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 ≠ 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

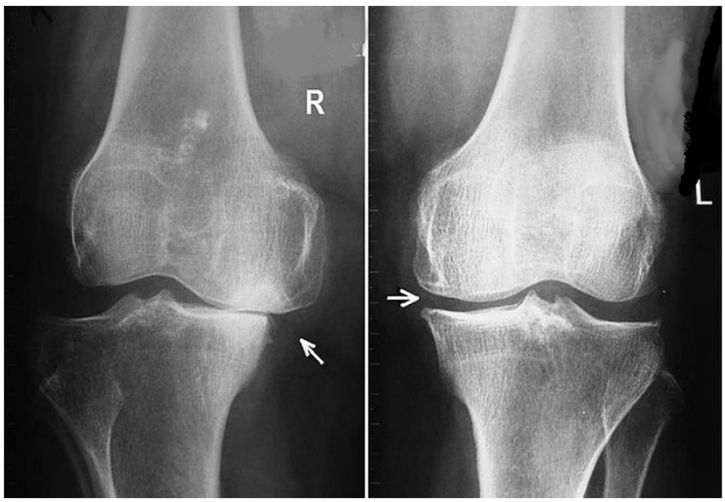
- X-ray almost always sufficient for AO Dx
- Weight-bearing views
- MRI rarely needed– adds anxiety
- Imaging ≠ symptoms, must correlate

