Different prostate cancer bone metastasis models respond differently to treadmill exercise (Abstract only)

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delayed bone regeneration, and increased risk of fractures. The use of electroacupuncture (EA) for postmenopausal osteoporosis treatment is recent and has been positive for bone quality improvement.

**Objective:** To verify the effects of EA on the regeneration process in the bone defect in the tibias of ovariectomized rats.

**Methods:** 48 female Sprague-Dawley rats (aged six weeks) were subdivided into four groups (n=12): OVDX: OVX; OVDX: OVX + bone defect; SHAM: SHAM surgery + bone defect; and SD: SHAM surgery + bone defect. After 90 days, the tibial bone defect was performed bilaterally. EA protocol started after 24h of the bone defect, and used the Zusanli (ST36) Sanyinjiao (SP6) acupoints. Therapy occurred once a day for 20 minutes, for three cycles of 10 days, with one day intervals between them. After euthanasia, bone microarchitecture evaluation by computed bone microtomography (Micro-CT) was performed. Statistical significance between groups were tested using analysis of variance (ANOVA); (P< 0.05 was considered statistically significant). The OVX group had lower values for micro-CT, being statistically significant.

**Conclusions:** It can be concluded that EA may present the improvement of bone microarchitecture in the bone defect model in osteopoenic tibias. Further studies in this area are suggested.


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**ND-P04**

A novel mouse model to study fracture healing at the proximal femur

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The majority of fractures especially in elderly and osteoporotic patients occurs in metaphyseal bone due to the susceptibility of trabecular bone to microstructural damage. While these injuries are important from a clinical standpoint, adequate small animal models to study them are lacking. Therefore, the aim of the current study was to develop a novel mouse model to study metaphyseal fracture healing at the proximal femur. 12 weeks old female C57BL/6J mice were used for the study (n=6 per group; p< 0.05). We successfully combined an open osteotomy approach to the proximal femur with a closed approach for intramedullary stabilization. No animals were lost due to surgical issues or anesthesia. All animals displayed normal limb loading and a physiological gait pattern within the first three days after fracture. µCT analysis revealed successful implementation of the osteotomy between the lesser and the third trochanter in all animals. Bony bridging score increased significantly between d14 and d21 (0.2 vs. 3.5). Bone volume ratio also increased significantly between d14 and d21. Total callus volume decreased significantly between d14 and d21. Histomorphometric analysis of Safranin O-stained sections revealed that all fractured healed via endochondral ossification, whereas relative amount of cartilage decreased and relative amount of bone increased between d14 and d21. All fracture calluses at d21 displayed less than 10% of cartilage tissue, indicating that fracture callus remodelling has already started at d21 after fracture. Our novel model provides a fast, reliable and inexpensive way to study metaphyseal fracture healing in mice. Future studies using osteoporotic mice might help to unravel molecular mechanisms of delayed osteoporotic fracture healing.


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**ND-P05**

Effects of the escitalopram oxalate on densitometric parameters at the intact and bone callus in growing and young adult rats

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**Objective:** to assess the effect of the escitalopram oxalate intake on densitometric analysis at the intact femur and at the fracture callus in growing and young adult rats.

**Methods:** Four-week-old and 8-week-old Hannover rats (n=28) were distributed into four groups: GP: growing and placebo; AP: adult and placebo; GE: growing and escitalopram; and AE: adult and escitalopram. Daily administration of 2.0 mg/kg of escitalopram (or saline solution) were orally administered for 35 days. Additionally, a fracture at the right femur was produced in all animals on day 21. Densitometric analysis (BMD and BMC) was performed at the distal metaphysis and at the neck of the intact femur, and in the whole bone callus. Analysis of variance with Bonferroni adjustment was made for comparisons (p<0.05).

**Results:** both the BMD at the distal femur (p=0.039) and BMC femoral neck (p=0.043) were higher in adult than growing animals. The drug-treated growing and young adult animals showed significantly lower BMC (p=0.042) and BMD (p=0.027) at the distal femur, which infer a negative effect of the drug on bone mass. This decrease in bone density did not differ among immature and mature animals (p=0.207). Conversely, the escitalopram oxalate intake did not affect the callus density in either group (p=0.184).

**Conclusion:** the escitalopram oxalate administration equally impaired bone density at the intact femur both in immature and mature animals. However, bone callus density remained unchanged with the pharmacological agent.


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**ND-P06**

Different prostate cancer bone metastasis models respond differently to treadmill exercise

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**Background:** Prostate cancer (PCa) is a leading cause of death in men with a predilection to metastasize into bone, when the disease is considered to be incurable. Exercise has been suggested to improve the health of patients with PCa but no current studies on its effects on PCa bone metastasis.

**Hypothesis:** Treadmill exercise can prevent the progression of PCa bone metastasis.

**Methods:** Human xenograft PCa cell line PC3 and murine syngeneic RM1-BM cells were intracardiacally injected (~1x10 cells/injection) into BALB/c nude (n=8) and C57BL/6J mice (n=12),...
respectively. The following day, the mice were subjected to treadmill exercise (12 meters/minute, 5° inclination, 30 minutes/day, 5 days/week) for 3 weeks. Bioluminescence assay was used to track skeletal tumour growth weekly and micro-CT was used to analyse bone morphometrics ex vivo. Naïve mice (n=6) were subject to the same treadmill protocol and used to assess the osteogenic response. Animal procedures were ethically approved by The University of Sheffield, UK.

Results: In the xenograft model, the treadmill exercised mice developed significantly higher tumour burden (p<0.05, Mann-Whitney test) in their hindlimbs compared to sedentary controls. The bone structure was not improved by treadmill exercise according to micro-CT analysis. In contrast, the syngeneic model showed significantly lower tumour burden in exercised mice compared to controls (p<0.05, Mann-Whitney test) and a tendency to significantly improved survival curve (p=0.07, Gehan-Breslow-Wilcoxon test). The trabecular thickness (Tb.Th) was found significantly higher compared to controls (p<0.001, unpaired t-test). In the naïve baseline study, the trabecular BV/TV had a 7.5% increase in C57BL/6j but 8.5% reduction in BALB/c nude mice, compared between exercised to sedentary controls.

Conclusion: Treadmill exercise alleviates PCa growth in bones of syngeneic RM1-BM/C57BL/6j but not the xenograft PC3/BALB/c nude model, a possible consequence of different osteogenic response to treadmill by the two mouse strains.


ND-P07

Estrogen-mediated downregulation of HIF-1α signaling in B lymphocytes influences postmenopausal bone loss

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ND-P08

Type 2 diabetes impairs mesenchymal stem cells functions and differentiation

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ND-P09

SLIT2/ROBO1-axis intensifies inflammation, M1 macrophage polarization, and alveolar bone loss in periodontitis, possibly via the activation of MAPK pathway

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