Healing of Partial-Thickness Rotator Cuff Lesions

Balancing Biomechanics and Biology

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Disclosures

Consultant:
- Rotation Medical
- Applied Biologics

The Problem:

PT-tears

- Partial-thickness rotator cuff tears represent a significant challenge to the orthopaedic surgeon.
- Unfortunately, there is no consensus on a single algorithmic treatment approach for a patient with a symptomatic, partial-thickness rotator cuff tear.

Finnan and Crosby, JSES 2010
The Problem:  

- Studies have documented spontaneous healing in a limited number of partial-thickness cuff tears as manifested by a reduction in size or disappearance of the defects.  

  Yamanaka and Matsumoto, CORR 1994  
  Maman et al, JBJS 2009

- 40 patients with partial-thickness joint tears @ 2 year follow-up  
  - 4 lesions decreased in size (healing?)  
  - 4 lesions disappeared (healed?)  
  - 32 lesions enlarged or progressed to full-thickness lesions  

  Yamanaka and Matsumoto, CORR 1994

The Problem:  

- Studies have demonstrated that small, full-thickness tears and partial-thickness rotator cuff tears have an active cellular response and thus, do possess some intrinsic healing ability.  

  Yamada et al, JOR 1997  
  Matthews et al, JBJS 2006

  H & E x 100  
  H & E x 100
The Problem:  

Partial-thickness tears of the supraspinatus tendon have been shown to progress to full-thickness tears:

- 6.5% to 34.6% (Strauss, et al., Arthroscopy 2011)
- 8% (Maman, et al., J Bone Jt Surg 2009)
- 26% (Ozbaydar, et al., Acta Orthop Traumatol 2006)
- 27.5% (Yamanaka and Matsumoto, Clin Ortho 1994)
- 44% (Keener et al., J Bone Jt Surg 2015)

Why don’t these tears heal??

While the biologic potential for healing may exist, other factors may adversely affect this process.
The Problem: PT-tears

Why don't these tears heal??

- While the biologic potential for healing may exist, other factors may adversely affect this process.
  - subacromial impingement
  - degenerative changes
  - age/systemic factors

- compromised vasculature: Biberthaler et al 2003
- increased enzymatic activity: Li et al 2004; Robertson et al 2012

- increased local strain at the injury site

The Problem:

PT-tears

- The increase in local strain at the injury site is thought to contribute to impaired healing and tear propagation

A new concept

Balancing Biology and Biomechanics

- Goal: To augment the biomaterial properties of mechanically compromised rotator cuff tendons by enhancing its natural biologic structure through the induction of new host tissue.

Bursal surface tear
47% reduction in peak strain

Articular surface tear
40% reduction in peak strain
Create an IDEAL Scaffold:

- 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.
**A new concept**

*Balancing Biology and Biomechanics*

Create an IDEAL Scaffold:

- 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.

A new concept

Implant Design:

- Highly-purified, bovine type I collagen (<50 ng/mg of DNA)
- Highly-oriented and highly-porous (85-90%)
- Minimally cross-linked and freeze-dried

Pre-clinical Study:

When placed on the superior surface of a rotator cuff tendon (T), the implant consistently induced a layer of highly-aligned, connective tissue (*), which continued to remodel over time without evidence of an inflammatory response. The implant was completely resorbed by 6 months and replaced by new host tissue.

Pre-clinical Study:
At 26 weeks, the new tissue (NT) was well-integrated with the native bone (NB). The bony insertion of the new tissue demonstrated evidence of a fibrocartilagenous (FC) component that suggests a normal, direct insertion.

![Image](image1.png)


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Pre-clinical 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.

![Image](image2.png)


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Key findings
- Rapid incorporation of the bioinductive implant by host tissues
- Implant stimulated both an inductive and conductive response
- Consistent production of a dense, regularly-oriented, connective tissue layer suggests functional adaptation, remodeling and maturation
- Excellent integration into bone with a fibrocartilagenous transition zone reminiscent of a normal direct insertion
- No Histologic evidence of a foreign body or inflammatory response at any time for any of the animals
- Histologic response of the host remained stable at 1 year
Objective: To assess the ability of a highly porous, collagen implant to induce new tissue formation and limit tear progression when placed on the bursal surface of unrepaired partial-thickness and repaired full-thickness rotator cuff tears.

Hypotheses:

H1: The reconstituted collagen implant would induce rapid new tissue ingrowth and create an environment that would permit the functional maturation and alignment of new tendon-like tissue over the surface of the injured tendon as determined by sequential MRIs over a 24 month period.

H2: The newly induced tissue would limit tear progression of partial-thickness lesions, re-tearing of full-thickness repairs, and prevent further degenerative changes within the tendon based on MRI evaluations.
First in Man Study

Study Design

- Case series (Level 4)
- Treated patients:
  - 13 partial-thickness tears (5 articular; 3 bursal; 5 intra-substance)
  - Ellman scale: 6 intermediate; 7 high grade
- 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


First in Man Study

Study Design

- Arthroscopic placement of a collagen implant over bursal surface of the cuff tendon; affixed to tendon with PLLA staples and to bone with PEEK staples.
- Post-op care similar to ASD;


First in Man Study

Results: MRI

At 3 months following surgery there was a significant (p<0.0001) increase in new tissue induction over the bursal surface of the supraspinatus tendon. (Mean thickness increase of 2.2 ± 0.26 mm).
First in Man Study

Results: MRI

- There was no MRI evidence of tear enlargement in any of the defects over time.
- Bursal-sided tear
  - There was no MRI evidence of tear enlargement in any of the defects over time.
  - 70% of the defects showed complete filling-in by 12 mos.
  - The remaining 30% of defects decreased in size but were not completely filled-in by 24 months.

