AUTOLOGOUS CHONDROCYTE IMPLANTATION (ACI) CLINICAL PRACTICE GUIDELINE

Background

Autologous chondrocyte implantation (third generation) is a two stage surgical procedure indicated for medium to large (≥2 cm^2) symptomatic full thickness chondral lesions. Stage one is performed arthroscopically, where a small sample of healthy cartilage is harvested from a non-weight bearing area of the knee. The chondrocyte sample is sent to a laboratory where the cells are cultivated on a scaffold for 4-6 weeks. Stage two is performed through an open procedure, or arthrotomy. The cartilage defect is exposed and debrided to an area with vertical margins. The scaffold implant is placed in the defect and secured fibrin sealant. These third generation ACI techniques eliminate the suture fixation previously required with second-generation ACI procedures. The various implantation procedures are as follows:

- Matrix-Induced Autologous Chondrocyte Implantation (MACI)- thin scaffold seeded with chondrocytes
- NeoCart- chondrocytes growing and producing extracellular matrix throughout scaffold
- NovoCart- full thickness scaffold seeded with chondrocytes

Disclaimer

Progression is time and criterion-based, dependent on soft tissue healing, patient demographics and clinician evaluation. If you are working with an Ohio State Sports Medicine patient and questions arise, please call 614-293-2385.

Summary of Recommendations

Expectations	• PT and CPM should begin at post-op day 7-10 days • Return to sport: 12-15 months • Please review operative report as lesion size and location may dictate speed of progression
Risk Factors	• CI requires extensive rehabilitation and can often exhaust insurance approved PT visits. Consider decreasing initial visit frequency, use of home NMES unit and daily self-ROM. • Long-term quadriceps strength deficits typically present >1 year post-operatively.

Concomitant Procedures	• Do not change protocol based on multiple defects, meniscus repair or ligamentous reconstruction
	  • If multiple defects include a patellofemoral lesion, following the patellofemoral precautions
	• TTO Adjustments:
	  • Open brace to 0-35° at weeks 5-6
	  • All CKC interventions performed through protected ROM (90-45°) before transition to full ROM

Weight Bearing Progression	**Tibiofemoral (No Brace)** • Phase 1 *(week 1):* NWBing • Phase 2 *(week 2-3):* 25% BW (weeks 1-2) to 50% BW (week 3) • Phase 3 *(weeks 4-5):* 60% BW (week 4) to 80% BW (week 5) • Phase 4 *(weeks 6-7):* 90% to100% BW • Phase 5 *(weeks 8-10):* Full BW with normal gait pattern	**Patellofemoral (TROM Extension Brace)** • Phase 1-3 *(weeks 1-5):* Full BW, brace locked in full extension ○ Open brace at week 5-6 • Phase 4 *(weeks 6-7):* Discharge brace • Phase 5 *(weeks 8-10):* Normal gait without brace
Range of Motion Progression	• Phase 1/2 *(weeks 1-3):* 0-45° (week 2) to 0-90° (week 3) • Phase 3 *(weeks 4-5):* 0-105° (week 4) to 0-120° (week 5) • Phase 4 *(weeks 6-7):* 0-125° (week 6) to 0-135° (week 7) • Phase 5 *(weeks 8-10):* Full AROM • **Same ROM progression for tibiofemoral and patellofemoral lesions**	

Functional Testing	• Isometric testing: 4-5 months (at 90 degrees)
	• Isokinetic testing: 6, 9, 12 months and discharge
	• Hop testing (Appropriate after 80% symmetry achieved on isokinetic testing)
	  ○ SL hop for distance
	  ○ Triple hop
	  ○ Cross over hop
	  ○ Timed 6m hop
	Functional strength testing and hop testing should be reserved for patients returning to high-level activity	

Patient Reported Outcomes	Collect at least one of the following at initial evaluation, every 6 weeks and discharge. Be consistent with which outcome tool is collected. • Knee Injury and Osteoarthritis Outcome Score (KOOS) • International Knee Documentation Committee (IKDC)	
Criteria to Discharge Assistive Device	1. ROM: Full active knee extension; no pain on passive overpressure 2. Strength: Able to perform strong quad isometric with full tetany and superior patellar glide and able to perform 2x10 SLR without quad lag 3. Effusion: 1+ or less is preferred (2+ acceptable if all other criteria are met) 4. Weight Bearing: Demonstrates pain-free ambulation without visible gait deviation **Tibiofemoral lesions: PWBing for 6-8 weeks. See above WBing progression**	
Criteria to Initiate Running and Jumping	1. ROM: full, pain-free knee ROM, symmetrical with the uninvolved limb 2. Strength: Isokinetic testing 80% or greater for hamstring and quad at 60º/sec and 300º/sec 3. Effusion: 1+ or less 4. Weight Bearing: normalized gait and jogging mechanics 5. Neuromuscular Control: Pain-free hopping in place	
Criteria for Return to Sport	1. ROM: full, painfree knee ROM, symmetrical with the uninvolved limb 2. Strength: Isokinetic testing 90% or greater for hamstring and quad at 60º/sec and 300º/sec 3. Effusion: No reactive effusion ≥ 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	

