DEBATE: PATCH AUGMENTATION- SAVE IT FOR THE LAB

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JOHNS HOPKINS MEDICINE

Disclosure

- **The following relationships exits:**
  1. **Royalties and stock options-none**
  2. **Consulting income-none**
  3. **Research and education-none**
  4. **Other support**
     - No conflict related to this talk

Identifying the problem…

- Galatz LM, Ball CM, Teefey SA, Middleton WD, Yamaguchi K. The outcome and repair integrity of completely arthroscopically repaired large and massive rotator cuff tears. J Bone Joint Surg Am. 2004;86:219-224.
- 80% anatomic failure rate.

Historically used rotator cuff allografts

- Neviaser, J S; Neviaser, R J; Neviaser, T J
- The repair of chronic massive ruptures of the rotator cuff of the shoulder by use of a freeze-dried rotator cuff.

Journal of Bone & Joint Surgery - American Volume. 60(5):681-684, July 1978.

Imaging showed universal anatomic failure

- Moore et al. Allograft Reconstruction for Massive, Irreparable Rotator Cuff Tears. AJSM 2006;34(3):392-396.
- 15/15 failed on MRI.

Orthobiologic Rotator Cuff Augmentation

- PRP
- patches
- Bone Marrow aspirate and Stem Cell
- Grafting rotator cuff repair not new "Been there…done that"

FDA

- Closely regulates-most drugs/devices-require FDA approval
- Regulates many orthobiologics
  - Stem cells regulated
  - Others (PRP, marrow concentrating devices) slide in under 510K clearance
  - Xenografts/synthetics require 510K clearance. Still others used "off label" in interpostional use (rotator cuff patches)
  - Allografts regulated under section 361
- Use of orthobiologics in investigational products not approved by FDA limited to IRB approved and registered human clinical trials (HCT)

How are HCT/Ps regulated?

361 HCT/Ps:

- That meet the criteria set forth in 21 CFR 1271.10(a).
- Are regulated solely under PHS Act Section 361 and 21 CFR 1271.

351 HCT/Ps:

- That do not meet the criteria in 21 CFR 1271.10(a) are not regulated solely under Section 361.
- Are regulated as either a drug, device, and/or biological product under the FD&C Act, and/or Section 351 of the PHS Act, and applicable regulations, including 21 CFR Part 1271.
- Premarket review is required.

Off Label Use

- Allows use of previously cleared products for used not approved or cleared by the FDA
- 85% of BMP used off label
- 30% of medications used off label with little support (AAOS Now 2014)
- Concerns
  - No premarket review for adverse events
  - "can lead to unsupervised experimentation"
  - Serious problems developed with off label use of BMP
- To check status:
  - Biologics Products Establishments (http://www.fda.gov/-BloodVaccines/ucm121134.htm)

