Healing of Partial-Thickness Rotator Cuff Lesions

Balancing Biomechanics and Biology

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Disclosures

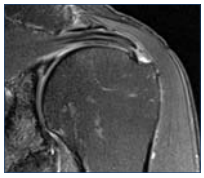
Consultant:

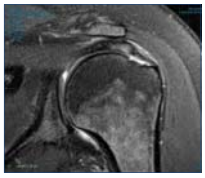
- Rotation Medical
- Applied Biologics

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: *PT-tears*

- **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

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40 patients with partial-thickness joint tears @ 2 year follow-up

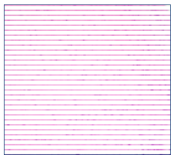
- **4 lesions decreased in size (healing?)**
- **4 lesions disappeared (healed?)**
- **32 lesions enlarged or progressed to full-thickness lesions**

Yamanaka and Matsumoto, CORR 1994

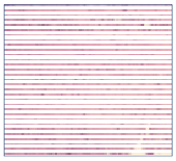
The Problem: *PT-tears*

- **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.**

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



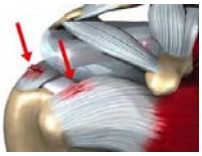
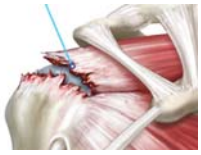
H & E x 100



H & E x 100

The Problem: *PT-tears*

- **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)

The Problem: *PT-tears*

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- **While the biologic potential for healing may exist, other factors may adversely affect this process.**

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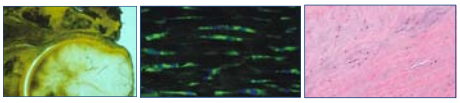
- While the biologic potential for healing may exist, other factors may adversely affect this process.
  - subacromial impingement
  - degenerative changes
  - age/systemic factors

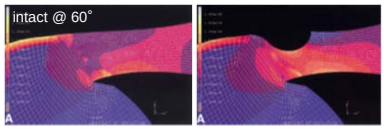


- compromised vasculature *Biberthaler et al 2003*
- increased enzymatic activity *Lo et al 2004; Robertsen et al 2012*
- apoptosis/decreased cellularity *Yuan et al 2002.*

The Problem: *PT-tears*

Why don't these tears heal??

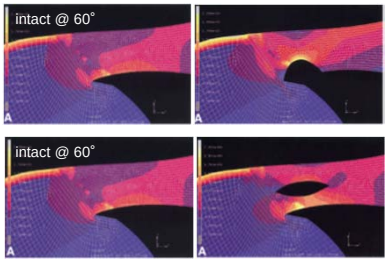
- While the biologic potential for healing may exist, other factors may adversely affect this process.
  - subacromial impingement
  - degenerative changes
  - age/systemic factors
  - increased local strain at the injury site



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: 100-105, 2006

The Problem: *PT-tears*

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



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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*.**

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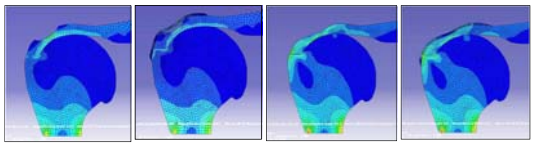


Bursal surface tear

47% reduction in peak strain

Articular surface tear

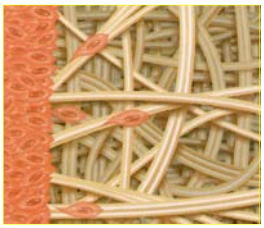
40% reduction in peak strain

Dr. Chen, Material and Structural Testing Core, Mayo Clinic, Rochester, MN

A new concept

Balancing Biology and Biomechanics

Create an IDEAL Scaffold:



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

A new concept

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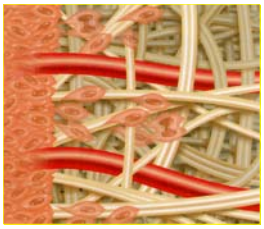

- Provide a matrix scaffold to support the ingrowth of host tissues.
- Provide an inductive and conductive stimuli for cell and vessel migration.

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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.

