with knee osteoarthritis (OA) stages in a nonlinear way. We determined whether the baseline TB texture, measured by DFS parameters, is associated with the risk of tibio-femoral (TF) OA incidence over 30 months.

Methods: The Multicenter Osteoarthritis (MOST) study is a longitudinal cohort study of subjects with or at risk for knee OA.

Posteroanterior radiographs were acquired at baseline and 30 months follow-up and read for Kellgren-Lawrence (KL) grade. Of 6052 knees from 3026 subjects of the MOST, 2028 knees (1407 subjects) with KL grade 0 or 1 at baseline considered eligible for the incidence of TFOA (KL≥2 at the follow-up). Exclusions were screen overlapping (vertical lines), under- and overexposure of X-ray (white or black bone image), knee injury and surgery, rheumatoid arthritis, osteonecrosis, undetermined TF status at 30 months, or missing knee alignment measurement. On baseline X-rays TB texture regions were automatically selected on medial and lateral compartments of the tibia under cortical plates. A variance orientation transform method was applied to each region, and seventeen fractal parameters were calculated at small (S), medium (M) and large (L) ranges of trabecular image sizes, i.e.: four fractal dimensions FD_{MEAN}, FD_V, FD_H, FD_{Sta}; nine FSs along the direction of the texture roughest part (FS_{Sta_S}, FS_{Sta_M}, FS_{Sta_L}), the horizontal (FS_{H_S}, FS_{H_M}, FS_{H_L}) and vertical (FS_{V_S}, FS_{V_M}, FS_{V_L}) directions; four aspect ratios (Str, $StrS_S$, $StrS_M$, $StrS_L$). FSs and FDs measure the roughness of bone texture and aspect ratios measure the texture anisotropy. We categorized the knees into quartiles of each fractal parameter (Q1, Q2, Q3, Q4). In compartment-specific analyses we assessed the association of baseline texture parameters and incident TFOA by means of logistic regression adjusted for covariates. GEE methods were used to account correlations between knees in one subject. Odd ratios (ORs) were calculated for each of quartiles in comparison with the lowest (reference). Trends were tested. $p < 0.05$ was considered as significant.

Results: Results were stratified by clinics since UAB and UIowa X-rays were acquired using different techniques and resolutions. In the longitudinal study, 54 (out of 874, UAB) and 80 (out of 1154, UIowa) knees had TFOA at 30 months follow-up. For digitized films, statistically significant ORs were 1.94 for Q3 of $StrS_M$ (medial) and 0.46 for Q2 of FS_{H_M}, 0.54 for Q3 of Str and 0.42 for Q3 of $StrS_S$ (lateral). For CR, ORs were 0.32 for Q3 of FS_{Sta_L} (medial) and 2.56 for Q3 of FD_{MEAN}, 2.95 for Q2 of FD_V and 4.08 for Q2 of FS_{V_M} (lateral) (Table 1). For other texture parameters ORs were not statistically significant.

Conclusions: Baseline TB texture parameters are significantly associated with an increased risk of TFOA incidence. In digitized films, the higher medial bone isotropy and the lower lateral bone roughness (horizontal and roughest part FSs) have support in previous studies (OA bone realignment and thickening). In CR, the lower medial and higher lateral bone roughness are associated with the risk of OA.

Table 1, Risk of TFOA incidence by quartile of baseline fractal texture parameters

