



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

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Disclosures

- Consultant for
 - Arthrex
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Objectives

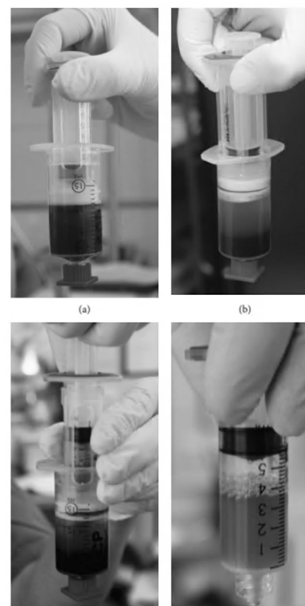
- Discuss definition and preparation methods for PRP
- Discuss data supporting PRP for musculoskeletal indications
- Define currently used 'stem cell' procedures and compare outcomes to PRP

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

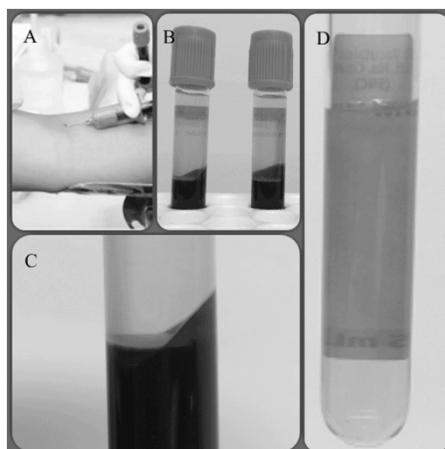
- Plasma-based method
 - Small volume of peripheral blood is drawn
 - Spin for 5 minutes to separate cells
 - Withdraw top layer to extract the PRP



C. Eichler, C. Baucks, J. Üner, C. Pahmeyer, D. Ratiu, B. Gruettner, W. Malter, M. Warm, "Platelet-Rich Plasma (PRP) in Breast Cancer Patients: An Application Analysis of 163 Sentinel Lymph Node Biopsies", *BioMed 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



Danieli 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](#) , [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 1st 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 ¹, Mandeep S Dhillon, Sameer Aggarwal, Neelam Marwaha, 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

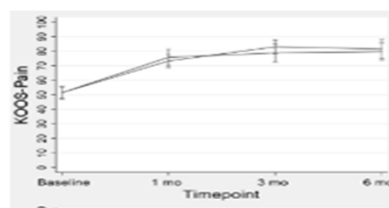
Stem Cells: Buyer Beware

- 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

Randomized Controlled Trial > Am J Sports Med. 2022 Mar;50(3):618-629.
doi: 10.1177/03635465211072554.

Bone Marrow Aspirate Concentrate Is Equivalent to Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis at 2 Years: A Prospective Randomized Trial

Adam W Anz¹, Hillary A Plummer¹, Achraf Cohen², Peter A Everts³, James R Andrews¹, Joshua G Hackel¹



A Randomized Controlled Trial. Orthop J Sports Med. 2022 Sep 16;10(9):23259671221120678. doi: 10.1177/23259671221120678. PMID: 36147791; PMCID: PMC9486262. (CC BY-NC-ND 4.0)

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# (b)(4) Donor # (b)(6)) into (b)(4) vials (2cc each). The microbial sample of starting material (umbilical cord blood) showed one colony of growth on 21 May 2018. These vials (all (b)(4)) were shipped to customers in (b)(4) and (b)(4) among other locations.

On 18 AUGUST 2018, your firm processed an umbilical cord blood product (label# (b)(4) and Donor # (b)(6)) into (b)(4) vials (1 or 2cc each). The serology testing for the donor showed positive markers for Chagas disease and Hepatitis B (HBsAg). (b)(4) of these vials were shipped to customers in (b)(4) and (b)(4) among other locations.

On 9 JUNE 2018, your firm processed an umbilical cord blood product (label# (b)(4) and Donor # (b)(6)) into (b)(4) vials (1 or 3cc each). The sterility testing of plasma separated during the process showed growth of Gram Positive Cocci. (b)(4) of these vials were shipped to customers in multiple locations, including (b)(4).

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 1;21(5):155-158. doi: 10.1249/JSR.0000000000000959.