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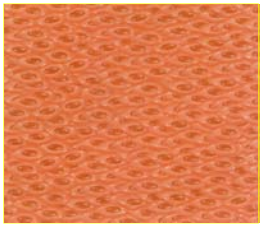
Create an IDEAL Scaffold:

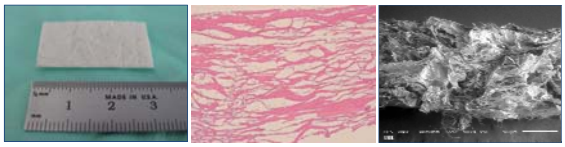


- **Provide a matrix scaffold to support the ingrowth of host tissues.**
- **Provide an inductive and conductive stimuli for cell and vessel migration.**
- **Allow for normal tissue remodeling.**
- **Eventually be removed by the host.**

A new concept

Balancing Biology and Biomechanics

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

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.

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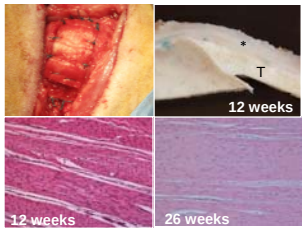
Pre-clinical Study:

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.*



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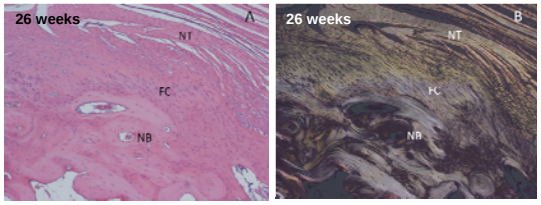
Pre-clinical Study:

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.



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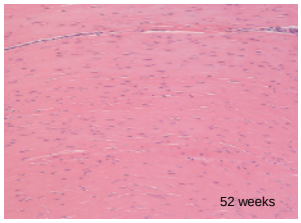
Pre-clinical Study:

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.



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Balancing Biology and Biomechanics

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

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.

First in Man Study — Study Design

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.*

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Hypotheses:

H_1: *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.*

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H_2: *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.*

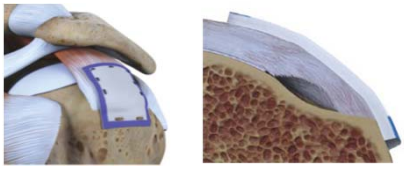
First in Man Study — Study Design

- **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**

Bokor DJ *et al:* Evidence of healing of partial-thickness rotator cuff tears following arthroscopic augmentation with a collagen implant: A 2 year MRI follow-up, *Muscle, Ligament,Tendon Journal 6:16-25,* 2016

First in Man Study — Study Design

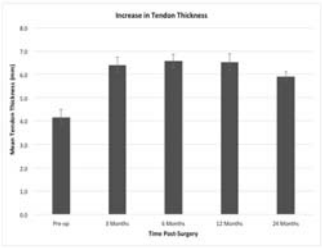
- **Arthroscopic placement of a collagen implant over bursal surface of the cuff tendon; affixed to tendon with PLLA staples and to bone with PEEK staples.**



- **Post-op care similar to ASD;**

Bokor DJ *et al:* Evidence of healing of partial-thickness rotator cuff tears following arthroscopic augmentation with a collagen implant: A 2 year MRI follow-up, *Muscle, Ligament,Tendon Journal 6:16-25,* 2016

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).

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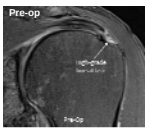
First in Man Study — Results: MRI

- There was no MRI evidence of tear enlargement in any of the defects over time.

First in Man Study — Results: MRI

- 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.

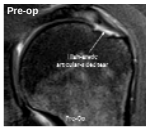
Bursal-sided tear



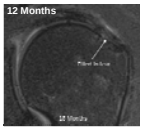
Tendon thickness = 3.3 mm

Total thickness = 5.4 mm

Articular-sided tear

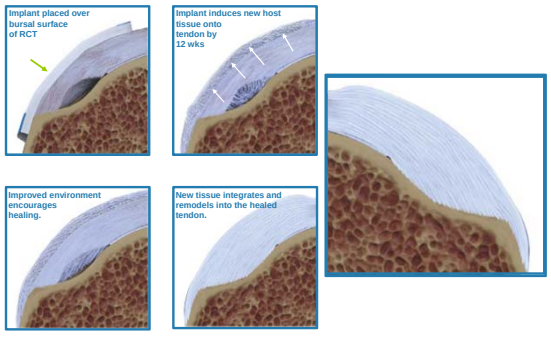


Tendon thickness = 2.9 mm



Total thickness = 4.8 mm

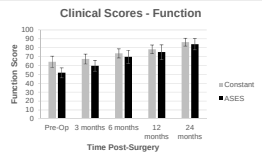
First in Man Study — Results: MRI

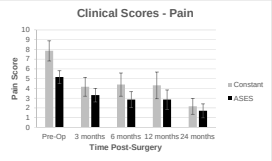


First in Man Study — Results: Clinical

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.**

First in Man Study — PT-Results: MRI

How do these results compare with published 'controls' ?

