental setup for estimating the angular motion accuracy using the digital angle calliper; a) CAD drawing and b) photo.

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

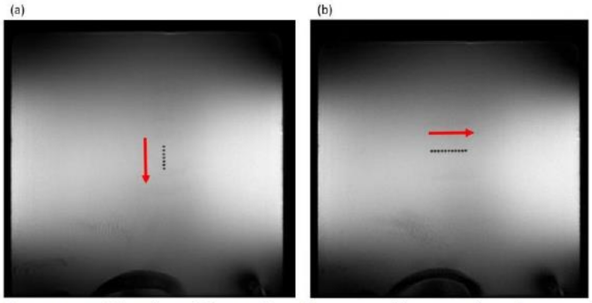


Motion accuracy of the robotic device (cont.)

MRI was also used to examine the accuracy of motion in the *X* and *Y* axes. The MR images acquired after execution of each 3 mm motion step in the *X* axis reverse and *Y* axis right directions were superimposed onto the images.



(a) The robotic device (i) as placed on the magnetic resonance imaging table, showing the location of the plastic marker (ii) and *the flex surface coil (iii), and (b) CAD drawing of the plastic marker used for accuracy measurements.*



Minimum intensity projection from a combination of fast spin echo coronal images that shows a (a) reverse step movement of 3 mm in the X direction and (b) right step movement of 3 mm in the Y direction.

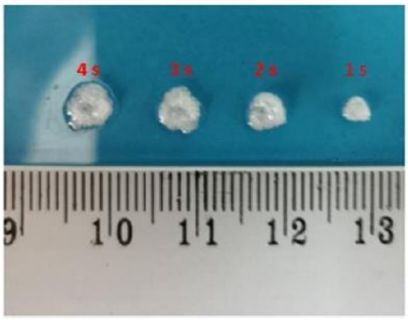
Linear axis	Commanded step (mm)	Range of actual displacement (mm)	Mean error ± SD forward (mm)	Mean error ± SD reverse (mm)
X	3	2.73–3.83	0.277 ± 0.007	0.342 ± 0.172
	5	4.92–5.47	0.339 ± 0.184	0.352 ± 0.179
	Commanded step (mm)	Range of actual displacement (mm)	Mean error ± SD right (mm)	Mean error ± SD left (mm)
Y	3	2.73–3.83	0.330 ± 0.166	0.278 ± 0.007
	5	4.37–5.47	0.171 ± 0.191	0.286 ± 0.239

The range of distance measurements as estimated by MRI at commanded spatial steps of 3 and 5 mm in X and Y axes bidirectional movements, and the corresponding mean motion error and standard deviation.

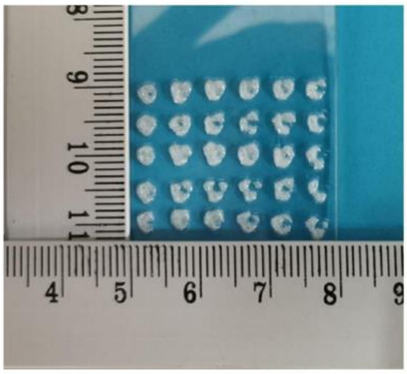
co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Motion accuracy of the robotic device (cont.)

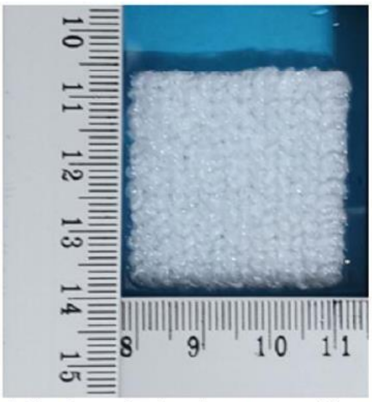
The motion accuracy was visually observed by sonicating plastic films. The effect of lesion formation on the plastic film was originally examined by varying the sonication time while keeping constant the acoustic power. The appropriate selection of sonication time and grid step allowed formation of discrete and overlapping lesions and visual evaluation of the accuracy of motion and alignment.



Effect of varying sonication time on lesion formation on the plastic film, using low power and a spatial step of 10 mm (transducer specifications: 1.1 MHz frequency, 50 mm diameter and 70 mm focal length).

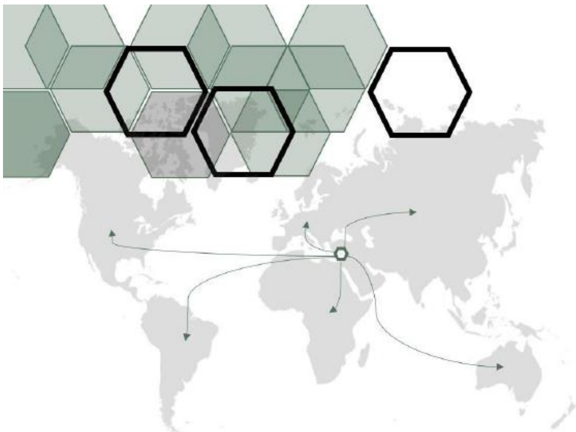


Discrete lesions as formed on the plastic film for sonications in a 6 x 5 grid pattern, with acoustical power of 10 W for 1 s and a step distance of 5 mm.



Overlapping lesions as formed on the plastic film for sonications in a 15 x 15 grid pattern, with acoustical power of 10 W for 3 s and a step distance of 2 mm.

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο
Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία
της Ευρωπαϊκής Ένωσης στην Κύπρο

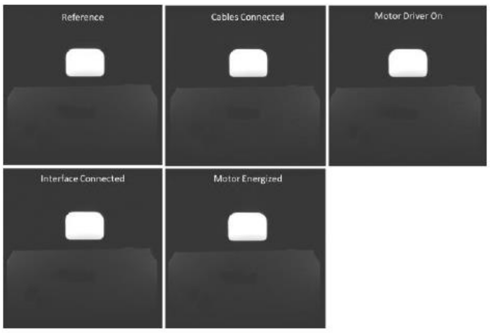


MR compatibility of the robotic device (version 2)

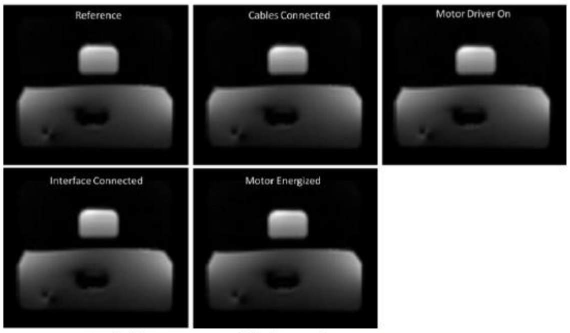
The MR compatibility of robotic device (version 2) that controls large piezoelectric motors was also examined. A phantom was scanned using fast spin echo (FSE), fast spoiled gradient-recalled echo (FSPGR) and echo planar imaging (EPI) sequence under the following activation states:

I. Reference image
II. Cables plugged, amplifier OFF, transducer OFF
III. Electronic system motor driver switched ON
IV. Interface connected
V. Motor energized

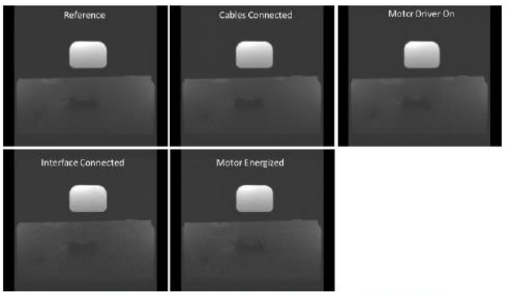
Visual assessment of the acquired images did not show a significant effect after transition between the different activation states.



