Low-intensity Pulsed Ultrasound Increases Vascularity During Fracture Healing in Patients With a Delayed Union of the Osteotomized Fibula

INTRODUCTION:
Recently, we reported that low-intensity pulsed ultrasound (LIPUS) affects bone healing at the tissue level in patients with a delayed union of the fibula [1, 2]. We found that LIPUS accelerates clinical fracture healing by increasing bone formation through increased osteoblast activity [1]. Angiogenesis and blood flow to the fracture site play an important role in fracture healing, and disturbed vascularity leads to impaired fracture healing. Given the relevance of blood flow to the fracture site in the fracture healing process, we speculated that LIPUS treatment affects the vascularity around the fracture gap thereby enhancing fracture healing. The aim of the present study was to investigate 1) whether LIPUS increases angiogenesis and blood flow in delayed union of the osteotomized fibula, and 2) if increased bone formation by LIPUS is correlated to increased angiogenesis and blood flow, by using histology and histomorphometric analysis.

METHODS:
Biopsies were obtained from 10 female and 4 male patients (age 41-63) with a delayed union of the osteotomized fibula after a high tibial osteotomy treated for 2-4 months with or without LIPUS in a randomized prospective double-blind placebo-controlled trial. Trial approval was obtained from the Medical Ethical Review Board of the VU University Medical Center. Patients were enrolled after informed consent was obtained. Mean fracture age at inclusion was 192 days (range 180-214, median 187 days) for sham-treated controls, and 222 days (range 180-331, median 190 days) for LIPUS-treated patients.

Biopsies were embedded in methylmethacrylate without decalcification, and stained with Goldner’s trichrome method. In the histological sections, 3 areas of interest were distinguished in the zone of newly formed bone. UA1, a glycoprotein labeled with fluorescein isothiocyanate (FITC), binds specifically to alpha-L-fucose residues as found on endothelial cells.

RESULTS:
Blood vessels were found throughout the zone of newly formed bone. Increased blood vessel density and size was seen in area 2 of LIPUS-treated delayed unions compared to untreated controls (fig 2A,B). LIPUS did not affect the number of blood vessels compared to untreated controls in area 2 (fig 3C). LIPUS seemed to increase blood vessel size (64%) and blood vessel volume density (60%), but did not affect the number of blood vessels in area 3. Significant Pearson correlation was seen between blood vessel size in area 3 and osteoid volume at the fracture end in area 1 of LIPUS-treated (p=0.041) and healed untreated controls (p=0.052).

DISCUSSION:
This histologic and histomorphometric study shows that LIPUS initiates a better blood supply in bone from patients with a delayed union of the osteotomized fibula by increasing the size of the blood vessels as well as blood vessel volume density and angiogenesis, which is essential for accelerated fracture healing. The increased ostoid volume in healed untreated fractures and LIPUS-stimulated fractures, can largely be explained by increased blood flow and perfusion to the fracture site.

REFERENCES:

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