Project Acronym:

BRAINSONIC (ENTERPRISES/0223/Sub-Call1/0057)

MRI-guided Focused Ultrasound robotic system for brain tumors.

Deliverable number: 2.1

Title: Dissemination and Communication activities

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Date: 19/12/2025

BRAINSONIC

Funded by the European Union NextGenerationEU

Cyprus_tomorrow RECOVERY AND RESILIENCE PLAN

Republic of Cyprus

RESEARCH & INNOVATION FOUNDATION

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

Contents

Executive summary

This deliverable details the dissemination and communication activities undertaken to raise awareness of the BRAINSONIC project and engage stakeholders. These activities were primarily led by the partner organization: the Cyprus University of Technology (CUT), leveraging its extensive prior experience in this domain. The Host organization: LINAC-PET SCAN OPCO LTD (LINAC), was actively involved throughout the process, contributing to and supporting all efforts, including the creation of dissemination materials, social media promotion, presentations at scientific conferences and public events, and publications in scientific journals.

To enhance the project's branding, a logo was designed, and a website was launched to share key information with the public. Biannual newsletters were produced to initially introduce the project's objectives and consortium, followed by updates on progress. These newsletters, created in English, were distributed to stakeholders and made available on the project website. To engage a broader audience, the project's progress and activities were regularly communicated via social media platforms, particularly Facebook and LinkedIn.

Throughout the project, various aspects of the technology, anticipated outcomes, and progress updates were presented to key academic and governmental representatives during laboratory visits at CUT, depending on the stage of project development. Additionally, participants from both consortium partners attended various networking events related to the project's objectives throughout its duration, promoting the technology and establishing connections with experts from diverse fields, including academia, research, and clinical practice. Key research outcomes were shared with the scientific community through presentations at international conferences and publications in high-impact scientific journals, while ensuring that any potentially patentable information remained undisclosed.

Logo creation

Figure 1 displays the logo designed for the BRAINSONIC project (on 15 March 2024). The logo was featured on all dissemination materials and deliverables.

BRAINSONIC

Figure 1*: Logo of the project.*

Website creation

In the context of WP2, a project-specific website was developed as a key dissemination tool and integrated into the partner organization's website (Therapeutic Ultrasound Laboratory of CUT), aligning with corporate identity standards. The website was built using an open-source scripting language (PHP). ***Figure 2*** shows a screenshot of the main website page, which offers a brief project description and includes tabs linking to the list of deliverables and newsletters. Content updates are regularly performed by researchers from the project consortium. The page also acknowledges the source of funding.

The lab's website can be accessed at https://theralabcut.org and the project's webpage is available under the 'Ongoing Projects' tab.

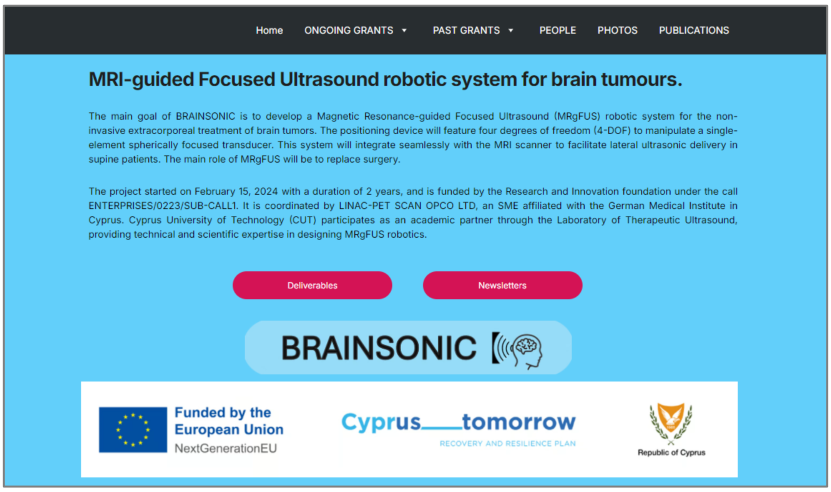

Figure 2*: Screenshot of the main page of the website.*

Dissemination through Social media

The project has effectively leveraged social media platforms, particularly **Facebook** and **LinkedIn**, to enhance its visibility and engage with a broader audience. Through targeted posts on these platforms, the project team has successfully shared the initial launch of the project, key milestones and project developments. This approach has not only increased awareness among stakeholders but also fostered valuable interactions with both the professional community and the public. The Facebook and LinkedIn posts announcing the launch of the project are displayed, respectively, in ***Figure 3*** and ***Figure 4***. These posts provide a brief overview of the project's main goals, highlighted the Host and partner organizations, and acknowledged the funding agency.

