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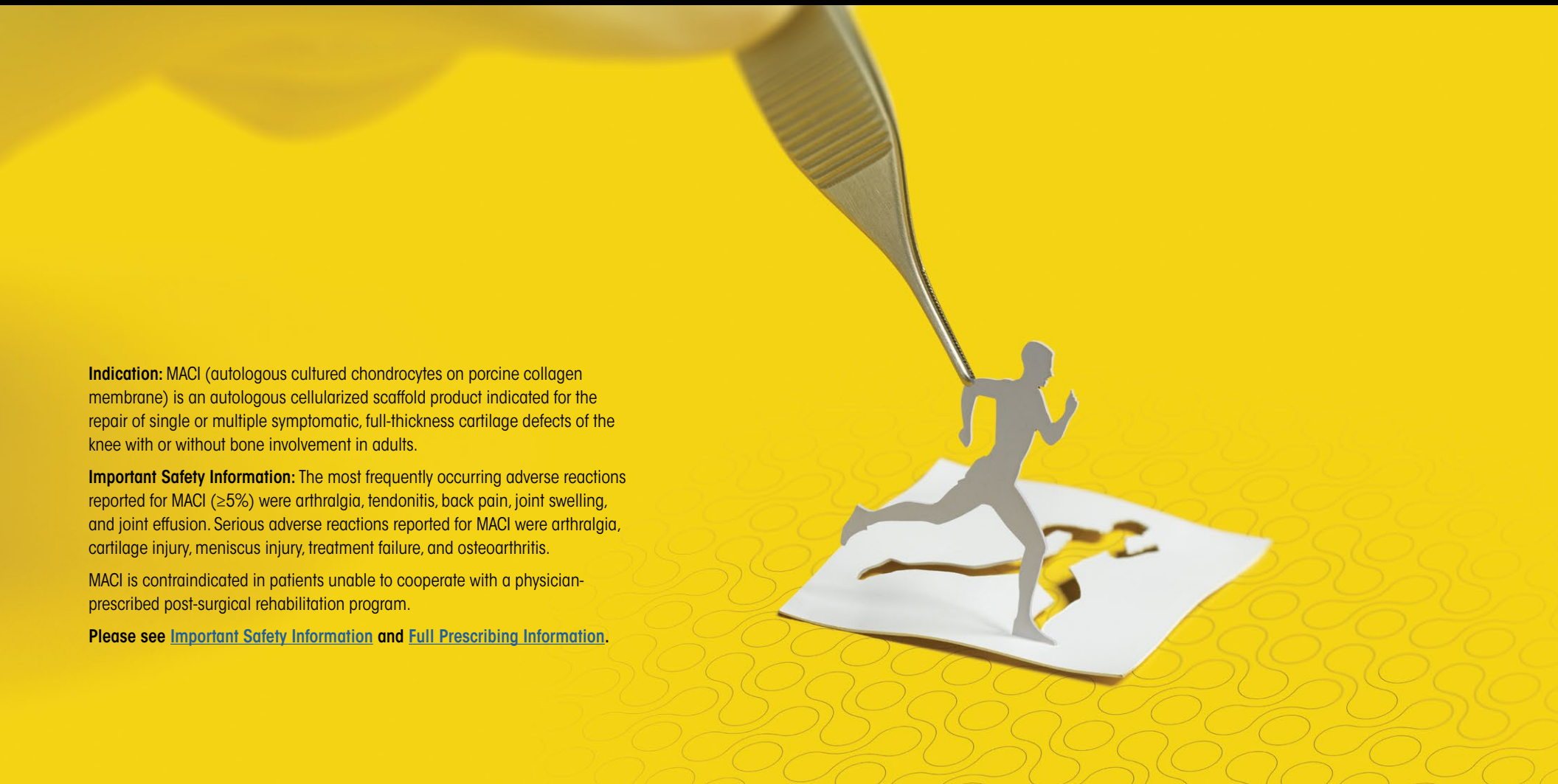
REHABILITATION MANUAL

Guidelines for the functional recovery of patients following MACI for the treatment of cartilage defects of the adult knee



Indication: MACI (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the knee with or without bone involvement in adults.

Important Safety Information: The most frequently occurring adverse reactions reported for MACI (≥5%) were arthralgia, tendonitis, back pain, joint swelling, and joint effusion. Serious adverse reactions reported for MACI were arthralgia, cartilage injury, meniscus injury, treatment failure, and osteoarthritis.

MACI is contraindicated in patients unable to cooperate with a physician-prescribed post-surgical rehabilitation program.

Please see Important Safety Information and Full Prescribing Information.

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REHABILITATION MANUAL

ABOUT THIS MANUAL

This manual provides guidance on how to develop an optimal physician-prescribed rehabilitation program related to MACI (autologous cultured chondrocytes on porcine collagen membrane).

The MACI rehabilitation program is intended to foster early mobilization and load protection, promote graft maturation, and reduce the risk of graft delamination, post-operative thromboembolic events, and joint stiffness. It outlines a path to a progressive return to full range of motion (ROM) and weight bearing (WB), as well as muscle strengthening and conditioning. The MACI rehabilitation program is comprised of three distinct phases. An overview is provided on page 3.

