



Accelerated Rehabilitation Guidelines for the Knee Using MACI® (matrix-induced autologous chondrocyte implant)



Dr. Jay R. Ebert, PhD, ESSAM

Dr. Brendan Joss, PhD, ESSAM

Winthrop Professor Timothy Ackland, PhD, FASMF



HOLLYWOOD FUNCTIONAL REHABILITATION CLINIC
VERDUN PHYSIOTHERAPY
Tomorrow's Treatment Today

genzyme
Biosurgery

Key points for consideration

The following document has been provided as a general guideline for rehabilitation following MACI® (matrix-induced autologous chondrocyte implant). The emphasis of this guideline is to protect the graft site, allowing regeneration of the cartilage, and return the patient to an optimal level of function. Notwithstanding the foregoing, the information provided in this document is intended for educational purposes. It is not a substitute for medical care nor should it be construed as medical advice. Consultation with the patient's treating surgeon is recommended prior to implementing a rehabilitation program. Individual results may vary.

- **Patient adherence** to the prescribed rehabilitation program is important and deviation from the program may compromise the clinical benefit of the MACI implant.
- **Lesion size, location and patient characteristics** are significant factors in determining a rehabilitation program for each patient.
- **Although timeframes have been established as a guide,** it is more important that goals are reached at the end of each phase prior to progression to the next.
- **It is important to avoid excessive load/weight bearing** on the graft site to allow proper healing. Take note of specific precautions mentioned in this guide. Information regarding the location, size and specifics of the implantation site should be obtained from the surgeon.
- **Pain and swelling must be carefully monitored** throughout the rehabilitation process. If either occurs in excess to what is routinely seen, the ensuing activity needs to be identified and appropriately adjusted to lessen the irritation. Ice packs may be used to control swelling. Ignoring these symptoms may compromise the success of the surgery and the patient's outcome.
- **At any time during or after the rehabilitation process,** if sharp pain with locking or swelling is experienced, the patient should notify his or her surgeon.

Introduction

Refer to *Accelerated Rehabilitation Guidelines for the Knee Using MACI® (matrix-induced autologous chondrocyte implant): Exercise Companion Guide* for detailed instructions and photographs of gym-based, hydrotherapy, and proprioception-based rehabilitation exercises for each postsurgical phase.

Articular cartilage defects are a common cause of pain and functional disability seen in orthopaedics and sports medicine practices. The avascular nature of articular cartilage predisposes individuals to progressive symptoms and degeneration due to the limited ability of articular cartilage to heal or regenerate. This guide provides an overview of specific rehabilitation guidelines following MACI implant, a treatment for articular cartilage defects. This suggested program is designed using knowledge of basic science, anatomy and biomechanics of articular cartilage, as well as the natural course of healing following implantation, and is not intended as a substitute for individual clinical judgment. The goal is to restore optimal function in each patient as quickly and safely as possible.



Accelerated Rehabilitation Guidelines

for the Knee Using MACI®
(matrix-induced autologous chondrocyte implant)

2	Postoperative Timeline: Accelerated Rehabilitation Guidelines for the Knee Using MACI Implant
4	Foreword
6	Acknowledgements
7	Overview of Cartilage Repair and Regeneration Techniques
9	Principles of post-MACI Implant Rehabilitation
15	Accelerated Rehabilitation Guidelines for the Knee Using MACI Implant
18	Phase One: Inpatient hospital stay (0-1 week postsurgery)
20	Phase Two: Weeks 2-3 postsurgery
22	Phase Three: Weeks 4-6 postsurgery
24	Phase Four: Weeks 7-12 postsurgery
26	Phase Five: Months 3-6 postsurgery
28	Phase Six: Months 6-9 postsurgery
30	Phase Seven: Months 9-12 postsurgery and return to sport
32	Recommended Readings
32	References

Accelerated Rehabilitation Guidelines for the Knee Using MACI® (matrix-induced autologous chondrocyte implant)