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*

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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

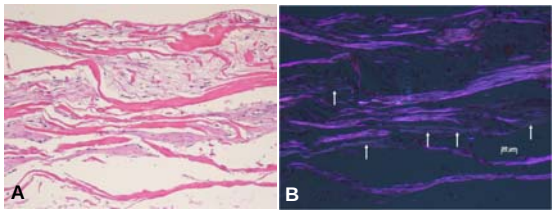
What type of tissue regeneration will occur in humans?

Patient # (sex/age)	Original Procedure	Time of Biopsy	Location of Biopsy	Reason for second look
1 46yo F	Primary FT-RCR massive	6 mos	Anterior aspect of repair	Staged hemi-arthroplasty
2 23 yo F	Primary FT-RCR medium	3 mos	Anterior aspect of repair	Patient fell and disrupted repair
3 50 yo F	Medium PT (B) tear	3 mos	Antero-lateral aspect of repair	Patient's arm was jerked while walking dog on leash
4 51 yo M	Revision FT-RCR medium	5 wks	Antero-lateral aspect of implant at bone attachment	Patient fell and disrupted repair
5 43 yo F	Primary FT-RCR large	3 mos	Postero-lateral aspect of repair	Pain; portion of tear not covered by implant was not healing
6 45 yo F	Coverted high-grade PT (B) to FT-RCR small	2 mos	Antero-lateral aspect of repair	Arthrofibrosis
7 55 yo M	Primary FT-RCR medium	2 mos	Multiple areas of the implant	Patient fell and disrupted repair

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, *(Arthroscopy* e-pub 2016*)*

Human Biopsy Study

Patient 4: 5 weeks

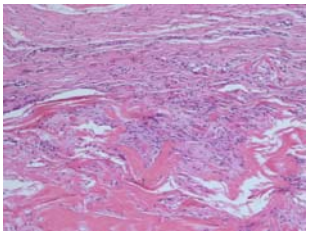


Light (A) and polarized light (B) photomicrographs of a highly porous collagen implant illustrating host cell ingrowth and early collagen production and alignment (arrows) at 5 weeks. H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, *(Arthroscopy* e-pub 2016*)*

Human Biopsy Study

Patient 2: 3 months



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

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Human Biopsy Study

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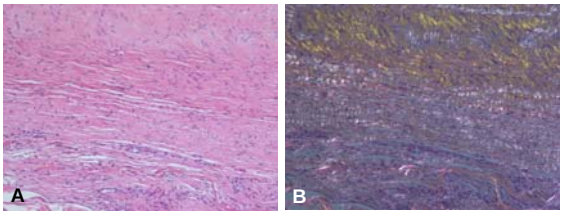
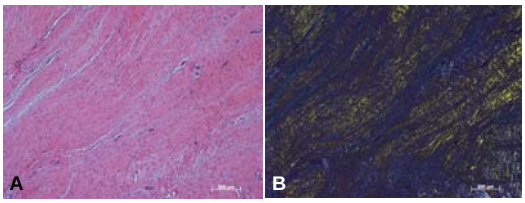


Light (A) and polarized light (B) photomicrographs of the newly regenerated host tissue overlying the implant at 3 months. There is evidence of maturation and a functional alignment of the dense, regularly oriented connective tissue. H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, *(Arthroscopy* e-pub 2016*)*

Human Biopsy Study

Patient 1: 6 months

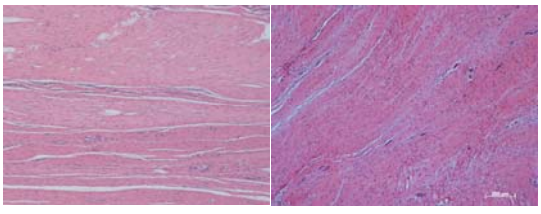


Light (A) and polarized light (B) photomicrographs of the newly regenerated host tissue by the implant at 6 months. This is dense, regularly-oriented connective tissue. There was no evidence of any remnants of the collagen implant at this time. H&E x100

Arnoczky SP, et al: Histologic evaluation of biopsy specimens obtained following rotator cuff augmentation with a highly-porous, collagen implant, *(Arthroscopy* e-pub 2016*)*

Human Biopsy Study

Comparison of implant-induced tissue in human and sheep at 6 months



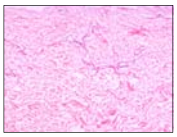
Sheep at 6 months **Human at 6 months**

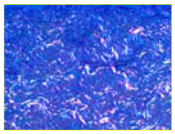
Implant completely resorbed, host regenerated tissue is dense, regularly-oriented connective tissue.

