



ORTHOBIOLOGICS IN A SPORTS MEDICINE PRACTICE

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MATA: Sip and Study Soiree
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DISCLOSURES

- No financial disclosures
- Orthobiologics considered off-label

LEARNING OBJECTIVES

- Review definitions pertaining to orthobiologics
- Understand the range of orthobiologic options
- Discuss the role and application of orthobiologic injections in a musculoskeletal practice

CASE

- 17-year-old male senior forward **hockey player**
- Right **anterior medial groin pain** that started gradually one month before
- Worse with skating, squatting, running
- Has had to sit out hockey due to the pain
- History of similar pain on the left, treated with physical therapy
- Goal: compete in upcoming Junior hockey season



CASE 1 - EVALUATION

- Exam:
 - Tenderness to palpation at the **proximal adductor tendons**
 - **Pain with passive hip abduction, resisted hip adduction and crunch** (strength was full)
 - Negative Stinchfield, log roll, FABER, FADER
- Right hip x-ray: mixed impingement morphology, but otherwise unremarkable



DIFFERENTIAL

- Adductor longus tendinosis
- Pubic plate disruption
- Core muscle injury
- Osteitis pubis
- Femoral acetabular impingement syndrome

CASE 1 - MANAGEMENT

- Initial Management
 - Activity modification
 - Physical therapy
- Follow-up
 - No significant improvement after 10 weeks of physical therapy



CASE 1 - MRI PELVIS

- Moderate grade **partial tear of the right adductor longus tendon**
- Mild osteitis pubis
- Mild tendinosis and low-grade partial tear of the left adductor longus tendon



T2 Sagittal View



NEXT STEPS?

TERMINOLOGY

Regenerative Medicine:

“Interdisciplinary therapeutic approach that aims to repair, replace, regenerate, and/or rejuvenate lost, damaged, or diseased cells, tissues, or organs to restore or establish normal form and function” (Finnoff 2021)

Orthobiologics:

“Use of biological substances to enhance biological healing of orthopedic injuries or alter the natural course of an orthopedic disease” (Finnoff 2021)



ORTHOBIOLOGICS IN SPORTS MEDICINE



Increasingly popular treatment option for athletes of all levels

Osteoarthritis

Tendinopathy

Cartilage defects

Muscular injury

Ligamentous injury

Labral pathology

Avascular necrosis



Stand-alone treatment (injection) or in conjunction with a surgical procedure



ORTHOBIOLOGICS IN SPORTS MEDICINE

- Survey of professional/collegiate level team physicians [\(Kantrowitz 2018\)](#)
 - **93% of physicians surveyed use PRP**
 - 98% used it in the clinic
 - 41% used it in the OR
 - 56% use PRP for all athlete levels
- Survey of AOSSM sports medicine physicians [\(Noback 2021\)](#)
 - **66.1% reported use of orthobiologics**
 - 76.1% reported use of PRP
 - 44.0% reported use of BMAC
 - 5.6% reported use of Ad-MSC

REGENERATIVE MEDICINE “HYPE”

- Hugely popular and highly marketed sub-specialty of medicine
- Misinformation is abundant
 - Public perception that true “stem cell” therapies are available/soon to be available → **unrealistic expectations**
 - Estimated 2,754 clinics offering “stem cell” treatments in 2021 (Turner 2016)
- Unproven stem cell interventions → public health threat (Master 2021)

We need to educate our patients and our colleagues regarding these injection/procedural options

CURRENT FDA COMPLIANT ORTHOBIOLOGICS

- FDA highly regulates use of human cells/tissues and tissue products (HCT/P) (FDA 2020, Finnoff 2021)
 - **Homologous use:** use of an HCT/P that performs the same basic function in the recipient as the donor
 - **Minimal manipulation:** no alteration to the original biologic characteristics of the HCT/P