University of Alabama (UAB), Birmingham (computer radiography (CR), 149 dpi)			University of Iowa (Ulowa), Iowa City (digitized film, 254 dpi)		
Quartile (range)	Incident TFOA/ No of knees (%)	Adj. OR* OR (95% CI)	Quartile (range)	Incident TFOA/ No of knees (%)	Adj. OR* OR (95% CI)
Medial compartment					
	FS_{Sta_L}			$StrS_M$	
Q1 (2.51 -2.71)	18 / 219 (8.2)	1.0 (ref)	Q1 (0.19- 0.57)	21/283 (7.3)	1.0 (ref)
Q2 (2.71 - 2.75)	8/218 (3.7)	0.46 (0.20-1.04)	Q2 (0.57-0.64)	17/287 (5.9)	0.89 (0.44-1.77)
Q3 (2.75 - 2.79)	6/220 (2.7)	0.32 (0.12 0.89)	Q3 (0.64-0.71)	23/291 (7.9)	1.91 (1.05-3.58)
Q4 (2.79- 2.96)	22/217 (10)	1.34 (0.65-2.79)	Q4 (0.71 - 0.96)	19/288 (6.6)	1.17 (0.56-2.44)
linear trend		p = 0.51	linear trend		P = 0.33
U shape trend		p = 0.04	U shape trend		p = 0.09
Lateral compartment					
	FD_{MEAN}			FS_{Sta_L}	
Q1 (2.59 - 2.77)	12/218 (5.5)	10 (ref	Q1 (2.45 - 2.66)	22/283 (7.6)	1.0 (ref)
Q2 (2.77 - 2.82)	10/218 (4.6)	1.04 (0.41-2.67)	Q2 (2.66-2.71)	20/289 (6.9)	0.81 (0.42-1.54)
Q3 (282 – 2.86)	20/217 (9.2)	2.56 (1.14-5.74)	Q3 (2.71 - 2.77)	12/289 (4.2)	0.46 (0.22-0.97)
Q4 (2.86-2.96%)	12/221 (5.4)	1.16 (0.45-2.97)	Q4 (2.77 -2.93)	26/288 (9.0)	0.97 (0.51-1.81)
linear trend		p = 0.34	linear trend		p = 0.65
U shape trend		p = 0.28	U shape trend		p = 0.39
	FD_V			FS_{H_M}	
Q1 (2.45-2.70)	10/220 (4.5)	1.0 (ref)	Q1 (2.28 -2.58)	22/288 (7.6)	1.0 (ref)
Q2 (2.70- 2.78)	18/218 (8.3)	2.95 (1.25-6.95)	Q2 (2.58-2.68)	12/289 (4.2)	0.46 (0.22-0.95)
Q3 (2.78-2.83)	15/219 (6.8)	2.06 (0.83-5.10)	Q3 (2.68 - 2.79)	19 / 289 (6.6)	0.81 (0.41-1.58)

93

IS THE RISK OF INCIDENT RADIOGRAPHIC KNEE OA RELATED TO SEVERITY OF CONTRA-LATERAL RADIOGRAPHIC KNEE STATUS? -DATA FROM THE OSTEOARTHRITIS INITIATIVE

S. Cotofana [†,‡], W. Wirth [†,‡], K.C. Kwoh [§], D.J. Hunter [‖], J. Duryea [¶], F. Eckstein [†,‡]. [†] *PMU-Salzburg, Salzburg, Austria;* [‡] *Chondrometrics GmbH, Ainring, Germany;* [§] *Div. of Rheumatology and Clinical Immunology, Pittsburgh, PA, USA;* [‖] *Univ. of Sydney, Sydney, Australia;* [¶] *Harvard Med. Sch., Boston, MA, USA*

Purpose: Radiographic knee osteoarthritis (ROA) frequently is a bilateral disease. The "Chingford-Knee-Study" found the 2-year incidence of ROA (KLG≥2 in extended radiographs) to be 47% in 58 obese, middle-aged women with unilateral ROA (one knee Kellgren Lawrence [KLG] 0/1; the contralateral KLG≥2). ROA incidence, however, was almost exclusively observed in KLG1 rather than in those without any sign of ROA (KLG0). The aim of this study therefore was to examine the incidence of ROA and joint space width (JSW) change in KLG0 knees using fixed flexion radiographs. We hypothesized that ROA incidence and JSW change are related to contralateral [CL] ROA status.

Methods: Baseline KLG0 knees of 4796 participants from the Osteoarthritis Initiative (OAI) were included based on central radiographic readings. After separating those from the healthy reference cohort, knees were stratified by CL KLG status and CL trauma history (OAI-variable: INJR/INJL). In each stratum (no CL ROA [KLG0/1]; moderate CL ROA [KLG2]; severe CL ROA [KLG3/4]), the percentage of knees with incident ROA (KLG≥2) was determined. JSW change (mJSW and x=225 fixed location) was available for a small subset. Statistical analysis (crude and with adjustment for age, sex, BMI) was performed in those with and without CL trauma history.