The rehabilitation program in this manual was designed using the knowledge of basic science, anatomy, and the biomechanics of articular cartilage, as well as the natural course of healing following implantation. Much of the program is driven by the work of Dr. Jay Ebert in Australia.[1,2]

This manual reflects clinical expertise derived from the Delphi technique—a method of congregating expert opinion through a series of iterative questionnaires, with a goal of coming to a group consensus—conducted with a panel of US orthopedic surgeons experienced with MACI implantation.[3]

Please see Important Safety Information and Full Prescribing Information or visit MACI.com

REFERENCES:

1. MACI Rehabilitation Manual: Guidelines for the functional recovery of patients following MACI for the treatment of cartilage defects of the knee. 2018. Vericel Corporation.
2. 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.
3. Flanigan, D. C., Sherman, S. L., Chilelli, B., Gersoff, W., Jones, D., Lee, C. A., Toth, A., Cramer, C., Zaporojan, V., & Carey, J. (2021). Consensus on Rehabilitation Guidelines among Orthopedic Surgeons in the United States following Use of Third-Generation Articular Cartilage Repair (MACI) for Treatment of Knee Cartilage Lesions. Cartilage, 13(1_suppl), 1782S-1790S.
4. Gillogly SD, Myers TH, Reinold MM. Treatment of Full-Thickness Chondral Defects in the Knee With Autologous Chondrocyte Implantation. J Orthop Sport Phys Ther. 2006;36(10):751-764.
5. McGee TG, Cosgarea AJ, McLaughlin K, Tanaka M, and Johnson K. Rehabilitation After Medial Patellofemoral Ligament Reconstruction. Sports Medicine and Arthroscopy Review, 25(2), 105–113.

Each patient's MACI rehabilitation physical therapy needs are unique.

A rehabilitation program should take into account the patient's specific medical history and individual goals. Modifications may be needed based on specifics of the cartilage lesion(s) as well as any concomitant procedures performed at the time of MACI implantation.

The information presented in this manual is not intended to be a substitute for your individual clinical judgment. Rehabilitation is a highly individualized process and the following recommendations are intended to help inform your development of a unique rehabilitation program specific to each patient's needs.

The goal is to restore optimal function in each patient as quickly and safely as possible. Rehabilitation progression is criterion-based. Although timeframes have been established as a guide, it is more important that goals are reached at the end of each phase prior to progressing to the next.

MACI is contraindicated in patients who are unable to follow a physician-prescribed post-surgical rehabilitation program.

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PHASES OF MACI REHABILITATION

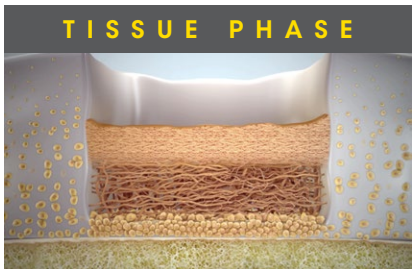
Individual results for timeline and repair tissue progress will vary.

Please see Important Safety Information and Full Prescribing Information or visit MACI.com

0-3 months following surgery >>>>> 3-6 months following surgery >>>>> 6-9 months following surgery >>>>>

ACHIEVE ROUTINE

After the immediate post-surgery phase, patients work to quickly achieve pain-free and full passive knee extension while gradually increasing weight bearing and knee flexion range of motion. Over time, the goal is to achieve unassisted ambulation and activities of daily living while becoming thoroughly independent with rehabilitation exercises.

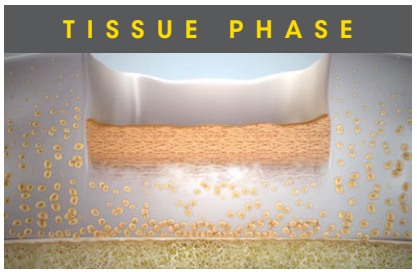


Implantation & Protection

Cells adhere to bone and begin to proliferate throughout the defect

BUILD STRENGTH

During this phase, patients should begin to feel comfortable returning to recreational activities. An exercise program will help re-build muscle strength and endurance. Patients may feel ready for more strenuous activity, so you may need to give explicit direction on what activities they are ready for at this stage.

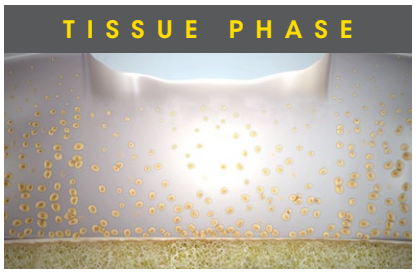


Transition & Proliferation

Continued proliferation forms a defect-spanning matrix

BE ACTIVE

Patients may enjoy a return to recreational activities and sports by gradually increasing the difficulty of their exercises. Every patient's recovery is unique and should be guided by your assessment of graft maturation as well as mental preparedness of the patient and the general physical function and level of specific knee strength, stability, and support.



