Biologic Patch for the Partial Rotator cuff tear

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Disclosure

• Consultant
  – Mitek
  – Smith & Nephew
Team Affiliations

[Images of baseball players and team logos]
Spring Training 2017
My Disclosure

I’m a Yankees Fan
Incidence of Partial Rotator Cuff Tears

• Fukuda et al., 2000
  – Prevalence of PTRCTs 13% - 32%
  – strong correlation to patient age.

• Sher J. S. et al., 1995

• MRI study of asymptomatic individuals
  – prevalence of PTRCTs 20%
  – 4% patients under the age of 40
  – 26% patients over the age of 60
Incidence of Partial Rotator Cuff Tears

- Milgrom et al., 1995
  - prevalence of full or partial thickness rotator cuff tears
    - 5%–11% in subjects aged 40–60
    - 80% in those aged 70 years or older

However, the true prevalence of PTRCTs may in fact be underreported.
Incidence of Partial Rotator Cuff Tears

• *Fukuda*. 2003
  – Investigation of 249 cadaveric supraspinatus tendons
    • 13% had PTRCTs
    • 55% were intratendinous
    • 27% were articular surface
    • 18% were bursal surface

• Suggesting that the vast majority of these intratendinous tears may have gone unnoticed
Incidence of Partial Rotator Cuff Tears

• prevalence of PTRCTs high in overhead athletes.

• prevalence of rotator cuff tears (i.e., partial or full thickness) was 40% in the dominant throwing shoulder.

• Connor et al. 2003
How Does An Injury Occur

- **Intrinsic Mechanisms**
  - Direct overload vs. internal degeneration
  - **Overuse**
    2° submaximal repetitive loading
  - **Traumatic failure**
  - **Degenerative failures** (most common)

Insertion site = Biomechanical weak
Hypovascular “Critical” Zone
Articular side less vascularity (?) ↑ Tears)
Tear Size – Partial Thickness

- **Ellman’s Classification:**
  - Based on Depth of Defect
    - Grade 1 < 25%
    - Grade 2 < 50%
    - Grade 3 > 50%
Tear Pattern

- Partial Articular
Tear Pattern

• Bursal Sided
Tear Pattern

- Intratendinous
Disease Progression of the Rotator cuff

- Severe Tendinosis (Failed Conservative Treatment)
- Partial-Thickness Tear
- Full-Thickness Tear
Disease Progression of the Rotator cuff

- Yamanaka et al., 1994
  - 40 Subjects with Partial Rotator Cuff Tears
  - Follow-Up Arthrography @ 1y
  - 53% showed enlargement of tear size
  - 28% progressed to Full Thickness Tear
Disease Progression of the Rotator cuff

Significant percentage of partial-thickness tears of the supraspinatus tendon progress to full-thickness tears:

- 27.5% (Yamanaka and Matsumoto, 1994)
- 8% (Maman et al., 2009)
- 26% (Ozbaydar et al., 2006)
- 6.5% to 34.6% (Strauss et al., 2011)
Disease Progression of the Rotator cuff

Partial-thickness and small full-thickness rotator cuff tears

– active cellular response and thus do possess some intrinsic healing ability
  • (Hamada et al., 1997; Matthews et al., 2006).
Disease Progression of the Rotator cuff

- The majority of imaging studies have demonstrated that healing of PTRCTs is rare
  - Mall N. et al. 2010
- Fukuda et al. 1994
  - PTRCTs do not have the ability to heal themselves over time.
What the &$!#%

• Why don’t partial-thickness tears heal?
Connective Tissue Healing

Healthy Tissue

Access to Reparative Cells

Availability of Bioactive Factors

Synthesis outpaces degradation

Biologics in Rotator Cuff Repair

Intrinsic Tissue Repair and Regeneration
Reasons for failed cuff healing:

Biological: local factors affecting RCT repair

- compromised vasculature \cite{Biberthaler2003}
- increased enzymatic activity \cite{Lo2004, Robertsen2012}
- apoptosis/decreased cellularity \cite{Yuan2002}
Reasons for failed cuff healing:

• While the biologic potential for healing may exist, other factors may adversely affect the healing process, such as:
  – Subacromial impingement
  – Degenerative changes
  – Age/systemic factors
  – Increased local strain at the injury site
Reasons for failed cuff healing:

• A key contributor to impaired healing and tear propagation is thought to be an increase in local strain at the injury site.

