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# A Scoping Review of Focused Ultrasound Enhanced Drug Delivery for Across the Blood-Brain Barrier for Brain Tumors

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## Abstract

**Background and objectives:** Previous mechanisms of opening the blood-brain barrier (BBB) created a hypertonic environment. Focused ultrasound (FUS) has recently been introduced as a means of controlled BBB opening. Here, we performed a scoping review to assess the advances in drug delivery across the BBB for treatment of brain tumors to identify advances and literature gaps.

**Methods:** A review of current literature was conducted through a MEDLINE search inclusive of articles on FUS, BBB, and brain tumor barrier, including human, modeling, and animal studies written in English. Using the Rayyan platform, 2 reviewers (J.P and C.Y) identified 967 publications. 224 were chosen to review after a title screen. Ultimately 98 were reviewed. The scoping review was designed to address the following questions: (1) What FUS technology improvements have been made to augment drug delivery for brain tumors? (2) What drug delivery improvements have occurred to ensure better uptake in the target tissue for brain tumors?

**Results:** Microbubbles (MB) with FUS are used for BBB opening (BBBO) through cavitation to increase its permeability. Drug delivery into the central nervous system can be combined with MB to enhance transport of therapeutic agents to target brain tissue resulting in suppression of tumor growth and prolonging survival rate, as well as reducing systemic toxicity and degradation rate. There is accumulating evidence demonstrating that drug delivery through BBBO with FUS-MB improves drug concentrations and provides a better impact on tumor growth and survival rates, compared with drug-only treatments.

**Conclusion:** Here, we review the role of FUS in BBBO. Identified gaps in the literature include impact of tumor microenvironment and extracellular space, improved understanding and control of MB and drug delivery, further work on ideal pharmacologies for delivery, and clinical use.

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