Meniscus Root Tears: A Clinical Review

Elena Randazzo¹, Robert Duerr², Michael R Baria¹

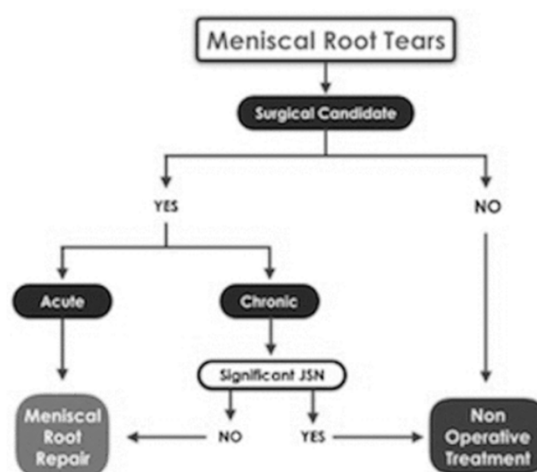
Affiliations + expand

PMID: 35522439 DOI: 10.1249/JSR.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

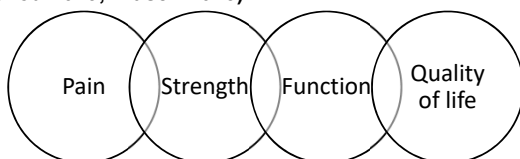
John DeWitt, PT, DPT, AT
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Objectives

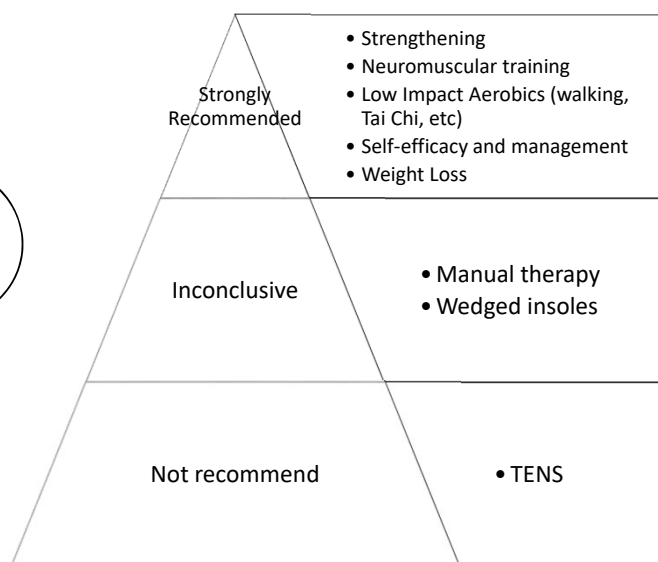
1. Review value of PT to manage knee OA
2. Identify key components to improve knee OA outcomes
3. Describe meniscal root injuries rehabilitation milestones
4. Discuss functional assessment use to reduce injury risk
5. Provide resources for rehabilitation guidelines

Discuss the Value of Physical Therapy with Knee OA Pain

Physical therapy improves (Skou 2019, Frasen 2015)

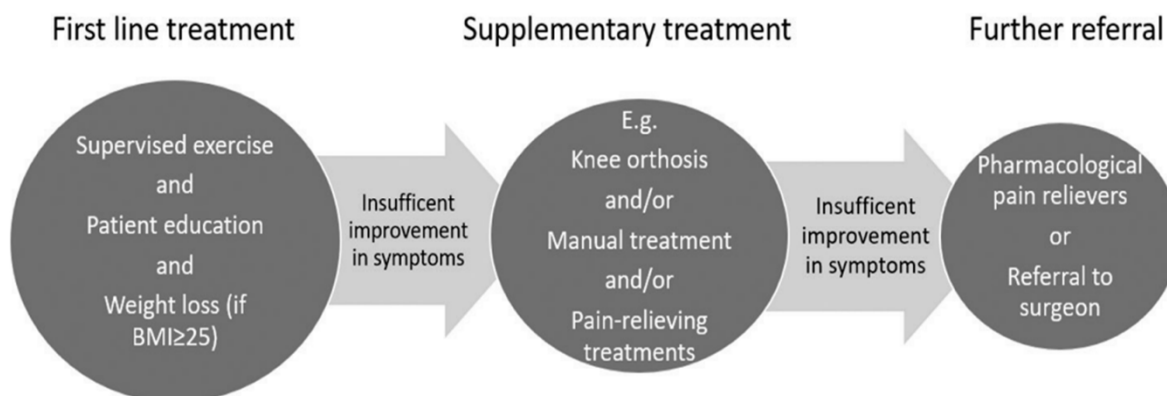


3 out of 4 delayed TKA for 1 year, 2 out of 3 delayed TKS for >2 years (Skou 2015, 2018)



