ANIMAL MODELS FOR KNEE INJURY FREQUENTLY UNDERESTIMATE THE MECHANICAL CONDITIONS OF THE CLINICAL SITUATION

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Introduction

The sheep has become a standard model for investigating biological and healing responses, as well as understanding the mechanical conditions after injury and investigating surgical treatments such as ligament reconstruction [1] and osteochondral defect repair [2]. Whilst biology plays a role in the long term outcome of these surgical treatments, the mechanical forces, recognized to be multiples of body weight [3, 4], are also known to influence the healing. Hip contact forces in sheep have been investigated using telemetric prostheses [5], where significant intra- and inter-individual variability in the measured hip contact forces was observed. Additionally, the internal skeletal forces have been examined using musculoskeletal models [6], but these were limited to 2D skeletal kinematics.

Although much research has been performed in sheep, no study has yet evaluated the joint contact forces that occur in the sheep, after surgical treatment. It is therefore unclear whether their mechanical conditions are comparable to those in man. The relevance of such healing results may therefore be questionable. By establishing accurate 3D kinematics of the sheep hind limb throughout the gait cycle, we aimed to determine the in vivo loading conditions that occur across the tibio-femoral joint of the sheep knee for comparison against the mechanical conditions in man [4].

Materials and Methods

Three Merino-mix sheep (two years, weights 59 kg, 62.5 kg and 55 kg) were trained to walk freely over a gangway which included a force measurement platform (Kistler, Kistler Instrumente AG, Winterthur) to determine the pre-operative ground reaction forces (GRFs). Schanz’ screws were then surgically inserted into the pelvis, femur, tibia, metatarsus (Ø 4.5 mm) and the patella (Ø 2.5 mm in order to minimize weight) of the right hind limb of all sheep. All soft tissues were carefully preserved and lesions sutured, and the sheep received an analgesic (Finadyne®, Germany) until gait analysis, performed three days postoperatively. All animal experiments were carried out according to the policies and principles established by the Animal Welfare Act, the NIH Guide for Care and Use of Laboratory Animals and the national animal welfare guidelines.

During postoperative gait analysis, light aluminum frames, each holding four reflective markers (3 for the patella), were attached to the Schanz’ screws. The position of each marker was recorded at a rate of 60Hz using an infrared optical measurement system (PC Reflex, Qualysis, Sweden; accuracy ±0.1 mm) for each gait repetition. A GRF triggered infrared light ensured synchronization of the movement and force data. All animals were then sacrificed and the complete hind limb was CT scanned (Siemens, Germany; voxel size 1 x 0.742 x 0.742 mm).

The surface of each bone was reconstructed from the CT scan data (Amira v2.3, ZIB, Berlin) and each muscle origin, insertion and wrapping attachment site, to be individually transformed into the local bone coordinate systems using an inverse dynamics approach. The physiological cross sectional area of each muscle was then determined in vivo [3] and scaled to the body weight of each sheep. The muscle and joint contact forces were then computed throughout each gait cycle repetition using static optimization techniques [4] to minimize the square of the muscle stresses. Finally, both the hip and the tibio-femoral joint contact forces were calculated as the sum of the intersegmental resultant force and all muscle forces crossing the relevant joint, throughout the gait cycle for a minimum of 2 repetitions in each of the three sheep.

Results

Average peak pre-operative GRFs were 0.48 BW. Postoperatively, the sheep walked with speeds varying from 0.7 to 1.0 ms⁻¹ (average 0.8 ms⁻¹), with average peak axial GRFs of 0.34 BW. Average peak tibio-femoral contact forces of 2.12 BW were calculated across the 3 sheep (Figure 1, right), with A-P shear forces averaging 0.7 BW. Only small M-L forces were determined. Joint contact forces across the hip showed an average peak of 1.36BW.

Discussion

For the first time, this study has reported the in vivo forces that occur in the sheep knee, valuable for understanding what surgical treatments must withstand. Importantly, this provides direct knowledge on the relevance and relationship of experimental animal models, such as those used for understanding osteochondral defect healing or ligament reconstruction, to the clinical situation.

The calculated hip joint contact forces, used for validation of the musculoskeletal analysis, were in accordance with those measured in vivo [2], and showed considerable inter- and intra-individual variation. Although postoperative unloading of the limb was observed, as seen in the GRFs, the good comparison of the forces attained at the hip in sheep does provide a level of confidence in the knee forces determined in the present study.

Knee contact forces of up to 3.2 BW during walking and 5.6 BW during stair climbing have been reported in vivo in humans [4]. The corresponding forces of 2.1 BW in sheep, as determined in this study, demonstrate that reconstruction studies in animal models might significantly underestimate the mechanical conditions that surgical treatments in the human situation are required to withstand. Further investigation, using the information presented here, is therefore required to determine if this difference is critical on a tissue level. Based on the sheep tibio-femoral forces presented in this study, however, it should now be possible to more carefully estimate the mechanical conditions under which healing of osteochondral defects and ligament reconstructions in experimental animal models occur.

References


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