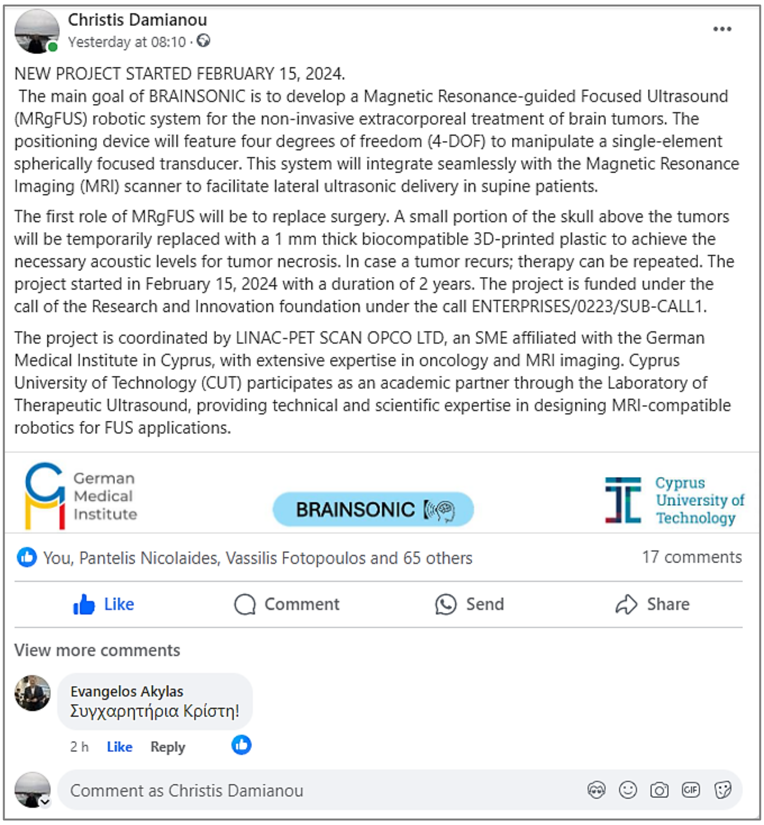

Figure 3: *Screenshot of the Facebook post announcing the launch of BRAINSONIC.*

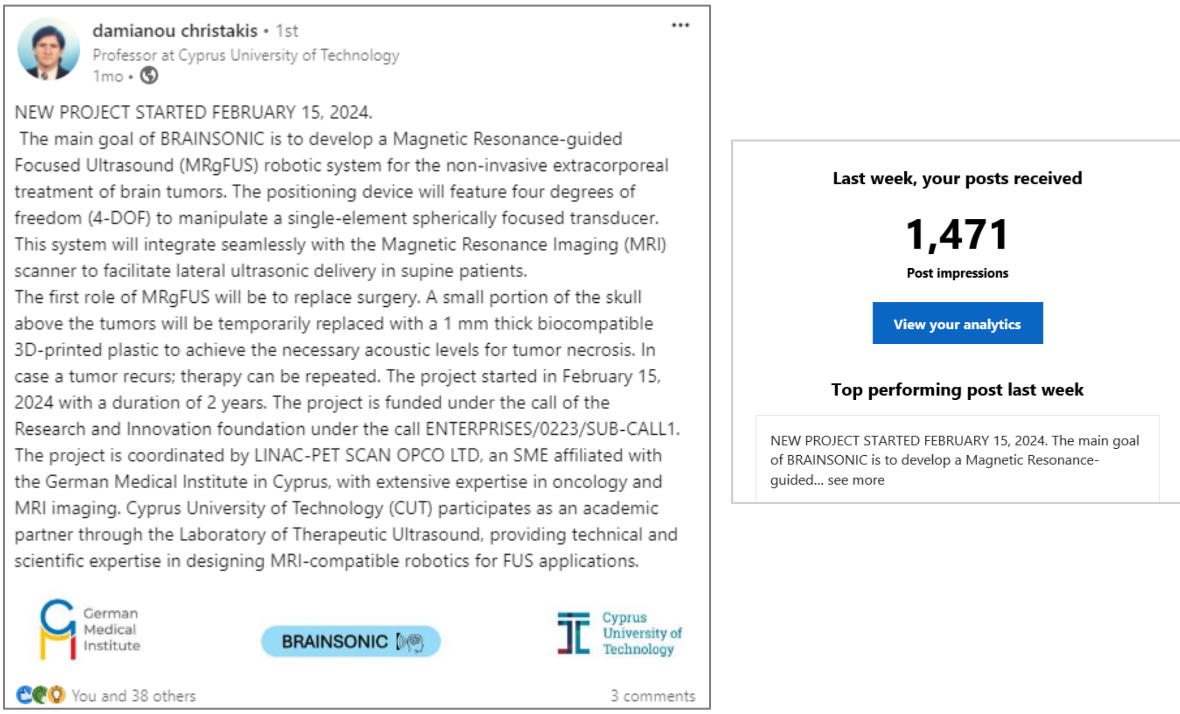

Figure 4: *Screenshot of the LinkedIn post announcing the launch of BRAINSONIC (left) and post impressions data provided by LinkedIn showing its high engagement (right).*

Throughout the project, updates and team activities were actively disseminated via social media platforms to enhance visibility and engagement. ***Figure 5*** shows a Facebook post highlighting the visit of the scientific coordinator to the premises of the Medical School, University of Patras, where he introduced the technology, supported the establishment of focused ultrasound, and fostered connections for potential future collaborations.

Figure 5*: Facebook post showcasing the visit of the scientific coordinator to the Medical School, University of Patras (March 2025).*

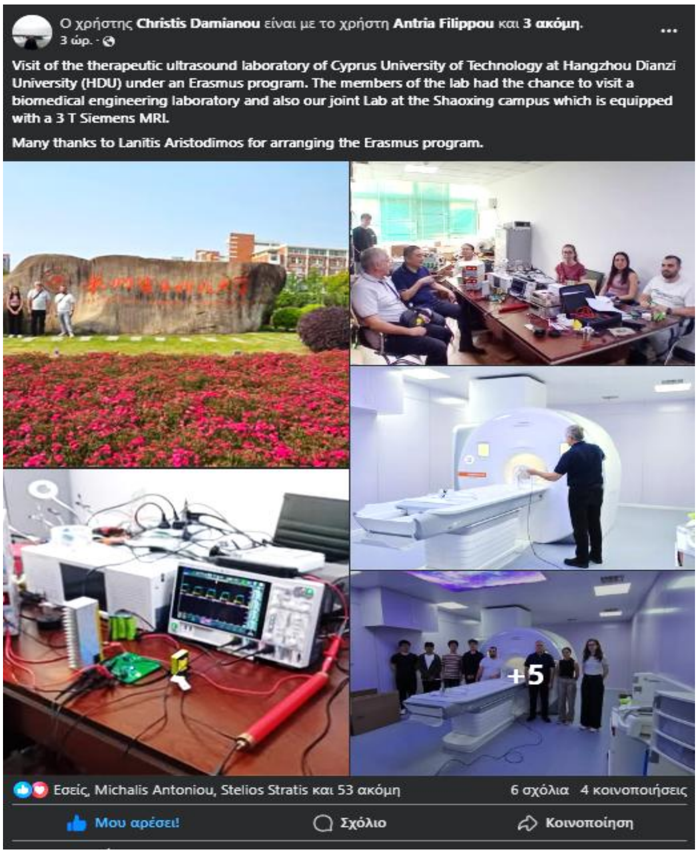

Figure 6*: Screenshot of a Facebook post about the team's visit to the Therapeutic Ultrasound Lab in China.*

Another example is provided in

Figure 6, which shows a screenshot of a Facebook post shared during the team's educational visit to the Collaborative Research Laboratory of Therapeutic Ultrasound at the Biomedical Integrated Application Technology Center in Shaoxing, Zhejiang, China. The post features photos taken both inside the MRI room and during the visit to the university's collaborative laboratories.

In addition to the educational activities, the team carried out initial experimental work on-site—complementing the visit with a hands-on research component. Further details on this visit are provided in later sections of this deliverable.

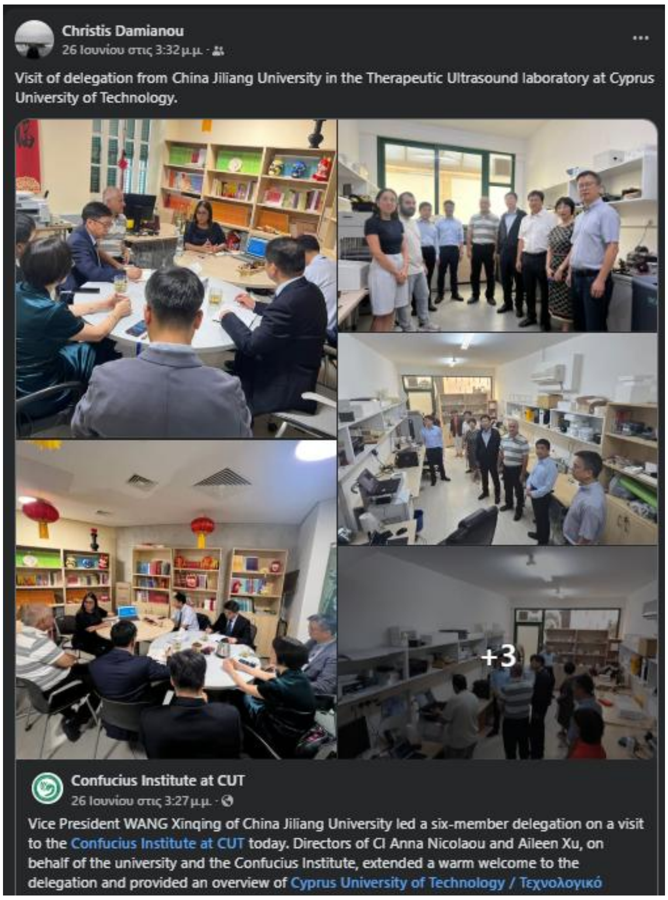

Figure 7: *Screenshot of a Facebook post disseminating the visit of the delegation of China Jiliang University at the laboratory of Therapeutic Ultrasound, CUT.*

Figure 7 shows a Facebook post highlighting the visit of a six-member delegation led by Vice President Prof. Wang Xinqing of China Jiliang University to the Therapeutic Ultrasound Laboratory.

The post emphasizes the delegation's keen interest in the laboratory's cutting-edge research and innovative technologies under development, underscoring their potential to advance the field of therapeutic ultrasound. It also reflects the collaborative spirit and shared commitment to driving progress in this rapidly evolving field.

