## Low intensity pulsed ultrasound therapy: A potential adjuvant treatment for osteonecrosis of alveolar bone grafting

## Sir,

Alveolar bone grafting (ABG) has become an essential part of orofacial cleft deformities since last century. Although, ABG is a routine operation in alveolar cleft surgery nowadays, osteonecrosis is still an intractable complication, and it is also the chief culprit of ABG failure.<sup>[1]</sup> The current treatment of osteonecrosis is limited and it is hard to achieve a satisfying result. Therefore, seeking an effective method to resolve osteonecrosis is necessary for ABG.

The goal of treating osteonecrosis is to eliminate postoperative infection, enhance blood circulation and energy metabolism, strengthen bone cellular vitality and recover the bone defect.<sup>[2]</sup> Various attempts have been made to achieve complete resolution of osteonecrosis, such as debridement, local or systemic antibiotics, absorbable biomembrane induced bone regeneration, etc.<sup>[3]</sup> But the current treatments are hard to achieve a satisfying result. Debridement is just for post-osteonecrosis, local or systemic antibiotics had only limited effects on microbiological parameters, while effect of absorbable biomembrane is still need to be evaluated.

Although, the biophysical mechanisms of low intensity pulsed ultrasound (LIPUS) for osteonecrosis is undefined, there are abundant clinical and experimental studies demonstrate the enhancing effect of LIPUS on bone regeneration. Claes found that LIPUS treatment involves nonthermal mechanisms that influence cell membrane permeability and increase cellular activity. Moreover, histological studies suggest that LIPUS influences all major cell types involved in bone regeneration, including osteoblasts, osteoclasts, chondrocytes and mesenchymal stem cells.[4] The results of Takayama's study demonstrated that<sup>[5]</sup> LIPUS stimulation directly affects osteogenic cells, leading to mineralized nodule formation. Romano<sup>[6]</sup> held that LIPUS has been proved to significantly stimulate and accelerate fresh fracture healing in animal studies and in randomized controlled clinical trials. LIPUS also appears as an effective and safe home treatment of aseptic or septic delayed unions and non-unions, with a healing rate ranging from 70% to 93% in different studies.

However as a non-invasive treatment, LIPUS therapy has not ever been reported to be utilized in ABG. We propose a hypothesis is that LIPUS may be an adjunct treatment for osteonecrosis by controlling infection, accelerating bone regeneration and promoting osseointegration after ABG. This hypothesis is based on the following three points: (1) The LIPUS has a bactericidal effect on pathogens relevant to osteonecrosis; (2) The LIPUS can accelerate bone regeneration; (3) The LIPUS may promote osseointegration between in situ bone and bone graft. The formation of osseointegration is similar to bone fracture healing. The LIPUS has demonstrated abilities to enhance osteoblast activities and promote growth and differentiation of bone-marrow stromal cells towards osteoprogenitors. And its favorable effect on healing of delayed union and non-union of bone fracture has been verified by numerous animal and clinical experiments. Similarly, LIPUS may be useful for ABG by inhibit bacteremia and promote osseointegration.

Considering the application of this treatment, further studies are needed to confirm its effect in clinical cases. The effectiveness of LIPUS on controlling infection, accelerating alveolar bone regeneration and promoting osseointegration should be verified firstly by animal experiments through which optimal energy flux density, impulse number and frequency of the treatment will be investigated. The likelihood of its negative influence on nearby vascular and nerve system should be minimized. When these concerns are clear, we believe that LIPUS could be used as a biophysical technique to assist in preventing and treating osteonecrosis after ABG.

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