



The Intersection of Regenerative Medicine and Women's Health: A Workshop



SESSION IV: Non-Cellular Innovations in Women's Health

Temporomandibular Disorders, the TMJ Disc, and Acellular Therapies

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No disclosures

The Temporomandibular Joint



- Mandible (jaw), temporal bone, TMJ disc
- Synovial Joint → Complex joint movements
 - Rotation
 - Translation
- Important for eating, talking, facial expression
 - Disruption of healthy movement has debilitating impacts on health and mental wellbeing



Temporomandibular Disorders

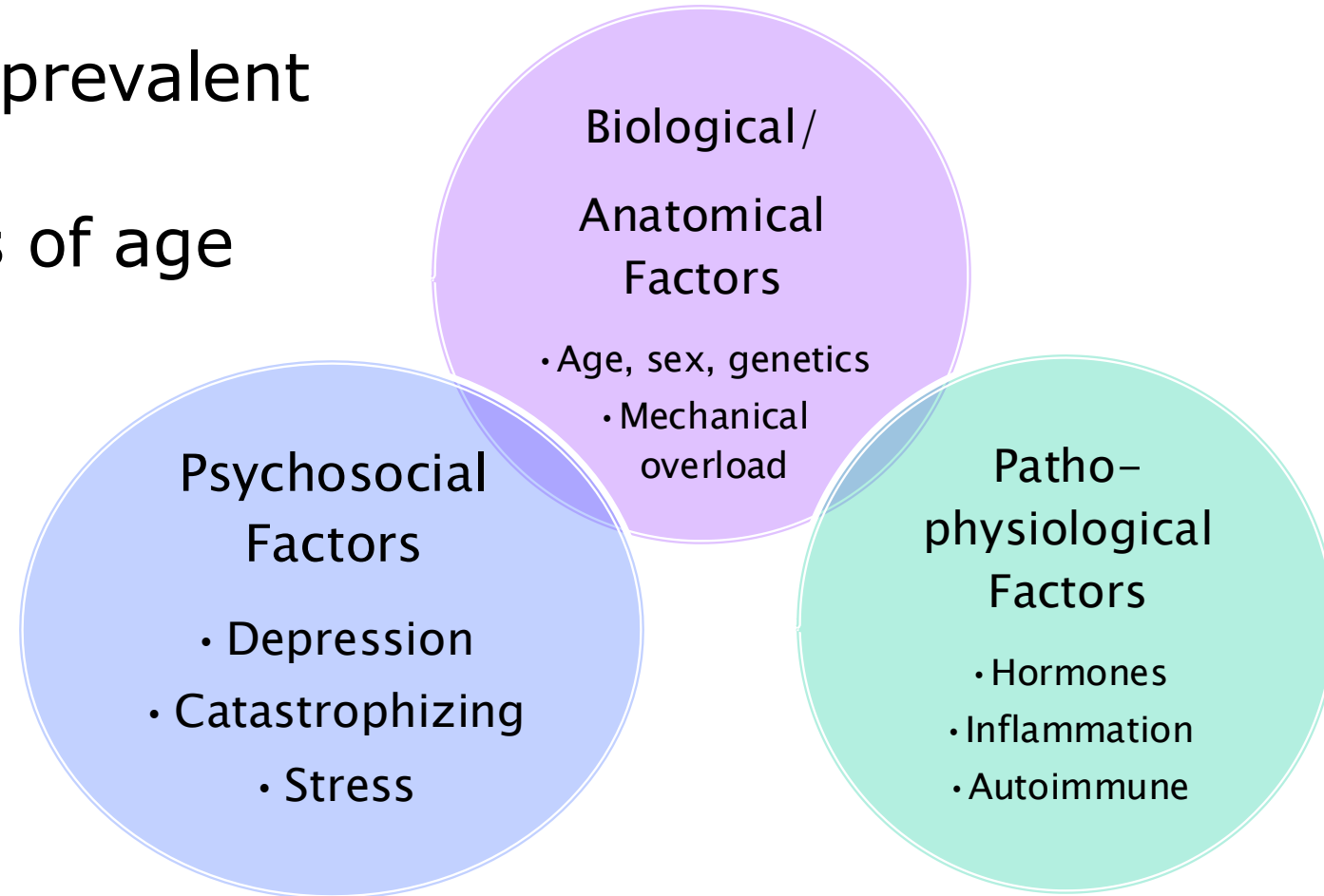
- ▶ Umbrella term for at least 30 different conditions
- ▶ 3–4% of population seek treatment
- ▶ Variety of symptoms
 - Acute and Chronic Pain
 - Loss of jaw motion
 - Joint noises: clicking/popping, grinding

Bio-psychosocial model

- Biological
 - Sex: TMDs are 2-3x more prevalent in **women**
 - Age: Between 20-50 years of age

Comorbidities

- Pathophysiological
 - Chronic low back pain
 - Fibromyalgia
 - Irritable bowel syndrome
 - Endometriosis
 - Headache conditions



