



# The Essential Role of Primary Care in the Management of Knee Osteoarthritis

Anne Sullivan, MD

*Associate Professor of Orthopaedics  
The Ohio State University Wexner Medical Center*

**MedNet21**  
Center for Continuing Medical Education

 **THE OHIO STATE UNIVERSITY**  
WEXNER MEDICAL CENTER

## Objectives

- Review knee OA diagnosis
- Utilize appropriate imaging
- Review non-operative management
- Understand how to access and apply AAOS CPG and AUC
- Identify timing and management for surgical referral

## Important Note

- Evidence Based strategies from AAOS CPG and AUC
- CPG / AUC offers summaries – not mandates
- Individual patient context matters
- Clinical judgment required

## What Is Knee Osteoarthritis?

- Degenerative joint disease--Pain and dysfunction
- Knee is most common joint involved
- Common but variable, 1/3 people > age 75 have it
- Primary care handles greatest burden

## Why This Matters in Primary Care

- Very common condition
- Long-term management
- Information often misleading to patients
- Expectations shape outcomes

## Diagnosis of Knee OA

- Clinical + radiographic
- OA often coexists with other conditions
- Imaging  $\neq$  pain
- Context matters, not all pain is OA

## Clinical Presentation

- Pain and stiffness
- Swelling
- ROM limitation
- Decreased function

## Differential Diagnosis

- Spine / radiculopathy
- Hip pathology, other bony issues
- Inflammatory arthritis, soft tissue injury
- Infection or neoplasm
- Vascular claudication

## Diagnostic Caution

- Do not inject blindly
- Image first
- Rule out red flags
- Safety first

## Imaging Approach

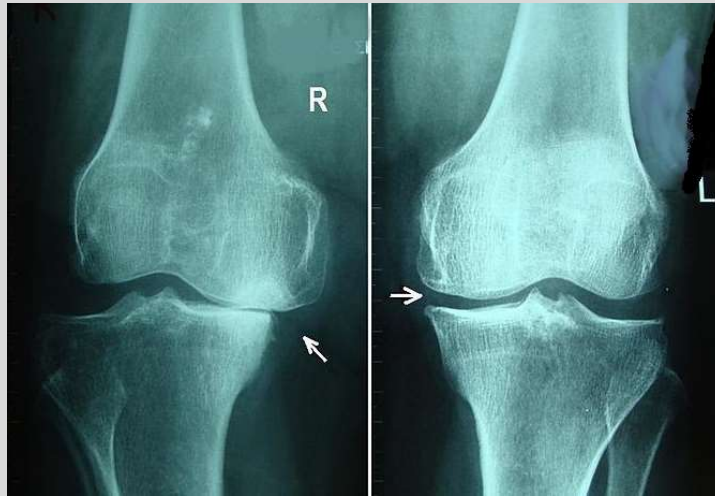
- X-ray almost always sufficient for AO Dx
- Weight-bearing views
- MRI rarely needed– adds anxiety
- Imaging  $\neq$  symptoms, must correlate

## Kellgren–Lawrence Grading

- Describes radiographic severity
- Used in guidelines, for imaging reliability
- Descriptor, Not a pain scale,
- Does not dictate treatment

Kellgren- Lawrence	OA Grading Scale
Grade 0–1	No or doubtful OA, possible osteophytes
Grade 2	Definite osteophytes, possible joint space narrowing
Grade 3	Joint space narrowing, sclerosis , osteophytes
Grade 4	Severe OA with deformity, joint space narrowing, osteophytes

## K-L Grade 4 on R; Grade 3 on L



## Non-Operative Treatment Goals

- Reduce pain
- Improve function, preserve motion and activity
- Slow progression of disease and morbidity
- Manage expectations

## **CPG STRONG Recommendations**

- Topical NSAIDs
- Supervised exercise
- Neuromuscular training
- Self-management programs

## **CPG MODERATE Recommendations**

- Weight loss
- Assistive devices
- Bracing
- Corticosteroid injections

## **CPG Limited Evidence Treatments (Select Patients)**

- Manual therapy
- Massage
- Acupuncture
- Laser therapy

## **Adjunctive Modalities (Limited Evidence)**

- Electrical stimulation (TENS / PENS)
- Extracorporeal shockwave therapy
- Percutaneous denervation
- Dry needling