Kolasinski 2019, McMurray 2017

Get into Physical Therapy Early



Skou, 2019

Physical Therapy is Effective in Managing Knee OA

Timeframe: 12 weeks 1-2x/week

Education	Strengthening	Neuromuscular Balance	Physical Activity
<ul style="list-style-type: none"> • Self-efficacy • Shared-decision making • 0-5/10 pain is ok 	<ul style="list-style-type: none"> • Focus on quad and hip strength 	<ul style="list-style-type: none"> • Single limb positions • Movement/gait corrections 	<ul style="list-style-type: none"> • 8,000-10,000 step/day • Match activity based on response • Weight loss

Van Doormaal 2020, Skou 2019, Fransen 2015

Quad Strength is Critical

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

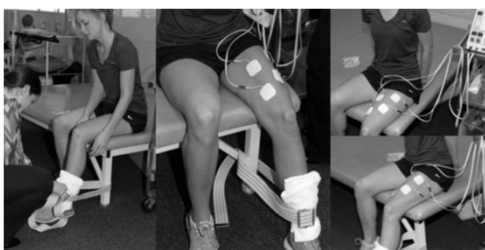
Avoid underdosing

- 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

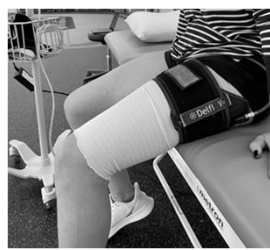


Effective Supplements to Improve Quad Strength



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 hyper-flexion/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

Sanjeev Bhatia ¹, Christopher M LaPrade ², Michael B Ellman ³, Robert F LaPrade ⁴

