Purpose: Several MRI features in osteoarthritis (OA) have been found to associate with radiological progression. As these MRI features are known to be highly correlated with each other, we investigated the presence of patterns of MRI features by principle component analysis (PCA) and their association with radiological progression over 6 years’ time.

Methods: 205 patients (mean age (SD) 60 (7) years, 79.5% woman, median BMI (range) 26 (20-40), were investigated. These patients were part of the Genetics, Osteoarthritis, and Progression (GARP) study, that includes probands and their siblings with symptomatic OA at multiple sites; patients were followed for 6 years. MRI of one knee, median (range) Kellgren-Lawrence (KL) score 1 (0–3), was made in every patient and included in the present study. At baseline coronal, axial and sagittal proton density and T2-weighed images as well as sagittal 3D T1-weighted spoiled gradient echo frequency-selective fat-suppressed images were made at 1.5T MRI. Cartilage damage (thinning and focal lesions), osteophytes (central and marginal), cysts, bone marrow lesions (BMLs) and effusion/synovitis were scored according to the Knee Osteoarthritis Scoring System (KOSS) score for presence or absence in 9 compartments, including the patellofemoral joint (PFJ) and tibiofemoral joint (TFJ). Baseline and 6-year semi-flexed posterior-anterior and lateral knee radiographs were scored (0–3) for both osteophytes and joint space narrowing (JSN) at both TFJ and PFJ according to the Osteoarthritis Research Society International (OARSI) atlas and Burnett atlas, respectively. Radiographic progression was defined as an increase of ≥1 point in JSN. Patterns of MRI features were investigated in the whole joint, using principal component analysis (PCA). A factor was considered to load significantly on a component when loading exceeded 0.4. Subsequently, the association of patterns of MRI features with radiological progression adjusted for age, gender, BMI and baseline JSN was investigated, using generalized estimation equation (GEE) models to correct for possible family effects.

Results: Of 205 patients 139 (68%) had KL score ≥1 at baseline. 55% had an JSN score ≥1 and 50% osteophyte score ≥1 in PFJ or TFJ. Radiological follow-up was available in 133 patients. In TFJ progression of JSN was seen in 28.6% of patients and progression of osteophytes in 293% of patients. In PFJ progression of JSN was in 9.2% of patients and progression of osteophytes in 15.4% of patients. PCA of MRI features of the whole joint of all patients resulted in extraction of 6 components (Eigen value > 1), explaining 65% of variance. Component 1 was characterized by medial and lateral cartilage damage and osteophytes of the PFJ and medial and lateral osteophytes of the TFJ and was associated with JSN progression in the TFJ (OR(95%CI)1.8 (1.1–2.5)). Component 2 included lateral cartilage damage, cysts and BMLs of the PFJ and was significantly associated with JSN progression of the PFJ (OR(95%CI) 8.2 (1.8–41.6), not with JSN progression of the TFJ. Component 3 consisted of medial cartilage damage, cysts and BMLs of the TFJ and was associated with JSN progression in the PFJ (OR(95%CI) 12.3 (3.3–46.7)), whereas a trend was observed with JSN progression in the TFJ (OR(95%CI)1.8 (1.1–3.1), whereas a trend was observed with progression of JSN in the PFJ (OR(95%CI) 4.9 (1.9–12.5)). Component 4 was characterized by medial cartilage damage, cysts and BMLs of the PFJ, in component 5 the lateral MRI features cysts and BMI were incorporated and component 6 included cartilage damage and osteophytes on both sides of the TFJ. Component 4, 5 and 6 did not associate with JSN progression. Interestingly effusion/synovitis was not incorporated in any of the components. When analysing only patients with KL grade ≥1 at baseline comparable associations of component 1, 2 and 3 with JSN progression were seen.

Conclusions: Investigation of patterns of MRI features show that cysts and BMLs are related with cartilage damage in all compartments except in the lateral TFJ. Components including medial TFJ BMLs and lateral PFJ BMLs are associated with JSN progression. Furthermore, also components characterized by medial and lateral cartilage damage and osteophytes of both PFJ and TFJ are associated with JSN progression. These results suggest that JSN progression in PFJ and TFJ is related.

452 MICE NULL FOR THE ALTERNATIVELY SPliced EDA SEGMENT OF FIBRONECTIN EXHIBIT REDUCED KNEE INFLAMMATION AFTER TIBIAL COMPRESSION INJURY

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Purpose: The alternatively spliced EDA-III segment of fibronectin (FN) is required for several types of inflammatory tissue injury and has been observed to regulate chondrocyte function. We therefore wished to determine if it participates in the inflammatory response to joint trauma.