**Platelet-Rich
Plasma (PRP)**

Blood Based

**Bone Marrow
Aspirate
Concentrate
(BMAC)**

Cell Based

**Micro
Fragmented
Adipose Tissue
(MFAT)**

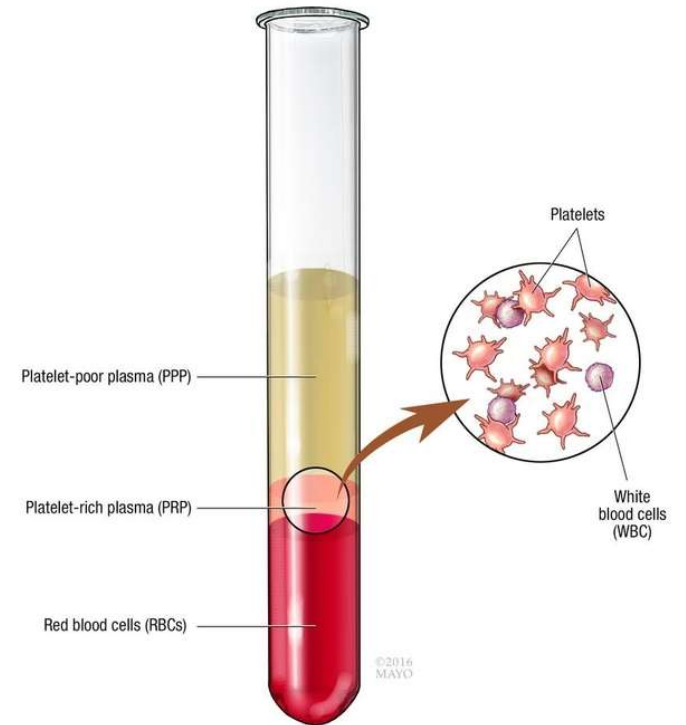
Cell Based

PLATELET-RICH PLASMA

- “Blood plasma enriched in **platelets**, which contains cytokines and growth factors in **higher concentrations than in blood plasma**” (Finnoff 2021)
- Can be characterized by its composition, i.e. leukocyte-rich or leukocyte-poor PRP
- Mechanism of Action (Finnoff 2021)
 - Modulate inflammation and healing
 - Release of growth factors, chemokines, cytokines
 - PDGF, TGF, VEGF, EGF, IGF

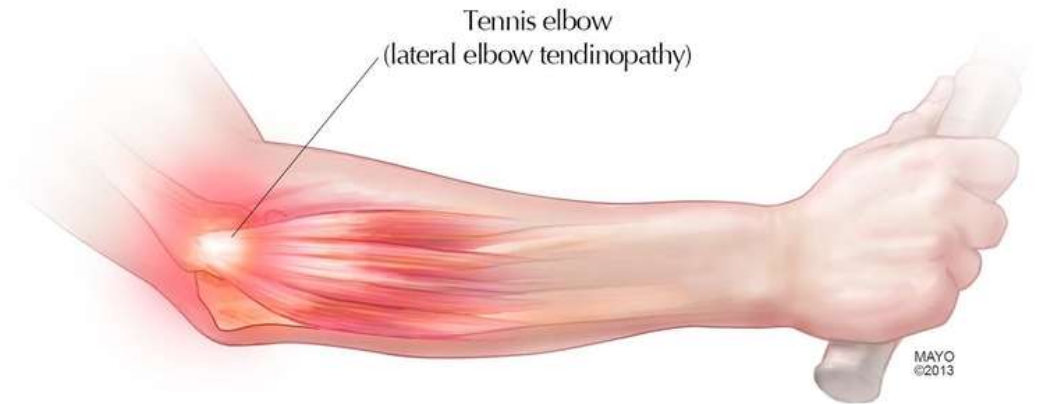


PLATELET-RICH PLASMA



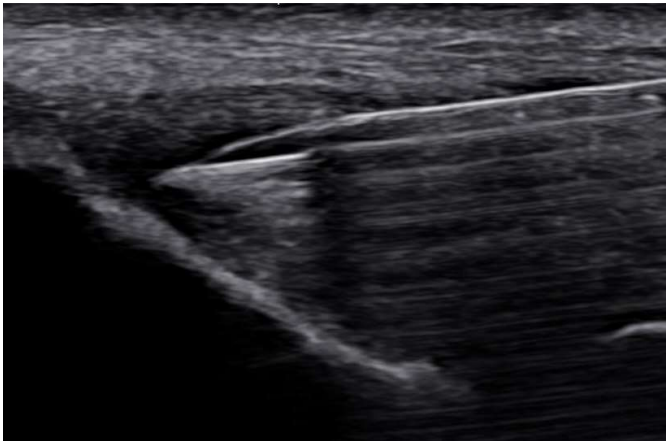
TENDINOPATHY

- Often related to overuse/repetitive mechanical load (Millar 2021)
 - “Degenerative process” → pain, swelling, loss of function
 - **23.9% lifetime prevalence in athletes**
 - **30% of elite athlete injuries related to tendinopathy**
- Phases of Healing
 - Inflammation
 - Proliferation
 - Remodeling