• Sano et al. (2006)
  – Demonstrated significantly increased strains at the injury site for bursal-sided, articular-sided, and intra-substance tears of the supraspinatus tendon
Figure 3. A. Intact supraspinatus tendon. B. Bursal-sided tear. C. Articular-sided tear. D. Intra-substance tear. (from Sano et al., 2006)
Reasons for failed cuff healing:

Biological: systemic factors affecting RCT repair

- smoking/nicotine \textit{Mallon et al. 2004; Galantz et al. 2006;}
- diabetes \textit{Bedi et al. 2010}
- hypercholesterolemia \textit{Abboud and Kim 2010}
- age \textit{Boileau et al. 2005; Flurin et al. 2005}

Biomechanical factors: poor tissue quality/tear size

\textit{George MS, Khazzam M 2012}
Addressing the Problem

Collagen Scaffolds

Optimizing Tissue Repair and Regeneration
It’s All About Mechanics

60% OF THE TIME

IT WORKS, EVERY TIME

Get More Funny Stuff @ funnyasduck.net
Collagen Scaffolds

**Goal:** augment the biomaterial properties of mechanically compromised rotator cuff tendons.

- Variety of tissue types (dermis, fetal dermis, small intestine submucosa [SIS], pericardium), donor species (allograft, xenograft), and processing techniques.

Collagen Scaffolds

• Allograft dermis has been shown to improve clinical scores in large (>3cm) tears involving two tendons. *Barber et al 2012*

• SIS did not improve clinical outcomes in large RTC repairs *Walton et al 2007; Iannotti et al 2006.*

• Dermal collagen scaffold augmentation of an extended double row technique did not improve the initial strength of the repair in healthy tendons. *Van derMeijden et al 2013*
Collagen Scaffolds

How might they help:

- Provide a ‘bio-inductive’ matrix to enhance cell migration and augment tissue healing.

New tissue induced by ‘onlay’ dermal collagen scaffold at 5 years. H&E x100. 

*courtesy of Dr. Stephen Snyder*
BIOLOGICS

- Increased stress on the repair site
- Rotator cuff tendon contains a zone of diminished blood supply—a watershed area
Biologic Patch to Increase Healing
Concept of a Biologic Patch

- A highly-porous, low modulus, collagen scaffold will induce the formation of a new layer of tendon-like tissue on the bursal surface of the supraspinatus tendon.
- This new tissue will reduce the peak strain at the site of the tear, thereby creating an environment conducive for healing.
Concept of a Biologic Patch

• Finite element analysis (FEA) demonstrated that a 2mm layer of new tissue on the bursal side of the supraspinatus tendon could significantly reduce stress at the site of a partial tear.
  • *Chen, 2011*
Concept of a Biologic Patch

- This FEA study demonstrated a reduction in peak strain
- 40% for an articular-sided tear
- 47% for a bursal-sided tear
  - Chen, 2011
Factors to Perpetuate Healing

Hypothesis:

The induction of a layer of new tendinous tissue on the bursal side of the supraspinatus tendon could reduce micro-strains within the tendon and could:

• Provide an optimized, mechanical environment for tendon healing
• Inhibit or arrest tear propagation

Bursal Surface Tear
47% reduction in peak strain

Articular Surface Tear
40% reduction in peak strain
Concept of a Biologic Patch

- Highly porous (85-90%)
- Low tensile modulus.
  - Produce tendon-like strain necessary to induce the fibroblasts to organize the collagen fibers into a tendon-like structure.
  - Bone anchors at one end ensures that the implant will undergo the same strain as the underlying tendon.
  - During rehabilitation the tendon will undergo about 2% strain, which for a 25 mm length of tendon equates to only 0.5 mm of elongation.
  - Necessitates need for low modulus
  - The low modulus also enables the appropriate strain to be transferred from the tendon to the implants without excessive loads at the fixation sites, thus enabling the use of small, low profile fixation components.
Concept of a Biologic Patch

