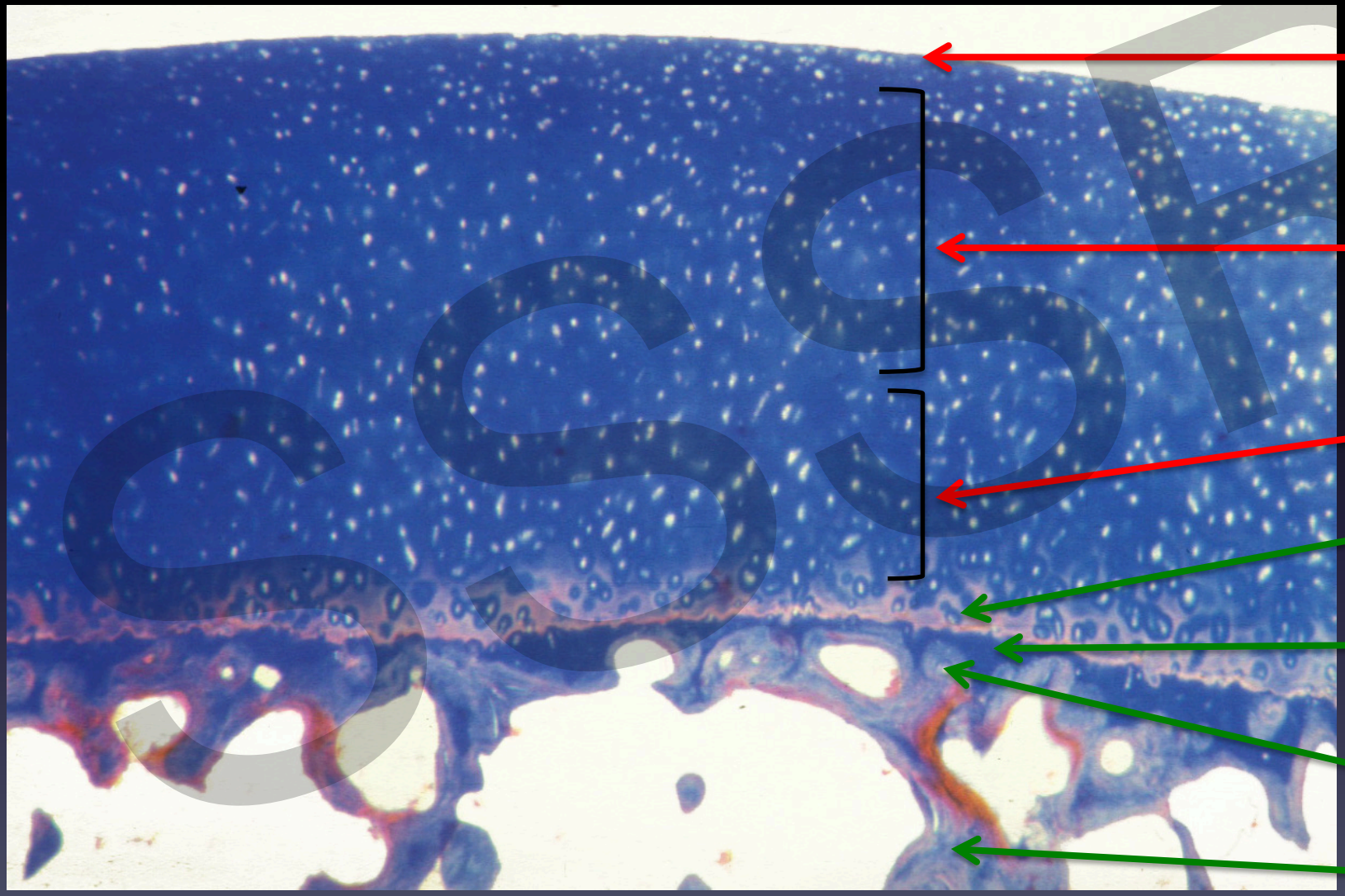
Cartilage defects and the subchondrale plate

Martin Kretzschmar
Radiology, University hospital Basel

University Hospital Basel

Bone-Cartilage Unit

University Hospital Basel



By courtesy of Mueller-Gerbl M, Anatomy Basel

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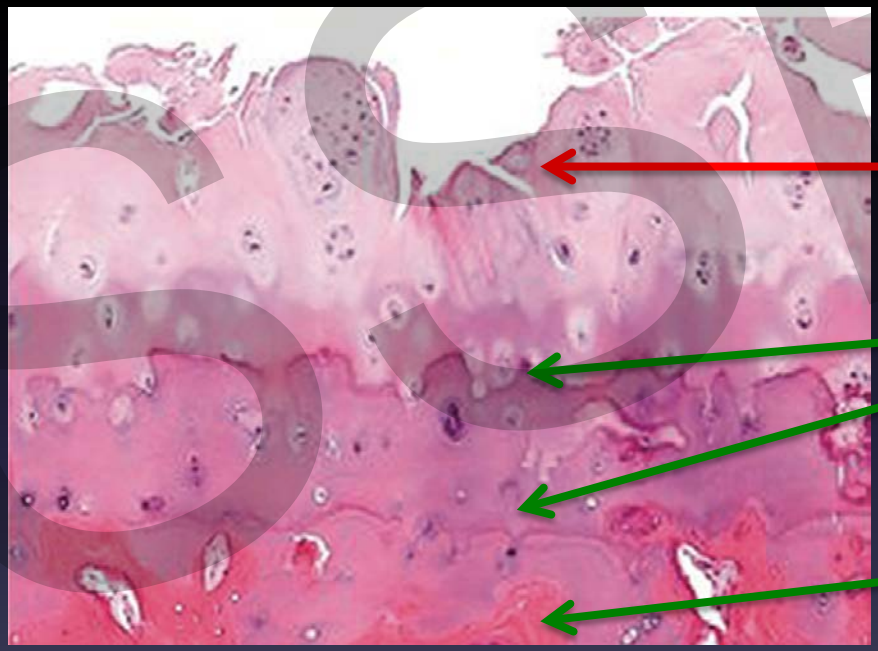
Structural changes of the bone-cartilage unit in OA