Methods: Transgenic mice were obtained that were either constitutively negative for FN-EDAIII (A−/−), or constitutively positive (A+/+). Immunohistochemistry was used to compare FN distribution between wild-type (WT) and FN-EDA null (A−) male C57Bl6 mice, aged 10–12 weeks. To create a joint injury, each strain was subjected to right knee Tibial compression injury and sham injury to the left knee. To measure glucose uptake as an indication of increased metabolic activity, knees were imaged with combined positron emission tomography (PET)/computerized tomography (CT) 30 minutes after tail vein injection of 200 μCi 18fluoro-deoxyglucose (FDG), n = 5 animals/group. To measure inflammatory cell activity, knees were imaged 6–12 hours after injection of ProSense-750 Fast (PerkinElmer), n = 9 animals/group. To estimate the extent of bone remodeling, knees were imaged 6–12 hours after injection of CatK-680 Fast (PerkinElmer) (n = 9 animals/group). uCT was performed post-mortem to assess subchondral trabecular bone volume/posterior volume (BV/TV) (n = 6 per group).

Results: Preliminary experiments revealed similar spatial patterns of total FN deposition in articular cartilage and synovial membranes of WT and A− mice (Fig. 1). Overall, with all 10 mice combined, injured knees had significantly greater PET signal than the paired uninjured contralateral knees 13 days post-injury (4.6 ± 0.66 vs. 3.7 ± 0.46, p = 0.035, avg ± 95%CI). When the mice were further stratified by genetic background, the injured knee had significantly higher PET signal than the uninjured knee in WT mice (5.3 ± 0.73 vs. 4.0 ± 0.75, p = 0.034) whereas PET signal was not increased in the injured vs. uninjured knees of A− mice (4.0 ± 0.75 vs. 3.4 ± 0.52, p = 0.297). Further, the average injured knee PET signal was significantly less in A− vs. WT mice, whereas UI signal did not differ significantly between groups (Fig. 1). Interestingly, at 24 days post-injury there were no significant differences in PET signals between Injured and Uninjured knees. Injury caused a significant increase in the activity of CatK and ProSense 4 days post-injury (Fig. 2) (p < 0.0001 for both probes) but there were no significant effects of EDA deletion on ProSense (n = 9 each group, p = 0.95) or CatK (p = 0.15) signals in either the injured or uninjured knee (Fig. 2). Subchondral bone density, which was significantly reduced in injured versus uninjured knees in both groups 7 days post-injury, was significantly greater in both uninjured and injured A− than WT knees (Fig. 3).

Conclusions: Fibronectin EDA −/− mice exhibit a less robust acute articular inflammation-associated metabolic response to trauma than WT mice, suggesting that the EDA segment participates in early inflammatory events related to post-traumatic OA development. Despite this, we found no evidence for reduced activity of cathepsins related to inflammation or bone-remodeling in A− compared to WT mice, suggesting that EDA promotes activity of an as-yet untested subset of inflammatory effector agents. Surprisingly, EDA deletion was found to be associated with increased subchondral bone density.
BONE-SEEKING SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES (SPIONS) FOR MAGNETIC RESONANCE IMAGING OF BONE TURNOVER IN EARLY OSTEOARTHRITIS

Purpose: Diagnosing osteoarthritis (OA) at an early stage would likely play a vital role in treatment and management of the disease. Etiology of OA is still unknown, however, it has been suggested that the primary initiating event(s) occur in subchondral bone, leading to subsequent cartilage degeneration. Bone turnover is routinely imaged clinically using nuclear medicine 99mTechnetium MDP bone scans, but at the cost of ionizing radiation and poor spatial resolution. If a marker of bone turnover can be visualized under MRI, then a single scan can provide greater resolution, no radiation side-effects, and the opportunity to image both cartilage integrity and the pattern of bone remodeling at the same patient sitting. The purpose of this study was to develop a bone-targeting contrast agent for MRI, to image altered bone turnover at the early stages of OA without ionizing radiation.

Methods: Superparamagnetic Iron Oxide Nanoparticles (SPIONS) with narrow size distribution were synthesized and conjugated with alendronate, a bisphosphonate (BP) drug which targets bone. The structure of SPIONS conjugated with alendronate (SPIONS-ALN) was characterized with various methods such as TEM, FT-IR, XPS, and affinity of SPIONS-ALN towards hydroxyapatite (HA) was evaluated in-vitro. Post-traumatic OA was induced in rats surgically by removing medial meniscus and...