

2nd Annual Workshop on Imaging Based Measures of Osteoarthritis:

"Why Aren't We There Yet?"

June 25-28, 2008
Wyllie Conference Center
Beverly, Massachusetts



130 attendees from 12 countries

Radiologists, orthopaedists, biologist, imaging scientists,
pharmaceutical and MRI industry, government agencies

Why aren't we there yet?

Where are we now?

Where is "There"???

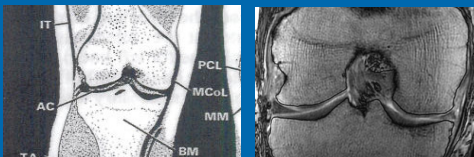
Case Study
Mr. A. Symptomatic
50 y.o. without prior health problems
Physical exam, 2008

Joint evaluation → Analgesics...
pain, mobility Total joint

Blood pressure → Diet changes
Blood lipids → Stress test / angio
Colonoscopy Biopsy

Detection of early disease process ;
prevention of pain, end stage disease and disability

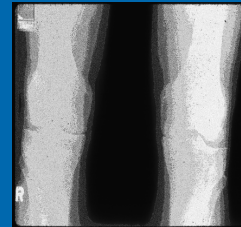
In the early 1980s there was hope that MRI could impact this situation;



1984

2008

While MRI has progressed...



X-ray

- Radiography is the primary diagnostic imaging procedure for OA
- Radiography is the mainstay of OA clinical investigations
- Few bench studies utilize MRI for research purposes

Why hasn't MRI made more of an impact in the diagnosis, study, and understanding of joint diseases?

- I. Current paradigms are limiting how we design studies, view the data, and how we interpret the implications for clinical trials, ultimately limiting MRI's utility.
- II. We have been seeing what we can image, instead of imaging what we need to see
- III. Resource limitations

The red universe...

Radiography is appropriate as a primary imaging tool for OA (K/L, joint space)

OA is a progressive disease of cartilage loss

The green universe...

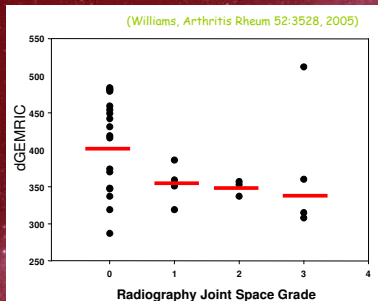
MRI can interrogate molecular parameters of joint structures to investigate early disease

OA is a reversible multi-tissue disease state; "end-stage" disease can be avoided

Example of Red Universe Paradigm:

Cohort delineation for clinical trials should be along the lines of radiographic criteria (JSG, KLG)

