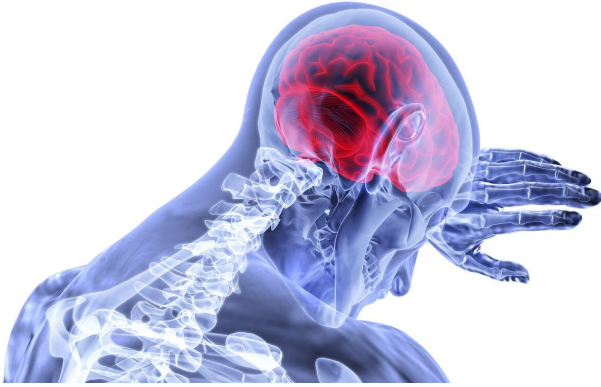


# Ultrasound blasts potent glioblastoma drug into brain tumor

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One of most potent drugs for treatment of glioblastoma, the most deadly type of brain tumor, can't be used in patients because of two problems. First, it can't reach its target because it's blocked by the blood-brain barrier, a microscopic structure that protects the brain from toxins in the blood. And the conventional formulation for this drug is toxic to the brain.

But now Northwestern Medicine scientists have used a novel technology for opening the [blood-brain barrier](#) with an implantable [ultrasound](#), and have delivered the powerful drug to the tumor in mice. In a new paper, they report on their findings of extensive preclinical research.

The scientists also discovered [brain](#) toxicity for the conventional formulation for this drug—paclitaxel—to the brain was caused by the solution required to dissolve the drug (cremophor.) Scientists tested a new formulation of the drug that uses albumin as opposed to cremophor, and it was not harmful to the brain.

Opening of the blood-brain barrier with an ultrasound increased the concentrations of this

paclitaxel in the brain by five-fold. The study also showed that the brain tumor-bearing mice live much longer when treated with the powerful cancer-fighting drug paclitaxel, and survival was even further extended when treated in combination with ultrasound to open the blood-brain barrier.

The study will be published Dec. 12 in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

In the laboratory, paclitaxel is much more potent than the currently used chemotherapy temozolomide. When paclitaxel was tested against the brain tumor in a dish outside an organism, a 1,400-fold lesser drug concentration was necessary to kill same number of tumor cells, compared to the conventional chemotherapy used for this cancer.

The scientists are now applying to the U.S. Food & Drug Administration to launch a clinical trial to test this concept of a new formulation of paclitaxel in combination with the novel ultrasound technology to open the blood-brain barrier in patients. The planned trial aims to determine if the treatment is safe, and if it prolongs survival of patients with brain cancer.

"Glioblastoma currently has no cure, and when the [tumor](#) recurs there are not many treatment options," said the principal investigator for this study, Dr. Adam Sonabend, an assistant professor of neurological surgery at Northwestern University Feinberg School of Medicine and a Northwestern Medicine physician. "We urgently need effective new treatments."

The ultrasound technology may have broader benefits. "This ultrasound technology now will enable us to use many agents established in other cancers for patients with brain tumors," said co-investigator Roger Stupp, chief of neuro-oncology and the Paul C. Bucy Professor of Neurological Surgery at Feinberg.

Other [clinical trials](#) are testing ultrasound-based opening of the blood brain barrier with various chemotherapy agents, but none are using such a potent drug as paclitaxel.

### How does it work?

The tiny ultrasound would be implanted during surgery into a window in the skull that does not contain bone. It is used in combination with microscopic gas bubbles injected into the blood at the same time the ultrasound begins. When the bubbles hit the sound waves, these vibrate and mechanically disrupt the blood-brain barrier. The opening is immediate, allowing penetration of the drug molecules. The blood-brain [barrier](#) opening is reversible and lasts for several hours after the sonication. The ultrasound emitter remains in the skull for repeated delivery of the [drug](#).

**More information:** Daniel Y. Zhang et al.

Ultrasound-mediated Delivery of Paclitaxel for Glioma: A Comparative Study of Distribution, Toxicity, and Efficacy of Albumin-bound Versus Cremophor Formulations *Clinical Cancer Research*. Published OnlineFirst December 12, 2019. [DOI: 10.1158/1078-0432.CCR-19-2182](#)

Provided by Northwestern University

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