PLATELET-RICH PLASMA FOR TENDINOPATHY

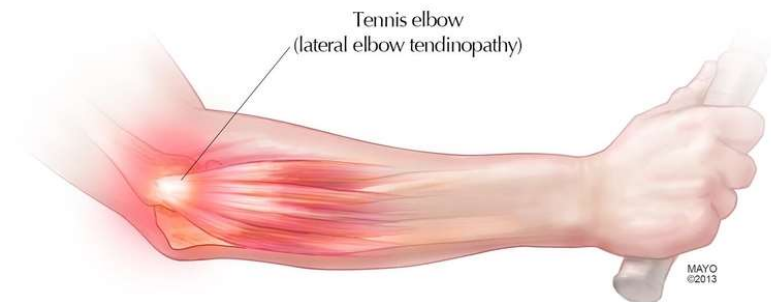
- US-guided platelet-rich plasma injection to the area of damaged tissue (Finnoff 2021)
 - +/- needle tenotomy to initiate a “controlled injury”
 - Growth factors released from the platelets initiate the healing cascade



PLATELET-RICH PLASMA FOR TENDINOPATHY

Fitzpatrick 2017
Finnoff 2021

- Lateral epicondylopathy* (Niemiec 2022)
 - +/- needle tenotomy
 - Pain and functional improvement at 4-8 weeks → 2 years
 - Gluteal tendinopathy* (Migliorini 2021)
 - More effective than CSI at 2 years
 - Plantar fasciosis* (Hurley 2020)
- Patellar tendinosis
 - Rotator cuff tendinopathy
 - Achilles tendinosis
 - Proximal hamstring



OSTEOARTHRITIS

- Affects 1 in 7 adults in the US (CDC 2020)
- Osteoarthritis “treatment gap”
 - Not responding to conservative care
 - Not yet a candidate/appropriate for arthroplasty
- Patellofemoral chondromalacia
- Degenerative changes related to femoral acetabular impingement





PLATELET-RICH PLASMA FOR OSTEOARTHRITIS

- No clear evidence to reverse OA processes or delay progression
- **Knee***
 - Multiple systematic reviews/meta-analyses demonstrating efficacy
 - Best for younger, mild-moderate OA
 - 6-12 weeks for initial relief
 - 9-12 month duration
- **Hip***
- Ankle, foot, hand, TMJ

PLATELET-RICH PLASMA INDICATIONS

- Limited evidence
 - Ligamentous injury
 - Partial thickness UCL tears? [\(Dines 2016\)](#)
 - Muscular injuries [\(Chellini 2019\)](#)
 - Use of platelet-poor plasma?
 - Articular cartilage/osteochondral defects [\(Baria 2023, Liang 2022\)](#)
 - Meniscal pathology [\(Li 2022\)](#)
 - Labral pathology (glenoid, acetabulum) [\(De Luigi 2019\)](#)
 - Adhesive capsulitis [\(Nudelman 2023\)](#)

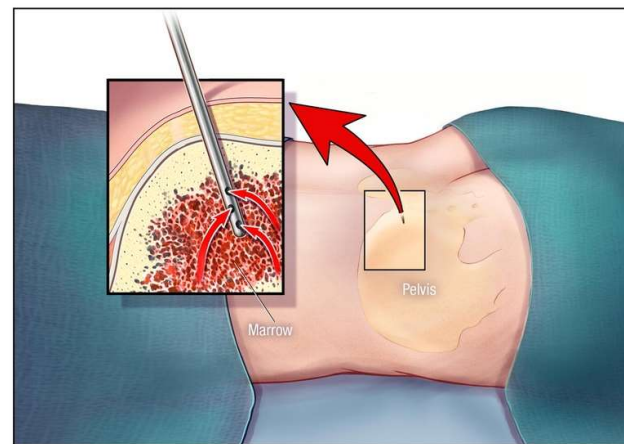


CELL-BASED THERAPIES (BMAC, MFAT) (Finnoff 2021)