Project newsletters

Project newsletters were produced biannually to provide updates on the project's progress.

Newsletter 1 introduced the project objectives and consortium partners.

Newsletter 2 focused on the four-degree-of-freedom robotic device and its evaluation for MRI compatibility.

Newsletter 3 detailed the development of a head phantom with tumor mimics and the evaluation of the system's thermal heating capabilities and proposed therapeutic protocol using MR thermometry in a 3T MRI scanner at the GMI MRI facility.

Newsletter 4 summarized the evaluation of the therapeutic system and protocol in a mouse model of Glioblastoma (GBM).

All four newsletters are provided in **Appendix I.**

Presentations and Networking Engagements

Conference presentations

1st Net4Brain annual meeting: Closing the translation gap in Brain cancer treatment, organized by COST (CA22103).

The project's scientific coordinator, Prof. Christakis Damianou (CUT) gave a poster presentation entitled "Robotic system for MRI-guided focused Ultrasound therapy of brain cancer" at the Net4Brain annual meeting organized by COST in Ljubljana, Slovenia between 4-6 September 2024. ***Figure 8*** shows indicative photos acquired during the meeting.

Figure 8*: Photos of the presentation room at the meeting venue (left) and the poster displayed on its dedicated stand (right).*

23rd Annual International Symposium on Therapeutic Ultrasound (ISTU 2024)

Christakis Damianou (CUT) presented a poster paper prepared during the BRAINSONIC project entitled "Robotic system for MRI-guided focused ultrasound therapy of brain cancer" at the *23rd Annual International Symposium on Therapeutic Ultrasound;* organized by the International Society for Therapeutic Ultrasound (ISTU). This conference took place between 19-22 September 2024 in Taipei, Taiwan. Participation in this prestigious conference provided valuable exposure for our project, fostering meaningful connections with industry experts and researchers. ***Figure 9*** shows photos taken during the conference.

Figure 9*: Conference photos showing the brain clinical panel discussion (left) and the poster displayed in the designated area at the conference venue (right).*

Peripheral Nerve Society (PNS) 2024 Annual Meeting

The work of the team on the topic “Ultrasound-Induced Enhanced Access of Therapeutics to Peripheral Nerves in a Demyelinating Charcot-Marie-Tooth Mouse Model,” in collaboration with the Cyprus Institute of Neurology and Genetics, was presented at the *PNS 2024 Annual Meeting*, which took place from June 22 to 25 in Montreal, Canada. This presentation provided valuable exposure for the team’s technology. The abstracts have been published in the *Journal of the Peripheral Nervous System* (Vol.29, Suppl.1, p.S3-S193, DOI: 10.1111/jns.12648). A screenshot showing the inclusion of the relevant abstract is provided in ***Figure 10***.

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ABSTRACT

WILEY

PNS Abstracts 2024

O 373 | ULTRASOUND-INDUCED ENHANCED ACCESS OF THERAPEUTICS TO PERIPHERAL NERVES OF A DEMYELINATING CHARCOT-MARIE-TOOTH MOUSE MODEL

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[2]*Cyprus University of Technology, Limassol, Cyprus*

Introduction: In order to facilitate the potential of systemically delivered viral vectors to transduce Schwann cells in peripheral nerves for gene therapy, we studied the use of a Focused Ultrasound System (FUS) to enhance AAV9 vector penetrance through the blood nerve barrier (BNB) to achieve better biodistribution and expression in peripheral nerves.

Methods: We first determined the optimal ultrasound electric power needed to induce transient BNB leakiness using different electric powers ranging from 20 to 120 Watt in wild type mice and the effects of FUS on sciatic nerve morphological and functional properties. We further tested the efficacy of AAV9 at different doses (2×, 1× and 0.5×1012 vg) to transduce Schwann cells following FUS application in Gjb1-null mice, a model of X-linked Charcot-Marie-Tooth disease (CMT1X). We assessed biodistribution by vector genome copy numbers (VGCNs) and expression rates of connexin 32 (Cx32).

Results: Our data show that an electric power of 120 W is needed to achieve BNB disruption. We did not observe any morphological and functional abnormalities or inflammatory responses up to 4 h post-sonication. VGCNs showed a trend for increase in sonicated nerves compared to non-sonicated controls in all groups. Cx32 expression rates were significantly increased in the high (61.1±4.98 % in control vs. 80.2±5.67 % in sonicated nerves, $p = 0.0027$) and mid-dose group (50.4±3.29 % in control vs. 64.6±4.80 % in sonicated nerves; $p = 0.0281$) and showed a trend for increase in the low dose group as well (49.5±3.69 % vs. 60.1±2.86 %, $p \geq 0.05$).

Conclusions: FUS application in sciatic nerves results in transient BNB disruption without any functional or morphological abnormalities or any inflammatory responses. Furthermore, FUS facilitates viral vector penetration into sciatic nerves and higher expression rates in Schwann cells. Application of the FUS may facilitate the delivery of therapeutics to peripheral nerves using lower systemic doses.

Grant Support: This work was funded by Muscular Dystrophy Association (MDA 963041 to AK).

Keywords: Charcot-Marie-Tooth disease, gene therapy, focused ultrasound system, Schwann cells

Figure 10*: Screenshot showing the inclusion of the abstract in the ‘PNS Abstracts 2024’, published in the ‘Journal of the Peripheral Nervous System’.*

11th International Conference on AUTOMATION, ROBOTICS, AND APPLICATIONS (ICARA2025)

Prof. Christakis Damianou (CUT) presented an article prepared during the BRAINSONIC project entitled “MRI-guided focused ultrasound robot for brain interventions” at the *11th International Conference on Automation, Robotics, and Applications.* This conference took place between 12 – 14 February 2025 in Zagreb, Croatia. Participation in this prestigious conference provided valuable exposure for the project, fostering meaningful connections with industry experts and researchers. ***Figure 11*** shows a photo taken during the conference and an image of the presented poster.

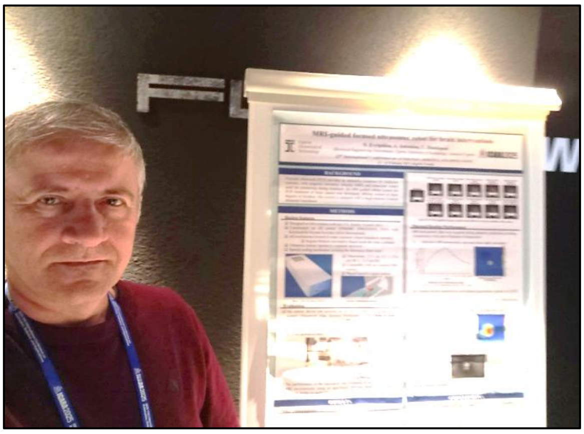
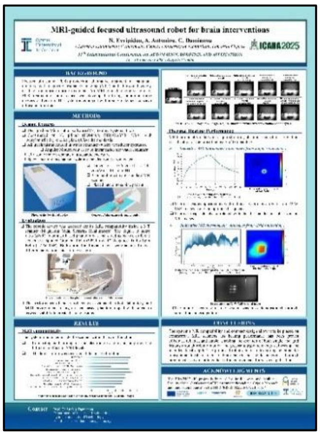
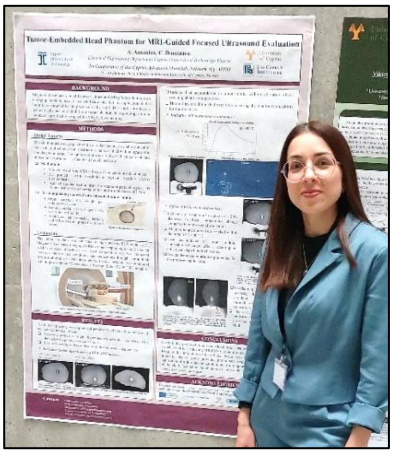
 

Figure 11*: Conference photo showing the poster displayed in the designated area at the conference venue and presenter (left), and the presented poster (right).*

1st Conference of the Cyprus Advanced Materials Network (Cy-AMN)

Anastasia Antoniou, a key researcher in the project, participated in the *1st Conference of the Cyprus Advanced Materials Network*, held on 13–14 January 2025, at the Library Auditorium of the University of Cyprus, Nicosia. She presented the topic 'Tumor-Embedded Head Phantom for MRI-Guided Focused Ultrasound Evaluation,' which provided an opportunity to engage with researchers from diverse disciplines and introduce this innovative technology to the national research community. Photos from the event can be seen in ***Figure 12***.



