UNIVERSITY of VIRGINIA
ORTHOPAEDIC SURGERY

Volumetric Muscle Loss

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Disclosures

- Research Supported by KeraNetics and through AFIRM (Armed Forces Institute of Regenerative Medicine)

The Problem

Volumetric Muscle Loss

- The Problem
  - Severe musculoskeletal injuries often associated with loss of muscle
  - Surrounding muscle can hypertrophy but does not fully compensate
  - If complete loss of muscle unit- limited options to recover function

Volumetric Muscle Loss

- The Problem
  - Reconstruction of bony defects (meta-diaphyseal) can be routinely accomplished.
  - Soft tissue coverage reliably closes wounds
  - Continued muscular functional deficits
    - Long term- atrophy/ joint contractures
  - Cosmetic defects

Limb Salvage

www.Stripes.com

Volumetric Muscle Loss

- **Volumetric muscle loss leads to permanent disability following extremity trauma**
- Corona BT1, Rivera JC, Owens JG, Wenke JC, Rathbone CR.
- J Rehabil Res Dev. 2015;52(7):785-92

- Evaluated medically retired servicemembers from recent conflicts
  - 65% retired for orthopaedic reasons had muscle injury
  - 92% of orthopaedic conditions involved muscle injury in those retired for non-orthopaedic reasons

Volumetric Muscle Loss

- Current treatment options
  - Bracing
    - AFO
    - IDEO

AFO

IDEO

Source: Curr Orthop Pract © 2013 Lippincott Williams

From Bobwoodruffinfoundation.org website

Volumetric Muscle Loss

- Physical Therapy
  - Compensatory gait training
  - Activity modification
  - Strengthening (limited efficacy in large VML)

Volumetric Muscle Loss

- Surgical options
  - Tendon transfers
    - Need nearby functional tendon (which can be "borrowed"
    - Lose 1 muscle grade of power
    - Often out of phase
    - Limited in size/scope

- Maybe the lost muscle can be regrown?

- Functional and Cellular Analysis of Engineered Skeletal Muscle Units following 28 days In Vivo Keith W. VanDusen, M.S., Brian C. Syverud, M.S., Jonah D. Lee, Ph.D., Lisa M. Larkin, Ph.D..
- University of Michigan, Ann Arbor, MI, USA.

- ORS 2015-Described nerve/muscle unit grown from cells.
- Very small scale currently

Volumetric Muscle Loss

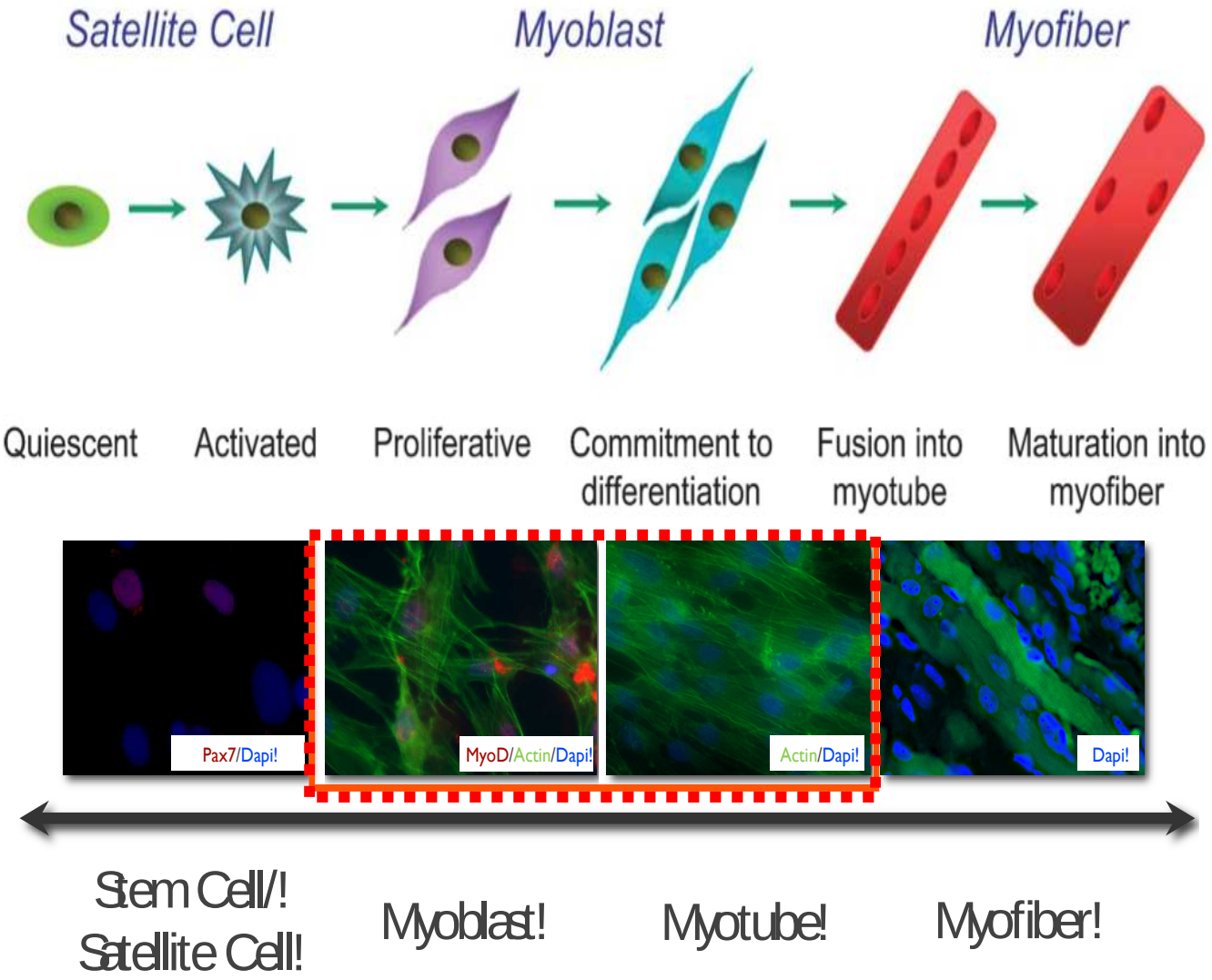
- Is there a way to replace lost muscle with scaffold to allow regeneration of new/functional muscle?

