Maryland man with fatal brain cancer lives, sparking hope for an experimental treatment to better guide chemo to tumors

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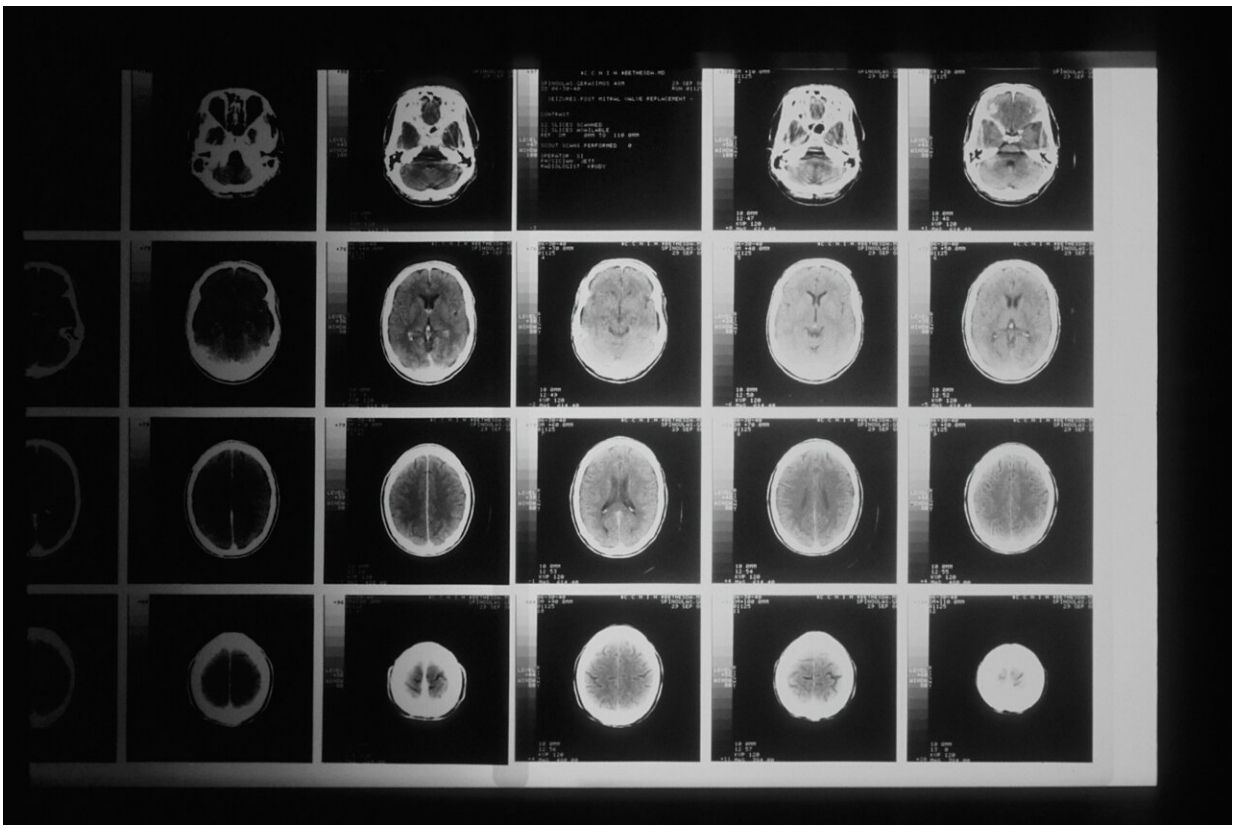

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The brain cancer diagnosis was so grim for Rick Miller that he says a social worker told him to "get my affairs in order." Glioblastomas

typically kill people in about 12 to 15 months.

But that was not the end of Miller's journey. He and his wife, Diana, took a trip from their Eastern Shore home to the University of Maryland Medical Center in Baltimore to hear other options and signed up for a clinical trial.

That was three years ago.

Miller, 65, isn't just alive. There is no sign of cancer, and he's getting back to his boat maintenance business. Two months ago, he and Diana traveled to their son's wedding in Florida.

"It worked," declared a smiling Miller, standing in front of his next boat project, his own 40-footer, at his property near Chestertown.

His doctors can't say he's cured, nor guarantee the cancer won't return or even yet officially credit the treatment he received in the clinical trial for his life and health. But, they say, he and most of the 14 people who participated in the initial study are alive. After years with little progress in discovering new treatments for glioblastomas, they are in the unusual position of having hope.

Glioblastomas are the kind of brain cancer that killed U.S. Sens. Ted Kennedy and John McCain and President Joe Biden's son Beau. They are normally treated with surgery, chemotherapy and radiation, but the tumors almost always come back. Federal figures show about 14,000 people a year are diagnosed in the United States, but as few as 5% survive five years, according to the Glioblastoma Foundation.

The foundation cites the method used on Miller, focused ultrasound, as one of only a few avenues of promising research. Others include repurposing older drugs and earlier detection.

Miller was receiving standard care when he entered the Phase 1 trial. Such trials are intended to assess safety and show whether a process works. Surgeons on the Eastern Shore already had removed a large, late-stage tumor from the right side of Miller's brain in 2019.

