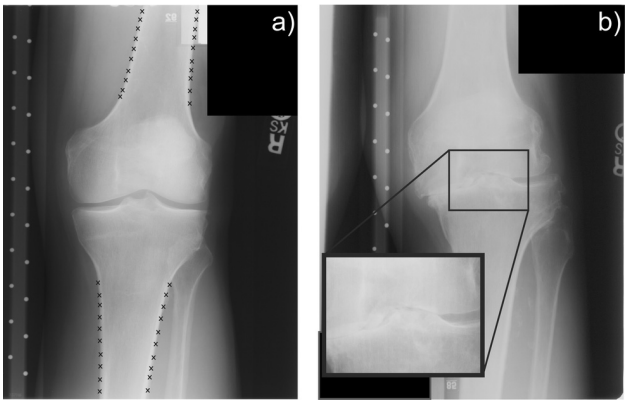


Figure 1. a) Illustration of the demarcated edges of the tibial and femoral bone shafts. b) In a patient with advanced OA and decreased JSW, demarcation of the tibial spine tips is not possible due to occlusion by the femoral head.

advanced OA and decreased joint-space width, such that the tibial spines were obscured by the femoral head (Figure 1b.)
**Conclusions:** Knee alignment is recognized as an important factor in the incidence and prevalence of knee OA. The bone shaft method agrees well with the previously validated lines-to-spines method of measuring knee alignment angle. Both demonstrate high reproducibility and fine precision. The bone shaft method does not rely on demarcation of the tibial spine tips, and can therefore be applied across a cohort that includes patients with advanced OA. Additionally, the method is more feasible for use in longitudinal studies when the tibial spine tips may become radiographically obscured over time. Finally, the bone shaft method demonstrates the feasibility of an automated measurement using edge-detection.

## P259

### CORRELATION OF BONE LESION CHANGES WITH CARTILAGE VOLUME LOSS IN KNEE OSTEOARTHRITIS PATIENTS AS ASSESSED BY QUANTITATIVE MRI OVER A TWO-YEAR PERIOD

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**Purpose:** To evaluate in knee osteoarthritis (OA) patients the size changes in bone hypersignal (edema) and hyposignal (cysts) over 24 months, and to contrast these changes with cartilage volume loss using quantitative magnetic resonance imaging (MRI).
**Methods:** A subset of 107 OA patients from a large clinical trial evaluating the impact of a bisphosphonate on knee OA was studied. This subset represented a standard study (mean age 62.4; 64% female; average BMI 30.6 kg/m$^2$). Patients with Kellgren-Lawrence grade IV radiographs were excluded. MR images of the knees were analyzed at baseline and 24 months. Edema, cysts and cartilage volume were quantitatively assessed.
**Results:** At baseline, 86 patients of the cohort showed the presence of at least one type of bone lesion: 71 had edema, 61 cysts and 51 both. At 24 months, the mean change in the edema size was an increase of 2.09 mm, and in cyst lesion size of 1.09 mm, but due to the high variability these did not reach statistical significance (one sample t-test). No impact of the bisphosphonate regimen was found on the bone lesion changes (edema, p=0.52; cysts, p=0.70; one-way ANOVA). Interestingly, when the knees were analyzed according to sub-regions, a statistical increase was found for the cysts in the trochlea (+0.67 mm, p=0.02) with a trend in the lateral tibial plateau (+0.15 mm, p=0.09), and for the edema in the medial tibial plateau (+1.73 mm, p=0.05). When the data on the bone lesion changes at 24 months were contrasted to corresponding cartilage volume loss, statistically significant correlations were seen in the medial sub-region between edema size change and the condyle cartilage volume loss (-0.40, p=0.0001; Spearman correlation test) and the tibial plateau (-0.23, p=0.03). Moreover, in the medial condyle, the cyst size changes were also correlated to the cartilage change (-0.29, p=0.01). No statistical correlation was seen for the lateral compartment. A multivariate analysis (multiple linear regression: age, gender, BMI, meniscal extrusion, meniscal tear) showed that edema size change was strongly and independently associated with cartilage volume loss (-0.31, p=0.0004).
**Conclusions:** These data demonstrate that bony lesions are prevalent in knee OA. The correlation of the edema and cyst size increase over time in the medial compartment with the loss of cartilage volume juxtaposed to the location of the lesions, underlines the importance of the subchondral bone remodeling in OA pathophysiology.

