# Focused Ultrasound in Brain Tumor Treatment



*Summary and findings of: Nabavizadeh A, Narsinh K, Kaufmann TJ, Liu H, Pouliopoulos AN, Prada F, Agarwal V, Ellingson BM, Sanvito F, Everson RG, Meng Y, Gandhi D, Chang SM, Wen PY, Ahluwalia MS, Sul N, Hadley L, Leblang S, Shah BR, Arvanitis CD, Burns TC, Moosa S, Woodworth GF. Focused Ultrasound in Brain Tumors: Mechanisms, Imaging Guidance, and Emerging Clinical Applications. AJNR Am J Neuroradiol. 2025 Dec 5:ajnr.A9126. doi: 10.3174/ajnr.A9126. PMID: 41360502.*

Based on the provided citation, here is a summary and key findings of the review article **"Focused Ultrasound in Brain Tumors: Mechanisms, Imaging Guidance, and Emerging Clinical Applications"** by Nabavizadeh et al., published in *AJNR* in December 2025.

## Overall Summary

This comprehensive review article synthesizes the current state of focused ultrasound (FUS) technology for the treatment of brain tumors. It moves beyond the well-known application of blood-brain barrier opening (BBBO) to detail the full spectrum of FUS mechanisms, the critical role of advanced imaging for guidance and monitoring, and the expanding horizon of clinical trials and applications. The paper positions FUS as a versatile, minimally invasive platform that is becoming an integral part of neuro-oncological therapy.

## Key Findings and Themes

### 1. Mechanisms of Action Beyond BBB Disruption

While BBBO (using low-intensity FUS with microbubbles) is a primary application to enhance drug delivery, the review emphasizes other important mechanisms:

- **Thermal Ablation:** High-intensity FUS can create precise thermal lesions, used for tumor ablation (e.g., in brain metastases) or creating surgical cavities.
- **Sonodynamic Therapy (SDT):** A combination of FUS with sonosensitizing agents to generate cytotoxic reactive oxygen species within the tumor.
- **Immunomodulation:** FUS can alter the tumor microenvironment, potentially stimulating a systemic immune response against the tumor, which is a major area of emerging research.
- **Histotripsy:** A non-thermal mechanical ablation technique that uses very short, high-intensity pulses to liquefy tissue, which is under investigation.

### 2. Central Role of Multi-Parametric Imaging

The paper highlights that imaging is not just for targeting but is essential for every step:

- **Guidance:** Real-time MRI thermometry (MRgFUS) is the gold standard for monitoring temperature during thermal procedures.
- **Targeting & Planning:** Advanced MRI sequences (perfusion, diffusion, spectroscopy) and PET are used to define tumor margins and biologically active regions.
- **Verification & Biomarkers:** Imaging confirms BBBO (via contrast enhancement), assesses treatment effect (via changes in diffusion/perfusion), and detects early complications. The review likely discusses quantitative imaging biomarkers of response.

**3. Emerging Clinical Applications and Trial Evidence**
The article surveys the broadening clinical landscape:

- **Glioblastoma (GBM):** The major focus is on repeated BBBO to facilitate delivery of chemotherapeutics (e.g., temozolomide, carboplatin), monoclonal antibodies, and novel agents. Early-phase trials show safety and promising efficacy signals.
- **Brain Metastases:** Applications include thermal ablation of deep-seated metastases and BBBO to improve penetration of targeted therapies and immunotherapy agents.
- **Pediatric Brain Tumors:** An area of growing interest, particularly for diffuse midline gliomas (DMG), where FUS-BBBO offers a potential route for drug delivery to previously inaccessible locations.
- **Sonodynamic Therapy:** Clinical trials are underway combining FUS with 5-ALA or other sonosensitizers for recurrent GBM.

**4. Safety Profile and Technical Considerations**

- The procedure is generally well-tolerated. The main risks are **hemorrhage** and **edema**, which are minimized with real-time monitoring.
- **Skull-related challenges** (attenuation, heating) are addressed through phased-array transducers and patient-specific planning.
- The importance of **standardized protocols** and defining biologically effective dose (beyond acoustic parameters) is emphasized.

**5. Future Directions and Conclusion**
The review concludes that FUS is a **transformative, platform technology** in neuro-oncology. Key future directions include:

- Integration with **novel therapeutic agents** (immunotherapies, viral therapies, antibody-drug conjugates).
- Exploration of **immunomodulatory** effects to turn "cold" tumors "hot."
- Development of **portable systems and implantable ultrasound devices** for repeated treatments.

- Larger, randomized **phase II/III clinical trials** to establish efficacy.

**In essence**, this article presents FUS not as a standalone treatment, but as a versatile, image-guided **enabling technology** that can potentiate the effects of existing and future brain tumor therapies by overcoming anatomical, biological, and delivery barriers. It marks the field's evolution from a technical novelty to an integrated component of multi-modal neuro-oncologic care.