Affiliations + expand

PMID: 24623276 DOI: 10.1177/0363546514524162

Bhatia 2014

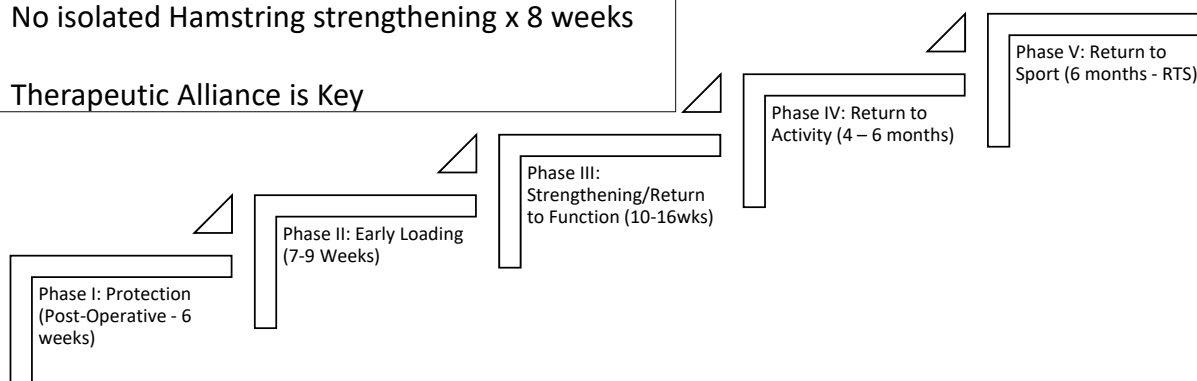
Meniscal Root Rehab Precautions

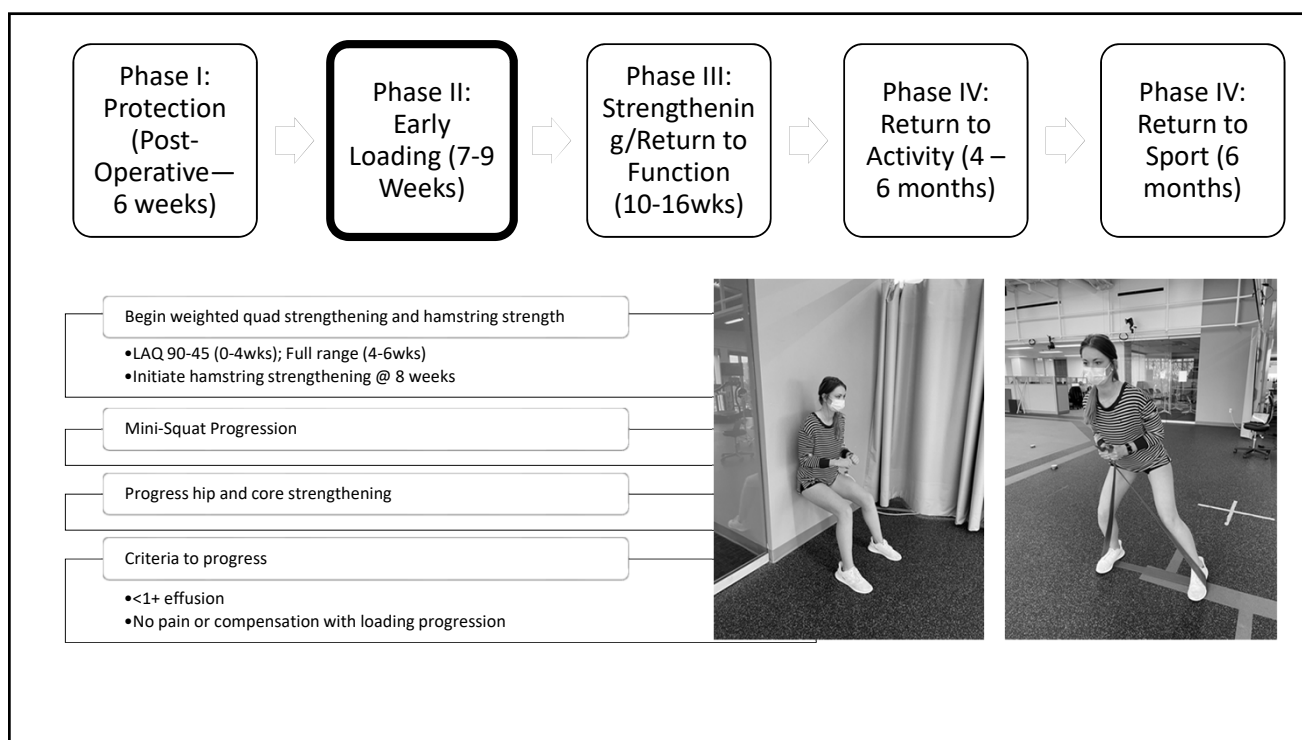
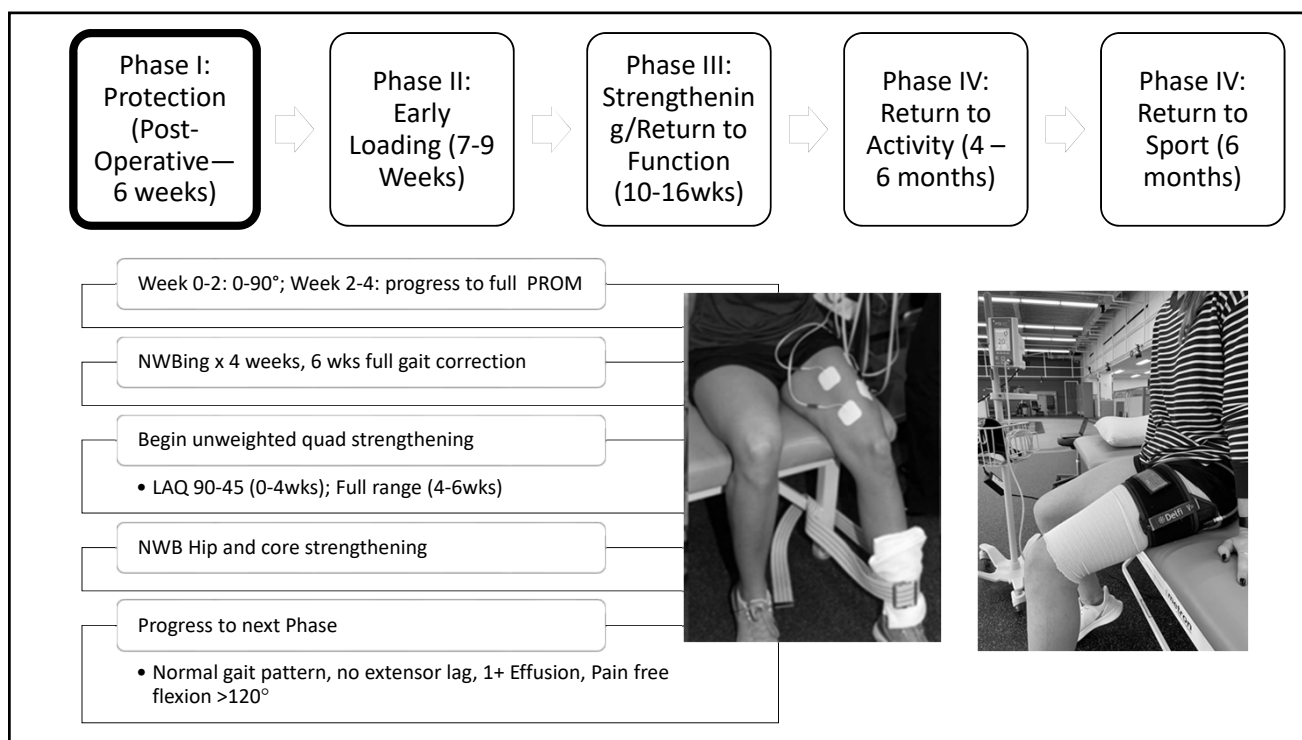
TROM immobilizer for first 10-14 days post-op