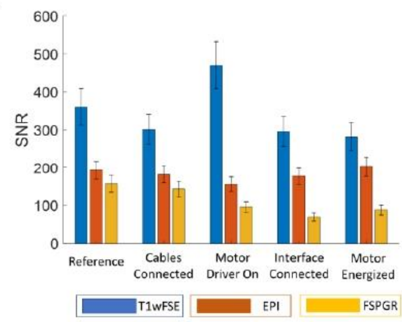
Axial image acquisition using FSE sequence.



Axial image acquisition using EPI sequence.

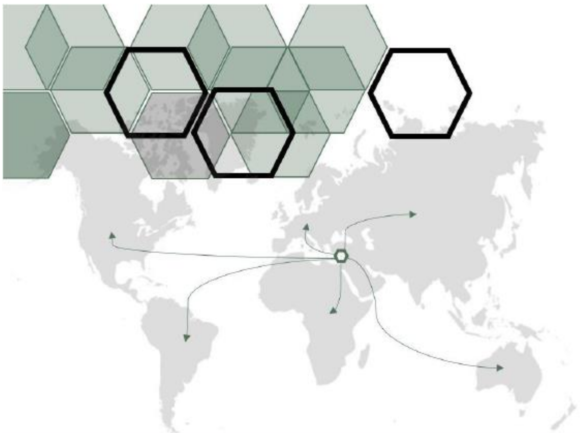


Axial image acquisition using FSPGR sequence.



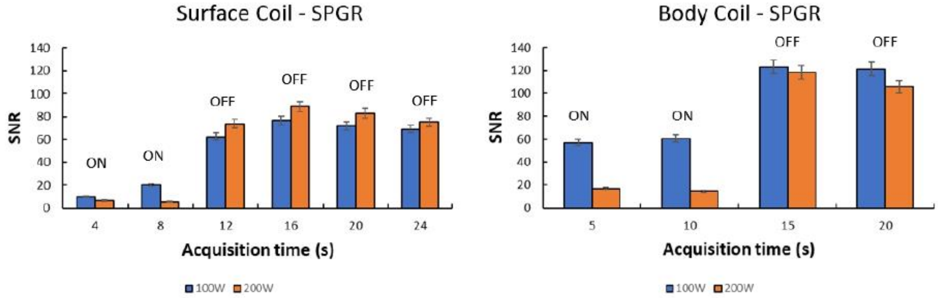
Bar chart of measured SNR (with error bars) for the various robot activation states for both electronic systems used and different pulse sequences; fast spin echo (FSE), echo planar imaging (EPI) and fast spoiled gradient-recalled echo (FSPGR).

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



MR compatibility of the robotic device (version 2)

The MR compatibility of the robotic device (version 2) was tested using two different coils, the GP FLEX coil, and the body coil. A combination of MR compatible positioners were used to increase the distance between the coils and the transducer. SNR measurements for both coils with the power of the US transducer ON and then OFF. The image acquisition was dynamic, i.e., images were acquired in succession at a specific temporal resolution while the power of the US transducer was set from ON state to OFF state.



(Left) Bar chart of SNR (with error bars) for the different acquisition times using the surface coil and a SPGR sequence, (Right) Bar chart of SNR (with error bars) for the different acquisition times using the body coil and a SPGR sequence. Both power settings (100W and 200W) are displayed.

CONNECT WITH US

https://www.facebook.com/soundpet

cy.linkedin.com/in/medsonic-ltd-cyprus-288286153

www.soundpet.eu

JULY 2021

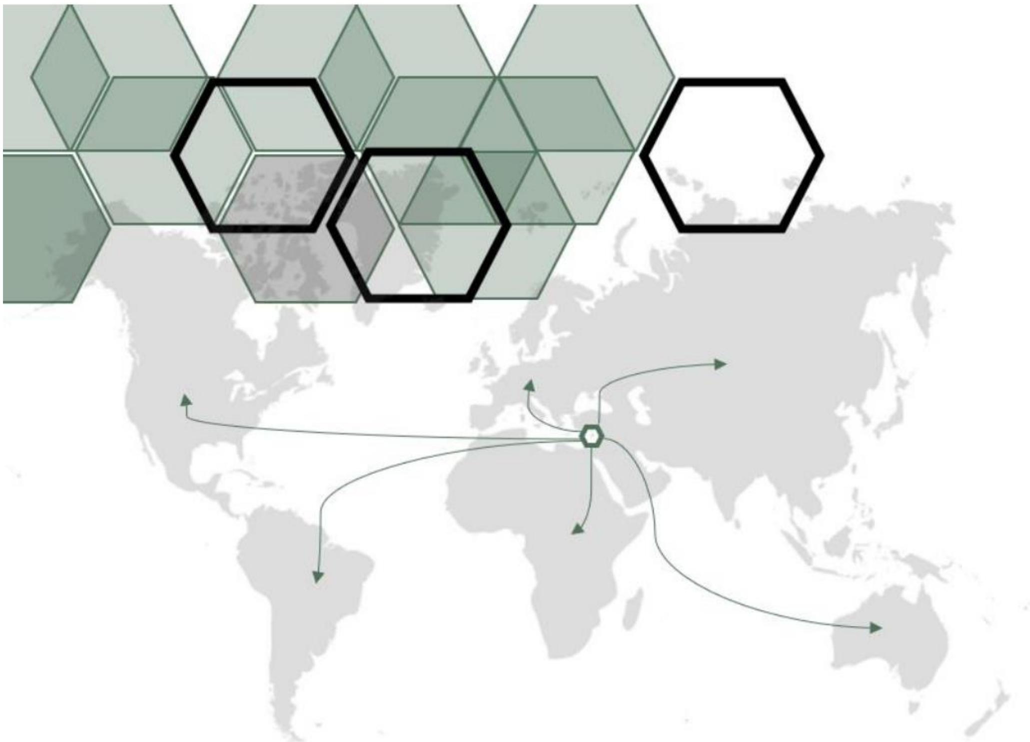
co-funded by

Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο
Περιφερειακής Ανάπτυξης

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία
της Ευρωπαϊκής Ένωσης στην Κύπρο