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

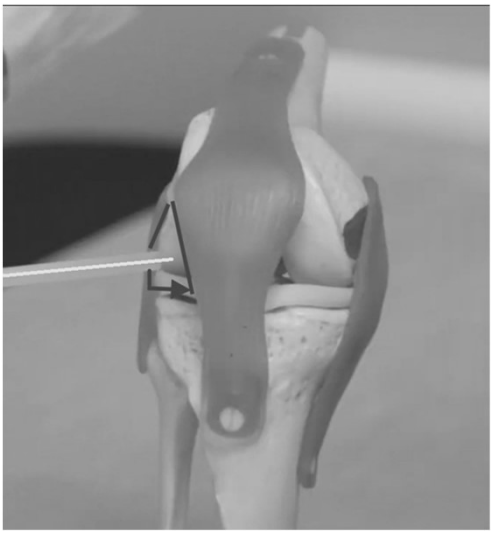
CPG Generally Avoid

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

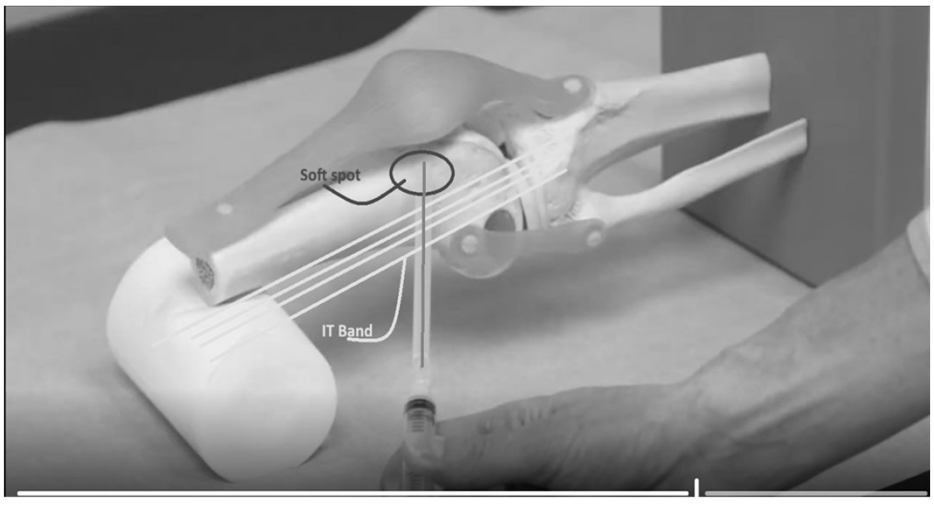
Knee Injection Principles

- 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

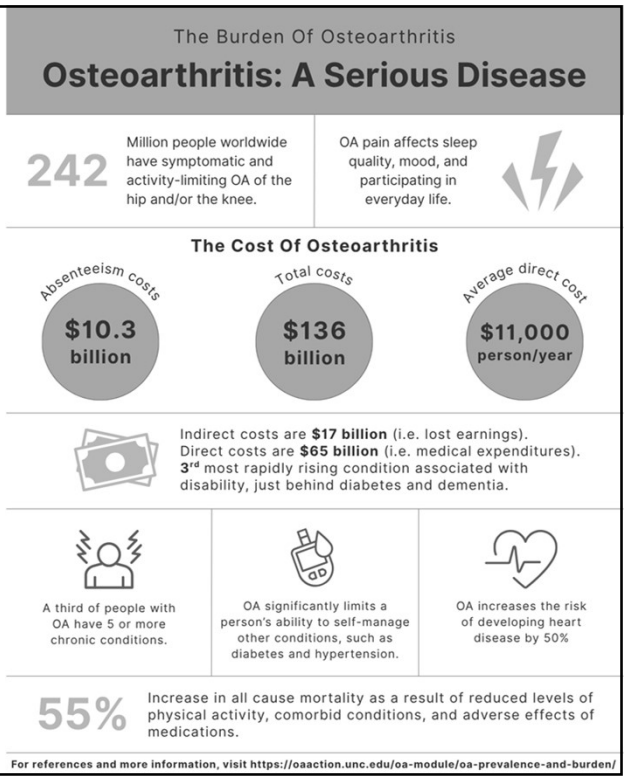
The Ohio State University
Wexner Medical Center

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**



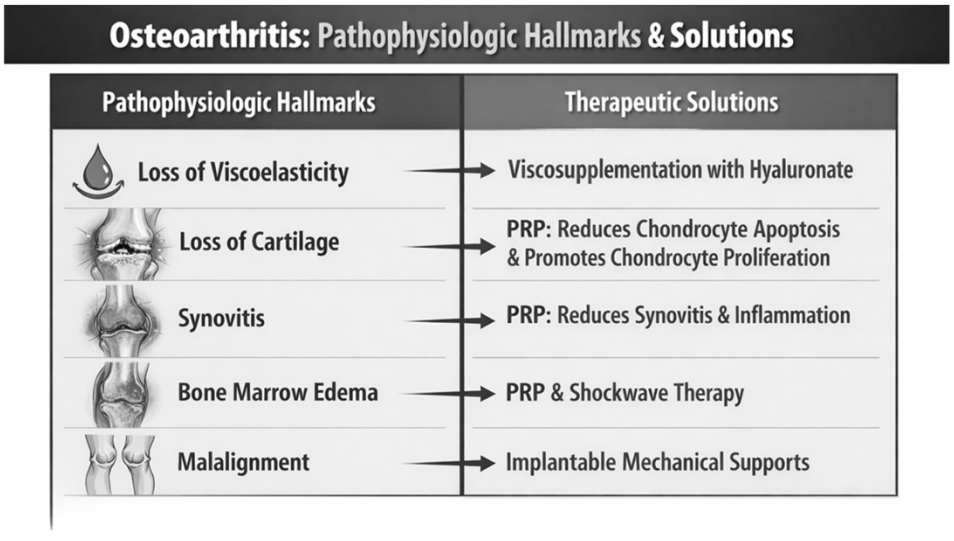
The Importance of Joint Preservation

- 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



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

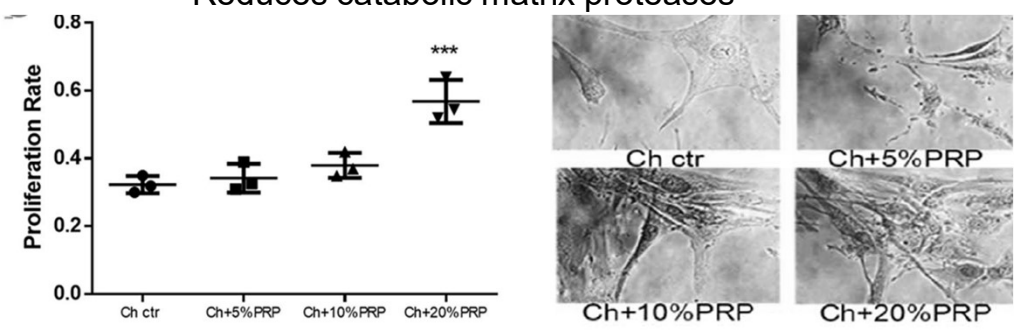
- Given the increased scrutiny on viscosupplement products, this created a new gap in treatment options
- At the same time, cohort studies were being published from Italy on positive patient outcomes after treatment with platelet-rich plasma (PRP)
- Originally used to aid in sternal wound closures and 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
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,*† 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

