Biopsies and Imaging at ACL Reconstruction

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Dx MRI

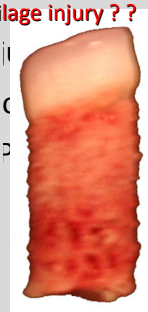
Sagittal Proton Density

Sagittal T2 Fat Saturated

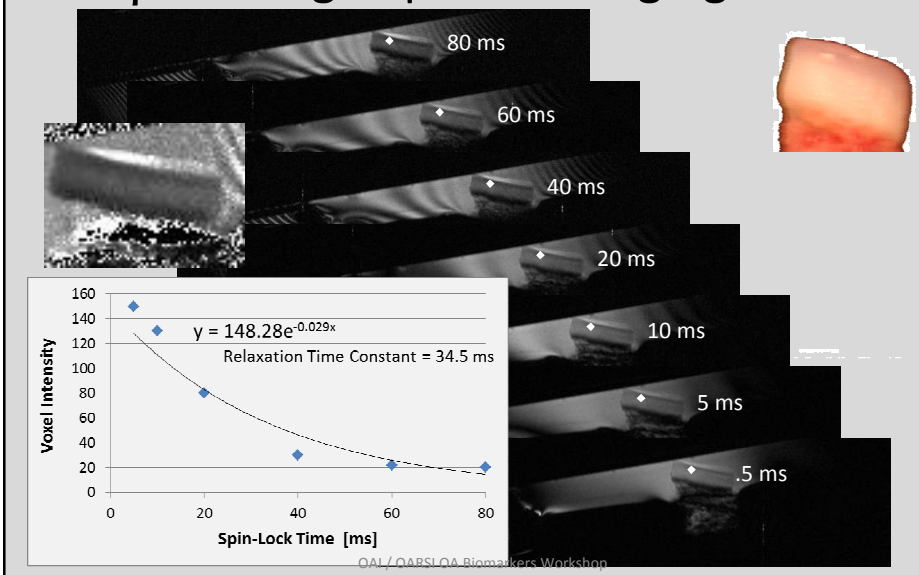
Blunt impact often leaves a visible bone bruise.

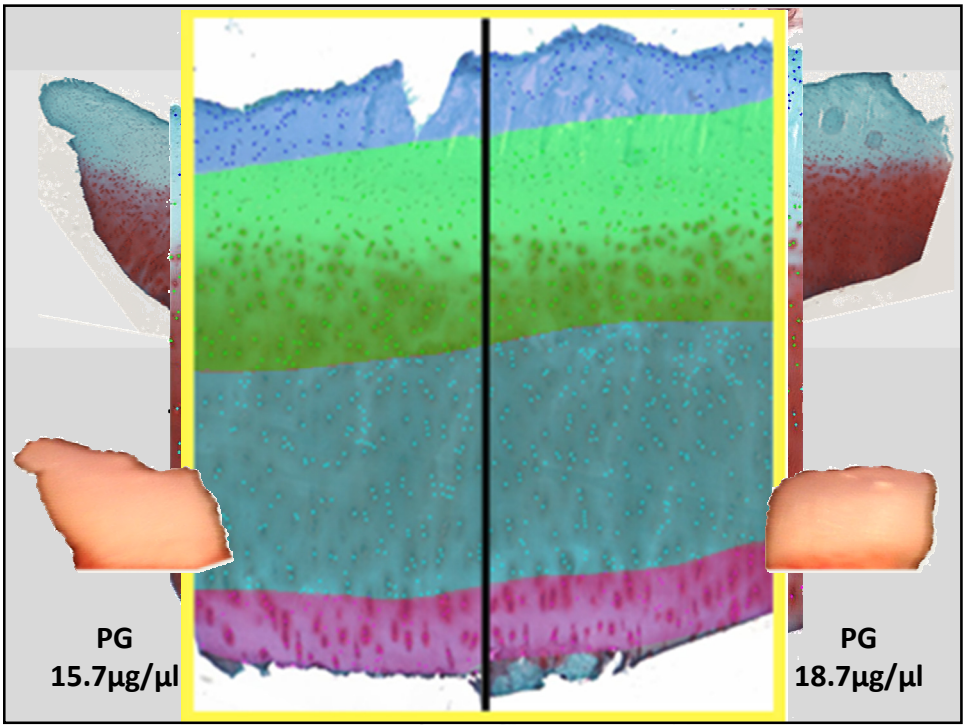
What about the overlying cartilage injury ? ?

