



## Platelet-rich Plasma in Musculoskeletal Medicine: 10 years in 10 minutes

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## Disclosures

- Consultant for
  - Arthrex
  - RION

## Objectives

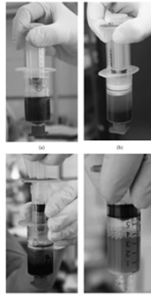
- Discuss definition and preparation methods for PRP
- Discuss data supporting PRP for musculoskeletal indications
- Define currently used 'stem cell' procedures and compare outcomes to PRP

## Introduction

- What is platelet-rich plasma (PRP)?
  - Solution of platelets elevated at least 2x over baseline compared to peripheral blood
  - Variety of preparation methods available
  - Each will change the precise cellular / protein content

### Examples of PRP Preparation Methods

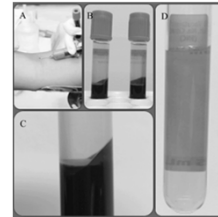
- Plasma-based method
  - Small volume of peripheral blood is drawn
  - Spin for 5 minutes to separate cells
  - Withdraw top layer to extract the PRP



C. Eichler, C. Baucks, J. Öner, C. Pahnmeier, D. Ratku, B. Gruettner, W. Malter, M. Warm, "Platelet-Rich Plasma (PRP) in Breast Cancer Patients: An Application Analysis of 163 Sentinel Lymph Node Biopsies", *Bioméd Research International*, vol. 2020, Article ID 3432987, 7 pages, 2020. <https://doi.org/10.1155/2020/3432987>

### Examples of PRP Preparation Methods

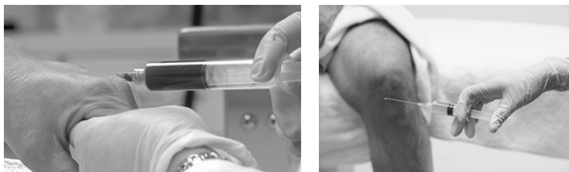
- Buffy-coat method
  - Spins at higher speeds to increase platelet concentration
  - Middle layer is the buffy-coat PRP



Daniell MV (2016) The Chondral Tissue and PRP: Theory to Support the Use. *J Musculoskelet Disord Treat* 2:020.

### Examples of PRP Preparation Methods

- Gel-based systems
  - Similar to the plasma systems, but it utilizes a thixotropic gel to provide the separation
  - Concern that platelets get trapped in gel, resulting in subtherapeutic doses



Author: Alice Pien MD

Author: KimLantz

### Foundational Mechanisms of PRP

- When platelets degranulate, they release their alpha-granules
  - Releases anabolic proteins like
    - TGF-beta
    - IGF
    - FGF
- In vitro studies have shown a reduction in chondrocyte apoptosis and induction of tendon stem-cell differentiation

### Evidence for PRP in Musculoskeletal Medicine

- Earliest reports using PRP for knee osteoarthritis (OA) were published in 2010

Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions

Elizaveta Kon, Roberto Buda, Giuseppe Filardo, Alessandro Di Martino<sup>1,2</sup>, Antonio Timoncini, Annarita

- Kon et al followed 100 patients treated with PRP and found durable improvements for 1 year in IKDC scores

### Evidence for PRP in Musculoskeletal Medicine

- Over time, the quality of these studies improved from uncontrolled case-series or cohort studies to rigorous randomized controlled trials
- Smith P performed the 1<sup>st</sup> FDA-sanctioned DB-RCT of PRP for knee OA
- Small sample size due to safety as the primary endpoint
  - PRP (n=15) vs saline (n=15)

### Evidence for PRP in Musculoskeletal Medicine

- Despite small sample size, the effect size of the treatment group was large enough to detect a clinically and statistically significant difference
- A clinical difference was seen by 2 weeks with durability at least for 1 year

Randomized Controlled Trial > Am J Sports Med. 2016 Apr;44(4):884-91.  
doi: 10.1177/0363546515624678. Epub 2016 Feb 1.

**Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis: An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial**

### Evidence for PRP in Musculoskeletal Medicine

- Patel et al performed a 3-arm, DB-RCT comparing
  - Single PRP injection (N=27)
  - Series of 2 PRP (N=25)
  - Placebo (N=26)
- Clinical improvement in PRP groups by 6 weeks
- Durable for at least 6 months
- No difference between PRP protocols
  - May suggest a ceiling effect

Randomized Controlled Trial > Am J Sports Med. 2013 Feb;41(2):356-64.  
doi: 10.1177/0363546512471299. Epub 2013 Jan 8.

**Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial**

Sandeep Patel<sup>1</sup>, Mandeeep S Dhilon, Sameer Aggarwal, Neelam Manwaha, Ashish Jain

### Evidence for PRP in Musculoskeletal Medicine

- After demonstrating superiority over placebo, the next obvious comparison was against the standard of care for knee OA (viscosupplement)
- Cole et al conducted a DB-RCT comparing PRP (same formulation used in the Smith / FDA study) vs Synvisc
  - Higher bar given that Synvisc has proven efficacy and longstanding use in clinical practice
  - PRP (N=49)
  - Synvisc (N=50)

### Evidence for PRP in Musculoskeletal Medicine

- Cole et al found improvement in both groups
- No difference on the WOMAC score
- PRP was superior on IKDC and VAS-Pain scores
- Depending on the outcome, at least as good as viscosupplement, in some respects superior

Randomized Controlled Trial > Am J Sports Med. 2017 Feb;45(2):339-346.  
doi: 10.1177/0363546516665809. Epub 2016 Oct 21.

**Hyaluronic Acid Versus Platelet-Rich Plasma: A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis**

### Evidence for PRP in Musculoskeletal Medicine

- Repeatedly, PRP has been superior to placebo, steroid, and viscosupplement injections for knee OA
- Several meta-analyses summarizing these studies have demonstrated the value of PRP for knee OA

**Platelet-Rich Plasma Versus Hyaluronic Acid for Knee Osteoarthritis: A Systematic Review and Meta-analysis of Randomized Controlled Trials**

- Belk et al performed a meta-analysis of level I studies and found PRP superior to viscosupplement injections

### Evidence for PRP in Musculoskeletal Medicine

- The evidence has grown significantly over the past decade
- So much so that a recent review by the American Academy of Orthopedic Surgery (AAOS) supports the use of PRP for knee OA

### What about Stem Cells?

- With PRP having demonstrated significant benefit, many patients are attracted not just to PRP, but to the notion of stem cells
- While there is robust data supporting the use of PRP, no such data exists for so-called 'stem cell' therapy in the United States

### Stem Cells: Buyer Beware

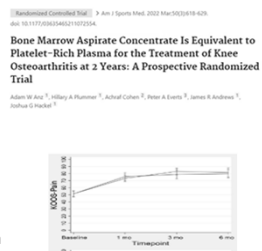
- The 3 major products used in the United States touted as 'stem cells' are
  - Bone marrow aspiration concentrate (BMAC)
  - Adipose
  - Amniotic / placental / umbilical cord products

### Stem Cells: Buyer Beware

- First, these products are not meaningful sources of stem cells
  - In BMAC, approximately .01% of the cells are stem cells
  - While adipose has more stem cells, as the patient has excess adiposity, those stem cells are not primed for therapeutic use
    - As we'd expect, more adiposity results in increased cellular senescence and inflammation
  - Studies have proven that in off-the-shelf amnio products, there are no living stem cells

### Stem Cells: Buyer Beware

- Second, unlike PRP, these products have limited data and none have outperformed standard of care options (including PRP)
- Anz et al demonstrated in a large RCT that bone marrow concentrate was not superior to a much simpler PRP (at 2 years)
- Our group at Ohio State showed that adipose derived cells were not better than PRP at 6 months and 1 year



### Stem Cells: Buyer Beware

- Thirdly, significant patient harm has resulted from the use of amnio / placental products
- These are now considered illegal to market for OA
- Regulatory environment is murky
- Because of poor quality control, vials of amnio tainted with e. coli were injected into patients

The New York Times

**12 People Hospitalized With Infections From Stem Cell Shots**

### Stem Cells: Buyer Beware

- Investigations of amnio companies have found poor lab conditions
- Report from FDA investigation found more tainted vial and tissue donors who were positive for hepatitis and Chagas disease

On 17 MAY 2018, your firm processed an umbilical cord blood product (label# [REDACTED] Donor # [REDACTED]) into [REDACTED] vials (2cc each). The microbial sample of starting material (umbilical cord blood) showed one colony of growth on 21 May 2018. These vials (all [REDACTED]) were shipped to customers in [REDACTED] and [REDACTED] among other locations.