Goldring SR *Ther Adv Musculoskel Dis 2012*

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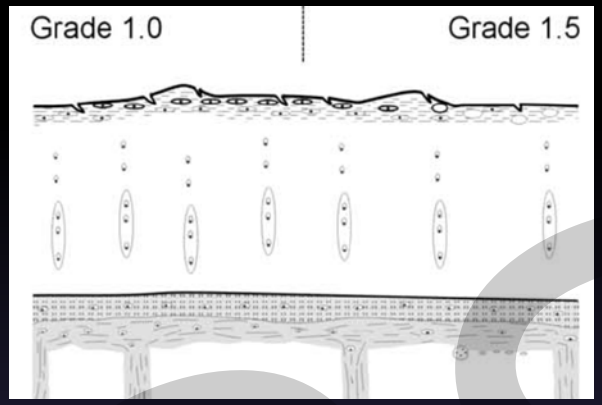
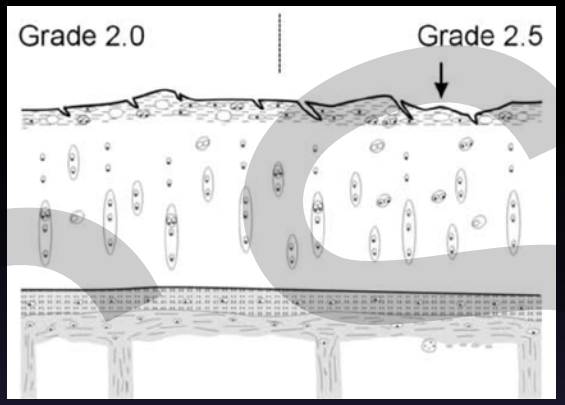
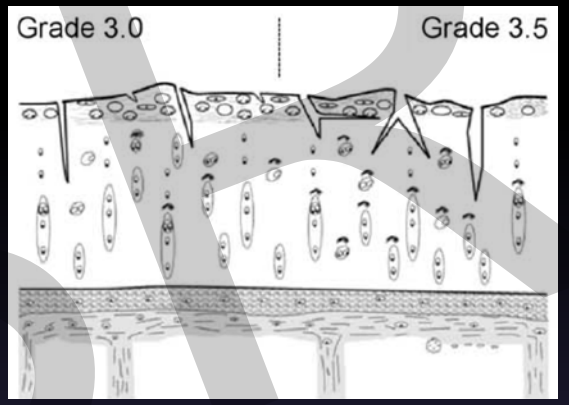
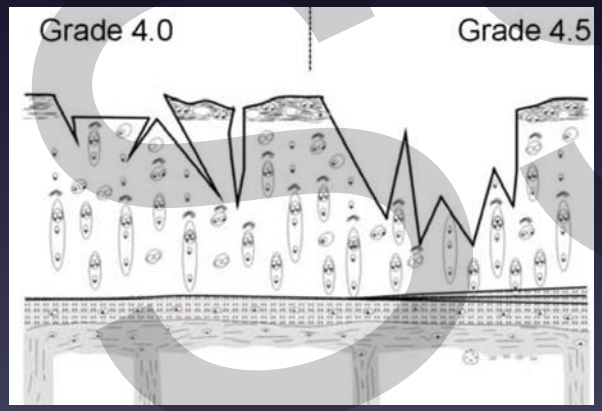
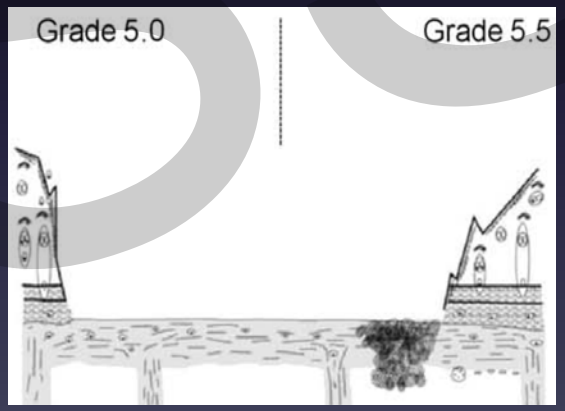
Structural progression in OA
OARSI Histology Grading System

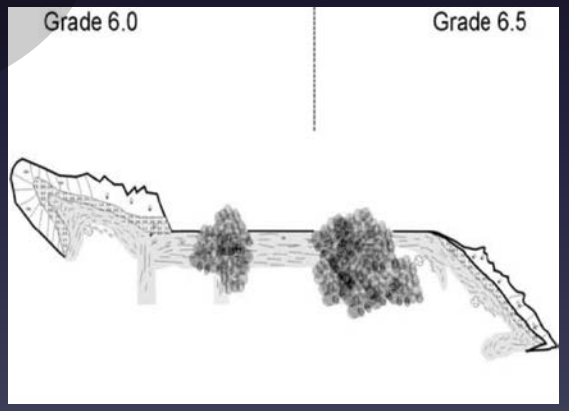












Pritzker KP *Osteoarthritis Cartilage* 2006

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Alternative Hypothesis: Bone is the primary tissue of degeneration

Discrepancy between bone scan activity and radiographic OA
Hutton CW et al. *Annals of the Rheumatic Diseases* 1986, McCray F et al *Annals of the Rheumatic Diseases* 1992

Bone scan uptake predicts radiographic OA
Hutton CW et al. *Annals of the Rheumatic Diseases* 1986

Progression of cartilage lesions may require increased stiffness of the subchondral bone
Radin EL et al. *Clin Orthop Relat Res* 1986