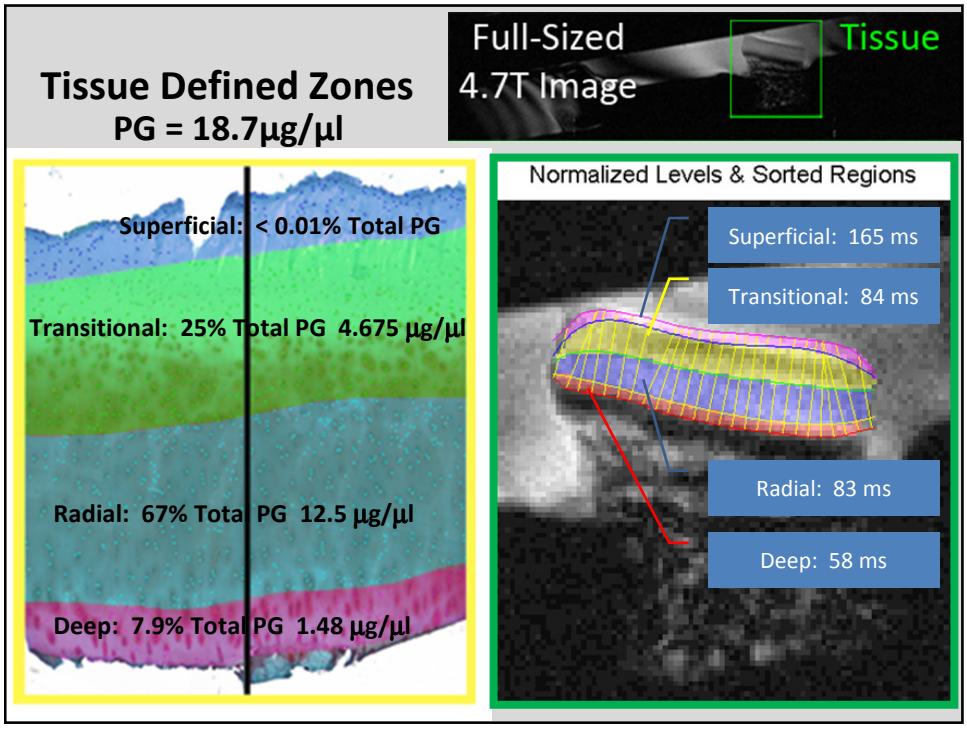
T1ρ
140mm x 140mm
array size 256 x 256
Voxel size:
0.55mm x 0.55mm x
3mm slice thickness

