BACKGROUND: The poor prognosis of pediatric diffuse midline gliomas, including diffuse intrinsic pontine gliomas (DIPGs), is partly due to the blood-brain barrier (BBB). The BBB can be opened by ultrasound (US), but few studies have focused on its characteristics in DIPGs, especially when submitted to US. We aimed to characterize the BBB in DIPGs and the influence of US on its characteristics, and to evaluate the effect of US-induced BBB opening on the kinetics of AsiDNA™ in DIPG murine models.

METHODS: US-induced BBB opening was performed with the SonoCloud® device and controlled with Evans blue dye. Permeability of DIPGs' BBB was assessed with fluorescent dextrans. A histological evaluation of BBB markers was carried out by immunohistochemistry and immunofluorescence, including endothelial markers (CD34, GLUT1, PLAP), tight junctions proteins (claudin 5, Zona occludens 1), and the efflux transporter ABCB1. An in vivo and ex vivo kinetic study of AsiDNA™ was performed with fluorescence. RESULTS: We could repeatedly open the BBB with low intensity US (acoustic pressure 0.4 Mpa). In vivo, 3 kDa and 70 kDa dextrans delivery to DIPG tissue was increased by US-induced opening of the BBB, while 500 kDa dextrans did not cross the BBB spontaneously or after US. ABCB1 gene expression was variable at baseline in different DIPGs but was downregulated after US-induced BBB opening. The spontaneous passage of AsiDNA™ through the BBB was limited but could be increased after US-induced BBB opening. CONCLUSIONS: We have shown that the BBB was specific in DIPG murine models, particularly in the expression of ABCB1. This BBB can be modulated and permeabilized by US, a technique that could allow for an improved delivery of AsiDNA. This study is a preliminary step before the introduction of a such technique and treatment in future clinical trials in children and adolescents with DMGs.

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DIPG-43. CHARACTERIZATION OF THE BLOOD BRAIN BARRIER IN DIPG MURINE MODELS AND EFFECT OF ULTRASOUND ON ITS SPECIFICITIES AND PERMEABILITY TO ASIDNA™

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