Remodeling & Maturation

Expansion of the cell matrix into puttylike consistency, progressive hardening until durable repair tissue forms

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PATIENT PROFILES

While all patients will progress through the three phases of rehabilitation, the specific recommendations vary from patient to patient. In order to help you develop the best rehabilitation plan for your patient, this manual contains guidance for **four general patient types**, shown in the table below.

Patient Profiles (Stratified by Defect Location)

	Patellofemoral (PF)		Tibiofemoral (TF)	
	Patient 1[a] (PF single defect) ▼ challenging	**Patient 2[b] (PF multiple defects)** ▲ challenging	**Patient 3[a] (TF single defect)** ▼ challenging	**Patient 4[b] (TF multiple defects)** ▲ challenging
No. of defects treated	One	Multiple	One	Multiple
Defect location(s)	Patella	Patella/trochlea	Femoral condyle	Femoral condyle (2×)
Primary lesion size, cm^2 (postdebridement)	<3	≥5	<3	≥5
Age, years	24	50	24	50
Activity level	Office worker/low to moderate exercise	Heavy labor (construction/police/etc.)	Office worker/low to moderate exercise	Heavy labor (construction/police/etc.)

[a] **Patients 1 and 3 are considered to have a "▼ less challenging" rehabilitation** due to treatment of a single defect, smaller lesion size, younger age, and lower job-level physical activity.

[b] **Patients 2 and 4 are considered to have a "▲ more challenging" rehabilitation** due to treatment of multiple defects, larger lesion size, older age, and higher job-level physical activity.

Patient profiles were developed with the intent of establishing boundaries for the timing of rehabilitation steps. Patient types were divided into categories by lesion type and more (▲) versus less (▼) challenging rehabilitation. The assumption was that patients had normal alignment and normal meniscus and ligament status.

Lesion location and concomitant surgeries are important factors in rehabilitation decision-making, specifically in relation to weight bearing. Surgeons in the rehabilitation study indicated that in some cases, an osteotomy might also be performed, which would likely extend the timing of many of the rehabilitation steps.

The content presented in the MACI Rehabilitation Manual is for informational purposes only and does not constitute medical advice. Individual results for rehab may vary.

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ADDITIONAL REHABILITATION FACTORS

When determining the best rehabilitation program to suit a particular patient's needs, the patient's specific medical history, goals, lesion location(s), and concomitant procedures should be taken into account.

PATIENT CONSIDERATIONS

Patient Age: rate of cartilage repair

Body Mass Index (BMI): less than 30 vs. greater than 30

Individual Goals: demands required of the repaired tissue

Other Considerations: fear of reinjury and self-efficacy and patient traits

Past Medical History: previous surgical history

PROCEDURE-MODIFIED REHABILITATION CONSIDERATIONS

Defect considerations

Lesion Size Large lesion size results in greater exposure of the membrane to compression and sheer forces, based on the radius of curvature of the joint surface

Lesion Location Understand the joint in which the lesion is located as well as the degree at which the lesion articulates against the opposing joint surface

Duration of Symptoms Longer duration of symptoms (greater than 12 months) may result in patient deconditioning at the time of post-operative rehabilitation

Cartilage Quality Cartilage quality (normal vs. chondropenia) may alter the progression of rehabilitation

Meniscus Status Consideration of progression following meniscectomy

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Concomitant Procedures

Rehabilitation course is modified based on concomitant procedures performed and the biological and biomechanical considerations of those procedures (it is important to maintain communication with the treating surgeon)

Anterior Cruciate Ligament Reconstruction

- Rehabilitation varies by ACL graft selection
- Weight bearing is similar to isolated femoral condyle lesions
- Range of motion rate of progression may be increased to avert motion loss for femoral condyle lesions

Medial Patellofemoral Ligament Reconstruction

- In single patellofemoral lesion, weight bearing may be decreased for (up to) the initial 2 weeks
- Range of motion is similar to patellofemoral lesions

Meniscal Allograft

- Weight bearing rate of progression may be decreased compared to isolated femoral condyle lesions
- Range of motion rate of progression is commonly decreased, with no active knee flexion past 90° for the first 6-8 weeks

High Tibial Osteotomy

- Weight bearing rate of progression may be decreased compared to isolated femoral condyle lesions
- A slightly increased rate of range of motion progression may be implemented to avert motion loss depending on radiographic healing

Distal Realignment

- Weight bearing rate of progression may be decreased compared to isolated patellofemoral condyle lesions
- Range of motion rate of progression is decreased, 0°-90° for up to the initial 4 weeks
- Active knee extension exercises may be limited during the first 6-8 weeks

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IMMEDIATE POST-OP AND INITIAL PHYSICAL THERAPY VISIT

Immediately following surgery, it is important to maintain joint mobility and muscle tone without placing undue stress on the implant area. Prior to discharge, the patient also must be proficient in, and comfortable with, all aspects of home exercise and functional activities.