Microcracks induce enchondral ossification advanement of tidemark and thinning of cartilage from below
Burr DB, Radin EL *Rheum Dis Clin North Am* 2003

Imbalance between adaptive capacities of bone and cartilage may trigger progression
Goldring MB, Goldring SR *Ann. N.Y. Acad. Sci.* 2010

Hutton CW et al. *Annals of the Rheumatic Diseases* 1986

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Adaptive structural bone changes in OA

Variety of different phenomena:

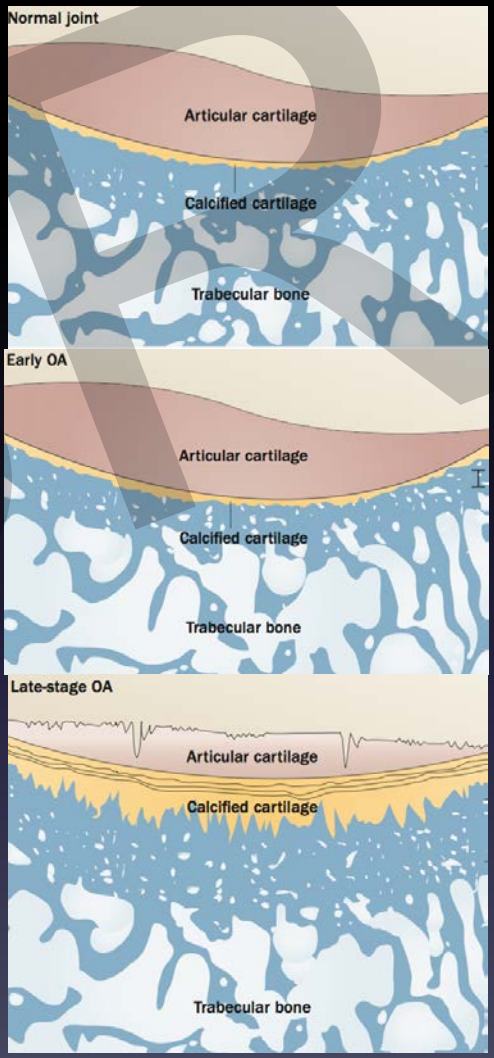
- Sclerosis
- BME
- Cysts
- Attrition
- Osteophytes
- Bone metabolism

Subchondral sclerosis and cartilage lesions

Subchondral remodelling in OA is a biphasic process:

1. Increased remodelling in early OA
2. Decrease of remodelling rate and sclerosis in advanced OA
3. Imbalance of osteoblast and osteoclast activity leads to "softer" bone

Burr DB, Gallant MA Nature Rev Rheumatol 2012.



From Burr DB, Gallant MA Nature Rev Rheumatol 2012.

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BME and cartilage lesions

Histology:

Predominant normal bone marrow with fibrosis, necrosis and abnormal trabeculation and a small proportion of edema

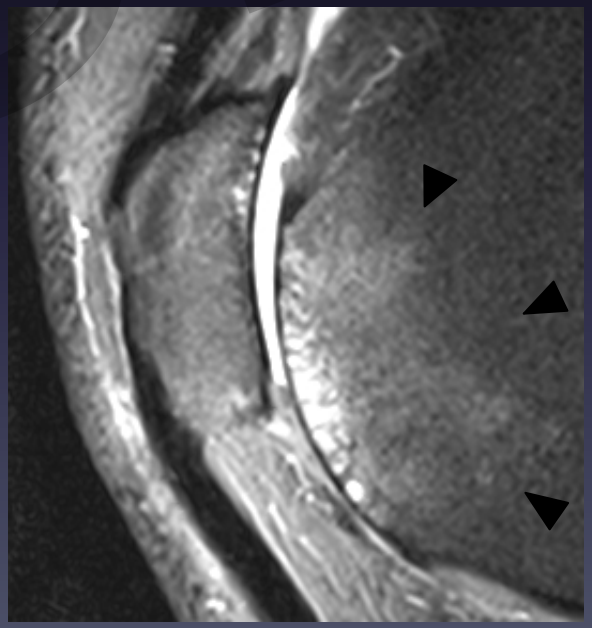
Zanetti M et al. *Radiology* 2000

Ingrowth of fibrovascular tissue and increased remodelling

Sadaat et al. *Eur Radiol* 2008

Microfracture in hip OA

Taljanovic MS et al. *Skeletal Radiol* 2008



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BME and cartilage lesions

Are crosssectionally associated with cartilage lesions
Baranyay FJ et al. *Semin Arthritis Rheum* 2007

Predict radiographic progression in association to limb alignment
Felson DT et al. *Ann Intern Med. 2003*

Increased risk for progression of cartilage lesions in the same subregion (OR 3.88 adjusted for age gender and BMI)
Kothari A et al. *Arthritis Care Res* 2010

Predict loss of cartilage volume at the same site. Cartilage lesions predict worsening of BME
Dore D et al. *Arthritis Research & Therapy* 2010

Moderate evidance that BME is associated with pain
Yusuf E et al *Ann Rheum Dis* 2011

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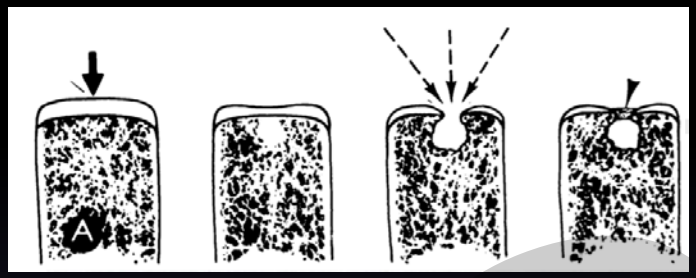
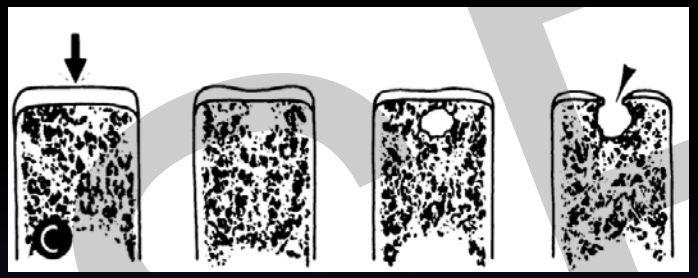
Cysts and cartilage lesions

