Update on the role of bone in OA

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Bone in OA

- Peri-articular bone and calcified cartilage alterations
- Imaging techniques to assess peri-articular bone
- "Bone marrow lesions": histopathology and pathogenic mechanisms
- "Anti-resorptives": effects on peri-articular bone remodeling
  - –Bisphosphonates
  - –Calcitonin
- Lessons from genetic models
- *Bone cell microarray gene profiling*

Relationship between subchondral bone, calcified cartilage and articular cartilage

- The composition and structural organization of the peri-articular bone and cartilage are optimally adapted to maintain their structural and functional integrity during joint loading

OA Pathogenesis: A model of remodeling disequilibrium

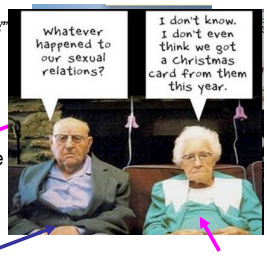
-The capacity of joint components to adapt to environmental signals differ, e.g. mechanical load, inflammation, injury

- periarticular bone adapts relatively rapidly (via remodeling or modeling) to alterations in local biomechanical signals
- chondrocytes have limited capacity to remodel their matrix

-Lack of synchrony in the *adaptative capacity* of the individual joint components disturbs the physiological equilibrium that is necessary to maintain their optimal structural and functional properties and relationships

Relationship between subchondral bone, calcified cartilage and articular cartilage

Bone and cartilage: "the later days"

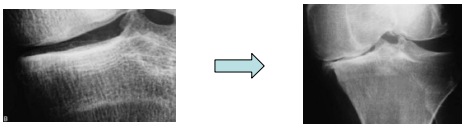


Cartilage

Bone

Cartilage

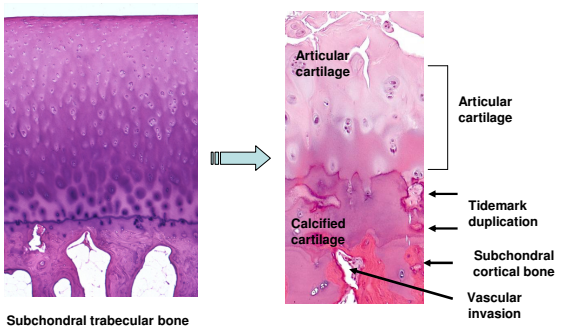
Progression of subchondral bone changes in knee OA



- **Increased cortical plate thickness**
- **increased thickness of horizontal trabeculae**
- **New bone, hypomineralized, often woven**
- **Tidemark duplication**
- **Decreased subchondral trabecular bone mass ("stress-shielding")**
- **Flattening and deformation of articular contour (late)**

Buckland-Wright et al. Rheumatology 2007;46:257-64
Taljanovic et al. Skeletal Rad 2008; 37:423-31

Osteoarthritis

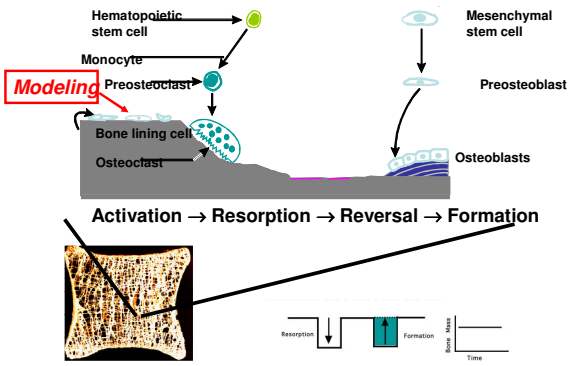


Physiologic Bone Remodeling

- **Adapt shape and structural organization to alterations in biomechanical forces**
  - **"Mechanostat"**
- **Maintain structural integrity**
  - **Repair microdamage**
- **Maintain mineral ion homeostasis**
  - **Source of calcium ions**

Increased load=Increased bone
-modeling (new bone directly on bone surface)
-remodeling (new bone via resorption/formation
Decreased load=Decreases bone
-remodeling

Physiologic bone remodeling cycle



Skeletal imaging in OA

•Relationship between trabecular bone structure and articular cartilage morphology and relaxation time in early OA of the knee joint using parallel MRI at 3T

–Bolbos et al. Osteoarthritis Cartilage 2008; In Press

•Prevalence of bone attrition on knee radiographs and MRI in a community-based cohort

–Reichenbach et al. Osteoarthritis Cartilage 2008; 16:1005-10

•Differences in trabecular bone texture between knees with or without radiographic osteoarthritis detected by fractal methods

–Podsiadlo et al. Osteoarthritis Cartilage 2008; 16:323-329

Fractal signature analysis (FSA) is a computerized system for quantitating trabecular subchondral bone structure (number, spacing and connectivity) using standard radiographs. In this study the FSA data has been augmented with a Hurst orientation transform (HOT) method that permits more detailed analysis of microarchitecture.

