Allograft Treatment of Partial Thickness Rotator Cuff Tears

Detroit, MI
July 28, 2016

Biologic Xenograft Implant for Partial Thickness Rotator Cuff Tears

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Partial Rotator Cuff Tears

Disclosures

- Paid Consultant
  - DePuy Synthes
  - Zimmer Biomet
  - Arthrex
  - Rotation Medical
  - Ceterix

- Surgeon Advisory Boards
  - Mitek Sports Medicine
  - Rotation Medical

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Partial Rotator Cuff Tears

Shoulder Pain

- United States:
  - 4-6 Million People Per Year Seek Medical Attention
  - 1.5 Million Visits Per Year to Orthopaedic Surgeons


Partial Rotator Cuff Tears

Basic Science

- Causes
  - Macrotomra
    - Usually leads to acute full thickness injury
  - Repetitive Microtrauma
  - Degenerative Pathologic Process

Partial Rotator Cuff Tears

Overuse Injury Algorithm

- Overuse During Overhead Activity
- Occult Anterior Instability
- Injury to Static Ligamentous Restraints
- Fatigue Develops, Reducing The Dynamic Stabilization Leading to Eccentric Tendon Fiber Failure

Partial Rotator Cuff Tears
Basic Science

- Histopathologic Changes to the Torn Rotator Cuff
  - Matthews et al. 2006
  - Small Sized Tears
    - ↑ Fibroblast Cellularity
    - ↑ Intimal Hyperplasia
    - ↑ Expression of Leukocyte and Vascular Markers
  - Large and Massive Tears
    - ↑ Edema and Degeneration
    - ↑ Chondroid Metaplasia and Amyloid Deposition
    - No Increase in Inflammatory Cells or Blood Vessels
  - Small Tears Have the Ability to Heal, Large Tears Need to Be Repaired

About Rotator Cuff Disease

- There are no good options for early surgical intervention
- Chronic rotator cuff tendinopathy has been identified as a primary cause of rotator cuff tears (Hashimoto et al., Clin Orthop. 2003)
- There are no good options for early surgical intervention
- Significant incidence (25%) of re-tears and impaired function after repair (Flurin et al.)

Partial Rotator Cuff Tears
Defining the Tear

- Understanding the Footprint
  - Average maximum length of 23 mm (range: 18 to 33 mm)
  - Average maximum width of 16 mm (range: 12 to 21 mm)
Why Don’t Tears Heal?

- While the biologic potential for healing may exist, several factors, such as subacromial impingement, may adversely affect this process.
- Growing belief that local strain at the injury site is thought to contribute to impaired healing and tear propagation.

How Can We Create An Optimum Environment For 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.

What are the attributes of an ideal scaffold for tissue regeneration?

- Provide a matrix scaffold to support the ingrowth of host tissues.

The IDEAL Scaffold:
What are the attributes of an ideal scaffold for tissue regeneration?

- Provide a matrix scaffold to support the ingrowth of host tissues.
- Provide an inductive and conductive stimuli for cell and vessel migration.
- Allow for normal tissue remodeling.
- Eventually be removed by the host.

The IDEAL Scaffold:
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 tendon induced by dermal patch at 2 years.

RM BioInductive Implant

- BioInductive implant reabsorbed, new connective tissue induced, thicker tendon.
- No induction of new host tissue by dermal patch, no evidence of any functional remodeling of the dermal patch at 2 years.

Target Patients Span Rotator Cuff Disease Spectrum

<table>
<thead>
<tr>
<th>Tear Progression</th>
<th>Severe Tendinosis (Failed Conservative Treatment)</th>
<th>High-Grade Partial-Thickness</th>
<th>Small Full-Thickness</th>
<th>Med-Large Full-Thickness</th>
<th>Massive Full-Thickness</th>
</tr>
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<tbody>
<tr>
<td>In lieu of standard repair</td>
<td>In lieu of in conjunction with Acromioplasty</td>
<td></td>
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- Patients at risk for tear progression, compromised healing potential
- Suboptimal tissue quality, thin tendons
- Patients with a recently failed repair
- Patients where only limited footprint can be restored
- Want to avoid over-tensioning

The Rotation Medical Rotator Cuff System™

<table>
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<tr>
<th>Scaffold</th>
<th>Novel Instrument Sets</th>
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</table>

- Five Years of R&D
- 100+ Cadaver Labs
- Third-Generation Instrumentation
- Two Options: Arthroscopic and Mini-Open
Unique Scaffold Design Induces Biological Response*  

Unique Characteristics:  
- Reconstituted, bovine collagen with 90% porosity  
- High purity to avoid inflammatory response  
- Low strength material not intended for mechanical augmentation  
- Permanent strength comes from patient’s induced, remodeled tissue  
- Bioabsorbable  
- Ability to implant arthroscopically as well as mini-open  

* Induces a layer of new, tendinous tissue on the surface and fills in defects

Breakthrough Instruments

- Differentiated and integrated system  
- Intuitive and easy  
- Reproducible procedure time (average 15-20 min.)  
- Disposable components

Demonstrated Healing: Articular-Sided, Partial-Thickness Tear (No Repair)

- Patient pain returned at 12 months; MRI indicated significant bursitis  
- Arthroscopic clean-up procedure was performed; histology showed minimal reaction to scaffold  
- Six months post clean-up patient was pain-free and MRI showed normal bursa  
- Tissue induction and defect filling was not compromised by bursal reaction in this patient
**Key Advantages**

- Quick procedure, average time ~15 minutes
- Instrumentation enables reproducible placement of the scaffold
- Minimal learning curve with training
- Patient acceptance excellent

**Conclusions**

- Rotation Medical Scaffold was able to:
  - Induce new tissue similar to tendon on MRI
  - Maintain increased thickness of compromised tendon on MRI (Dr. Ho)
  - Lead to an improvement in Constant, ASES and SF-36 scores comparable to that seen in patients undergoing rotator cuff repair
  - MRI scans at 12 months indicate that there may be induction of healing at the site of the partial-thickness tear in the cuff
  - Rotation Medical Scaffold may offer an alternative treatment option for those patients with a deep partial-thickness cuff tear who are unable to comply with cuff repair rehabilitation
  - Rotation Medical Scaffold did not interfere with routine cuff healing following repair, but in fact enhanced the radiological appearance of the repaired tendon

**The Rotation Medical Difference: Addressing Tendon Biology**

**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
- Load sharing implant
RM BiInductive 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.