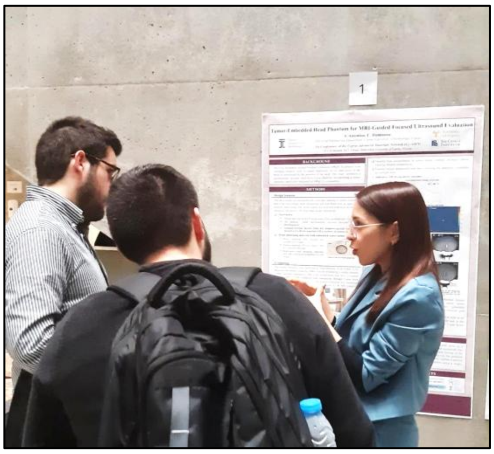


Figure 12: *Conference photos showing the poster displayed in the designated area at the conference venue and presenter.*

7th International Conference on BioMedical Technology (ICBMT 2025)

The scientific coordinator, Prof. Christakis Damianou presented BRAINSONIC at the *7th International Conference on BioMedical Technology* (ICBMT 2025), held on 16-19 January 2025, in Bangkok, Thailand. His oral presentation, titled 'MRI-Compatible Focused Ultrasound Phantom for Brain Targets,' focused on an advanced phantom developed to evaluate the BRAINSONIC system, highlighting its ability to replicate key biological tissue properties and produce tissue-like MRI signals. While the emphasis was on the tissue-mimicking head phantom, he also discussed the objectives, current status, and potential of the BRAINSONIC system. He was awarded with the **Best Presentation Award**. Photos acquired during his presentation can be seen in ***Figure 13***.

Figure 13: *Photos taken during the presentation (left) and when receiving the Best Poster Presentation award (right).*

International Society for Magnetic Resonance in Medicine (ISMRM 2025)

Indicative outcomes of BRAINSONIC performance, demonstrated through focused ultrasound sonications in a tumor-bearing head phantom within a high-field MRI scanner, were presented at the ISMRM 2025 Annual Meeting held in Honolulu, Hawaii, USA (10–15 May 2025, in-person attendance). The digital poster was title "Focused Ultrasound sonications in a tumor-bearing head phantom within a high field MRI scanner."

Net4Brain Second Annual Meeting 2025, organized by COST (CA22103).

The project's scientific coordinator, Prof. Christakis Damianou (CUT) gave a poster presentation entitled "MRI-Guided Focused Ultrasound Robotic Platform for Brain Cancer Therapy" at the Net4Brain annual meeting organized by COST in Bucharest, Romania between 2-4 July 2025. ***Figure 14*** shows indicative photos acquired during the meeting.

Figure 14*: Photographs taken at the meeting venue; the presentation room following the coordinator's presentation (left) and a group photo outside the venue (right).*

Networking - Knowledge sharing activities

Artificial Intelligence in Modern Oncology event in Cyprus

An event on 'Artificial Intelligence in Modern Oncology,' collaboratively hosted by GMI, CUT, and the Cancer Research and Innovation Centre, took place on 22 March 2024, at the university's facilities in Limassol, Cyprus. Dr. Yiannis Roussakis, the project coordinator, moderated a panel discussion with representatives from various key organizations, including those involved in cancer care, research, and ethics. Prof. Damianou and a key project researcher; Anastasia Antoniou from CUT attended the event.

Throughout the event, the project and scientific coordinators had the chance to connect and engage with a diverse group of attendees, including representatives from national and international academic institutions and regional cancer patient organizations, as well as prominent physicians in the field of clinical oncology. Importantly, several attendees were stakeholders and clinical advisors already engaged with the BRAINSONIC project, which facilitated productive interactions related to its potential clinical applications. Notably, Mr. Theodoros Loukaidis, Director General at the Cyprus Research and Innovation Foundation, was also present at the event. ***Figure 15*** presents selected photos from the event.

Figure 15*: Photos acquired during the Artificial Intelligence in Modern Oncology event.*

Visit of the Scientific Coordinator to the Medical School, University of Patras.

During his visit to the Medical School at the University of Patras (27 March 2025), the scientific coordinator introduced FUS technology to the faculty and researchers and demonstrated the capabilities of the BRAINSONIC system. This visit played a key role in supporting the establishment of FUS technology at the institution, helping integrate it into ongoing research. Additionally, he fostered valuable connections, paving the way for potential future collaborations aimed at advancing the developed technology towards clinical translation. A photo taken during the visit is shown in ***Figure 16***.

Figure 16*: Photo from the scientific coordinator's visit to the Medical School, University of Patras.*

Educational visit at the collaborative research Laboratory of Therapeutic Ultrasound, Biomedical Integrated Application Technology Center, Shaoxing, Zhejiang, China.

As part of the project's dissemination and communication activities, the team travelled to China to visit a collaborative laboratory recently established under the scientific guidance of Prof. Damianou. The lab was developed to promote the application of MRgFUS technology and is now fully equipped to support advanced research—generating data towards future clinical translation and commercialization. During the visit, the team conducted initial experimental work on site. ***Figure 17*** shows a photo of the participants together with Chinese students in the MRI room during the execution of an experiment.

Figure 17: *Photo of the participants together with Chinese students in the MRI room during the execution of an experiment at the Collaborative Research Laboratory of Therapeutic Ultrasound in Shaoxing, Zhejiang, China.*

Visits to the laboratory premises of CUT

Visit of Hangzhou Dianzi university (HDU) officials

On 9 May 2024, the rector of HDU, Professor Chen Jiming, and his delegation visited the Therapeutic Ultrasound Laboratory at CUT. Prof. Damianou (CUT) introduced the BRAINSONIC project, and attendees were notably impressed by the promising potential of the technology under development. Indicative photos from the visit are shown in ***Figure 18***.