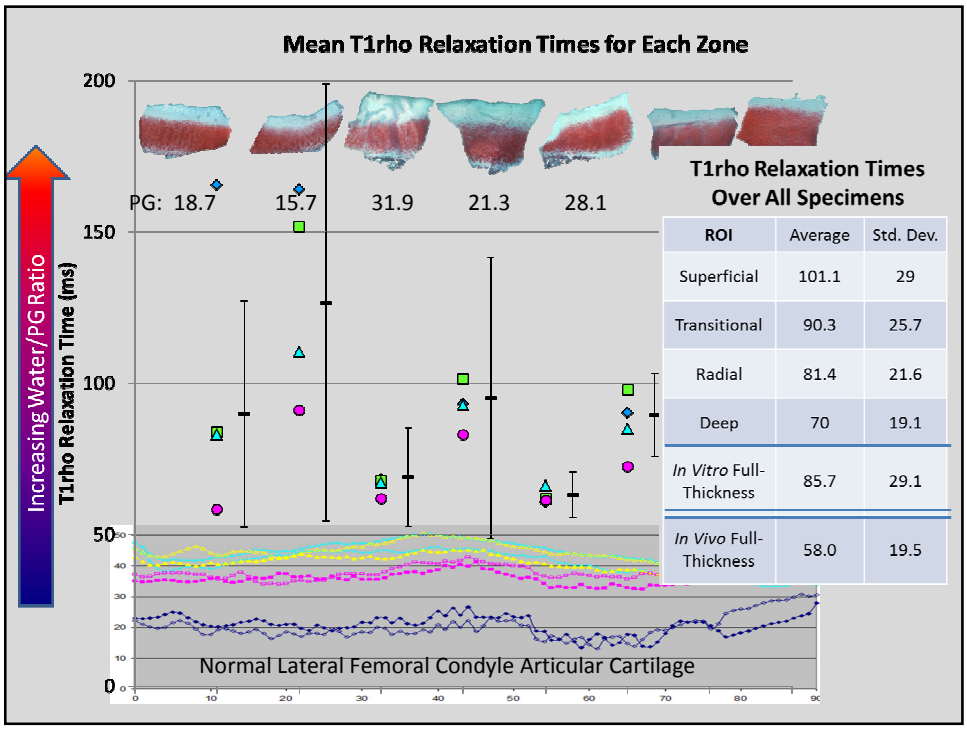


T1ρ Cartilage-Specific Imaging at 4.7T



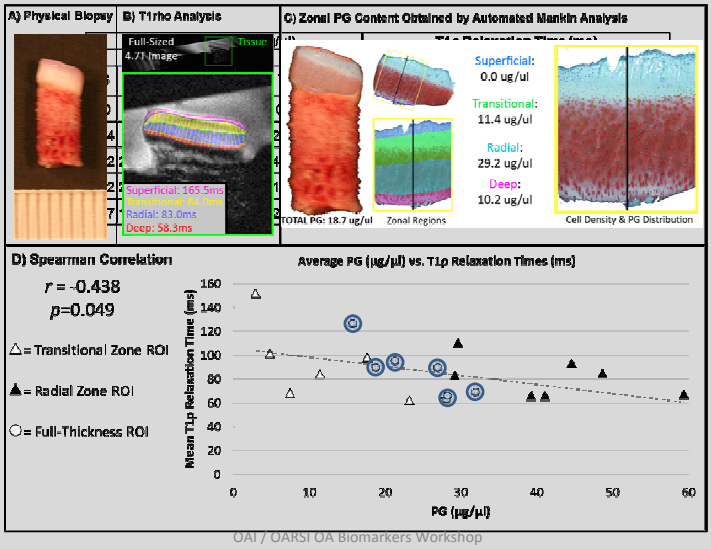






ROI	Average	Std. Dev.
Superficial	101.1	29
Transitional	90.3	25.7
Radial	81.4	21.6
Deep	70	19.1
In Vitro Full-Thickness	85.7	29.1
In Vivo Full-Thickness	58.0	19.5

T1ρ Relaxation Time and PG



Sera Collected from 3 Patient Cohorts

within 30 Days of Injury

1. Tibial plafond fractures (IAF)
   20-75 years old
2. Normal – no joint injury
   21-70 years old
3. Anterior cruciate ligament tears (ACL)
   23-40 years old

Marker	Units	IAF			Normal			ACL		
		Mean	Std.Dev	n	Mean	Std.Dev	n	Mean	Std.Dev	n
C2C	ng/mg	1795	900	18				705	99	4
BAP	µg/mg	0.065	0.034	19	0.072	0.031	10	0.095	0.021	4
Trap	mU/mg	17.0	6.9	18	12.4	4.4	28	1.3	1.8	4
3B3	ng/mg	3.9	4.4	19	4.7	2.2	27	28.4	8.5	4