- Numerous Studies
  - Extracellular matrix (ECM) as scaffold
    - Porcine mucosa
    - Porcine Bladder
    - De-cellularized muscle
    - Other variations

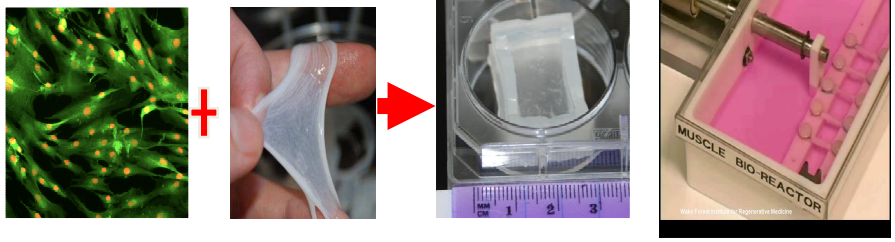
      Variable results- most show some improvement and increased muscle cells

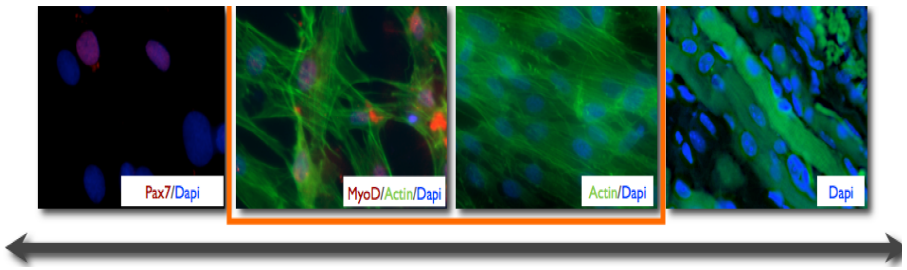
      Goal is decreased scarring and environment conducive to new growth

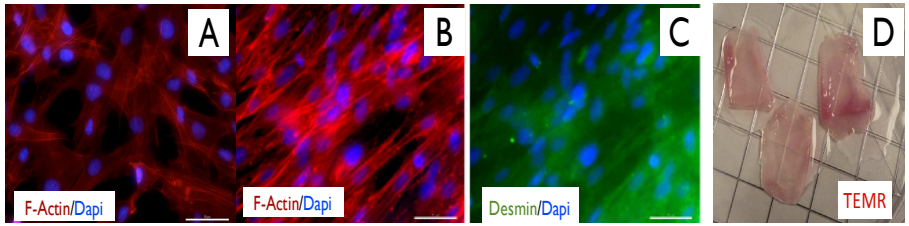
Tissue Engineered Muscle Repair (TEMR)



TEMR Creation Process







Volumetric Muscle Loss

- Is there a way to replace lost muscle with scaffold to allow regeneration of new/functional muscle?