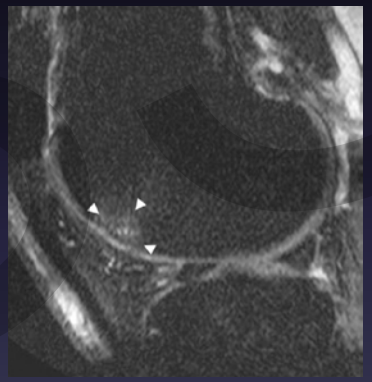


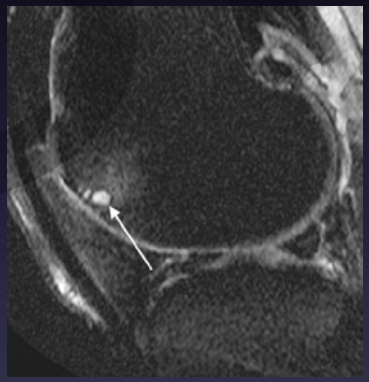


Resnick D et al. *Am J Roentgenol* 1977

Develop in regions with BME

Carrino JA et al. *Osteoarthritis Cartilage* 2006





Incident cysts are strongly associated to prevalent BME (OR 12.9, Full thickness Cart lesions 1.4)

Crema MD et al. *Radiology* 2010

No significant risk for progression of cartilage lesions in the same subregion (OR 1.66 adjusted for age gender and BMI)

Kothari A et al. *Arthritis Care Res* 2010

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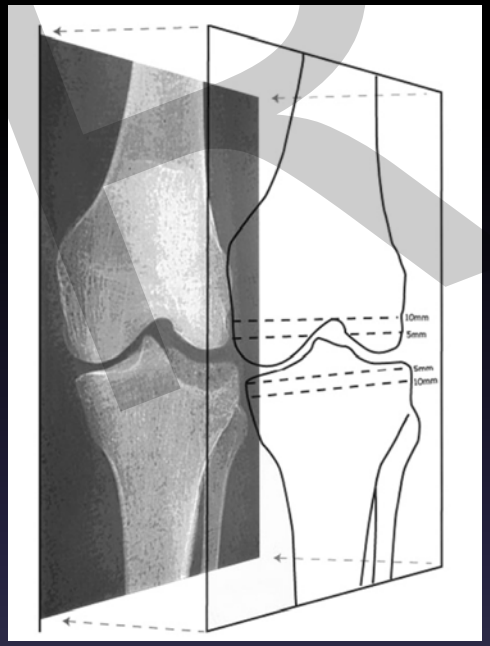
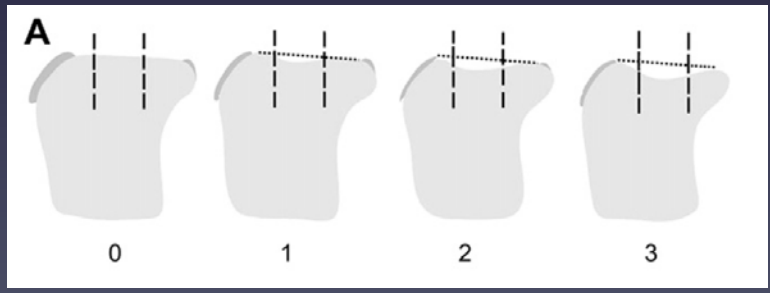
Attrition and cartilage lesions

Appears early in disease and is associated to cartilage lesions
Reichenbach S et al. *Osteoarthritis Cartilage* 2008

Is associated with cartilage loss over 30 months (OR 7.5)
Neogi T et al. *Arthritis & Rheumatism 2009*



Dieppe PA et al. *Arthritis Rheum* 2005



Peterfy CG et al. *Osteoarthritis Cartilage* 2004

Osteophytes and cartilage lesions

Central osteophytes are less common (prevalence 15%) compared to marginal osteophytes

Central osteophytes are regularly associated with full or near full thickness lesions of the overlaying cartilage Mc Cauley TR, et al. *AJR* 2001

Underlying mechanism of the development of central osteophytes remains unclear.

Mc Cauley TR, et al. AJR 2001

Osteophytes and cartilage lesions

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Central osteophytes develop in cartilage with abnormal structure and composition: data from the OAI cohort.

