Suitability of Various Non-Invasive Imaging Techniques to Analyze Bone, Muscle and Fat Tissues in Ovariolectomized Mice

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Introduction

Musculoskeletal disorders are a broad range of diseases that affect various tissue types including bone, muscle and fat. Preclinical evaluation of drug candidates for treating musculoskeletal disorders could benefit from an integrated approach analyzing the pharmacological effects on various tissue types. A broad range of non-invasive imaging techniques are now available in animal models to address this evaluation, including dual-energy X-ray absorptiometry (DXA), peripheral quantitative computed tomography (pQCT), echo magnetic resonance imaging (MRI), and high-resolution micro-computed tomography (µCT). Currently, mice are used increasingly in studies of musculoskeletal disorders. This is mainly due to an availability of genetically modified mice that mimic musculoskeletal disorders including various rare bone diseases.

Materials and Methods

Animals: experiments: The study was conducted using female C57BL/6 mice (S/GNIR Research, Karlsruhe, Germany), unless an animal experiment license granted by National Animal Experiment Board, Regional State Administrative Agency for Southern Finland, Finland. Six to 12 post-surgery weeks mice were randomized to subcutaneous injection of saline, 0.01%, 0.05%, 0.1%, 0.5% rodan dosage, or 0.5% rodan dosage, respectively. Their relative weight in study were determined, and their long bone and femur were assessed by scintillation bone analyses.

The regional Bone health of bone and soft tissues of the mouse femur were analyzed using the SkyScan 1176 microtomography system (SkyScan, Kontich, Belgium). The bone mineral density (BMD) and trabecular bone content (TBC) were determined using a pQCT system (pQCT, XCT Research Systems, Amersham, UK). The bone area (BA), bone mineral area (BMA), bone mineral content (BMC), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tbs), and bone volume fraction (BV/TV) were determined using µCT (µCT, SkyScan, Kontich, Belgium). The bone area (BA), fat mass (FM), and fat content (FC) were determined using a µCT (µCT, SkyScan, Kontich, Belgium).

Aims of the Study

The purpose of this study was to evaluate the suitability of non-invasive imaging techniques to analyze bone, muscle and fat tissues in mice using the ovarioectomy (OVX) model of human postmenopausal osteoporosis. Non-invasive imaging techniques evaluated included DXA, pQCT, Echomer and high-resolution µCT.

Body, Soft Tissue and Uterine Weight

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Muscle Tissue

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Fat Tissue

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Summary

- Surgical ovarioectomy increased body weight and soft tissue weight, and decreased relative uterine weight in young adult mice after 9 post-surgery weeks (Fig. 1).
- In the bone of OVX mice after 9 post-surgery weeks: DXA demonstrated a reduction in areal BMD in long bone and lumbar vertebra (Fig. 2A,B), pQCT showed a reduction in volumetric BMD and trabecular BMD in long bone metaphysis (Fig. 2C,D), µCT demonstrated a reduction and an impairment in the volume microarchitecture of metaphyseal trabecular bone and in the volume and distribution of diaphyseal cortical bone (Fig. 2E,F,H-I).
- In the muscle of OVX mice after 9 post-surgery weeks: DXA showed a reduction in lean percentage (Fig. 3B), Echomer demonstrated a reduction in relative lean mass (Fig. 3D).
- In the fat of OVX mice after 9 post-surgery weeks: DXA demonstrated an increase in fat mass and fat percentage (Fig. 4A,B). Echomer showed an increase in fat mass and relative fat mass (Fig. 4C,D), pQCT demonstrated an increase in fat area in proximal and mid-call (Fig. 4E,F).

Conclusions

This study demonstrated that in young adult OVX mice, DXA, pQCT and µCT can be used to analyze bone tissue, and DXA, Echomer and pQCT to analyze muscle and fat tissues. These non-invasive imaging techniques are valuable for a follow-up of drug effects in animal models as well, including in various genetically modified mice used as models for rare bone diseases.

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References