At the Baltimore hospital, neurosurgeon Dr. Graeme F. Woodworth and medical staff secured Miller's head with a metal halo and screws. They put him in a magnetic resonance imaging, or MRI, machine and injected a bubbling agent into his arm. Then they used ultrasound, or high-frequency sound waves, to guide the tiny bubbles to the precise site and shape of the tumor.

Woodworth watched images from the MRI on a computer screen from a control room as the commotion from the bubbles created temporary leaks in the protective layer around the brain known as the blood-brain barrier. The barrier of cells and blood vessels normally protects the brain from toxins, but it also blocks helpful therapeutics.

The openings lasted hours, long enough for Miller to return home and follow separate instructions from his cancer doctors for taking standard chemotherapy pills.

He returned monthly for more focused ultrasound treatments.

Woodworth has not yet submitted findings in a peer-reviewed journal, but he is working with pharmaceutical leaders and seeking funding for more and bigger trials to learn more about the efficacy of the technique and get it approved by the U.S. Food and Drug Administration for wider use. They also are working to determine whether there are more effective drugs generally or that help people with different types of glioblastomas.

"All we can say now is that we did it safely," said Woodworth, also a

professor and chair of neurosurgery in Maryland's School of Medicine. "Today, it feels promising. But we need more proof."

Already doctors have refined the process of shaping the opening to the tumor site and eliminated that immobilizing metal halo, which Miller called the worst part of the trial.

Focused ultrasound is a growing area of research, with more than a dozen companies investing nearly $400 million last year to potentially deliver better treatment for multiple kinds of cancers, not all in the brain, according to the Focused Ultrasound Foundation.

Woodworth is working with an Israeli medical device company, Insightec Ltd., that developed the tools for the procedure.

Three years in, the Millers couldn't be more pleased with the results, whether they're due to the trial, really successful surgery or his general good health before his cancer diagnosis.

The absence of Miller's cancer has been confirmed in regular scans by Dr. Mark Mishra, University of Maryland School of Medicine's director of clinical research and associate director for the hospital system's cancer network. He presented the trial option to the couple.

"As soon as I mentioned it, they were both very interested and were among the first enrolled," Mishra said about Miller and his wife, who is a nurse. "He stands out because he's done so well. He's not had any recurrence, but more importantly, he's maintained his quality of life and is getting back out and doing things he used to do before his cancer diagnosis."

Mishra noted the "tough talks" they had before the treatment about the diagnosis and the rarity of long-term survival. Now, he said, "Mr.

Miller's case shouldn't be a unique one, and the only way to raise that bar is through clinical trials."

He said they will happen at Maryland, other universities and the National Institutes of Health, and doctors will look at different types of drugs for new or recurrent tumors, as well as for different subtypes of glioblastomas. Because there can be different molecular features at different stages in different patients, they may be treated uniquely in the future, in a move toward personalized, or precision, medicine.

There also are other focused ultrasound trials planned unrelated to Maryland's trials, including at Johns Hopkins Medicine.

Dr. Chetan Bettegowda, a Hopkins neurosurgeon-scientist, is working on those trials. He said he and Woodworth informally share some information about the technology to advance the research and are collaborating in a separate trial in another area.

Bettegowda said news of Miller's health was "truly remarkable," and said focused ultrasound had the potential to be a "paradigm shift " in treatment for glioblastomas.

"We've long understood the brain has natural mechanisms to prevent drugs from entering, and we've tried other ways, such as with catheters or polymers or local injection into the brain after surgery," he said.

"Some have shown some effects, but unfortunately not sufficient effects to cure large numbers of people," he said. "That's where having something like this that is noninvasive and can be done repeatedly and be focused and tuned to individual tumors is quite powerful. There is a lot of enthusiasm about this."

The area where Bettegowda and Woodworth are collaborating involves

improving the assessment of how well treatment is working. For now, that's limited to the occasional MRI. That's because biomarkers from tumor cells, which could offer more information, are blocked by the blood-brain barrier from entering the body's circulation, where they could be picked up in a blood test.

Focused ultrasound could provide the openings for that blood test—or liquid biopsy—showing how tumor cells are responding down to their DNA to chemotherapy, radiation or other treatment.

The possibility to offer better outcomes, Bettegowda said, is what keeps him going into the operating room and the lab.

Diana and Rick Miller are glad for the research, though they hope Rick never needs another trial.

Diana Miller, who is being treated for breast cancer, remembered how her husband passed out several times while on an earlier trip to Florida, episodes she initially thought were related to his heart. After they returned home, he texted gibberish to his wife during another episode. At that point, she rushed him to an emergency room and they learned about the advanced tumor soon after.

She's thankful to the doctors on the shore and in Baltimore and also their network of friends providing support. She specifically noted those who helped move their customers' boats to and from the water for maintenance and storage.

Rick Miller plans to continue some work, but expects to sell some stock from his shop and yard and head closer to retirement. He can't manage 12-hour days anymore at Miller's Marine, the business he built over the past couple of decades between the Chester River and the Chesapeake Bay.

His mind, however, still knows his way around a boat's engine, HVAC unit and electrical systems. He'll tap that knowledge to restore the 40-foot boat he keeps in a large shed across from his house for "when he wakes up with a little more ambition."

For now, the couple's journey continues on a 17-foot boat Rick gave Diana awhile back and taught her how to operate. They often take it out to enjoy the evening together and let their dog swim.

"It's my wife's boat," he said, "but sometimes she takes me."