



Structural and Biochemical Changes From Injury to Joint Replacement: Potential Roles of the ATC


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 June 28, 2014


Potential Roles for the AT

1. The healthy joint
2. Post-injury
3. Osteoarthritis progression
4. Before a joint replacement
5. After a joint replacement


I have no professional or financial affiliations that would bias this work.



It's One of Our Domains


"Injury/Illness Prevention & Wellness Protection"


- We must strive to not only prevent injuries
- But to also prevent chronic diseases (e.g., OA)
- We must consider our athletes' wellness not just today but for the next few decades
- In a community focused on today we need to think about tomorrow



The Healthy Joint

- Healthy articular cartilage
 - chondrocytes
 - no blood supply
 - collagen and proteoglycan
- Healthy synovium
- Healthy bone
- Intact ligaments and meniscus






Bone Shape

- Hip shape is an important risk factor for hip OA
 - Cam-type deformities may be a key risk factor¹
 - Athletes (e.g., soccer, football, hockey) may be more likely to have cam deformities²
 - The formation of cam deformities may be related to high-impact activities during growth³


1. Agricola R et al., 2013; 2. Agricola R et al., 2012; Philippon MJ, et al., 2013; Larson CM et al., 2014; 3. Agricola R et al., 2014



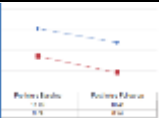
How Healthy is Healthy?

- On average 21 months before injury
 - Increased collagen breakdown and synthesis
 - No difference in breakdown:synthesis ratio

2 Markers of Collagen Breakdown



Collagen Synthesis



Svoboda SJ et al., 2013 (Am J Sports Med)



Goal: Preserve and Protect

There are no accepted treatments to reverse, slow, or prevent the development or progression of osteoarthritis

Wait! Don't leave yet.




Prevention: Modify Risk Factors

- We can influence two key risk factors
 1. Joint Injury
 2. Obesity




Good overview: Hunter DJ (2011) Br J Sports Med

Injury is a Risk Factor for OA

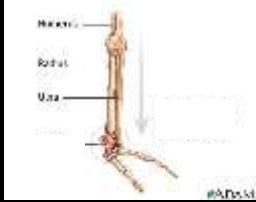
- Knee injuries
 - 3 to 6 times more likely to have OA¹
 - 26% of knees with ACL injury have OA within 5 yrs²
 - Meniscal injuries may be a key knee injury that increases the risk of OA



1. Muthuri SG et al., 2011; 2. Frobell R et al., 2013.
Image from: <https://www.flickr.com/photos/joncandy/8048470875/>

How does OA affect my practice?

- Intra-articular fractures
 - 65% of wrists with intra-articular fractures had OA ~ 7 years post-injury



Knirk JL & Jupiter JB 1986.

What about my patient?*


- 20 years of age: injures ACL and meniscus
- 25-35 years: radiographic osteoarthritis
- 45-64 years: total knee replacement
- 90 years: death

* Mock Case Study

This cannot be an acceptable outcome by clinicians that emphasize injury and illness prevention.

Injury Prevention

- 15-25% of symptomatic knee OA could be prevented by preventing knee injuries¹
 - We can prevent > 40% of lower extremity injuries²



1. Felson & Zhang 1998.
 2. Pamphlet @ nata.org, Leppanen M et al., 2013; Lauersen JB et al., 2013; Taylor JB et al., 2013; Myer G et al., 2013; Gagnier JJ et al., 2013, Sadoghi P et al., 2012

Obesity

- 25-50% of symptomatic knee or hip OA could be prevented by eliminating obesity¹
- A 5-10% change in body weight may influence the risk of symptomatic osteoarthritis²
- We should advise and educate our patients
- We should serve as a gatekeeper

1. Felson & Zhang 1998. 2. Tanamas SK et al. 2013, Hart & Spector 1993

What about my patient?*

- 15 year old, female, HS athlete in soccer
- BMI = 20 kg/m²
- No history of any major joint trauma
- **Let's get this athlete (and her team) engaged in injury prevention programs**

* Mock Case Study

What about my patient?*

- 21 year old, female, college athlete in soccer
- BMI = 22 kg/m²
- Diagnosed with cam-type deformity
- *Advise patient to maintain a healthy lifestyle*
 - For example: maintain healthy body weight


* Mock Case Study

AT's Role: Healthy Joint

Primary Protection



We Can't Prevent Every Injury

- Traditional radiographic changes may be slow
- Magnetic resonance imaging and other imaging modalities open new doors