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.

- 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 – 38+ months
- Median implantation time -15 minutes

Demonstrated Healing: Bursal Partial-Thickness Tear
(No Repair)

- Tendon thickness = 3.3 mm
- Total thickness = 5.4 mm
- Healing demonstrated at 12 months with a regain of normal tendon and tear filled in.
Demonstrated Healing: Articular Partial-Thickness Tear (No Repair)

Partial-Thickness Tear – Pre-Op

Healed Tear – 12 Months

Tendon Thickness = 2.9 mm

Tendon Thickness = 4.0 mm

Demonstrated Healing: Intra-Substance Partial-Thickness Tear (No Repair)

Partial-Thickness Tear – Pre-op

Healed Tear – 12 Months

Tendon thickness = 6.2 mm

Total thickness = 9.2 mm

Repairs Heal with Increased Thickness and Fully Restored Footprint

Approximate lateral edge of footprint preoperatively

Extract of restored footprint
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
- Cuff repairs are all intact at two year post-operative MRI evaluation
  - Footprint fully restored in all patients
- No foreign body/inflammatory reaction
- No implant related complications

AU Clinical Study Post-Operative Rehab

Partial-Thickness Tears (No Repair) Treated Post-Operatively Similar To ASD
- Sling discarded when comfortable (max 1 week)
- Graduated progression of motion as tolerated from
  - PASSIVE \(\rightarrow\) ACTIVE ASSISTED \(\rightarrow\) ACTIVE
- Active ROM allowed with:
  - Forward flexion 0 – 100° for first 4 weeks
  - External rotation allowed with arm by side (No ABER for 6 weeks)
  - No resistance exercises for 6 weeks
- No restriction of motion or use of arm after 6 weeks

Full-Thickness Tears (Implant with Cuff Repair)
- Patient treated as for rotator cuff repair
- NO changes to routine post-operative protocol

AU Clinical Scores Show Improvements in Partial-Thickness and Full-Thickness

The differences in all scores compared to pre-op (shoulder Constant scores and Shoulder Pain Visual Analog Scale) are statistically significant (p < 0.05)
U.S. Clinical Study Summary

- Enrollment closed 3/31/2016
- 64 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)
  - 31 full-thickness tears, with repair
    - (Medium (1-3 cm): 22, Large (3-5 cm): 9)
- 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.

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.

Baseline MRI

- 11 mm x 14 mm, high-grade bursal tear
- 2.0 mm tendon thickness at location of tear
- MRI 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

1-Year MRI

- 9.0 mm tendon thickness at location of tear; Thickness \(\Delta\) = +6 mm
- 100% defect fill-in with new, amorphous, immature material

Newly induced tissue; similar to 3-month MRI, with 75-100% fill-in of tear
Demonstrated Healing: Full-Thickness Tear with Repair

- 71 year old active, retired male with 8 month history of medically managed shoulder pain
- Repaired with a single row 4.5mm anchor

Baseline MRI 3-Month MRI 1-Year MRI

8mm x 12mm full-thickness tear
Mild subacromial, subdeltoid, subacromial

Newly induced inhomogeneous tissue; Mild subacromial, subdeltoid, subacromial

Tissue quality better defined vs. 3-month MRI
Mild subacromial, subdeltoid, subacromial

Clinical Results Compellingly 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
Early results validating AU study, > 70% increase in tendon thickness

Physician Recommended 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 sling 3 to 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 affected arm in front of body, no lifting of objects over 10lbs., no excessive shoulder extension, no supporting body weight by hands
- Phase II: Intermediate phase (1 to 6 weeks post-op)
  - Should be weaned out of using sling
  - Begin formal physical therapy (ROM, AAROM, AROM, 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.
- Phase III: Active strengthening phase (6 weeks and beyond)
  - Must be able to perform full ROM and no pain or tenderness on examination to proceed to this phase
  - Continue dumbbell strengthening, progress thoracic exercises to 90/90 position for internal rotation and external rotation

Partial-Thickness Tears (Implant with Cuff Repair)

- Patient treated as for rotator cuff repair
- NO changes to routine
Patient Biopsy Case Study

Patient
- Custodial engineer, female 45 years old
- Full thickness tear repair failed
- Very poor, degenerated rotator cuff tissue
- Osteoarthritis in humeral head, required reverse total shoulder arthroplasty but not good candidate
- Performed rotator cuff surgical revision with Rotation Medical implant to potentially generate new rotator cuff tissue and allow for arthroplasty

Patient Biopsy Case Study – Rotator Cuff Repair – October 2014

Patient Biopsy of Degenerated Rotator Cuff Tissue Before RM Implant

Poorly organized collagen, dying cells, poor vascularity

Polarized Light Image

*H&E 50x original magnification
Patient Biopsy Case Study – Hemiresurfacing – April 2015

Comparison Between Sheep And Human – 6 Months Biopsy

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

Thank You
Bio-Inductive Implant Arthroscopic Technique PEARLS

- Please customize as you see fit -

- 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.