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Response to letter: The effect of whole body vibration training on bone and muscle function in children with osteogenesis imperfecta

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We thank Hoyer-Kuhn et al for their comments on our paper which investigated the effects of whole body vibration (WBV) on muscle and bone in children with osteogenesis imperfecta (OI) and limited mobility. (1)

Their first comment states that children in our study may have been too mildly affected for WBV to be effective. Our study included only OI children with limited mobility, and baseline data clearly demonstrated significantly decreased muscle function; hence there was sufficient capacity to demonstrate improvement during the study. Hoyer-Kuhn et al quote improvements in mobility reported from their uncontrolled, observational study in children with a wide range of OI severity (2) where WBV was used not in isolation, but within a functional training concept that included resistance, treadmill and neurodevelopmental training. In their study, only 26/53 children had DXA scans which showed no effect of 12-months intervention on bone density Z-scores (2). Such observations in retrospective studies are important but cannot replace randomised controlled studies in well-defined, homogenous cohorts. To date, our study is the only such study in OI, and recruiting 12 pairs matched for age, gender and pubertal stage from three large OI centres took 5 years since OI children are recurrently fracturing. We did not demonstrate an effect of WBV, in isolation, on bone mass or muscle function. Whether the Cologne functional training concept, with or without WBV, is effective remains to be shown in a randomised controlled trial.

The second concern questions whether the duration of WBV therapy was long enough to exert an effect on bone as measured by DXA. Our study used DXA and pQCT and showed no significant bone effects over 5 months. We have already discussed the limitation that longer treatment duration may possibly have resulted in measurable effects on muscle function and bone. However, substantial effort is required for the patient and the family using this intensive WBV protocol and longer treatment durations are likely to affect compliance. Whilst paediatric studies of cerebral palsy have generally positive effects on muscle function, and some as well on bone (3,4), cerebral palsy and OI are entirely separate, non-comparable conditions. In contrast to cerebral palsy, OI represents a bone formation and composition defect and our data indicate reduced or delayed biomechanical responsiveness to vibration. We disagree with Hoyer-Kuhn et al that the underlying condition does not matter for biomechanical responsiveness.

Their third point relates to our remark on potential safety concerns in OI children. The two patients who dropped out of the study with fractures in the WBV arm had the lowest muscle function at baseline. One of them developed an atraumatic pelvis fracture, a fracture type which we have never observed in any child with OI. Hoyer-Kuhn et al are misquoting us when they claim we had concluded that those 2 fractures "gave evidence for a significant increase of fracture rates under WBV". It is good scientific practice to list adverse events in randomised trials. We are not claiming that the fractures of these 2 children (out of 12

randomised to WBV) were caused by WBV, but our observations led us to raise potential safety concerns.

Finally, there was a remark on our study being insufficiently powered to conclude that WBV is ineffective. Our study was a pilot study, designed to test a concept, and we have already mentioned the small sample size, and in fact OI severity and treatment duration, as limitations.

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