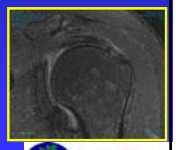
~~Allograft Treatment of~~ Partial Thickness Rotator Cuff Tears

Detroit, MI
July 28, 2016

Associated Orthopedists of Detroit, PC
Sports Medicine, Shoulder Surgery and Hip Arthroscopy
Assistant Professor, Michigan State University College of Osteopathic Medicine
Assistant Professor, Oakland University William Beaumont School of Medicine
Professor, Detroit Medical Center Sports Medicine Fellowship
Past-President, American Osteopathic Academy of Orthopedics Sports Section
Past-President, Detroit Academy of Orthopaedic Surgery





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Biologic Xenograft Implant for Partial Thickness Rotator Cuff Tears

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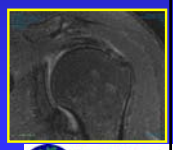

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Partial Rotator Cuff Tears Disclosures

- Paid Consultant
  - DePuy Synthes
  - Zimmer Biomet
  - Arthrex
  - Rotation Medical
  - Ceterix
- Surgeon Advisory Boards
  - Mitek Sports Medicine
  - Rotation Medicial

DePuy Synthes
Pioneering inspired.

ZIMMER BIOMET
Your progress. Our promise.

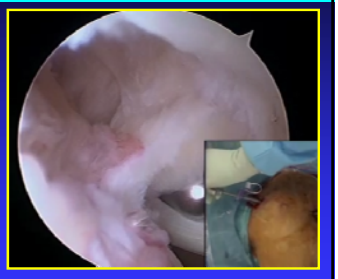
Arthrex

rotation MEDICAL

CETERIX ORTHOPAEDICS

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



Lehman RC: Shoulder pain in the competitive tennis player. *Clin Sports Med.* 7: 309-327, 1988.

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Partial Rotator Cuff Tears
Basic Science

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

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Partial Rotator Cuff Tears
Overuse Injury Algorithm

Kuhn JE, Hawkins RJ: Surgical Treatment of Shoulder Injuries in Tennis Players. Clin Sports Med. 1995. 14: 139-161.

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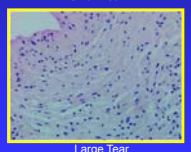
Partial Rotator Cuff Tears
Basic Science

- 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 Inflammatory Cells or Blood Vessels
    - Small Tears Have the Ability to Heal, Large Tears Need to Be Repaired


Small Tear


Large Tear

Matthews TJW, Hand GC, Rees JL, Athanasou NA, Carr AJ. Pathology of the Torn Rotator Cuff Tendon,Reduction in the Potential For Repair as Tear Size Increases. *J Bone Joint Surg Br.* 2006; 88: 489-495.

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About Rotator Cuff Disease

DISEASE PROGRESSION


Severe Tendinosis (Failed Conservative Treatment)


Partial-Thickness Tear


Full-Thickness Tear

- 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)

Significant Debate On Most Effective Treatment

- Transtendon: Difficult with bursal sided lesions, tissue quality can be an issue, poor results in high demand shoulders (throwers)
- Takedown and Repair: Morbidity of cuff repair, potential to heal, proper tensioning? Patient rehab is long, painful, disruptive
- ~44% have been reported to progress to full-thickness tears. (Keener *et al, JBJS* 2015)

- Significant incidence (25%) of re-tears and impaired function after repair (Flurin et.al.)

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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)

Curtis AS, Burbank KM, Tierney JJ, Scheller AD, Curran AR. The Insertional Footprint of the Rotator Cuff: An Anatomic Study. Arthroscopy 2006: 22 (6)603-609.

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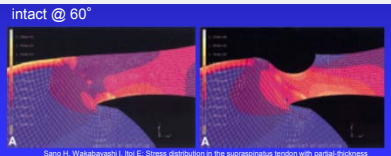
Why Don't Tears Heal?

10

- 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

intact @ 60˚



Sano H, Wakabayashi I, Itoi E: Stress distribution in the supraspinatus tendon with partial-thickness tears: an analysis using a two-dimensional, finite element model. *J Shoulder Elbow Surg* 15: 100-103, 2006

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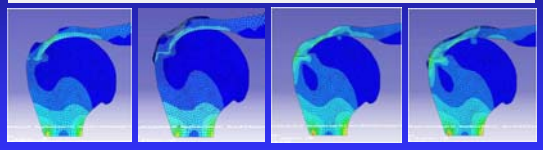
How Can We Create An Optimum Environment For Healing?

