Background:

The evolution of pain in relation to damage in the synovium, bone and cartilage in osteoarthritis (OA), coupled with their relation to wet biochemical markers are not well understood.

Objectives:

In this study we evaluated the relation between structural damage by MRI, clinical and pain sensitisation measures and wet biochemical biomarkers in knee OA.

Methods:

We recruited 130 participants fulfilling ACR criteria with advanced OA requiring total knee replacement (TKR) (n=80), mild OA having standard care (n=42) and non-OA controls (n=8). Knee MRI in 90 subjects (72 F, 18 M) was acquired and assessed by two radiologists with the MRI Knee Osteoarthritis Score (MOAKS). Overall MOAKS scores were created for Bone Marrow Lesions (BML), Cartilage Degradation (CD) and effusion/Hoffa synovitis (tSyn). Type II collagen cleavage products (CTX-II) were determined by ELISA. Clinical scoring was performed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain levels (WOMAC_P), Hospital Anxiety and Depression Scale (HADS), Body mass index (BMI) and pain sensitisation with pain pressure thresholds (PPT) of the patella by Quantitative Sensory Testing (QST).

Results:

The mild OA group had a mean age of 63 +/-9 yr and the advanced OA group 69 +/- 9 yr. The advanced OA group had higher levels of pain, with a mean WOMAC_P of 58 +/- 22 compared with the mild OA group who had a mean WOMAC_P of 40 +/-22. WOMAC_P correlated with the total number of regions with cartilage damage (nCD) (R=0.225, p=0.033) and total number of BMLs (nBML) (R=0.195, p=0.065) using BMI, age and HADS as covariates. Levels of CTX-II correlated with tSyn (R=0.313, p=0.03), nBML (R=0.252, p=0.019), number of osteophytes (R=0.33, p=0.002) and nCD (R=0.218, p=0.042), using BMI and age as covariates. The correlation for urinary CTX-II with tSyn (p=0.006) is shown in Figure 1 using a partial linear regression analysis of MOAKS, BMI and age. We also found CTX-II correlated with lesion load scores (total number of lesions multiplied by MOAKS size by % damage scores) for CD (R=0.277, p=0.009) and BML (r=0.308, p=0.004). PPT correlated with patella MOAKS scores for nBML (R=-0.221, p=0.038) and nCD (R=-0.279, p=0.009), with HADS, BMI and age as covariates.

Conclusion:

There is a direct correlation between the degree of cartilage damage and BMLs with pain in OA. Type II collagen degradation products were higher when there was more severe MRI-detected synovitis, BMLs and cartilage damage in the knee joint, suggesting that the source of enzymes degrading type II collagen in OA, including matrix metalloproteinases, are also likely to be produced by synovium and bone (1) and not just cartilage, as previously hypothesised in other studies. There was also a correlation between pain sensitisation and

frequency of BMLs and cartilage degradation, suggesting that molecular mediators of pain sensitisation, which we have shown are produced by BMLs (1), are a cause of patient-reported OA pain.

References:

1. Kuttapitya et al. Annals Rheumatic Diseases, 2017; 76(10): 1764-73

Figure 1.