## **CPG Limited Evidence: Orthobiologics and Supplements**

- Platelet-rich plasma (PRP)
- Other orthobiologics
- Dietary supplements
- Select patient benefit

## **Limited Evidence – Clinical Framing**

- Low to moderate evidence
- May be early in development/ need further study
- Generally low harm
- May benefit select patients
- Shared decision-making

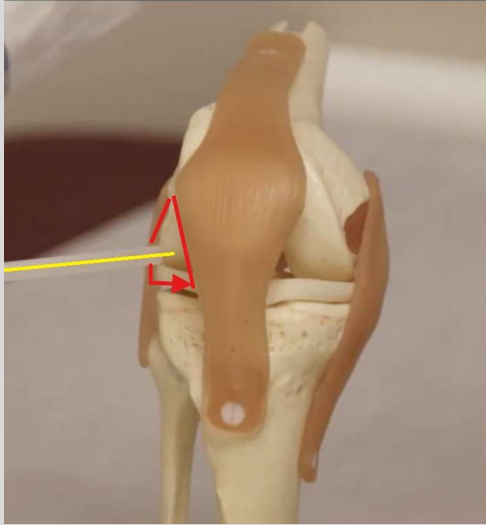
## **CPG Generally Avoid**

- Chronic narcotics incl tramadol
- Arthroscopic debridement
- Routine HA injections

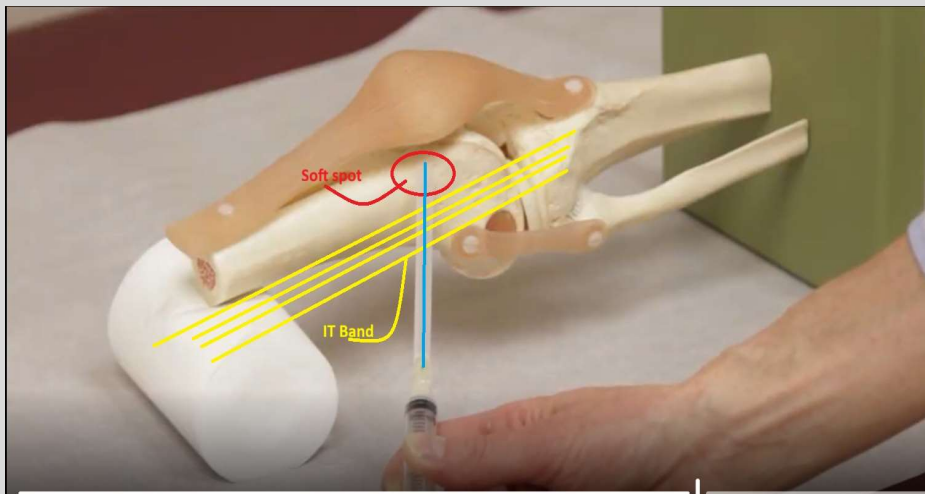
## **Knee Injection Principles**

- Several techniques work
- Use what you know
- Sterility critical
- Patient comfort matters

## Lateral and Medial injection sites



## Superolateral (Pouch) injection



## Video - Knee injection, Superolateral (suprapatellar pouch access) Approach



## When to Refer for TKA

- Pain limits daily life
- OA explains symptoms
- Non-op care failed
- Patient engaged and open to surgery

## **Prerequisites for Considering TKA**

- Mental and emotional readiness
- Diagnosis is correct and explains symptoms
- Modifiable Risks identified and mitigated
- Expectations aligned

## **Medical Optimization Before Referral**

- Optimize chronic disease management
- Strongly Encourage smoking cessation
- Address nutrition and weight
- Coordinate care early

## Relative Contraindications to TKA

- Minimal pain or dysfunction–Little benefit, poor satisfaction
- Incorrect diagnosis
- Poor engagement- patient not ready
- Unsafe social situation
  
- Not necessarily permanent contraindications

## Modifiable Medical Risk Factors

- Poor diabetes control ( Hgb A1c>7)
- Tobacco or nicotine exposure
- Morbid obesity ( BMI>40) malnutrition
- Active infection
- Other medical co- morbidities: CAD, PVD, HTN

## **Largely Unmodifiable Contraindications**

- End-stage renal disease on dialysis
- Permanent non-ambulatory state
- Life expectancy less than 6 months

