

## ORIGINAL REPORT

# EFFECT OF DETRAINING ON BONE AND MUSCLE TISSUE IN SUBJECTS WITH CHRONIC SPINAL CORD INJURY AFTER A PERIOD OF ELECTRICALLY-STIMULATED CYCLING: A SMALL COHORT STUDY

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**Objective:** To investigate adaptive changes in bone and muscle parameters in the paralysed limbs after detraining or reduced functional electrical stimulation (FES) induced cycling following high-volume FES-cycling in chronic spinal cord injury.

**Subjects:** Five subjects with motor-sensory complete spinal cord injury (age 38.6 years, lesion duration 11.4 years) were included. Four subjects stopped FES-cycling completely after the training phase whereas one continued reduced FES-cycling (2–3 times/week, for 30 min).

**Methods:** Bone and muscle parameters were assessed in the legs using peripheral quantitative computed tomography at 6 and 12 months after cessation of high-volume FES-cycling.

**Results:** Gains achieved in the distal femur by high-volume FES-cycling were partly maintained at one year of detraining: 73.0% in trabecular bone mineral density, 63.8% in total bone mineral density, 59.4% in bone mineral content and 22.1% in muscle cross-sectional area in the thigh. The subject who continued reduced FES-cycling maintained 96.2% and 95.0% of the previous gain in total and trabecular bone mineral density, and 98.5% in muscle cross-sectional area.

**Conclusion:** Bone and muscle benefits achieved by one year of high-volume FES-cycling are partly preserved after 12 months of detraining, whereas reduced cycling maintains bone and muscle mass gained. This suggests that high-volume FES-cycling has clinical relevance for at least one year after detraining.

**Key words:** bone loss, detraining, functional electrical stimulation, osteoporosis, spinal cord injury.

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## INTRODUCTION

Spinal cord injury (SCI) leads to a rapid and distinct reduction in bone tissue in the paralysed regions (1). The most affected areas are the metaphyseal-epiphyseal regions of the distal

femur, and of both the proximal and distal tibia, where bone mineral content (BMC) is reduced by approximately 50% and 70%, respectively, within the first few years post-injury (2). The clinical significance of this bone loss and associated reduction in bone strength is that it exposes those with SCI to a high risk of low-energy fractures, with a lifetime risk of suffering a fracture in the lower limbs being twice as high as in able-bodied people (3).

In order to increase bone strength in the paralysed limbs and reduce fracture risk, the application of load on bones in people with SCI was investigated. Active loading i.e. through muscle contractions by means of functional electrical stimulation (FES)-induced cycling was found to lead to a site-specific recovery in bone mineral density (BMD) in the paralysed legs up to 14% (4–6). However, despite the positive effect of FES-cycling on bones after SCI, little is known about bone behaviour in the paralysed limbs once the FES-cycling is discontinued. To our knowledge only 2 groups (4, 5) have as yet investigated the impact of a reduced FES-cycle training programme or detraining on bone status in the paralysed limbs. Both groups found that the partially reversed bone loss after initial FES-cycling was lost within the subsequent 6 months of either reduced FES-cycling or detraining. However, whether an initial phase of high-volume FES-cycling causes similar bone adaptations during detraining or reduced FES-cycling remains unclear.

The aim of the present study was therefore to investigate the impact of detraining or reduced FES-cycling following a one-year high-volume FES-cycle training on bones and soft tissue in the paralysed limbs of people with chronic complete SCI by detailed peripheral quantitative computed tomography (pQCT) assessment. For this purpose, we performed a follow-up study of the subjects who participated in the previously published study on the osteogenic effects of high-volume FES-cycling (6).

## MATERIALS AND METHODS

The study was conducted as a multi-centre design at the Queen Elizabeth National Spinal Injuries Unit and the University of Glasgow, Glasgow, UK as well as at the Swiss Paraplegic Research, Nottwil, Switzerland. The study was approved by the local ethics committees.

### Subjects

Eleven people with a chronic SCI participated in a high-volume FES-cycling programme (up to 5 sessions per week, for one year) as published previously (6). Of those, 4 men and one woman aged 38.6 (standard deviation (SD) 8.1) years (age range 27.7–48.4 years) who showed a significant training effect on bone parameters attended follow-up investigations after termination of the high-volume FES-cycling programme. All subjects had motor-complete post-traumatic paraplegia (grade AIS A, i.e. American Spinal Injury Association (ASIA) impairment scale (AIS) (7)), with a lesion level between T4 and T7 and a lesion duration of 11.4 (SD 7.0) years (range 3.6–19.8 years). Exclusion criteria were current or past unhealed bone fractures, diseases known to affect bone metabolism and use of bone acting drugs. All subjects were informed about the protocol for the bone measuring procedure and were required to sign an informed consent form.