Newsletter 3



NOVEMBER 18th, 2021

INTEGRATED/0918/0008

SOUNDPET NEWSLETTER

ISSUE 3

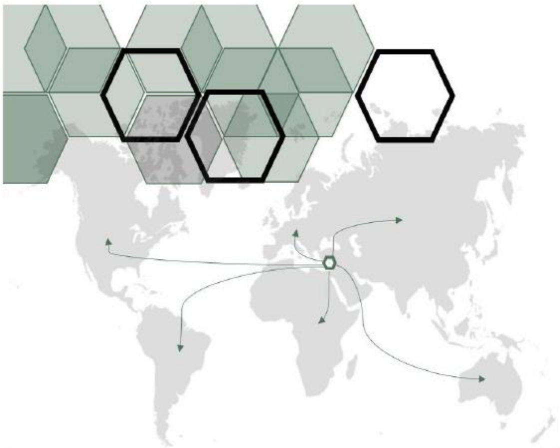
Providing with news on MRI guided Focused Ultrasound technology in the field of oncology, in the framework of the SOUNDPET project!

co-funded by

Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



Ultrasonic transducer

Two transducers were specially designed to be single element, spherically focused, MR compatible and compact. The structural characteristics and operating frequency of the manufactured transducers were estimated by simulation studies, which investigated the power field and heating effects of different candidate transducers. Purchased piezoelectric elements were housed in 3D printed plastic cases and covered by an encapsulant. Specifically, an ultrasonic transducer element made out of P762-type piezoceramic, with the selected specifications of 1 MHz central frequency, 70 mm radius of curvature and 60 mm diameter, was provided by Ferroperm (Kvistgaard, Denmark) company. The other selected element of 2.5 MHz frequency, 50 mm diameter and 65 mm radius of curvature was provided by Piezo Hannas (Wuhan, China) company. Special emphasis was placed on the selection of the suitable materials for safe long-term high-power operation of the transducers.

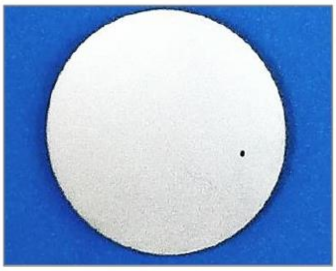
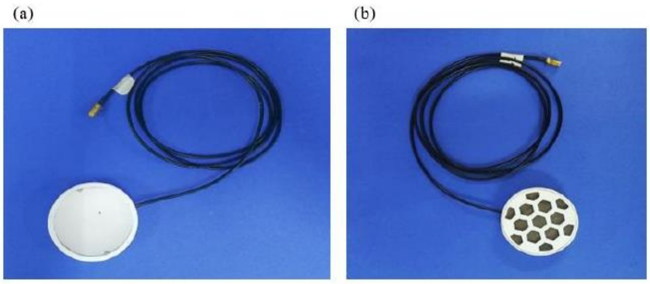
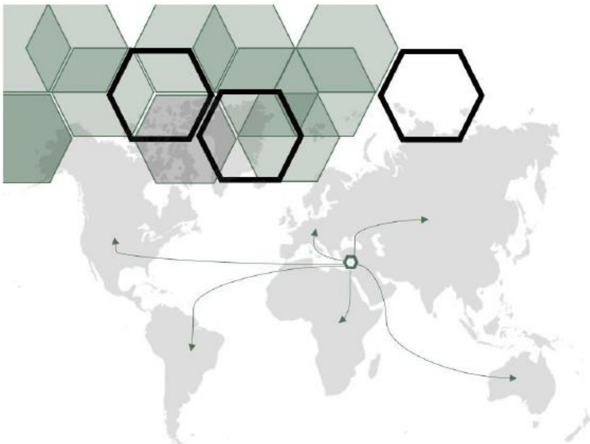


Photo of the ultrasonic element.



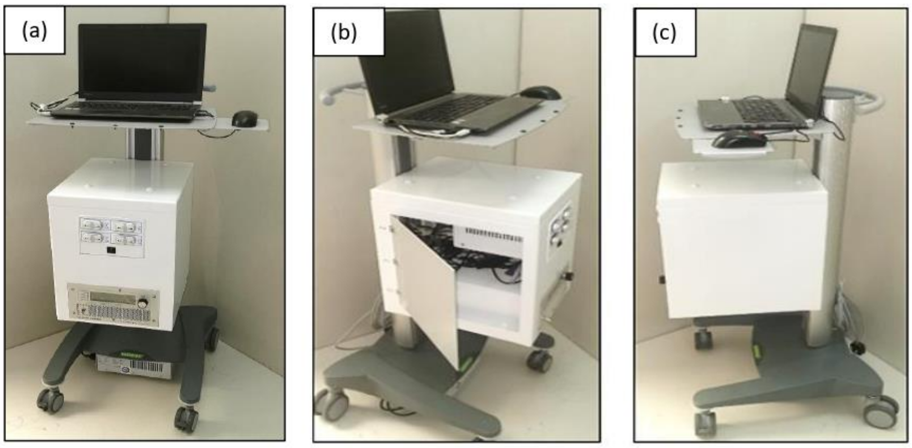
Photos of the developed transducer: a) top view, and b) bottom view.

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



Medical Cart

A medical cart was designed to host all the electronic devices needed for proper operation of the SOUNDPET system. An already existing cart of the Haeberle company was modified according to the requirements and specifications of the present system, which consists of a laptop, an electronic driving system, and an amplifier.



Photos of the developed medical cart: (a) front view and (b) & (c) side views.

CONNECT WITH US

https://www.facebook.com/soundpet

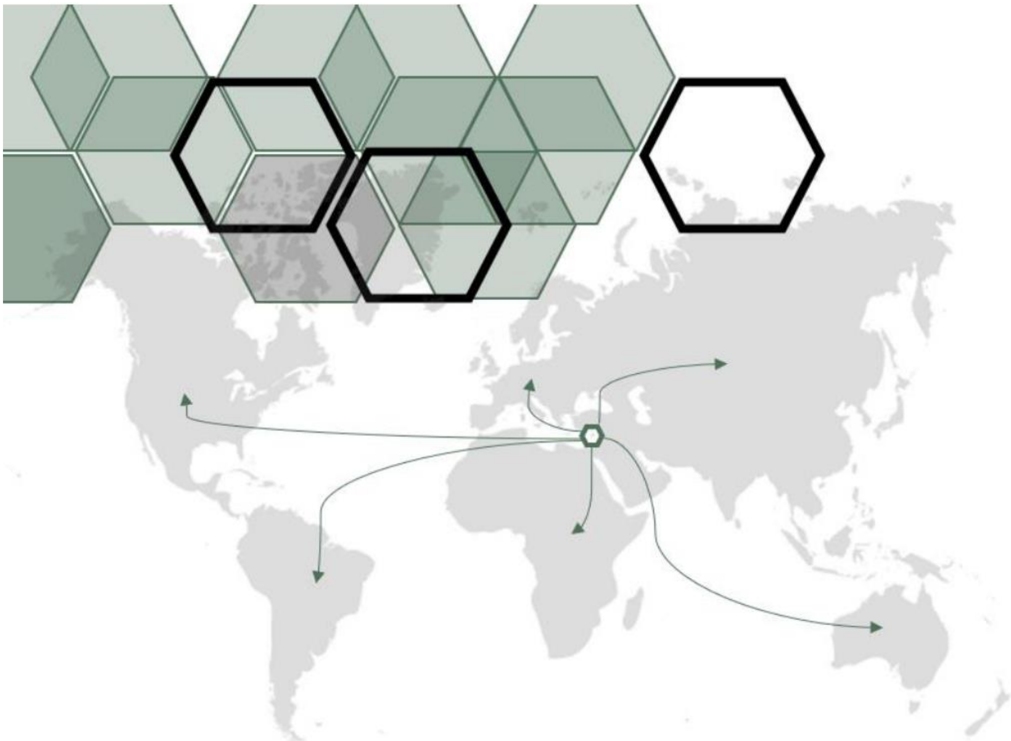
cy.linkedin.com/in/medsonic-ltd-cyprus-288286153