- Implant is made from highly-purified, type 1 collagen fibers
- The implant is minimally cross-linked and freeze-dried
- designed to be completely absorbed within 6 months.
Augmentation with Biologics Patch

- Decrease tension to the repair site by adding mass to the tendon
- Increase blood vessels to the area
- Results: re-tear rate of 0 after two years (full and partial tears)
- Healed tendon by 3 months
- Completely normal tissue at one year
The Smith and Nephew Biologics Patch

RM Bioinductive Implant

- Implant derived from bovine Achilles tendon, highly purified, highly porous, highly oriented design

- Bioinductive Implant gradually absorbs within six months, leaving a layer of new tendon-like tissue to biologically augment the existing tendon
RM Bioinductive Implant: How It Works

- Proprietary implant design allows for rapid infiltration of fibroblasts and new blood vessels facilitating the formation of new tendon-like tissue – unlike any collagen scaffold on the market today.
- New tissue reduces the peak strain at the site of the tear and creates an environment conducive for healing.
- Strength comes from patient’s own induced tissue, not the implant.
Novel, Disposable Instruments Enable Quick And Easy Procedure

- Minimal learning curve with training
- Fast, reproducible procedure (10 - 15 min. or less)
Pre-Clinical Animal Study

When placed on the superior surface of a rotator cuff tendon (T), the implant consistently induced a layer of highly-aligned, connective tissue (*).

• The implant was completely resorbed by 6 months and replaced by new host tissue.

• Tissue continued to remodel over time without evidence of an inflammatory response.

Pre-Clinical Animal Study

At 26 weeks, the new tissue (NT) was well-integrated into the native bone (NB).

The bony insertion of the new tissue demonstrated evidence of a fibrocartilagenous (FC) component that suggests a normal, direct insertion.

Pre-Clinical Animal Study

- The histologic response demonstrated functional remodeling of the tissue at 52 weeks.
- The maturing tissue histologically resembled tendon-like, (dense, regularly-oriented) connective tissue.
- The mean thickness of the new tissue was 86% of the thickness of the underlying rotator cuff tendon.

AU Clinical Study Overview

• Conducted at five hospitals in Sydney
  – Drs. David Sonnabend, Des Bokor, Ben Cass and Allan Young
• 24 treatment patients and 6 comparison patients
• Treated patients:
  – 15 partial-thickness tears (14 ASD only, 1 ASD plus repair)
    • Ellman scale: 1 small, 5 medium, 4 large; 5 intra-substance (2 large)
  – 9 full-thickness tears (1 ASD only, 8 ASD plus repair)
    • Cofield scale: 1 small, 8 medium
• Comparison patients
  – Partial-thickness tears, acromioplasty only
• Implant attached to bursal surface of supraspinatus
• MRI, ASES, Constant, and SF-36 Scores
  – Pre-operative, 3 months, 6 months, 12 months, 24 months
  – All MRIs read by one independent radiologist, blinded to clinical outcomes
• Mean follow-up time – ~ 24.9 months
• Median implantation time -15 minutes
Demonstrated Healing: **Bursal Partial-Thickness Tear (No Repair)**

**Partial-Thickness Tear – Pre-op**
- **Tendon thickness = 3.3 mm**

**Healed Tear – 12 Months**
- **Total thickness = 5.4 mm**

- High-grade bursal tear
- Maturation of new tissue and tendon and tear filled-in
Demonstrated Healing: **Articular Partial-Thickness Tear (No Repair)**

**Partial-Thickness Tear – Pre-Op**

Tendon Thickness = 2.9 mm

**Healed Tear – 12 Months**

Tendon Thickness = 4.0 mm
AU MRI Results for Partial-Thickness and Full-Thickness Tears

- 100% induction of new tendinous tissue in all patients
  - Increase in thickness in both partial and full-thickness tears
  - Mean increase in thickness of 2.4 mm (64%)
  - No increase in thickness in controls

- Filling in of defect observed in partial-thickness tears
  - Observed in all patients in which pre-op MRI showed a clear defect

- No foreign body/inflammatory reaction

- No implant related complications
AU Clinical Scores Show Improvements in Partial-Thickness and Full-Thickness

The differences in all scores compared to pre-op (except Constant overall at 3 months) are statistically significant (p < 0.05)
U.S. Clinical Study Summary

