RESEARCH AWARD: VAN FOREEST AWARD

SUSTAINED RELEASE OF CELECOXIB AFTER INTRA-ARTICULAR INJECTION AS A TREATMENT OF OSTEOARTHRITIS IN MAN AND DOG

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Osteoarthritis (OA) is a common cause of pain and lameness in dogs and humans. Anti-inflammatory drugs are effective in reducing pain and inflammation but have limited duration after oral/local administration while their prolonged use can be accompanied by systemic side effects. These limitations can be addressed by local administration of drugs in controlled release systems. The aim of this study was to investigate the safety and effectivity of Celecoxib-loaded poly-ester-amide microspheres as a basis for translation towards veterinary and human patients.

Knee OA was induced in 32 rats. After six weeks, rats randomly divided into five groups received intra-articularly either unloaded microspheres, microspheres loaded with Celecoxib (0.03, 0.23, and 0.4 mg in 25µL) or a bolus injection of Celecoxib (0.4 mg in 25 µL). During the 16 week follow up, systemic Celecoxib values were determined; pain and limb function were monitored weekly (pressure plate). Histology and µ-CT were utilized to measure OA progression, synovitis and subchondral bone changes.

After induction of OA, load bearing was significantly reduced in the operated limb, but normalized a month after surgery in all groups. Systemic effects were absent on post mortem analysis. There was significantly more OA in the operated than in the healthy control joints. Celecoxib-loaded microspheres, but not bolus Celecoxib injection, reduced the formation of osteophytes, subchondral sclerosis, bone cysts and loose bodies on µ-CT (figure 1). Sustained presence of Celecoxib reduced synovial inflammation and the presence of macrophages in the synovial lining.

Intra-articular injection of Celecoxib-loaded microspheres was proven to be safe in OA joints. While there was no clear regenerative effect of Celecoxib at the histological level, its prolonged presence reduced subchondral bone changes and synovitis. Currently, a randomized double-blind placebo controlled clinical trial is performed in client-owned dogs with knee OA to determine efficacy.

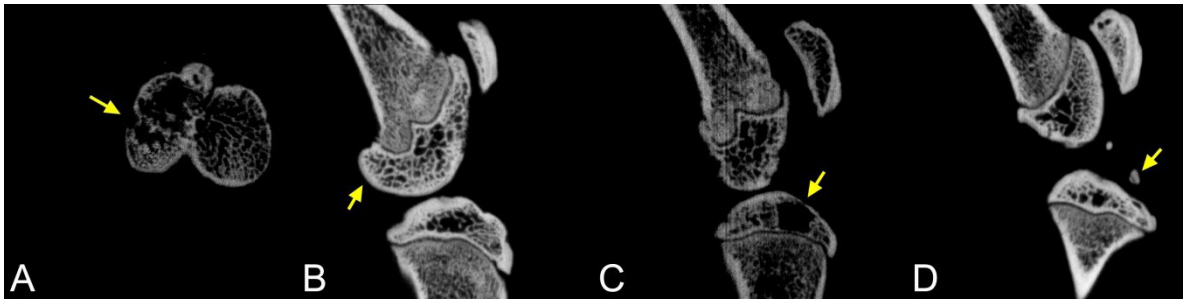

Figure 1. Appearance of osteophytes (A), subchondral sclerosis (B), bone cysts (C) and loose bodies (D) in a rat knee joint 20 weeks after OA induction surgery. Treatment with sustained release of celecoxib significantly reduced these subchondral bone changes.