## **Higher-Risk but Possible Situations**

- Long-term immunosuppression
- Active or recent cancer treatment
- Sickle cell disease
- Cognitive or mental health differences
- Prior joint infection

## **Role of Primary Care**

- The Heavy Lifting
- Longitudinal OA management
- Risk factor modification
- Expectation-setting
- Appropriate referral

## **Transitional Q & A**



# Non-Arthroplasty Treatments for Knee Osteoarthritis

**Michael R. Baria, MD, MBA**

*Director of Orthobiologics*

*Professor, Department of Physical Medicine and Rehabilitation*

*The Ohio State University Sports Medicine Research Institute*

**MedNet21**  
Center for Continuing Medical Education

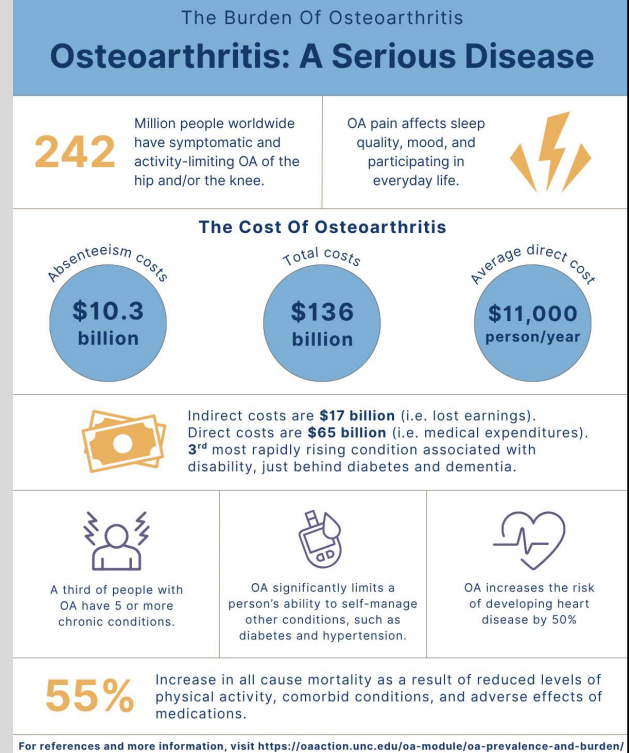
 **THE OHIO STATE UNIVERSITY**  
WEXNER MEDICAL CENTER

## The Importance of Joint Preservation

- Why should we care about joint preservation?
  - The Burden of Osteoarthritis (OA)
  - Patient Apprehension
  - The Potential for Regeneration

## The Importance of Joint Preservation

- Why should we care about joint preservation?
  - The Burden of Osteoarthritis (OA)
    - High expenditures on patient care, time lost from work
    - Worsens co-morbid conditions and increases risk of heart disease
    - **55% increase in all-cause mortality**








## The Importance of Joint Preservation

- Why should we care about joint preservation?
  - Patient Apprehension
    - Fear of infection, VTE, poor outcome
  - The Potential for Regeneration
    - OA has traditionally been understood as progressive, with no disease-modifying treatments
    - New(er) treatments show disease-modifying potential that may further prolong the lifespan of the native joint

## OA Pathophysiology and Therapeutic Targets

- OA is a multi-factorial degenerative condition with hallmark pathophysiologic features
  - Loss of synovial fluid viscoelasticity
  - Cartilage degradation (apoptosis)
  - Subchondral bone resorption (manifested as bone marrow edema and insufficiency fractures)
  - Synovitis
  - Mechanical axis deviations (malalignment and flexion contractures)

## OA Pathophysiology and Therapeutic Targets

Osteoarthritis: Pathophysiologic Hallmarks & Solutions	
Pathophysiologic Hallmarks	Therapeutic Solutions
 Loss of Viscoelasticity	→ Viscosupplementation with Hyaluronate
 Loss of Cartilage	→ PRP: Reduces Chondrocyte Apoptosis & Promotes Chondrocyte Proliferation
 Synovitis	→ PRP: Reduces Synovitis & Inflammation
 Bone Marrow Edema	→ PRP & Shockwave Therapy
 Malalignment	→ Implantable Mechanical Supports