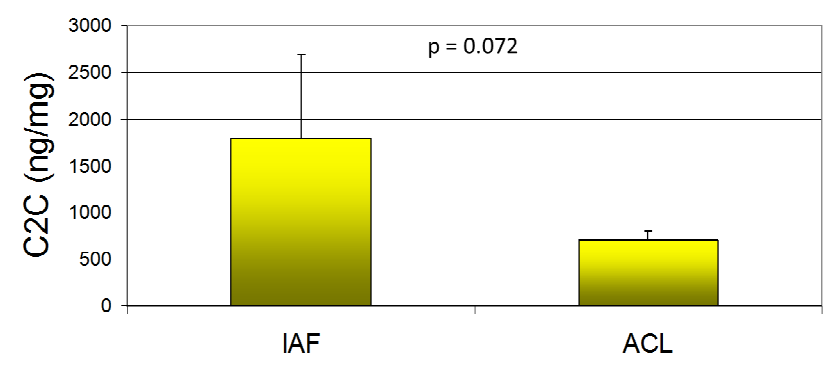
Serum Biomarkers

1. *Acute* indicators of bone and cartilage turnover in patients with:

- **Intra-articular fractures**
  - matrix turnover from fracture healing
- **Anterior cruciate ligament damage**
  - turnover from cartilage or ligament repair?

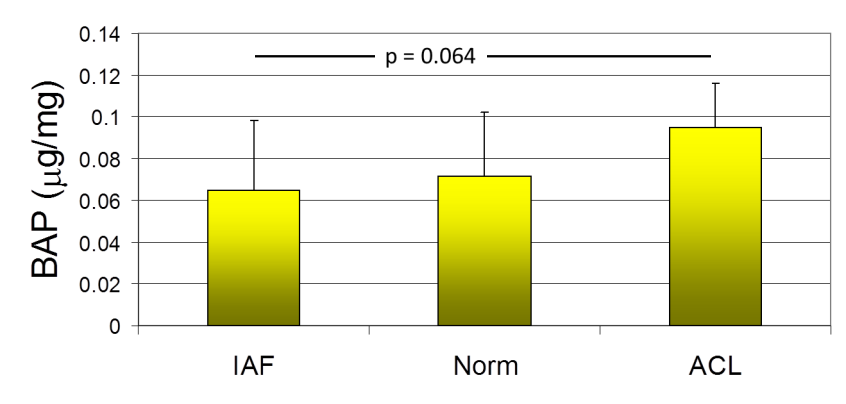
2. CS3B3 - an OA marker in these patients?

Collagen Degradation Marker: C2C



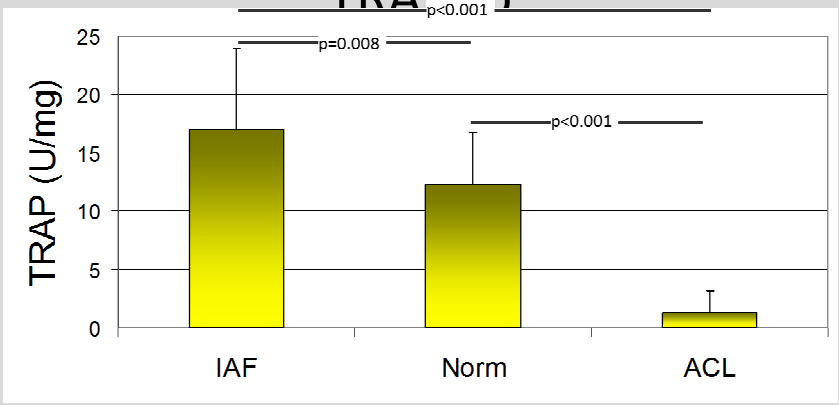
AKA "Col2-. 3/4Clong", C2C is a marker for collagen degradation by collagenases.