Bio-psychosocial model

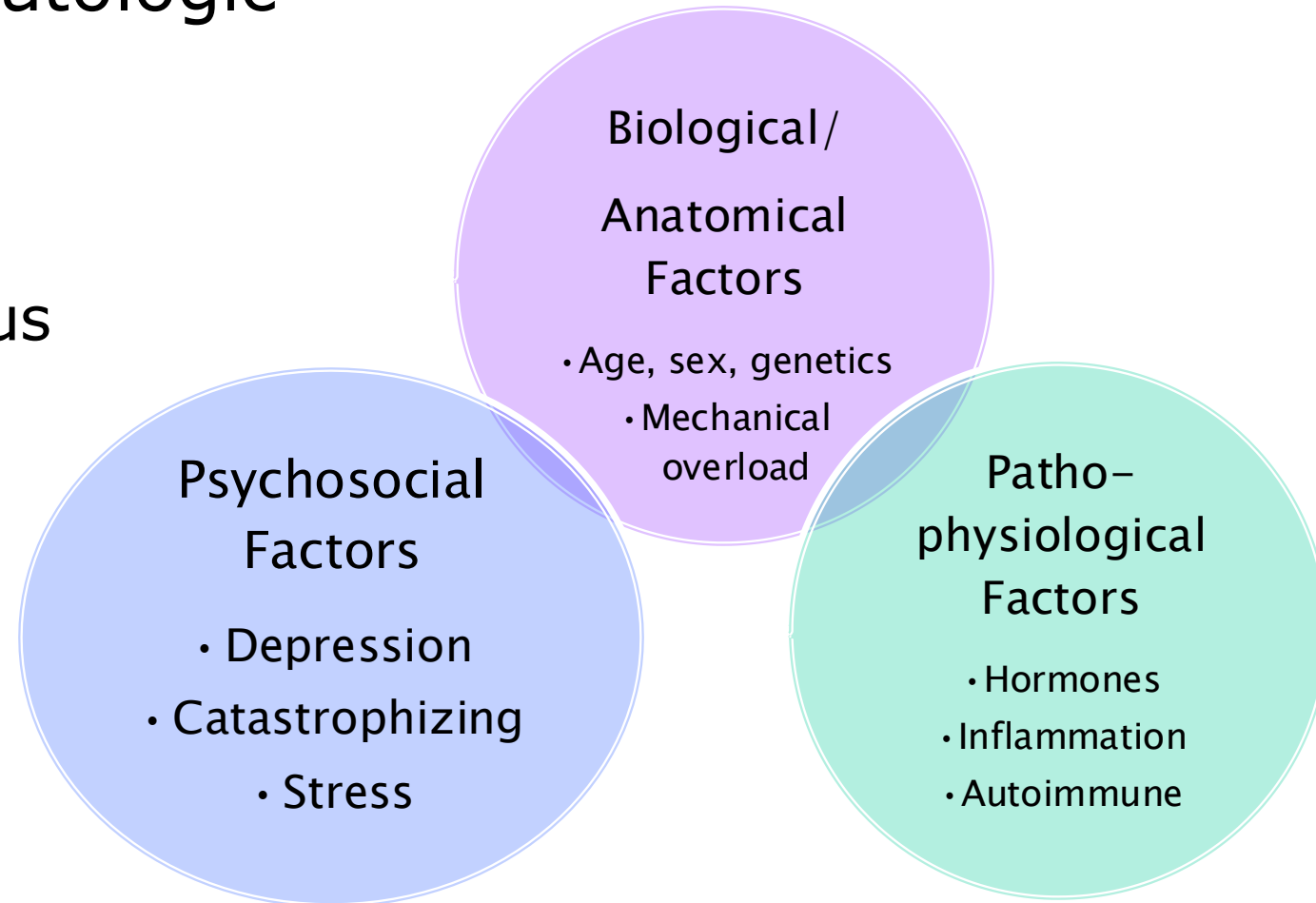
- Pathophysiological-Rheumatologic diseases

- Rheumatoid arthritis
- Ankylosing spondylitis
- Systemic lupus erythematosus
- Sjogren's syndrome