Human Biopsy Study — Dermal Allografts

Do currently available rotator cuff augmentations remodel in a similar manner?

dermal allografts





- freeze-dried dermal allograft
- distinct collagen pattern

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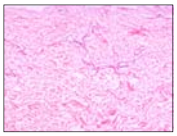

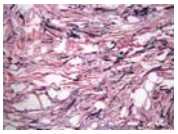

- freeze-dried dermal allograft
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- contains elastin fibers

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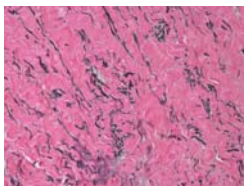

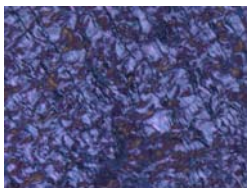

Light (A) and polarized light (B) photomicrographs demonstrating that at 8 months the implant still retains the histological character (collagen pattern and the presence of elastin fibers) of human dermis. Verhoeff-Van Gieson Stain X 100

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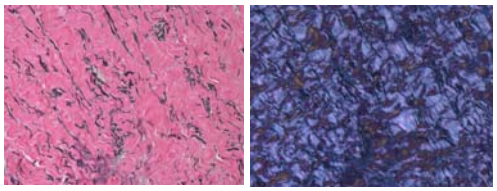

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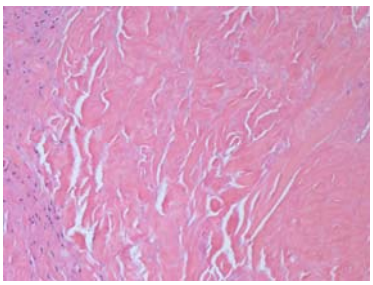

Photomicrographs of the dermal implant at 8 months showing large areas in the deeper aspects of the implant which are devoid of host cell infiltration. H&E X 100

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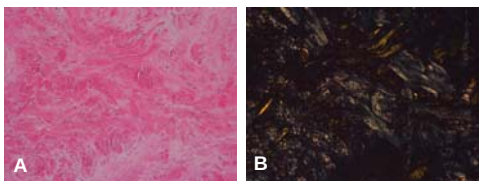

Light (A) and polarized-light (B) images of biopsy of dermal allograft rotator cuff augmentation at 8 years. While the allograft has been repopulated with host cells, the collagen arrangement seen in the polarized image is more similar to dermis than tendon.

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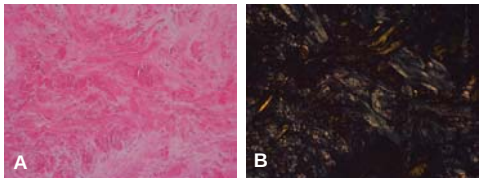

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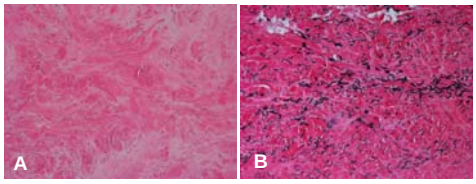

H&E (A) and Van Giesen(B) stained images of biopsy of dermal allograft rotator cuff augmentation at 8 years. The dense elastin staining suggests that the scaffold retains its dermal character and is not remodeled into tendon.

A new concept

Balancing Biology and Biomechanics

- 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.

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- 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.

A new concept

Balancing Biology and Biomechanics

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.

Bokor *DJ et al:* Preliminary investigation of a biological augmentation of rotator cuff tears using a collagen implant: 2 year MRI follow-up *Muscle, Ligament, Tendon Journal* 5:144-150, 2015

Bokor DJ *et al:* Evidence of healing of partial-thickness rotator cuff tears following arthroscopic augmentation with a collagen implant: A 2 year MRI follow-up, *Muscle, Ligament,Tendon Journal 6:16-25,* 2016

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: Sept 2016)*

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Healing of Partial-Thickness Rotator Cuff Lesions

Balancing Biomechanics and Biology