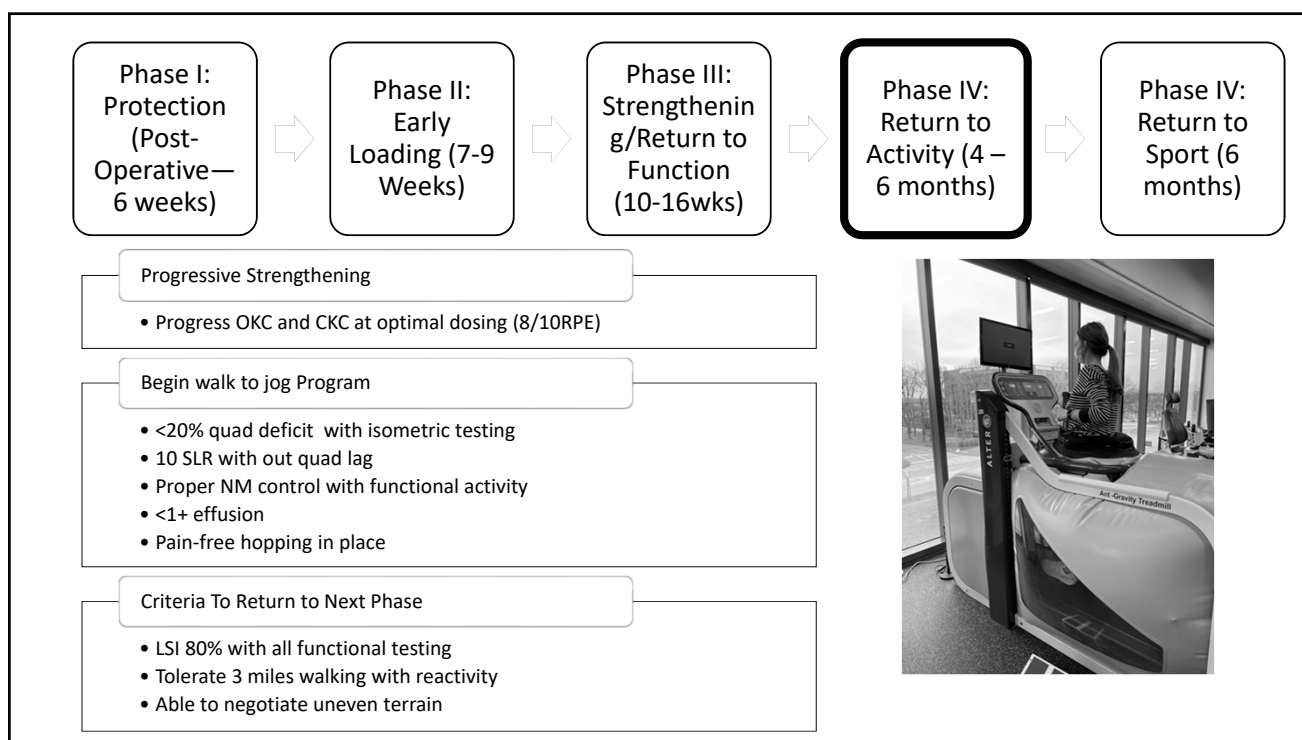
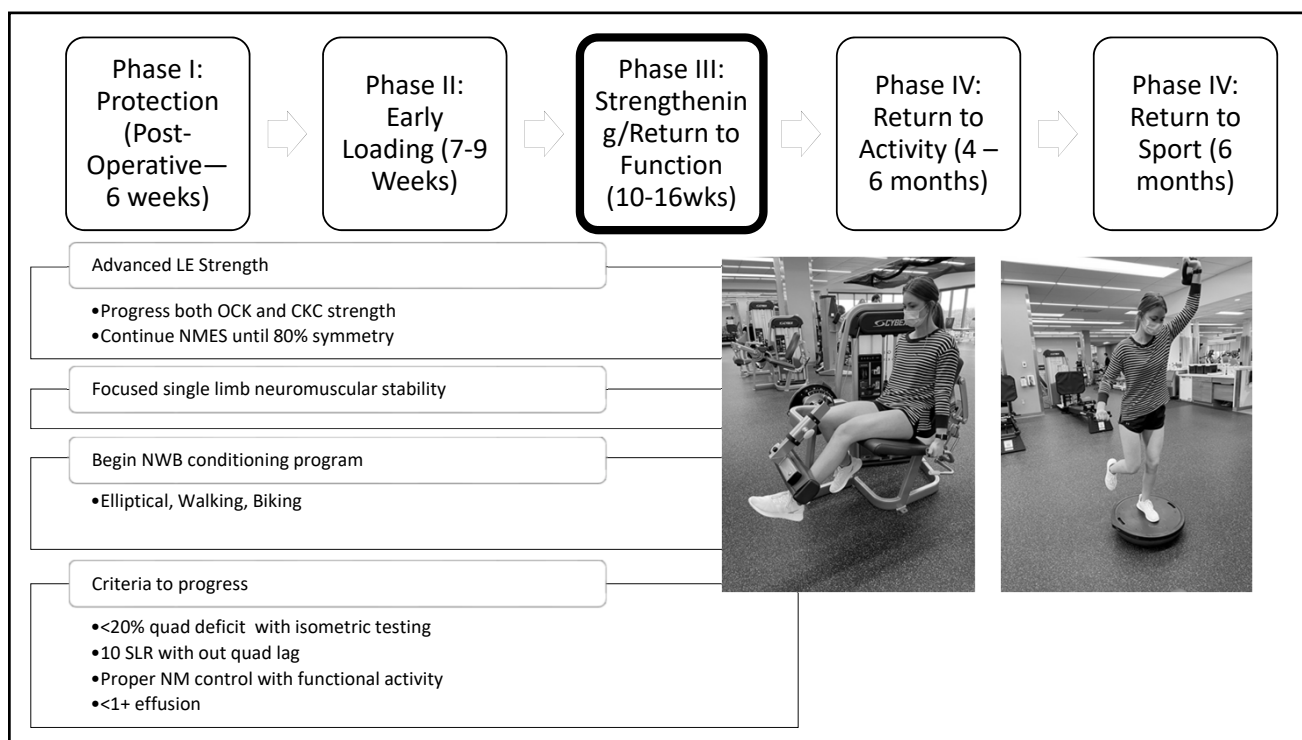
NWBing x 4 weeks, with a goal of crutch discharge by 6 weeks