## Viscosupplement

- Approved by the FDA in 1997, this is either avian-derived or fermented (from streptococcus metabolism) and then purified for patient application
- Although widely used, it came under scrutiny when the AAOS recommended against it in its 2013 clinical practice guideline
- That posed a major issue for patients
- This left steroid as the only other injectable therapy
  - Known to be chondrotoxic and is associated with increased rate of knee arthroplasty
- This created a significant need for knee OA injectables

## An Opportunistic Window

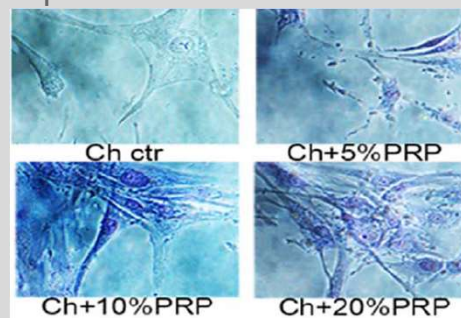
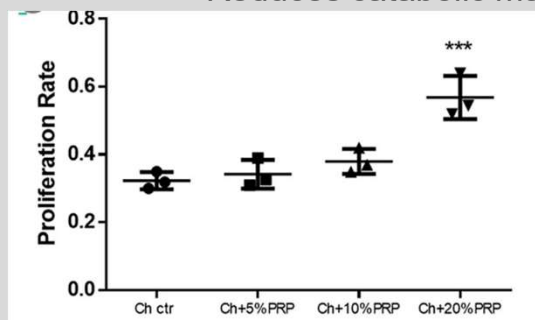
- Given the increased scrutiny on viscosupplement products, this created a new gap in treatment options
- At the same time, cohort studies were being published from Italy on positive patient outcomes after treatment with platelet-rich plasma (PRP)
- Originally used to aid in sternal wound closures and gum grafting, PRP was applied to OA
  - Rationale: OA is a non-healing condition, so a boost of growth factors may improve symptoms and / or disease progression

## PRP: Mechanistic Insight

- Complex interplay of tissue healing, anti-inflammatory, and anti-catabolic effects
- When platelets contact damaged collagen, they degranulate and release their anabolic 'cargo'
  - Growth factors (TGF, IGF, FGF, VEGF, etc)
  - Exosomes
- These GF and proteins then exert a paracrine effect and incorporate into cells (like synoviocytes)
  - Alters phenotypic expression to one more resilient in the face of chronic disease

## Mechanisms of Tissue Healing

- PRP results in dose-dependent effects
  - Anabolic
    - Promotes chondrocyte proliferation
    - Increases vacuole formation as a marker of autophagy, promoting balanced cellular turnover
  - Anti-catabolic
    - Reduces arthritic chondrocyte apoptosis
    - Reduces catabolic matrix proteases



Moussa, Exp Cell Res, 2017

CC BY-NC-ND 4.0

No changes made

<https://doi.org/10.1016/j.yexcr.2017.02.012>

## ACP



### Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis

An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial

Patrick A. Smith,<sup>\*†</sup> MD

*Investigation performed at the Columbia Orthopaedic Group, Columbia, Missouri, USA*

**Confirmed safety and efficacy of ACP with statistical and clinical significance up to 1 year**

## Mechanisms of Tissue Healing

- These cellular level changes have potential to cause macroscopic improvement
- Yoshioka et al completed a RCT comparing 3 LP-PRP vs saline
- **MRI improvement** seen by 24 weeks