During this time, patients should:

- Understand that the week immediately following surgery will be spent managing pain and swelling with the careful introduction of movement
- Know that a comfortable setting is recommended and unnecessary movement should be restricted to protect the implant (rest, immobilization)
- Use RICE as directed (rest, ice, compression, elevation)
- Follow continuous passive motion (CPM) and basic exercises and activities as directed

Post Surgical Care Tip: use R-I-C-E as your guide

REST General rest is incredibly important. Stay off your knee and use crutches as instructed. Follow your surgeon's advice on how long to keep weight off your knee.

ICE Ice your knee for 20 minutes every 2 hours.

COMPRESSION Use an elastic (ACE-type) wrap or compression bandage on your knee if instructed to do so.

ELEVATION Lie down with your knee propped up on pillows.

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IMMEDIATE POST-OP AND INITIAL PHYSICAL THERAPY VISIT

Immediate post-op:

- ☐ Ensure the patient has an initial appointment (or appropriate contacts) for outpatient physical therapy.
- ☐ Ensure the patient is aware of when the next post-operative appointment with their orthopedic surgeon is scheduled.
- ☐ If required, ensure that patient has an appointment for the removal of sutures/staples, or is aware when they must be removed.
- ☐ Instruct and educate the patient on the importance of following the RICE guidelines for edema control.
- ☐ Reinforce WB and brace guidelines.
- ☐ Ensure the patient is educated in wound healing, and how to assess changes in the wound and surrounding soft tissue that may indicate infection.

If applicable:

- ☐ Review the home exercise regimen, ensuring the patient is proficient in safely performing these activities.
- ☐ Review (and educate on) techniques for performing functional activities (i.e., stairs, bed transfers, showering, etc.), ensuring the patient is independent in safely performing these activities.

Initial outpatient physical therapy session:

- ☐ Review the patient's level of pain and medication use.
- ☐ Ensure the appropriate knee brace is obtained, correctly fitted, and adjusted appropriately.
- ☐ Ensure proficiency with crutches, both during normal ambulation and while negotiating stairs.
- ☐ Provide appropriate education, training, and proficiency with the desired level of partial WB.
- ☐ Review instructions and movement contraindications outlined by the orthopedic surgeon and hospital physical therapist as needed.
- ☐ Review and progress the home exercise program based on the current post-operative timeline and patient status.

REHAB CONTRAINDICATIONS

- Excessive load bearing (>20% of patient body weight) for tibiofemoral defects and uncontained patellofemoral defects, especially in combination with knee flexion
- Ambulation without crutches and a protective knee brace
- Generation of shear forces within the knee
- Knee flexion beyond 45° for tibiofemoral and patellofemoral grafts
- Active knee extension ROM (especially against resistance)

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0-3 months following surgery

ACHIEVE ROUTINE

Patients make tremendous strides during this initial phase, beginning with their recovery from surgery and then working towards a pain-free and full passive knee extension with limited weight bearing. By the end of this phase, patients will be thoroughly independent with rehabilitation exercises and should expect to achieve the following goals.

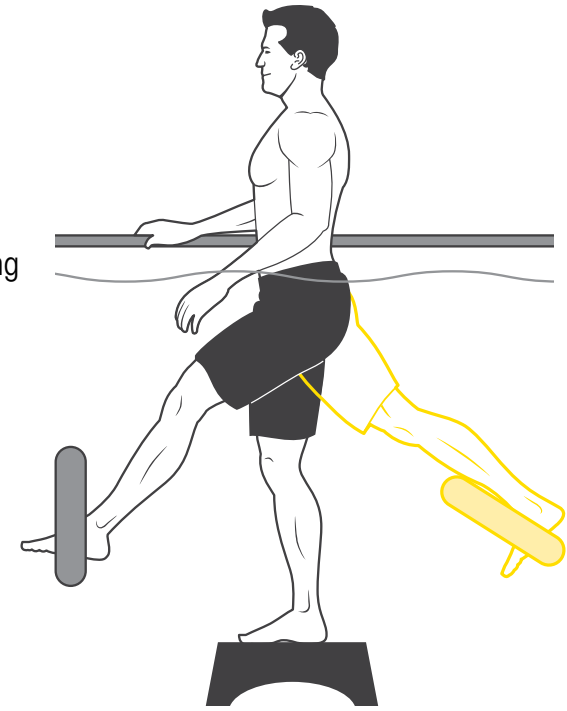
Individual results will vary.