• 66 treated patients
  – Mean age: 56.6 years (Range 33.5 to 74.8)
• 12 implanting surgeons
• Treated patients:
  – 33 partial-thickness tears, no repair
    • (13 Bursal, 16 Articular, 4 Intrasubstance)
  – 33 full-thickness tears, with repair
    • (Medium (1-3 cm): 22, Large (3-5 cm): 11
• Implant attached to bursal surface of supraspinatus
• MRI, ASES, Constant, and SF-36 Scores
  – Pre-operative, 3 months, 12 months, 24 months
  – All MRIs read by one independent radiologist, blinded to clinical outcomes
Demonstrated Healing: **Bursal** High-Grade Partial-Thickness Tear (No Repair)

- 55 y.o Caucasian Male
- Grade 3 (> 50%) bursal tear

**Treatment**
- RM Bioinductive Implant placed on bursal side of tendon
- No repair

**Recovery data**
- Returned to work in 7 days
- Sling removed after 14 days
- Satisfied with procedure and would recommend it to a friend.

**Baseline MRI**
- 11 mm x 14 mm, high-grade bursal tear
- 2.0 mm tendon thickness at location of tear
- Mild subacromial, sub deltoid bursitis

**3 Month MRI**
- 7.5 mm tendon thickness at location of tear; Thickness $\Delta = +5.5$ mm
- 100% defect fill-in with new, amorphous, immature material
- Tendon thickness at tear = 2.0 mm
- Tendon thickness at tear = 7.5 mm

* U.S. Clinical Study
**Demonstrated Healing: Articular Partial-Thickness Tear (No Repair)**

- 61 y.o. active, retired male with chronic shoulder pain for 15 months previously managed with cortisone injections, PT, and OTC pain medication.

<table>
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<tr>
<th>Baseline MRI</th>
<th>3-Month MRI</th>
<th>1-Year MRI</th>
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<tr>
<td><img src="image1" alt="Baseline MRI" /></td>
<td><img src="image2" alt="3-Month MRI" /></td>
<td><img src="image3" alt="1-Year MRI" /></td>
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- **Grade 2 articular-sided partial-thickness tear**
  - Tendon thickness at tear 2.6mm
  - Slight bursitis with mild capsulitis

- Newly induced tissue; indistinct margins, amorphous appearing texture with 75-100% fill-in of tear
  - Tendon thickness at tear 4.6mm ($\Delta +2$ mm)
  - Mild/moderate bursitis, debris

- Newly induced tissue; similar to 3-month MRI, with 75-100% fill-in of tear
  - Tendon thickness at tear 4.0mm ($\Delta +1.5$ mm)
  - Mild bursitis
Host Cell Ingrowth And Early Collagen Production And Alignment

Patient 4: 5 weeks

Light (A) and polarized light (B) photomicrographs of a Rotation Medical Collagen implant illustrating host cell ingrowth and early collagen production and alignment (arrows) at 5 weeks. H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, (Arthroscopy e-pub on line)
Increased Collagen Formation, Maturation and Orientation Over the Surface of the Implant

Photomicrograph showing increased collagen formation, maturation, and orientation over the surface of the implant at 3 months. H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant. (Arthroscopy e-pub on line)
Evidence Of Maturation And Functional Alignment Of Dense, Regularly Oriented Connective Tissue

Patient 2: 3 months

Light (A) and polarized light (B) photomicrographs of the newly regenerated host tissue Overlying the implant at 3 months. There is evidence of maturation and a functional alignment of the dense, regularly oriented connective tissue.  H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, (Arthroscopy e-pub on line)
Dissolution Of Collagen Implant By Invading Fibroblasts

Patient 2: 3 months

Photomicrograph showing what appears to be dissolution of the collagen implant by invading fibroblasts at 3 months (arrows). H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, (Arthroscopy e-pub on line)
Patient 1: 6 months

Light (A) and polarized light (B) photomicrographs of the newly regenerated host tissue by the implant at 6 months. This is dense, regularly-oriented connective tissue. There was no evidence of any remnants of the collagen implant at this time. H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, (Arthroscopy e-pub on line)
Comparison Between Sheep And Human – 6 Month MRI