Bone Synthesis Marker: BAP



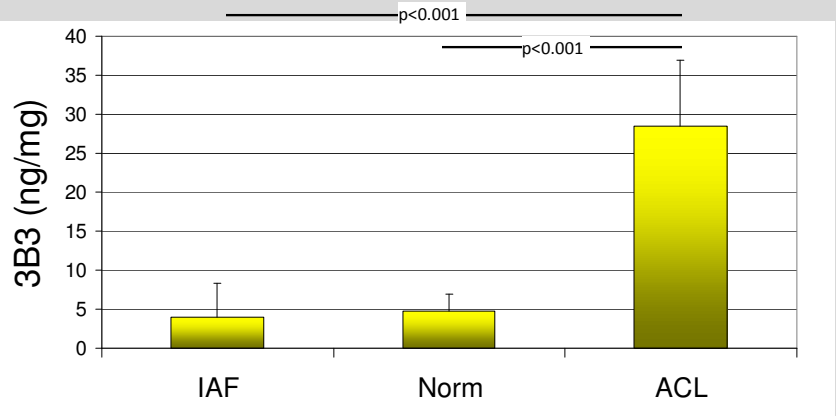
Bone alkaline phosphatase is an enzyme involved in matrix mineralization by osteoblasts (bone turnover).

Bone Degradation Marker: TRAP5b



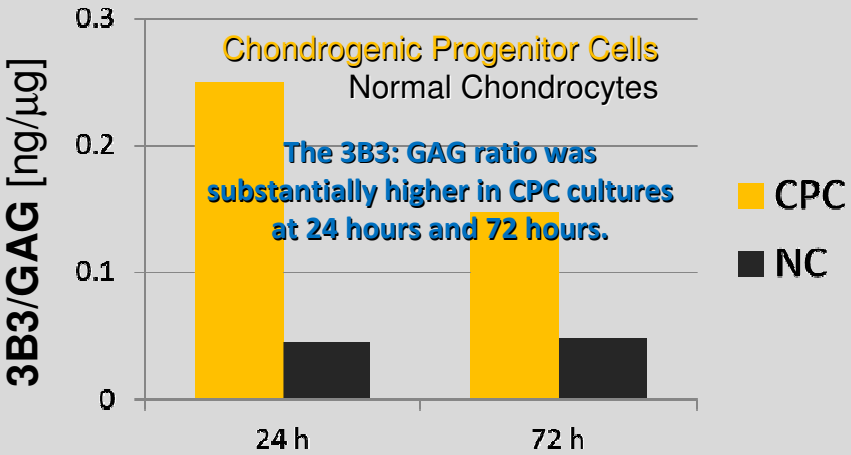
Tartrate-resistant alkaline phosphatase is a bone mineral-degrading enzyme synthesized by osteoclasts (bone turnover).

Osteoarthritis Marker: CS3B3



The 3B3(-) chondroitin sulfate epitope is made in immature & osteoarthritic cartilage, Possibly synthesized by injury-responsive chondrogenic progenitor cells [1,2]

1. Hayes AJ, Tudor D, Nowell MA, Caterson B, Hughes CE. Chondroitin sulfate sulfation motifs as putative biomarkers for isolation of articular cartilage progenitor cells. J Histochem Cytochem. 2008 Feb;56(2):125-38.
2. Seol D, McCabe DJ, Choe H, Zheng H, Yu Y, Jang K, Walter MW, Lehman AD, Ding L, Buckwalter JA, Martin JA. Chondrogenic Progenitor Cells Respond to Cartilage Injury. Arthritis Rheum. 2012 (accepted)



The 3B3(-) epitope and total glycosaminoglycans (GAG) were measured in medium samples from primary cultures of chondrogenic progenitor cells (CPC), and medium from primary cultures of normal chondrocytes (NC).
The columns are averages of two different experiments.