11

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

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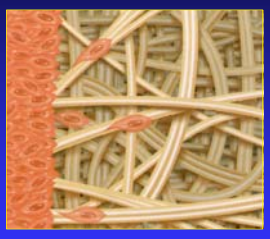
What are the attributes of an ideal scaffold for tissue regeneration?



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

The IDEAL Scaffold:

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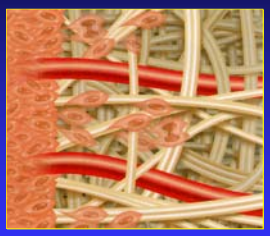
What are the attributes of an ideal scaffold for tissue regeneration?



- Provide a matrix scaffold to support the ingrowth of host tissues.
- Provide an inductive and conductive stimuli for cell and vessel migration.

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.

The IDEAL Scaffold:

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

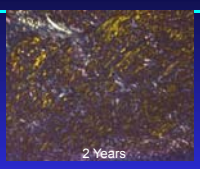
- Provide a matrix scaffold to support the ingrowth of host tissues.
- Provide an inductive and conductive stimuli for cell and vessel migration.
- Allow for normal tissue remodeling.
- Eventually be removed by the host.

The IDEAL Scaffold:

BioInductive Implant First To Clinically Demonstrate Tendon Tissue Induction

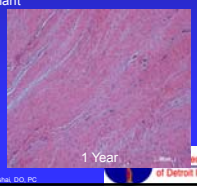
Dermal Collagen Patch

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



RM BioInductive Implant

BioInductive Implant reabsorbed, new connective tissue induced, thicker tendon



Target Patients Span Rotator Cuff Disease Spectrum

TEAR PROGRESSION

Severe Tendinosis (Failed Conservative Treatment)	High-Grade Partial-Thickness	Small Full-Thickness	Med-Large Full-Thickness	Massive Full-Thickness
In lieu/ conjunction with Acromioplasty	In lieu of standard repair	In conjunction with standard repair to enhance tendon healing		

- Patients at risk for tear progression, compromised healing potential
- Suboptimal tissue quality
- Demanding lifestyle (can't afford to take time from work, very active)
- Patient likely will not or can't comply with current repair rehab protocols
- Young athletes, including overhead athletes

- Patients at risk for re-tears, compromised healing potential
- Suboptimal tissue quality, thin tendons
- Patients with previously failed repair
- Patients where only limited footprint can be restored
- Want to avoid over-tensioning

Not intended to bridge a gap

The Rotation Medical Rotator Cuff System™

Scaffold + Novel Instrument Set

Five Years of R&D

100+ Cadaver Labs

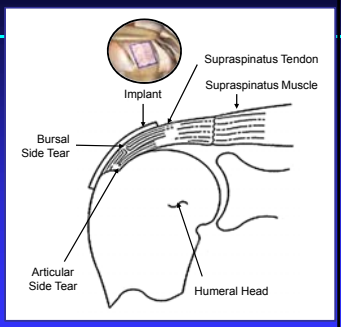
Third-Generation Instrumentation

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

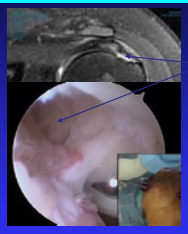
Location and Delivery System

Tendon Fixation System

Bone Fixation System

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

Partial-Thickness Tear – Pre-Op



Tendon Thickness = 2.9 mm

Healed Tear – 12 Months

Tendon Thickness = 4.0 mm

- 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

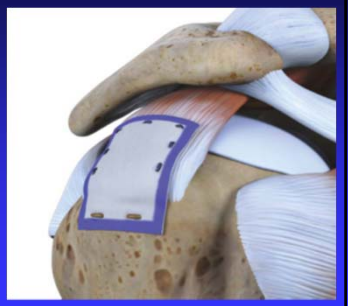
Conclusions

- 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

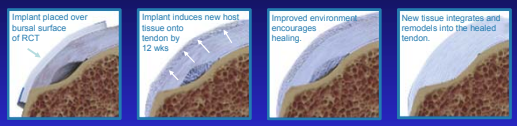
The Rotation Medical Difference: Addressing Tendon Biology