Sheep

- Regularly-oriented collagen, fibroblasts and blood vessels
- No evidence of implant, no inflammatory response
- Sheep and human are essentially identical

Human

CONFIDENTIAL
BioInductive Implant First To Clinically Demonstrate Tendon Tissue Induction

Dermal Collagen Patch

No induction of new host tissue by dermal patch, no evidence of any functional remodeling of the dermal patch at 2 years

Bioinductive Implant

Bioinductive Implant reabsorbed, new connective tissue induced, thicker tendon
Clinical Results Consistent

- **Pre-Clinical Study**
- **AU Clinical Study**
- **U.S. Post-Market Clinical Study**

Consistently induced highly-aligned, connective tissue, 86% thicker tendon

**64% thicker tendons in partial thickness tears with no re-tears for FT patients**

**Interim 1-year results validate AU study, 61% increase in tendon thickness**

**Partial-Thickness Tear Patients**

- **Sheep Model**
  - 52 weeks

- **Graph**
  - Mean Thickness Increase (mm)
  - Time Post-Surgery:
    - 3 Months
    - 6 Months
    - 1 Year
    - 2 Years
Bio-Inductive Implant Arthroscopic Technique

PEARLS

• Make lateral portal parallel to supraspinatus in both coronal and axial planes or use accessory anterolateral portal

• Tendency is to place graft too far posterior and medial. Make sure graft comes out lateral enough for proper bone staple insertion

• Make sure staple gun insertion angle is not more than 45 degrees, separate portals for staples near edge of acromion

• Pay close attention to maintaining position of bone stapler while switching from punch to staple
Where Does This Really Pay Off

• Partial rotator cuff tears can be addressed with the patch
• Maintain the shoulders normal anatomy
• No conversion to a rotator cuff repair
• Return to full activity in 3 months
Comparison Of Rehab Protocols

Partial tear traditional repair
• Sling/ immobilizer 4 weeks
• Full range of motion 12 weeks or more
• Return to full activity 6 months or more

Repair with Biologic Patch
• Sling 1 week
• Full range of motion 5 weeks
• Return to full activity 3 months or more
Rehab Protocols

Partial-Thickness Tears (No Repair)

- Phase I: Immediate post-op (first 5 to 7 days after surgery, prior to starting PT)
  - Use sling for 24 – 48 hours
  - Remove 4 or 5 times daily to do pendulum exercises, supine external rotation, supine passive arm elevation, scapular retraction, shoulder shrug
  - Sleep with sling in place
  - May use affect arm in front of body, no lifting of objects over 5lbs., no excessive shoulder extension, no supporting body weight by hands
Rehab Protocols

Partial-Thickness Tears (No Repair)

- Phase II: Intermediate phase (1 to 6 weeks post-op)
  - Should be weaned out of using sling
  - Begin formal physical therapy (ROM, AAROM, AROM, Pendulums, Pulleys, Cane Exercises, Self Stretches)
  - Once patient has pain free full ROM and no tenderness (Initiate isotonic program with dumbbells, PNF)
  - Continue to ice regularly
  - Unless instructed otherwise, okay to drive, allowed to actively use arm for daily living, bathing, dressing, typing on computer, etc.
Rehab Protocols

• Phase III: Active strengthening phase (6 weeks and beyond)
  – Must be have full painless ROM and no pain or tenderness on examination to proceed to this phase
  – Continue dumbbell strengthening, progress theraband exercises to 90/90 position for internal rotation and external rotation, etc.
Reimbursement Overview

Current Situation

• There are existing CPT codes in which the SN technology fits into
  – Procedure is billed under CPT Code 29827, Arthroscopic, shoulder, surgical; with rotator cuff repair (see Rotation Medical Coding Guidance for complete list) among other codes

• Physician’s payment is separate from hospital
  – Receive same payment for a procedure performed with Rotation Medical’s technology as they do today for a rotator cuff repair

• A large number of hospitals do have provisions in their private payer contracts to pay for devices not covered under the CPT code payment
  – Carve outs for expensive implantable devices
  – Payment based on a percent of charges
  – Payment based on a percent of Medicare
  – (i.e. 150% of Medicare payment)
Thank You
Life Lessons

Good

Bad