Results: 1618 OAI participants had ≥1knee with baseline KLG0 status (892 women, BMI: 27.2±4.3kg/m^2, age: 59.6±9.1yrs, 757 right knees). Of these, 837 were CL KLG0, 304 KLG1, 253 KLG2, 111 KLG3, and 35 KLG4. Of those 466 had a CL trauma history, and 77 were from the healthy reference cohort. Incidence rates and JSW change between baseline and year 2/4 follow up are shown in Table 1. In the group without CL trauma, ROA incidence at year 4 in the healthy reference cohort was 1.4%. In KLG0 knees with risk factors incidence was 2.8%; the relative risk (RR) was significantly greater in knees with moderate CL ROA (7.9%; RR=2.8; 95%CI 1.4-5.6) and particularly in those with severe CL ROA (16.7%; RR=6.3; 95% CI 3.1-12.8). The 4-year minimal JSW change in KLG0 knees did not significantly differ between categories when excluding knees with CL trauma, but was significantly (p=0.004) greater in those with severe (-570μm) than in those without CL ROA (-424μm) when including those with CL trauma (Table 1).

(*continued*)

University of Alabama (UAB), Birmingham (computer radiography (CR), 149 dpi)			University of Iowa (Ulowa), Iowa City (digitized film, 254 dpi)		
Quartile (range)	Incident TFOA/ No of knees (%)	Adj. OR* OR (95% CI)	Quartile (range)	Incident TFOA/ No of knees (%)	Adj. OR* OR (95% CI)
Q4 (2.84 - 2.98)	11 / 217 (5.1)	1.64 (0.60-4.48)	Q4 (2.79 - 3.04)	27/288 (9.4)	1.23 (0.63-2.40)
linear trend		p = 0.49	linear trend		p = 0.36
U shape trend		p = 0.13	U shape trend		p = 0.04
	FS_{V_M}			Str	
Q1 (2.40 - 2.69)	8/218 (3.7)	1.0 (ref)	Q1 (0.31 -0.51)	29 / 287 (10)	1.0 (ref)
Q2 (2.69 - 2.77)	207/219 (9.1)	4.08 (1.65-10.10)	Q2 (0.51 -0.57)	18/291 (6.2)	0.59 (0,32-1.08)
Q3 (2.77 - 2.84)	14 / 220 (6.4)	2.18 (0.83-5.69)	Q3 (0.57 - 0.63)	15/288 (5.2)	0.54 (0.29-1.00)
Q4 (2.84 - 3.00)	12/217(5.5)	2.37 (0.89-6.32)	Q4 (0.64 - 0.88)	18 / 288 (6.3)	0.67 (0.36-1.25)
linear trend		p = 0.31	linear trend		p = 0-19
U shape trend		p = 0.18	U shape trend		p = 0.04
–	–	–		$StrS_S$	
–	–	–	Q1 (0.27-0.50)	28/288 (9.7)	1.0 (ref)
–	–	–	Q2 (0.50 - 0.58)	20/289 (6.9)	0.72 (0.38-1.34)
–	–	–	Q3 (0.58-0.68)	12/289 (4.2)	0.42 (0021-0.83)
–	–	–	Q4 (0.68 - 0.93)	20/288 (6.9)	0.72 (0.37-1.40)
–	–	–	linear trend		p = 0.19
–	–	–	U shape trend		p = 0.35
–	–	–		$StrS_M$	
–	–	–	Q1 (0.20 - 0.47)	30/288 (10)	1.0 (ref)
–	–	–	Q2 (0.47-0.55)	23/289 (8.0)	0.76 (0.43-1.35)
–	–	–	Q3 (0.55 - 0.63)	9/290 (3.1)	0.33 (0.15-0.70)
–	–	–	Q4 (0.64-0.91)	18/287 (6.3)	0.62 (0.33-1.19)
–	–	–	linear trend		p = 0.06
–	–	–	U shape trend		p = 0.13

*Adjusted for sex, age, race, body mass index (BMI), leg alignment, TF status of contralateral knee and baseline KL grade.

Conclusions: The findings support the concept that idiopathic OA is a bilateral disease, and that the risk of incident ROA and structural change in radiographically normal knees is strongly related to (the severity of) CL ROA status. KLG0 knees with CL KLG≥2 may thus be considered an "accelerated" ROA incidence model for studying early (pre-radiographic) changes in OA.

Table 1
ROA incidence and JSW change (subset) in baseline non-ROA (KLG0) knees, depending on contralateral (CL) knee ROA status and trauma history.