- **KeraNetics** is an advanced biomaterials company focused on creating keratin-based products for therapeutic and regenerative medical applications.(from their website)
- - Developed Keratin Gel scaffold which can serve as void filler and potentially as carrier for molecules to assist with muscle growth

Volumetric Muscle Loss

- Keratin Gel

- Basic Science work ongoing
- Animal study (rat TA) ongoing
- Clinical trial next

Treatment variety is necessary for diversity of Sheet-Like VML injuries

Cell delivery capable biomaterials

Tunable degradation rates

Drug delivery capable

Sheet

Solid geometry

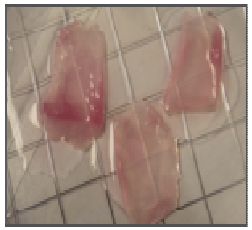
Space filling

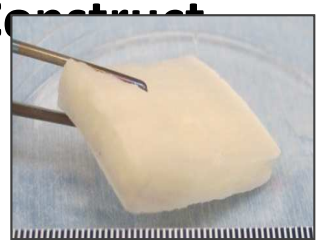
TEMR

Silk Sponge Construct

Fibrin

Keratin Hydrogel





Volumetric Muscle Loss

- Previous studies
  - Evaluated strength- Biodex
  - Muscle Mass- CT/MRI
  - Functional scores
  - Pain scores

Volumetric Muscle Loss

- Keratin Gel
  - 1st step- 5 healthy volunteers
    - Evaluate processes
    - Set baselines
    - Establish testing parameters
      - Biodex
      - Treadmill
      - Plyometric

MRI/CT

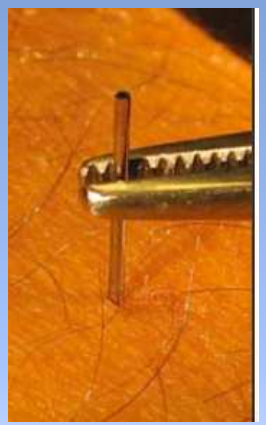
US

Volumetric Muscle Loss

Minimally invasive high-speed imaging of sarcomere contractile dynamics in mice and humans

Michael E. Llewellyn[1], Robert P. J. Barretto[1], Scott L. Delp[1] & Mark J. Schnitzer[1]

- Zebrascope
  - Allows visualization of sarcomeres
  - Previous studies unable to quantify contribution of scaffold to overall function
  - Will be able to sample any area of interest
  - Similar to needle biopsy of soft tissue



Volumetric Muscle Loss

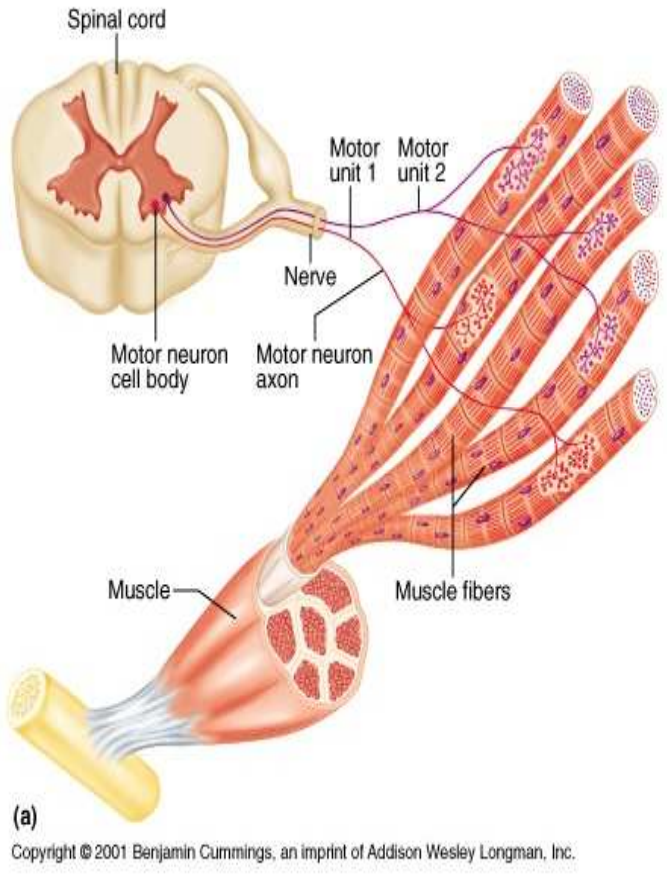
Limited clinical data- most studies in animals

- Big issue in Wounded Warriors
  - ? VA involvement
- Clinical trial
  - Utilized data from UVA studies on muscle to form materials/methods
  - Plan for 5 patient trial
  - 25-30 cc VML in anterior tibialis after injury
  - Fill defect with Keratin gel
    - Plain gel now to test safety
    - Next trial with additives

What about Polytrauma?