www.soundpet.eu

NOVEMBER 2021

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Newsletter 4



JULY 29th, 2022

SOUNDPET

Animal therapies with focused ultrasound

INTEGRATED/0918/0008

SOUNDPET NEWSLETTER

ISSUE 4

Providing with news on MRI guided Focused Ultrasound technology in the field of oncology, in the framework of the SOUNDPET project!

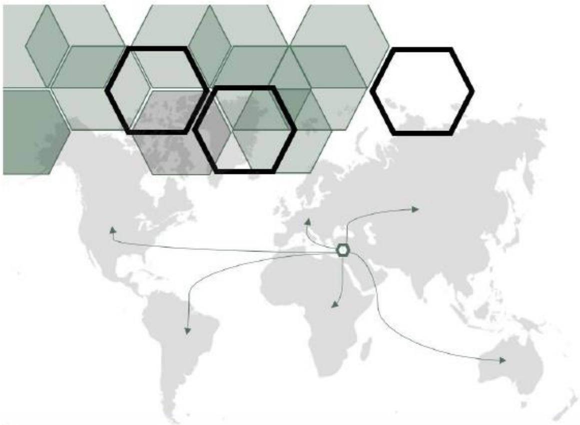
co-funded by

Ευρωπαϊκή Ένωση

Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



Software Development

An advanced software platform was developed to integrate with the SOUNDPET system for MRI guided Focused Ultrasound therapy. The software platform interfaces with the amplifier, electronic driving system and robotic device (as placed within the table of the MRI scanner) offering functions for treatment planning, therapy and monitoring. The software was mainly developed using the C # language (Microsoft Corporation, Washington, USA) with some scripts written in Python (Python Software Foundation, Wilmnington, Delaware, USA). Emphasis was placed in the development of a modern and user-friendly interface that integrates the following features on a single panel:

I. Precise robot localization
II. Ultrasonic parameters control
III. Treatment planning on MRI images
IV. Treatment monitoring with MR thermometry

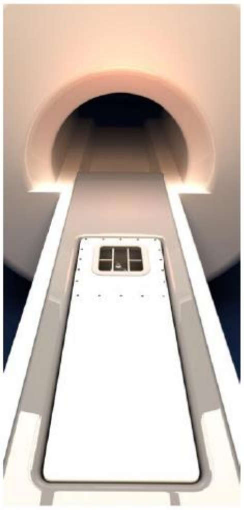
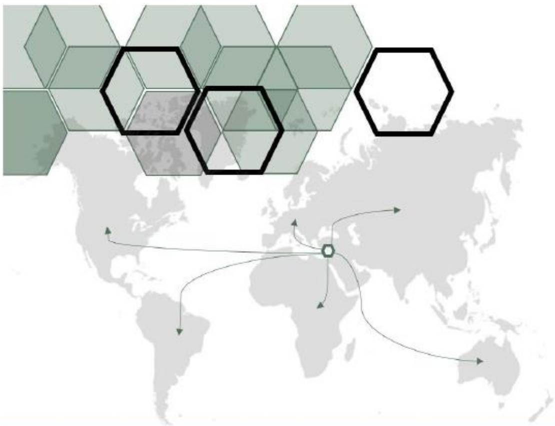


Photo of the robotic device within the table of the MRI scanner.

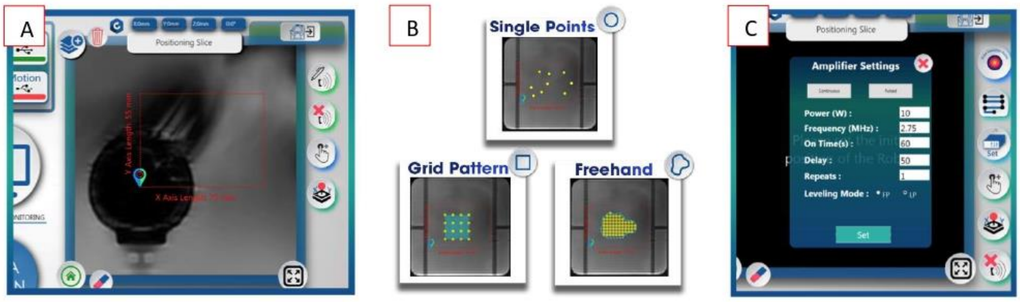
Photo of the developed software platform interfaced with the electronic driving system.

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



Software Features

Precise robot localization is initially achieved by simply clicking on the center of the transducer as visualized on MRI images. A marker automatically appears on the center, translating the position of the transducer on the image. Complex treatment plans can be performed on MRI images using various drawing tools. The single points, grid pattern and freehand drawing tools can be respectively employed to design random point, grid operation or non-uniform sonication areas overlayed on the MRI image. Ultrasonic treatment parameters can be easily defined by the user on a simple pop-up panel. The treatment procedure is then executed according to the user-defined treatment plan and monitored with MRI. The software interfaces with the MRI, enabling MR thermometry calculations for near-real time monitoring of the temperature increase through display of thermal maps and temperature graphs.



Photos of the software features. A) Robot localization, B) the three sonication area drawing tools, and C) pop-up panel for ultrasonic treatment parameter setting.