### Reduced FES-cycle training or detraining

At the end of the 12-month high-volume FES-cycling programme (for more training details see Frotzler et al. (6)), subjects were free to stop or continue the FES-cycling at their own desired training volume (as determined by the number and duration of sessions per week and the training intensity, i.e. resistance). Four subjects stopped the FES-cycling programme and one subject decided to continue a reduced FES-cycle training and performed 2–3 training sessions per week, each lasting 30 min.

### Measurements

Bone and soft tissue measurements were performed with a pQCT scanner (model XCT 3000, Stratec Medical, Pforzheim, Germany) with regard to volumetric BMD and bone geometry, as well as muscle and fat cross-sectional areas. Image processing and calculation of numerical values were performed using the manufacturer's software package (version 6.0 B). Peripheral QCT scans were performed 4 times: at baseline prior to the FES-intervention ( $t_1$ ), at the end of the high-volume FES-cycling programme ( $t_2$ ), as well as after 6 ( $t_3$ ) and 12 months ( $t_4$ ) of detraining or reduced training. Bone data at  $t_1$  and  $t_2$  have been published previously (6). In the tibial and femoral epiphyses, BMC, total BMD (BMDtot) and trabecular BMD (BMDtrab) were calculated. In the diaphyses, BMC and cortical BMD (BMDcort) were calculated. In addition, muscle cross-sectional area (CSAmuscle) and fat CSA (CSAfat) both in the thigh and the shank were also identified.

### Statistical analysis

Due to the small number of subjects, only descriptive statistics were performed. The mean and SD of the changes in bone and soft tissue parameters between  $t_2$  and  $t_3$ , and between  $t_3$  and  $t_4$  were calculated to analyse the impact of detraining or reduced FES-cycling. To describe the effect of detraining or reduced FES-cycling, changes in bone and soft tissue parameters between  $t_1$  and  $t_2$  were compared with those between  $t_2$  and  $t_4$ .

## RESULTS

### Impact of detraining on bone and soft tissue

Within 12 months of detraining, a mean of 73.0% (SD 13.4) of the total bone gain achieved between  $t_1$  and  $t_2$  in BMDtrab in the distal femur was still preserved at  $t_4$  (Fig. 1). At this site, 63.8% (SD 8.0) gained in BMDtot and 59.4% (SD 3.9) gained in BMC during the FES-cycling period were also preserved at  $t_4$ . In the femoral shaft, BMC and BMDcort decreased by 1.8% (SD 0.8) and 3.6% (SD 2.8) between  $t_2$  and  $t_4$ , which is comparable to the decreases in this site found between  $t_1$  and  $t_2$ . With regard to the impact of detraining on soft tissue in the thigh, 22.1% (SD

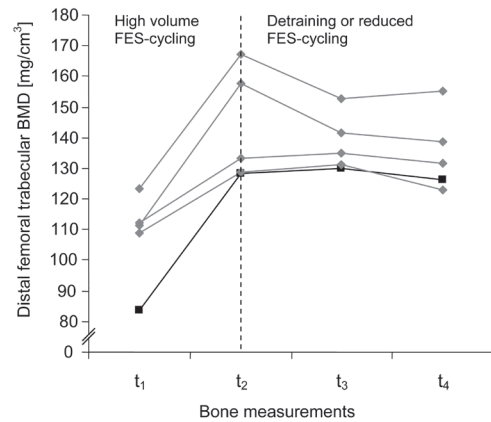


Fig. 1. Adaptive changes in trabecular bone mineral density (BMD) of the distal femur. Values are shown at baseline ( $t_1$ ), after 12 months of high-volume functional electrical stimulation (FES)-cycling ( $t_2$ ), and after 6 ( $t_3$ ) and 12 months ( $t_4$ ) of detraining or reduced FES-cycle training. Note that one subject (black line) continued reduced FES-cycling between  $t_2$  and  $t_3$ , whilst 4 participants (grey lines) stopped high-volume FES-cycling at  $t_2$ . The dashed line indicates the start of the detraining or reduced FES-cycling following high-volume FES-cycling.