Postoperative Timeline

Week 1 (Phase 1)	WB Status <ul style="list-style-type: none"> TF joint: ≤ 20% BW PF joint: 20-30% BW 	KEY BW = body weight CPM = continuous passive motion CKC = closed kinetic chain OKC = open kinetic chain PF = patellofemoral ROM = range of motion TF = tibiofemoral WB = weight bearing
	Ambulatory Aids <ul style="list-style-type: none"> TF joint: 2 crutches used at all times PF joint: 2 crutches used at all times 	
	Knee ROM <ul style="list-style-type: none"> TF joint: passive & active ROM from 0-30° PF joint: passive & active ROM from 0-20° 	
	Knee Bracing <ul style="list-style-type: none"> TF joint: 0-30° PF joint: locked at full knee extension Hospital/Clinic – Phase 1 exercises 	
Week 2-3 (Phase 2)	WB Status <ul style="list-style-type: none"> TF joint: ≤ 20% BW (week 1-2) to 30% BW (week 3) PF joint: 20-30% BW (week 1-2) to 50% BW (week 3) 	
	Ambulatory Aids <ul style="list-style-type: none"> TF joint: 2 crutches used at all times PF joint: 2 crutches used at all times 	
	Knee ROM <ul style="list-style-type: none"> TF joint: active ROM from 0-30° (week 2) to 0-90° (week 3) PF joint: active ROM from 0-30° (week 2) to 0-60° (week 3) 	
	Knee Bracing <ul style="list-style-type: none"> TF joint: 0-30° (week 1-2) to 0-45° (week 3) PF joint: locked at full knee extension Initial postoperative review (pain, swelling & wound) Education on appropriate WB & crutch ambulation Review home-based exercise program Hydrotherapy – Phase 1-2 exercises Clinic – Phase 1-2 exercises Remedial massage, soft tissue and patella mobilisation, CPM and cryotherapy 	
Week 4-5 (Phase 3)	WB Status <ul style="list-style-type: none"> TF joint: 40% BW (week 4) to 50% BW (week 5) PF joint: 75% BW 	
	Ambulatory Aids <ul style="list-style-type: none"> TF joint: 2 crutches used at all times PF joint: 1 crutch used at all times 	
	Knee ROM <ul style="list-style-type: none"> TF joint: active ROM from 0-110° (week 4) to 0-125° (week 5) PF joint: active ROM from 0-90° (week 4) to 0-120° (week 5) 	
	Knee Bracing <ul style="list-style-type: none"> TF joint: 0-60° (week 4) to 0-90° (week 5) PF joint: locked at full knee extension Hydrotherapy – Introduce Phase 3 exercises Clinic – Introduce Phase 3 exercises Remedial massage, soft tissue mobilisation and patella mobilisation CPM and cryotherapy as required 	

Table 1. Generic progression of postoperative weight bearing (WB), knee range of motion (ROM) status and exercise rehabilitation.

Week 6-7 (Phase 3-4)	WB Status <ul style="list-style-type: none"> TF joint: 60% BW (week 6) to 80% BW (week 7) PF joint: full WB
	Ambulatory Aids <ul style="list-style-type: none"> TF joint: 1 crutch used at all times PF joint: 1 crutch as required
	Knee ROM <ul style="list-style-type: none"> TF joint: active ROM from 0-125° (week 6) to 0-135° (week 7) PF joint: active ROM from 0-125° (week 6) to 0-135° (week 7)
	Knee Bracing <ul style="list-style-type: none"> TF joint: full knee flexion PF joint: no brace Hydrotherapy – Introduce Phase 4 exercises Clinic – Introduce Phase 4 exercises Remedial massage, soft tissue mobilisation and patella mobilisation
Week 8-10 (Phase 4)	WB Status <ul style="list-style-type: none"> TF & PF joint: full WB as tolerated
	Ambulatory Aids <ul style="list-style-type: none"> TF & PF joint: 1 crutch as required
	Knee ROM <ul style="list-style-type: none"> TF & PF joint: full active ROM as tolerated
Week 11-12 (Phase 4)	Knee Bracing <ul style="list-style-type: none"> TF joint: full knee flexion PF joint: no brace Hydrotherapy – Phase 1-4 exercises Clinic – Phase 1-4 exercises Commence proprioceptive/balance activities Remedial massage, soft tissue mobilisation and patella mobilisation
	<ul style="list-style-type: none"> Hydrotherapy – Phase 1-4 exercises Clinic/gym – Phase 2-4 exercises Progress proprioceptive/balance activities Introduce cycling, walking, resistance and CKC activities
3-6 Months (Phase 5)	<ul style="list-style-type: none"> Clinic/gym – Introduce Phase 5 exercises Progress proprioceptive/balance activities Progress to more demanding CKC exercises, rowing ergometry and elliptical trainers
6-9 Months (Phase 6)	<ul style="list-style-type: none"> Clinic/gym – Introduce Phase 6 exercises Progress proprioceptive/balance activities Increase difficulty of OKC & CKC exercises (i.e., step ups/downs, modified squats) Introduction of controlled mini trampoline jogging
9-12 Months (Phase 7)	<ul style="list-style-type: none"> Clinic/gym – Introduce Phase 7 exercises Progress proprioceptive/balance activities Increase difficulty of OKC & CKC exercises (i.e., lunges/squats on unstable surfaces) Introduction of agility drills relevant to the patient's sport Return to competitive sport suggested after 12 months Graded increase in stress based on maturation of chondral repair

Foreword

Accelerated Rehabilitation Guidelines for the Knee Using MACI[®] (matrix-induced autologous chondrocyte implant) are the culmination of almost 10 years clinical experience and research in the pre- and postoperative management of patients undergoing this surgical procedure. The team at the Hollywood Functional Rehabilitation Clinic (HFRC) has developed these guidelines in collaboration with Genzyme Biosurgery; collectively we seek to share our knowledge in order to better equip other professionals to treat patients during post-MACI implant rehabilitation.