## P260

### LOWER EXTREMITY ALIGNMENT, RADIOGRAPHIC OSTEOARTHRITIS AND ABNORMAL SCINTIGRAPHY IN A COHORT WITH KNEE OA

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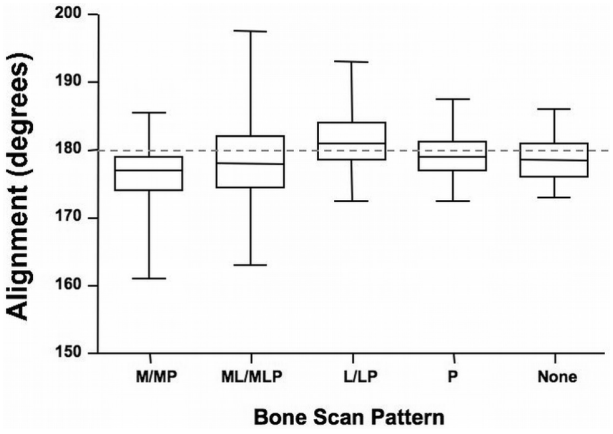
**Purpose:** The goal of this study was to evaluate lower extremity alignment and knee abnormalities in a cohort with knee OA, using knee and full leg radiographs, and bone scintigraphy, a sensitive method for detecting metabolic abnormalities of joints. We hypothesized that the localization and intensity of bone scan uptake and the severity of radiographic knee OA would be associated with the direction and severity of knee malalignment.
**Methods:** Participants in the Prediction of Osteoarthritis Progression (POP) study (n=159; 118 female, 41 male; mean age 64 years), met ACR criteria for knee OA and had Kellgren-Lawrence (KL) grades 1-4 radiographic OA in at least one knee. Late phase uptake (at 2.5 hours post injection) of technetium-99m methylene diphosphonate was scored semi-quantitatively as normal, mild, moderate or severe (graded 0-3) in the medial (M), lateral (L) and patello-femoral (P) compartments of the knee. Knees were categorized into mutually exclusive groups by location of any (grade $>$0) bone scan abnormality based upon the involved compartment(s) as M, L, P, ML, MP, LP, or MLP. Knee alignment was defined as the angle formed by the intersection of 2 lines, one from the center of the head of the femur to the center of the tibial spines, and a second from the center of the talus to the center of the tibial spines. Knee alignment of 180° was taken as the reference value and considered neutral for the purposes of these analyses. Statistical analyses were performed with JMP software (SAS, Cary, NC).
**Results:** A total of 308 knees were imaged; 10 knees were excluded due to a history of total knee replacement (TKR). The proportions of knees in each KL grade were 0.05% KL0, 29%KL1, 18%KL2, 42%KL3, 10%KL4. The proportions of knees in each alignment category were: 64%varus ($<$180°), 31% valgus ($>$180°), 4% neutral; range 161° to 197.5°. By linear trend analysis there was a significant positive association between KL grade and severity of malalignment (r=0.27 p$<$0.0001). Isolated patello-femoral uptake was the most common (20%) pattern of bone scan abnormality followed by MP (17%), MLP (17%),

isolated M (7.5%) or isolated L (8.5%) uptake. Total intensity of uptake score for the M and L compartments was associated positively with severity of malalignment (Spearman's rho=0.25, $p<0.0001$). Bone scan abnormalities of the medial compartment (M, MP) were associated with varus malalignment (mean 176°) (see Figure). Bone scan abnormalities of the lateral compartment (L and LP) were associated with valgus malalignment (mean 181°). Simultaneous abnormalities of both compartments were associated with a range of alignment angles and a mean angle of 178°, near neutral and the reported 1.1°-1.5° varus alignment of normal knees. By ANOVA and Tukey's post-hoc test, the mean knee alignment angle associated with L and LP patterns was significantly different ($p<0.001$) from that associated with M, MP, and MLP patterns of uptake.




