THE PROS AND CONS OF STUDIES OF ANIMAL JOINTS TO IMPROVE ARTICULAR CARTILAGE REGENERATION

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Animal models of articular cartilage repair/regeneration have greatly contributed to the understanding of the biology of the repair mechanisms and our capacity to manipulate or enhance these events. Many factors need to be considered when choosing an animal model for novel cartilage repair strategies. The ideal model should be similar to humans in respect to anatomy, joint mechanics and cell biology. However, in reality, this ideal is impossible to achieve because of the great heterogeneity which already exists in the target human population (genetic profile, age, weight, joint geometry…). Adult animals should preferably be used to mimic the adult human joint environment, when attempting to predict the response of the intervention in humans. However they may not be easily available and it is costly to house them until they attain an adult age. The animals should at least be skeletally mature (growth plate closure on radiographs). It is possible to obtain adult horses, but the majority of studies include 2-3 year old (post – pubertal) horses and are consequently models of acute injury in young athletes.

An advantage of all the animal models is that the anatomy of the knee joint is similar to that of humans. On the other hand, all, except primates, are quadrupeds and consequently joint mechanics and loading are very different from humans. It should be borne in mind that differences also exist at the cartilage structural and cellular level that could affect outcome. It is interesting that the size of the chondrocytes do not differ between species, but differences in cell volume density exist (1.7% human v 12.2% rabbit femoral condyles) which could impact cell dosing[1]. There is also considerable variation in cartilage thickness between species [2] and the thickness of mature equine femoral cartilage most closely approximates that of humans.

The characteristics of the cartilage defect in the animal model (partial or full thickness/area/depth/shape,) should also mimic that encountered in humans. The larger animals, because of the increased cartilage thickness, are preferable for studies of partial thickness defects confined to the hyaline cartilage.

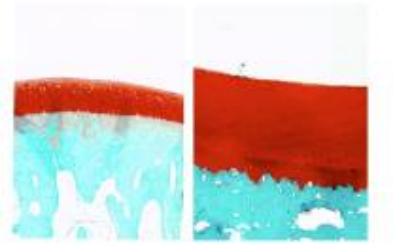

Fig. 1: Differences in cartilage structure between species x25 (rabbit left, horse right)

One of the most valuable contributions of animal models is that they allow the determination of the kinetics of repair mechanisms and efficacy of cartilage repair strategies temporally. The ability to assess the treatment strategy non-destructively *in vivo* is an important consideration. Repeated imaging with MRI & CT is possible in all species but resolution is problematic in small animals such as rabbits where the cartilage is thin and powerful magnets are required to accurately quantify cartilage changes.[3] Large animals (goat, sheep, pig, horse) are required when studying efficacy and functionality of the intervention as the size of the joints more closely approximate the human knee. The large joints facilitate minimally invasive surgical procedures such as arthroscopy to visualize, biopsy and assess the mechanical properties of the repair site. They also permit harvest of undiluted synovial fluid and yield abundant joint tissues for assessment. Joint function analyses (force plate and kinematics) also make the larger animals more appealing. The ultimate test however for any novel repair strategy is a long term clinical trial in the target species-homo sapiens.

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