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Anticancer drug delivery by focused ultrasound-mediated blood-brain/tumor barrier disruption for glioma therapy: From benchside to bedside

Charlotte Bérard [1], Charles Truillet [2], Benoit Larrat [3], Frédéric Dhermain [4], Marie-Anne Estève [5], Florian Correard [6], Anthony Novell [7]

Affiliations

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Abstract

The therapeutic management of gliomas remains particularly challenging. Brain tumors present multiple obstacles that make therapeutic innovation complex, mainly due to the presence of blood-tumor and blood-brain barriers (BTB and BBB, respectively) which prevent penetration of anticancer agents into the brain parenchyma. Focused ultrasound-mediated BBB disruption (FUS-BBBD) provides a physical method for non-invasive, local, and reversible BBB disruption. The safety of this technique has been demonstrated in small and large animal models. This approach promises to enhance drug delivery into the brain tumor and therefore to improve survival outcomes by repurposing existing drugs. Several clinical trials continue to be initiated in the last decade. In this review, we provide an overview of the rationale behind the use of FUS-BBBD in gliomas and summarize the preclinical studies investigating different approaches (free drugs, drug-loaded microbubbles and drug-loaded nanocarriers) in combination with this technology in in vivo glioma models. Furthermore, we discuss the current state of clinical trials and devices developed and review the challenges to overcome for clinical use of FUS-BBBD in glioma therapy.

Keywords: Blood-brain barrier; Brain tumor; Drug delivery; Focused ultrasound; Glioma.