Open-LIFU 2.0 Specification v. 2.1

Note: the specification is nearing finalization. We are seeking comments from the community prior to finalizing to give you the best system we can.

Product Summary

Open-LIFU 2.0 is Openwater's Low Intensity Focused Ultrasound (LIFU)[1] platform for researching the treatment of a variety of conditions. The platform is flexible, easy-to-use, and can deliver LIFU to targets located nearly anywhere in the head or body. While Open-LIFU 2.0 devices are ready to set up "out of the box", their open-source design allows customization and modification to support clinical research across diverse users and applications. At the same time, Open-LIFU 2.0's controlled design features make it an effective solution for developing regulated medical devices that are portable and low-cost. By filling the gap between expensive research hardware available for proof-of-concept studies and commercially manufacturable hardware suitable for regulated medical devices, Open-LIFU 2.0 greatly facilitates the translation of novel therapies from bench to bedside.

Figure 1: Industrial Design enabling use of one or many transducers driven by a small console. Allows enormous flexibility in using LIFU transducers in many places on most bodies. Comments to community@openwater.health

[1] During sonication, MI, ISPPA, ISPTA, TI, and TIC will all remain within the FDA limits for diagnostic ultrasound.

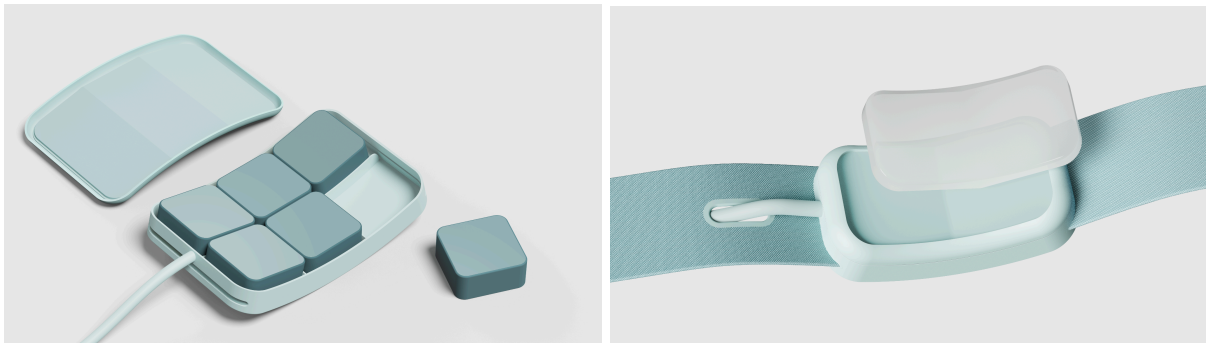


Figure 2: Left: Flexible reconfigurability of various housing options (with per transducer purchase added_ transducers driven by a small console. Allows enormous flexibility in using LIFU transducers in many places on most bodies. Right: the coupling pad to enable close contact the body. Please send comments to community@openwater.health

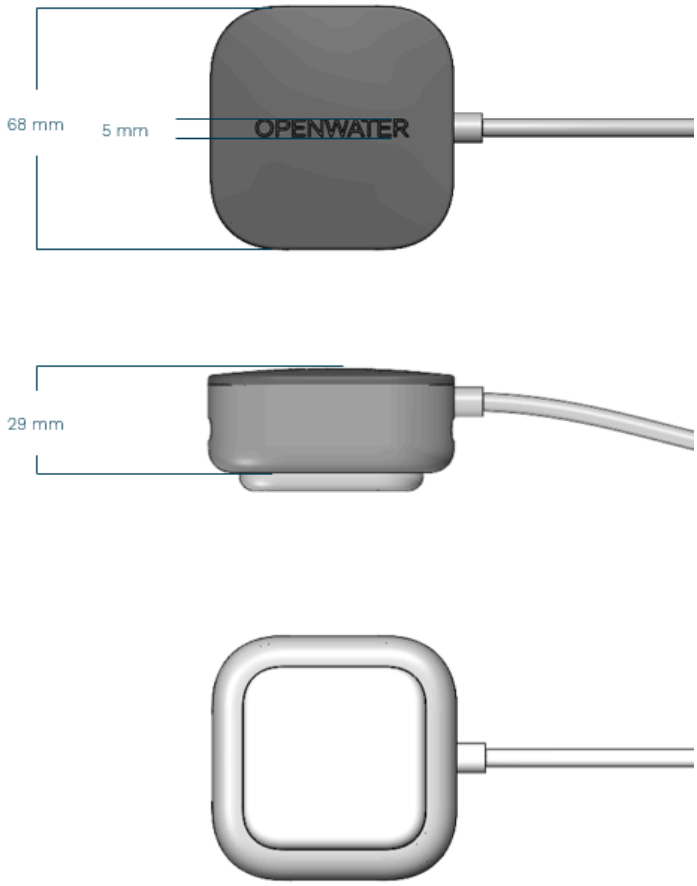


Figure 3: Dimensions of singlet transducer array module - estimated.

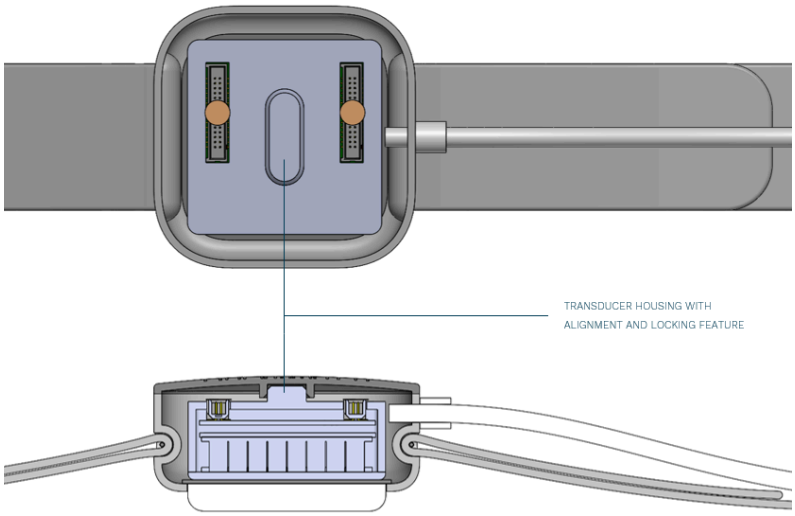


Figure 4: "Xray" view of internals of the module housing the transducer array.

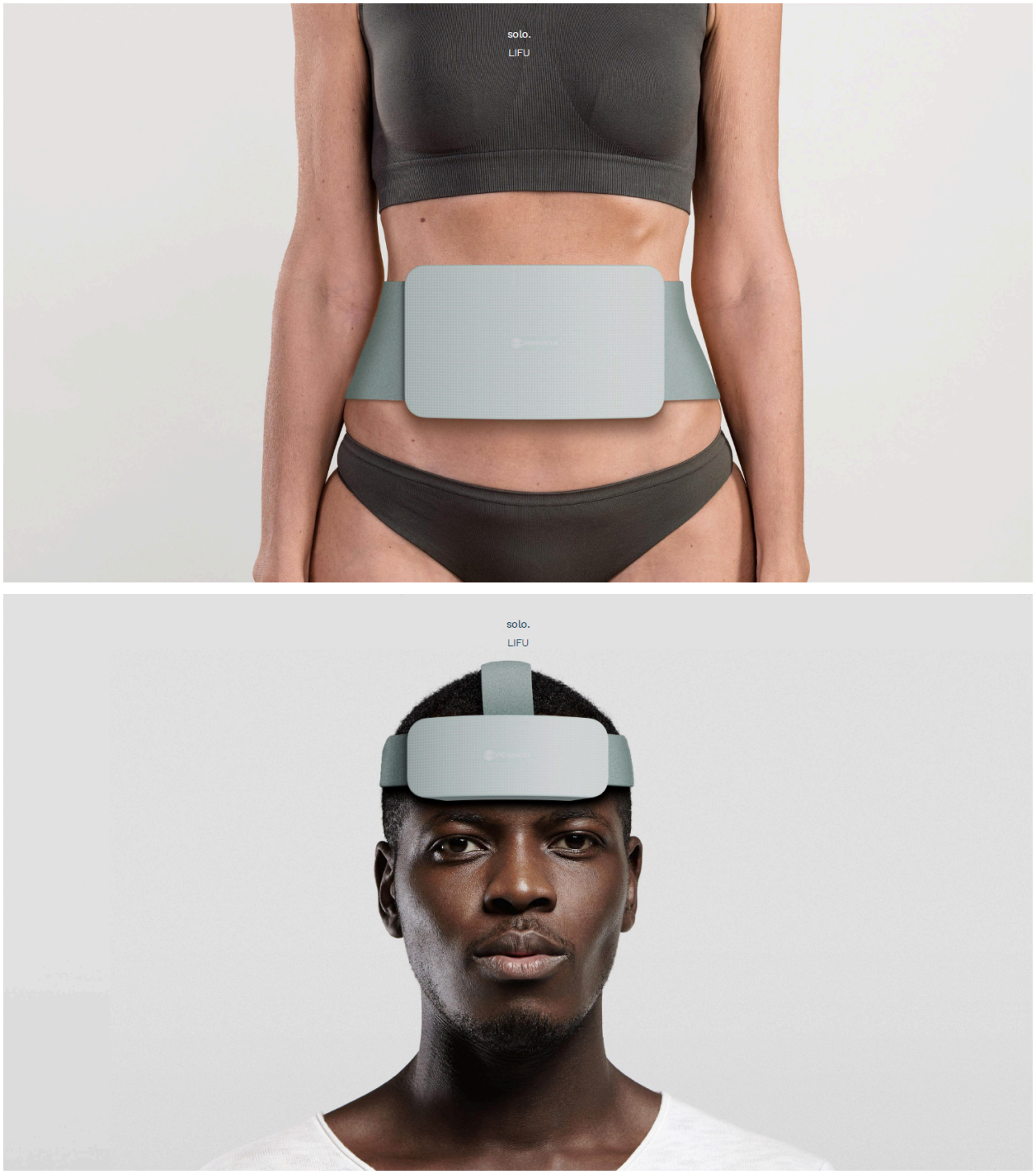


Figure 5,6,7: Designed to be used in multiple configurations in most parts of the body with housings that can be populated with one or multiple transducers easily. Default configuration is one console and the single transducer housing. Other housings available with more transducers and can run all off of the same console.

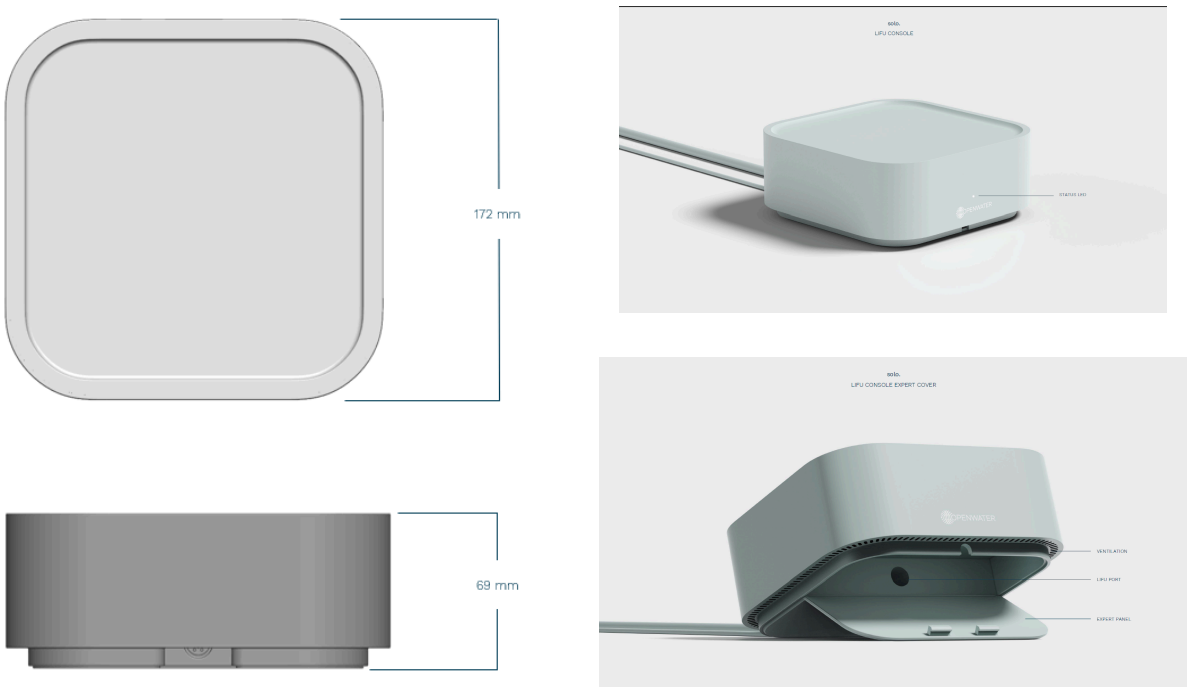


Figure 8: Dimensions and styling of the console housing.

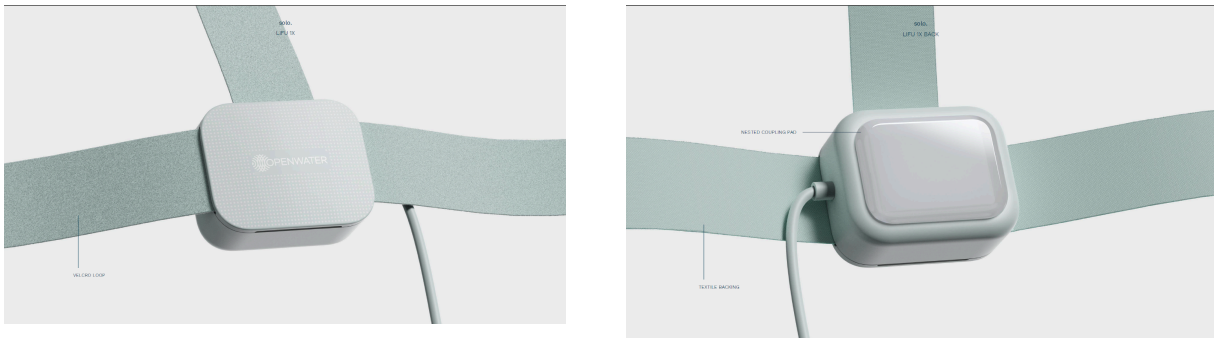
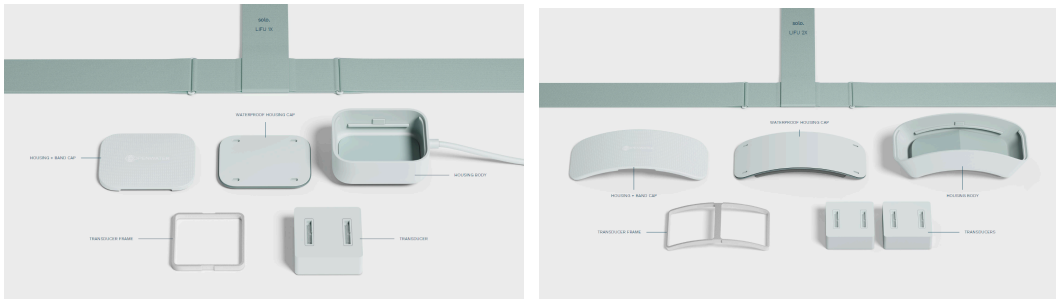


Figure 9,10: Details of Open-LIFU wearable



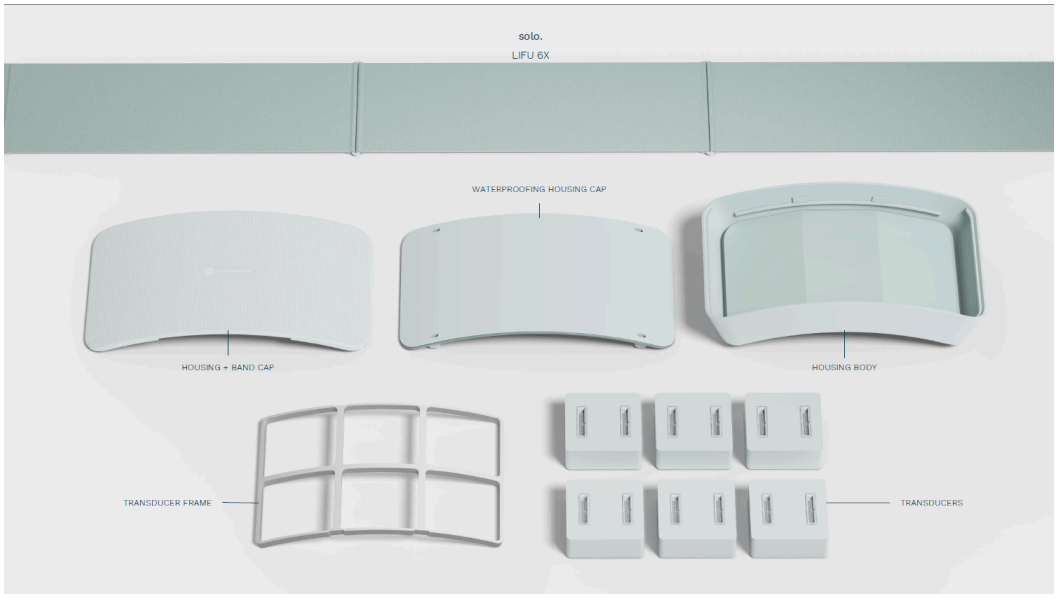


Figure 11,12,13: 1-up, 2-up and 6-up configurations. Can be assembled with the waterproofing assembly supplied. Other configurations can be 3D printed.

Key Components & Features

- Transducers in a variety of form factors, made from one or more steerable matrix arrays and arranged rigidly to meet the focusing and beamforming demands of any just about any target in the body.
- Sonications controlled by PC software, relayed to transducers via small console connected via USB to the PC
- Unique two-stage targeting: position the transducer on the body roughly over the target of interest, capture its precise location and let software focus LIFU precisely to the target.
- Flexibility from Research to Commercialization
    - Ready to set up “out of the box”
    - Open-source design enables innovation and modification
    - Quality controls provide compatibility with regulatory approvals
    - Same modules used for research and commercial products

Target Specifications[2]

Category	Parameter	Value
Sonication Parameters	Center frequencies	100-500 kHz
	Mechanical Index at focus	0-1.9 MI
	Pulse length	0-100 ms
	Duty Cycle	0-50%
	Duration	0-15 minutes
	Focusing range (1 module)	3cm (150kHz), 6cm (400kHz)
	Focusing range (multi-module)	11cm (deeper may be possible with more modules than 4x2 grid)
	Apodization	Binary
	Focal Patterns	Singe, Multi (rastered)
Transmit Modules	Number of Elements	64 (8x8 grid) per single transducer
	Transmit Electronics	On-module
	Center frequencies	150kHz, 400kHz
	Footprint	4x4 cm
	Communication	I2C, TTL
	Expansion ports	I2C
	Receive Channels	Expansion header
Transducers	Number of transmit modules	*Depending on frequency & duty cycle- Use of many transducers simultaneously at max power may require custom power supply - TBD*
	Connection to console	Flexible Cable
	Affixation to body	Multiple strap configurations
Console	Input Power	120V / 240V AC
	Output Voltage	+/- (5-96V) DC
	Output Power	60W Peak
	Input Communication Port	USB C
	Size	6” x 6” x 2”
Software	Operating System Memory Storage Connections GPU	Windows 11 or later 8 GB of RAM 100 GB of free storage 1 available USB-C port (at least USB 3.0) NVIDIA Recommended
	Simulation Engine	K-Wave (python version)
	Language	Python
	Components	1. Underlying Python Modules. 2. Access controlled GUI
Transducer Tracking	Method	3D Scanning
	Accuracy	TBD – requires < 2mm
Compliance[3]	IEC Standards	60601-1-1, 60601-1-2, 60601-1-6, 60601-2-5, 60601-2-37, 60601-2-62, 62304
	ISO Standards	13485, 10993

[2] Preliminary specification for informational purposes only. Subject to change.
[3] Openwater has not yet been certified for compliance to these standards.

Intended Use Statement

Open-LIFU 2.0 is intended to help researchers study the effects of Low-Intensity Focused Ultrasound (LIFU) in laboratory, pre-clinical, and clinical research settings. The system is designed to be flexible and re-programmable so that a wide array of sonication and targeting parameters can be explored by researchers, while also allowing constrained operation modes so that trained operators can use the system to complete specified workflows, and entities seeking regulatory approval for specific indications can use realizations of the platform in commercial products. Open-LIFU 2.0 has not been evaluated by the FDA and is intended for research use only.

Open Source

All hardware and software will be released under an aGPLv3 open-source license, the Creative Commons Attribution-ShareAlike 4.0 International (license available at https://creativecommons.org/licenses/by-sa/4.0/legalcode), or equivalent licensing terms.

Safety

This notification serves as a safety disclosure for our Open-LIFU 2.0 and Open-Motion medical components intended exclusively for research purposes. Openwater acknowledges that, as of January, 2024 the device has not undergone review and clearance or approval by the U.S. Food and Drug Administration (FDA) for commercial distribution and use.

Research-Only Purpose: The devices discussed on this site are exclusively intended for research purposes and are not cleared or approved by the FDA for clinical use or commercial distribution. It is solely available to researchers and research institutions.

Lack of FDA Review: The safety and effectiveness of these components have not been established through the FDA's formal review process. Researchers should be aware that the device has not undergone the regulatory scrutiny required for general medical use.

Risk Awareness: The potential risks associated with these components are not fully known. Researchers and research institutions are advised to exercise caution and fully inform all involved parties about the investigational nature of the device and the uncertainties surrounding its safety and efficacy.

Informed Consent: Researchers using these components are responsible for obtaining informed consent from participants, clearly communicating the experimental nature of the device and any potential risks associated with its use.

Monitoring and Reporting: Researchers are urged to closely monitor the use of these components during research activities and promptly report any adverse events or unexpected side effects to Openwater safety@openwater.cc. This information is crucial for ongoing evaluation and refinement of these devices.

Restricted Use: These components should be confined to research settings and not used in clinical practice or commercial applications. Their use should be limited to researchers and research institutions with the expertise to manage and monitor the investigational nature of the device. For inquiries or additional information, please contact safety@openwater.cc

Note: the specification is nearing finalization and incrementing to v. 1.0. We are seeking comments from the community prior to finalizing to give you the best system we can.
Send your comments to community@openwater.health

Appendix - LIFU Literature

Low Intensity Focused Ultrasound (LIFU) refers to therapeutic ultrasound whose intensity levels are within the bounds that the FDA generally considers safe for use in diagnostic imaging. LIFU is being studied for potential uses in a range of diseases and conditions, including neuromodulation in the brain for the treatment of mental diseases[4][5], neuromodulation of peripheral nervous targets to relieve pain or reduce inflammation[6], selective damaging of certain types of cancer cells[7][8], and selective treatment of clotting[9], among many others. These studies are typically performed with customized one-off research setups or expensive research platforms, and there are currently no FDA approved LIFU products on the market. Open-LIFU 2.0 fills the need for a flexible, low cost, quality built platform to accelerate research to treat these critical diseases.

Openwater has been creating LIFU systems for some time and has preclinical results on glioblastoma with our units as well as clinical feasibility results on humans in a study on treatment to severe depression using our units. Link to more of our clinical work at Openwater. For more information on LIFU and other focused ultrasound research, https://www.fusfoundation.org contains many resources for researchers, industry, clinicians, and patients.

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[4] Pasquinelli, Cristina, et al. "Safety of transcranial focused ultrasound stimulation: A systematic review of the state of knowledge from both human and animal studies." *Brain Stimulation* 12.6 (2019): 1367-1380.
[5] Yu, Kai, et al. "Intrinsic functional neuron-type selectivity of transcranial focused ultrasound neuromodulation." *Nature communications* 12.1 (2021): 2519.
[6] Zanos, Stavros, et al. “Focused ultrasound neuromodulation of the spleen activates an anti-inflammatory response in humans”, Brain Stimul. 2023 May-Jun;16(3):703-711
[7] David R. Mittelstein, Jian Ye, Erika F. Schibber, Ankita Roychoudhury, Leyre Troyas Martinez, M. Houman Fekrazad, Michael Ortiz, Peter P. Lee, Mikhail G. Shapiro, Morteza Gharib; Selective ablation of cancer cells with low intensity pulsed ultrasound. Appl. Phys. Lett. 6 January 2020; 116 (1): 013701. https://doi.org/10.1063/1.5128627
[8] Schibber, E. F., et al. "A dynamical model of oncotripsy by mechanical cell fatigue: selective cancer cell ablation by low-intensity pulsed ultrasound." Proceedings of the Royal Society A 476.2236 (2020): 20190692.
[9] Papadopoulos, N., Kyriacou, P. A. and Damianou, C. (2017). Review of Protocols Used in Ultrasound Thrombolysis. Journal of Stroke and Cerebrovascular Diseases, 26(11), pp. 2447-2469. doi: 10.1016/j.jstrokecerebrovasdis.2017.07.032