Polytrauma

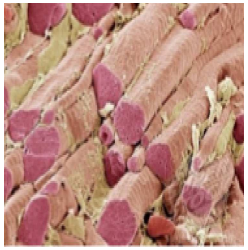
- **Tissue Damage**
  - functional nerve signal, no contraction
- **Nerve damage**
  - Perceived tissue damage exaggerated
  - Important model consideration
- **Combination**

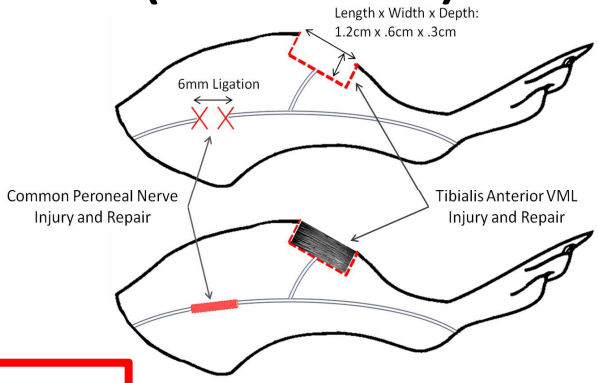


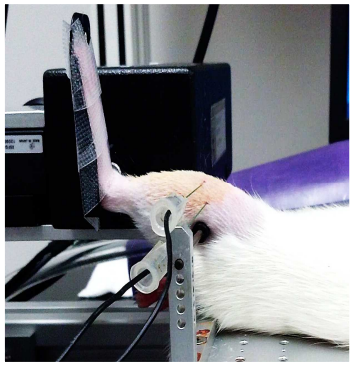
http://www.sivabio.50webs.com/mus.htm

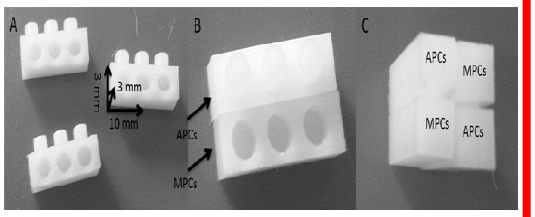
Muscle-Nerve Tissue Integration System (MuNTIS)

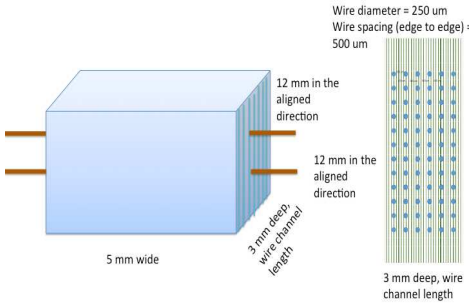
Native Muscle

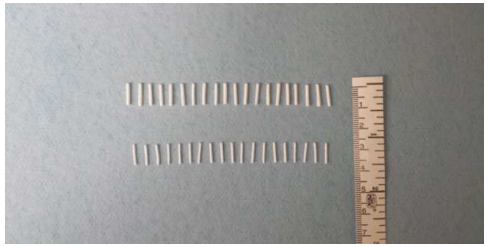


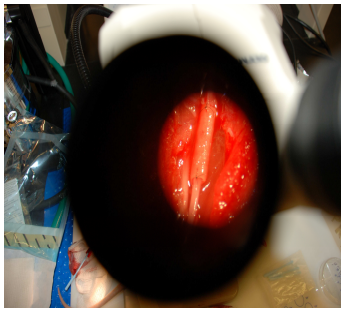


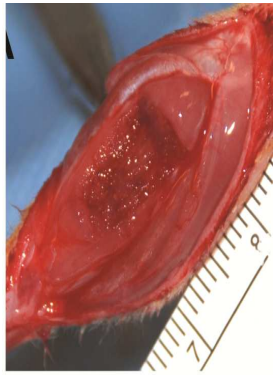












Volumetric Muscle Loss

Summary

-Identified as significant problem in military and civilian population

-Several areas of ongoing research but no clear path forward yet

UVA with several trials in works to look at Keratin Gel efficacy as a tool for regeneration of skeletal muscle cells.