Use Of Small Animal Multi-modality Imaging For In Vivo Assessment Of Tendon-to-Bone Healing

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Disclosures:

Introduction: Relatively little is known about the sequence of events that occur during healing between the tendon autograft and bony reconstruction tunnels. Specifically, the spatial and temporal progression of bone ingrowth and the effects of mechanical stimuli on tendon-bone healing are poorly understood. In previous work we showed that bone formation at the tendon-bone interface is essential for healing [1]; however, the limited availability of a non-invasive means to evaluate healing in vivo impeded a more refined analysis. Positron Emission Tomography (PET) is a minimally invasive imaging modality that measures the distribution of tracers labeled with positron emitting radionuclides. 18F-Fluoride is a bone-seeking agent that reflects bone turnover and can be used to evaluate soft tissue and bone metabolic processes [2]. The aim of this study was to evaluate the use of micro (µ) PET/computed tomography (CT) to serially characterize and quantify anterior cruciate ligament (ACL) graft healing in vivo, using an established rat reconstruction model. We hypothesized that serial µ PET/CT scans would be feasible and safe, and that this method would capture differences in bone turnover along the graft tunnel, allowing us to better define the sequence of events occurring during the healing process.

Methods: Six male Sprague-Dawley rats underwent ACL reconstruction using a flexor digitorum longus autograft. An external fixator was placed across the knee. The rats were assigned to immobilization (N=3) or daily loading (N=3, daily 50 cycles of ROM from 0-90°) groups. The animals were scanned using µ PET/CT scans (spatial resolution 1.4mm) and 18F fluoride as a tracer to monitor bone turnover at 7, 14, 21 and 28 days after ACL reconstruction (Fig 1c). Each bone tunnel and the surrounding bone were divided into three equal regions of interest (ROI) along each tunnel (intraarticular aperture (IAA), midtunnel (MT), and extraarticular aperture (EAA)). Standard uptake values (SUV) were calculated for each ROI. All rats were euthanized at 28 days and ex vivo high-resolution µ CT analysis was performed on all ACL tunnels.

Results: The µ PET/CT imaging provided quantifiable evidence of bone turnover in and around the bone tunnels over time (Fig 1). On the tibial side, there was a gradient in SUV, with most bone turnover at the IAA and least at EAA in both groups. The same pattern was observed for the immobilized group on the femoral side at 14, 21 and 28 days. The lack of significant differences in PET scans could be due to the small sample size. The µ CT scan at 28 days showed a significantly higher bone volumetric density in the loaded group at the femoral IAA when compared to the immobilized animals. A gradient was seen on the tibial side, with most bone volume at the EAA and least at IAA. In the loaded group, all the femoral ROIs showed bone volumetric densities of ~40%.

Discussion: Our study indicates that the use of repetitive µPET/CT scans is feasible and highly sensitive for the evaluation of tendon-bone healing processes in a small animal in vivo model. Considering the current lack of knowledge of the tendon-bone healing process due to the limited availability of in vivo studies, our data highlights the feasibility and potential of repetitive µPET/CT scanning to provide further insight into the healing process and to directly measure the effect of interventional strategies in tendon-bone healing.

Significance: There is a current lack of knowledge of the tendon-bone healing process due to the limited availability of in vivo studies. Our data highlights the feasibility and potential of repetitive µPET/CT scanning to directly measure the effect of interventional strategies in tendon-bone healing and provide further insight into the healing process.

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Fig. 1a: 18F-Fluoride standard uptake values of the femoral and tibial IAA, MIT, and EAA at 7, 14, 21, and 28 days postoperative.

Fig. 1b: μCT scan at 28 days postoperative.

Fig. 1c: Representative 18F-fluoride PET/CT image of the right femoral ACL tunnel (arrow) in a rat. **p<0.05