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Improved survival in rats with glioma using MRI-guided focused ultrasound and microbubbles to disrupt the blood-brain barrier and deliver Doxil MUNA ARYAL, BWH, Harvard Medical School/Department of Physics, Boston College, YONG ZHI ZHANG, NATALIA VYKHODTSEVA, JUYOUNG PARK, CHANIKARN POWER, NATHAN MCDANNOLD, Department of Radiology, BWH, Harvard Medical School — Blood-brain-barrier (BBB) limits the transportation of most neuropeptides, proteins (enzymes, antibodies), chemotherapeutic agents, and genes that have therapeutic potential for the treatment of brain diseases. Different methods have been used to overcome this limitation, but they are invasive, non-targeted, or require the development of new drugs. We have developed a method that uses MRI-guided focused ultrasound (FUS) combined with circulating microbubbles to temporarily open BBB in and around brain tumors to deliver chemotherapy agents. Here, we tested whether this noninvasive technique could enhance the effectiveness of a chemotherapy agent (Doxil). Using 690 kHz FUS transducer and microbubble (Definity), we induced BBB disruption in intracranially-implanted 9L glioma tumors in rat's brain in three weekly sessions. Animals who received BBB disruption and Doxil had a median survival time of 34.5 days, which was significantly longer than that found in control animals which is 16, 18.5, 21 days who received no treatment, BBB disruption only and Doxil only respectively This work demonstrates that FUS technique has promise in overcoming barriers to drug delivery, which are particularly stark in the brain due to the BBB.

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