INTRODUCTION: Bone lengthening by distraction osteogenesis is a well-described method of addressing segmental deficits due to either congenital or acquired conditions. It is both technically demanding and associated with a relatively high incidence of complications. While plastic deformation and refracture have been associated with premature removal of the fixator device, other complications such as infection, malunion and delayed union are also prevalent. The purpose of this study was to determine if Low Intensity Pulsed Ultrasound (LIPU) accelerated the maturation of regenerate bone when applied during the distraction and early consolidation phases in a rabbit model.

MATERIALS AND METHODS: A mid-tibial osteotomy was performed in 44 adult New Zealand White rabbits and an external fixator was applied anteromedially. The animals were randomly divided into treatment and control groups. After a 7-day latency period, the tibiae were distracted 0.5 mm every 12 hours for 10 days. The treatment groups received a 20-day course of LIPU for 20 minutes daily (200 µsec bursts of 1.5 MHz sine waves repeating at 1 kHz, 30 mW/cm²), coinciding with the initiation of the distraction phase on postoperative day 7 (Fig. 1). The control groups received sham LIPU. Bone labeling was accomplished by injecting each of the animals with oxytetracycline on postoperative days 17 and 31, and alizarin complexone on postoperative day 24. Radiographs were taken weekly after distraction and the total and mineralized areas of the regenerate callus were analyzed. Animals were sacrificed at 1.5 and 3 weeks after the end of distraction. All procedures were done in full compliance with institutional guidelines for care and use of animals. Torsional testing to failure was performed using an MTS mechanical testing machine on both the experimental and the contralateral intact sides after sacrifice to determine torsional stiffness and maximum torque. Specimens were prepared after mechanical testing for the undecalcified histological sections. Longitudinal sections were used to measure the tissue composition and the transverse sections were used to determine the mineral apposition rate of the regenerate bone. The results of the treatment and control groups were compared by unpaired t-test. Data were presented as mean and standard error of the mean.

RESULTS: Radiographic analysis: There was no significant difference in regenerate callus area between treatment and control tibiae immediately after distraction, or at 1 week, 2 weeks or 3 weeks after distraction (p=0.54, 0.61, 0.90 and 0.95, respectively). There was also no difference in percent of callus mineralization (p=0.35, 0.78, 0.96 and 0.31, respectively). Mechanical testing (Table 1): There was no significant difference in structural stiffness of the lengthened bone construct at 1.5 or 3 weeks (p=0.79 and 0.98, respectively). Additionally, there was no significant difference in maximum torque at 1.5 or 3 weeks after distraction (p=0.51 and 0.42, respectively). Any of the values normalized by those of the contralateral intact tibia revealed no significant difference between treated and control tibiae. Histomorphometric analysis (Table 2): There was no significant difference in bone mineral apposition rates between treatment and control groups at either interval (p=0.72 and 0.29, respectively). Additionally, there was no significant difference in any of the tissue compositions at 1.5 or 3 weeks after distraction.

DISCUSSION: A modality effective in improving the rate and quality of regenerate bone maturation may improve clinical outcome. Recent studies of LIPU applied during the consolidation phase of distraction osteogenesis have demonstrated a positive effect early in the course of treatment (1). This study used a model of resective shortening followed by lengthening, which has been reported to provide greater callus than the simple lengthening due to the different microenvironment at the osteotomy site (4). Our previous study (5) and the current study used the simple lengthening model to investigate the effect of LIPU on the limb lengthening simulating the most popular clinical setting for limb lengthening. In the previous study using the identical model to the current study except the timing of LIPU stimulation (from day 17 to 37) did not show biomechanical positive results (5). While the mechanism of action of ultrasound stimulation is not fully understood, it has been found to increase expression of genes coding for cartilage such as aggrecan and α1(II) procollagen (2). Controversy exists regarding the mode of ossification in distraction osteogenesis. Nests of cartilage more prevalent in the earlier stages suggest a transition from early endochondral to later intramembranous ossification. Theoretically, a modality affecting endochondral bone formation would potentially have its maximal influence at the time of greatest chondroid activity, that is, during the distraction and early maturation phases. Therefore, the earlier timing of the LIPU stimulation was chosen for the current study. In this study though, LIPU applied during the distraction phase of bone lengthening did not appear to have a beneficial effect with regards to radiographic, histologic or mechanical parameters. A recent study, employing identical ultrasound wave characteristics to an acute fracture model, investigated the effect of stimulation during various stages of fracture healing. It demonstrated a positive effect independent of the timing of treatment (3). This suggests that ultrasound may play a role in several reactions taking place during the various phases of acute fracture healing. While LIPU applied during distraction osteogenesis remains a promising option, further work is necessary to determine the mechanism of action, optimal timing, wavelength and interval of application.


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