Chondrocyte Rehabilitation Maturation Phases

Phases of post-operative rehabilitation and the associated graft maturation timeline

Rehabilitation Phase	Stage of Repair Tissue
Phase 1: weeks 0-1	Implantation and protection (0-6 weeks)
Phase 2: weeks 2-3	
Phase 3: weeks 4-6	
Phase 4: weeks 7-12	Transition and proliferation (6-12 weeks)
Phase 5: months 3-6	Remodeling (12-26 weeks)
Phase 6: months 6-9	
Phase 7: months 9-RTS	Maturation (26 weeks onward) ***The graft will continue to remodel for up to 1 year post-op****

Red/Yellow Flags

Red Flags ***(signs/symptoms that require immediate referral for re-evaluation)***	• Signs of DVT *(Refer directly to ED)*
	  • Localized tenderness along the distribution of deep venous system
	  • Entire LE swelling
	  • Calf swelling >3cm compared to asymptomatic limb
	  • Pitting edema
	  • Collateral superficial veins
	• Mechanical block or clunk *(Refer to surgeon for re-evaluation)*
	• Lack of full knee extension by 4-6 weeks *(Refer to surgeon for re-evaluation)*

Yellow Flags (*signs/symptoms that require modification to plan of care)*	• Persistent reactive pain or effusion following therapy or ADLs • *Decrease intensity of therapy interventions, continue effusion management and provide patient education regarding activity modification until reactive symptoms resolve*

Phase I: Weeks 0-1

Patients will not begin physical therapy until post-operative days 7-10. Phase 1 will be completed independently through a home exercise program provided on the day of surgery. Formal physical therapy will begin in Phase 2.

Goal	Maintain joint mobility and muscle tone while adhering to all post-operative precautions
Range of Motion	• 0-45° • CPM to start at day 7-10
Weight Bearing	Tibiofemoral**:** ≤20% BW Patellofemoral: Full BW, brace locked in full extension
Suggested Interventions	• Ankle pumps • Quadriceps, hamstring and gluteal isometrics • Diaphragmatic breathing • Effusion management strategies, including RICE

Phase II: Weeks 2-3

Goals	The patient should achieve pain-free and full passive knee extension. Focus is placed on maintaining muscle tone, ensuring proper wound healing and effusion management.
Range of Motion	**0-90°** **Achieved though CPM and AAROM (heel slides, wall slides, AAROM row machine)** • *Total volume: 300+ repetitions per day* *Goal: early AROM though safe range*
Weight Bearing	Tibiofemoral**:** 30% to 50% BW Patellofemoral: Full BW, brace locked in full extension
Suggested Interventions	• Ankle pumps • Quadriceps, hamstring and gluteal isometrics • Prone TKE • SLR-4 way • Patellar mobilization in all directions • Gait training • Extension ROM: Seated towel stretch, prone hang, bag hang • Flexion ROM: heel slides, wall slides, AAROM row machine • Recumbent cycling- for ROM only (week 3) • SAQ (no resistance) • LAQ (no resistance, through protected ROM (90-45 degrees) • Continue CPM, effusion management and NMES in long sitting For PF lesions only: *(Must be performed in locked knee brace)* o Weight shifting o DL heel raise o SL balance • NMES in long sitting
NMES Parameters (in long sitting)	• NMES pads are placed on the proximal and distal quadriceps • Patient: Seated in long sitting (knees extended) • The patient is instructed to relax while the e-stim generates at least 50% of their max volitional quadriceps contraction OR maximal tolerable amperage without knee joint pain • 10-20 seconds on/ 50 seconds off x 15 min
Criteria to Progress to Phase 3	By the end of week 3: • Pain-free knee flexion of 90° • Pain-free and full passive knee extension • Proficient heel-to-toe gait with 50% BW for tibiofemoral grafts or full BW for patellofemoral grafts • Reduced and well-controlled post-operative pain and edema • Ability to perform a strong isometric quadriceps contraction (full tetany and superior patellar glide) • Proficiency with home-exercise program