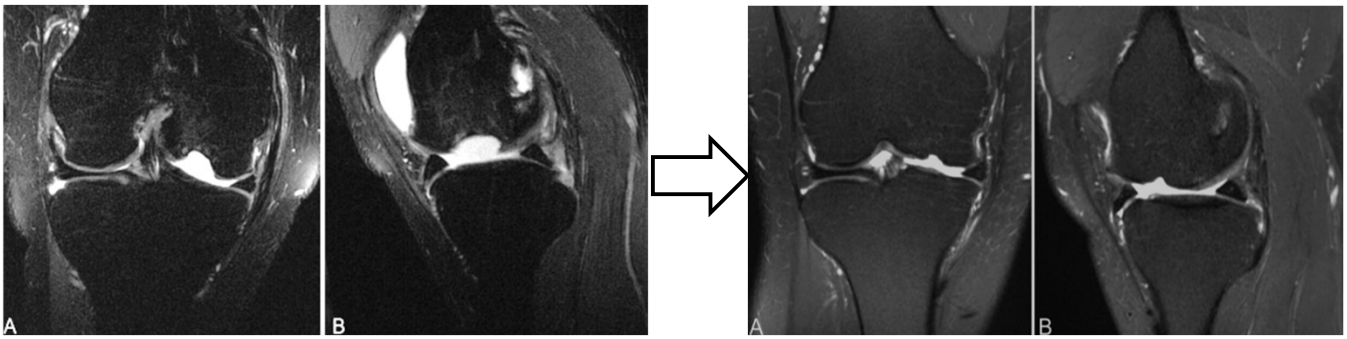
Yoshioka, AJSM, 2024

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

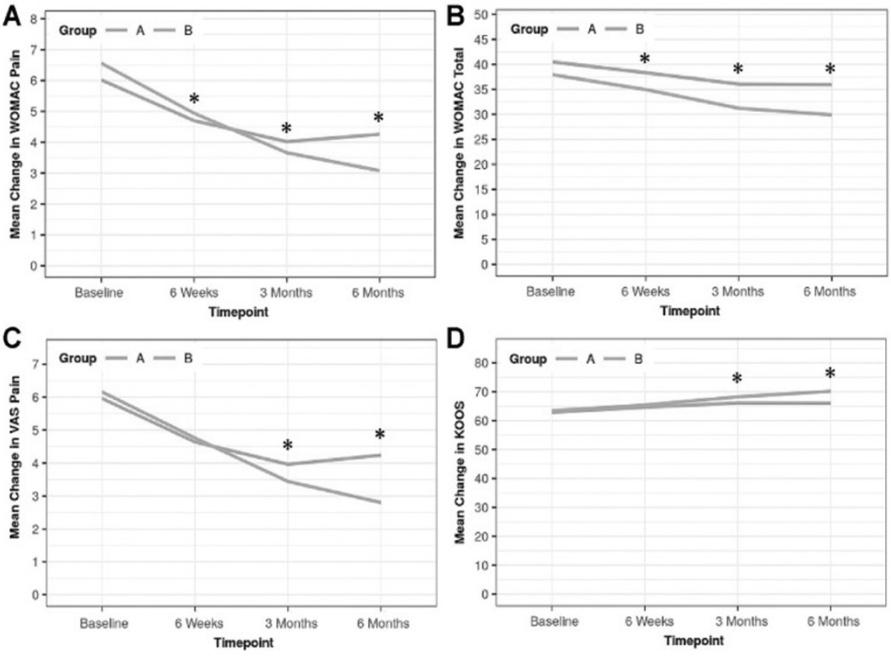
Chu, KSSTA, 2022

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

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

https://doi.org/10.1177/0363546519899923

SAGE journals

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[*], Richard E. Campbell, BS[†], Fotios P. Tjoumakaris, MD[†], Kevin B. Freedman, MD[†], Lawrence S. Miller, MD[‡], Daniel Santa Maria, MD[§], and Bradford S. Tucker, MD[†,‖]

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

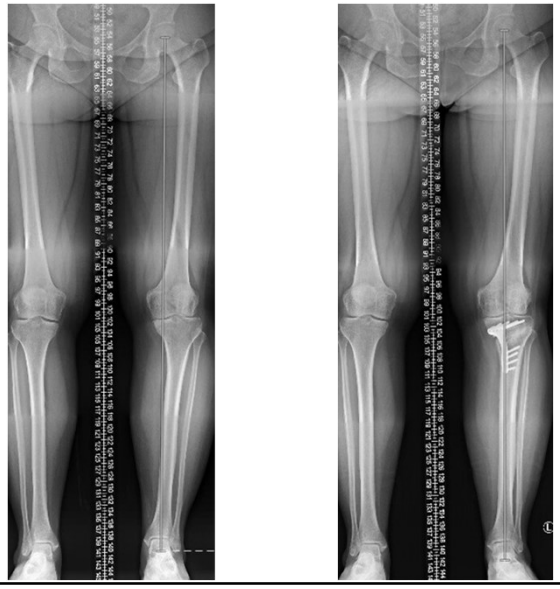
- Bracing intuitively helps patients
- Address malalignment
- Improves muscle contractility
- However, patients cannot brace 24/7
- Two surgical, non-arthroplasty treatments are worth considering

Surgical Innovations for Knee OA

- **M**edial **I**mplantable **SH**ock **A**bsorber (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