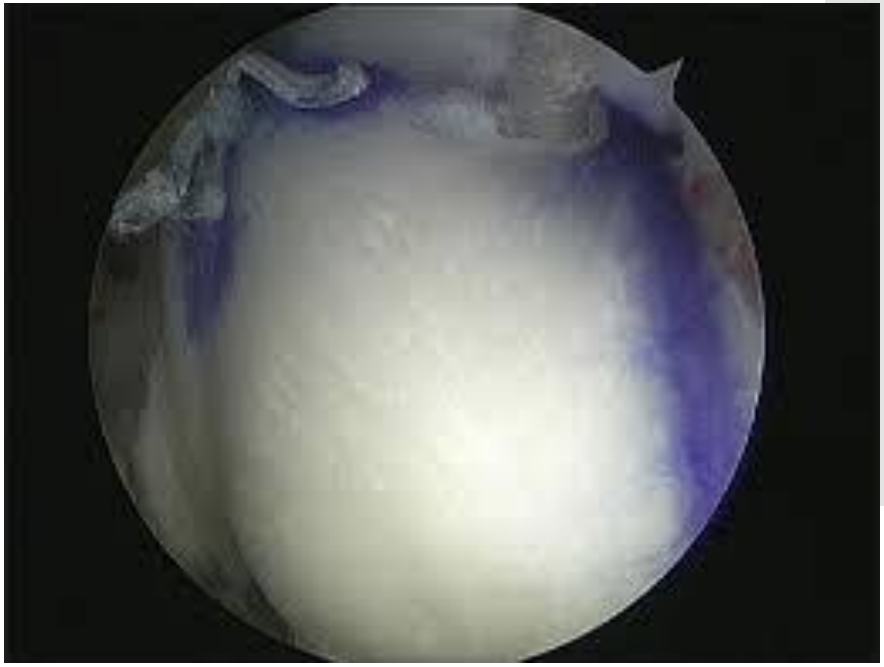
Medtronic Bone Graft Lawsuit Update

Medtronic Infuse Bone Graft

The ***Medtronic Infuse Bone Graft*** has been linked to life-threatening complications in patients who were given ***Medtronic off-label***. ***Medtronic bone graft complications*** include swelling of the airways, which can cause difficulty breathing, speaking and swallowing. Medtronic Infuse has also been linked to retrograde ejaculation which can lead to male sterility. A number of ***Medtronic lawsuits*** allege the manufacturer illegally promoted the Medtronic bone product for off-label uses.

Patches

- Variety of patches
  - Xenograft
  - Allograft
  - Synthetic
- Used to reinforce repair (FDA approved) and to bridge gaps (off label for xenografts /synthetics)



Restore patch

- Acellular porcine submucosa
- Approved for reinforcement
- Widespread off label use
- Ianotti et al. JBJS 2006 PRCT halted because of inferior results w/ Restore
- Walton JBJS 2007 "Restore implant not recommended for RCR"
- Porcine DNA recovered post product release from implants (Derwin et al. JBJS 2006)

RM bioinductive implant

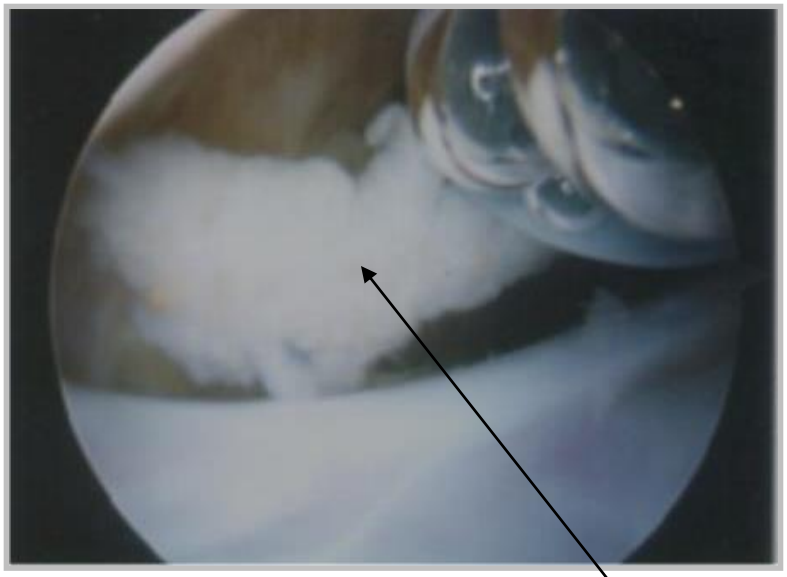
- Schlegel T et al. Radiologic and clinical evaluation of a bioabsorbable collagen implant to treat partial-thickness tears: a prospective multicenter study. JSES 2018
  - Bovine achilles tendon
  - For reinforcement of partial tears
  - Innovative staple attachment
  - 61% increase in tendon thickness
  - No adverse responses

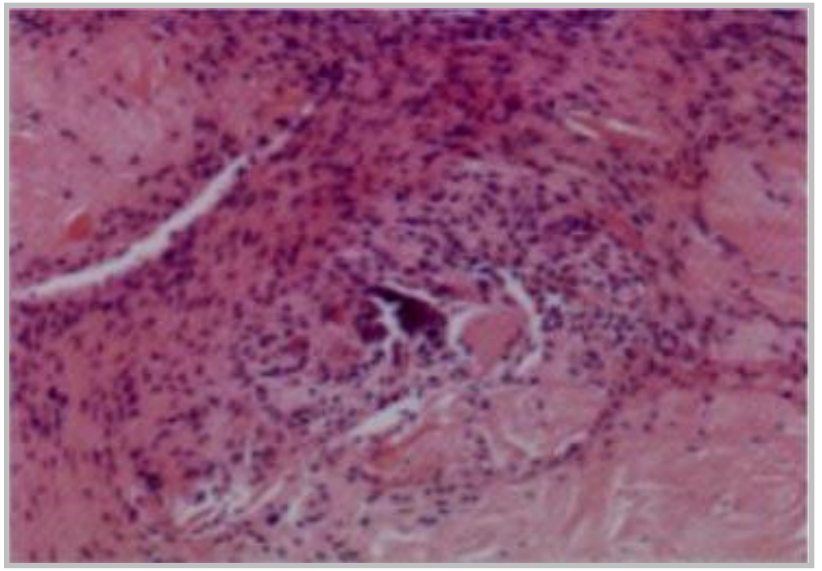
Cai et al.