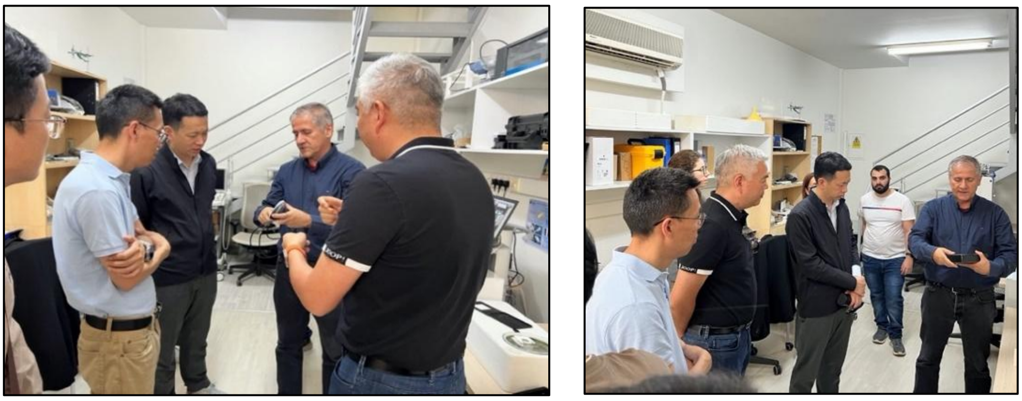


Figure 18*: Photos taken during the visit of the rector of HDU and his delegation to the Therapeutic Ultrasound Laboratory.*

Visit of the chief scientist for Research, Innovation and Technology of Republic of Cyprus

On 16 May 2024, the chief scientist for Research, Innovation and Technology of the Republic of Cyprus, Dr. Demetris Skourides, along with various delegates from CUT, visited the laboratory at CUT to gain direct insight into the research and activities being conducted. In this context, the BRAINSONIC project was introduced, the technology was explained, and its potential application in the treatment of brain cancer was discussed. Dr. Skourides found the therapeutic potential particularly compelling, recognizing its ability to offer significant advancements in treatment options and potentially revolutionize current approaches to therapy. ***Figure 19*** shows indicative photos acquired during the visit.

Figure 19*: Photos taken during the visit of the chief scientist for Research, Innovation and Technology of the Republic of Cyprus at the Therapeutic Ultrasound Laboratory.*

Visit of distinguished guest

On 26 June 2025, a distinguished guest, Mr. George Karagiannopoulos (Dextera Consulting Limited; scientific and technical consulting firm) visited the CUT's laboratory and was introduced to the BRAINSONIC technology. He expressed strong appreciation for the innovative approaches demonstrated and recognized the significant potential of the technology to revolutionize brain cancer therapy. ***Figure 20*** shows a photo acquired during the visit.

Figure 20*: Photos taken during the visit of Mr. Karagiannopoulos at CUT's lab.*

Visit of Delegation from China Jiliang University

On 26 June 2025, a six-member delegation led by Vice President Wang Xinqing of China Jiliang University visited CUT's laboratory. During the visit, the delegation was introduced to ongoing research activities and the technology developed under the BRAINSONIC project. Vice President Wang expressed gratitude for the detailed presentation and highlighted the potential for enhanced collaboration between the two institutions in areas such as student exchanges and joint research projects. Photos from the visit can be seen in ***Figure 21***.

***Figure 21**: Photos taken during the visit of the delegation from China Jiliang University at the Therapeutic Ultrasound Laboratory.*

List of Conference papers

1. Evripidou N, Antoniou A, and Damianou C, "Robotic system for MRI-guided focused ultrasound therapy of brain cancer", *1st Net4Brain annual meeting: Closing the translation gap in Brain cancer treatment*, Ljubljana, Slovenia, 4-6 September 2024, Poster presentation (in person attendance).
2. Evripidou N, Antoniou A, Spanoudes K, and Damianou C, "Robotic system for MRI-guided focused ultrasound therapy of brain cancer", *23rd Annual International Symposium on Therapeutic Ultrasound (ISTU)*, Taipei, Taiwan, 19-22 September 2024, Poster Presentation (in person attendance).
3. Kombou M, Antoniou A, Damianou C, Kleopa K, and Kagiava A, "Ultrasound-induced enhanced access of therapeutics to peripheral nerves of a demyelinating Charcot-Marie-tooth mouse model", *2024 Peripheral nerve society (PNS) Annual Meeting*, Montreal, Canada, 22-25 June 2024, DOI: 10.1111/jns.12648, Volume 29 (S3).
4. Evripidou N, Antoniou A, and Damianou C, "MRI compatible Focused Ultrasound Phantom for Brain Targets", *7th International Conference on BioMedical Technology (ICBMT 2025)*, Bangkok, Thailand, 16-19 January 2025, Oral presentation (in person attendance).
5. Evripidou N, Antoniou A, and Damianou C, "MRI-guided focused ultrasound robot for brain interventions", *11th International Conference on Automation, robotics, and applications,* Zagreb, Croatia, 12 – 14 February 2025, Poster presentation (in person attendance).
6. Antoniou A and Damianou C, "Tumor-Embedded Head Phantom for MRI-Guided Focused Ultrasound Evaluation", *1st Conference of the Cyprus Advanced Materials Network (Cy-*

AMN), Library Auditorium of the University of Cyprus, Nicosia, 13–14 January 2025, Poster presentation (in person attendance).
7. Antoniou A, Evripidou N, Georgiou L, Chrysanthou A, Christofi A, Roussakis Y, Ioannides C, and Damianou C, "Focused Ultrasound sonications in a tumor-bearing head phantom within a high field MRI scanner", *The International Society for Magnetic Resonance in Medicine (ISMRM 2025)*, Honolulu, Hawaii, USA, 10-15 May 2025 (in person attendance).
8. Damianou C, Antoniou A, and Evripidou N, "MRI-Guided Focused Ultrasound Robotic Platform for Brain Cancer Therapy", *2nd Net4Brain annual meeting*, Bucharest, Romania, 2-4 July 2025, Poster presentation (in person attendance).

List of Journal Papers

Published:

1. Antoniou A, Georgiou L, Chrysanthou A, Christofi A, Roussakis Y, Ioannides C, Spanoudes K, Zhao J, Yu L, Damianou C, "Impact of 3D-Printed Skull Inserts of Different Thickness on MRgFUS Heating in a Head Phantom", *Journal of Medical Ultrasound* (2025). doi: 10.4103/jmu.JMU-D-24-00014.
2. Antoniou A, Evripidou N, Giannakou M, Georgiou L, Chrysanthou A, Christofi A, Roussakis Y, Ioannides C, Spanoudes K, Zhao J, Yu L, Damianou C, Utilizing an Agar/Silica Phantom for MRgFUS Evaluation: Lesion formation, MRI manifestation, and Comparison with Porcine Tissue, *Journal of Medical Ultrasound* (2025). doi: 10.4103/jmu.JMU-D-25-00008.
3. Antoniou A, Chrysanthou A, Georgiou L, Christofi A, Roussakis Y, Ioannides C, Spanoudes K, Zhao J, Yu L, and Damianou C, "Focused Ultrasound Sonications of Tumor Model in Head Phantom under MRI Monitoring: Effect of Skull Obstruction on Focal Heating", *Journal of Medica Physics* (2025), doi: 10.4103/jmp.jmp_177_24.
4. Antoniou A, Evripidou N, Georgiou L, Christofi A, Zhao J, Yu L, Li W, Kagadis G, Damianou C, "Magnetic Resonance Imaging monitoring of Histotripsy effects in agar phantom", *Medical physics* (2025), doi:10.1002/mp.18054.
5. Antoniou A, Evripidou N, Filippou A, Georgiou L, Chrysanthou A, Christofi A, Roussakis Y, Ioannides C, Lyu Y, Zhao J, Yu L, Li W, Damianou C, "Phantom-based Assessment of Focused Ultrasound Thermal Effects with Conventional Magnetic Resonance Imaging", *Physica Medica* (2025), doi: 10.1016/j.ejmp.2025.105078.
6. Antoniou A, Evripidou N, Georgiou L, Christofi A, Weng Y, Zhao J, Yu L, Li W, Damianou C, "Multi-channel Flow Phantom for MRI-Guided Focused Ultrasound," *Physica Medica* (2026), doi: 10.1016/j.ejmp.2026.105730.
7. A. Antoniou, C. Damianou, "Phantoms for MRI-guided focused ultrasound and associated robotic systems research", *Digital Medicine - Review article* (2025), Status: Accepted for publication. DOI: 10.1097/DM-2025-00007.