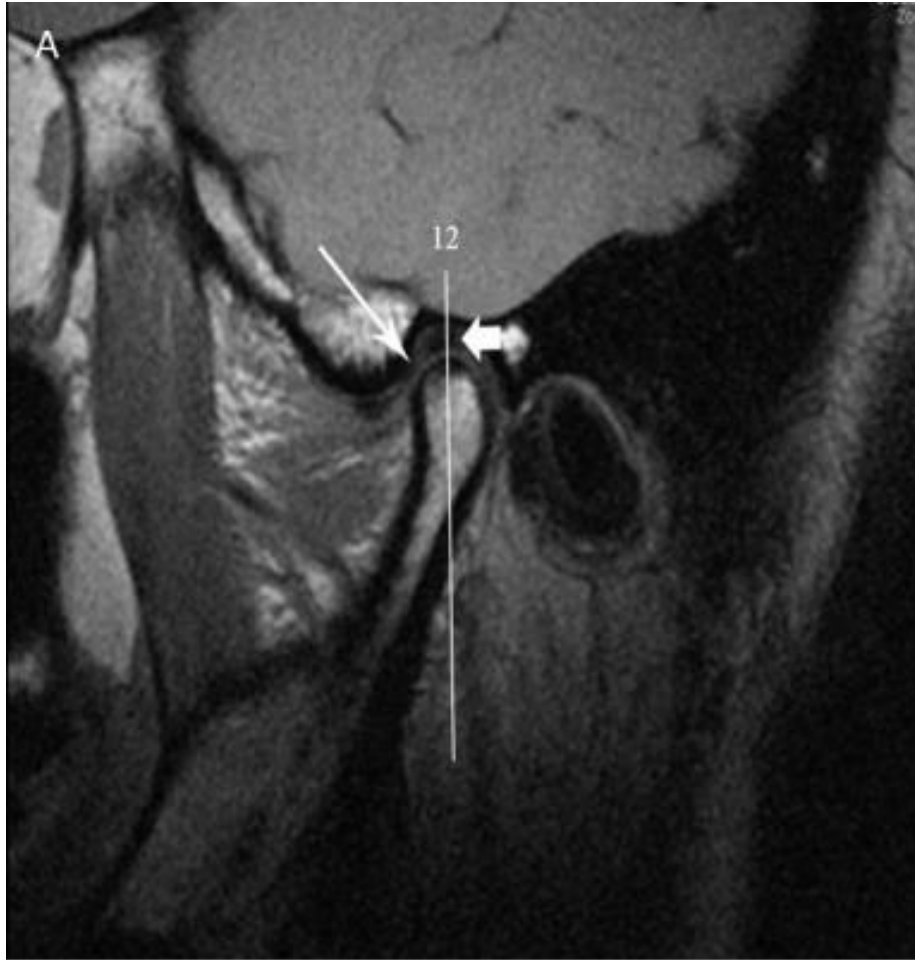
- Psychosocial

- Depression
- Stress
- Catastrophizing

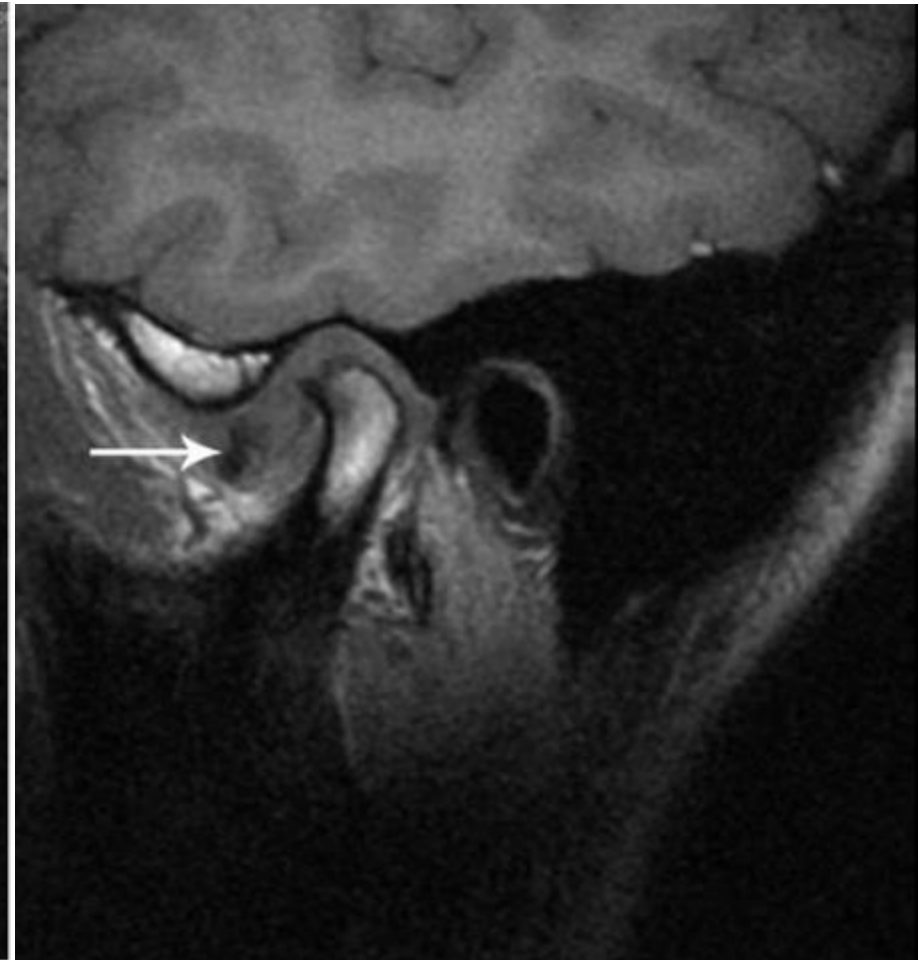
- Social and economic status



MRI of Normal joint

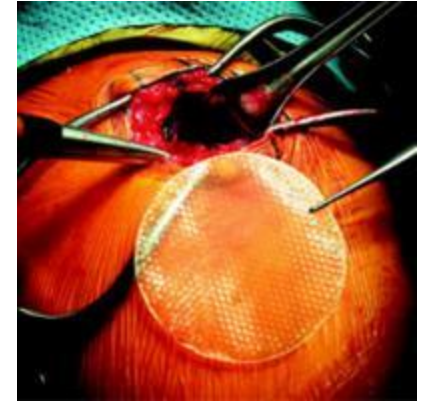


MRI of disc displacement



Extracellular Matrix Scaffolds

- ECM scaffolds have successfully used in many orthopaedic TE applications Badylak, 2004
 - Rotator cuff, Achilles tendon, biceps tendon, triceps tendon
- Contains growth factors/cytokines
- Promotes constructive tissue remodeling
- Acellular therapy with approved FDA devices