21.0) of the total increase in CSAmuscle achieved between  $t_1$  and  $t_2$  was preserved after 12 months of detraining. The main decrease of the total gain in CSAmuscle (68.6% (SD 34.0)) occurred within the first 6 months of detraining, i.e. between  $t_2$  and  $t_3$ . CSAfat in the thigh did not change considerably during the FES-cycling programme, but increased in the phase of detraining and was, on average, 7.6% higher at  $t_4$  than at  $t_1$ . With regard to the impact of detraining on the tibia, bone parameters at this site only changed by between -1.3% and 1.6%. This is similar to the negligible bone changes found during the high-volume FES-cycling programme between  $t_1$  and  $t_2$ . Soft tissue parameters in the lower leg also showed only minor changes between  $t_2$  and  $t_4$ : both CSAmuscle and CSAfat increased on average by 3.2% and 3.5%.

### Impact of reduced FES-cycling on bone and soft tissue

One subject continued a reduced FES-cycle training programme between  $t_2$  and  $t_4$  and was able to preserve 96.2% and 95.0% of the total gain in distal femoral BMDtot and distal femoral BMDtrab (Fig. 1) achieved during high-volume FES-cycling.

In the femoral shaft, BMC and BMDcort decreased by 7.3% and 5.4%, respectively, between  $t_2$  and  $t_4$ . It should be noted that BMC at this site showed similar decreases during high-volume FES-cycling, i.e. between  $t_1$  and  $t_2$ . With regard to the impact of reduced FES-cycling on the soft tissue in the thigh, both CSAmuscle and CSAfat decreased by 1.5% and 17.0%. Thus, nearly the complete gain in muscle tissue achieved during high-volume FES-cycling was still preserved at  $t_4$ . In the tibial epiphysis and diaphysis, bone parameters showed decreases of between 1.3% and 4.8% in the phase of reduced FES-cycling. Interestingly, these decreases are less pronounced than those observed in this subject during high-volume FES-cycling with decreases in tibial bone parameters of up to 18.6%.

## DISCUSSION

The effect of detraining or reduced FES-cycle training following 12 months of high-volume FES-cycling on bones in the lower extremities of 5 persons with chronic complete SCI was investigated. This is the first study with such a long FES-intervention and follow-up period and the first to measure bone and soft-tissue parameters by pQCT. Despite the small number of subjects the present study shows a clear tendency: between 59% and 73% of the gain achieved in BMC, BMD<sub>tot</sub> and BMD<sub>trab</sub> in the distal femoral epiphysis following high-volume FES-cycling were still preserved after 12 months of detraining. This finding is in contrast to the documentations of Chen et al. (5), who found that after stopping FES-cycling (from 5 to zero FES-cycle training sessions per week) bone values returned to baseline levels within 6 months of detraining. According to our results, it appears to take more than 12 months of detraining to resorb the bone tissue that was gained within 12 months of high-volume FES-cycling. In addition, according to Wilmet et al. (8) who found a decrease of BMC of approximately 4% per month in areas rich in trabecular bone during the first year of SCI, bone loss following high-volume FES-cycling in people with chronic SCI seems to be slower with an average decrease in distal femoral BMC of 0.5% per month. The reason for this finding remains unclear, and needs to be investigated in further studies. We speculate that factors that affect bone metabolism, such as vascular atrophy after SCI, may slow down bone loss in people with chronic SCI. Regarding the muscle tissue in the paralysed legs, more than two-thirds of the muscle gain achieved during high-volume FES-cycling was lost within one year of detraining. This is comparable to the atrophy in CSA muscle found in people after acute SCI (9). Reduced FES-cycle training (2.5 training sessions of 30 min per week) seemed to preserve the increase in both the bone at the distal femur and the muscle tissue of the thigh that resulted from high-volume FES-cycling. The present results are in contrast to the findings of Mohr et al. (4), who found the total gain in areal BMD (+10%) in the proximal tibia following FES-cycling for 30 min per day, 3 days per week for 12 months to be lost after a further 6 months with only one training session per week. It may be that there is an important difference between 1 and 2 training sessions per week, with one weekly training session turning a bone's disuse mode "on", thus resulting in resorption of the gained bone substance (as described by Frost (10)). According to Frost's Mechanostat-theory (10), load-induced strains in bones provide the primary control signal underlying the biological responses of bone to its mechanical usage. Thus, strains above a certain threshold turn modelling "on", resulting in an increased bone mass and strength. On the other hand, if strains are too small or absent, a disuse mode of remodelling turns "on" and bone will be resorbed until bone strength is adapted to its new mechanical usage. Consequently, one weekly training session may not be enough to preserve an adequate muscle mass necessary to induce large enough bone strains, while 2 sessions per week may preserve the previously achieved gain in muscle mass sufficiently in order to preserve the achieved gain in BMC.