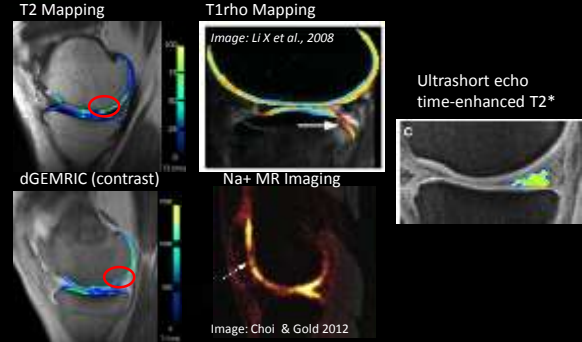
No Longer Out of Sight, Out of Mind

- Cartilage changes within 2 years of ACL injury
 - Femoral trochlea: thinning
 - Central medial femur: thickening (swelling)

Frobell RB et al., 2011 (JBJS)

Subtler Changes



T2 Mapping
Image: Li X et al., 2008

T1rho Mapping
Image: Choi & Gold 2012

dGEMRIC (contrast)

Na+ MR Imaging

Ultrashort echo time-enhanced T2*

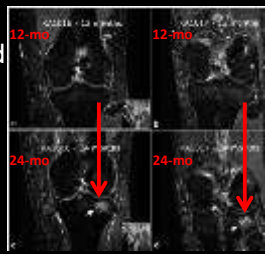
Images: Roemer et al 2011 (OARSI Primer)

What does it mean?

- We can detect subtle changes within 2 yrs
- Key Questions:
 1. Are some of these changes normal adaptations to new joint loading?
 2. Are some of these changes pathologic changes that represent early OA?
 3. How do athletic trainers optimize cartilage health over time in a joint with a history of injury?

Re-emerging Bone Marrow Lesions

- “bone bruise”: > 90% of knees with an ACL injury
- 34% of knees developed a new bone marrow lesion (BML) within 24-mo of injury¹
- BMLs may predict OA progression²




1. Frobell RB et al., 2011 (JBJS);
2. Felson DT et al., 2003; Tanamas SK et al., 2010; Driban et al., 2013

Key Questions to Ask Ourselves

- Do the new lesions represent early signs of OA?
- Why do these lesion appear?
 - Overloading due to training to soon?
 - Do we need to try to prevent them?
 - What can we do to prevent them?
 - Modify return to play?
 - Treatments?

Shaping the Future?

- Bone shape changes begin within 3 months
 - Flattening of articular surfaces of the femur
 - Inc. tibial curvature
- Change in first 3 mo. predicted change over 5 years




Hunter DJ et al., 2014
Images: Bowes M et al 2008, 2011 (OARS abstract)

Key Questions to Ask Ourselves

1. Are some of these changes normal adaptations to new joint loading?
2. Are some of these changes pathologic changes that represent early OA?

Back to the Basics

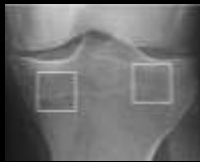
- New semi-automated methods to measure joint space width
 - 20 to 32% of participants experience joint space narrowing within 4 years of an ACL injury




Tourville T 2013, 2014 (images from Am J Sports Med)

Back to the Basics

Fractal Signature Analysis



Bone Mineral Density



FSA: Buckland-Wright JC et al., 1996; Kraus V et al., 2009; Wlodoszynski T et al. 2011
 Bone Mineral Density: Lo GH et al. 2006, 2012, 2012 (OARSI Abstract)

Losing Control for a Bit

- Post-ACL injury
 - Aggrecan turnover is elevated during 1st year^{1,2}
 - Collagen breakdown is elevated for 1st year¹
 - Collagen synthesis is elevated for at least 2 years¹
 - Elevated ratio of collagen breakdown/synthesis at 1 year and 4 years²
 - Increased inflammation for weeks; possibly years
 - ↑ Interleukin (IL)-6, IL-8, TNF-alpha, ↓ IL-1ra³

1. Beynon et al., 2005; 2. Larsson et al., 2013 (abstract) 3. Cameron et al., 1997



A Key Time Period?

- First two years after an injury
 - Cartilage changes
 - Reemerging bone marrow lesions
 - Changes in bone shape
 - Abnormal collagen and aggrecan turnover
 - Elevated Inflammation
- Some changes may be healthy adaptations but others may be early OA



A Key Time Period?