Under Peer‒Review:

1. Lyu Y., Filippou A., Antoniou A., Evripidou N., Zhao J., Yu L., Li W., and Damianou C, “Effect of agar concentration, acoustic power, pulses and pulse repetition period on histotripsy-induced fractionation in agar-based phantoms,” Journal of Applied Clinical Medical Physics; submitted on 22/08/2025—In Peer-Review.
2. Filippou A, Lyu Y, Georgiou L, Christofi A, Zhao J, Yu L, Li W, Damianou C, “MRI-based assessment of focused ultrasound parameters on histotripsy lesions in agar-based phantoms,” Physica Medica; submitted on 27/08/2025—In Peer-Review.
3. Antoniou A, Damianou C, “Artificial Intelligence in MR-Guided Focused Ultrasound: A Decade of Progress and Challenges,” Journal of Medical Ultrasound; revised version submitted on 04/02/2026—In Peer-Review.
4. Antoniou A, Evripidou N, Georgiou L, Christofi A, Zhao J, Yu L, Li W, Kagadis G C, Damianou C, “MRI-Guided Large-Scale Lesion Patterning with High-Intensity Focused Ultrasound in Homogeneous Phantoms,” Medical Physics; submitted on 10/12/2025—In Peer-Review.
5. Antoniou A, Evripidou N, Georgiou L, Christofi A, Zhao J, Yu L, Li W, Damianou C, “MRI Evaluation of Near-Field Heating in a High Intensity Focused Ultrasound Phantom,” Physica Medica; submitted on 21/01/2026—In Peer-Review.

The project was acknowledged as follows: «The study was` funded by the Recovery and Resilience Facility of the NextGenerationEU instrument, through the Research and Innovation Foundation (RIF) of Cyprus, under the project BRAINSONIC (ENTERPRISES/0223/Sub-Call1/0057)».

Appendix I: Newsletters

ISSUE 1 | 01/ 07/ 2024

MRI-guided Focused Ultrasound robotic system for brain tumors.

Funded by the European Union NextGenerationEU

Cyprus tomorrow RECOVERY AND RESILIENCE PLAN

Republic of Cyprus

BRAINSONIC

ENTERPRISES/0223/SUB-CALL1/0057

NEWSLETTER

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German Medical Institute

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Cyprus University of Technology

PROJECT OBJECTIVES

Robotic system: The main goal of BRAINSONIC is to develop a **Magnetic Resonance-guided Focused Ultrasound (MRgFUS) robotic system** for the non-invasive extracorporeal treatment of brain tumors. The positioning device will feature four degrees of freedom (4-DOF) to manipulate a single-element spherically focused transducer. This system will integrate seamlessly with the Magnetic Resonance Imaging (MRI) scanner to facilitate lateral ultrasonic delivery in supine patients.

Therapeutic Protocol: The **first role of MRgFUS will be to replace surgery**. A small portion of the skull above the tumors will be temporarily replaced with a 1 mm thick biocompatible 3D-printed plastic to achieve the necessary acoustic levels for tumor necrosis. In case a tumor recurs; therapy can be repeated. The **second role of MRgFUS will be to open the Blood brain barrier (BBB)**, enabling the delivery of killer drugs to the tumor. Tissue heating will be accurately monitored by MR thermometry.

CONSORTIUM PARTNERS

The project is coordinated by **LINAC-PET SCAN OPCO LTD**, an SME affiliated with the German Medical Institute in Cyprus, with extensive expertise in oncology and MRI imaging. LINAC aims to pioneer novel medical devices, leveraging its clinical experience to optimize the BRAINSONIC prototype system for clinical practice. **Cyprus University of Technology (CUT)** participates as an academic partner through the Laboratory of Therapeutic Ultrasound, providing technical and scientific expertise in designing MRI-compatible robotics for FUS applications.

The project started on February 15, 2024, and will run for 2 years. It is funded by the Research and Innovation foundation under the call ENTERPRISES/0223/SUB-CALL1.

For technical questions contact the scientific coordinator:
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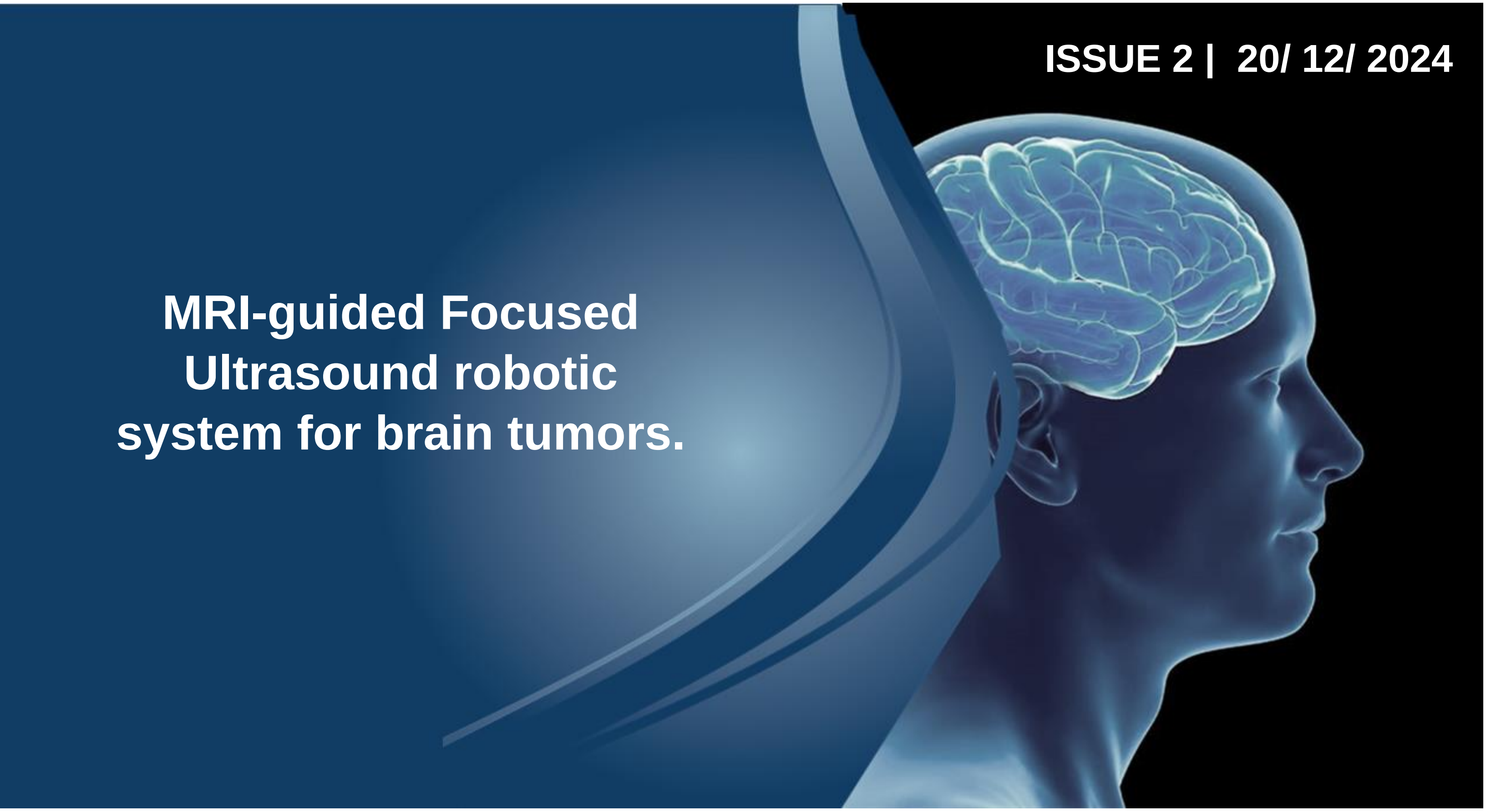