On 18 AUGUST 2018, your firm processed an umbilical cord blood product (label# [REDACTED] and Donor # [REDACTED]) into [REDACTED] vials (1 or 2cc each). The serology testing for the donors showed positive markers for Chagas disease and Hepatitis B (HBsAg). [REDACTED] of these vials were shipped to customers in [REDACTED] and [REDACTED] among other locations.

On 9 JUNE 2018, your firm processed an umbilical cord blood product (label# [REDACTED] and Donor # [REDACTED]) into [REDACTED] vials (1 or 2cc each). The sterility testing of plasma separated during the process showed growth of Gram Positive Coec [REDACTED] of these vials were shipped to customers in multiple locations, including [REDACTED].

### Recommendations for Clinicians

- PRP has robust evidence demonstrating safety and top-tier efficacy for knee OA
- PRP has level I evidence for other conditions like greater trochanteric pain and plantar fasciitis
- Other products like bone marrow, adipose, and amnio
  - Are NOT stem cells
  - Should be avoided as they are not superior to a safer, less expensive, less invasive PRP

### Part 2: Meniscus Root Tears

### Meniscus Root Tears

- Most of us received education on meniscal pathology like degenerative tears or bucket-handle tears
- However, root tears have only been recognized in the last 10-15 years, so many of us were not given education or experience with this unique injury

### Root Tears Defined

- The meniscus root is the anchor of the meniscus to the tibia
- We'll focus on the posterior root as it is the most commonly injured
- Function of the root is to translate contact forces through the meniscus as hoop stresses
- If the root is disrupted, it results in a complete loss of meniscus function and the contact pressures in the knee are the same as if there was no meniscus at all

### The Importance of Root Tear Recognition

- Because of the increased contact pressures, articular cartilage degeneration happens rapidly
- Results in premature need for knee replacement
- Prompt recognition and treatment (root repair) can delay the need for joint replacement

### Root Tear: Presentation

- Patient demographics and risk factors
  - Middle-age
  - Women > men
  - Obesity
  - Varus alignment

### Root Tear: Presentation

- Unlike sport-related meniscus tears which occur with a cut / pivot movement, the mechanism of injury for a root tear is generally unimpressive
  - Deep knee bend during daily tasks like cleaning or gardening
  - Stair climbing
  - Common forces across the joint are axial load + knee flexion (no rotation)
- Patients experience
  - Sudden, severe pain
  - Often posterior
  - Significant difficulty with weight bearing for the first few days
  - Traditional mechanical symptoms of meniscus tears (locking, catching) are usually not reported
  - Rapid improvement over the first week
    - Quick improvement plus lack of mechanical symptoms can lead to a missed diagnosis

### Root Tear: Physical Exam

- Variable degrees of antalgia
- Usually do not have a knee effusion
- Posterior pain with hyperflexion of the joint
  - May feel clunk / click with any degree of joint flexion
- + McMurray's
- Meniscal extrusion with varus stress (compression causes extrusion)

### Root Tear: Imaging

Review > Curr Sports Med Rep. 2022 May 12;15(1):155-158. doi: 10.1249/RSR.0000000000000959.

#### Meniscus Root Tears: A Clinical Review

Elena Randazzo<sup>1</sup>, Robert Dueri<sup>2</sup>, Michael R Baris<sup>3</sup>

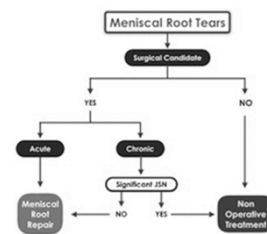
Affiliations + expand

PMID: 35522439 DOI: 10.1249/RSR.0000000000000959

- Plain films either normal or mild OA
- MRI is definitive
- Ghost sign is pathognomonic
  - On sagittal imaging, the posterior horn / root of the meniscus sudden disappears indicating the gap of the root tear

### Root Tear: Indications for Surgical Referral

- Surgical referral is key for joint preservation
- Root repair (not debridement) has been shown to decrease the rate of OA development and need for joint replacement
- All acute injuries should be referred to a surgeon
- Chronic injuries with preserved joint spaces on PA flexion views may also benefit
- If there is significant joint space narrowing on plain films, these patients should be treated according to OA guidelines



To cite Cinque ME, Chahla J, Moatshe G, et al. Br J Sports Med 2018;52:872-876.



