Dual-frequency ultrasound (DFU) has emerged as a new treatment modality for improving inflammatory skin disorders

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Neural stem/progenitor cells (NSPCs) have the potential to serve as the basic materials for treating severe neural diseases and injuries. Ultrasound exposure is an effective therapy for nonunion fractures and healing fresh wounds through an easy and noninvasive application. According to the results of a preliminary study, low-intensity ultrasound (LIUS) promotes the attachment and differentiation of NSPCs. However, the parameters of and mechanisms by which LIUS induces NSPC differentiation remain unclear. To the best of Lee et al., knowledge, no published studies have reported and compared the biological effects of dual-frequency and single-frequency LIUS on NSPCs. The purpose of a study was to systematically compare several LIUS parameters, including single-frequency, single-transducer dual-frequency ultrasound, burst, and continuous cycling stimulation at several intensities. Furthermore, synergistic effects of single-/dual-frequency LIUS combined with neural growth factor addition on NSPCs were also evaluated. Based on the results of the cytotoxicity assay, low-intensity (40 kPa) ultrasound does not damage NSPCs compared with that observed in the control group. The morphology and immunostaining results show that all experimental groups exposed to ultrasound exhibit neurite outgrowth and NSPC differentiation. In particular, dual-frequency ultrasound promotes NSPCs differentiation to a greater extent than single-frequency ultrasound. In addition, more complicated and denser neural networks are observed in the dual-frequency group. Neural growth factor addition increased the percentage of neurons formed, particularly in the groups stimulated with ultrasound. Among these groups, the dual-frequency group exhibited significant differences in the percentage of differentiated neurons compared with the single-frequency group. This study may the first to prove that dual-frequency LIUS exposure further enhances NSPC differentiation and the utilization of growth factors than single-frequency LIUS. Moreover, the result also revealed that dual-frequency ultrasound generated higher calcium ion influx and extended the channel opening time. A potential explanation is that dual-frequency ultrasound generates more stable cavitation than single-frequency LIUS, which may stimulate cell membrane mechanochannels and enhance calcium ion influx but does not damage them. This in vitro study may serve as a useful alternative for ultrasound therapy [1].

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Lee IC, Wu HJ, Liu HL. Dual-Frequency Ultrasound Induces Neural Stem/Progenitor Cell Differentiation and Growth Factor Utilization by Enhancing Stable Cavitation. ACS Chem Neurosci. 2019 Jan 4. doi: 10.1021/acschemneuro.8b00483. [Epub ahead of print] PubMed PMID: 30608667.