Phase III: Weeks 4-6

Goals	Emphasis is placed on increasing knee flexion ROM and improving quadriceps, gluteal and core strength
Range of Motion	**0-105° (week 4) to 0-125° (week 6)** **Achieved though CPM and AAROM (heel slides, wall slides, AAROM row machine)** • *Total volume: 300+ repetitions per day* *Goal: early AROM though safe range*
Weight Bearing	Tibiofemoral**:** 60% BW (week 4) to 80% BW (week 5) Patellofemoral: Full BW, open brace at weeks 5-6

Suggested Interventions	• Continue Phase 1 and 2 interventions
	• SLR-Flexion progressions
	  ○ Semi-reclined or seated
	  ○ Add ER
	  ○ Perform with eyes closed (cortical training)
	  ○ Speed
	  ○ Isometric holds at end-range
	• Heel slides
	• Clamshells
	• Seated or standing hip ab/adduction (depending on WBing status)
	• Trunk stability interventions
	  ○ TrA isometric progression
	  ○ Prone/side planks
	• Upright cycling (weeks 5-6)
	• Standing TKE (weeks 6-8)
	• Partial BW Shuttle Press (week 6-8)
	• OKC Hamstring strengthening (week 6-7)
	• Progress NMES to seated with tibia fixed at 60° of knee flexion
	• Discharge CPM at 6 weeks
	• Continue effusion management strategies

NMES Parameters (with tibia fixed at 60° of knee flexion)	• NMES pads are placed on the proximal and distal quadriceps • Patient: Seated with the knee in at least 60º flexion, shank secured with strap and back support with thigh strap preferred. The ankle pad/belt should be two finger widths superior to the lateral malleoli • The patient is instructed to relax while the e-stim generates at least 50% of their max volitional contraction against a fixed resistance OR maximal tolerable amperage without knee joint pain • 10-20 seconds on/ 50 seconds off x 15 min
Criteria to Progress to Phase 4	By the end of week 6: • Pain-free active knee flexion to 125° • Pain-free gait with 80% BW for tibiofemoral grafts or full BW for patellofemoral grafts • 3x10 SLR without quadriceps lag • Proficiency with home exercise program

Phase IV: Weeks 7-12

Goals	The patient works toward movement independent of ambulation devices and knee braces. Full ROM should be achieved and balance/proprioception interventions are initiated.
Range of Motion	0-125° (week 6), 0-135° (week 7) to full ROM (week 8-10)
Weight Bearing	Tibiofemoral**:** 90% BW (week 6), 100% BW (week 7) to full WBing without obvious gait deviation (week 10) Patellofemoral: Discharge brace
Suggested Interventions	• Continue Phase 2 and 3 interventions • Continue ROM interventions until symmetrical ROM is achieved • Partial BW Shuttle Press (week 6-8) • OKC Hamstring strengthening (week 6-7) • Multi-angle isometrics • Balance and proprioception interventions • Mini squats: 0-45 degrees (week 8-10) • Heel Taps: 2-4" (weeks 10-12) • Step Ups: 6-8" (weeks 10-12) • Resisted OKC quadriceps strengthening through 90-45° protected ROM (week 10-12) • Continue NMES (seated with tibia fixed at 60° of knee flexion) • Continue effusion management strategies as needed
Criteria to Discharge Assistive Device	1. ROM: Full active knee extension; no pain on passive overpressure 2. Strength: Able to perform strong quad isometric with full tetany and superior patellar glide and able to perform 2x10 SLR without quad lag 3. Effusion: 1+ or less is preferred (2+ acceptable if all other criteria are met) Weight Bearing: Demonstrates pain-free ambulation without visible gait deviation
Criteria to Progress to Phase 5	By week 12: • Pain-free active ROM • Pain-free upright cycle ergometry • Pain-free ambulation without visible gait deviation • Proficiency in home exercise program

Phase V: Months 3-6

Goals	The majority of patients return to work either on a part-time or full-time basis. Patients should continue skilled physical therapy to progress functional, CKC strengthening.
Range of Motion	Full AROM
Weight Bearing	Full WBing, normal gait without brace
Suggested Interventions	• Continue Phase 3 and 4 interventions • Bridging • Standing SL calf raises • Resisted OKC quadriceps strengthening through full ROM (week 12-14) • Lunges • SL sit to stand, through protected ROM • Elliptical • Outdoor cycling if desired (months 5-6) • Rowing ergometry as tolerated (months 5-6) • Continue NMES until 80% symmetry is obtained • Continue effusion management as needed
Isometric Testing	Isometric testing is appropriate at 4-4.5 months
Criteria to Progress to Phase 6	By 6 months: • Ability to negotiate stairs and mild gradients without pain or reactive effusion • Return to work, depending on the demands of the job • Ability to perform 3x10 heel raise on 6” step with neutral frontal and sagittal plane alignment • Proficiency in home exercise program