Table 1: Subject characteristics

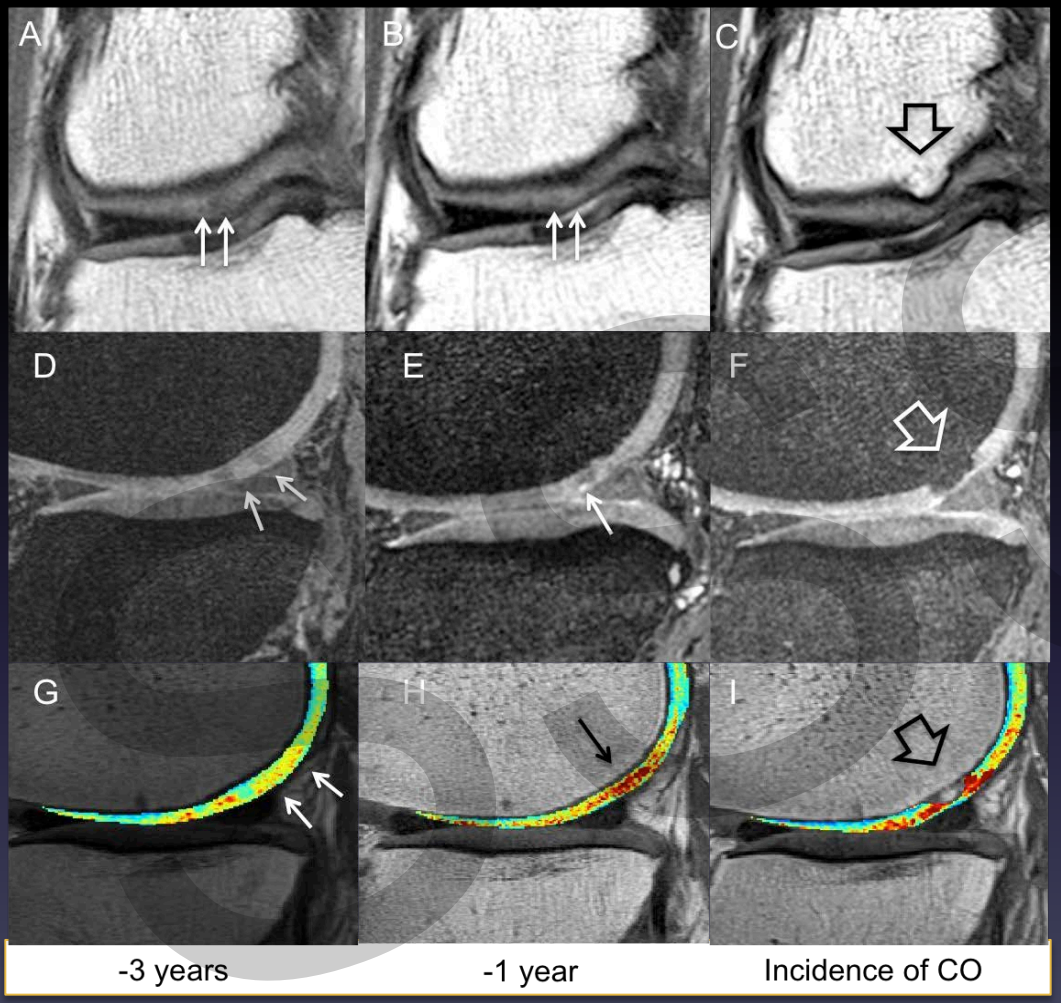
	MRI sample	Subjects with incident CO	p
	n = 400	n = 28	
Age	55.5 (±6.2)	54.4 (±6.8)	0.360
BMI	27.7 (±4.5)	27.8 (±3.9)	0.959
Sex (%)			0.312
Male	30	39	
Female	70	61	
KL grade (%)			**< 0.0001**
KL 0	65	46	
KL 1	28	32	
KL 2	7	21	
KL 3	/	/	
KL 4	/	/	
WOMAC Knee Pain	1.33 (±2.36)	1.54 (±2.0)	0.843

WORMS = Whole Organ Magnetic Resonance Imaging Score, CO = central osteophyte, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Kretzschmar M et al. unpublished data

OSSR

Osteophytes and cartilage lesions



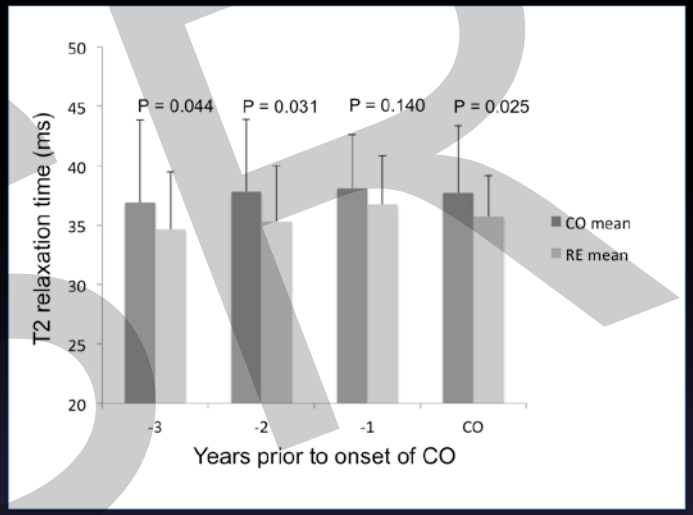
Kretzschmar M et al. unpublished data

Osteophytes and cartilage lesions

Table 2: Focal cartilage structure and regional and focal cartilage T2 prior to and at the onset of osteophytes

	Year of MRI prior to the onset of a CO			
	-3	-2	-1	CO
WORMS cartilage*	n = 18	n = 24	n = 31	n = 31
Grade 0	/	/	/	
Grade 1	9	5	4	2
Grade 2	7	12	17	16
Grade 2.5	1	/	/	2
Grafe 3	1	6	9	10
Grade 4	/	/	/	
Grade 5	/	1	1	1
Grade 6	/	/	/	
Mean cartilage lesions (SD)**	1.33 (0.57)	2 (0.81)	2.17 (0.41)	2.38 (0.48)
BMEP	0.43 (0.85)	0.63 (1.01)	0.85 (1.09)	0.63 (0.93)
T2 (ms)				
Cartilage of Region	34.6 (4.9)	35.4 (4.3)	36.9 (4.1)	35.8 (3.8)
Focal cartilage prior to CO	36.9 (6.9)	37.8 (5.0)	38.1 (4.5)	37.7 (5.8)
WOMAC knee pain	1.5 (1.4)	0.95 (1.3)	0.97 (1.3)	1.54 (2.0)
WOMAC stiffness	1.40 (1.59)	1.05 (1.27)	1.00 (1.19)	1.00 (1.55)
WOMAC disability	4.47 (4.98)	4.11 (5.51)	3.67 (6.24)	3.50 (6.28)

WORMS = Whole Organ Magnetic Resonance Imaging Score, CO = central osteophyte, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, * = number of cases with lesions of different grades. ** mean of focal cartilage lesions at the site of onset.