- **Mesenchymal “stem cells” (MSC):**
 - Multipotent cells that differentiate into different tissues of mesenchymal lineage (bone, cartilage, adipose, etc.)
- **Medicinal “signaling cells” (MSC):**
 - Primary mechanism is trophic/paracrine → **anti-inflammatory, immunomodulatory, pro-angiogenic, anti-apoptotic, anti-fibrotic, proliferative effects**
 - Growth factors (PDGF, TGF-B, VEGF, IGF1), cytokines, chemokines
- ◆ Insufficient research to support a preventative or restorative potential for cartilage degradation in vivo

BONE MARROW ASPIRATE CONCENTRATE (Finnoff 2021)

- “A concentrate of BMA (bone marrow aspirate) containing multiple cell types including a small number of MSCs, typically created through a centrifugation process”
- Marrow cells have anti-inflammatory, immunomodulatory effects and secrete growth factors, cytokines, chemokines



Removing bone marrow from pelvis

©2016
MAYO

MICROFRAGMENTED ADIPOSE TISSUE

- Adipose derived MSCs
 - “isolated from homogenized adipose tissue located in the capillary and perivascular adventitia of large blood vessels within adipose tissue”
(Malanga 2019)
- Harvest from the abdominal wall/flank region → mechanical forces/washing





MSC INDICATIONS (BMAC/MFAT)

- Osteoarthritis
 - **Spectrum of studies with varying levels of evidence**
 - Pain and functional improvement with BMAC and MFAT (Shapiro 2017, Boffa 2022, Whitney 2020, Screpis 2022)
 - No clear difference between the two (Mautner 2019)
 - No clear superiority of MSC to PRP (? Duration) (Baria 2022, Anz 2022)
 - Lack of evidence for regenerative capacity
 - Good safety profile
 - Need further studies to compare efficacy



MSC INDICATIONS

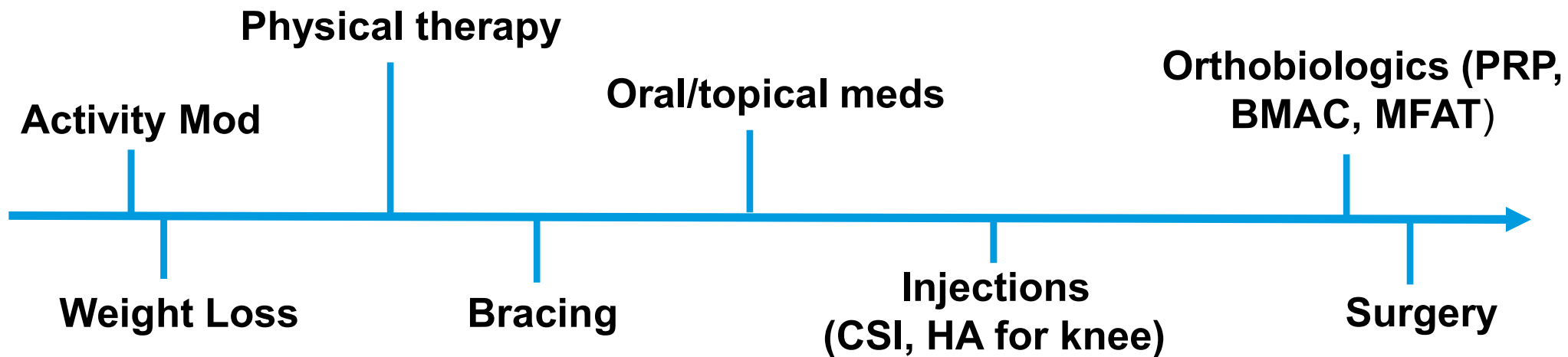
- Few studies evaluating MSCs for tendinopathy
 - ? augment rotator cuff repair
- Focal articular cartilage defect
 - Several studies demonstrating benefits when used to augment surgical procedures ([Southworth 2019](#))
- Avascular necrosis in combination with core decompression ([Kumar 2022](#))



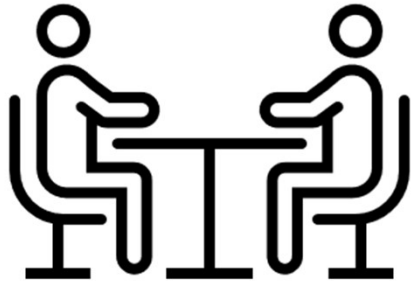
HOW DOES THIS FIT INTO A SPORTS MEDICINE PRACTICE?

