Conclusions: 1. Detectable contrast peak by CEUS was associated with lower KOOS indices  
2. Detectable arrival time correlated with number of synovial blood vessels  
3. In some patients CEUS and PDU can offer discrepant results. Further investigation is needed in cases of longer AT (> 30 sec) when CEUS might be more informative than PDU in detection of low blood flow  
4. Using CEUS and performing time/intensity analysis enables to distinguish states of increased vascularity in the KOA

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SENSITIVITY TO CHANGE OF KNEE IMAGES DIGITAL ANALYSIS COMPARED TO ALTMAN GRADING FOR CLASSIFICATION OF RADIOGRAPHIC PROGRESSION IN EARLY OSTEOARTHRITIS (CHECK)

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Purpose: Grading radiographic osteoarthritis (OA) on an ordinal scale commonly results in low sensitivity to change. Measurement of separate radiographic OA features on a continuous scale using Knee Images Digital Analysis (KIDA) theoretically enables more precise measurement and greater sensitivity to change. The longitudinal Cohort Hip & Cohort Knee (CHECK) evaluates radiographic progression early in OA. The objective of this study was to determine whether the sensitivity to change was greater by using KIDA than by using ordinal grading according to the Altman atlas.

Methods: Sensitivity to change was determined by calculation of the smallest detectable difference (SDD), which is a measure for the variability of the radiographic procedure and digital analysis. SDD was determined for the KIDA measures of the joint space narrowing (JSN; lateral and medial), osteophyte area (lateral and medial femur, lateral and medial tibia), and bone density (BD; lateral femur and medial tibia). Since no repeated radiographs were available, subsets of unchanged radiographic pairs from baseline to 2 year follow-up were selected based on an Altman grade of 0 at both time points. Radiographic pairs were selected from 1002 CHECK participants (2004 knees) for the JSN, osteophyte, and BD parameters separately (313, 303, and 213 pairs respectively). Next, of all CHECK participants available baseline and follow-up radiographic pairs were evaluated. The percentage of pairs changing on the radiographic parameters was determined for KIDA, defined as a change larger than the SDD, and for the Altman atlas defined as a change of at least one grade. Further, for each parameter radiographic pairs with a change on KIDA and/or Altman were evaluated using cross-tabulations.

Results: The SDD was on average 1.8mm for JSN, 3.4mm² for osteophyte area, and 11.6mmAL equivalents for BD parameters. Using KIDA, an average increase in OA features was found in 6.4% (JSN), 7.6% (osteophyte), and 3.5% (BD) of radiographic pairs. Using Altman, an increase in OA severity was found in 7.4% (JSN), 7.5% (osteophyte), and 0.8% (BD) of pairs. Interestingly, of the radiographic pairs with a change, only a small percentage changed both on KIDA and Altman grading, and a substantial percentage changed on either KIDA or Altman. E.g. for medial JSN 17% of radiographic pairs changed on KIDA and Altman, 38% changed only on KIDA, and 44% changed on Altman only. Agreement was 10% for osteophyte, and 0% for BD parameters.

Conclusion: Sensitivity to change of KIDA is comparable to Altman grading in patients with early OA and relatively short follow-up, despite the measurement on a continuous scale with KIDA. Importantly, KIDA and Altman grading identified different OA progressors. The latter needs thorough evaluation and might involve the quality of radiographic procedures leading to non-comparative radiographs over time.

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RESORPTIVE BONE REMODELING IS A PROMINENT FEATURE OF BONE MARROW LESIONS DETECTED BY MAGNETIC RESONANCE IMAGING (MRI) IN OSTEOARTHRITIS

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Purpose: Bone marrow lesions (BMLs) are an important source of symptoms and risk for disease progression in osteoarthritis (OA). Prior studies have suggested increased bone remodeling within these lesions. The objective of this study was to begin to test the hypothesis that BMLs in OA knees result from microfracture of pathologic bone with subsequent remodeling associated with secondary bone healing. Specifically, bone remodeling in BMLs was characterized histologically and presence and activity of osteoclasts in BMLs were histochemically evaluated.

Methods: Magnetic resonance imaging (MRI): Fourteen patients with predominantly medial compartment osteoarthritis scheduled for total knee replacement (TKR) were included in this study. MRI was performed using a 1.5T scanner with a dedicated extremity coil. After TKR, the patients were eligible for MRI 2 weeks after surgery. Standard T1, T2, and T2* images were obtained. BMLs were identified on T2* images as hyperintense regions on the femoral and tibial condyles that were larger than 0.5 cm².

Surgical excision of BMLs: BMLs were excised from both the femoral and tibial condyles of the TKR specimens. BMLs were defined as areas of subchondral bone that were identified on MRI as hyperintense regions on the femoral and tibial condyles. BMLs were sectioned into 3 mm slices. H&E staining was performed to qualitatively evaluate for active bone remodeling, endochondral ossification, and distribution of lesions. Osteoclastic bone resorption: Osteoclast presence and activity in the lesions were confirmed by positive TRAP, CD68 and Cathepsin K staining.

Results: Subchondral bone below regions of denuded cartilage was a consistent finding. Sclerosis was frequently accompanied by evidence of active bone remodeling, including reversal lines, presence of osteoid, and increased numbers of osteoblasts and osteoclasts. In some lesions there were islands of either necrotic bone or cartilage cores (variably mineralized) within these areas of active remodeling. Some of these islands were encased within bone, while others were in the process of active remodeling characterized predominantly by osteoclastic resorption.

Conclusion: BMLs exhibited enriched populations of osteoclasts compared to non-lesion bone, as evidenced by the presence of TRAP positive multinucleated osteoclasts in both the Haversian canals and marrow spaces of subchondral bone. The presence of osteoclasts in BMLs was characterized by endochondral ossification and presence of TRAP+ osteoclasts in regions of demineralization. The appearance of the classic osteoclast “ruffled border” and presence of Howships Lacunae on the bone surface. BMLs were associated with active bone remodeling, especially in regions below denuded cartilage. Endochondral ossification is involved to some extent in new bone formation in a number of these lesions. These results suggest increased bone remodeling in development and progression of BMLs in OA knees, and may be attributed to increased osteoclastic activity. Further investigation of the role of pathologic bone remodeling in the development and progression of BMLs is warranted given their pathological and clinical significance.

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INCREASED VASCULAR PENETRATION AND NERVE GROWTH IN THE MENISCS: A POTENTIAL SOURCE OF PAIN IN OSTEOARTHRITIS

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Purpose: Meniscal damage increases the risk of osteoarthritis (OA), accelerating disease onset and severity. This study describes vascular penetration