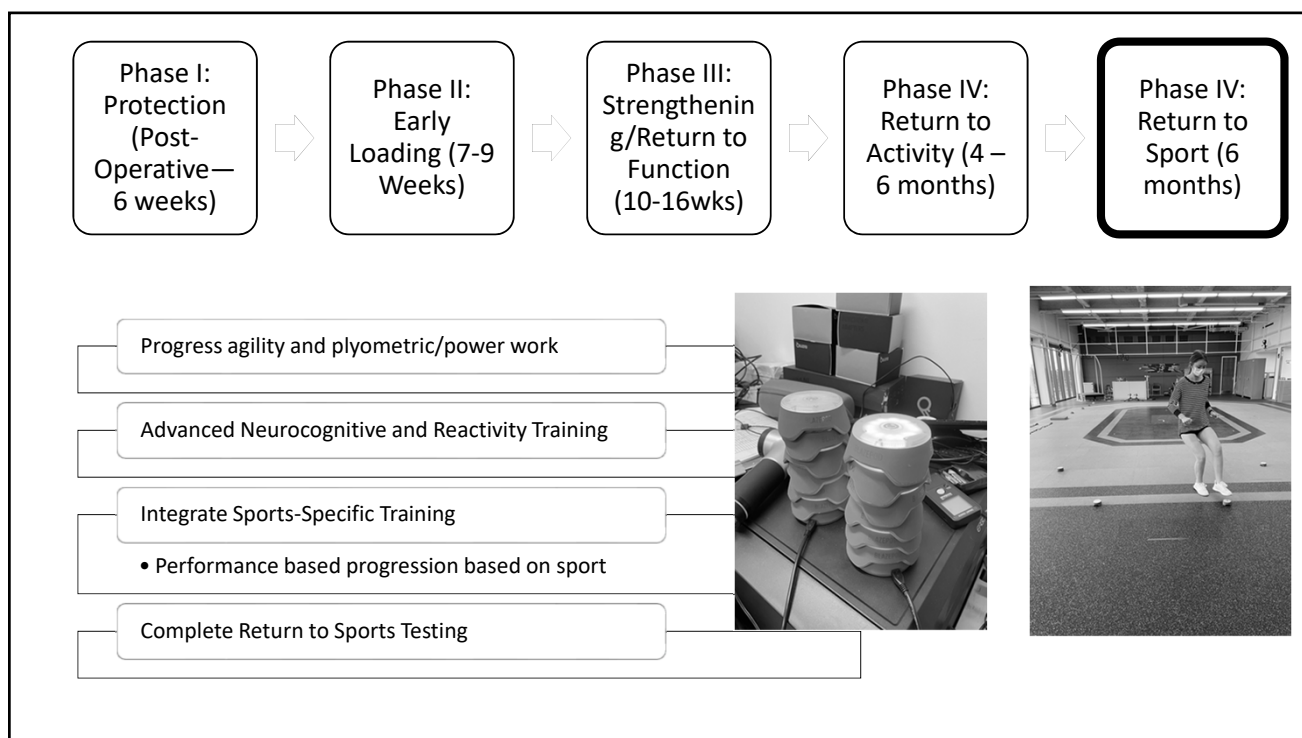
No isolated Hamstring strengthening x 8 weeks