CONNECT WITH US

https://www.facebook.com/soundpet

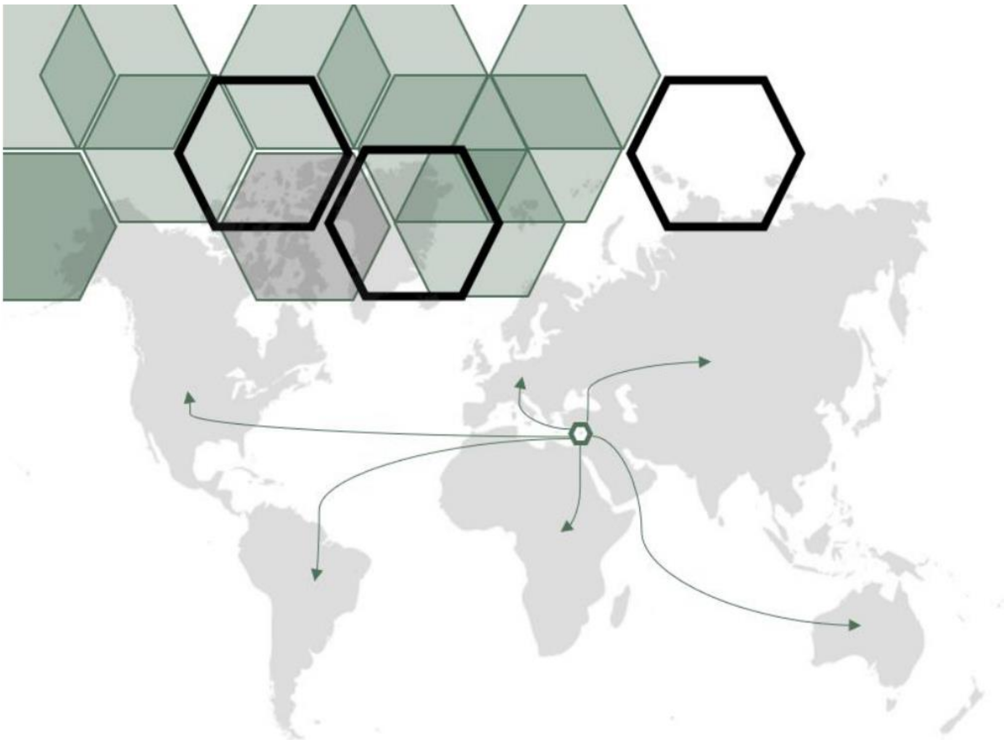
cy.linkedin.com/in/medsonic-ltd-cyprus-288286153

www.soundpet.eu

JULY 2022

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης | Κυπριακή Δημοκρατία | Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Newsletter 5



JANUARY 23rd, 2023

SOUNDPET
Animal therapies with focused ultrasound

INTEGRATED/0918/0008

SOUNDPET NEWSLETTER

ISSUE 5

Providing with news on MRI guided Focused Ultrasound technology in the field of oncology, in the framework of the SOUNDPET project!

INDEX

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

SOUNDPET MRI-guided Focused ultraSOUND system for cancer in PETs (dogs and cats)

MRI Thermometry of Focused Ultrasound

The SOUNDPET robotic system was accommodated on the table of a 1.5 T (Signa HD16, GE Healthcare, Chicago, Illinois, USA) and 3 T (Magnetom Vida, Siemens Healthineers, Erlangen, Germany) MRI scanners and focused ultrasound (FUS) sonications were executed on agar-based phantoms. The in-house software platform developed in C# (Visual Studio, Microsoft Corporation), was employed for monitoring the sonications and generating MR thermometry data. MR thermometry data in the form of colour-coded thermal maps overlapped on MRI images and time-series temperature graphs, were presented on the software's interface, next to the treatment planning window, providing temperature monitoring during sonications. Dependencies of the temporal and spatial resolution of MR thermometry temperature measurements with the magnetic field strength, the FUS sonication parameters and the MRI image acquisition parameters were examined.

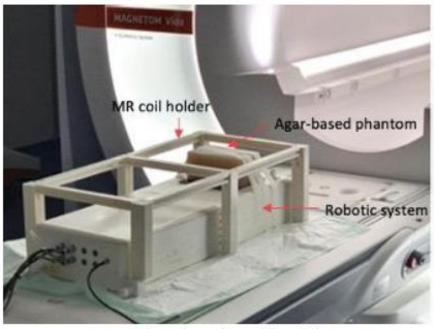
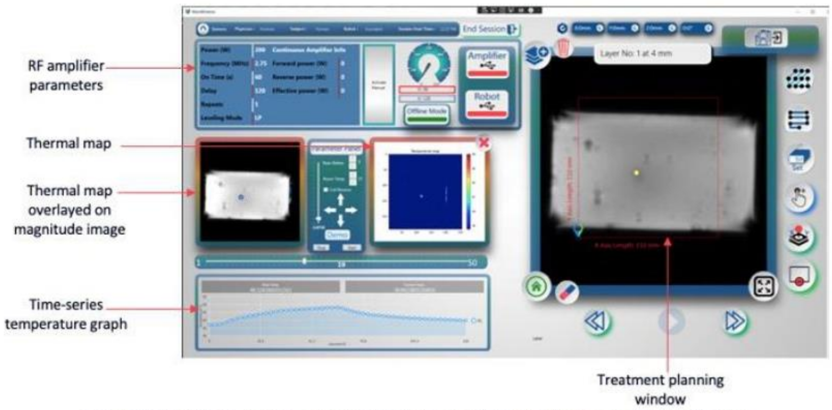
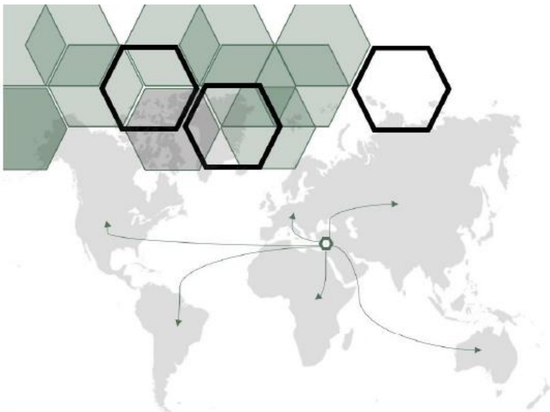


Photo of the robotic system accommodated on the table of the MRI scanner with the agar-based phantom positioned on top for sonications.



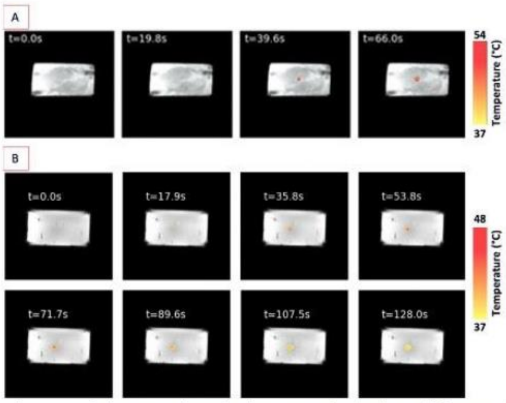
Screenshot of the in-house software platform providing MR thermometry monitoring.

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

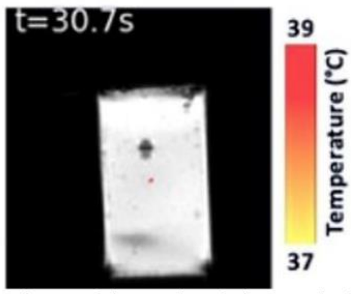


MRI Thermometry of Focused Ultrasound (cont.)