COUNSELING

- Should fit in as part of the entire “treatment spectrum”
- Trial non-invasive, safe, cost-effective options first



COUNSELING



- Informed consent
- Discussion of evidence-based rationale for use of orthobiologics
- Avoid anti-inflammatories (NSAIDs, turmeric)
- Avoid anti-platelet medications (if safe to do so)
- Post-procedure activity recommendations vary by provider, location of treatment, type of tissue

COUNSELING

- Generally thought to be safe
- Contraindications
 - Active infection
 - Cancer
 - Platelet dysfunction/low platelets
 - Currently on blood thinners → be cautious with BMAC or MFAT
 - Lean individuals → be cautious with MFAT due to harvest site pain



FUTURE DIRECTIONS

- Appropriate counseling and education of our patients
 - Training Guidelines
 - Standardized pre- and post-procedure protocols
 - Reporting Standards
 - Quality Control/Analysis
-
- Who is the best candidate? When is the best time? What is the best “dose“? How frequent to repeat?





CASE 1

CASE 1 - HISTORY

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T2 Sagittal View

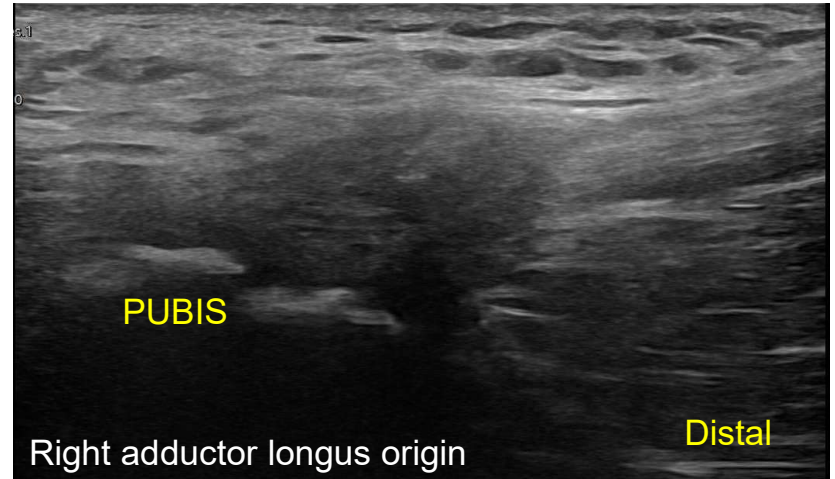


CASE 1 - TREATMENT

- Treatment options
 - Continued physical therapy, adjustment of skating/activities
 - Extracorporeal shockwave therapy
 - ~~US-guided corticosteroid~~
 - US-guided needle tenotomy/PRP
 - Surgical referral

CASE 1 - PRP

- US-guided adductor longus needle tenotomy with PRP injection
- Post-procedure
 - 3 days non-weight bearing
 - Days 3-14 partial-weight bearing
 - Gradual resumption of strengthening/skating





CASE 1 – FOLLOW-UP

- Returned to light skating 7 weeks post-procedure
- Helped his junior hockey team to the Fraser Cup Championship this past March
- 11 goals and 16 assists this past season