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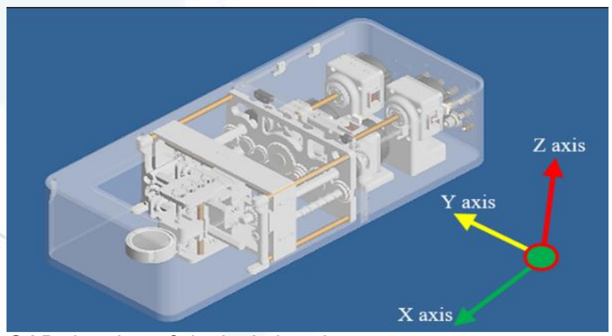
DEVELOPMENT OF 4-DOF ROBOTIC SYSTEM

The robotic device was designed on Microstation software. The various parts were manufactured on a 3D printer (FDM400, STRATASYS, USA) using Acrylonitrile Styrene Acrylate (ASA) material.

All mechanisms were arranged inside the water container, except for the ultrasonic motors, which operate in a separate enclosure.



CAD drawing of device's interior.

The positioning mechanism enables motion of a single-element FUS transducer operating at a frequency of about 1 MHz along four axes: forward/backward (X), left/right (Y), upward/downward (Z) and rotational.

Photo of manufactured device.

The four stages are driven by piezoelectric ultrasonic motors (Shinsei Kogyo Corp., Japan), further incorporating optical rotary encoders (US Digital Corporation, USA) to ensure accurate movement.
The robotic device has compact dimensions, making it suitable for integration with any conventional high-field MRI scanner, laterally to a patient lying in supine position.

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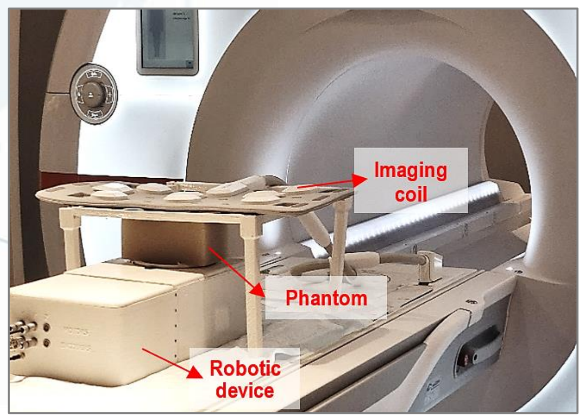
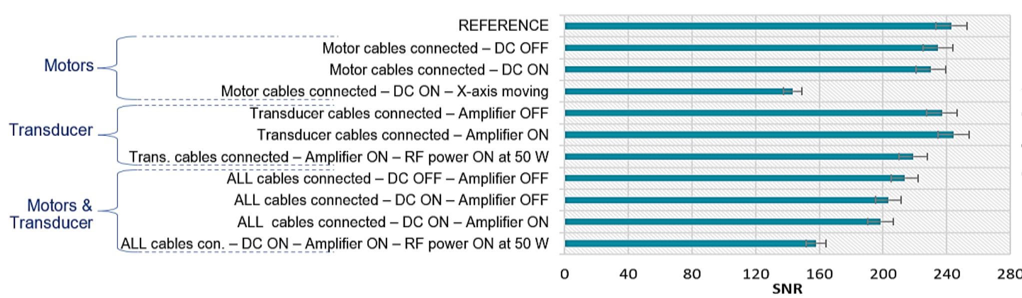
MRI COMPATIBILITY ASSESSMENT

This task was performed in a 3T MRI owned by LINAC. The Signal to noise ratio (SNR) served as the main metric for assessing MRI compatibility. The device was positioned on the patient couch and an agar-based phantom was placed on its acoustic opening. The phantom was scanned using Spoiled Gradient Echo (SPGR) and T2-W Turbo Spin Echo (TSE) sequences. A series of 2D coronal and axial images were acquired under different activation states of the electronic system and amplifier.



Experimental set-up in 3T MRI scanner.

The BRAINSONIC system operated seamlessly within the MRI scanner, experiencing no malfunctions or operational issues. Sufficient SNR for high quality imaging was achieved for both employed sequences and maintained among different activations of the robotic system.



Bar chart of SNR values calculated for the different activation conditions (from coronal SPGR images).

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MRI-guided Focused Ultrasound robotic system for brain tumors.

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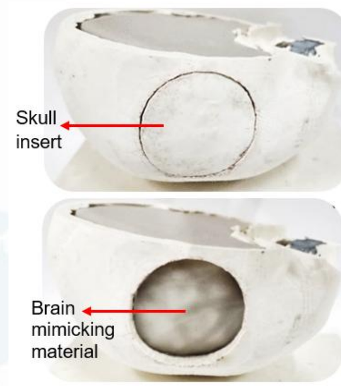
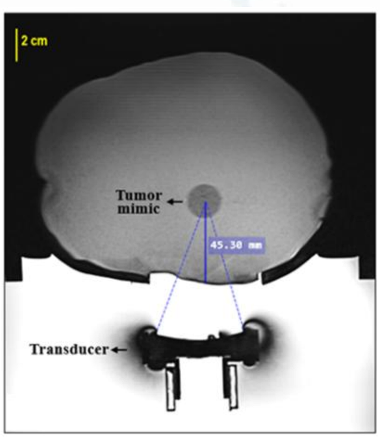
DEVELOPMENT OF HEAD PHANTOM WITH TUMOR MIMICS

An advanced tumor-bearing head phantom was developed following a comprehensive characterization of various inclusion concentrations. This phantom consists of a skull mimic filled with a tissue-mimicking material composed of 6% w/v agar, embedding a tumor mimic with the same agar concentration and supplemented with 4% w/v silica.

The skull bone model was derived by segmenting computed tomography (CT) head scan images from an anonymized female volunteer. A circular segment of the temporal-parietal skull area was isolated (referred to as circular skull insert), resulting in a two-compartment skull model. The designed skull model was 3D-printed with 100% infill and filled with a tissue mimicking material to form the head phantom.



Tumor-bearing brain tissue-skull phantom with removable insert.



T2-Weighted Turbo Spin Echo (T2-W TSE) image of the phantom, with skull opening aligned over the transducer.

The attenuation coefficient of the brain mimicking material (6% agar) at 1 MHz was measured to be 0.743 ± 0.027 dB/cm, aligning sufficiently with reported literature values for brain tissue, which typically range around 0.8 dB/cm.[1]
In addition, the silica-doped (4%) phantom exhibited significantly greater heat accumulation and temperature increase compared to the pure 6% agar gel, mimicking the higher density of tumors in real tissue. The specific inclusion compositions also provided excellent contrast between the tumor and its surroundings in MRI scans.
This phantom model served as a critical component in evaluating the BRAINSONIC robotic system and relevant therapeutic protocol, which relies on Magnetic Resonance Imaging-guided Focused Ultrasound (MRgFUS) delivery through a thin skull implant to enable efficient ultrasonic transmission while minimizing off-target heating effects.

