

Comment to a BMJ Editorial

Is LIPUS the baby in the bathwater?

Low-intensity pulsed ultrasound stimulation (LIPUS) is commonly used to stimulate healing of tibial fractures. One-fifth of Canadian trauma surgeons sometimes use it (Busse et al. 2008). Still, it apparently does not work. A recent multicenter, blind, placebo-controlled randomized trial involving 501 reamed and nailed tibial fractures showed no effect (Busse et al. 2016). It was published in the BMJ together with an editorial that gave the impression that this treatment is now finally out (Griffin 2016). This contrasts with the pioneering multicenter randomized trial that showed a reduction in healing time for unoperated tibial fractures of about one-third (Heckman et al. 1994). This early study was regarded as being of the highest methodological quality at the time, but nowadays it is noted that 3 of the 5 authors had an economic interest in the result (Griffin et al. 2012). So which study was correct?

LIPUS has been around since the 1990s, when randomized trials showed that it shortened the radiographic healing time—not only for tibial fractures (Heckman et al. 1994) but also for distal radial fractures (Kristiansen et al. 1997). Notably, both trials pertained to closed, non-operative treatment. A later high-quality trial on scaphoid fractures, also with closed treatment, again showed a positive effect of LIPUS (Mayr et al. 2000). But all these trials only measured radiographic variables, and no trial performed so far has shown a beneficial effect perceived by the patient, even though this might be a power issue. More recently, a series of trials has failed to show any positive effect of LIPUS, but all these studies except 1 (Lubbert et al. 2008) pertained to internally fixed fractures (Griffin et al. 2012).

The new, strong evidence suggests that we should abandon LIPUS altogether, but this might be throwing out the baby with the bathwater. It is entirely possible that the early studies on unfixed fractures were correct, i.e. that LIPUS works in fractures without internal fixation. Positive effects of LIPUS have been shown in animal models, but we have no mechanistic rationale for a role of ultrasound in fracture healing. Still, internal fixation alters the mechanics at the fracture site, and because sound waves could interact with biomechanical signaling, a different response in fixed and unfixed fractures might be possible.

LIPUS is marketed not only for improved fracture healing, but also for use in atrophic non-unions. Here, there is no evidence at all for a positive effect. In non-union, there is a lack of cartilaginous or bony callus with a potential for bone formation that might be stimulated. Instead, there is scar tissue.

It is difficult to believe that sound waves would change scar into bone.

The early positive trials were sponsored by the manufacturer of the LIPUS apparatus. As the company attempted to interfere with the conduct and interpretation of the latest, large trial (Busse et al. 2016), it cannot be ruled out that similar attempts were more successful in the early trials. The effect of LIPUS on the fractures with closed treatment appeared to be so evident that either there was a strong positive effect, or the data were wrong. The first author in the old tibial trial is also one of the authors in the new one, and he has confirmed that he had full access to all the data before and after unblinding and that he was vigilant concerning commercial bias when performing the old trial (J.D. Heckman, personal communication).

With the current trend towards a revival of the art of non-operative fracture treatment, there is room for a new, modern trial with LIPUS in such treatment.

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