**Conclusions:** Lower extremity malalignment and bone scan abnormality of the knee are known potent risk factors for knee OA progression. Malalignment has been associated with compartmental specific abnormalities by MRI including cartilage volume loss, bone marrow edema, and lower dGEMRIC indices. To our knowledge, this is the first study describing a relationship between knee malalignment and compartmental specific abnormalities by bone scintigraphy. Longitudinal analysis of this cohort is ongoing to determine the prognostic value of various patterns of uptake for knee OA progression.

## P261

### COMPARISON OF DIFFRACTION ENHANCED IMAGING TO MAGNETIC RESONANCE IMAGING FOR CARTILAGE LESIONS, IN SITU

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**Purpose:** To map the immunolocalization of type X collagen (col X), the tyrosine kinase cSRC, and S-100, a $Ca^{2+}$-binding protein in talar dome cartilage with calcium pyrophosphate dihydrate (CPPD) deposition.
**Methods:** 14 tali displaying CPPD crystals on the trochlea, 4 tali displaying cartilage degeneration and no CPPD, and 4 control tali displaying no cartilage degeneration were used. Each talus was divided into 6 regions, and full-thickness uncalcified cartilage was harvested from each region and prepared for Safranin O/fast green histology, Alizarin red for polarizing light microscopy, and immunohistochemistry for col X, cSRC, and S-100. Each of the parameters measured was scored from grade 0 (no presence) through 3 (greatest presence). Cartilage was graded for integrity. Statistical correlations were determined with the Spearman's test. Significance was taken at $p \leq 0.05$.
**Results:** Polarized light microscopy revealed that CPPD tali displayed crystals on the articular surface as well as in the middle and/or deep zones in varying amounts, and some as large cysts depending upon the specimen. The level of CPPD visible on the articular surface was not necessarily representative of the level of CPPD found beneath the surface. There was a significant positive correlation between the amount of CPPD crystal deposition and the level of col X and cSRC staining, but not with the level of S-100 staining. However, a high level of S-100 staining could be found in cell clones located adjacent to CPPD cysts. Col X was found in particularly high levels around CPPD crystals, but not associated with enlarged chondrocytes. However, Col X could be found in regions not associated with CPPD if CPPD was found somewhere on the talar surface. Col X was not found in control cartilages but it was found in talar cartilages displaying signs of degeneration but without CPPD. The most interesting finding was that there were several CPPD tali in which crystals could be found on the articular surface and creating intracartilagenous cysts, but in which the articular surface, including the entire superficial zone was intact and without cell loss or cloning. This made grading the cartilage integrity more difficult since often there were only isolated, but large CPPD cysts within the cartilage, the surface remaining intact.
**Conclusions:** To our knowledge, this is the first study on the mapping of immunolocalization of Col X, cSRC, and S-100 in CPPD cartilages. Col X, known to be associated with the late phase of hypertrophic chondrocytes, was found in all CPPD cartilages but was not associated with enlarged chondrocytes and thus raises the question as to the significance of Col X in CPPD cartilage. One possibility is that it is made by the chondrocytes in response to local inflammation-induced hypertrophy. cSRC was correlated to the level of CPPD in the immediate vicinity, which substantiates its role in CPPD-associated kinase cascade signaling. S-100 protein was found at greater levels in cell clones adjacent to CPPD cysts thus supporting the suggestion that it plays a role in matrix calcification and also in local inflammation-induced chondrocyte hypertrophy. In contrast to a previous report S-100 was not found in higher levels in enlarged, hypertrophic chondrocytes. The most interesting finding was that the superficial zone could be intact in the presence of overlying CPPD crystals.

## P262

### COMPARISON OF QUANTITATIVE CARTILAGE MEASURES BETWEEN 3D FAST LOW ANGLE SHOT (FLASH) AND REFORMATTED 3D DOUBLE ECHO STEADY STATE (DESS)

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**Purpose:** To cross-validate the precision of 3D FLASH and 3D DESS MR image contrast for the assessment of osteoarthritis (OA) based on measures of cartilage volume, cartilage thickness, and cartilage surface area.
**Methods:** Unilateral MR images of 12 persons (6 healthy persons, 6 with clinical OA of the knee) from an Osteoarthritis Initiative (OAI) pilot study were obtained. Each subject was imaged twice at 3 Tesla on a Siemens Trio to permit measurement