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

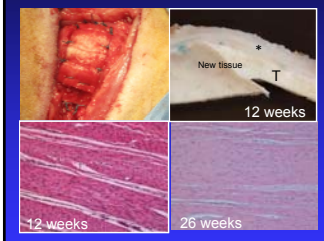


RM BioInductive Implant: How It Works



- 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

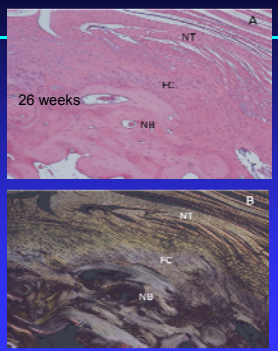
Pre-Clinical Animal Study



- 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

Van Kampen C, et al., Tissue-engineered augmentation of a rotator cuff tendon using a reconstituted collagen scaffold: A histological evaluation in sheep. *Muscles, Ligaments and Tendons Journal* 3:229-235, 2013.

Pre-Clinical Animal Study

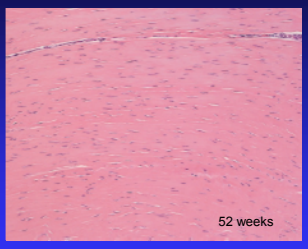


26 weeks

- 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

Van Kampen C, et al, Tissue-engineered augmentation of a rotator cuff tendon using a reconstituted collagen scaffold: A histological evaluation in sheep. *Muscles, Ligaments and Tendons Journal* 3:229-235, 2013.

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.

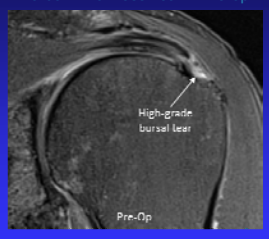
Van Kampen C, et al, Tissue-engineered augmentation of a rotator cuff tendon using a reconstituted collagen scaffold: A histological evaluation in sheep. *Muscles, Ligaments and Tendons Journal* 3:229-235, 2013.

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

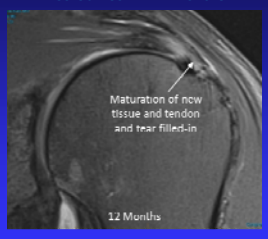
Demonstrated Healing: Bursal Partial-Thickness Tear (No Repair)

Partial-Thickness Tear – Pre-op



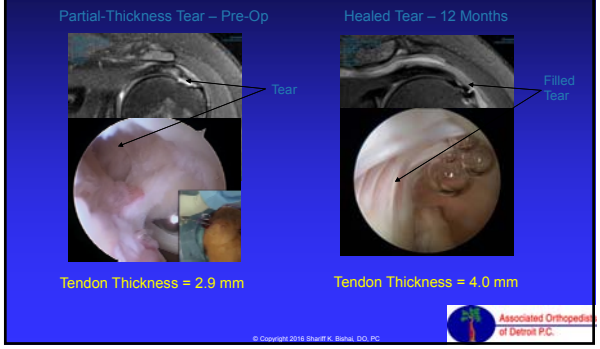
Tendon thickness = 3.3 mm

Healed Tear – 12 Months

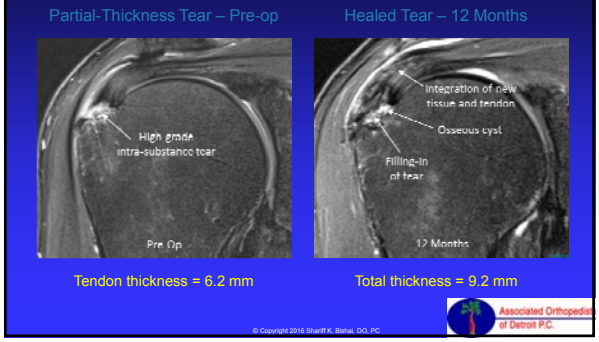


Total thickness = 5.4 mm

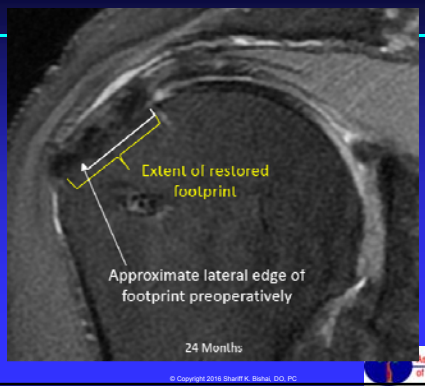
Demonstrated Healing: Articular Partial-Thickness Tear (No Repair)