FUNCTIONAL GOALS

- Mobile with crutches within first week
- Limited weight bearing and pain-free, full knee extension by 2-3 weeks
- Independent home exercise as early as 1 month
- Immediate weight bearing for single PF defect, full weight bearing by 5-6 weeks for multiple PF defects with full knee ROM by 7-9 weeks (single or multiple PF defects)
- Full weight bearing and full knee range of motion by 7-9 weeks for TF defects
- Free from knee brace by 8-12 weeks post-surgery

ACTIVITY MILESTONES

- Return to light recreational exercise including walking and stationary cycling
- Perform daily routine and activities of daily living (navigating stairs, showering, etc.) with the assistance of crutches
- Start driving again and return to office or seated work



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0-3 months following surgery >>>>>
ACHIEVE ROUTINE

Patient	Weight Bearing (WB)	Range of Motion (ROM)	Work & Activities of Daily Living (ADL)	Recreational Activities & Sports
Patient 1 **PF** Single Defect	**Time to WB:** Immediately **% of body weight:** 81-100% **Full WB:** Immediately	**Time to passive ROM:** Immediately **Time to early active ROM:** 2 weeks **Time to full active ROM:** 6 weeks **ROM progression:** 0° to 45°, increasing by 15° each week following week 1 **Full ROM:** 7-9 weeks	**Release to unrestricted ADLs:** As early as 3 months **Release to sedentary work:** As early as 2 weeks	**Stationary cycling:** 3-4 weeks
Patient 2 **PF** Multiple Defects	**Time to WB:** Immediately **% of body weight:** <20% (uncontained lesion), increasing by 15-20% each week following week 1 81-100% (contained lesion) **Full WB:** 5-6 weeks *Nonkissing lesions; neutral joint alignment	**Time to passive ROM:** Immediately **Time to early active ROM:** 4 weeks **Time to full active ROM:** 8-10 weeks **ROM progression:** 0° to 45°, increasing by 15° each week following week 1 **Full ROM:** 7-9 weeks	**Release to unrestricted ADLs:** As early as 3 months **Release to sedentary work:** As early as 4 weeks	**Stationary cycling:** 5-6 weeks
Patient 3 **TF** Single Defect	**Time to WB:** Immediately **% of body weight:** <20%, increasing by 10-15% each week following week 1 **Full WB:** 7-9 weeks	**Time to passive ROM:** Immediately **Time to early active ROM:** Immediately **Time to full active ROM:** As tolerated, 4 weeks **ROM progression:** 0° to 45°, increasing by 15° each week following week 1 **Full ROM:** 7-9 weeks	**Release to unrestricted ADLs:** As early as 3 months **Release to sedentary work:** As early as 2 weeks	**Stationary cycling:** 3-4 weeks
Patient 4 **TF** Multiple Defects	**Time to WB:** Immediately **% of body weight:** <20%, increasing by 10-15% each week following week 1 **Full WB:** 7-9 weeks	**Time to passive ROM:** Immediately **Time to early active ROM:** Immediately **Time to full active ROM:** As tolerated, 4 weeks **ROM progression:** 0° to 45°, increasing by 15° each week following week 1 **Full ROM:** 7-9 weeks	**Release to unrestricted ADLs:** As early as 3 months **Release to sedentary work:** As early as 4 weeks	**Stationary cycling:** 5-6 weeks

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0-3 months following surgery >>>>>
ACHIEVE ROUTINE

WEEKS 0-1

Pain Control
- Provide appropriate analgesics for pain control

Exercises
- Start 0°-45° CPM of knee flexion (12-24 hours post-surgery for at least 1 hour each day)
- For first 3 weeks, wear ROM control brace (Set at 0°-30° of knee flexion)
- Apply cryotherapy (20 minutes of ice, at least 3 times per day)
- Perform active ankle plantarflexion and dorsiflexion
- Encourage contraction of quadriceps, hamstrings, and gluteal muscles

Reminders
- Ensure proper breathing techniques during exercise
- Offer information on proper ambulation with crutches, bed transfers, and stairs
- Provide written and verbal instruction on performing daily living activities while limiting weight bearing on knee implant

	Ambulatory Aids	Knee Bracing	
PF	2 crutches	Locked at full knee extension	>>>>>
TF	2 crutches	Progress from 0˚-30˚	>>>>>
PF+ TF	2 crutches	Locked at full knee extension	>>>>>

WEEKS 2-3

Range of Motion and Flexibility
- Use CPM at end of session for 20-30 minutes
- Passive and active heel slides
- Passive knee extension
- Careful patellar mobilization in all directions

Exercises
- Contraction and co-contraction of quadriceps
- Contractions of hamstrings, adductor, calf, and gluteal muscles
- Straight-leg-raise activities

Hydrotherapy Exercises
- Deep water walking and calf raises
- Straight-leg hip flexion, extension, abduction, and circumduction (with or without floatation devices)
- Passive knee flexion
- Hamstring and calf stretching

	Ambulatory Aids	Knee Bracing	
PF	2 crutches	Locked at full knee extension	>>>>>
TF	2 crutches	Progress from 0˚-30˚ to 0˚-45˚	>>>>>
PF+ TF	2 crutches	Locked at full knee extension	>>>>>

Number of Defects: Rehabilitation may vary if single or multiple lesions.

PF + TF: Rehabilitation may be altered to address healing constraints of both PF and TF lesion locations.

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0-3 months following surgery >>>>>
ACHIEVE ROUTINE

After the immediate post-surgery phase, patients will work towards a pain-free and full passive knee extension with limited weight bearing. Over time, the goal is to be free of ambulation devices and knee braces while becoming thoroughly independent with rehabilitation exercises.