		2-year follow up			4-year follow up		
	CL ROA status (n= incidence / JSW analysis)	% ROA incidence	Δ mJSW (μm) (mean/SEM)	Δ x=225 JSW (mean/SEM)	% ROA incidence	Δ mJSW (μm) (mean/SEM)	Δ x=225 JSW (mean/SEM
	Healthy ref. (n=77/77)	0	-161 / 50	-171 / 49	1.3	-189 / 51	-261 / 42
All KLG0 knees n=1618	No CL ROA (n=1142/174)	1.3	-148 / 39	-138 / 38	2.7	-365 / 55	-360 / 48
	Mod. CL ROA (n=253/89)	6.3	-84 / 52	-107 / 48	9.9	-340 / 84	-377 / 74
	Severe CL ROA (n=146/86)	5.5	-286 / 70	-225 / 58	14.4	-622 / 87	-522 / 78
	Healthy Ref. (n=74/74)	0	-161 / 52	-169 / 51	1.4	-192 / 53	-264 / 43
KLG0 knees without CL trauma n=1152	No CL ROA (n=866/126)	1.3	-183 / 49	-142 / 45	2.8	-424 / 69	-389 / 60
	Mod. CL ROA (n=152/49)	6.6	-108 / 71	-191 / 74	7.9	-301 / 102	-410 / 95
	Severe CL ROA (n=60/35)	10.0	-203 / 103	-206 / 96	16.7	-570 / 142	-511 / 137

94
IN VIVO IMAGING OF NF-κB ACTIVITY AND CORRELATION TO PAIN IN A MODEL OF RADICULOPATHY

R.D. Bowles [†], I.O. Karikari [‡], K.J. Riebe [§], G.D. Sempowski [§], L.A. Setton [†,‖]. [†] *Dept. of BioMed. Engineering, Duke Univ., Durham, NC, USA;* [‡] *Dept. of Surgery, Duke Univ., Durham, NC, USA;* [§] *Dept. of Med. and Human Vaccine Inst., Duke Univ., Durham, NC, USA;* [‖] *Dept. of Orthopaedic Surgery, Duke Univ., Durham, NC, USA*

Purpose: Intervertebral disc (IVD) herniation is a protrusion or extrusion of disc material upon the ganglion that can contribute to back pain, radicular pain (radiculopathy), and nerve root dysfunction. Nerve root compression and biochemical irritation associated with IVD herniation may activate an immune system response characterized by monocyte infiltration into nerve and IVD tissues with an associated increase in expression of pro-inflammatory cytokines. Much neuroinflammation in IVD herniation falls downstream of activation of the transcription factor, NF-κB. The goal of this study is to test for a correspondence between painful symptoms and NF-κB activation using longitudinal luminescence in vivo imaging of NF-κB activity in combination with testing of pain sensitivities.
Methods: Transgenic mice engineered to carry cDNA for luciferase downstream of NF-κB response elements were used in this study (n=24, BALB/c-Tg(NFκB-RE-luc), age 12 weeks, Taconic). Mice were subjected to either a chronic constriction injury (CCI) of the sciatic nerve (n=12) or a sham surgery (n=12). Mice undergoing surgery were sacrificed on day 3 (n=6/group; CCI, Sham) or day 28 post surgery (n=6/group; CCI, Sham). All mice underwent live animal luminescence imaging (IVIS Spectrum, PerkinElmer) of NF-κB activity with quantitative determination of luminescence acquired for regions of interest (ROI) corresponding to the sciatic nerve. Ex vivo imaging of NF-κB activity immediately upon sacrifice was also obtained for nerve, muscle and other tissues to confirm specificity of the ROI signal. In addition, animals underwent von Frey testing of mechanical allodynia to determine a threshold of 50% paw withdrawal, and the Hargreaves method of testing thermal hyperalgesia preoperatively and at multiple timepoints after surgery. Data was analyzed with two-factor analysis of variance (Tukey post hoc tests) and Spearman ρ correlations.
Results: The CCI model produced painful symptoms consistent with IVD herniation induced radiculopathy and increased NF-κB activity in the transgenic NF-κB reporter mouse. NF-κB activity was increased ($p<0.05$) in the ipsilateral ROI of the CCI group compared to the sham group on days 3, 7, and 14 (Fig 1A). Von Frey testing demonstrated