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Bone metabolism and cartilage lesions

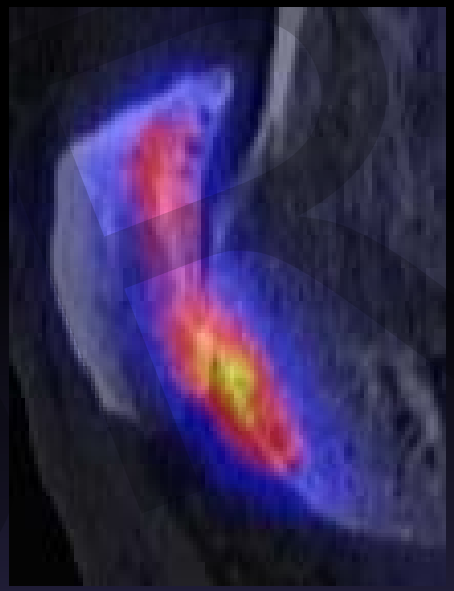
Accumulates in bone via chemical adsorbtion into crystalline form of hydroxyapatite
Kanishi D, Oral Surg Oral Med Oral Pathol. 1993

Indicates enhanced bone remodeling

Increased uptake is associated with OA
McCray F et al. *Annals of the Rheumatic Diseases* 1992

Correlation with BME
McAlindon TE 1991, Boegard T 1999

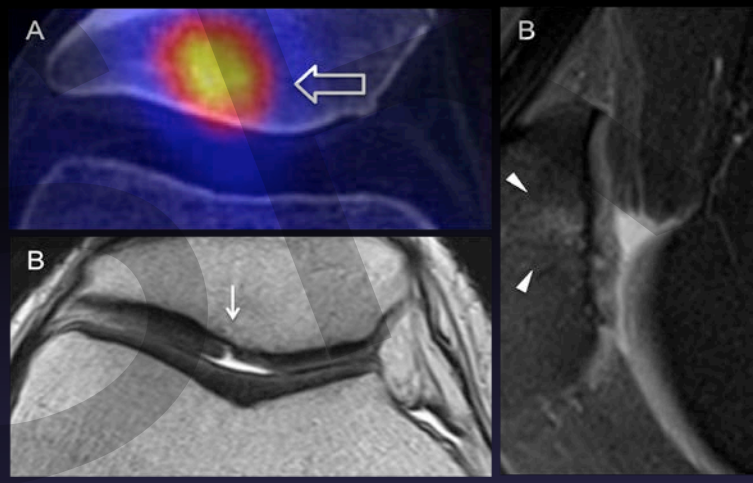
Correlates with pain
Buck F et al. Skeletal Radiol 2009, Kretzschmar M et al. EJR 2011



Maas O et al. Osteoarthritis Cartilage 2015

Bone metabolism and cartilage lesions

Association between cartilage degeneration and subchondral bone remodeling in patients with knee osteoarthritis comparing MRI and ^{99m}Tc-DPD-SPECT/CT.



Maas O et al. Osteoarthritis Cartilage 2015

Retrospective cross-sectional analysis of 162 regions of 27 knees

Comparison of SPECT-uptake and MRI structure of the overlaying cartilage

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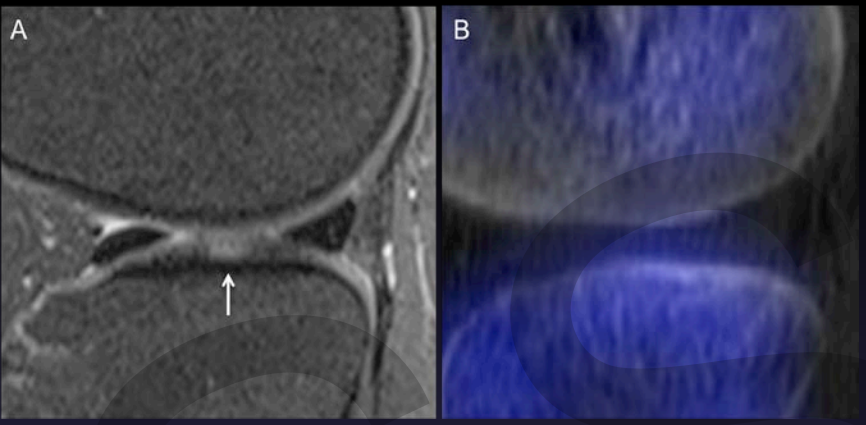
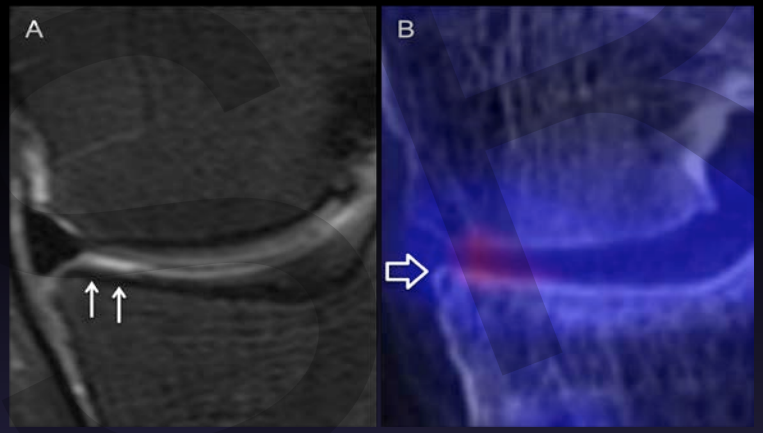
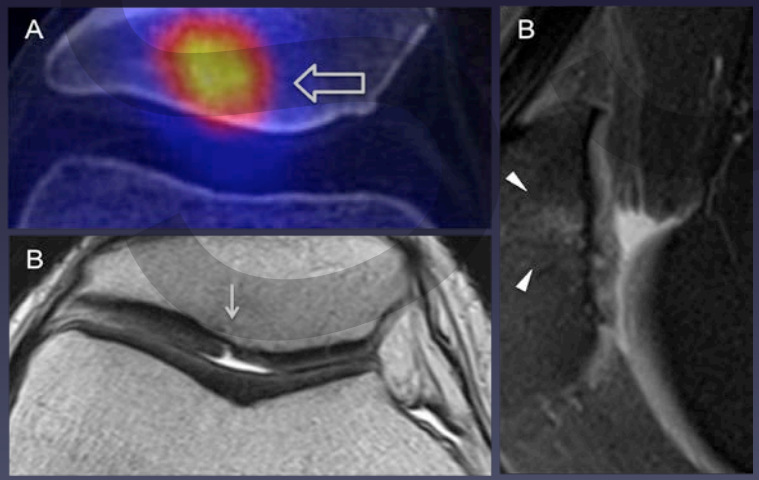
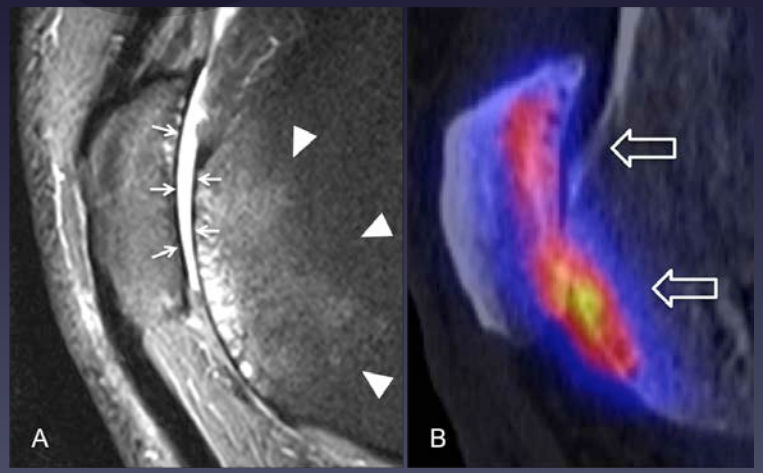
Bone metabolism and cartilage lesions