Phase VI: Months 6-9

Goals	Patient progress OKC interventions. Strength testing is performed to determine readiness to initiate light plyometrics and walk-jog progression.
Range of Motion	Full AROM
Weight Bearing	Full WBing, normal gait without brace

Suggested Interventions	• Continue phase 3-5 interventions
	• Progress and increased difficulty of OKC exercises
	• Continue to progress SL eccentric strengthening through body weight and machine interventions
	• Once strength criteria have been met, perform the following progression:
	  ○ PBW jumping on the shuttle (DL → SL)
	  ○ Full body weight jumping progression
	• Walk-jog program

Isokinetic Testing	Isokinetic testing is appropriate at 6 and 9 months **Functional strength testing should be reserved for patients returning high-level activity**
Criteria to Initiate Running and Jumping	1. ROM: full, pain-free knee ROM, symmetrical with the uninvolved limb 2. Strength: Isokinetic testing 80% or greater for hamstring and quad at 60º/sec and 300º/sec 3. Effusion: 1+ or less 4. Weight Bearing: normalized gait and jogging mechanics 5. Neuromuscular Control: Pain-free hopping in place
Criteria to Progress to Phase 7	By 9 months: • Quadriceps and hamstring symmetry of 80% or greater • Ability to tolerate walking distances of 3 miles or greater without reactive pain or effusion • Ability to effectively negotiate uneven ground, including soft sand, without reactive pain or effusion • Ability to return to pre-operative low-impact recreational activities, including cycling, elliptical and weight training

Phase VII: Months 9-Return to Sport

Goals	The patient is able to resume all normal functionality and will continue to progress towards return to sport.
Range of Motion	Full AROM
Weight Bearing	Full WBing, normal gait without brace
Suggested Interventions	• Continue phase 3-6 interventions • Step-hold progression to SL hop progression • Sports-specific training • Agility • Plyometrics
Isokinetic Testing	Isokinetic testing is appropriate at 12 months and discharge **Functional strength testing and hop testing should be reserved for patients returning high-level activity**
Criteria to Return to Sport	1. ROM: full, painfree knee ROM, symmetrical with the uninvolved limb 2. Strength: Isokinetic testing 90% or greater for hamstring and quad at 60º/sec and 300º/sec 3. Effusion: No reactive effusion ≥ 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
	Activities that generate high compression, shear and rotational loads are to be avoided until 12-18 months, or as directed by orthopaedic surgeon ***Full RTS expected between 12-15 months post-operatively***

Author: Caroline Lewis, PT, DPT, SCS, AT
Reviewers: Laura C. Schmitt, PT, MPT, PhD; David C. Flanigan, MD, Jay Ebert, PhD

References

Minas T, Peterson L. Autologous chondrocyte implantation. *Op Tech in Orth.* 1997;7(4):323-333.

O'Driscoll S, Keeley F, Salter R. Durability of regenerated articular cartilage produced by free autogeneous periosteal grafts in major full-thickness defects in joint surfaces under the influence of continuous passive motion. *J Bone Joint Surg Am.* 1988;70:595-606.

Rodrigo J, Steadman R, Fulstone H. Improvement of full-thickness chondral defect healing in the human knee after debridement and microfracture using continuous passive motion. *Am J Knee Surg*. 1994;7:109-16.

Salter RB. The physiologic basis of continuous passive motion for articular cartilage healing and regeneration. *Hand Clin.* 1994;10(2):211-9.

McAllister DR, Joyce MJ, Mann BJ, Vangsness CT Jr. Allograft update: the current status of tissue regulation, procurement, processing, and sterilization. *Am J Sports Med.* 2007;35:2148-2158.

Minas T. The role of cartilage repair techniques, including chondrocyte transplantation, in focal chondral knee damage. *Instructional Course Lectures.* 1999;48:629-43.

Ebert JR, Ackland T, Lloyd DG, Wood DJ. Accuracy of partial weight bearing after autologous chondrocyte implantation. *Arch Phys Med Rehabil.* 2008;89(8):1528-34.

Ebert JR, Robertson WB, Lloyd DG, Zheng MH, Wood DJ, Ackland T. Traditional vs accelerated approaches to post-operative rehabilitation following matrix-induced autologous chondrocyte implantation (MACI): comparison of clinical, biomechanical and radiographic outcomes. *Osteoarthritis Cartilage.* 2008;16:1131-40.

Enright PL. The six-minute walk test. *Respir Care.* 2003;48(8):783-5.