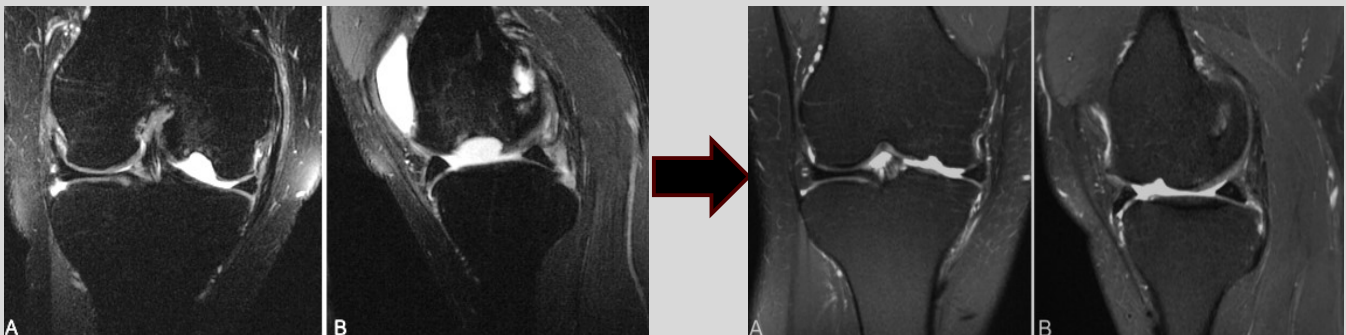
Yoshioka, AJSM, 2024

## Mechanisms of Tissue Healing

- Chu et al randomized over 600 knee OA patients to either a series of 3 LP-PRP or saline
- After only 1 treatment session (series of 3 weekly injections), the LP-PRP group had less cartilage loss compared to placebo at 5 years
- Take home point: A single treatment changed the disease course over 5 years

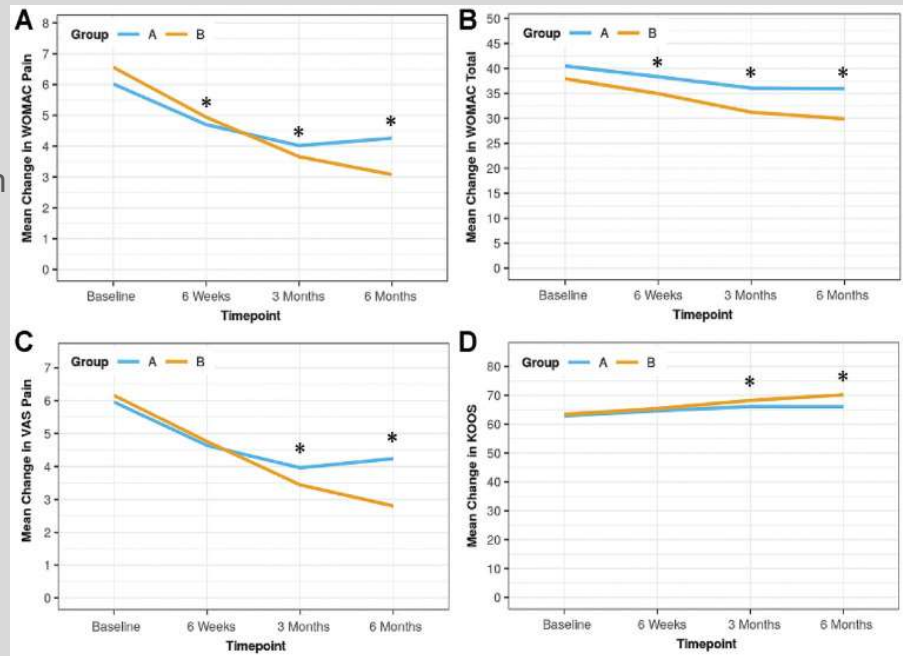
Chu, KSSTA, 2022

## Clinical Observations of Structural Healing



## Dosing Primer

- Patel et al performed a dose comparison study
  - 5.6 billion vs 2.8 billion platelets (LP-PRP)
  - PRP concentrated approximately 3.5x over baseline
  - 5.6 billion superior as an initial dose



Patel et al. OJSM, 2024

doi: 10.1177/23259671241227863

CC BY-NC-ND 4.0 No changes made

## Dosing Primer

- Gobbi et al demonstrated that a proactive 'booster' cycle at 1 year promotes further symptom relief compared to a single series without repeat administration

Gobbi, KSSTA, 2014

## Autologous “Stem Cell” Therapies

- Both bone marrow and adipose are known sources of mesenchymal stem cells (MSC)
  - Relative concentration of MSCs in both cell populations is quite low
  - Stem cells are unlikely to be the primary driver of effect
- Despite the popularity due to stem cell content, there are no studies showing either are superior to either placebo or PRP
- More invasive
- More costly

## Off-the-Shelf “Stem Cell” Therapies

- Usually derived from birth tissue
  - Umbilical cord
  - Placenta
  - Amniotic fluid
- Studies have shown these products have no stem cell content
  - Mainly composed of hyaluronate
- None are FDA approved
- Substantial harm has occurred
  - Sepsis / septic arthritis
  - Reactive arthritis in HLA –B27+ patients
- Not indicated for any clinical use
  - Off-label use doesn't apply since this is allogeneic