Maas O et al. Osteoarthritis Cartilage 2015

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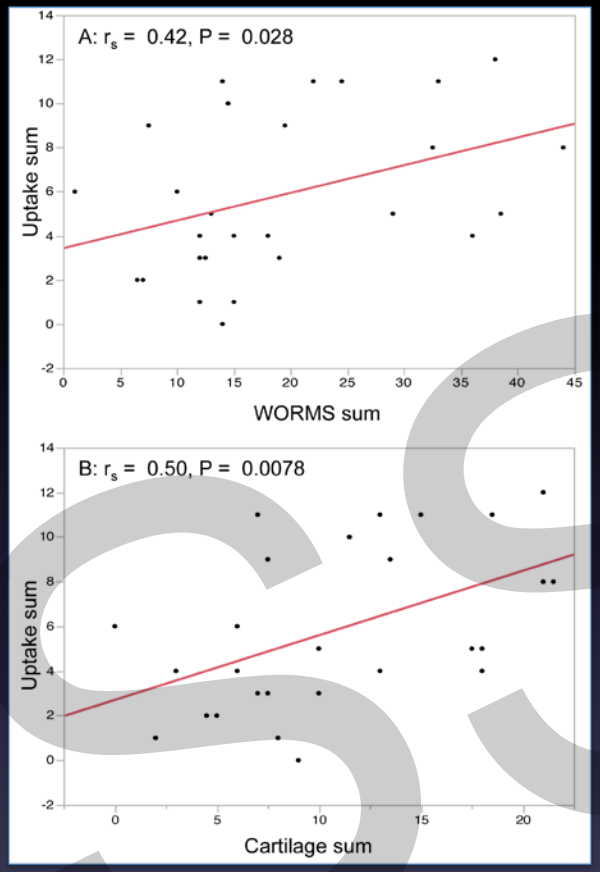
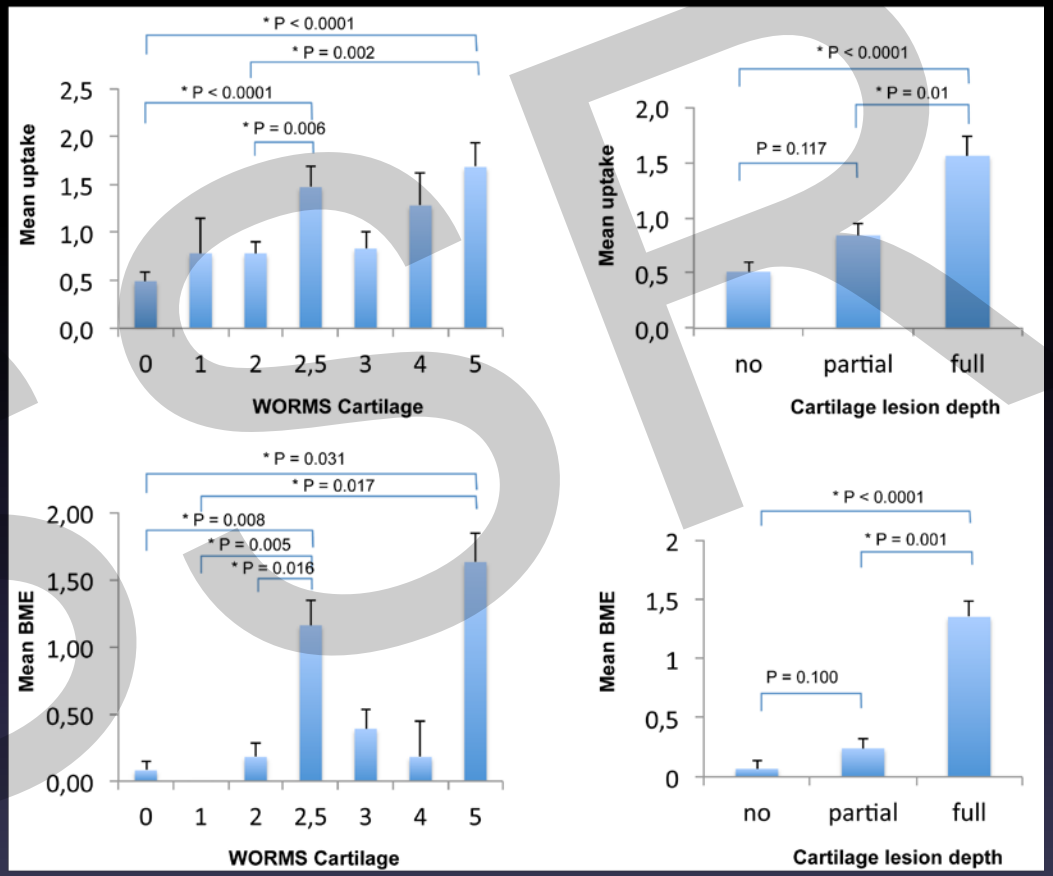
Bone metabolism and cartilage lesions