Symptom Control: Perform clearance and lymphatic remedial massage, cryotherapy, compression, and elevation as required for edema

WEEKS 4-6

Range of Motion and Flexibility
- Continue flexibility/stretching exercises
- Stretch hamstrings and calf musculature
- Careful patellar mobilization in all directions
- Use CPM to maximum comfortable range as required
- Begin recumbent cycling

Exercises
- Continue strengthening exercises
- Progress straight-leg-raise activities
- Introduce gluteal, calf, hip, and trunk strengthening exercises

Hydrotherapy Exercises
- Continue hydrotherapy exercises
- Introduce active knee flexion exercises, shallow water walking, shallow water calf raises, deep water squats, and pool cycling

	Ambulatory Aids	Knee Bracing	
PF	1-2 crutches (Weeks 4-5); 1 crutch as required (Week 6)	Use brace as required (Week 6)	>>>>>
TF	1-2 crutches	Progress from 0˚-45˚ to full flexion	>>>>>
PF+ TF	1-2 crutches	Progress from 0˚-45˚ to full flexion	>>>>>

WEEKS 7-12

Range of Motion and Flexibility
- Continue Week 2-6 flexibility/stretching exercises
- Stretch quadriceps musculature (Weeks 9-10)
- Begin passive knee ROM on rowing ergometer (Weeks 9-10)
- Careful patellar mobilization in all directions
- Use CPM to maximum comfortable range as required
- Begin upright cycling

Exercises
- Continue Week 2-6 strengthening exercises
- Introduce standing hip and weighted knee flexion strengthening exercises

	Ambulatory Aids	Knee Bracing	
PF	No crutches	No brace	>>>>>
TF	1 crutch as needed in outdoor/unfamiliar	Allow full knee flexion within brace	>>>>>
PF+ TF	1 crutch as needed in outdoor/unfamiliar	Allow full knee flexion within brace	>>>>>

3-6 months following surgery

BUILD STRENGTH

Having achieved full weight bearing and range of motion in the previous phase, patients spend this phase focused on rebuilding muscle strength and endurance. Patients may feel ready for more strenuous activity, so you may need to give explicit direction on what activities they are ready for at this stage.

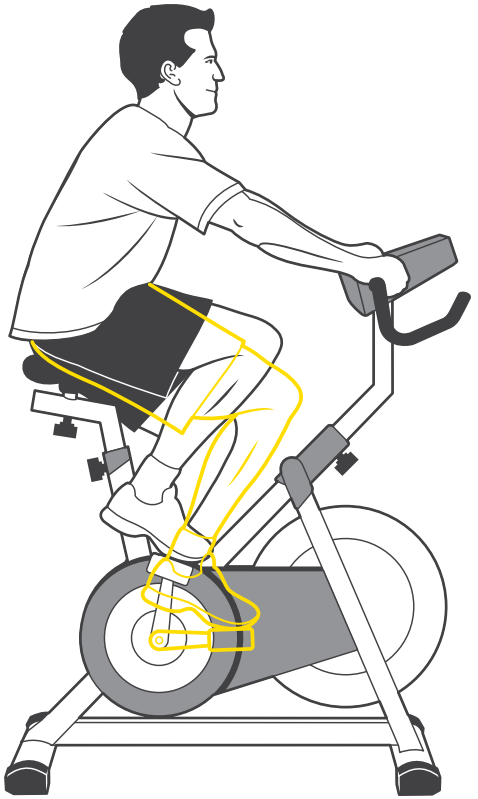
Individual results will vary.

FUNCTIONAL GOALS

- Full and pain-free weight bearing and range of motion
- Continue progression of strengthening exercises without pain or swelling
- Transition to gym/home based rehab
- Free from crutches

ACTIVITY MILESTONES

- Return to low-impact recreational activities including: cycling, golf, yoga & pilates, rowing & kayaking, swimming, dancing, elliptical & treadmill
- Return to more physically active jobs such as nursing or construction (as directed)
- Return to daily activities that require strength and endurance



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3-6 months following surgery >>>>>
BUILD STRENGTH

Patient	Weight Bearing (WB)	Range of Motion (ROM)	Work & Activities of Daily Living (ADL)	Recreational Activities & Sports
Patient 1 **PF** Single Defect	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work** **Release to heavy labor:** 3-6 months	**Outdoor cycling:** 5-6 months **Evaluation for running:** 6 months **Low-impact recreational activities:** As directed
Patient 2 **PF** Multiple Defects	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work**	**Outdoor cycling:** 5-6 months **Low-impact recreational activities:** As directed
Patient 3 **TF** Single Defect	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work** **Release to heavy labor:** 3-6 months	**Outdoor cycling:** 3-4 months **Evaluation for running:** 6 months **Low-impact recreational activities:** As directed
Patient 4 **TF** Multiple Defects	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work**	**Outdoor cycling:** 5-6 months **Low-impact recreational activities:** As directed

RECOMMENDATIONS

During this phase, patients should be performing exercises that help rebuild muscles and increase endurance.

