Figure 1. CALC2 measurements in HEX model.


THE PATTERN OF JOINT INFLAMMATION IN THE CAIA MOUSE MODEL OF ARTHRITIS

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Background: Animal models of inflammatory arthritis such as the collagen-antibody induced arthritis (CAIA) have a variable disease incidence in hind paw arthritis, complicating experimental design.

Objectives: To investigate the use of 18FDG µPET/CT as a guide for inflammation in joints otherwise inaccessible for clinical scoring, enabling the use of additional joints for histological analysis.

Methods: CAIA was induced in 8 male DBA/1 mice using the ArthritisMab Antibody cocktail (4mg/mouse on day 0), followed by 100 µg LPS at day 3. Body weight, clinical signs of arthritis such as paw swelling and grip strength losses were recorded 3 times per week in both front and hind paws. Whole body 18FDG µPET/CT was performed at day 11, the estimated time of peak inflammation, and inflammation was scored visually on images scaled to the same standardised uptake value. At day 28, animals were euthanized and peripheral joints were harvested for histological assessment.

Results: Cumulative disease incidence based on paw swelling dropped from 100% to 87.5% when looking only at hind paws, and to 75% when taking into account only the region suitable for histological analysis, namely the ankle and midfoot of the hind paws. Symmetrical, bilateral hind paw arthritis was not observed. While hind paw arthritis showed a tendency to be less severe in comparison to front paw arthritis, grip strength was equally affected, indicating possible involvement of other hind limb joints. µPET/CT images detected inflammation in the hind paws (at least unilateral involvement in 62.5% of the mice, bilateral involvement in 0%), knee joints (at least unilateral in 75%, bilateral in 50%), hip joints (at least unilateral in 50%, bilateral in 0%), elbow joints (at least unilateral in 50%, bilateral in 37.5%) and shoulder joints (at least unilateral in 25%, bilateral in 25%). Histology could confirm this inflammation with the presence of inflammatory infiltrates and bone erosions. Grip strength loss in hind limbs without paw swelling correlated only weakly with knee inflammation detected by µPET/CT.

Conclusion: In the CAIA model, inflammatory arthritis can develop in all peripheral joints, in particular with a high incidence in knee joints, which are highly suitable for subsequent histological analysis. Since clinical scoring seems insufficient for detecting these affected joints, implementation of in vivo imaging modalities such as µPET/CT, offers a substantial benefit in disease monitoring and assessment.