Conclusions at 2-4 weeks post injury

- T1ρ relaxation times were elevated from normal.
- Serum biomarkers TRAP and C2C were significantly higher in IAF patients, consistent with bone and cartilage turnover expected during fracture healing.
- CS3B3 was significantly higher in ACL patients, consistent with early osteoarthritic changes? Or activation of chondrogenic progenitor cells

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What does it mean?

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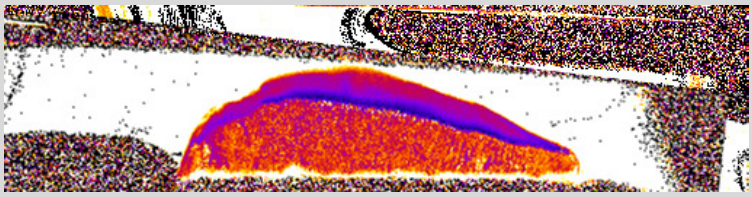
NIAMS
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Conclusions

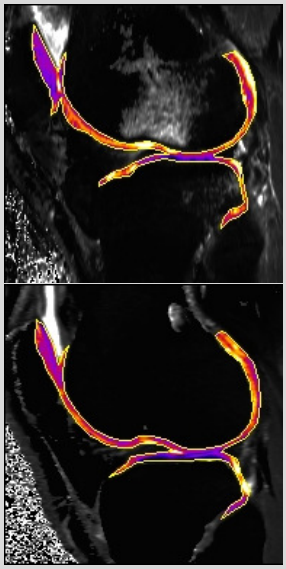
- We propose that swelling and soft-tissue fluid infusion associated with the inflammatory response to injury were responsible for some difference[illegible]perative imaging markers of cartilage composition.

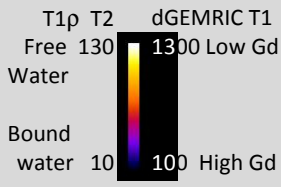


ACLR 12 days post-injury with follow-up at 141

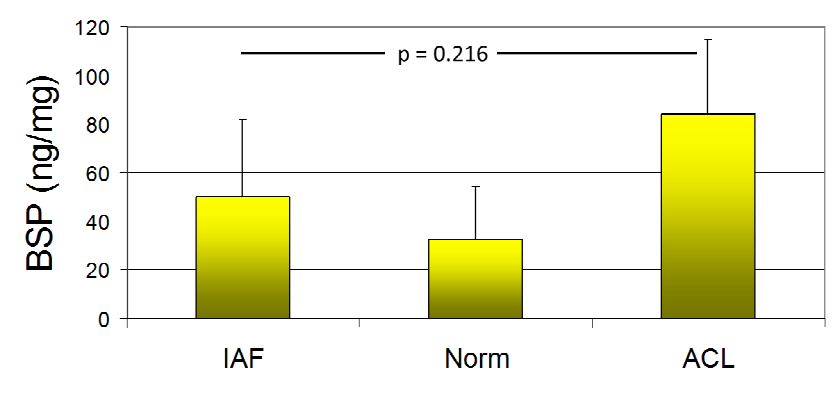
$T1\rho^{days}$ ACL01

Pre-surgery





Bone Turnover Marker: BSP



Bone sialoprotein is normally trapped within bone, but is released by osteoclast activity (bone degradation).

Conclusions at 2-4 weeks post injury

- T1ρ relaxation times were elevated from normal.
- There were significant differences in serum biomarkers in blunt trauma injured ACL and IAF patients.
  - TRAP and C2C were significantly higher in IAF patients, a finding consistent with bone and cartilage turnover expected during fracture healing.
  - CS3B3 was significantly higher in ACL patients, consistent with early osteoarthritic changes.
- The relationships of these imaging and biomarker data are inconclusive, but continued complementary sample collection and recommendations of this workshop should enhance that search.