The CABMM writes about new animal models for augmentation of cancellous bone in sheep

Augmenting cancellous bone

The augmentation of cancellous bone is a developing field in orthopaedic surgery and represents a treatment option for various disease states in conjunction with loss of bone mass and stability. Such loss of bone integrity may be observed in a range of clinical diseases caused by osteolytic tumours, osteoporosis and bone deformities leading to fragility fractures.

These fractures have become a major public health problem, particularly in the elderly population due to increased life expectancy, affecting up to nine million people worldwide each year. Prophylactic local treatment has emerged as a new treatment strategy to enhance bone mineral density involving percutaneous injections of biodegradable and osteoconductive augmentation materials into bones at risk of fractures (e.g. proximal femur, distal radius, proximal humerus and vertebrae). Although new implants and biomaterials could be mechanically tested in a fresh cadaveric specimen, *in vivo* experiments are required for proof of principle and safety reasons. Therefore, adequate animal models are needed.

Our group developed two *in vivo* animal models for the augmentation of cancellous bone in sheep to evaluate the biocompatibility, osteoconductivity and degradation properties of new injectable composites. Both animal models give an accurate situation for bone augmentation, but also for side effects such as pulmonary embolisation and cardiovascular changes as observed in humans.

Using fluoroscopy and a customised aiming device for each animal model (Fig. 1 and 2), the biomaterials could be successfully injected with high accuracy and repeatability within the inter-trabecular space of the intact femoral condyle and proximal tibia metaphysis (first animal model) or the cervical vertebral bodies (second animal model). The suitability of various biomaterial formulations has already been investigated using specialised evaluation procedures. *In vivo* fluorescent staining at six and 12 weeks as well as 16 weeks post-surgery for the cervical augmentation model was performed to detect enhanced bone activity in the region of interest at each time point. After a 12-week follow-up for the tibia and femur augmentation, and a 16-week follow-up for the cervical augmentation, the sheep were sacrificed and the injected bones harvested and evaluated. For evidence of new bone formation, radiographs were taken after sacrifice using a Faxitron. Micro-computed tomography measurements of the regions of interest were taken to qualitatively assess bone volume density and trabecular thickness. Qualitative and quantitative histological evaluations were performed to assess bone structure, bone remodelling, percentage of new bone formation and remaining material as well as cellular reactions to the material.

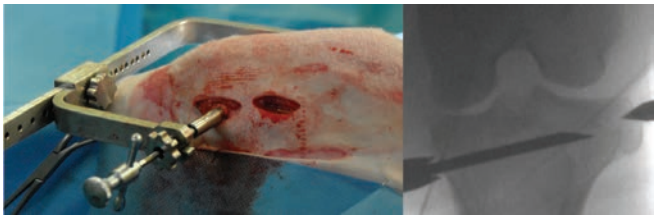

Fig. 1 Correct placement of aiming device for the tibia and femur augmentation model; the left picture shows aiming device in the correct position; fluoroscopy pictures (shown in right picture) were used to validate correct placement of aiming device and needle as well as subsequent material injections (Reference: Klein *et al.* *BMC Musculoskeletal Disorders* 2013, 14:200)

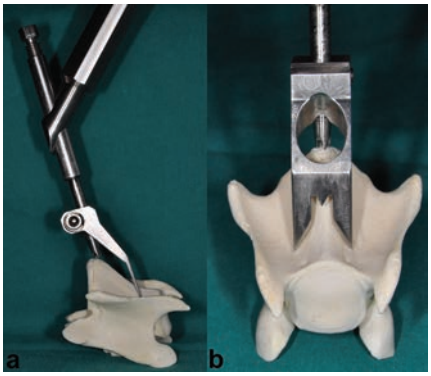

Fig. 2 Correct placement of aiming device for the cervical augmentation model. (a) The lateral view represents the central drill guide in correct position on promontorium of the caudal aspect of the vertebral body. (b) The craniocaudal view shows drill guide positioned on promontorium, with aiming targeting tip lined up with vertebra midline and two sharp long dents, arranged symmetrically lateral of the midline, resting on the cranial deeper part of the vertebral body (Reference: Klein *et al.* Vet. Sci. 2014, 1, 96-120; doi:10.3390 /vetsci1020096)

Both animal models revealed to be suitable for the evaluation of new biomaterials for prophylactic augmentation of cancellous bone in sheep. While the tibia and femur augmentation model showed to be particularly suitable for screening studies to evaluate new biomaterial formulations, the cervical augmentation model revealed to be more challenging due to a high rate of clinical relevant pulmonary emboli with subsequent cardiovascular alterations.

Therefore, this animal model could be chosen to particularly study the development of a pulmonary embolism and its consequences following augmentation of cancellous bone, as these complications also occur in humans.

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