- The first two years after an injury are a busy time...
 - Tissue healing
 - Rehabilitation/surgery
 - Return to play
- Very little is known about how rehabilitation, surgery, and return to play influence the risk of OA at different joints



How does this affect my patient?

1. We can detect subtle changes within 3 to 24 months
 - We may start to monitor early changes in our patients before they graduate
2. If we can identify, which changes are bad...
 - Develop and implement prevention strategies
 - Modify return to play, interventions
 - Identify high-risk patients and implement long-term wellness programs




What can we do today?

- Educate about their risk for OA, proper body weight, and healthy lifestyle
- Prevent secondary damage
- Prevent new injuries



What's the Future

- Monitor patients after an injury
- Implement wellness protection programs
- Biochemical and biomechanical interventions
- Adapted treatment strategies
 - Rehabilitation progression
 - Return to play
- We are in an ideal position to help these patients




AT's Role: Injured Joint

Secondary Protection




Development of Osteoarthritis

- A complex disease
 - Biochemical and biomechanical factors
 - Altered tissues throughout the joint



OA: Bone

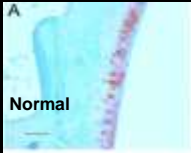
- Early changes in bone either coincide or precede early changes in cartilage
- Resorption of subchondral bone
- Osteophyte (bone spur) formation
- Eventual sclerosis



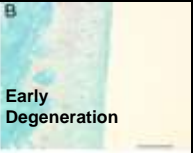
Sandell L 2012; Goldring SR, 2009; Images: Wolski M et al. 2011; Buckland-Wright et al., 2000; Lo GH et al., 2012; Zanetti M et al., 2000; Hunter DJ et al., 2009; Driban J et al., 2013

OA: Cartilage

- Changes in composition before structure
- Eventually leading to small cracks
- Chondrocytes try to save the cartilage but fail
- Fragments enter the synovial fluid



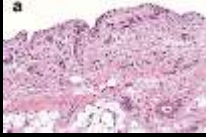
Normal



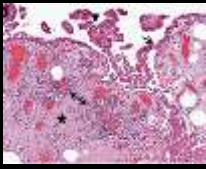
Early Degeneration

OA: Synovium

- Inflammation
- Express catabolic mediators
- Increased synovial surface
- Increased blood vessels
- Increased cells
- Capsular thickening and fibrosis



Normal



Osteoarthritis

Haynes et al. 2002, Linblad & Hedfors 1987, Myers et al. 1990, Revell et al. 1988, Bondeson et al. 2006, Grau et al. 2006, Fernandez-Madrid et al. 1995, Roach et al. 2007, Image: Scanzello & Goldring 2012

OA: Synovial Fluid

- Normally lubricates and nourishes the cartilage
- The Wastelands
 - Becomes less viscous
 - Becomes a depository for cartilage fragments, inflammatory mediators, catabolic mediators, and other proteins



1. Jones EA et al. 2008

Other Changes

- Articular structures (e.g., labrum, meniscus)
- Ligaments
- Musculotendinous Structures
- These structures may undergo degenerative changes and ultimately fail
- OA is not a disease of one or two tissues

Progression: The Whole Patient

- The entire body can contribute and react to OA
 - Central nervous system
 - Depression and anxiety
 - Peripheral nervous system
 - Other joints?
 - Adipose tissue

The Vicious Cycles

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graph TD
    Pain --> Disability
    Disability --> Fatigue
    Fatigue --> DepressedMood[Depressed Mood]
    DepressedMood --> Inflammation
    Inflammation --> Pain
    Pain <--> Disability
    Fatigue <--> DepressedMood
            