[1] *Guo J et al. Mathematical Model of Ultrasound Attenuation With Skull Thickness for Transcranial-Focused Ultrasound. Front Neurosci, 15:778616, 2022.*

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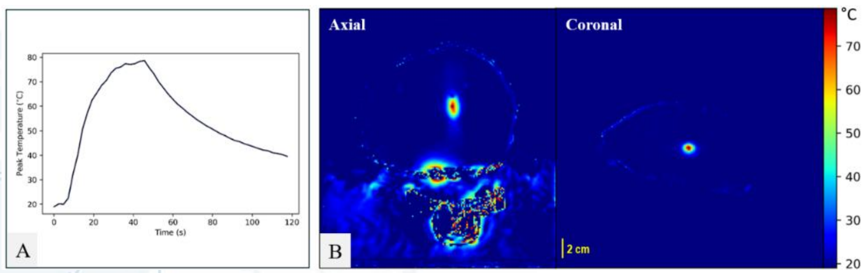
ASSESSMENT OF THERMAL HEATING CAPABILITIES

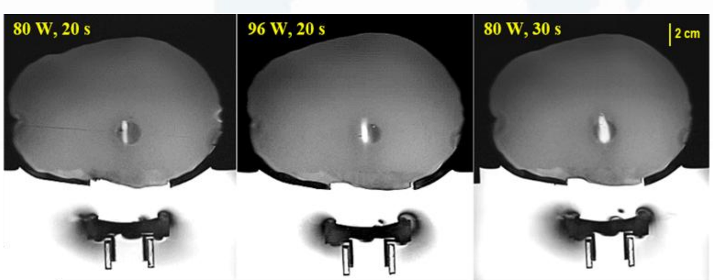
A rigorous investigation of various MRgFUS protocols for both partial and robotic-assisted complete ablation of the tumor simulators was conducted. Typical FUS parameters were applied, with acoustic power ranging from 60–120 W for up to 60 s. Increasing either the power or duration resulted in lesions of larger dimensions. The system demonstrated the capability to generate thin, cigar-shaped lesions within the tumor, regardless of its location, without significant shifting effects, provided that an appropriate transducer was selected.

Typical thermometry outcomes from high-power exposure targeting the tumor mimic without skull obstruction :

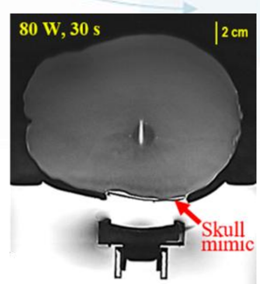


(A) Focal temperature profile during and after a 40-s sonication at 120 W (6397 W/cm^2) at 7 cm depth. (B) Corresponding thermal maps showing temperature distribution in tumor.

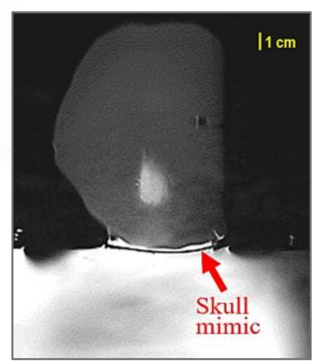
Tumor ablation results with and without skull mimic interference :



*T2-W TSE phantom images post-sonication at increasing energy levels (left to right), **no skull interference**.*



TSE image after sonication through 1-mm resin skull.



T2-W TSE sagittal image showing lesion formed by 3x3 sonication at 80 W for 60 s, with 60-s cooling, at a 3.5 cm focal depth through 1-mm Resin skull.

Indicatively, for a typical exposure of 80 W (1838 W/cm²) over 30 s of unobstructed sonication at 4.5 cm focal depth, the focal temperature increased by 54.6 °C. The corresponding rise with the 1-mm resin skull was 41.7 °C, resulting in a thin, cigar-shaped thermal lesion, compared to a larger, oval-shaped lesion for unobstructed sonication.

Importantly, overlapping lesions were successfully created covering the entire tumor using robotic-assisted grid sonication both in free field and with the 1-mm Resin obstructing the beam. **Precise thermal ablation of tumor mimics through the 1-mm resin skull model demonstrated proof of concept for the proposed strategy of treating inoperable brain tumors via FUS delivered through specialized skull implants**.

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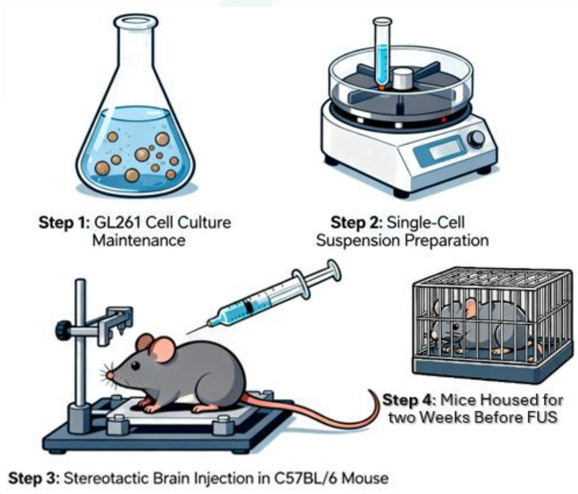
FOCUSED ULTRASOUND IN GLIOBLASTOMA MICE: STUDY OVERVIEW

This study explored the use of focused ultrasound (FUS) for targeted ablation of glioblastoma (GBM) tumors in a mouse model, using the BRAINSONIC robotic system.

A mouse model of GBM was established using GL261 tumor cells to enable FUS targeting of well-defined intracranial tumors. Tumor-bearing mice received a single FUS exposure directed at the tumor site, while a group of healthy mice served as control to provide a procedural reference. All sonications were performed using predefined intensity and duration parameters that were applied consistently across all subjects.



Tumor development in C57BL/6 mice

The 3 degrees-of-freedom (DOF) robotic system, incorporating a single-element spherically focused ultrasonic transducer operating at 2.75 MHz, was employed. The accompanying treatment-planning, control, and monitoring software platform enabled automated triggering and coordinated control of robotic motion and FUS exposure.

The study focused on evaluating the acute tissue response to FUS under controlled conditions. Histological analysis using hematoxylin and eosin (H&E) staining was performed shortly after treatment to characterize immediate structural changes and assess short-term tissue integrity.

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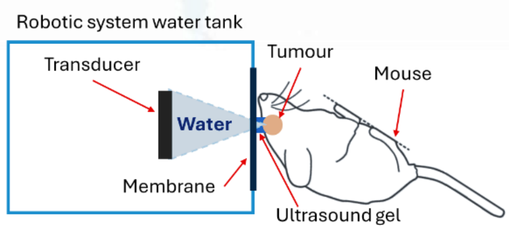
KEY EXPERIMENTAL RESULTS

Histological Outcomes

Acute histological evaluation revealed clear tissue alterations within the sonicated GBM regions. Treated tumor areas exhibited coagulative necrosis, characterized by eosinophilic staining, loss of nuclear detail, marked neuronal dropout, and localized tissue rarefaction consistent with ablative effects.

In contrast, unsonicated brain regions in control samples and in tissue surrounding the FUS-treated GBM region showed preserved architecture, indicating that areas outside the focal zone remained unaffected under the tested conditions.



Schematic of FUS delivery to mouse brain tumor

Key Findings

- Localized coagulative necrosis observed in sonicated tumor tissue.
- Loss of nuclear structure and reduced cellular integrity in ablated regions.
- Unsonicated brain regions preserved normal cytoarchitecture.
- No acute complications noted during or immediately after the procedure.

Outlook

These early results support the feasibility of robotic FUS delivery for targeted tumor ablation in a small-animal GBM model. Future studies may incorporate longer-term follow-up to evaluate tumor growth dynamics and overall treatment response. Overall, the findings validate the BRAINSONIC platform for experimental neuro-oncology research and motivate further in-vivo experimentation.

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