Red Universe Design of Trial and Interpretation of Data

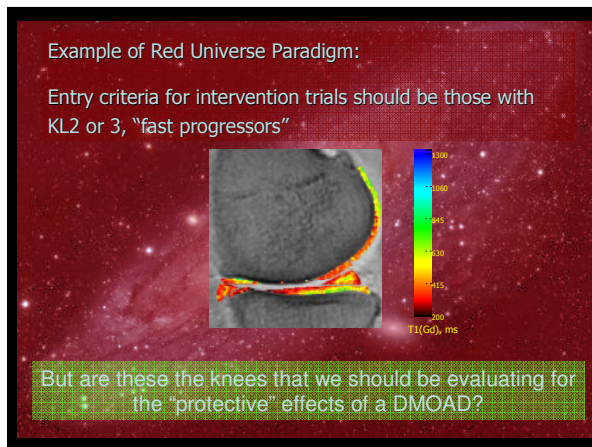
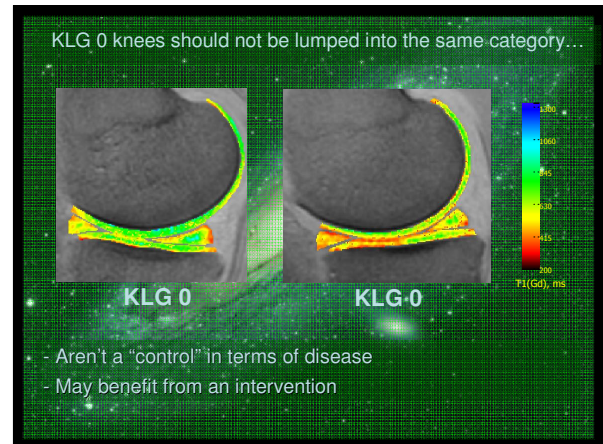
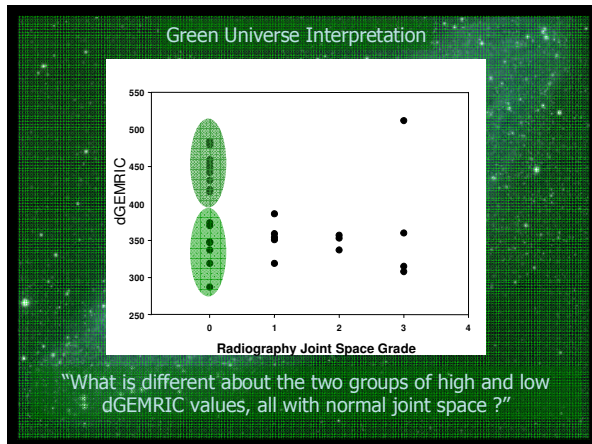


Design: Cohort is grouped by JSG

Interpretation: "dGEMRIC decreases with joint space grade"

If MRI metrics are mainly presented as correlating with standard radiographic metrics (and therefore we can already differentiate those groups), there is no advantage to using the much more expensive MRI...

The additional information achievable with MRI is not elucidated.



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But, there are major differences between tissues of the joint and those of other major organ systems:

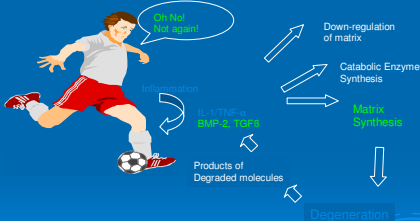
- I. Articular cartilage is relatively acellular (5% vs 70%)
- II. Articular cartilage / meniscus has little or no vascularization
- III. The tissue function is mainly a property of the extracellular matrix, not the cells (although cells produce the matrix)

Therefore, the interpretation of "standard" MRI metrics of tissues of the joint may not be appropriate or optimal.

*Instead of seeing what we can image,
we need to think more about finding ways
to image what we want to see...*

What do we know?
What do we need to learn?

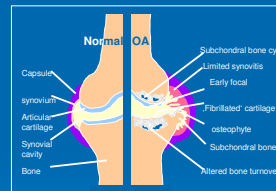
BIOLOGY:



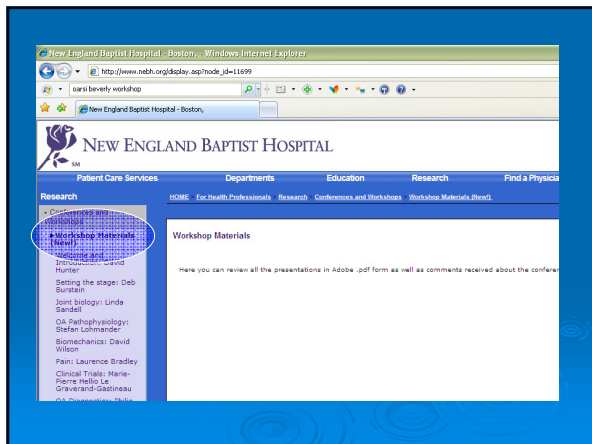
- e.g.
- Are there regional variations in the permeability of the subchondral bone?
 - Can we image cell death in cartilage?

What do we know?
What do we need to learn?

PATHOPHYSIOLOGY:



- What is a BML lesion in OA? (water, cells, blood)
- At what point can tissue / joint still be repaired to pre-injury or pre-disease state, i.e. is the disease fully reversible?



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