

Identifying radiographic phenotypes of early knee OA

Towards more targeted treatment

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OA phenotypes



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- OA symptoms and radiography vary between patients, between disease stages, and over time
- This may prove important in determining optimum (potential) treatment
- Identifying radiographic phenotypes would expectedly be facilitated by use of quantitative evaluation of separate radiographic OA features

Current goal

- To investigate whether different longitudinal radiographic phenotypes of very early-stage knee OA can be recognized...
- ... using continuous measures of individual radiographic OA features.

Cohort Hip & Cohort Knee

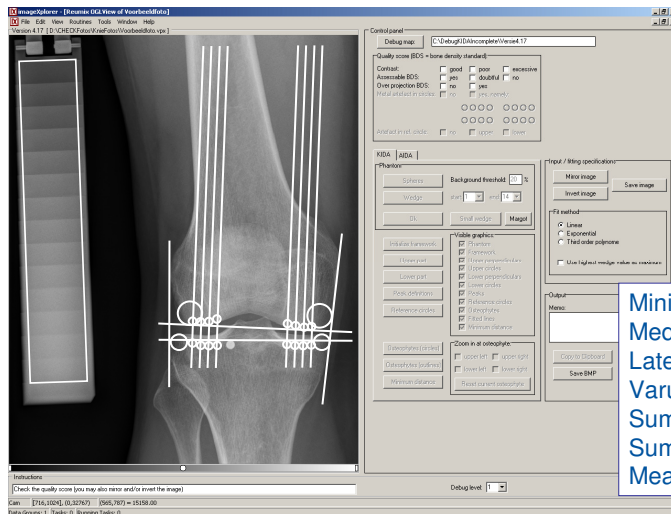
- 1002 Subjects
- Inclusion criteria:
 - Pain and/or stiffness of knee(s) and/or hip(s)
 - Never or no longer than 6 months ago visited a general physician because of these complaints
 - Age 45-65 years



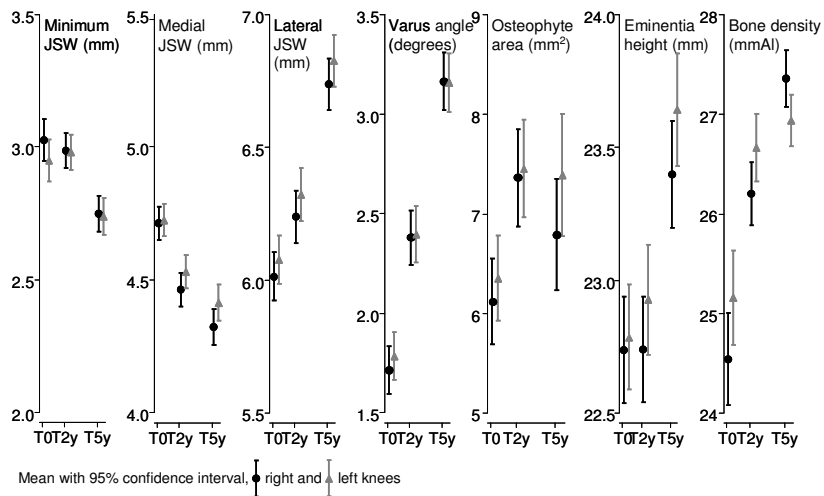
Knee radiographs

- Weight-bearing, semiflexed, posteroanterior
- At baseline, 2 year, 5 year
- Scoring
 - One observer
 - Blinded to sequence and clinical characteristics

Knee Images Digital Analysis (KIDA)