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

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Sports Medicine Rehabilitation Protocols

Our evidence-based post-procedure rehab guidelines helps facilitate a successful return to activity.

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Sports Medicine Academics and Research

Ohio State physicians and physical therapists work collaboratively to develop best clinical practices for post-surgical rehabilitation. The path to regaining range of motion, strength and function can require a sustained and coordinated effort from the patient, his or her family, the Ohio State Sports Medicine physical therapy team and sometimes, other healthcare providers. While each individual's progress differs based on their age, health, rehab compliance and injury severity, our team has established time frames, precautions and progression criteria that help ensure a safe return to sport.

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

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

Total knee arthroplasty (TKA), also known as a total knee replacement, is an elective surgical procedure to treat patients who experience pain and dysfunction from an arthritic knee joint. TKA is an effective option if the patient's pain does not respond to conservative treatment and has caused a decline in their health, quality of life, or ability to perform activities of daily living. This procedure removes the arthritic structures that make up the knee joint and replace them with artificial implants.

With advancements in modern medicine, there have been several effective surgical approaches developed for TKA. The surgeon will determine the best surgical approach to use for each individual. Patients are encouraged to participate in early mobilization while adhering to precautions in order to improve

Disclaimer: Progression is time and criterion-based, dependent on evaluation. Contact your orthopedic surgeon or surgical staff if you have care guidelines, please contact the author by calling our office at (614)