## Shockwave Therapy

- High-energy acoustic waves
- In-office administration
- Therapeutic effects
  - Promotes angiogenesis
  - Stimulates tissue regeneration
  - Reduces pain signaling
- Many RCTs demonstrate superiority for knee OA over control therapies (including physiotherapy and alendronate)



## On The Horizon

- Several biologics are in the developmental pipeline and worth monitoring
- Autologous
  - Stromal vascular fraction (SVF)
  - Adipose is harvested in a procedure room similar to a low-volume liposuction
  - Collagenase is mixed with the tissue to release MSCs from the collagen matrix
  - Tissue is centrifuged to concentrate a higher amount of true stem cells

## On The Horizon

- SVF
  - Passed Phase 2 FDA trials
  - Successfully complete phase 3 FDA trials
  - Awaiting regulatory review

The American Journal of Sports Medicine  
 Volume 48, Issue 3, March 2020, Pages 588-598  
 © 2019 The Author(s), Article Reuse Guidelines  
<https://doi.org/10.1177/0363546519899923>



Article - Knee

### **Clinical Efficacy of Intra-articular Mesenchymal Stromal Cells for the Treatment of Knee Osteoarthritis: A Double-Blinded Prospective Randomized Controlled Clinical Trial**

Jaime R. Garza, MD<sup>†</sup>, Richard E. Campbell, BS<sup>†</sup>, Fotios P. Tjoumakaris, MD<sup>†</sup>, Kevin B. Freedman, MD<sup>†</sup>, Lawrence S. Miller, MD<sup>‡</sup>, Daniel Santa Maria, MD<sup>§</sup>, and Bradford S. Tucker, MD<sup>†,‡</sup>

## On The Horizon

- Platelet-derived exosomes
  - Exosomes are small extracellular vesicles (sEV) found in blood cells and plasma
  - Consist of proteins, lipids, and nucleic acids (i.e. miRNA) that deliver cell signaling information
  - Promotes tissue restoration and homeostasis

## On The Horizon

- Exosomes; Two primary applications
  - Exosomes as the therapy
    - When derived from platelets, carry the same therapeutic information as PRP
    - Purified
    - Consistent dosing
    - Off-the-shelf (stable shelf life for years, eliminates need to draw / spin blood in the clinic)
  - Exosomes as the delivery vehicle
    - Exosomes can be loaded with another therapeutic drug / biologic
    - Lipid bilayer protects the therapeutic content
    - Improves targeted delivery

## On The Horizon

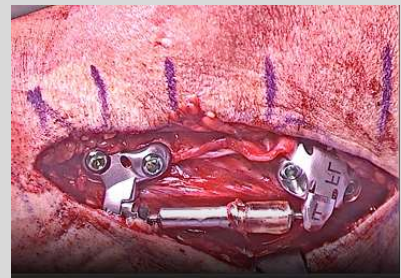
- Platelet-derived exosomes
  - Currently in phase I studies for
    - Knee OA
    - Radiation and fistulizing wounds
    - Myocardial infarction
  - In phase 2 for
    - Diabetic foot ulcers

## Surgical Innovations for Knee OA

- Bracing intuitively helps patients
- Address malalignment
- Improves muscle contractility
- However, patients cannot brace 24/7
- Two surgical, non-arthroplasty treatments are worth considering

## Surgical Innovations for Knee OA

- **Medial Implantable SHock Absorber (MISHA)**
- For medial knee OA
- Reduces impact by 30%
- In the Phantom Trial, 96% of patients had an improvement of 20% or more on the WOMAC scale
  - 4% removal rate
- Native joint preserved, OA injectables still an option



## Surgical Innovations for Knee OA

- Osteotomy
  - High tibial osteotomy for medial pain / varus knees
  - Distal femoral osteotomy for lateral pain / valgus knees
  - Corrects malalignment with no implants and no replacement
  - Native joint is preserved
    - OA injectables can still be performed



## Summary

- PRP has excellent safety and efficacy track record for over 10 years
- New biologic injectables may offer additional injection based care
  - Autologous and off-the-shelf options in FDA pathway
- Joint sparing surgical techniques (MISHA / HTO) may offer additional benefit when rehabilitation and injectable options have yielded suboptimal results