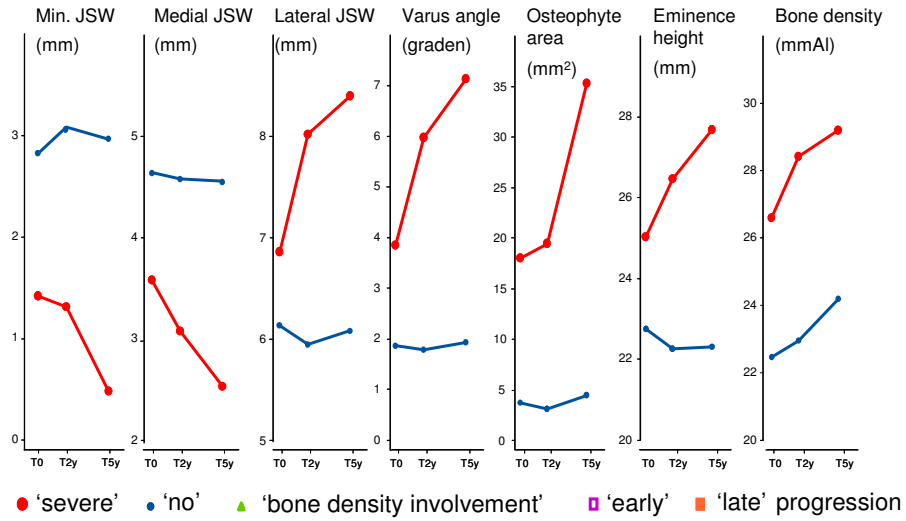
Overall progression



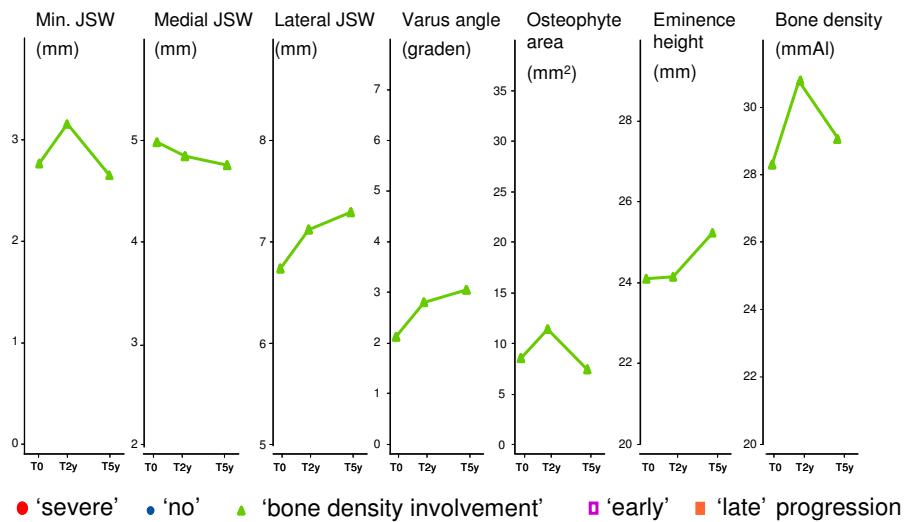
Identification of phenotypes

- Hierarchical cluster analysis (N=417)
 - Radiographic parameters left and right at T0, T2, T5
 - Change in radiographic parameters (T2-T0 and T5-T2)
 - Standardized using z-scores
 - Ward's method

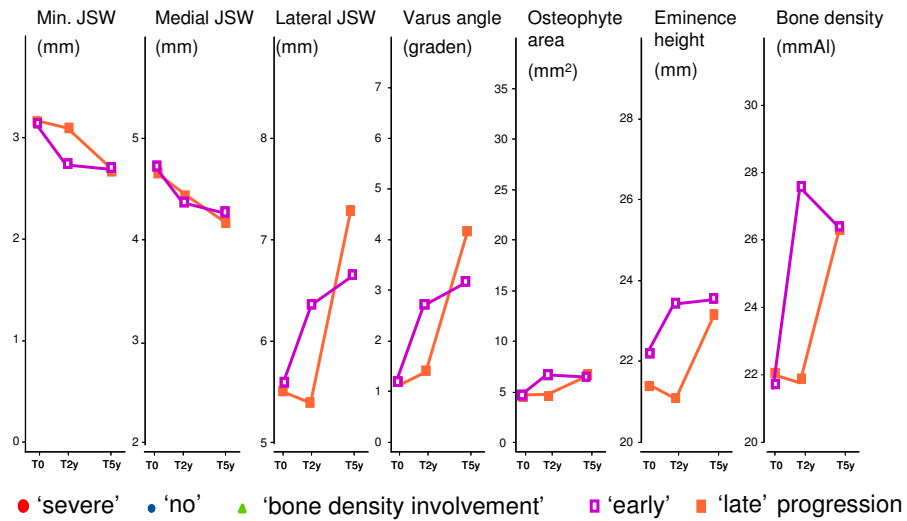
Radiographic progression phenotypes



Radiographic progression phenotypes



Radiographic progression phenotypes



Identified phenotypes

- Severe progression (N=17; 4%)
 - Bone density (N=113; 27%)
 - Early progression (N=110; 26%)
 - Late progression (N=69; 17%)
 - No progression (N=108; 26%)
- Can these longitudinal phenotypes be predicted by baseline characteristics?

Characteristics of phenotypes

	'Severe' (n=17)	'Bone density' (n=113)	'Early' (n=110)	'Late' (n=69)	'No' (n=108)	'p-value'
Age (yrs)	58 (4)	56 (5)	56 (5)	56 (5)	57 (5)	0.16
Female	82%	55%	81%	88%	92%	<0.0001
BMI (kg/m ²)	27 [25-31]	27 [24-30]	24 [23-27]	24 [23-27]	24 [22-27]	<0.0001
ESR (mm/hr)	9 [5-15]	6 [4-12]	8 [5-15]	8 [5-13]	9 [5-15]	0.07
K&L score \geq II	26%	4%	3%	2%	2%	<0.0001
Pain in knee	71%	44%	40%	30%	34%	0.002

Outcome T=5y

K&L score \geq II	39%	23%	16%	12%	6%	<0.0001
Pain in knee	53%	29%	30%	27%	21%	<0.0001

Mean (SD) and median [25-75 percentile]

Prediction of phenotype membership

	severe	bone	early	late	no
AUC	NA	0.91	0.79	0.76	0.72

Radiographic feature

Min JSW					
Medial JSW		+			
Lateral JSW				-	
Varus angle		+	-		+
Osteophyte		+			-
Eminence		+	-	-	+
Bone density		+	-	-	

Demographic & clinical

Age					+
Female gender		-		+	+
BMI					-


Conclusions and discussion

- Specific phenotypes of radiographic knee OA progression in early-stage OA
- Phenotypes represented the level (severe vs. no), the phase of progression (early vs. late), and the involvement of specific features (e.g. bone density)
- Baseline demographic and radiographic features could partly predict phenotypes

Conclusions and discussion

- Phenotypes might represent relevant subgroups for the evaluation of treatment strategies in clinical trials
- Validation needed
- Relation with long-term clinical outcome and treatment will determine usefulness
- Clustering on radiographical and clinical characteristics as next step

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