Range of Motion and Flexibility

- Continue flexibility/stretching exercises

Exercises

- Continue strengthening exercises
- Introduce bridging exercises and standing single-leg calf raises
- Introduce modified open kinetic chain (OKC) and closed kinetic chain (CKC) exercises
  OKC: terminal leg extension
  CKC: inner-range quadriceps; leg press activities
- Progress upright stationary and outdoor road cycling
- Begin rowing ergometry as tolerated

6-9 months following surgery

BE ACTIVE

Patients should enjoy a return to recreational activities and sports by gradually increasing the difficulty of their exercises. Every patient's recovery is unique and should be guided by your assessment of graft maturation as well as mental preparedness of the patient and the general physical function and level of specific knee strength, stability, and support.

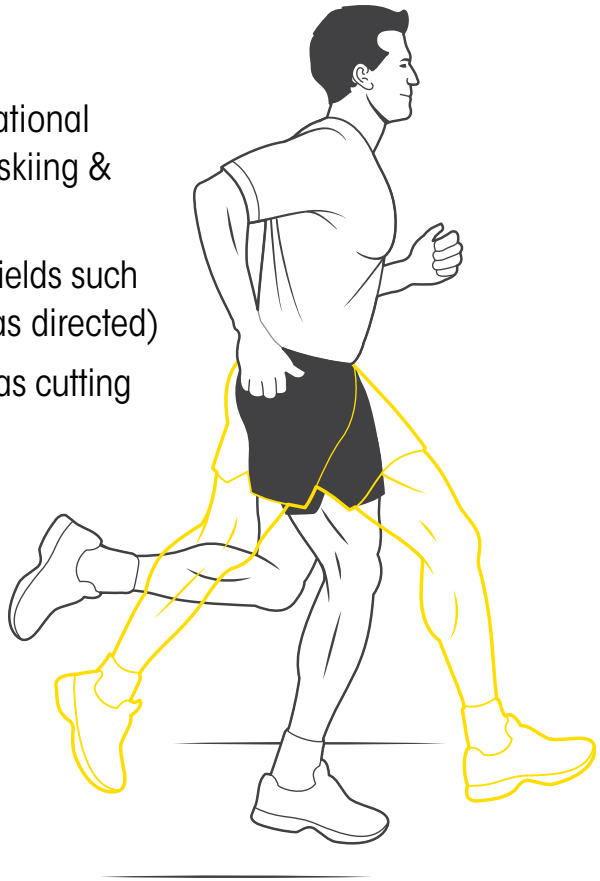
Individual results will vary.

FUNCTIONAL GOALS

- Increase distance, time, and difficulty of exercises
- Ability to tolerate lengthy walking distances
- Return to a pre-operative level of activity

ACTIVITY MILESTONES

- Return to pre-injury sports-based recreational activities including: running distances, skiing & snowboarding, weight training, tennis
- Return to work for those in heavy labor fields such as military deployment or firefighting (as directed)
- Over time, heavy impact activities such as cutting or pivoting can be reintroduced



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6-9 months following surgery >>>>>
BE ACTIVE

Patient	Weight Bearing (WB)	Range of Motion (ROM)	Work & Activities of Daily Living (ADL)	Recreational Activities & Sports
Patient 1 **PF** Single Defect	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work** **Release to heavy labor**	**Release to running:** 7-9 months **Release to tennis*:** 9 months
Patient 2 **PF** Multiple Defects	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work**	**Evaluation for running:** 8 months (as directed)
Patient 3 **TF** Single Defect	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work** **Release to heavy labor**	**Release to running:** 7-9 months **Release to tennis*:** 9 months
Patient 4 **TF** Multiple Defects	**Full WB**	**Full ROM**	**Release to unrestricted ADLs** **Release to sedentary work**	**Evaluation for running:** 8 months (as directed)

*Other examples of this type of sport are pickle ball, golf.

RECOMMENDATIONS

It's essential for patients to maintain a rehabilitation program in order to continue progressing. At this point, patients should be adept in all activities of daily living and their exercise program should support their return to all activities of daily living and even things like running, low-impact sports, and other recreational activities.

Range of Motion and Flexibility

- Continue flexibility/stretching exercises

Exercises

- Progression and increased difficulty of open kinetic chain exercises
- Progression and increased difficulty of closed kinetic chain exercises (e.g., step ups/downs, modified squat activities)
- Introduction of agility exercises
- Ability to navigate uneven ground, inclines and obstacles
- Return to running program
- Return to low-impact sports and recreational activities
- Return to all activities of daily living
- Maintaining rehabilitation program is essential for continued progression

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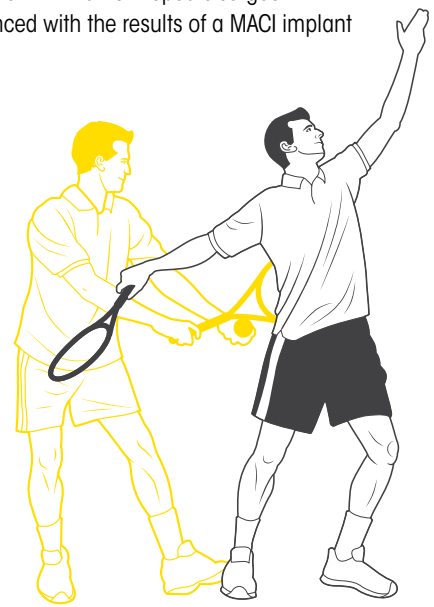
9+ MONTHS AFTER SURGERY

Patients should be able to resume normal functionality as well as low-compression recreational activities, which should initially be performed in isolation and then with the appropriate equipment. (It is not the purpose of this document to outline a protocol of specific exercises and activities.)