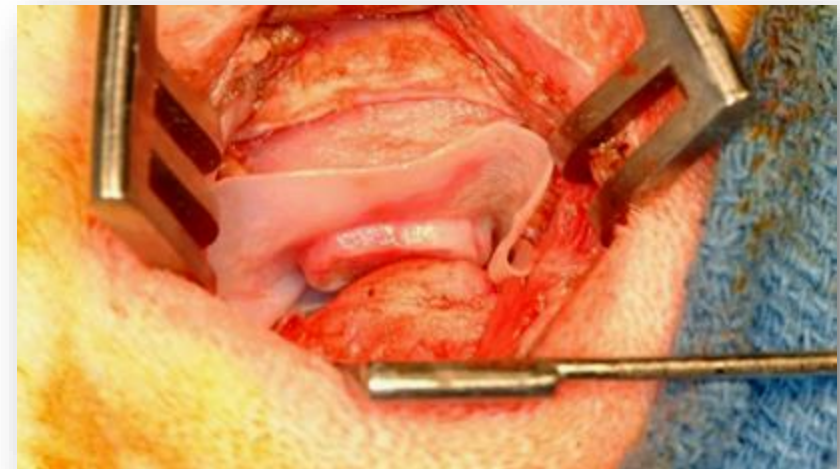
Restore® Orthobiologic
Soft Tissue Implant



ECM Sheet
Badylak et al ,2005

TMJ Disc Regeneration–Study1 Pilot study

- ▶ Bill Chung (OMS), Bryan Brown, and Steve Badylak (Surgery) developed TMJ disc implant
 - Extracellular matrix scaffolds
 - Acellular
- ▶ Very positive histological results (n=1)
 - 6 months after implantation
 - Discectomy model (canine)



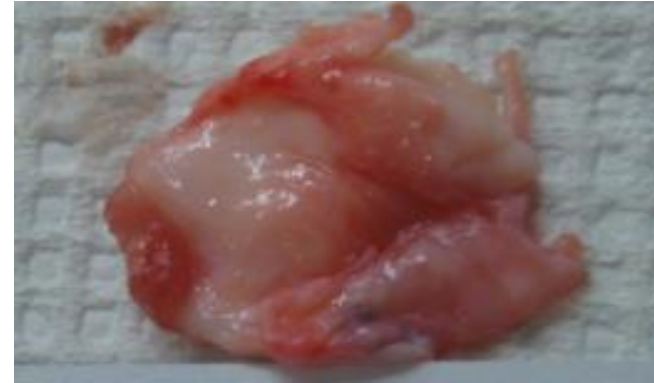
(PMID: 22365981)

Study 2– Long-term Study

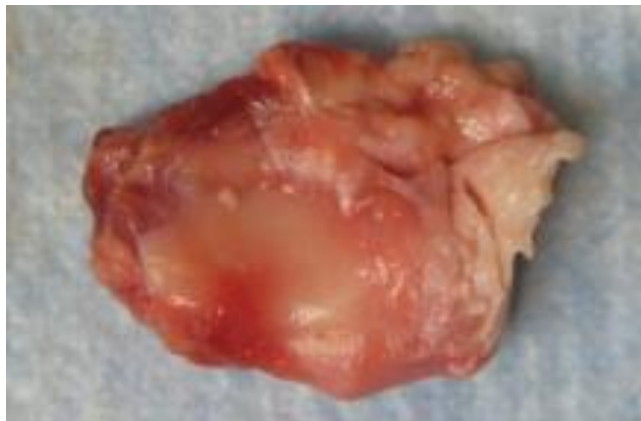
(n=6)



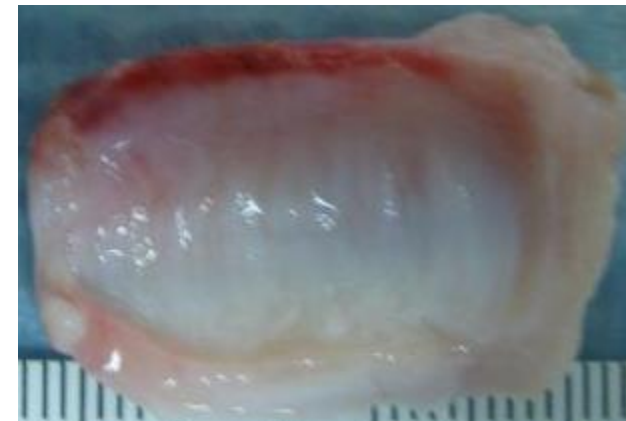
Remodeled ECM (1 month)



Remodeled ECM (3 month)