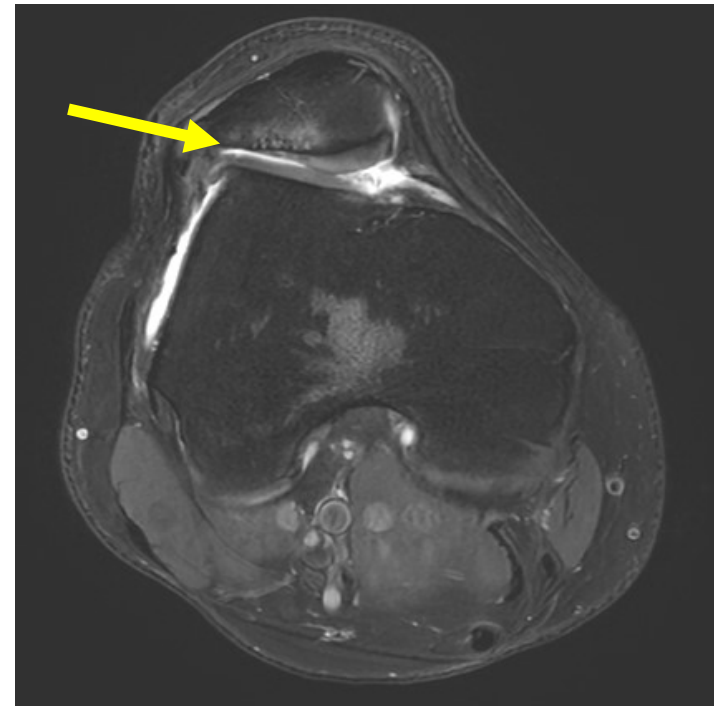
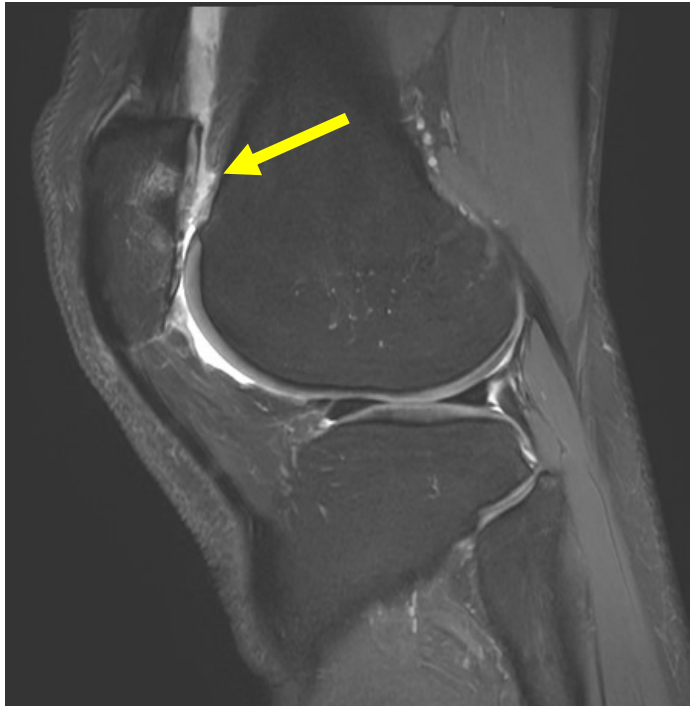
CASE 2

CASE 2 - HISTORY

- 22-year-old female collegiate/professional hockey player with **right anterior knee pain** and swelling with squats, running, jumping
- Frequent clicking but no mechanical symptoms
- Uses a patellofemoral brace with buttress with some improvement
- Home exercise program focusing on quad/hip/core strengthening
- Hx lateral retinacular release 6 years ago, loose body removal 3 years ago



CASE 2 - MRI



High grade fissuring/irregularity of the retropatellar cartilage predominantly at the distal aspect of the lateral patellar facet