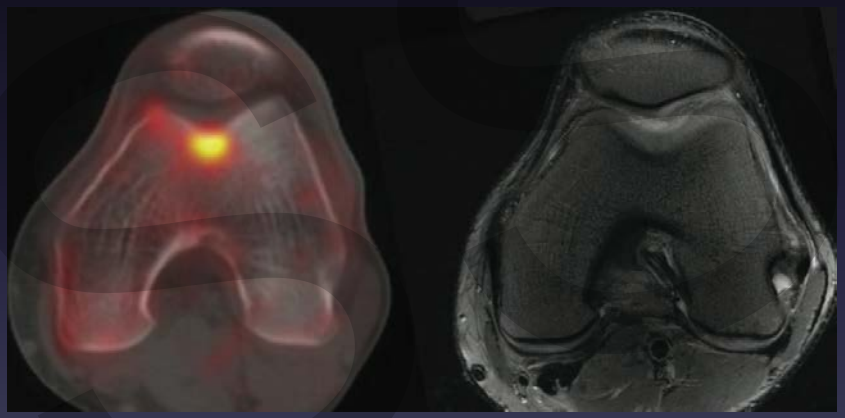
Maas O et al. Osteoarthritis Cartilage 2015

High prevalence of increased uptake under normal cartilage (35%)

Bone metabolism and cartilage lesions

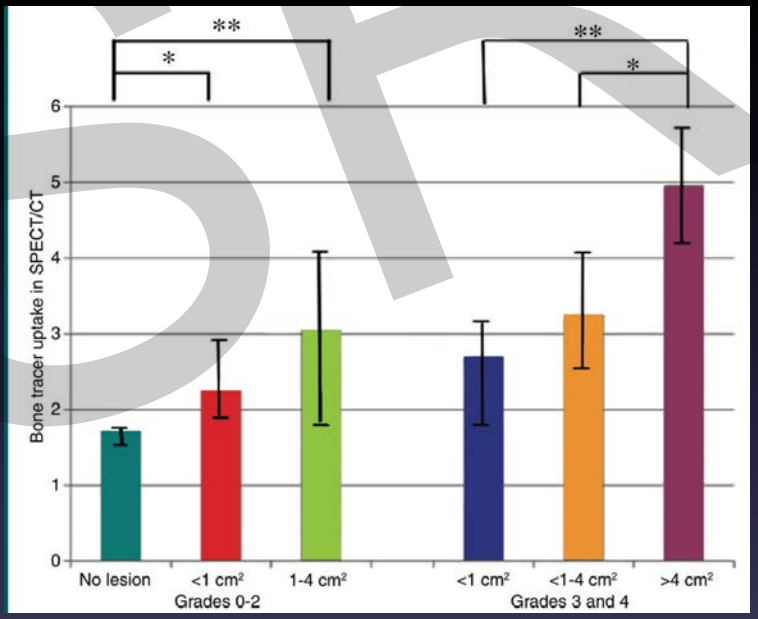
Draper et al.2012:
Cartilage lesions and BMEP lesions often co-occurred in regions with increased NaF uptake

But 49% of uptakes were detected without the presence of cartilage or bone marrow lesions



Draper CE et al. *JMRI* 2012

Dordevic et al. 2015:
Uptake increased with lesion depth and with diameter



Dordevic M et al. *Radiology* 2015

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Clinical Implications
The rheumatological perspective

Early intervention with disease modifying osteoarthritis drugs may prevent or slow the process of joint destruction.

Among others subchondral bone is a target tissue
e.g. Calcitonin, Bisphosphonates, Strontium

In vivo data about the interplay of cartilage and bone during disease initiation and progression may help to find appropriate biomarkers and to define stages of OA (eg. with active remodeling) that are most sensitive for DMOADs

Shirley Pei-Chun Yu & David John Hunter *Expert Opinion on Emerging Drugs* 2015

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Clinical Implications
The orthopedic perspective

Many techniques of cartilage repair utilize stem cells from the subchondral bone.

Metabolic and structural properties of subchondral bone may influence quality and outcome of cartilage repair

May influence the therapeutic strategy e.g. osteochondral vs. chondral repair
Dordevic et.al *Radiology* 2015

Chevrier A et al. *J Orthop Res 2015*

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Summary

Due to its high plasticity subchondral bone shows various distinct patterns of reactive and adaptive changes in OA

Many of these changes are closely related to cartilage lesions.

The presence of BME, Attrition and szintigraphic uptake is associated with progression of both, cartilage lesions and radiographic progression.

Further longitudinal observations are warranted to investigate the onset of bone changes in relation to the development of cartilage lesions

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Thank you