### Meniscus Root Tear: Summary

- A critical diagnosis to consider in patients with sudden onset of posterior knee pain after a flexion moment at the knee
- MRI and prompt referral to a surgeon may preserve joint health long term
- Early recognition and treatment can preserve joint health and quality of life for your patients



### Knee OA and Meniscal Root Rehabilitation

**John DeWitt, PT, DPT, AT**  
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*Assistant Professor, Clinical Practice*  
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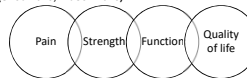
### Objectives

1. Review value of PT to manage knee OA
2. Identify key components to improve knee OA outcomes
3. Describe meniscal root injuries rehabilitation milestones
4. Discuss functional assessment use to reduce injury risk
5. Provide resources for rehabilitation guidelines

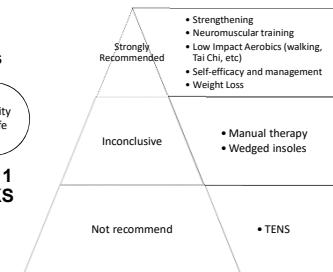
### Discuss the Value of Physical Therapy with Knee OA Pain

#### Physical therapy improves

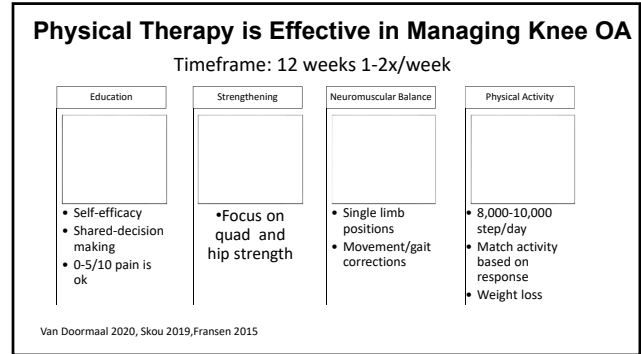
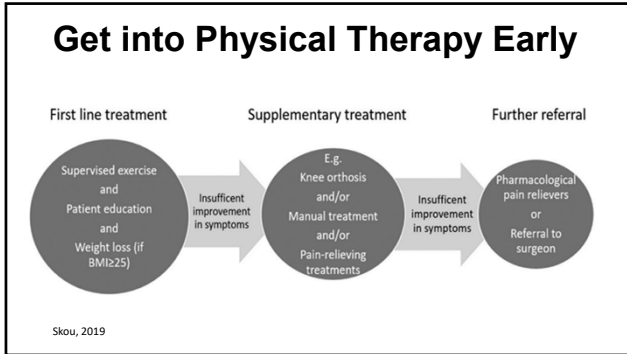
(Skou 2019, Fransen 2015)



**3 out of 4 delayed TKA for 1 year, 2 out of 3 delayed TKS for >2 years** (Skou 2015, 2018)



Kolasinski 2019, McMurray 2017



### Quad Strength is Critical

Needs to improve by 30-40% to impact pain and disability (Bartholdy, 2017)

**Avoid underdosing**

- Rep Max (80% 1rep Max)
- Ratings of Perceived Exertion(7-8/10)
- Reptations in reserve (2 RIR)

**Open & Closed chain ex are safe and effective**

### Effective Supplements to Improve Quad Strength

**Neuromuscular Estim (NMES) improve**

- Muscle fiber size
- Strength
- Functional performance
- Patient reported outcomes

**Blood flow Restriction Therapy**

- Limb occlusion using low resistance
- ↑ muscle strength, quad mass, and functionality to high resistance strengthening" (Ferraz 2018)