- Articular-sided tear
  - Tendon thickness = 2.9 mm Total thickness = 4.8 mm

First in Man Study

Results: MRI

- New tissue integrates and remodels into the healed tendon.
- Improved environment encourages healing.
- Implant placed over bursal surface of RCT
- Implant induces new host tissue onto tendon by 12 wks.
First in Man Study

Clinical Assessment

Constant and ASES scores showed steady improvement throughout the 24 month follow-up period.

- At 24 months 12 of 13 patients (92%) expressed satisfaction with the procedure.
- No adverse events associated with the implant.

Chi square analysis against published historic controls showed that a highly porous collagen implant resulted in a statistically significant benefit in limiting tear progression when used in partial-thickness rotator cuff tears.

Keener et al.: 44% tear progression  p<0.002
Yamanaka and Masamoto: 27.5% tear progression  p=0.000

Chi square analysis against published historic controls showed that a highly porous collagen implant resulted in a statistically significant benefit in the healing of partial-thickness lesions.

Yamanaka and Masamoto: 10% healing rate  p=0.000
**Human Biopsy Study**

**What type of tissue regeneration will occur in humans?**

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Age (yo)</th>
<th>Sex</th>
<th>Procedure</th>
<th>Time of Biopsy</th>
<th>Location of Biopsy</th>
<th>Reason for second look</th>
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<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>F</td>
<td>Primary FT-RCR</td>
<td>6 mos</td>
<td>Anterior aspect of repair</td>
<td>Suggest trial and replay</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>F</td>
<td>Primary FT-RCR</td>
<td>3 mos</td>
<td>Anterior aspect of repair</td>
<td>Patient fell and disrupted repair</td>
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<tr>
<td>3</td>
<td>50</td>
<td>F</td>
<td>Medium PT-B tear</td>
<td>3 mos</td>
<td>Antero-lateral aspect of repair</td>
<td>Patient's arm was jerked while walking dog</td>
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<tr>
<td>4</td>
<td>51</td>
<td>M</td>
<td>Revision FT-RCR</td>
<td>5 wks</td>
<td>Antero-lateral aspect of implant</td>
<td>Patient fell and disrupted repair</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>F</td>
<td>Primary FT-RCR</td>
<td>3 mos</td>
<td>Postero-lateral aspect of repair</td>
<td>Pain; portion of tear not covered by implant was not healing</td>
</tr>
<tr>
<td>6</td>
<td>45</td>
<td>F</td>
<td>Converted high-grade PT (B) to FT-RCR</td>
<td>2 mos</td>
<td>Antero-lateral aspect of repair</td>
<td>Arthrofibrosis</td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>M</td>
<td>Primary FT-RCR</td>
<td>2 mos</td>
<td>Multiple areas of the implant</td>
<td>Patient fell and disrupted repair</td>
</tr>
</tbody>
</table>


**Human Biopsy Study**

**Patient 4: 5 weeks**

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


**Human Biopsy Study**

**Patient 2: 3 months**

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

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


Human Biopsy Study

Patient 2: 3 months

Sheep at 6 months

Human at 6 months

Implant completely resorbed, host regenerated tissue is dense, regularly-oriented connective tissue.

Human Biopsy Study

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


Human Biopsy Study

Comparison of implant-induced tissue in human and sheep at 6 months
Do currently available rotator cuff augmentations remodel in a similar manner?

- freeze-dried dermal allograft
- distinct collagen pattern

- contains elastin fibers

Light (A) and polarized light (B) photomicrographs demonstrating that at 8 months the implant still retains the histological character (collagen pattern and the presence of elastin fibers) of human dermis. Verhoeff-Van Gieson Stain X 100
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Photomicrographs of the dermal implant at 8 months showing large areas in the deeper aspects of the implant which are devoid of host cell infiltration. H&E X 100

Light (A) and polarized-light (B) images of biopsy of dermal allograft rotator cuff augmentation at 8 years. While the allograft has been repopulated with host cells, the collagen arrangement seen in the polarized image is more similar to dermis than tendon.
Light (A) and polarized-light (B) images of biopsy of dermal allograft rotator cuff augmentation at 8 years. While the allograft has been repopulated with host cells, the collagen arrangement seen in the polarized image is more similar to dermis than tendon.

H&E (A) and Van Giesen (B) stained images of biopsy of dermal allograft rotator cuff augmentation at 8 years. The dense elastin staining suggests that the scaffold retains its dermal character and is not remodeled into tendon.

- The reconstituted collagen implant (RCI) is rapidly incorporated by host cells and induces the production of a dense, regularly-oriented, connective tissue layer over the bursal surface of a rotator tendon.
A new concept

- The reconstituted collagen implant (RCI) is rapidly incorporated by host cells and induces the production of a dense, regularly-oriented, connective tissue layer over the bursal surface of a rotator tendon.
- The implant provides no immediate additional strength but rather allows the rapid, functional adaptation, remodeling, and maturation of additional tendon.
- It is this new, host-derived tissue that optimizes the biomechanical and biological environment of the tendon allowing for better healing.
- The RCI demonstrates consistent biological performance in both pre-clinical animal studies as well as in clinical applications for the treatment of partial- and full-thickness rotator cuff tears.
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The RCI demonstrates consistent biological performance in both pre-clinical animal studies as well as in clinical applications for the treatment of partial- and full-thickness rotator cuff tears.

The RCI-induced tissue demonstrates an excellent integration into bone through a fibrocartilagenous transition zone which is reminiscent of a normal tendon insertion.

Animal and human biopsy specimens have shown that the RCI is completely resorbed by 6 months with no evidence of any foreign body or inflammatory reactions.
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