CASE 2

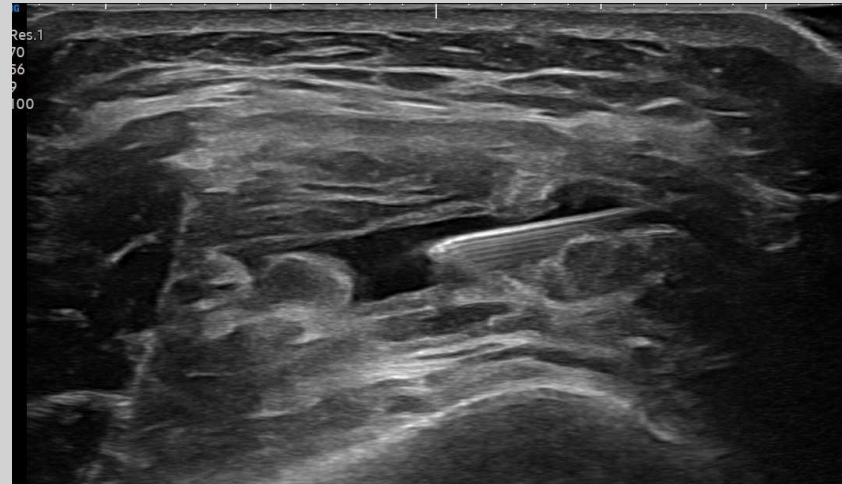
Treatment Options for Patellar Chondromalacia

- Physical therapy (quads, hip, core)
- Oral/topical medications
- Patellofemoral stabilizing brace
- Injections
 - CSI
 - HA
 - Orthobiologics

CASE 2 - PRP

US-Guided Right Knee PRP Injection

- Substantial improvement 3 months post-procedure with duration of 7-12 months
- Repeat PRP +/- HA injections
- Continues to play and skate at a high level





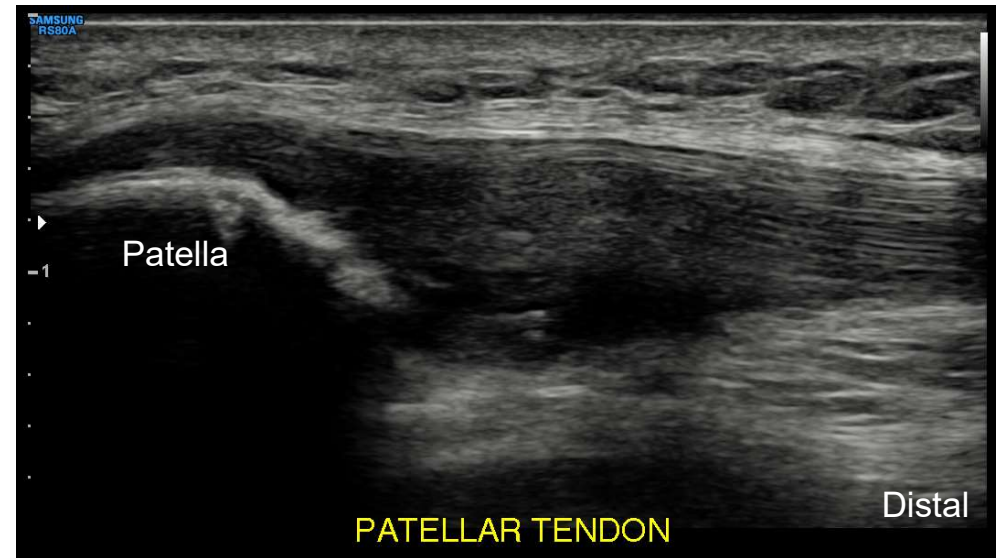
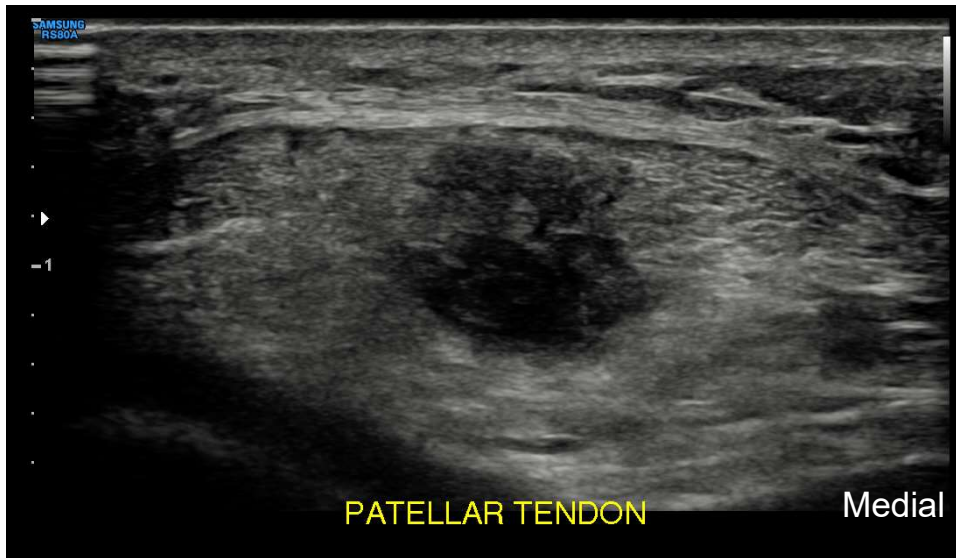
CASE 3