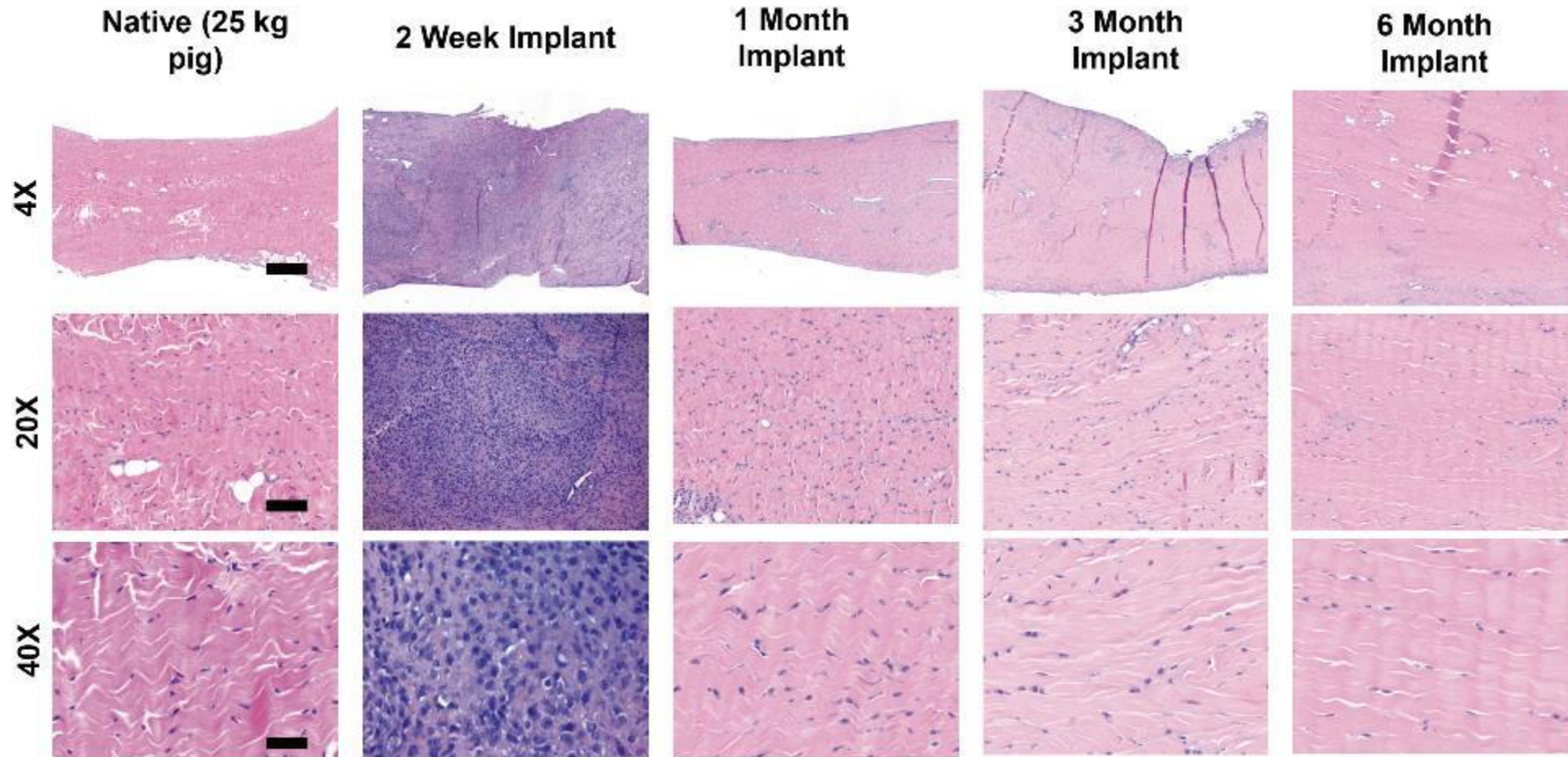
Remodeled ECM (6 month)



Native Porcine (~1 year)