Summary of Recommendations

Expectations	<ul style="list-style-type: none">Outpatient rehabilitation is expected for every patient after discharge from hospital. Home health may be performed initially to increase mobility and achieve community distance ambulation prior to independent rehab.
Precautions	<ul style="list-style-type: none">Signs of DVT: refer directly to IDT<ul style="list-style-type: none">Localized tenderness along the distribution of deep venous systemEdema LE swellingCalf swelling >3cm compared to asymptomatic limbDistal rednessConstant mechanical locking or clunk (refer to surgeon for re-evaluation)Lack of full knee extension by 4-6 weeks (refer to surgeon for re-evaluation)AD required for ambulation after post-op week 8 (NO follow up visit)
Weight Bearing Progression	<ul style="list-style-type: none">ROM: Full active knee extension, no pain on passive compressionStrength: Able to perform during gait training with full safety and superior gaitgait and able to perform 10-15 SLR without quad lag60 sec of SLR without compensation or painWeight Bearing: Demonstrates pain-free ambulation without visible gait deviation<ul style="list-style-type: none">Goal: GC AD to post-op week 10 (NO follow up visit)
Criteria to Discharge Assistive Device	<ul style="list-style-type: none">L solid - 2 weeksR solid - 4-6 weeksSee Phys for further criterion
Return to Driving	<ul style="list-style-type: none">L solid - 2 weeksR solid - 4-6 weeksSee Phys for further criterion
Range of Motion Progression	<ul style="list-style-type: none">Knee ext APROM:<ul style="list-style-type: none">Neutral extension - week 2Knee extension symmetrically between sides (as applicable) - week 4-6Proximal achieving full knee extension APROMKnee flex APROM:<ul style="list-style-type: none">Lack of full knee extension by 4 weeks (refer to surgeon for re-evaluation)80 by 1 week90 by 2 weeks100-110 by 4-6 weeks120 by 8-12 weeks130 by 12-14 by 6 weeks, refer to surgeon for re-evaluationConsider patient knee flexion ROM requirements based on social work noted response regarding desired level of more aggressive ROM may be required. Refer to surgeon for guidance as needed
Patient Reported Outcomes (PROs)	<ul style="list-style-type: none">Consistently collect at least one of the following PROs each visit:<ul style="list-style-type: none">Knee Injury and Osteoarthritis Outcome Score (KOOS)International Knee Declaration Committee (IKDC)Lower Extremity Functional Scale (LEFS)
Considerations Regarding Running and Plyometrics	<ul style="list-style-type: none">High impact activities such as plyometrics and running are generally not advised following total joint replacements. The first priority following these surgeries is to prevent damage to the new artificial joint and surrounding structures. Patients are advised to participate in low impact exercises/recreational activities. Patients should consult with their physician to resume contact sports should consult with their surgeon.

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

Disclaimer

The following rehabilitation guidelines are specific to patients who have undergone an advanced meniscus repair of a radial, root or horizontal cleavage tear. These refer to the Ohio State Sports Medicine website for

Progression is criterion-based and dependent on evaluation. The time frames identified in this guideline are not recommended as guide progression is based upon the achievement noted at the end of each phase.

Background

Meniscal root/cleavage tears present in a radial tears can have a profound effect on the mechanical environment of the knee joint and can lead to an advanced degeneration of the meniscus activity. The listed clinical recommendations

The rehabilitation recommendations are evidence-based practice. Progression patient demonstrating readiness by and

Summary of Recommendations

Precautions	<ul style="list-style-type: none">Weight and bearing recommendations are based on knee morphology and intra-operative findings. Recommendations are below. However, ALWAYS refer to the operative note or contact the surgical team for clarification.For root/cleavage tears - no resisted isometric hamstring strengthening at all weeksMany of these patients will be encouraged to wear a medial unloader brace for the first 12 months post-op
Risk Factors	<ul style="list-style-type: none">The patient should be monitored for signs and symptoms of DVT (see Red/Yellow Flag section)
Weight Bearing/Bracing	<ul style="list-style-type: none">Root Repair:<ul style="list-style-type: none">Refer to surgeon for first 10-14 days post-opWalking 4 weeks, with a goal of crutch discharge by 6 weeksRadial Repair:<ul style="list-style-type: none">Typically walking 4 weeks, with a goal of crutch discharge by 6 weeksWalking status and training are patient dependent - always refer to the operative note or contact the surgical team for clarificationHorizontal Cleavage Repair:<ul style="list-style-type: none">No braceWalking 2-4 weeks, crutches should be discharged no later than 6 weeks
Range of Motion	<ul style="list-style-type: none">Please refer to the "post-op plan" section of the operative note or contact the surgeon for clarificationWeek 0-2 90°Week 2-4 progress to full PROMSymmetrical knee extension should be achieved by week 4. If not achieved by week 4, contact surgeon
Outcome Tools	<ul style="list-style-type: none">Collect the LEFS at each visitYou may choose to include KOOS, KOOS ACLASL, Tegner or other questionnaires specific to your patient's needs
Hamstring Considerations	<ul style="list-style-type: none">No hamstring precautions for horizontal cleavage repairsRoot/Radial Repairs: No resisted isometric hamstring strengthening at all weeks
Functional Testing	<ul style="list-style-type: none">Isometric Testing:<ul style="list-style-type: none">Root/Radial Repairs: 4 monthsHorizontal Cleavage Repairs: 3 monthsIsokinetic Testing:<ul style="list-style-type: none">Root/Radial Repairs: 6 monthsHorizontal Cleavage Repairs: 4 monthsHigh testing should be avoided until 6 months post-op and is only appropriate after 80% symmetry is achieved on isokinetic testing<ul style="list-style-type: none">Crutch over topTaped to top*Functional strength testing and hop testing should be reserved for patients returning to high level activity

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