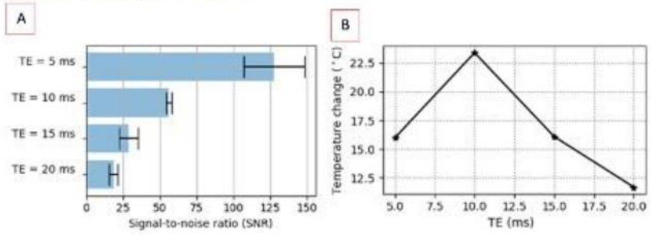
The effect of magnetic field strength was originally examined by executing identical sonications inside the 1.5 T and 3 T MRI scanners. MR thermometry data for sonications inside the 3 T scanner were produced 2.5 times more rapid compared to 1.5 T, while the generated thermal maps were of an increased image quality with decreased artifacts. Since the 3 T MRI scanner provided more accurate monitoring of the FUS sonications, it was employed to assess the effect of the sonication and imaging acquisition parameters on the MR thermometry. The effect of the applied acoustic power was investigated for a series of sonications executed at varied power for a constant sonication time. Increased acoustic power resulted in increased MR thermometry calculated temperature changes with the lowest acoustic power of 1.5 W producing reliable temperatures. Finally, a series of images were acquired with varied echo time (TE) during identical FUS sonications to evaluate the dependency of the temperature change with the acquisition parameters. Signal to noise ratio (SNR) measurements were performed for each TE to examine the image quality. Increased TE revealed a negative effect on image SNR with appropriate TE selection resulting in the highest temperature sensitivity.



Coronal thermal maps of the agar based phantom obtained at different timepoints during sonications with a 2.6 MHz transducer at acoustic power of 60 W for a sonication time of 60 s at 40 mm focal depth inside A) a 1.5 T scanner, and B) a 3 T scanner.

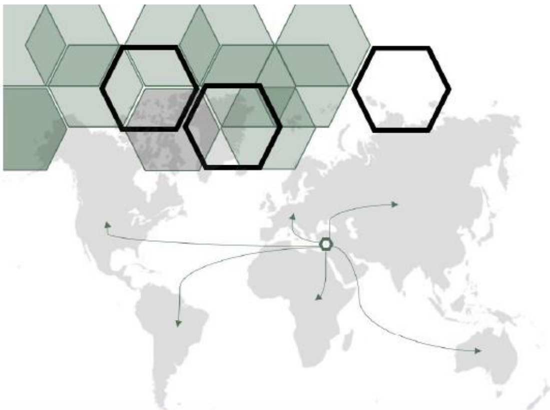


Coronal thermal maps of the agar based phantom obtained at the end of sonication at acoustic power of 1.5 W for a 30 s sonication time at 45 mm focal depth inside a 3 T scanner.



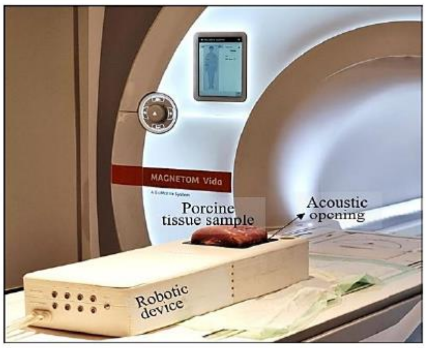
A) Bar chart of SNR for images acquired with different TE values, and B) Maximum temperature change measured for different TE values as a result of sonications executed at acoustic power of 45 W for a sonication time of 30 s at 35 mm focal depth inside a 3 T scanner.

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

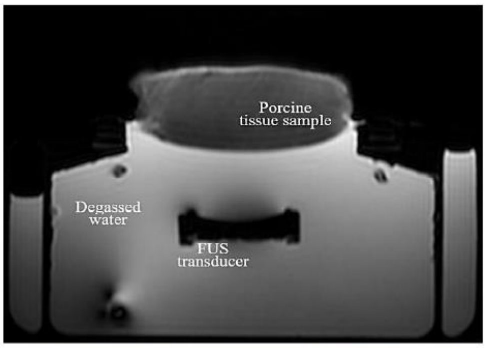


MRI Monitoring of lesions induced by Focused Ultrasound

Multiple sonications were planned on the custom-made software and executed by the SOUNDPET system in freshly excised porcine tissue. The impact of critical imaging parameters on the resultant contrast to noise ratio (CNR) between ablated and intact tissue was investigated to optimize lesion discrimination on T1-W and T2-W Fast Spin Echo (FSE) images. Both discrete and overlapping lesions were inflicted in pork tissue samples with simultaneous acquisition of T2-W images to visualize the heated area and assess lesion progression with time.

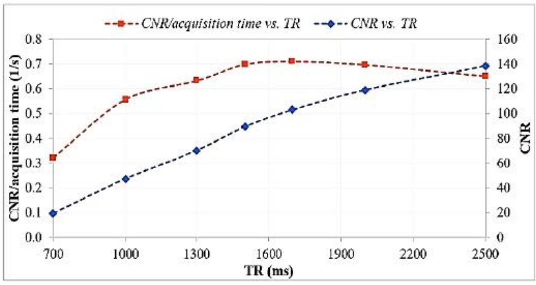


The robotic device positioned on the MRI table of the 3 T MRI scanner with the piece of meat mounted on the acoustic opening for ablation experiments.



T2-W FSE image of the setup showing the concept of tissue sample placement above the FUS transducer.

Critical MR parameters were optimized by balancing between the CNR and acquisition time, provided that the imaging time is an important parameter in the context of intraprocedural lesion monitoring. The use of CNR values above 80 was set as the criterion for proper lesion visualization on T1-W and T2-W FSE images.

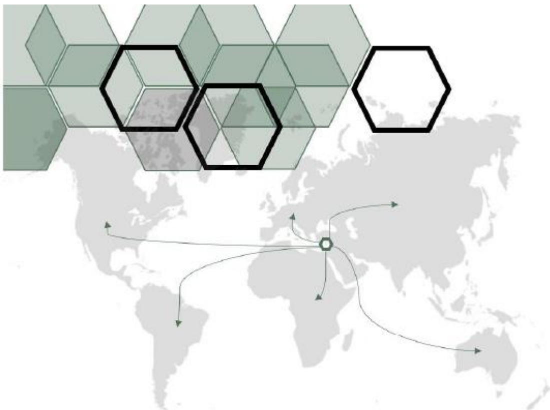


CNR between lesion (68 W acoustic power for 120 s at 2.6 MHz) and normal tissue and CNR/acquisition time of T1-W FSE images versus TR at 3 T.

MR parameter	T1-W FSE	T2-W FSE
TR (ms)	1500	2000
TE (ms)	10	50
ETL	60	60
NEX	1	1
pBW (Hz/pixel)	150	150
Matrix size	256×256	256×256
FOV (mm²)	280×280	280×280
Slice thickness (mm)	5	5

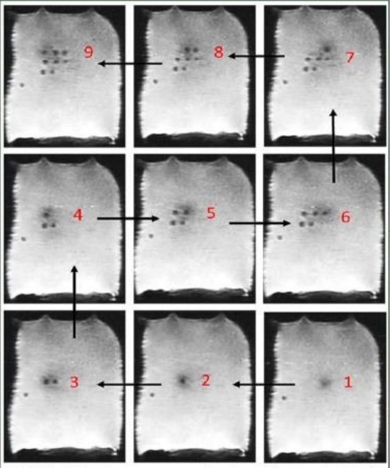
Summary of suggested MR parameters for optimizing CNR between lesion and tissue at the minimum time cost.

