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Overcoming the blood brain barrier in glioblastoma: Status and future perspective

[M H Ahmed](#)¹, [M Canney](#)², [A Carpentier](#)³, [A Idbaih](#)⁴

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Abstract

Glioblastoma is the most common primary brain malignancy in adults. Treatment of glioblastoma patients is based on neurosurgery, radiation therapy and chemotherapy. Despite this multimodal therapeutic regimen, the prognosis of glioblastoma patients is poor. Indeed, glioblastoma is very resistant to treatments due to multiple molecular and cellular mechanisms including the existence of the blood-brain barrier (BBB). The BBB consists of multiple layers surrounding brain vessels and limits drug penetration within the brain. Therefore, overcoming the BBB is a strategy to increase bioavailability and efficacy of therapeutic agents against glioblastoma cells. The development of two approaches is ongoing: i) enhancing the delivery of drugs to the brain and ii) improving the penetration of drugs into the brain. One way to enhance drug delivery to the brain is through high-dose intravenous chemotherapy, with or without bone marrow transplantation, or via intra-arterial chemotherapy, with or without disrupting the BBB through osmotic means. Conversely, improving drug penetration within the brain can be achieved through modifying either the drug itself or the BBB. Promising results in terms of safety and signals of efficacy were obtained with these approaches in early phase clinical trials. More advanced comparative clinical trials are needed to investigate the clinical benefit for glioblastoma patients.

Keywords: Blood-brain barrier; Drug delivery; Glioblastoma; Treatment; Ultrasound.

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