

OBCD Joints

<https://www.biorxiv.org/content/10.1101/836221v1>

This was a collaboration with the Origins of Bone and Cartilage Disease (OBCD) project:

At the end of the pipeline at 16 weeks of age, the left hind limbs of 7 male mutant and wild-type mice were collected at necropsy, skinned and fixed in 10% NBF for 24hr before being transferred to 70% ethanol and stored at 4°C. Prior to analysis, limbs were rehydrated in PBS for >24h. Soft tissues were removed and the knee joints were disarticulated under a microscope.

Signs of joint disease were detected using a multi-modal, three-dimensional imaging pipeline. Joint Surface Replication of the tibial plateau was used to assess articular cartilage surface damage. Three-dimensional replicas of the tibial plateaux were cast using Crystal Clear 202 acrylic resin (Smooth-On, Bentley Advanced Materials, London, UK) and imaged by back-scattered electron scanning electron microscopy (Vega3 XMU, Tescan, Cambridge, UK). Subchondral X-ray microradiography was used to assess subchondral bone sclerosis. Tibial epiphyses were imaged at 10µm pixel resolution (Faxitron MX20) alongside standards to quantify relative bone mineral content. Changes to articular cartilage and subchondral bone morphology were assessed by Iodine Contrast-Enhanced micro-Computerised Tomography (µCT-50, Scanco, Zurich, Switzerland). Tibial epiphyses (articular cartilage and subchondral bone) were imaged in an iodinated contrast agent (Lipiodol Ultra, Guerbet Laboratories, Solihull, UK) at 2µm voxel resolution.

Overall, 17 joint parameters were reported for each mouse and compared to reference data obtained from 100 16-week wild-type C57BL/6 male mice.

Mice were fed on Mouse Breeder Diet (5021, Labdiet) from weaning and anaesthetized with Ketamine/Xylazine at the end of the pipeline.