```

*Hawker GA et al., 2011;
Kyrkanides et al., 2011*

We Can't Prevent it All, Now What?

- There's A LOT of guidelines

To name a few

1. OARSI Guidelines for the Non-Surgical Management of Knee Osteoarthritis
2. American College of Rheumatology: 2012 Recommendations for the use of nonpharmacological and pharmacological therapies in osteoarthritis of the hand, hip, and knee.
3. American Academy of Orthopaedic Surgeons: The treatment of glenohumeral joint osteoarthritis: Guideline and Evidence Report
4. American Academy of Orthopaedic Surgeons: Treatment of osteoarthritis of the knee
5. EULAR: An evidence based approach to the management of knee osteoarthritis
6. EULAR: Evidence based recommendations for the management of hip osteoarthritis
7. EULAR: Evidence based recommendations for the management of hand osteoarthritis
8. EULAR: Recommendations for the non-pharmacological core management of hip and knee osteoarthritis
9. EULAR: Recommendations for the management of knee osteoarthritis
10. Ottawa Panel: evidence based clinical practice guidelines for the management of osteoarthritis in adults who are obese or overweight
11. Ottawa Panel: Evidence-based clinical practice guidelines for patient education programmes in the management of osteoarthritis
12. Ottawa Panel: Evidence-based clinical practice guidelines for therapeutic exercises and manual therapy in the management of osteoarthritis
13. Ottawa Panel: evidence-based clinical practice guidelines for aerobic walking programs in the management of osteoarthritis
14. NICE: National Collaborating Centre for Chronic Conditions: Osteoarthritis. National clinical guidelines for care and management in adults
15. National Health and Medical Research Council: Guidelines for the nonsurgical management of hip and knee osteoarthritis 2009
16. South African Arthritis Foundation: Osteoarthritis: Clinical Guideline 2003
17. MOVE Consensus: Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee
18. Turkish League Against Rheumatism: Evidence-based recommendations for the management of knee osteoarthritis: a consensus report
19. Portuguese Society of Rheumatology: Physiotherapy in hip and knee osteoarthritis

We Can't Prevent it All, Now What?

- There's A LOT of guidelines

- Relax. They have a lot of similarities.

Guidelines Overview

- Pharmacological Interventions
 - Oral/Topical: Acetaminophen, NSAIDs, tramadol, etc
 - Intra-articular: Corticosteroids
- Non-pharmacological Interventions
 - Physical Management: exercise, education, weight loss/diet, assistive devices, modalities, manual therapy, etc
 - Surgical Treatments: joint replacements

Physical Management

- Most common recommendations
 1. Exercise (16 of 17 guidelines)
 2. Patient education (13 guidelines)
 3. Assistive equipment (11 guidelines)
 4. Weight loss/diet (11 guidelines)

Larmer et al. 2013 (Arch Phys Med Rehabil): Systematic review of guidelines (physical management)

Exercise

- Individualized or tailored programs
 - Guidelines are vague
 - Often recommend individualized/tailored exercise



Larmer et al. 2013 (Arch Phys Med Rehabil): Systematic review of guidelines (physical management)

Exercise

- Summary recommendations: *Patients should be advised to engage in low-impact aerobic exercise (land or water based)...consideration can be given to range of motion/flexibility exercises, exercise in combination with manual therapy, endurance/strengthening exercises, and physical/occupational therapy referral.*



Nelson A et al., 2014

Strong Recommendation: Other

- Unspecified types of education (11 guidelines)
- Self-management (7 guidelines)
- Summary recommendations: *provide or refer patients to self-management programs; provide education, regular contact to promote self-care, joint protection strategies, and individualized treatment plans to patients with OA.*

Larmer et al. 2013 (Arch Phys Med Rehabil): Systematic review of guidelines (physical management); Nelson A et al., 2014

Strong Recommendation: Other

- Weight loss (10 guidelines)
- Wedged insoles for knee OA (10 guidelines)
- TENS (6 guidelines)
- Knee bracing for knee OA (5 guidelines)
- Appropriate footwear (4 guidelines)
- Balneotherapy/spa therapies (<3 guidelines)

Larmer et al. 2013 (Arch Phys Med Rehabil): Systematic review of guidelines (physical management)

Where do we fit in? Treatment

- Athletic trainers can be key figures in a team approach for all patients with osteoarthritis
- There are plenty of physically-active individuals with osteoarthritis
 - They may have unique goals/expectations
 - We are well trained for this population



What about my patient?*

- 50 year old, male, former college athlete in football
- BMI = 37 kg/m²
- Diagnosed with symptomatic hip OA
- *Educate (disease, home exercises, healthy lifestyle), therapeutic exercises as needed, weight loss, etc*