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

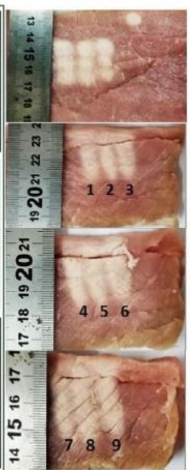


MRI Monitoring of lesions induced by Focused Ultrasound (cont.)

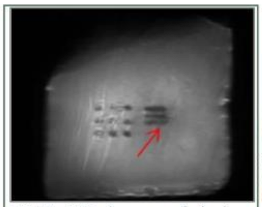
Lesion progression in both discrete and overlapping patterns was successfully monitored by MRI. During sonications, acute FUS lesions were visualized as spots of reduced intensity with excellent contrast from the surrounding intact tissue. It was demonstrated that multiple images should be acquired at varying depth in tissue to avoid non-detectability of shifted lesions. The T2-W FSE sequence yielded higher CNR and was considered preferred for lesion monitoring in *ex-vivo* tissue.



T2-W FSE images acquired with optimized parameters during ablation in a 3×3 pattern (ac. power of 54 W for 120 s, 10-mm step, 60-s delay) in the 1.5 T MRI scanner.



Photos of tissue sliced horizontally (top) and vertically (bottom, 1-9) showing the formed lesions.



T2-W FSE image of lesions formed in 3x3 discrete (left, 10 mm step) and overlapping (right, 5-mm step) patterns in the 3 T MRI scanner.

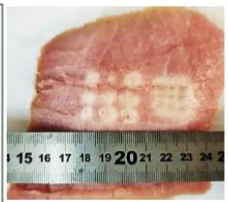


Photo of tissue cut horizontally showing the formed lesions.

CONNECT WITH US

https://www.facebook.com/soundpet

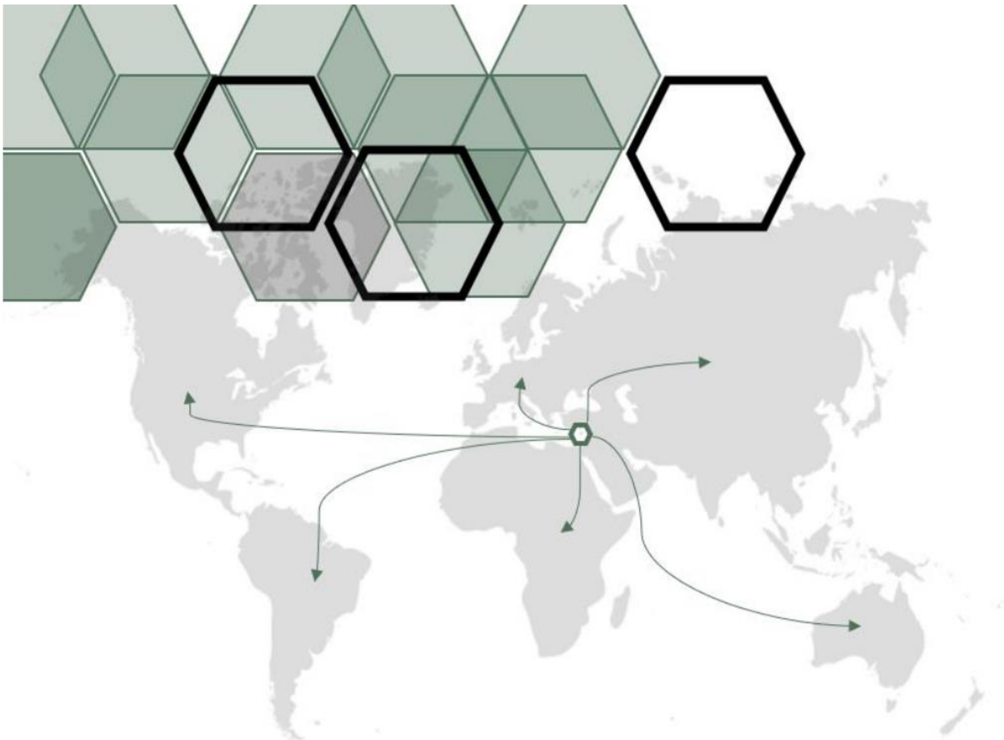
cy.linkedin.com/in/medsonic-ltd-cyprus-288286153

www.soundpet.eu

JANUARY 2023

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Newsletter 6



JULY 3rd, 2023

INTEGRATED/0918/0008

SOUNDPET NEWSLETTER

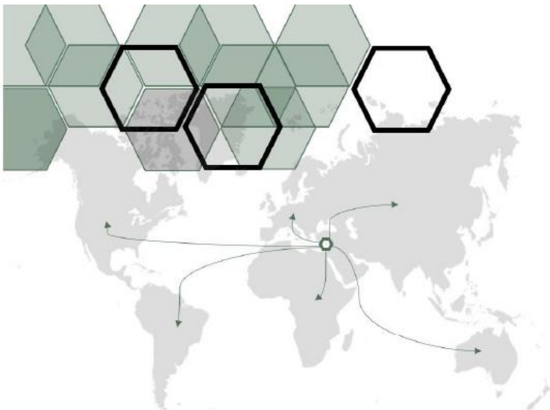
ISSUE 6

Providing with news on MRI guided Focused Ultrasound technology in the field of oncology, in the framework of the SOUNDPET project!

<u>INDEX</u>

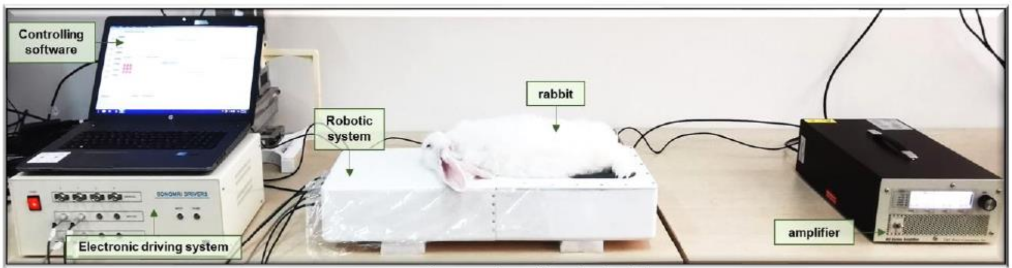
***In-vivo* Focused Ultrasound ablation in a rabbit thigh model & canine and feline mammary cancer patients**

co-funded by
Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης
Κυπριακή Δημοκρατία
Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