A 2 yr longitudinal radiographic study examining the effect of risedronate upon subchondral bone loss in osteoarthritis knee patients

Buckland-Wright, JC. Rheumatology 2007; 46:257-64

- Methods: In this study FSA used to calculate fratal dimension (FD) of vertical and horizontal trabeculae
- Results:
  - OA knees without JSN lost vertical and horizontal bone in placebo and low dose risedronate (ris) (5mg/da); no change in high dose ris (15mg/da or 50mg/wk)
  - In JSN-progressors, bone loss greater in placebo and low dose ris; in high dose ris, vertical trabecular number increased
- Conclusion: In patients with JSN>0.6mm, ris treatment associated with increased trabcular number, preserving structural integrity of the subchondral bone

KOSTAR: Bingham et al. Arhtritis Rheum 2006; 54:3494-507
No effect of risedronate on OA progression or symptoms

Effect of calcitonin in early and late stages of experimentally induced osteoarthritis. A histo-morphometric study

Papaioannou et al. Osteoarthritis cartilage 2007; 15:386-95

- Cruciate transection model in rabbits
- CT treatment
  - Smaller osteophytes
  - Less subchondral cystic formation
  - Smoother articular surfaces
  - Minimal signs of cartilage surface ulceration

Skeletal imaging in OA

Early identification of radiographic osteoarthritis of the hip using an active shape model to quantify changes in bone morphometric features

Gregory et al. Arthritis Rheum 2007; 56:3634-43

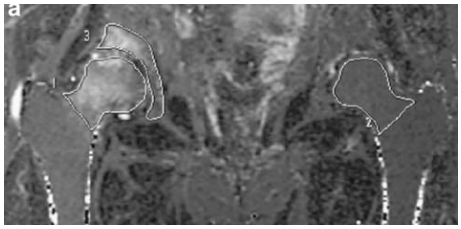
Methods: selected 110 subjects without radiographic hip OA from Rotterdam Study cohort to measure progression of OA
Results: ASM predicted subset of subjects who developed OA and progressed to THR
Conclusions: ASM can be used as an "imaging biomarker" to more precisely identify patients at risk for OA and TJR

MRI associated bone marrow lesions ("edema") in OA

- Strongly associated with cartilage and radiographic progressive joint space loss
- Associated with joint pain
- Associated with malalignment (e.g. medial lesions associated with varus alignment)

Hunter DJ et al. Arthritis Rheum 2006; 54:1529-1535
Felson DT et al. Arthritis Rheum 2007; 56:2986-2992

MRI associated bone marrow lesions ("edema") in OA



Taljanovic MS et al. Skeletal radiol 2008; 37:423-431l

Histopathology of bone marrow lesions ("edema") in OA

•Minimal bone marrow "edema"
•Subchondral sclerosis
•Subchondral cysts and geodes corresponding to regions of damaged cartilage
•Microfractures at different stages of healing
  •Osteoblasts adjacent to bone fragments
  •Woven bone
•Marrow fat necrosis
•Bone marrow fibrosis

Taljanovic MS et al. Skeletal radiol 2008; 37:423-431l

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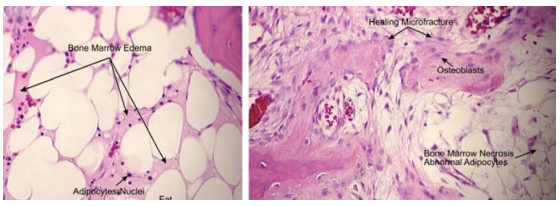

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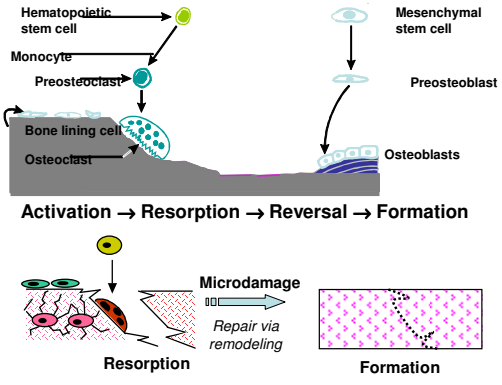
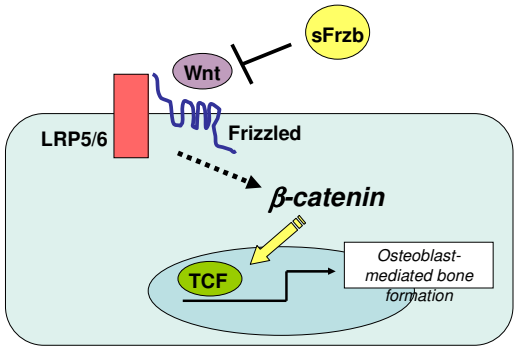


Articular cartilage and biochemical properties of the long bones in Frzb-knockout mice

Lories et al. Arthritis Rheum 2007; 56:4095-103

- Polymorphisms in FRZB gene (secreted WNT antagonist) associated with OA
- Three models: collagenase, papain, BSA-induced arthritis
- Frzb (-/-) phenotype:
  - –increased cortical bone thickness and density
  - –Increased bone stiffness
  - –Increased periosteal anabolic response to loading
  - –Increased cartilage damage (?increased MMP production)

Canonical Wnt/β-catenin signaling pathway



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