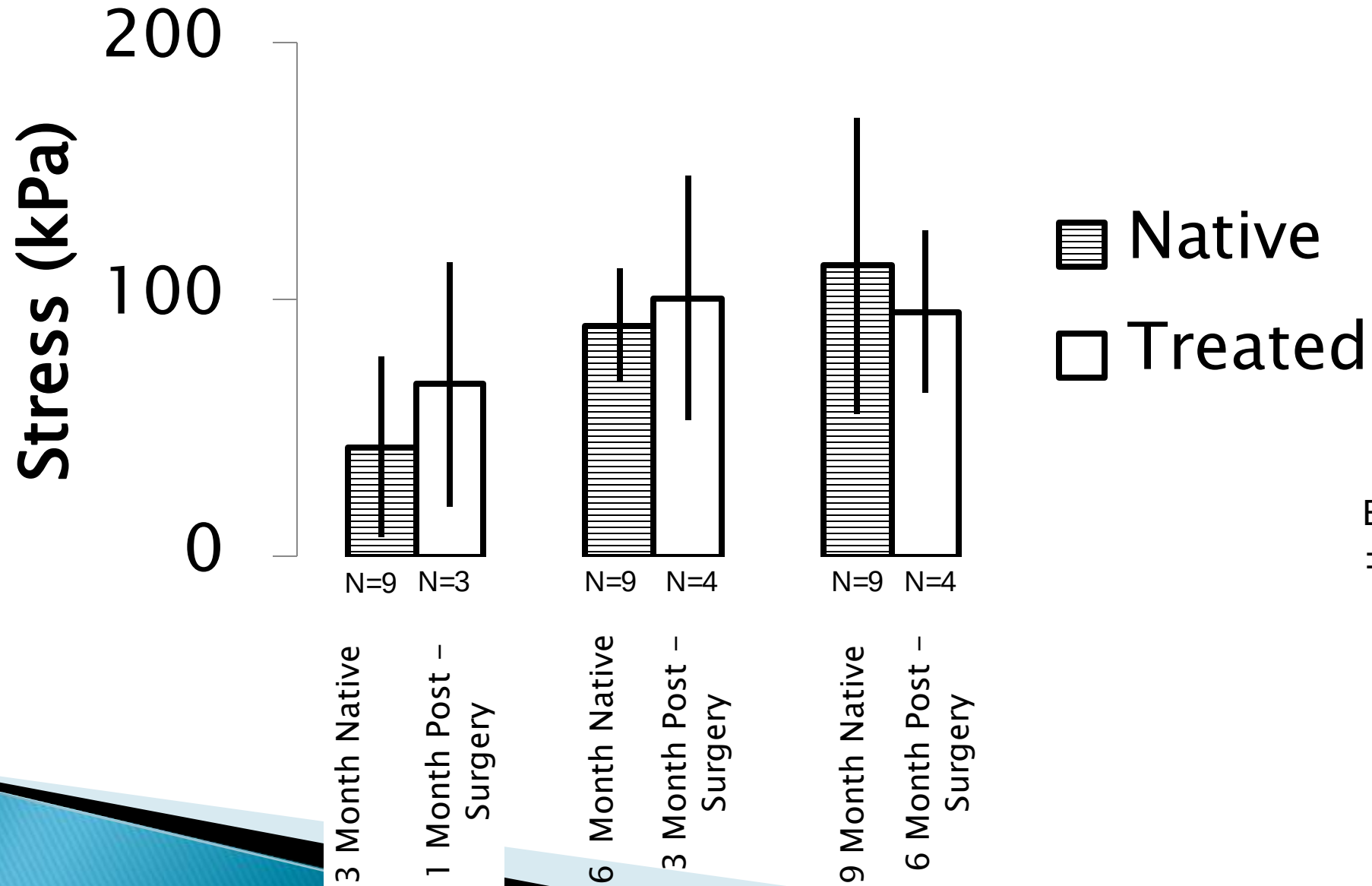
(PMID: 34809494)