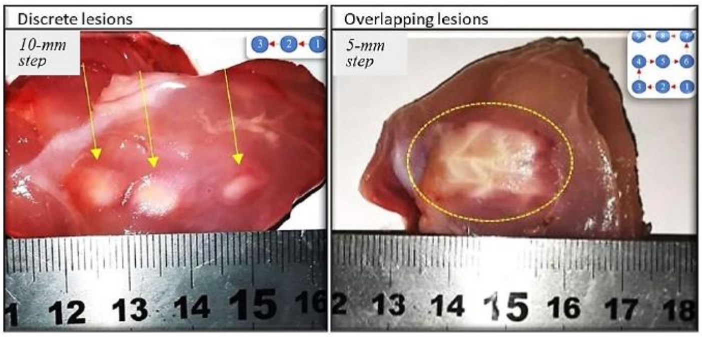
Focused ultrasound ablation in a rabbit thigh model

The *in-vivo* performance of the SOUNDPET robotic system was tested in a rabbit thigh model. The rabbit experiments were carried out at the premises of CUT by a qualified veterinarian. The rabbit thighs received multiple sonications in grid patterns. The spatial step between successive sonications and ultrasonic parameters were varied to assess their effect on lesion formation. After completion of the experiment, the animal was humanely euthanized.



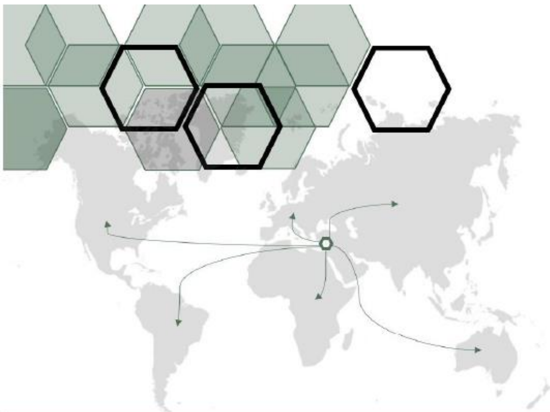
Experimental set-up for rabbit thigh ablation

Both discrete and overlapping lesions with variable diameter and length were inflicted In tissue, demonstrating that the **system is capable of creating reproducible and controllable lesions in live tissue**. No operational malfunctions that could compromise the animal's welfare were recorded. There were no indications of animal suffering or off-target burns.



Sample photos (top view) of rabbit thigh after muscle exposure showing lesions inflicted using focal intensity of 2116 W/cm², 10 s sonication time, and 60 s delay between sonications, at focal depth = 1 cm.

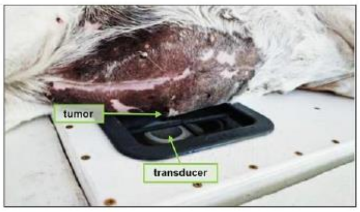
co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο



Focused ultrasound treatment of canine & feline mammary cancer

Nine (9) pets with local superficial tumors of the mammary glands were involved in the trial and treated with FUS followed by surgical removal of the entire tumor. The pet trials took place at the premises of the referring veterinarians. A comprehensive treatment protocol was adopted where the pet was placed on the device in a way to ensure that thermal heating is fully applied to the tumor, thus avoiding accidental heating of healthy tissue. Partial tumor ablation was performed by single or multiple grid sonications depending on the tumor size.

Animal placement on the device

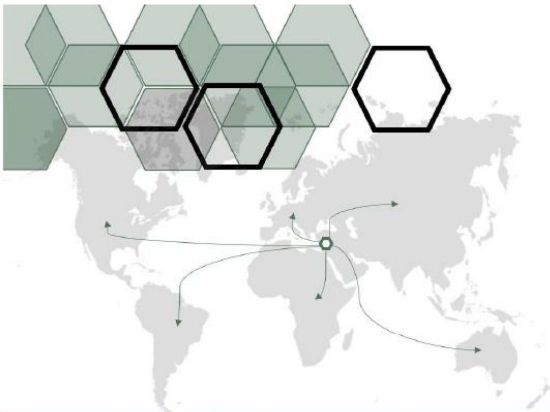


As part of these trials, the SOUNDPET system was integrated with a veterinary MRI system and a CT scanner. CT imaging was useful to visualize the animal placement and tumor location relative to the transducer. In the MRI, only anatomical imaging was possible because the specific MRI system uses ring-shaped coils that are placed around the pet, thus making ultrasonic penetration unfeasible. Since the device fits within the scanner, if in the future the vendor redesigns the coils, thermal ablation under MRI guidance will be feasible.

SOUNDPET device placed within the Vet-MR Grande veterinary MRI system (Esaote) at V3ts Veterinary Clinic (Larnaca, Cyprus).

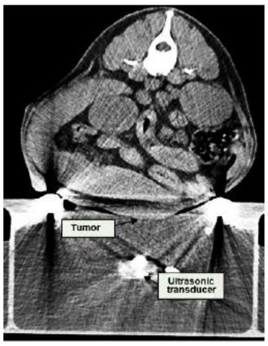
The SOUNDPET device integrated with the SOMATOM CT scanner (Siemens) at V3ts Veterinary Clinic.

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

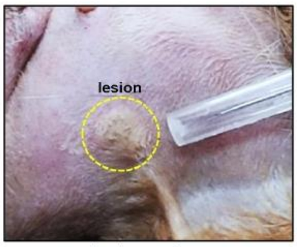


Focused ultrasound treatment of canine & feline mammary cancer (cont.)

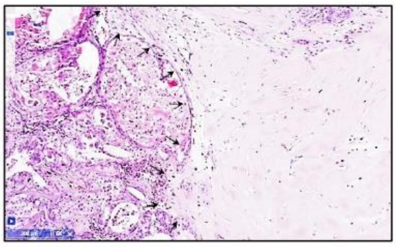
All pets were successfully treated with the SOUNDPET system with no recorded adverse events. Well-defined areas of coagulative necrosis were created in the treated canine and feline mammary tumors. The selected frequency (~2.5 MHz) offered good focusing and sufficient penetration of ultrasound in tissue. Hematoxylin and Eosin (H&E) staining demonstrated thermal necrosis in all treated tumors (9/9) without off-target effects, except from minor hemorrhage at the lesion borderline (1/9).



CT axial image of the dog placed on the device.



Example photo of mammary tumor in cat after FUS (45 W acoustic power, 20 s duration).



Indicative histological slide demonstrating thermal necrosis (indicated by the black arrows) at 5X magnification.

The findings are very promising and provide a good starting point for further research on FUS ablation of mammary neoplasia in pets. More trials with a larger patient population should be performed to confirm these findings and investigate the feasibility of safely ablating the entire malignancy, as well as deep-seated tumors.

CONNECT WITH US

https://www.facebook.com/soundpet

cy.linkedin.com/in/medsonic-ltd-cyprus-288286153

www.soundpet.eu

JULY 2023

co-funded by Ευρωπαϊκή Ένωση Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης Κυπριακή Δημοκρατία Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο