SCIENCE PRISM
Illuminating Science, Empowering Minds

Science Prism

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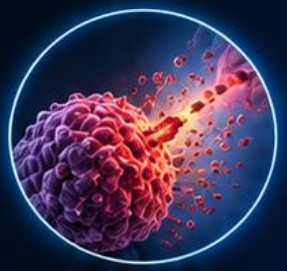
Issue 22
15 September 2026.

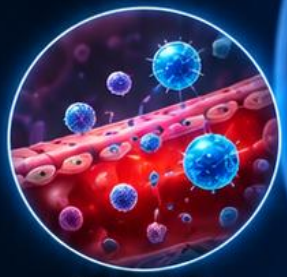
WHEN SOUND BECOMES MEDICINE

From imaging tumours to manipulating them

OPENING THE BLOOD-BRAIN BARRIER



DESTROYING TUMOURS



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In this Issue

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Welcome to *Science Prism* — your gateway to exploring the brilliance of science and discovery. Like a prism dispersing light into a spectrum of colours, we distil complex scientific ideas into clear, engaging, and thought-provoking insights. Delivered monthly, *Science Prism* is designed for students, researchers, and curious minds, bringing you the latest breakthroughs, timeless questions, and actionable ideas to fuel your curiosity and drive innovation. Guided by our tagline, "*Illuminating Science, Empowering Minds*," we aim to inspire fresh perspectives and connect the transformative power of science with the world around us. Join us each month as we explore knowledge, spark curiosity, and celebrate discovery, one insight at a time.

Welcome to the September 2026 Issue of *Science Prism*

If earlier issues have explored what happens when biology goes wrong, this month we ask a different question: what happens when we learn to control biology with sound?

For most of us, ultrasound means an image. But when acoustic energy is carefully controlled, it can do much more. It can heat tissues, generate mechanical forces, influence drug delivery, temporarily open the blood-brain barrier, and even activate engineered biological systems. This month, we explore how ultrasound is evolving from *a technology used primarily to see into one that can also change what happens inside the body.*

This issue opens with ***"When Sound Becomes Medicine: From Imaging Tumours to Manipulating Them,"*** following ultrasound from focused tumour ablation and microbubble-assisted drug delivery to blood-brain barrier opening, sonodynamic therapy and experimental approaches that use sound to control engineered immune responses. Some of these technologies are already in clinical use, others are being tested in early human studies, while the most ambitious remain preclinical.

This month's ***Science Shapers*** features **Prof. Kullervo Hynynen**, whose work has helped shape modern focused ultrasound research. His career provides a remarkable thread through this issue's central theme: how physics, engineering and medicine can come together to turn sound into a tool for interacting with living tissue.

Together, these stories invite us to rethink what ultrasound can become. Its future may not lie in replacing existing treatments, but in giving them greater control over where and when they act. The challenge now is to make these effects sufficiently controlled, reproducible and safe to become dependable medicine.

With curiosity and continuity,
The *Science Prism* Team

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WHEN SOUND BECOMES MEDICINE
From imaging tumours to manipulating them

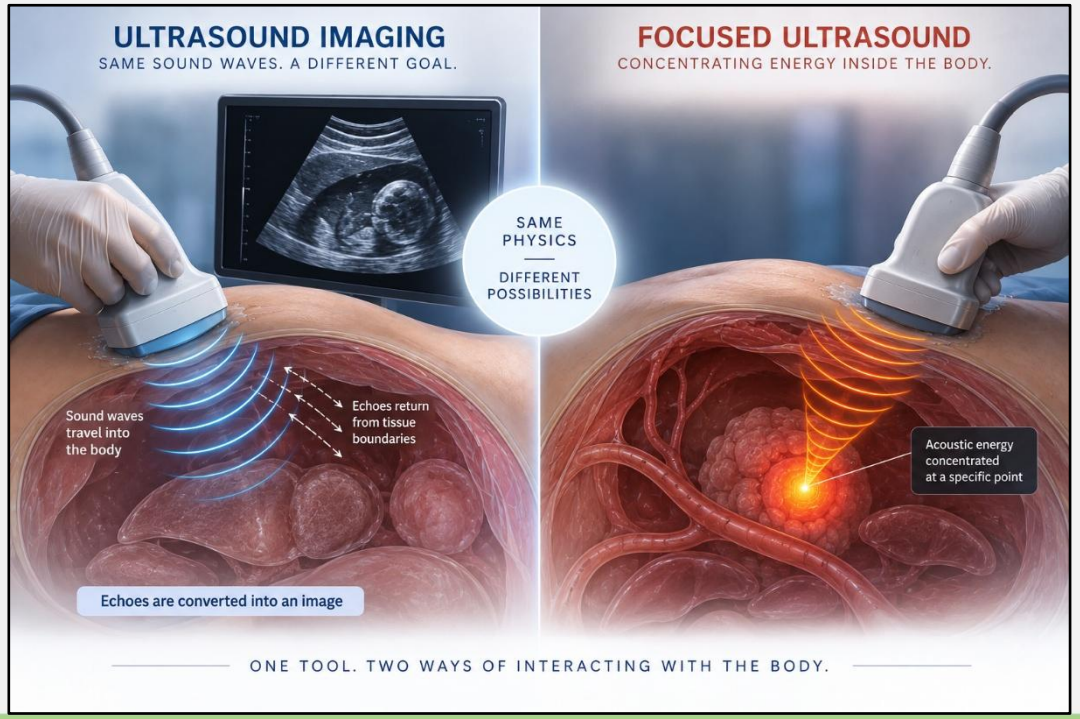
For decades, ultrasound has been one of medicine's most familiar ways of seeing inside the body. But the same sound waves used to create an image can also exert precise physical forces on living tissue. Researchers are now harnessing these effects to destroy tumours, improve drug delivery, temporarily open the blood-brain barrier, activate therapeutic molecules and even direct engineered immune responses. Ultrasound is no longer simply helping us see disease. It is beginning to help us change it.

For most of us, the word *ultrasound* brings to mind an image. A probe is placed against the skin, sound waves travel into the body, echoes return, and a computer turns those echoes into a picture. The technology has become so familiar that it is easy to forget how remarkable the original idea was: using sound to investigate structures hidden inside the body without an incision or ionising radiation.

Medical ultrasound was not the work of a single inventor. In the 1940s, Austrian neurologist Karl Dussik explored ultrasound imaging of the brain, while in Glasgow, Ian Donald and his colleagues helped establish ultrasound as a practical clinical imaging technology during the 1950s. But another possibility was already emerging. If sound waves could travel into the body and interact with tissue, could they also be used to deliberately change what they encountered? In 1942, physicist John G. Lynn and colleagues at Columbia University and the Piezo-Electric Research Laboratories showed that ultrasound could be focused to produce localised effects in biological tissue. The principle was simple but important: acoustic energy could be concentrated at a particular point, making its effect much stronger there than along the rest of the beam.

Turning that principle into practical medicine took decades. Early experiments demonstrated that focused ultrasound could produce precise lesions, but the technology lacked the imaging, targeting and monitoring systems needed for reliable clinical treatment. As medical imaging, computing and ultrasound engineering improved, researchers gained increasingly precise control over where acoustic energy was deposited. This eventually gave rise to *high-intensity focused ultrasound,* or *HIFU*. A specialised transducer concentrates acoustic waves on a selected region of tissue. At the focus, sufficient acoustic energy can be absorbed to raise the temperature and cause irreversible damage, while treatment is designed to minimise unwanted effects outside the target. Cancer became an important testing ground. Researchers in China, including groups at Chongqing Medical University, developed extensive clinical experience with ultrasound-guided HIFU for solid tumours. Their work helped establish that ultrasound could be used not merely to observe diseased tissue, but to physically treat it. Sound was no longer only an imaging signal. It could become a therapeutic tool.

Acoustic waves also produce rapidly changing pressures and mechanical forces. When ultrasound interacts with gas-filled microbubbles in the bloodstream, the bubbles can expand and contract in response to the acoustic field. Under appropriate conditions, their behaviour can influence nearby blood



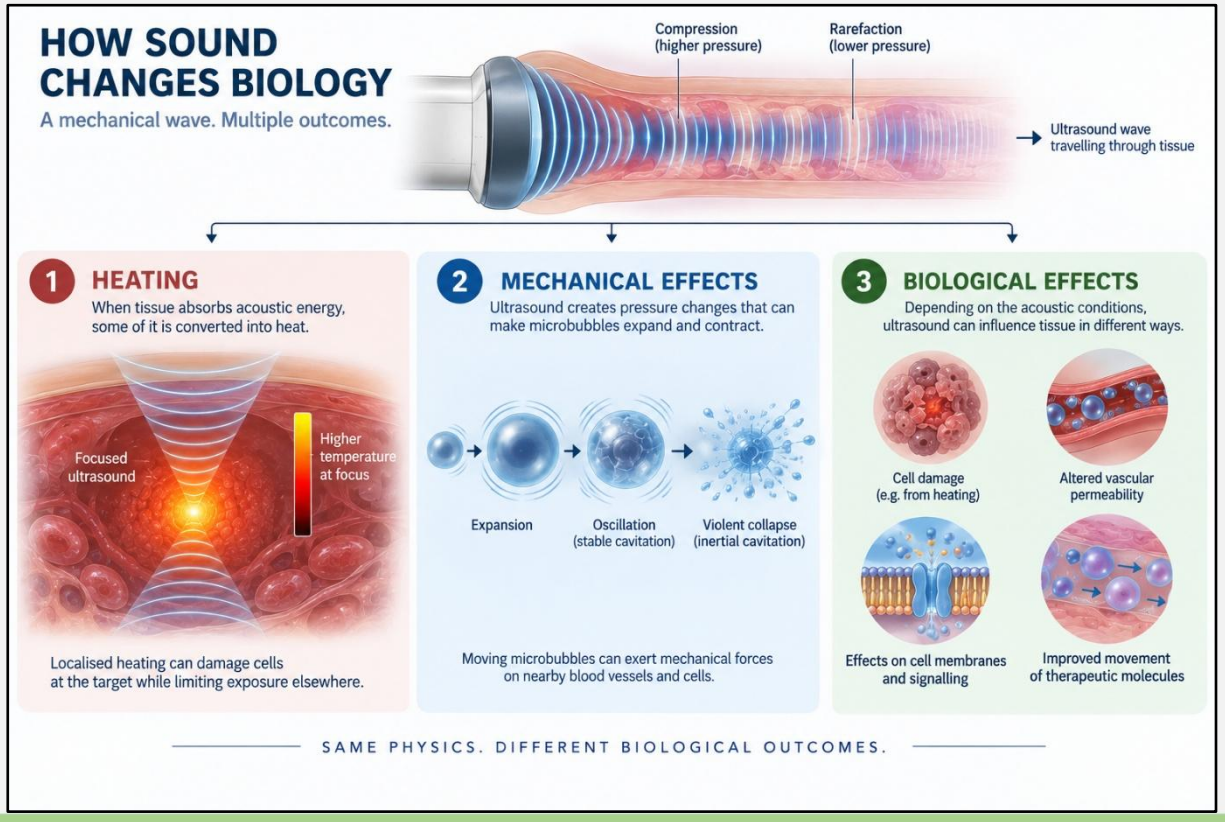
vessels and cells, producing effects very different from simple heating. This distinction between thermal and mechanical effects now underlies much of therapeutic ultrasound research. Depending on how the acoustic field is controlled, ultrasound can heat tissue, generate mechanical forces, alter vascular permeability, influence drug delivery or trigger other biological processes. Some of these approaches are already used clinically; others are being tested in early human studies or remain experimental. So the question that once sounded unusual is becoming increasingly important: Can sound do more than create an image? The answer is increasingly yes. The more interesting question now is not simply what ultrasound can do, but how well we can control what happens when sound meets living tissue.

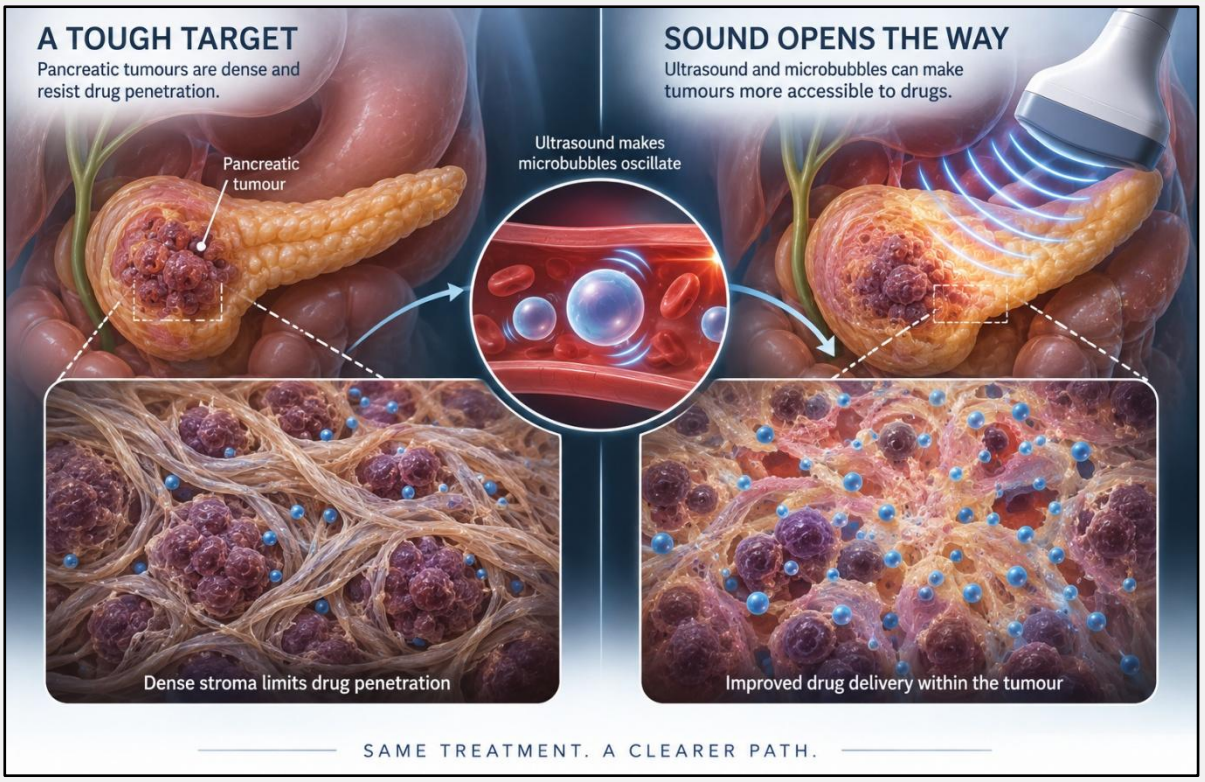
HOW SOUND CHANGES BIOLOGY. Ultrasound is a mechanical wave. As it travels through tissue, it creates alternating cycles of compression and rarefaction, producing small pressure changes. What happens next depends on how the acoustic energy is delivered, how strongly it interacts with the tissue and whether anything else, such as a microbubble, is present. One of the best-known effects is heating. When tissue absorbs acoustic energy, some of that energy is converted into heat. At sufficiently high intensities and with appropriate exposure times, the temperature can rise enough to damage cells. Focused ultrasound makes this useful by concentrating acoustic energy within a selected region while limiting exposure elsewhere. Rather than heating an entire area, the aim is to deposit enough energy at a defined target to produce a therapeutic effect.

But heat is only part of the story. Ultrasound can also produce mechanical effects. This becomes particularly important when microscopic gas-filled bubbles are introduced into the circulation. Known as microbubbles, these contrast agents expand and contract as the ultrasound wave's pressure changes. Under carefully controlled conditions, their movement can exert mechanical forces on nearby blood vessels and cells. Bubble behaviour depends strongly on the acoustic conditions. They may oscillate repeatedly without collapsing, a phenomenon known as *stable cavitation*. At higher acoustic pressures, they can undergo much more violent motion, known as inertial cavitation. These different behaviours can produce very different biological effects. For example, oscillating microbubbles can temporarily alter blood vessel behaviour and loosen connections between endothelial cells. This can increase vascular permeability, allowing substances that would normally remain outside tissue to cross the vessel wall. Mechanical forces can also affect cell membranes, the cytoskeleton and intracellular signalling pathways. This is why therapeutic ultrasound cannot simply be described as “turning up the power”. Frequency, pressure, pulse duration, exposure time, focusing, tissue properties and the presence of microbubbles can all change the biological outcome. Heating and mechanical effects may also occur together.

The same physical phenomenon can therefore produce very different biological effects. Depending on how the acoustic field is controlled, ultrasound can destroy tissue, alter blood vessels, change how drugs move through tissue, or temporarily modify biological barriers. The challenge is no longer simply producing ultrasound. It is controlling its interaction with living tissue well enough to produce the desired effect while avoiding unwanted damage. That principle will become increasingly important as we move from what ultrasound can physically do to what researchers are trying to make it do.

DESTROY AND DELIVER. Pancreatic ductal



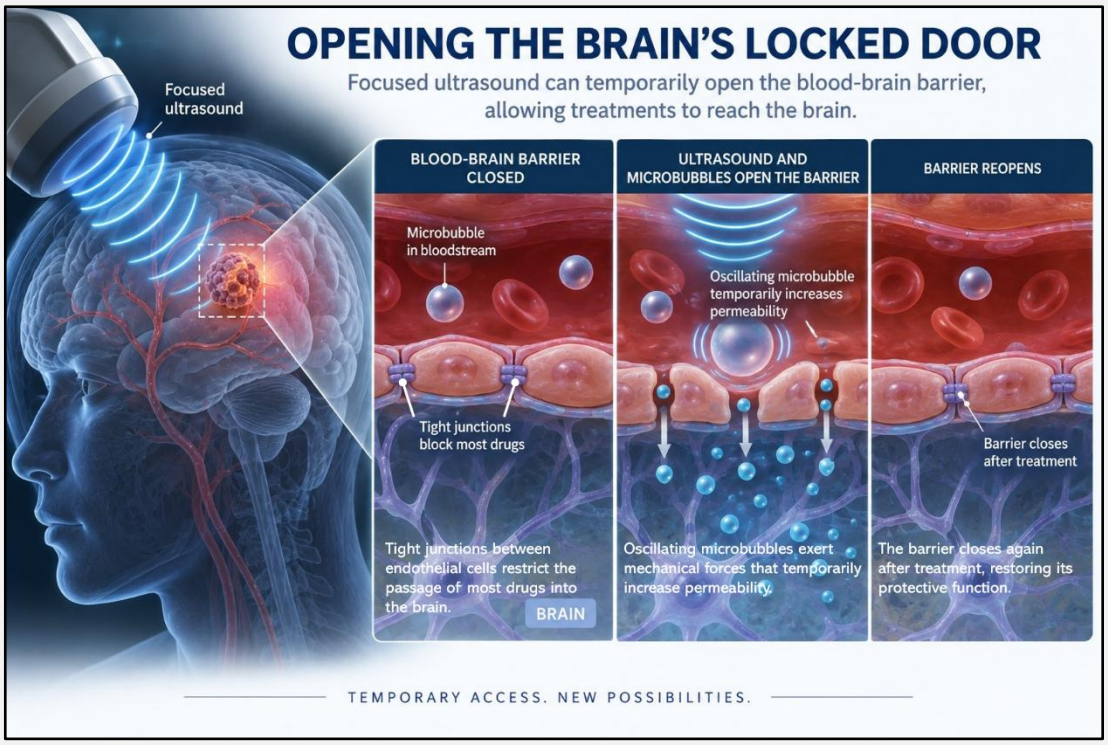


adenocarcinoma presents a problem that is not solved simply by finding a better drug. Many pancreatic tumours are surrounded by a dense, fibrous stroma that restricts the movement of drugs through the tumour. Even when chemotherapy reaches the tumour, getting enough of it to the right place can be difficult. Researchers in Bergen, Norway, began exploring whether ultrasound could help overcome this physical barrier. In clinical studies led by Georg Dimcevski, Odd Helge Gilja, Spiros Kotopoulis and colleagues, patients with pancreatic cancer received gemcitabine together with ultrasound and intravenously administered microbubbles. The idea was not to use ultrasound as another chemotherapy agent. Instead, the acoustic field would make the microbubbles oscillate near blood vessels, producing mechanical effects that could temporarily increase vascular permeability and alter the tumour environment.

The first clinical work was deliberately cautious. A 2013 case report demonstrated the feasibility of combining ultrasound, microbubbles and gemcitabine in patients with advanced pancreatic cancer. A subsequent phase I study involving 10 patients found the treatment to be feasible, with no additional toxicity clearly attributable to the ultrasound procedure. Tumour responses were observed, but the study was small and had no control group, so it could not establish that ultrasound improved survival. A larger randomised phase II study provided more encouraging evidence. Patients receiving ultrasound with gemcitabine had a median overall survival of 9.10 months compared with 6.10 months in the control group, together with a higher disease-control rate. But this result must be interpreted in context. A single trial does not establish a new standard of care, and subsequent studies have not produced uniformly positive results. That inconsistency is important. It suggests that ultrasound-mediated drug delivery is not simply a matter of adding sound to chemotherapy. Acoustic pressure, frequency, pulse duration, microbubble dose, treatment timing and the physical properties of an individual tumour can all influence the outcome. The biological response may therefore depend as much on *how* ultrasound is delivered as on whether it is used at all.

Laboratory studies have helped explain why. In tumour-like models containing dense collagen matrices, ultrasound combined with microbubbles can alter the extracellular environment and increase interstitial transport. In one organ-on-chip model developed by researchers including Delanyo Kpeglo, Stephen Evans and Sally Peyman, the approach improved fluid movement through a collagen-rich tumour-like matrix and increased gemcitabine delivery. Such experiments cannot predict what will happen in every patient, but they provide a possible mechanism for how acoustic forces might influence drug distribution. The broader lesson is more interesting than any single trial. Ultrasound does not necessarily have to replace a cancer treatment to make a difference. It may instead change the physical conditions under which that treatment operates. In pancreatic cancer, that means trying to make a difficult tumour more accessible to chemotherapy. In the brain, the barrier is even more formidable. There, the problem is not simply dense tumour tissue. It is a biological security system designed to keep many drugs out. The next question is whether ultrasound can open that barrier.

OPENING THE BRAIN'S LOCKED DOOR. The brain has its own defence system against the outside world. The blood-brain barrier (BBB) is formed largely by specialised endothelial cells lining cerebral blood vessels, supported by surrounding cells and tightly regulated junctions. It protects neural tissue from many potentially harmful substances in the bloodstream. For medicine, however, the same protection creates a formidable problem. Many drugs that could potentially



treat brain tumours do not cross the barrier in sufficient amounts. Researchers therefore began asking whether ultrasound could open the barrier temporarily rather than trying to bypass it permanently. The crucial ingredient was the microbubble. When microbubbles circulating in the bloodstream are exposed to focused ultrasound, they oscillate in response to the acoustic pressure. Their mechanical movement can exert forces on nearby blood vessels and temporarily increase permeability. Importantly, the goal is not to destroy the barrier. It is to create a controlled opening that subsequently closes.

On 5 November 2015, researchers at Sunnybrook Health Sciences Centre in Toronto reported the first non-invasive temporary opening of the human BBB using focused ultrasound and microbubbles. Kullervo Hynynen and Nir Lipsman led the work, which was carried out in patients with glioblastoma. It was a proof of principle, but an important one. A structure that had long been regarded primarily as an obstacle to drug delivery could be manipulated temporarily and locally using externally delivered acoustic energy. The concept has since moved beyond experimental demonstrations. One approach developed by Alexandre Carpentier and colleagues uses an implantable device called SonoCloud-9, containing nine ultrasound emitters positioned beneath the skull. In a phase I/II clinical trial published in 2024, patients with recurrent glioblastoma received repeated blood-brain barrier opening in combination with carboplatin chemotherapy.

Across 90 monthly sonication procedures, MRI evidence of blood-brain barrier disruption was observed in 90% of evaluated treatments in which the activated emitters could be assessed. The study also found substantially higher carboplatin concentrations in sonicated peritumoural brain tissue in exploratory pharmacokinetic measurements.

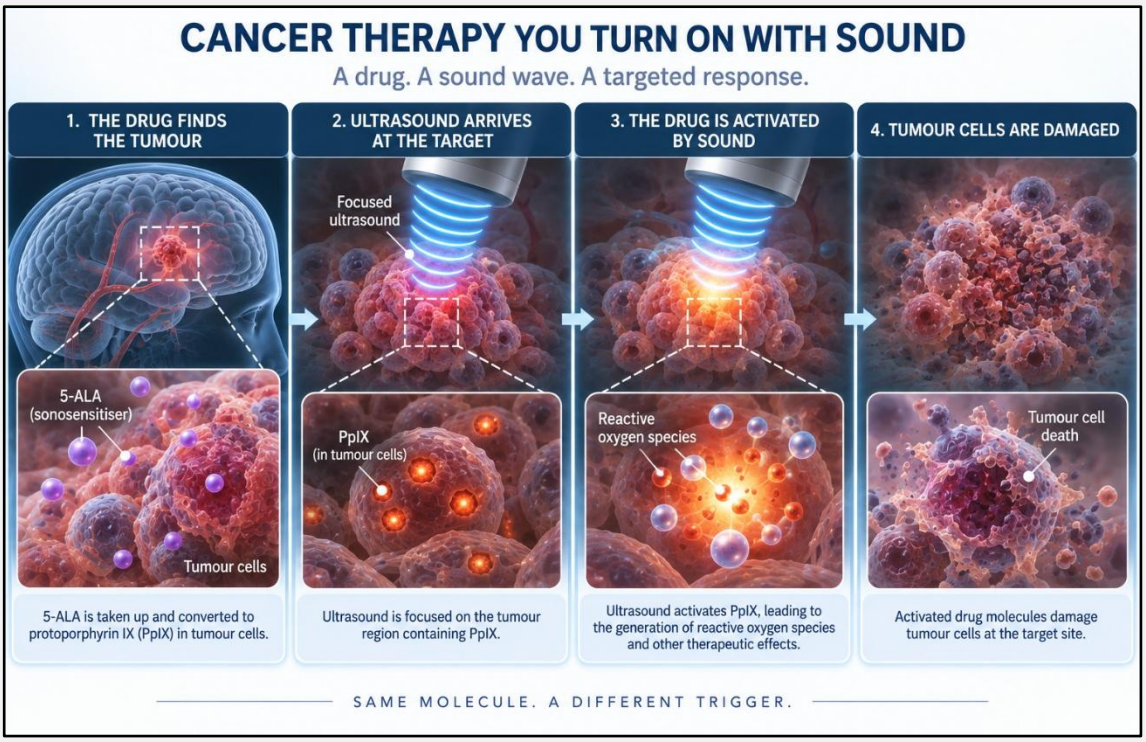
But the distinction between *reaching the tumour* and *treating the tumour* remains critical. These studies demonstrated that the barrier could be opened and that drug exposure could be increased. They did not definitively show that ultrasound-mediated BBB opening improves survival in glioblastoma. That distinction is central to the field. A drug cannot help a tumour if it cannot reach it, but increased delivery does not automatically translate into better clinical outcomes. Safety is therefore as important as access. The acoustic exposure must be controlled closely enough to produce the desired vascular response without causing unwanted injury. Researchers are developing methods to monitor acoustic emissions from the bubbles during treatment, helping distinguish controlled bubble activity from potentially damaging cavitation.

Instead of asking a molecule to defeat the brain's security system, researchers are trying to make that system open a door briefly, at a defined location and under controlled conditions. But once that door opens, another possibility emerges. What if ultrasound could do more than help a treatment reach the tumour? What if it could help activate the treatment once it got there?

CANCER THERAPY YOU TURN ON WITH SOUND.

Getting a treatment into a tumour is only one part of the problem. Another is making sure that it becomes active where it is needed. Sonodynamic therapy takes a different approach. It uses a compound called a sonosensitiser that ultrasound can activate, generating biological effects that can damage tumour cells. The concept resembles photodynamic therapy, in which light activates a photosensitising molecule, but ultrasound offers a potential advantage: acoustic energy can be focused into tissues that light cannot reach.

One of the most interesting candidates is 5-aminolevulinic acid (5-ALA). In malignant glioma cells, 5-ALA is metabolised to protoporphyrin IX, or PpIX. Neurosurgeons already use this property during fluorescence-guided surgery, because PpIX accumulates preferentially in many malignant glioma



cells and fluoresces under appropriate illumination.

Researchers have asked a provocative question: if PpIX can help identify tumour cells, can ultrasound also activate a therapeutic response in those same cells? The proposed mechanisms are complex. Ultrasound, particularly when mechanical effects such as cavitation are involved, can generate conditions that promote the formation of reactive oxygen species. Sonoluminescence, mechanical effects and other chemical pathways have all been proposed, but the precise mechanism of sonodynamic activation remains an active area of investigation.

The idea reached patients in an early clinical study reported in 2025 by Nader Sanai and colleagues at the Ivy Brain Tumour Centre at Barrow Neurological Institute. Nine patients with recurrent high-grade glioma received intravenous 5-ALA followed by MRI-guided focused ultrasound at escalating acoustic exposures. The study was designed primarily to establish feasibility and investigate biological effects, not to prove that the treatment prolongs survival. The researchers found no drug- or device-related toxicities attributable to the treatment and examined differences between sonicated and untreated tumour regions, including pharmacokinetics and markers associated with oxidative stress and cell death. That distinction matters. A biological response is not the same thing as tumour control. Tumour control is not the same thing as improved survival. Early clinical studies can show that a treatment reaches its intended target and produces the expected biological effect without demonstrating longer survival. And 5-ALA is only one example.

Researchers are exploring other sonodynamic approaches using different therapeutic molecules and delivery systems. Early human studies outside the brain remain exploratory, while most of the wider sonodynamic therapy literature is still preclinical. What makes the field interesting is not that sound has suddenly become a new chemotherapy. It is that ultrasound offers something drugs alone cannot easily provide: a physical signal delivered to a selected region at a selected time. The role of sound has changed again. It is no longer simply heating tissue or helping a drug cross a barrier. It is becoming a way of telling a therapeutic system when and where to act. And if ultrasound can control a therapeutic molecule, researchers can ask an even more ambitious question: Could sound control something alive?

WHEN ULTRASOUND TALKS TO IMMUNE CELLS.

CAR-T therapy has transformed the treatment of some blood cancers. The approach involves removing T cells from a patient, genetically engineering them to recognise a chosen target and returning them to the body, where they can seek out and destroy cells carrying that target. Solid tumours are a much harder problem. A tumour is not simply a collection of identical target cells. Cancer cells can vary from one region to another, the tumour may physically restrict immune-cell movement, and its local environment can suppress immune function. Choosing a target can also risk damaging healthy cells that carry the same molecule. Researchers are therefore exploring whether ultrasound could help control where an immune response is activated.

In a 2026 study published in *Nature Materials*, researchers including Chi Woo Yoon, Yingxiao Wang, and colleagues developed a system in which focused ultrasound activated a genetic circuit inside tumour cells. But one important detail: ultrasound did not simply make ordinary cancer cells express a CAR-T target. The tumour cells had first been equipped with genetic machinery designed to respond to mechanical stimulation. When focused ultrasound was applied, the engineered circuit responded through calcium signalling and activated an AND-gated genetic programme. This caused a subset of the tumour cells in the sonicated region to display CD19, a molecule recognised by CD19-directed CAR-T cells. The result

was conceptually different from conventional CAR-T therapy. Instead of relying entirely on a tumour-wide marker that may be absent from some cancer cells, the researchers attempted to create local "training centres" within the tumour. Ultrasound defined the region in which the engineered programme was activated, while the induced CD19 signal provided a target for the CAR-T cells. The approach produced tumour-suppressive effects in cell experiments, tumour organoids and animal models. But this is an important boundary: the work was *preclinical*. It has not shown that ordinary human tumours can be controlled this way, and the system first requires delivering the necessary genetic machinery to tumour cells.

A second study published in *Science Advances* in 2026 pushed the concept further. The researchers developed a system called SHIFTERS, in which ultrasound activation was gated by features associated with the tumour environment, including hypoxia. In experimental models, this helped restrict activation of the engineered programme and guide CAR-T-mediated tumour suppression.

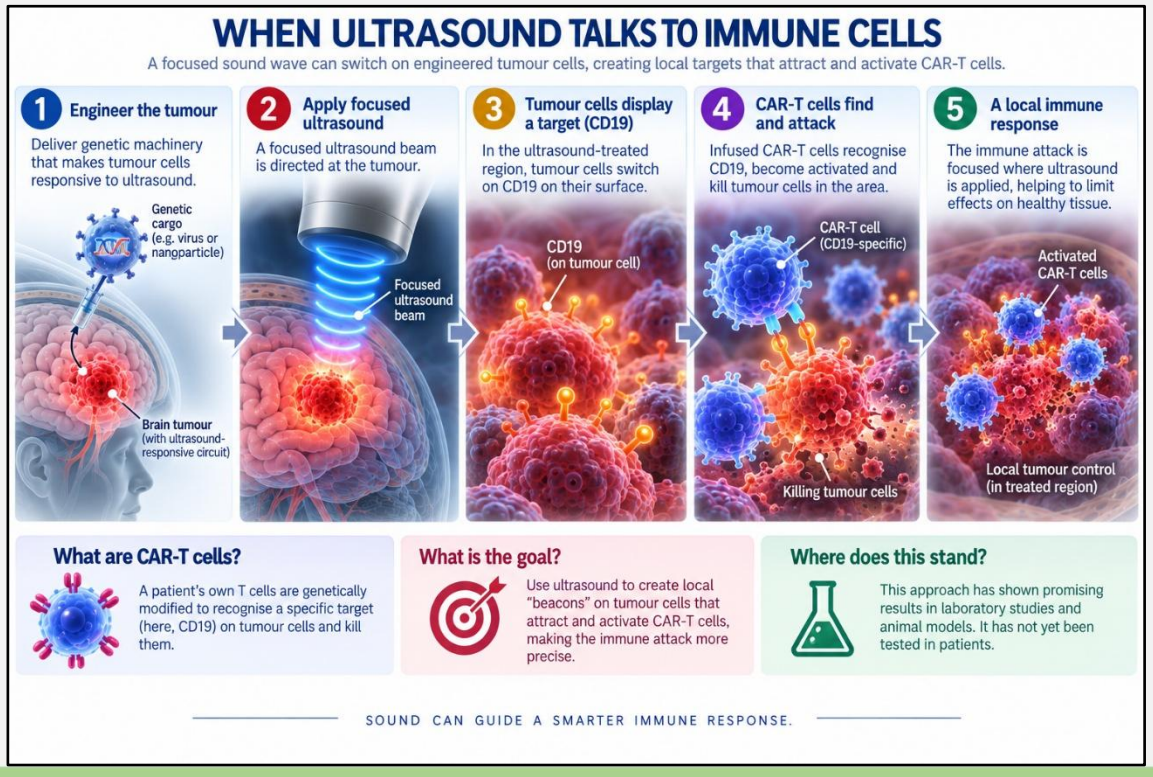
These experiments point towards a new role for ultrasound. The sound wave is no longer being used simply to destroy tissue or help a drug enter it. It is being used as a control signal for an engineered biological system. The concept is powerful, but the practical challenges are substantial. The genetic components must reach the appropriate tumour cells. Ultrasound must activate them where intended without affecting healthy tissue. CAR-T cells must still enter the tumour, remain functional and respond effectively. Every additional biological component also introduces another layer of safety and manufacturing complexity.

For now, this remains experimental biology rather than clinical therapy. But it changes the question we can ask of ultrasound. Instead of asking only, "What can sound do to tissue?", researchers can now ask: *Can sound tell an engineered biological system what to do, and where to do it?* That is a very different kind of medicine.

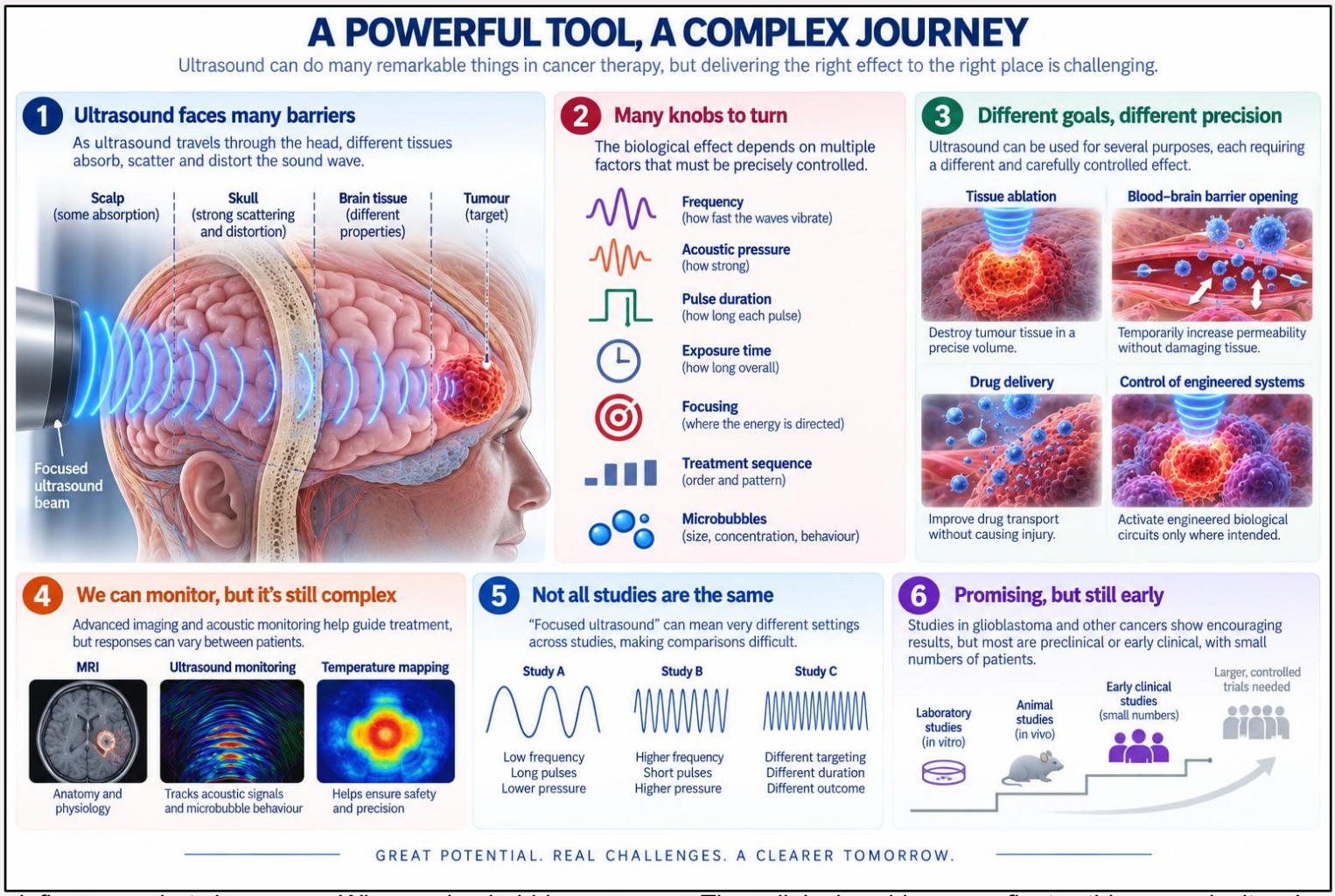
ONE BEAM, DIFFERENT JOBS. By now, ultrasound no longer looks like a single treatment. Across these examples, the same physical tool has been given very different jobs: destroying tissue, changing the tumour environment, opening the blood-brain barrier, activating therapeutic molecules and, in experimental systems, controlling engineered biological circuits. These approaches are not interchangeable, and they do not all belong to the same stage of development. Some focused ultrasound applications are already established clinical treatments. Others are being investigated in early human studies, while the most ambitious approaches remain preclinical.

What connects them is not a single biological mechanism, but a way of working. Ultrasound can deliver a physical signal to a selected region of the body and control it over time. The sound wave itself is not necessarily the treatment. It can control when and where a biological effect occurs.

THE PRECISION PROBLEM. If ultrasound can destroy tissue, open the blood-brain barrier, improve drug delivery and even control engineered biological systems, why is it not already routine treatment for every difficult tumour? Because controlling sound inside the human body is harder than controlling it in a laboratory.



Ultrasound does not travel through the body as though it were moving through a uniform material. Bone, blood, muscle, fat and tumour tissue all interact with acoustic waves differently. The skull presents an additional challenge in the brain, because it can absorb, scatter and distort the acoustic field before it reaches its target. Even when the intended target is reached, the biological response is not determined by one variable. Frequency, acoustic pressure, pulse duration, exposure time, focusing and treatment sequence can all



influence what happens. When microbubbles are involved, their size, concentration and behaviour within individual blood vessels add another layer of variability.

For tissue ablation, the goal is controlled destruction of a defined volume. For blood-brain barrier opening, the desired effect is temporary increased permeability without damaging the underlying tissue or blood vessels. For drug delivery, the challenge is to improve transport without causing unwanted injury. For experimental mechanogenetic systems, the requirements become even more demanding: the acoustic signal must activate the engineered system where intended while leaving surrounding tissue unaffected.

Researchers are developing increasingly sophisticated methods to measure acoustic emissions, temperature changes, tissue responses and microbubble behaviour during treatment. MRI can provide anatomical and physiological information, while acoustic monitoring can help identify how bubbles are responding to the ultrasound field. Standardisation is another challenge. Two studies may both describe their treatment as "focused ultrasound" while using substantially different frequencies, pressures, pulse structures, treatment durations or targeting strategies. Comparing their results is therefore not always straightforward.

The clinical evidence reflects this complexity. In glioblastoma alone, a 2026 systematic review identified studies spanning preclinical experiments and early clinical trials, but the number of treated patients remains small relative to established cancer therapies. Larger, well-controlled studies are still needed to determine which approaches improve meaningful clinical outcomes and which mainly demonstrate that a biological effect is possible.

The question is no longer whether ultrasound can affect living tissue. That has been demonstrated repeatedly. The harder question is whether researchers can control those effects reliably enough that a clinician can reproduce the intended therapeutic response from one patient to the next. That is what will determine whether therapeutic ultrasound becomes a collection of specialised procedures or a broader medical platform.

WHERE SOUND GOES NEXT. Ultrasound began in medicine as a way of seeing what was hidden inside the body. Today, researchers are learning to use the same physical phenomenon to do much more. Focused acoustic energy can destroy tissue. Microbubbles can alter blood vessels and help therapies reach difficult targets. The blood-brain barrier can be opened temporarily. Sonosensitisers can be activated deep inside tissue. In some of the most

experimental work, ultrasound is even being connected to engineered genetic circuits and immune cells. These approaches do not all belong to the same stage of medicine. Some are established clinical technologies. Others are being tested in early human studies, while several remain entirely preclinical.

The major challenge now is not demonstrating that ultrasound can affect biology. It is making those effects sufficiently controlled, reproducible and safe to become dependable medicine. That does not necessarily mean ultrasound will replace surgery, chemotherapy, radiotherapy or immunotherapy. Its value may instead be in giving those treatments something they have often lacked: greater control over where and when they act.

The field is moving towards a different idea of what ultrasound can be. It is no longer simply a tool for imaging, nor merely a source of heat. It is becoming a way of interacting with living tissue through carefully controlled physical forces. We once used sound to look inside the body. Now we are learning how to make the body respond to it.

Suggested Reading

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SCIENCE SHAPERS
Prof. Kullervo Hynynen

Temerty Chair in Focused Ultrasound Research
Professor, Department of Medical Biophysics
Cross-Appointed Professor, Institute of Biomedical Engineering, University of Toronto
Senior Scientist, Physical Sciences Odette Cancer Research Program
Sunnybrook Research Institute
Toronto, Ontario, Canada
Email: khynynen@sri.utoronto.ca
Webpage: https://research.sunnybrook.ca/researchers/kullervo-hynynen/

Some of the most transformative medical technologies begin with a deceptively simple question: can something already familiar be used in a completely different way? Ultrasound had long been one of medicine's most useful tools for seeing inside the human body without surgery or ionising radiation. But Kullervo Hynynen saw a much larger possibility. If sound waves could travel deep into the body and be focused with sufficient precision, perhaps they could do more than create images. Perhaps they could deliberately change tissue, deliver therapies, and eventually control biological processes without an incision.

Hynynen's scientific career has focused on turning that possibility into reality. After completing his PhD at the University of Aberdeen in the United Kingdom, he developed a research programme centred on biomedical ultrasound and its interaction with living tissues. His work brought together physics, engineering, medical imaging, biology, and clinical medicine, reflecting a central feature of his scientific approach: solving difficult medical problems often requires looking beyond the boundaries of a single discipline. Over more than three decades, he has helped transform focused ultrasound from an experimental technology into a sophisticated platform for non-invasive medicine. He is now the Temerty Chair in Focused Ultrasound Research and Professor in the Department of Medical Biophysics at the University of Toronto, while also serving as a Senior Scientist at Sunnybrook Research Institute in Toronto.

