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## MR-Guided Ultrasound Delivers Antibody Therapy to Brain Tumours



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Canadian researchers at Sunnybrook Health Sciences Centre, safely delivered trastuzumab antibody therapy to breast cancer brain metastases using magnetic resonance (MR)-guided focused ultrasound. This study provides the first visual confirmation that focused ultrasound can improve the delivery of targeted antibody therapy across the blood-brain barrier (BBB).

The team used MR to guide a focused ultrasound device, Insightec's Exablate Neuro, to open the BBB and allow intravenous trastuzumab to effectively reach Her2-positive brain tumours. The BBB presents a challenge for developing central nervous system (CNS) therapeutics because it transforms the CNS into an immunologically and pharmacologically privileged compartment. Antibodies do not normally cross the BBB, so treating Her2-positive brain tumours with trastuzumab is problematic, unless there the BBB can be made permeable. Furthermore, surgical or radiation options for brain tumours are highly invasive if available. The research team's method of inducing BBB permeability has the advantage of being localised, temporary, and non-invasive.

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Trastuzumab delivery into the tumour sites was confirmed using  $^{111}\text{In}$ -BzDTPA-NLS-trastuzumab SPECT imaging. Four patients with Her2-positive breast cancer brain metastases were enrolled in a clinical trial, phase 1, single-arm open-labelled study. Patients received 20 treatments consisting of MR-guided focused ultrasound along with intravenous trastuzumab-based therapies. No treatment-related serious adverse events occurred. With treatment, tumour measurements decreased by  $19 \pm 12\%$ .

This study shows the promise of this approach for CNS drug delivery. The technology can be applied to many CNS diseases where efficacious drugs for other organ compartments exist but cannot be used in the CNS because of poor BBB permeability.

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