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



Repairs Heal with Increased Thickness and Fully 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

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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 → ACTIVE ASSISTED → 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

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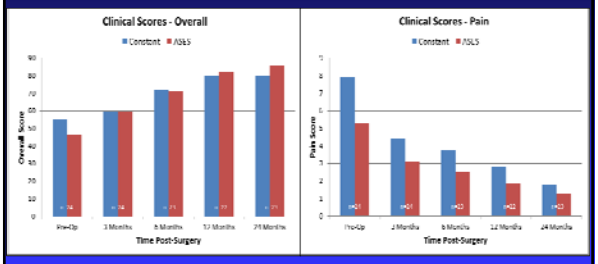
AU Clinical Scores Show Improvements in Partial -Thickness and Full-Thickness



The differences in all scores compared to pre-op (except Constant overall at 3 months) are statistically significant ($p < 0.05$)

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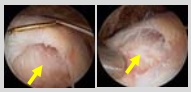
U.S. Clinical Study Summary

- 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

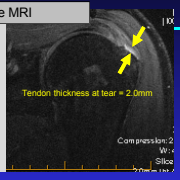


- Treatment
  - RM bioinductive implant placed on bursal side of tendon
  - No repair
- Recovery data
  - Returned to work in 7 days
  - Sling removed after 14 days
  - Satisfied with procedure and would recommend it to a friend.

** U.S. Clinical Study*

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

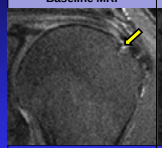
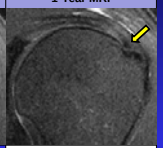


3 Month MRI

- 7.5 mm tendon thickness at location of tear; Thickness Δ = +5.5 mm
- 100% defect fill-in with new, amorphous, immature material

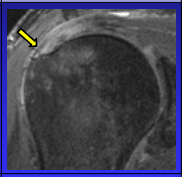
Demonstrated Healing: Articular Partial-Thickness Tear (No Repair)

- 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	3-Month MRI	1-Year MRI
		
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 (Δ +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 (Δ +1.5 mm)* *Mild bursitis*

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*

All MRI evaluations performed by Dr. Charles Ho.

AU IS Clinical Study

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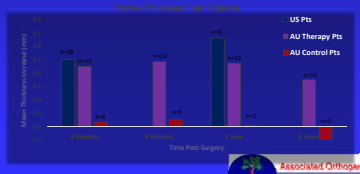
Clinical Results Compellingly Consistent

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**



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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 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
- **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.
- **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.

Full-Thickness Tears (Implant with Cuff Repair)

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

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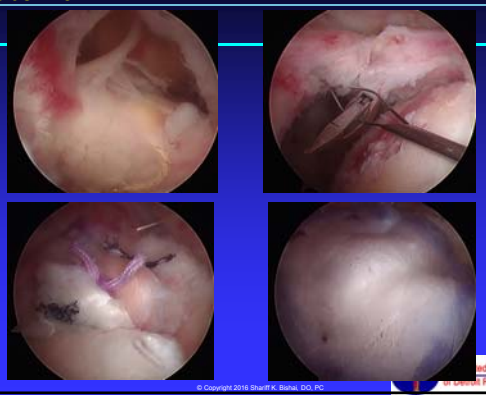
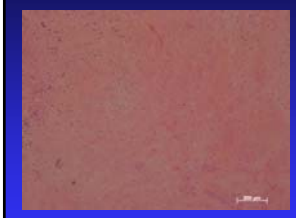
Patient Biopsy Case Study

- **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 shoudler 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

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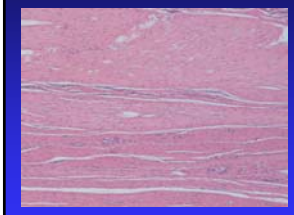
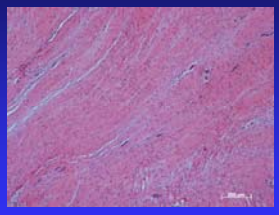
Comparison Between Sheep And Human – 6 Months Biopsy

Sheep



Human



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

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Thank You

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Surgical Technique

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Bio-Inductive ImplantArthroscopic 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

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