- Center for Stem Cell and Tissue Engineering, Zhejiang University
- prospective, randomized controlled study of "3D collagen augmentation"
- Source not described, but prior publications note porcine origin
- retear rate was 34.0% in the control group and 13.7% in the study group
- No difference in outcome scores

My experience- Xenografts:

- Removed a lot of fragmented Restore patches
- Never put one in
- Xenograft patches expensive and time consuming to put in
- European experience: "why hook a dead muscle up to the bone?"
- Clearly more data needed





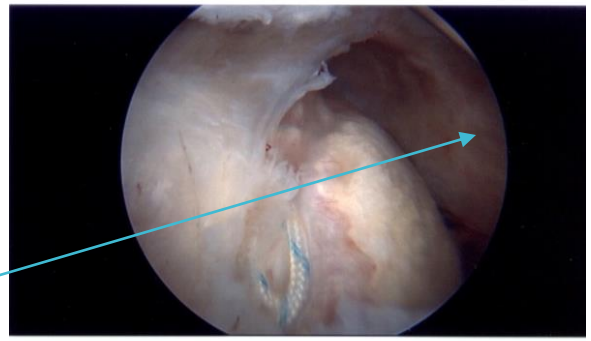
residual patch fragment

Allograft, synthetic better?

- Wong, Snyder JSES 2010 dermal allograft to bridge gaps
- Barber, et al. J Arth 2012 good results with allograft reinforcement ONLY HIGH-LEVEL STUDY
- Lenart et al. JSES 2015 poly-L-lactide synthetic polymer
- Mori et al. JSES facia lata autologous graft better than PRCR- level 3 study
- Millet, et al. JSES 2015 "additional studies are needed"
- These devices are EXPENSIVE and difficult to implant arthroscopically. Cost can make ASC use prohibitive

Dermal allograft patch

- Post op graft
- Healed to tuberosity
- Pulled off cuff remnant
- This side scheduled for reverse
- Contralateral side debrided, unrepairable tear-full ROM, no pain



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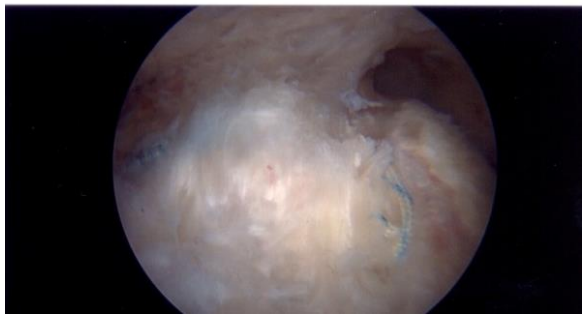


Karuppaiah and Sinha Scaffolds in the management of massive rotator cuff tears: current concepts and literature review EFORT Open Rev

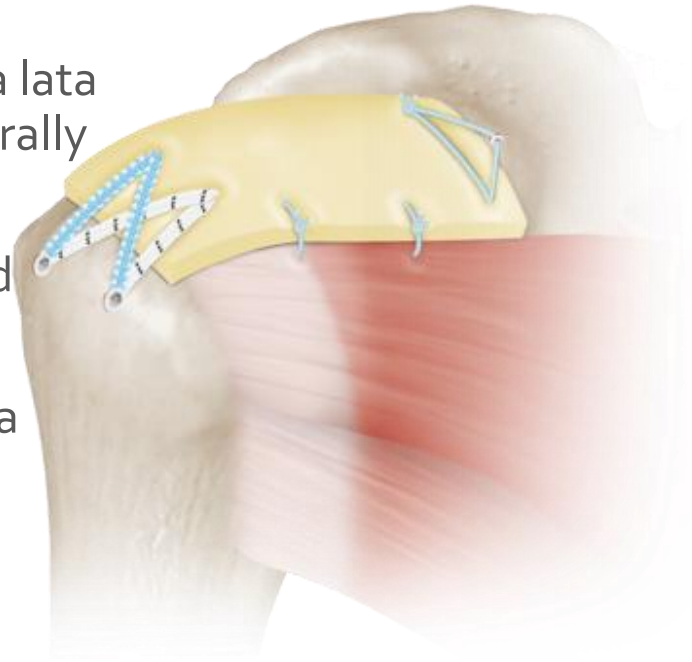
- Prospective randomized controlled trials from independent centres are needed beforewidespread use can be recommended.