### Functional Strength and Balance Measures

Outcome Measure	Interpretation	MCID/MDC
5x Sit to Stand	>15 sec = Risk for Falls	11.4 seconds
Berg Balance Scale	<45/56 = risk for falls	5 points
10 m Walk Test	<1.0m/s m/s = risk for falls <.8 = Limited Community Ambulator >1.2 m/s needs to safely cross stree	.06 m/s
6m Walk Test	5.38 m age/gender norms	50 m
Lower Extremity Functional Test	MCID = 9 points	

### If you Don't Use it.....

**PT gains only last 4-6 months if exercise is not continued**

**Physical activity guidelines**

- 150 min of mod activity/week
- 75 min vigorous activity/week
- 2 days of Strength Training



**Community Programs (Yoga, Tai Chi, etc.)**

### Meniscal Root Tear is Rare

10-20% of meniscal tears

Occurs with MLI and hyperflexion/squatting injuries

Leads to meniscal extrusion and OA advancement

Better outcomes than debridement

Review | Am J Sports Med. 2014 Dec;42(12):3016-30. doi: 10.1177/0363546514524162. Epub 2014 Mar 12.

**Meniscal root tears: significance, diagnosis, and treatment**

Sarjeov Bhatia<sup>1</sup>, Christopher M LaPrade<sup>2</sup>, Michael B Elman<sup>3</sup>, Robert F LaPrade<sup>4</sup>  
ARISiations • expand  
PMID: 24623276 DOI: 10.1177/0363546514524162

Bhatia 2014

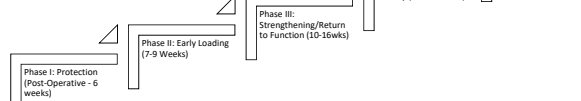
### Meniscal Root Rehab Precautions

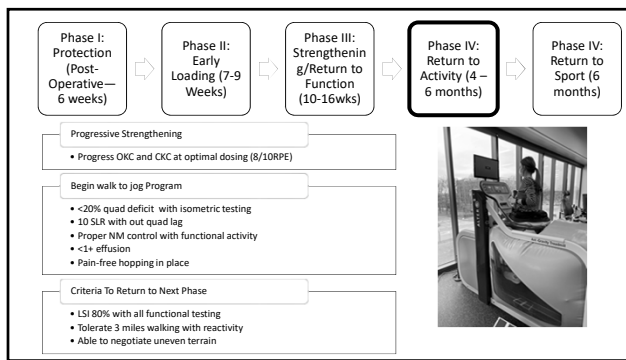
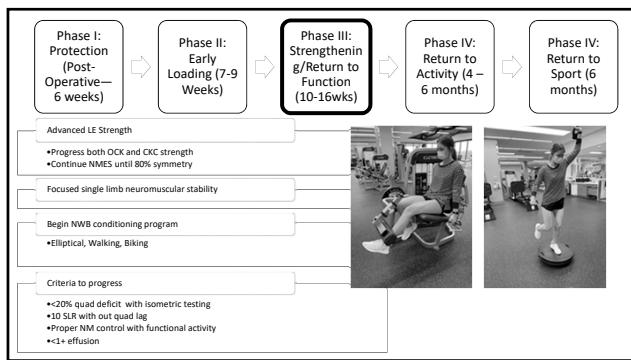
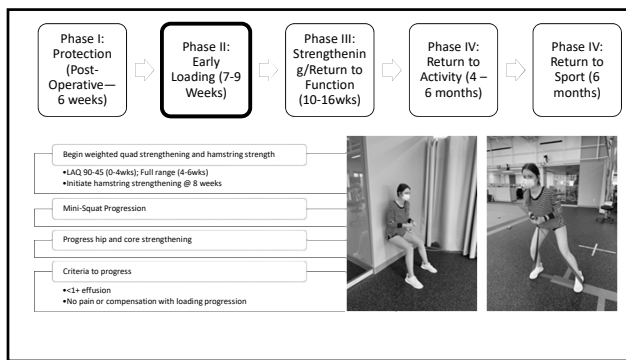
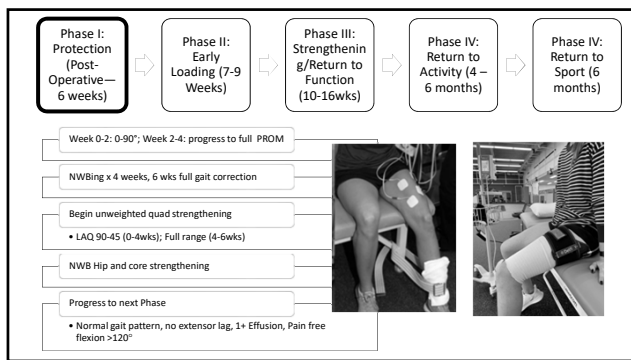
TROM immobilizer for first 10-14 days post-op