Histology–Cellularity

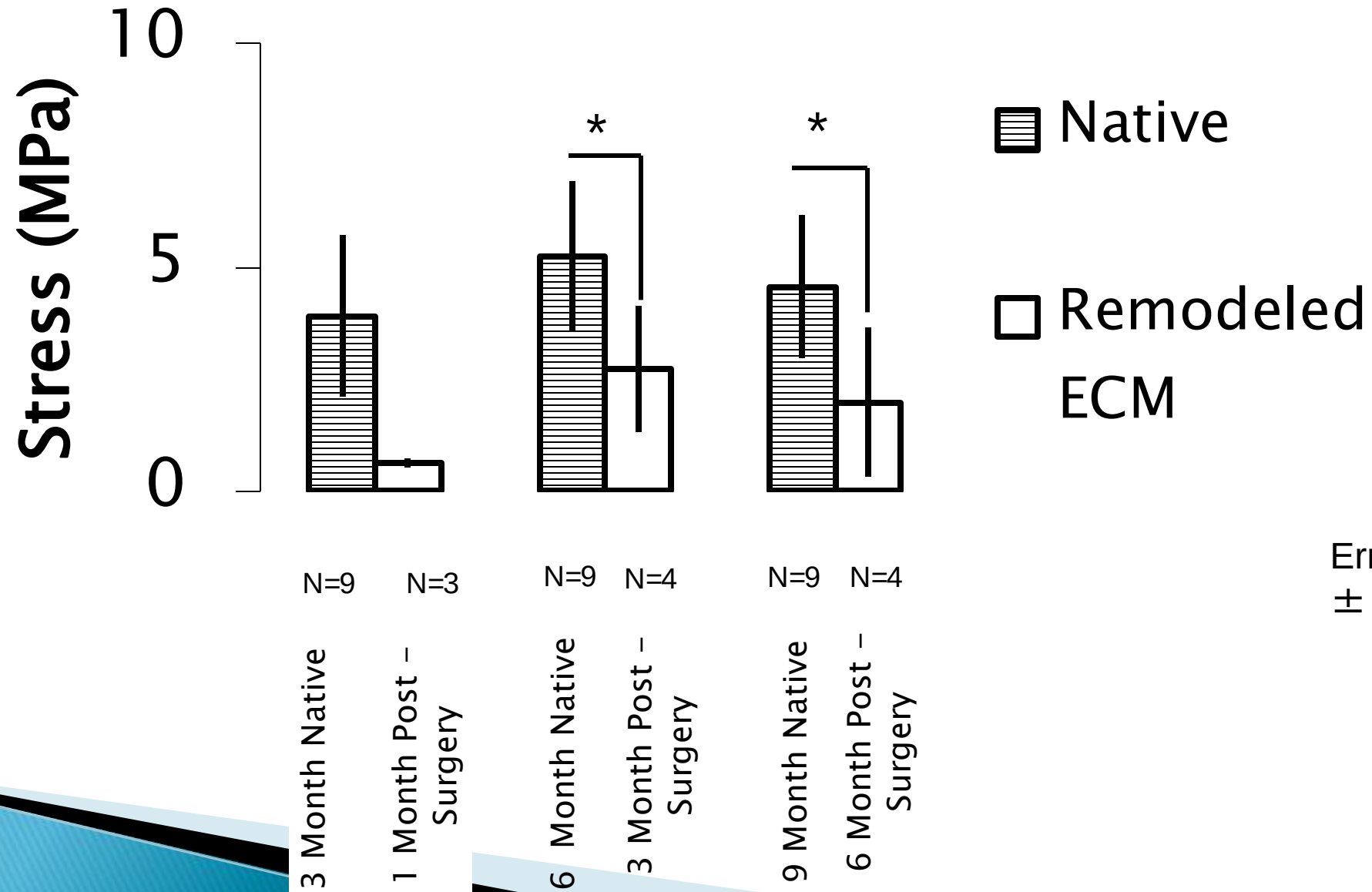


- Initial cell infiltration of macrophages is required for constructive remodeling
- Patient must have ability to mount robust inflammatory response

Compressive Properties



Tensile Properties

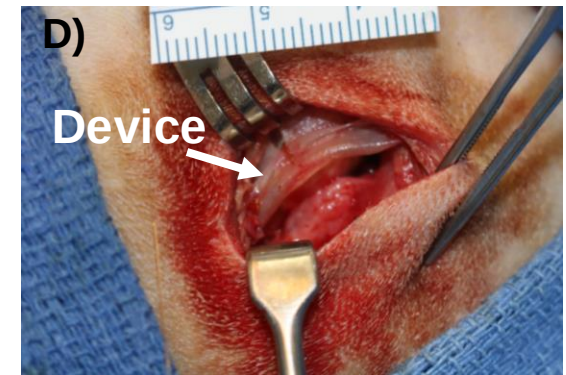
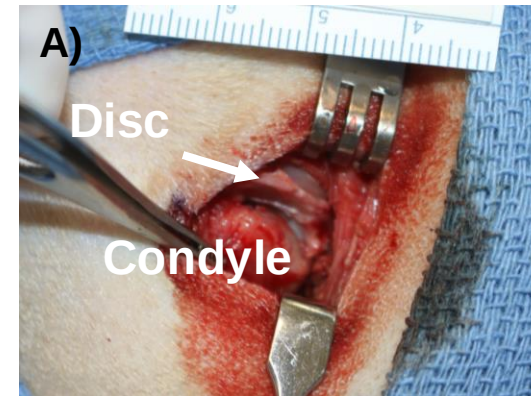


Translational Work (Study3)

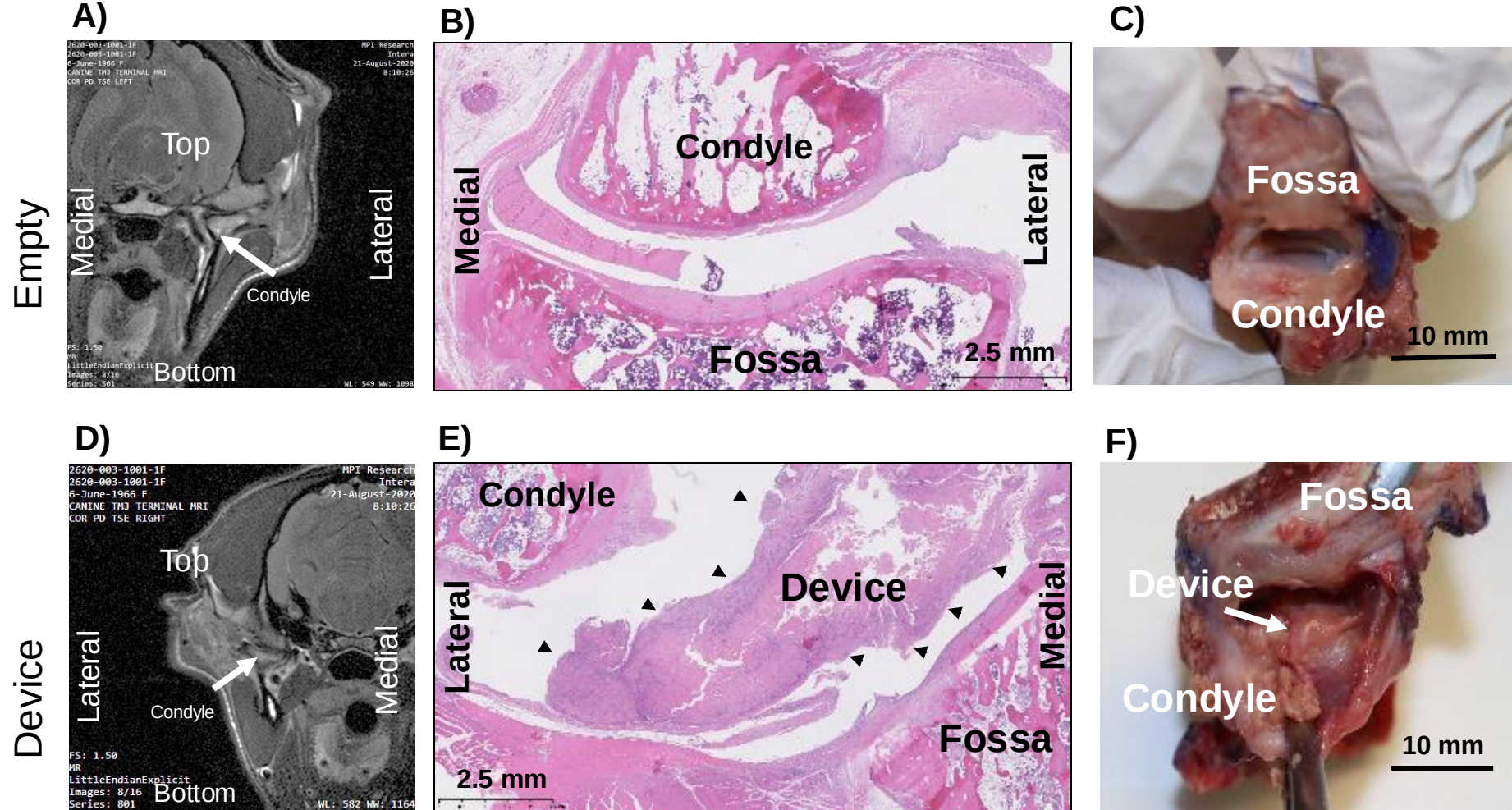
- ▶ FDA guidance
 - Need to show results with good manufacturing practices (GMP) device and perform in good laboratory practices (GLP) animal model
- ▶ Show safety
- ▶ Go to 1 year post implantation