Karuppaiah and Sinha
Scaffolds in the management of massive rotator cuff tears: current concepts and literature review
EFORT Open Rev 2019

- "Xenografts have higher retear rates and have shown less improvement in patient-reported outcomes, strength and range of motion than synthetic grafts and allografts"
- "Prospective randomized controlled trials from independent centres are needed before widespread use can be recommended"

Superior Capsular Reconstruction (SCR)

- Reported 90% success rate Mihata with autogenous fascia lata graft-85% structurally intact
- Used in US limited dermal allograft
- No long-term data



Early publications successful

- Burkhart et al. Arthroscopy Techniques, Vol 5, No 6 (December), 2016: pp e1407-e1418 describes technique
- Denard, Burkhart et al. Preliminary Results of Arthroscopic Superior Capsule Reconstruction with Dermal Allograft (J Arth 2017)
  - Forty-six (74.6%) cases were considered a success. Eleven patients (18.6%) underwent a revision procedure including 7 reverse shoulder arthroplasties.
  - 45% (9 of 20) of the grafts demonstrated complete healing

Others not so good

- AlRamadan et al. Presented AANA 2017
  - Failure rate of SCR by MRI study was 30.7% at five months
- Woodmass et al. JSES 2019
  - 34 patients at 6 centers
  - clinical failure in 65% (n= 22/34) at two years
  - Only 24% two-year anatomic success rate
  - 8/34 reoperated
  - Although described as a learning curve issue, no significant difference between first 10 and subsequent results

Others not so good

- Campbell et al. Clinical Imaging 2020
  - No significant increase in motion or strength
  - 50% one-year anatomic failure
  - Only 0.2mm change in AH distance
  - "The chronicity of this procedure's action to depress the humeral head and thereby affect AHI remains in question"
  - 3 mm graft

Host response not entirely benign

- Rashid et al. Rotator cuff repair with biological graft augmentation causes adverse tissue outcomes Acta Orthop 2020
- "there are no high-quality, low risk of bias, clinical studies evaluating their clinical efficacy"
- "Histological and immunohistochemical analysis of native rotator cuff tendon tissue after patch augmentation raises some concerns about a lack of benefit and potential for harm from these grafts."

Wide array of editorials

- Echinger Arth 2019 "Treating Irreparable Rotator Cuff Tears With a Patch or Balloon: Is It All a Bunch of Hot Air?"
- Favorito Arth 2019 "SCR: Substantial Confusion Remains"
- Savoie Arth 2019 "Shoulder Superior Capsular Reconstruction: When a Systematic Review of a Procedure Can Be Misleading" SCR "was applied with great enthusiasm, which has now (appropriately) tapered off to find its correct spot."

Actual role of superior capsule

- Hu et al. J Arth 2018
- "The anatomic SC has a negligible role in preventing the superior translation of the humeral head."
- "SC reconstruction is not a simple anatomic reconstruction, and its promising clinical outcome may be due to tensional fixation technique and choice of graft."

SCR graft thickness?

- Savoie Arth 2019 "apples to oranges" to compare 3mm to 8mm graft results
- Time will tell…

Any better than a balloon?

- Moon AS et al. Subacromial spacer implantation for the treatment of massive irreparable rotator cuff tears: A systematic review. J Arth 2019;35:607-614.
- Similar biomechanically balloon far cheaper

AAOS CPG lessons

- Very little high-quality level one data for most of what the first world does
- Doesn't mean it doesn't work
- "clinical equipoise" popularized by Pedowitz makes level one studies difficult
- Absence of level one evidence does not make orthobiologics unethical

RC CPG- Xenografts

- "Limited evidence does not support the use of xenografts to augment the repair of large and massive rotator cuff tears"
- One high quality study (Bryant, D. 2016), one moderate quality study (Ianotti, J. 2006), and three low quality studies (Flury, M. 2018 , Walton, J. 2007, Ciampi, P. 2015) addressed xenografts as an ancillary surgical technique.

RC CPG-Allografts

- "Limited evidence supports the use of dermal allografts to augment the repair of large and massive rotator cuff tears to improve patient reported outcomes."
- "There was one moderate strength study (Barber et al. 2016) and one low strength studies (Gilot 1545 et al. 2015)."

RC CPG-Patches

- "The risk and expense of orthobiologics in rotator cuff surgery remains difficult to fully assess, even though multiple high-quality studies are currently available. The use of either allograft or xenograft patches to either augment rotator cuff repair or as a superior capsular reconstruction requires additional high quality studies to prove efficacy."

Good enough summary for me!