Several studies documented the fact that people with SCI are at a higher risk of low-trauma fractures (3), and that fractures mainly occur in the distal femur and in the distal and proximal tibia (11). Since fractures may lead to comorbidity and a reduction in quality of life, improvement of bone parameters in the femur may have considerable clinical relevance. High-volume FES-cycling has the potential to increase bone strength of the distal femur in people with chronic and complete SCI (6). Hence, we assume that fracture risk at this site might be reduced after high-volume FES-cycle training and that this protective effect is subsequently sustained following a period of reduced FES-cycling, or even after 12 months of detraining. Indeed, the BMD<sub>trab</sub> in the distal femur is reported to be the most sensitive bone parameter distinguishing between SCI persons with and without fractures (11). Four of our subjects had baseline BMD<sub>trab</sub> values in the distal femur below the reported fracture threshold (11). However, at the end of the 30-month period of monitoring (including 12 months of high-volume FES-cycling and 12 months of detraining or reduced FES-cycling), all of our subjects, independent of whether they stopped or continued FES-cycling, remained above this fracture threshold. Thus, for a lasting improvement in bone parameters in the distal femur of people with chronic complete SCI we recommend a 2-phase FES-cycle training schedule, the first phase consisting of high-volume FES-cycle training in order to increase bone parameters, followed by the second phase consisting of reduced FES-cycle training in order to preserve bone parameters. Studies with even longer follow-up periods are needed to determine how long this second phase of reduced training volume may be.

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## REFERENCES

1. Biering-Sorensen F, Bohr HH, Schaadt OP. Longitudinal study of bone mineral content in the lumbar spine, the forearm and the lower extremities after spinal cord injury. *Eur J Clin Invest* 1990; 20: 330–335.
2. Eser P, Frotzler A, Zehnder Y, Wick L, Knecht H, Denoth J, et al. Relationship between the duration of paralysis and bone structure: a pQCT study of spinal cord injured individuals. *Bone* 2004; 34: 869–880.
3. Vestergaard P, Krogh K, Rejnmark L, Mosekilde L. Fracture rates and risk factors for fractures in patients with spinal cord injury. *Spinal Cord* 1998; 36: 790–796.
4. Mohr T, Podenphant J, Biering-Sorensen F, Galbo H, Thamsborg G, Kjaer M. Increased bone mineral density after prolonged electrically induced cycle training of paralyzed limbs in spinal cord injured man. *Calcif Tissue Int* 1997; 61: 22–25.
5. Chen SC, Lai CH, Chan WP, Huang MH, Tsai HW, Chen JJ. Increases in bone mineral density after functional electrical stimulation cycling exercises in spinal cord injured patients. *Disabil Rehabil* 2005; 27: 1337–1341.
6. Frotzler A, Coupaud S, Perret C, Kakebeeke TH, Hunt KJ, Donaldson N de N, et al. High-volume FES-cycling partially re-

- verses bone loss in people with chronic spinal cord injury. *Bone* 2008; 43: 169–176.
7. Maynard FM Jr., Bracken MB, Creasey G, Ditunno JF Jr., Donovan WH, Ducker TB, et al. International Standards for Neurological and Functional Classification of Spinal Cord Injury. American Spinal Injury Association. *Spinal Cord* 1997; 35: 266–274.
  8. Wilmet E, Ismail AA, Heilporn A, Welraeds D, Bergmann P. Longitudinal study of the bone mineral content and of soft tissue composition after spinal cord section. *Paraplegia* 1995; 33: 674–677.
  9. Castro MJ, Apple DF Jr., Hillegass EA, Dudley GA. Influence of complete spinal cord injury on skeletal muscle cross-sectional area within the first 6 months of injury. *Eur J Appl Physiol Occup Physiol* 1999; 80: 373–378.
  10. Frost HM. Bone “mass” and the “mechanostat”: a proposal. *Anat Rec* 1987; 219: 1–9.
  11. Eser P, Frotzler A, Zehnder Y, Denoth J. Fracture threshold in the femur and tibia of people with spinal cord injury as determined by peripheral quantitative computed tomography. *Arch Phys Med Rehabil* 2005; 86: 498–504.