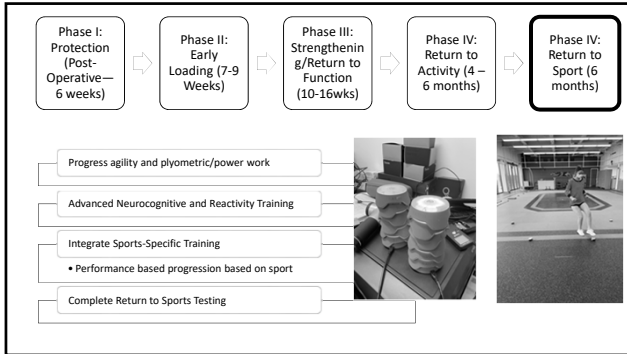
NWBing x 4 weeks, with a goal of crutch discharge by 6 weeks

No isolated Hamstring strengthening x 8 weeks

Therapeutic Alliance is Key







### Criteria for Return to Sport

1. ROM: full, pain free knee ROM, symmetrical with the uninvolved limb
2. Strength: Isokinetic testing 90% or greater for hamstring and quad at 60°/sec and 300°/sec
3. Effusion: No reactive effusion  $\geq 1+$  with sport-specific activity
4. Weight Bearing: normalized gait and jogging mechanics
5. Neuromuscular Control: appropriate mechanics and force attenuation strategies with high level agility, plyometrics, and high impact movements
6. Functional Hop Testing: LSI 90% or greater for all tests
7. Physician Clearance

## OSUWMC Sports Medicine Rehab Protocols

<https://medicine.osu.edu/departments/sports-medicine/education/medical-professionals/rehabilitation-protocols>

### TOTAL KNEE ARTHROPLASTY (TKA) POST-OP CLINICAL CARE GUIDELINE

**Objective:** Provide a standardized approach to the post-operative care of patients who have undergone total knee arthroplasty (TKA) to optimize patient outcomes and reduce the risk of complications.

**Background:** Total knee arthroplasty (TKA) is a common orthopedic procedure performed to relieve pain and improve function in patients with end-stage knee osteoarthritis. The post-operative care of these patients is critical to achieving the best possible outcomes.

**Summary of Recommendations:**

- Pain Management:** Multimodal analgesia is recommended, including acetaminophen, NSAIDs, and opioids. Opioids should be used sparingly and discontinued as soon as possible.
- Wound Care:** The surgical wound should be inspected daily for signs of infection, including redness, swelling, and drainage.
- Range of Motion (ROM):** Active and passive ROM exercises should be initiated immediately post-operatively to prevent stiffness and promote healing.
- Weight Bearing:** Patients should be encouraged to bear weight as tolerated, typically within the first 24 hours post-operatively.
- Discharge Planning:** Patients should be educated on home care instructions, including wound care, medication management, and activity restrictions.

### ADVANCED MENISCUS REPAIR: RADIAL ROOT, HORIZONTAL CLEAVAGE TEAR CLINICAL PRACTICE GUIDELINE

**Objective:** Provide a standardized approach to the post-operative care of patients who have undergone advanced meniscus repair (AMR) for radial root or horizontal cleavage tears to optimize patient outcomes and reduce the risk of complications.

**Background:** Advanced meniscus repair (AMR) is a surgical procedure performed to repair tears of the meniscus, which is a wedge-shaped piece of cartilage between the femur and tibia. The repair is typically performed using a radial root or horizontal cleavage tear repair technique.

**Summary of Recommendations:**

- Pain Management:** Multimodal analgesia is recommended, including acetaminophen, NSAIDs, and opioids. Opioids should be used sparingly and discontinued as soon as possible.
- Wound Care:** The surgical wound should be inspected daily for signs of infection, including redness, swelling, and drainage.
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