Quantitative joint alignment measurements for preclinical models of osteoarthritis

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Osteoarthritis (OA) is characterised, in part, by architectural and structural alteration to joint tissues which also adversely affects joint alignment and limb stability. The state-of-the-art preclinical diagnostic technique for joint tissue evaluation is histological sectioning, a destructive method which does not allow a 3D analysis of the whole joint. In this study, we use micro-computed tomography (μCT) of rat knee joints to investigate alignment changes in the OA-induced and contralateral whole joints, based on displacement and orientation of the femur and tibia.

Eight 3-month old male Wistar rats underwent medial meniscectomy/anterior cruciate ligament desmotomy on one knee joint (a mechanically-induced OA model), where the contralateral joint served as a control. Animals were sacrificed 6 weeks post-operatively and scanned using μCT (SCANCO Medical AG; 10 μm voxel size).

The micro-CT scans were processed and scans were rotated to a common orientation. Tibiae in all the samples were registered to the mean tibia shape obtained using a hybrid model. In this approach, the tibia of one sample is registered to another sample (a reference sample). The registered and reference images are then added to obtain a first stage hybrid. This is repeated for 8 random pairs, producing 8 hybrid images. The registration is then repeated until a single multi-stage hybrid is produced. Each femur is then registered using the same transformation as that used for the registration of the tibia to the hybrid.

The distance (λ) and orientation (α, β, γ) of the centre of mass of the femur relative to the centre of mass of the tibia along the three principle axes in a cartesian coordinate system (coronal view along YZ and sagittal view along XZ plane) were then measured, see Figure 1.

Results

Plots of the distance (λ) and orientation (α, β, γ) of the line segment joining the centre of mass of the femur and tibia are shown in Figures 2 and 3. Although the mean values for the operated and contralateral joints were comparable, the results showed a significant increase in the α, β, γ ranges of motion for operated (6.5°, 3.9°, 4.8°) compared to contralateral (1.1°, 1.1°, 1.1°) joints, indicating a marked increase in instability. Similarly, while the distance, λ, is not significantly different for the contralateral and operated joints; mean λ: 5.32 and 5.38 mm, respectively, the standard deviation is significantly altered; 0.05 and 1.67 mm, respectively.

OA affected joints show additional bone growth called osteophytes. Also the femurs in operated joints show a subtle tilt towards the lateral side.

Discussion & Outlook

The results for the orientation of the centre of mass of the femur with respect to the centre of mass of tibia about X, Y and Z axis show good agreement in all non-operated joints while the deviation from that trend in the operated joints can be seen in larger standard deviations of α, β, and γ. The standard deviation for the orientation was observed to be greatest for α which is indicative of a relatively higher freedom of movement in the femur relative to tibia about the X axis, or in other words an increasing posterior shift of the femur with the destabilisation of the joint. Variation in the standard deviation of λ supports this finding.

Additionally, the observation of consistent mean values for all measures between the contralateral and operated joints indicates that while the variance in the latter case is significantly larger, the change from the normal position is not unidirectional. Future studies will repeat this work in large animal models, as well as cross-correlate all results with standard bone and cartilage morphometry measures.

Figure 1: Sketch of the relative distance between the centre of mass of femur and tibia (λ) and the inclination of centre of mass of femur with respect to the centre of mass of the tibia along the X-axis (α), Y-axis (β) and Z-axis (γ) in a registered sample.

Figure 2: Distance between the centre of mass of the femur and tibia, λ, mean ± standard deviation. Operated joints display a significantly different variation from the mean compared to contralateral joints (p<0.05).

Figure 3: Inclination of the centre of mass of the femur relative to the centre of mass of the tibia (a) along the X axis, (b) along the Y axis, and (c) along the Z axis; mean ± standard deviation.

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