CASE 3 – HISTORY/EXAM

- 18-year-old freshman triple jumper/javelin thrower at a D3 college
- 3 years of **anterior knee pain** worse with jumping, impact activities, and prolonged immobility
 - Several trials of rest
 - Ice/heat
 - Slight improvement with physical therapy
- Exam: Tenderness to palpation at the proximal patellar tendon, pain with resisted knee extension

CASE 3 – MSK ULTRASOUND



Moderate to advanced proximal patellar tendinopathy with partial thickness intrasubstance tear

CASE 3

Treatment Options for Patellar Tendinosis

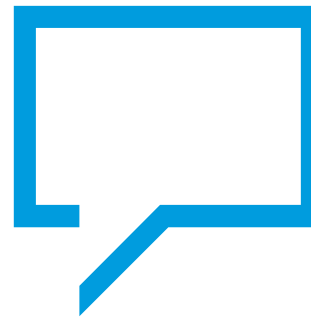
- Physical therapy
- Bracing/strap
- Extracorporeal shockwave
- Peritendinous injections
- Patellar tendon scraping (neovessel ablation)
- Ultrasonic tenotomy/vacuum debridement
- US-guided needle tenotomy + PRP

CASE 3

- Bilateral US-guided **patellar tendon scrapings** during her season
 - Felt that pain worsened
 - Limiting her ability to compete
- Bilateral (staged) **US-guided patellar tenotomy and PRP injection**
 - 20-30 passes with the needle
 - 3.5 ml LR-PRP
 - PWB with crutches for 2-3 weeks
- Lost to follow-up but able to compete in the outdoor 2023 season



QUESTIONS & ANSWERS





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INDICATIONS OSTEOARTHRITIS

- Affects 1 in 7 US adults
 - \$65.5 billion in medical costs/year
 - Aging population
 - Obesity epidemic
- “Osteoarthritis treatment gap”
 - Unresponsive to conservative care
 - Not yet considered for arthroplasty or not a candidate

A national public health agenda for osteoarthritis: 2020 Update.. CDC.





CASE – BMAC ANKLE

- 26-year-old professional dancer with right ankle pain for the past 4-5 years
- History of a motor vehicle collision six years ago and sustained a right open bimalleolar ankle fracture initially managed with external fixation but eventually went on to ORIF
- Gradual anterior and posterior ankle pain and stiffness, worse with standing, walking, squatting
- Treatments tried: activity modification, lace-up ankle brace, oral anti-inflammatories, multiple anterior ankle joint corticosteroid injections, last provided 2-3 weeks of relief, ice/heat, massage



X-RAY/DIAGNOSIS

- Advanced, post-traumatic tibiotalar joint osteoarthritis with loose bodies
- BMAC/PRP/HA
- 65% improved after four weeks
- Resumed biking, core strength, stretching
- Returned to work, walking her dog 0.5 miles
- Improved ankle ROM
- Returned to light jogging about four months after – has not been able to jog for 2 years
- Best it felt in 2-3 years, sustained at one year post injection





MANAGEMENT

- Hoping to avoid ankle fusion given profession as a dancer as well as activity level
- BMAC, PRP, HA injection

REGULATIONS

- FDA highly regulates use of human cells/tissues and tissue products (HCT/P) (FDA 2020)
- Must meet criteria for
 - **Homologous use:** use of an HCT/P that performs the same basic function in the recipient as the donor
 - **Minimal manipulation:** no alteration to the original biologic characteristics of the HCT/P
 - OK to rinse, cleanse, size, shape
- PRP/BMAC are exempt from traditional regulatory pathway because they are considered equivalent to a “currently marketed device”



CASE 5 – UCL PRP