* Mock Case Study



What about my patient?*

- 50 year old, female, former college athlete in soccer, still running
- History of ACL tear
- BMI = 24 kg/m²
- Diagnosed with symptomatic patellofemoral OA
- *Educate, therapeutic exercises as needed, maintain healthy lifestyle, taping/bracing*


* Mock Case Study



What about my patient?*


- 63 year old, female, strength trains
- History of an acromioclavicular (AC) sprain
- BMI = 24 kg/m²
- Diagnosed with symptomatic AC joint OA
- *Educate (e.g., activity modification), therapeutic exercises and modalities (limited benefit), short-term immobilization*

* Mock Case Study



AT's Role: OA Progression

Symptom Management

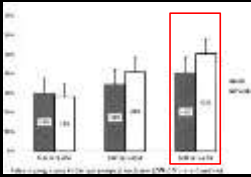


Treatments on the Horizon

- No accepted structure modifying therapies

Treatments on the Horizon

- Hip osteoarthritis
 - Avocado-soybean unsaponifiable
 - Extracts from avocado and soybean
 - May influence cartilage and bone
 - Over 3 years, less people progressed compared with a placebo
 - No effect on symptoms



Maheu E 2014 (Ann Rheum Dis)

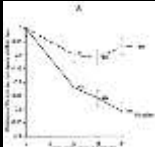
Treatments on the Horizon

- Knee osteoarthritis
 - Bisphosphonates (e.g., Risedronate, Zoledronic Acid)
 - Mainly influences bone
 - Over 1 to 2 years, participants on bisphosphonates had less biochemical evidence of cartilage degradation than those on placebo.
 - Bone marrow lesions became smaller among those with treatment
 - Radiographic evidence is limited
 - Improved symptoms

Bingham CO et al., 2006 (Arthritis Rheum); Spector TD, et al. 2005 (Arthritis Res Ther); Laslett LL., et al., 2012 (Ann Rheum Dis)

Treatments on the Horizon

- Knee osteoarthritis
 - Chondroitin sulphate
 - A component of articular cartilage
 - May influence cartilage and bone
 - Over 1-2 year, participants on chondroitin sulphate lost less cartilage than those on placebo
 - May also influence bone marrow lesions
 - No effect on symptoms



Wildi LM, et al., 2011 (Ann Rheum Dis); Raitlhad J, et al., 2012 (Clin Rheumatol); Kahan A et al., 2009 (Arthritis Rheum; figure)

Treatments on the Horizon

- Knee osteoarthritis
 - Doxycycline
 - Antibiotic
 - May influence cartilage
 - Over 30 months, participants on doxycycline lost less joint space than those on placebo
 - No effect on symptoms

Brandt KD et al., 2005 (Arthritis Rheum)

Treatments on the Horizon

- Knee osteoarthritis
 - Doxycycline
 - Biomechanics may be a very important

*Brandt KD et al., 2005 (Arthritis Rheum);
Mazucca SA et al., 2010 (Osteoarthritis Cartilage; Figure)*

Treatments on the Horizon

- Knee osteoarthritis
 - Biomechanical Interventions
 - Patellofemoral braces may modify BML size¹
 - Variable-stiffness shoes alter joint loading and may influence structural changes²

1. Felson D et al., 2013 (ACR Abstract), 2. Erhart JC et al., 2010 (J Orthop Res)

Treatments on the Horizon

1. No accepted as structure-modifying interventions
2. Only tested among individuals with OA
 - There is interest in testing interventions in early-stage OA or after an injury
3. May need to combine biomechanical and pharmacological interventions
4. May need to individualize treatment strategies

Future Role for ATs

- Identify high-risk patients
- Biomechanical interventions
 - Bracing
 - Insoles
 - Rehabilitation
- Promote Adherence
- Patient Education, etc



Prehabilitation before TJR

- 4 to 8 weeks before surgery
 - At home exercise programs
 - Supervised exercise programs
 - Strengthening and flexibility exercises
 - Neuromuscular electrical stimulation
 - Education

- Weak evidence so far

Matassi F et al., 2014; Brawn K et al., 2012; McKay C et al., 2012; Tungtrongjitt Y et al., 2012; Walls RJ et al., 2010; Figure from Topp R et al., 2009; Barbay K 2009.


AT's Role: Before a joint replacement

Improve Pain and Function

Postoperative Rehabilitation

- Early supervised rehabilitation (2-3 weeks)
 - Range of motion
 - Decrease swelling and pain
 - Gait retraining
 - Strengthening
- Supervised rehabilitation (4-6 weeks)
 - Strengthening and functional exercises
 - Neuromuscular electrical stimulation
 - Aerobic Exercise

Meier W et al., 2008



Postoperative Rehabilitation

- Semi-independent Phase (4-6 weeks)
- Progressive resistive training
- Aerobic training
- Encourage patient to meet exercise recommendations


Meier W et al., 2008



AT's Role: After a Joint Replacement


Improve Function and Independence

Meier W et al., 2008



Things to Consider

1. Prevention is key
2. We may soon be able to detect early OA
3. Early interventions may emerge
4. "Injury/Illness Prevention & Wellness Protection"
5. ATs can be a key part of treating OA



Structural and Biochemical Changes From Injury to Joint Replacement: Potential Roles of the ATC

Thank You.

