Blood-Brain Barrier Disruption by Low-Frequency Ultrasound

To the Editor:

Dr Reinhard and coworkers report a case of cerebral gadolinium extravasation after 300 kHz ultrasound “treatment” using the same device that has been applied in the Transcranial Low-Frequency Ultrasound Mediated Thrombolysis in Brain Ischemia Study (TRUMBI) trial.1,2 This interesting observation improves our understanding of the underlying pathophysiology of the hemorrhagic complications that occurred in stroke patients during the TRUMBI study. The assumption that low-frequency ultrasound might cause blood-brain barrier disruptions and thus increase the risk of intracerebral hemorrhage—particularly in the presence of recombinant tissue plasminogen activator—appears convincing and is corroborated by our rat experiments using 20 kHz ultrasound.3 In this MRI study, low-frequency insonation caused a dose-dependant increase in T2-relaxation time which serves as an indicator for vasogenic brain edema and thus indicates blood-brain barrier disruption. Increased ultrasound energy, furthermore, caused circumscribed cortical hemorrhagic lesions that appeared like traumatic cerebral contusions histologically.

These findings suggest that mechanical ultrasound effects might be responsible for blood-brain barrier disruptions and bleeding complications. Because mechanical effects decrease with higher frequencies, we would recommend the use of ultrasound frequencies in the upper kHz range (ie, >300 kHz) for treatment purposes. Extensive preclinical evaluation of new devices, however, is obligatory.

Disclosures

None.

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