The fundamental idea behind focused ultrasound is elegant. Instead of allowing acoustic energy to spread broadly through tissue, multiple ultrasound waves can be concentrated at a selected location, producing a much stronger effect at the focal point. Depending on how the acoustic energy is delivered, it can generate heat sufficient to destroy tissue or produce mechanical effects that influence cells and blood vessels. Hynynen's research helped develop increasingly precise methods to target and monitor these effects, including MRI-guided focused ultrasound. This work contributed to the emergence of non-invasive treatments that allow physicians to reach structures deep inside the body without physically entering them. One important clinical example is focused ultrasound treatment for essential tremor, in which acoustic energy is concentrated on a precisely selected region of the brain to produce a therapeutic effect without conventional brain surgery.

Perhaps the most remarkable extension of this work emerged from a problem that has frustrated neurological medicine for decades: the blood-brain barrier. This specialised vascular interface protects the brain from potentially harmful substances circulating in the bloodstream, but it also prevents many therapeutic drugs from reaching brain tissue in sufficient concentrations. Hynynen and his collaborators showed that focused ultrasound, combined with circulating microscopic gas-filled microbubbles, could temporarily increase blood-brain barrier permeability at a selected location. In 2015, researchers at Sunnybrook reported the first non-invasive temporary opening of the human blood-brain barrier using this approach in patients with

glioblastoma. Rather than destroying the barrier, the goal was to create a controlled opening that could subsequently close, providing a potential route for delivering treatments that would otherwise have difficulty entering the brain.

The implications of this discovery extend far beyond simply making a drug enter the brain. It introduced a different way of thinking about therapeutic delivery: instead of designing every treatment around the body's biological barriers, perhaps some barriers could be temporarily and precisely manipulated. This concept has since expanded into clinical research involving brain tumours and neurological disorders, while Hynynen's programme has continued to investigate focused ultrasound for drug delivery, cancer therapy, gene therapy, vascular interventions, and regenerative medicine. His work therefore illustrates how a physical phenomenon can become a biological tool when researchers learn to control its intensity, timing, location, and interaction with tissue.

Cancer has become an especially important area of this research. In glioblastoma, for example, researchers are investigating focused ultrasound and microbubbles to improve chemotherapy delivery by temporarily modifying the blood-brain barrier around the tumour. In 2025, a Sunnybrook-led clinical study reported encouraging evidence that combining focused ultrasound with chemotherapy could extend survival in patients with glioblastoma, showing how decades of work in ultrasound physics and engineering can eventually reach clinical testing. At the same time, researchers worldwide are exploring even more ambitious possibilities, including ultrasound-assisted drug delivery, sonodynamic therapy, and approaches that use ultrasound to control engineered biological systems and immune responses.

What makes Hynynen's scientific journey particularly remarkable is that ultrasound has gradually acquired entirely different roles. It can destroy tissue through focused heating, alter blood vessels through mechanical forces, improve the delivery of therapeutic molecules, and temporarily open the blood-brain barrier. Emerging research is now asking whether acoustic energy can also serve as a signal that tells engineered cells or therapeutic systems when and where to act. The field is therefore moving beyond the idea of ultrasound as simply an imaging or ablative technology and towards the possibility of using carefully controlled sound as an interface between physical energy and biology.

Hynynen's contribution extends beyond his own discoveries. Over the course of his career, he has mentored more than 100 graduate students and postdoctoral researchers, many of whom have gone on to careers in academia, industry, healthcare, and medical technology. His approach to mentorship has emphasised recognising individual trainees' strengths and interests and helping them develop those strengths through research. This is particularly relevant to a field such as focused ultrasound, where physicists, engineers, biologists, clinicians, imaging specialists, and computational scientists must work together to solve problems that no single discipline can address alone.

Today, Hynynen's research programme remains active at the University of Toronto and Sunnybrook Research Institute, where focused ultrasound research continues to expand across oncology, neuroscience and several other areas of medicine. Sunnybrook was renewed in 2026 as a global Centre of Excellence in Focused Ultrasound, reflecting the institution's continuing work in discovery science, technology development, and clinical translation. For young researchers, his career offers a valuable example of how fundamental science can move across disciplinary boundaries and eventually become a medical technology that can be tested in patients.

Earlier in this issue of *Science Prism*, we explored how ultrasound is evolving from a technology used primarily to see disease into one capable of interacting with living tissue in increasingly sophisticated ways. Kullervo Hynynen's career provides a remarkable thread through that transformation. His work demonstrates that the boundary between physics and medicine can be surprisingly productive: a question about how sound waves interact with tissue can ultimately lead to new approaches for treating cancer, reaching the protected brain, and manipulating biological processes without conventional surgery.

Perhaps the most inspiring lesson from Hynynen's career is that scientific innovation does not always require inventing an entirely new phenomenon. Sometimes it begins by looking at something familiar and asking a different question about what it can do. Ultrasound was already an extraordinarily powerful tool for seeing inside the body; the challenge was to discover whether it could also be controlled well enough to change what was happening there. For the next generation of researchers, that lesson extends far beyond ultrasound. The technologies already around us may contain possibilities we have not yet imagined, waiting for someone curious enough to ask the next question.

Dr. Kaushik P Sharma

Dr. Kanchan Bisht

Dr. Shreesh Raj Sammi

Dr. Manju Tewari

ABOUT THE TEAM:

Dr Kaushik P. Sharma and Dr Kanchan Bisht are neuroscientists at the Department of Neurology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun. With over a decade of extensive research experience at renowned institutions in India, Europe, Canada, and the USA, they are dedicated to making science accessible and inspiring the next generation of thinkers, innovators, and problem solvers.

Dr Shreesh Raj Sammi, an Assistant Professor in the Department of Translational Neuroscience at Michigan State University, USA, brings his expertise in neurotoxicology and neurodegenerative disorders to the team. In addition to his research pursuits, Dr Sammi is deeply committed to training the next generation of researchers and making science accessible to diverse audiences.

Dr Manju Tewari, an Assistant Professor at Kumaun University, is a neuroscientist specialising in neuron–glial interactions, microglial biology, and neuroinflammation. With training at NBRC, India, and postdoctoral research at Saint Louis University, USA, she brings strong expertise in cellular and molecular neuroscience and is dedicated to advancing research and mentorship in Uttarakhand.

This newsletter is our humble effort to empower readers with insights into scientific breakthroughs and foster a foundational understanding of nature, health, and science. We hope it sparks curiosity and supports students, educators, and young researchers in their journeys.

We'd truly love to hear from you. Your thoughts, questions, and reflections are greatly appreciated. Your feedback not only helps us grow but also motivates us to keep moving forward with these small but heartfelt efforts. Let's make Science Prism a two-way conversation where curiosity flows both ways.

Stay curious, stay connected.

– The Science Prism Team.

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