At this point:

- The patient's graft has matured to the point at which it is able to withstand the specific demands of the chosen activity
- The patient has been appropriately rehabilitated to the point at which he or she is able to physically and psychologically undertake the demands of the chosen activity
- The patient has undergone appropriate clinical assessment with an orthopedic surgeon experienced with the results of a MACI implant



Patient	Work / Sports
Patient 1 **PF** Single Defect	**Release to contact/collision sports†:** 12+ months
Patient 2 **PF** Multiple Defects	**Release to heavy labor:** 9-12 months **Release to running:** 10-12 months **Release to tennis*:** 10-12 months **Release to contact/collision sports†:** 10-12 months
Patient 3 **TF** Single Defect	**Release to contact/collision sports†:** 10-12 months
Patient 4 **TF** Multiple Defects	**Release to heavy labor:** 9-12 months **Release to running:** 10-12 months **Release to tennis*:** 12+ months **Release to contact/collision sports†:** 12+ months

*Other examples of this type of sport are pickle ball, golf.
†Examples are soccer, football, hockey, combat sports.

KEY POINTS

Each patient's MACI rehabilitation physical therapy needs are unique. A rehabilitation program should take into account the patient's specific medical history and individual goals. Modifications may be needed based on specifics of the cartilage lesion(s) as well as any concomitant procedures performed at the time of MACI implantation.

To help optimize outcomes, you need to consider:

- Patient adherence to the prescribed rehabilitation program is critical.
- Consider lesion size, location and patient characteristics when determining a rehabilitation program.
- Emphasis should be placed on reaching the goals of a given phase over rigid adherence to time schedule.
- It is important to avoid excessive load/WB on the graft site to allow proper healing.
- Pain and swelling must be carefully monitored throughout the rehabilitation process. Ignoring these symptoms may compromise the success of the surgery and the patient's outcome.
- If sharp pain with locking or swelling is experienced, the patient should notify their surgeon immediately. Activity should be adjusted to lessen the irritation. Cryotherapy may be used to control the swelling.

maci®
autologous cultured chondrocytes on porcine collagen membrane

Active cells help restore active patients

Indication

MACI® (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the knee with or without bone involvement in adults.

Limitations of Use

Effectiveness of MACI in joints other than the knee has not been established.

Safety and effectiveness of MACI in patients over the age of 55 years have not been established.

Important Safety Information

Contraindications: MACI is contraindicated in patients with a known history of hypersensitivity to gentamicin, other aminoglycosides, products of porcine or bovine origin; in patients with severe osteoarthritis of the knee, inflammatory arthritis, inflammatory joint disease, or uncorrected congenital blood coagulation disorders; in patients who have undergone prior knee surgery in the past 6 months, excluding surgery to procure a biopsy or a concomitant procedure to prepare the knee for a MACI implant; or in patients unable to cooperate with a physician-prescribed post-surgical rehabilitation program.

Warnings and Precautions:

- Malignancy: The risk of MACI in patients with malignancy in the area of cartilage biopsy or implant is unknown. Expansion of malignant or dysplastic cells present in biopsy tissue during manufacture and subsequent implantation may be possible.
- Transmissible infectious diseases: Because patients undergoing procedures associated with MACI are not routinely tested for transmissible infectious diseases, cartilage biopsy and MACI implant may carry risk of transmitting infectious diseases.
- Presurgical Comorbidities: Local inflammation or active infection in the bone, joint, and surrounding soft tissue, meniscal pathology, cruciate ligament instability, and misalignment should be assessed and treated prior to or concurrent with MACI implantation.
- Product Sterility: Final sterility test results are not available at the time of shipping.

Adverse Reactions: The most frequently occurring adverse reactions reported for MACI (≥5%) were arthralgia, tendonitis, back pain, joint swelling, and joint effusion. Serious adverse reactions reported for MACI were arthralgia, cartilage injury, meniscus injury, treatment failure, and osteoarthritis.

Specific Populations:

- Use of MACI in pediatric patients (younger than 18 years of age) or in patients over 65 years of age has not been established.
- The MACI implant is not recommended during pregnancy. For implantations post-pregnancy, the safety of breastfeeding to an infant has not been determined.

To report negative side effects, contact Vericel Corporation at 1-800-453-6948 or FDA at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch.

VERICEL

For more information, please see Full Prescribing Information or visit MACI.com

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