Surgical Removal of Disc and Implantation of Device

- ▶ Secured GMP manufacturing
- ▶ Obtained funding for GLP animal study (canine model) for short term safety study



► GMP device was shown to be safe



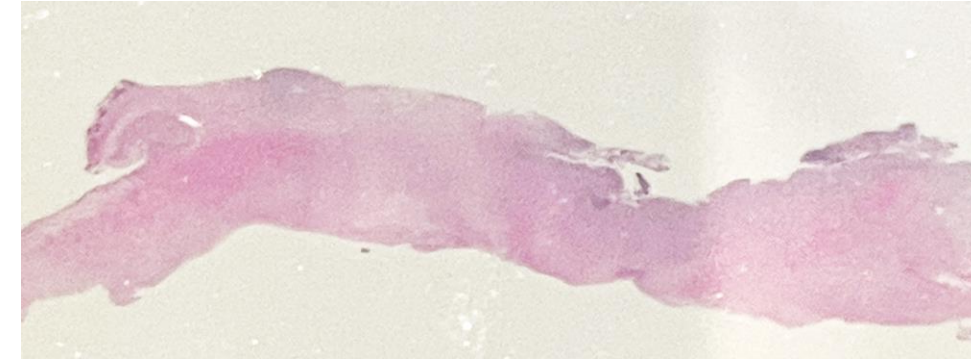
21-Day Safety Study. Coronal MRI of empty (A) and implanted (D), Sagittal H&E of empty (B) and implanted (E), Necropsy Picture of empty (C) and implanted (F). (females; n=5)

Problems with Translation

- ▶ There are no viable therapies to disc removal
- ▶ There are no competitors in the space
- ▶ Base materials are FDA approved
- ▶ Technology has shown efficacy in several animal models and safety in canine model
- ▶ The number of patients with dislocations of the TMJ disc is low
- ▶ FDA categorizes all TMJ technologies as Class III devices
 - Highest level of oversight and investment from industry to move technology through clinical trials
- ▶ No claims on pain relief

Current Work (Study 4) 21-Day Timepoint

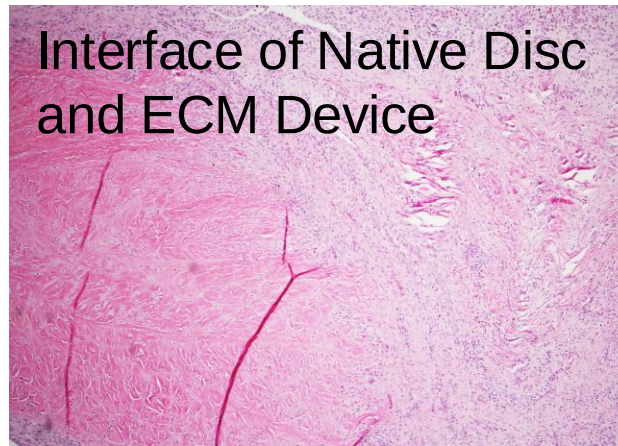
- ▶ Remodeling of both device and native disc (Goat)



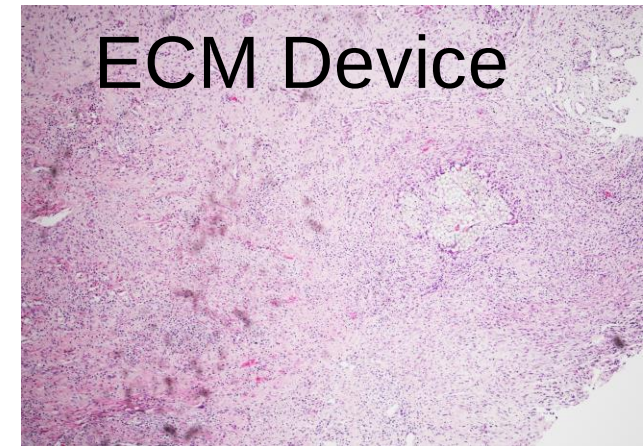
Native Disc



Interface of Native Disc
and ECM Device



ECM Device



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Questions?