A purpose-built rehabilitation facility, HFRC promotes a multidisciplinary team approach to patient management. The facility has treated in excess of 400 patients following MACI implantation and has also adopted a strong research focus into all aspects of MACI implantation, in particular, the pre- and postoperative education and management of patients. This has culminated in numerous scientific publications in the field, and is an integral part of the commitment to development as a centre of excellence in the area.

Published data reported the results of a prospective, randomised comparison of accelerated approaches to postoperative rehabilitation following MACI implant.¹ The study followed 70 patients for two years, assessing them pre-surgically, then at 3, 6, 12 and 24 months. While both groups continued to improve up to 24 months, the accelerated regime showed clinical and statistical advantages in several metrics. The accelerated group:

- Reported significantly less severe pain (Figure 1)
- Demonstrated superior 6-minute walk distance (Figure 2)
- Reached full weight bearing (WB) at 8 weeks, as compared with 11 weeks for the traditional group
- Demonstrated a significant group effect for maximal active knee extension range
- Showed no incidence of graft delamination up to 24 months that resulted directly from the 3-month postoperative rehabilitation program

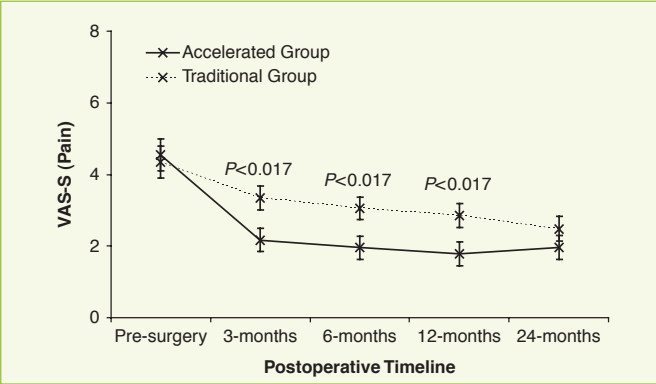


Figure 1. Changes in pain severity for the accelerated and traditional patient groups, throughout the pre- and postoperative timeline.¹ Figure adapted from reference 1: P values adapted to reflect the correct values in the study.

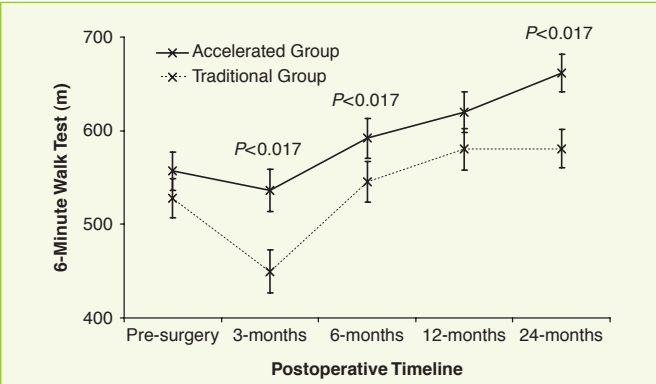


Figure 2. Changes in 6-minute walk distance (m) for the accelerated and traditional patient groups, throughout the pre- and postoperative timeline.¹ Figure adapted from reference 1: P values adapted to reflect the correct values in the study.

Weeks Postsurgery	2	3	4	5	6	7	8	9	10	11	12
Traditional Group Weight-bearing (% body weight)	≤20				50	60	70	80	90	100	
Crutches	2				1	1	1	1	1	1	0
Accelerated Group Weight-bearing (% body weight)	≤20	30	40	50	60	80	100				
Crutches	2	2	2	2	1	1	1	0			

Table 2. Comparative review of load-bearing gradients followed by MACI implant patients in the traditional and accelerated rehabilitation groups.²

In summary, the accelerated weight-bearing approach produced comparable, if not superior, clinical outcomes when compared with traditional methods, while demonstrating a faster return to normal function postsurgery¹. See **Table 2** for a comparative review of the two rehabilitation schedules.

Accelerated Rehabilitation Guidelines for the Knee Using MACI® (matrix-induced autologous chondrocyte implant) detail the accelerated approach; they are representative of HFRC's link between quality research and quality clinical application. The guidelines include:

- **An overview of the field of cartilage repair/regeneration surgery**
- **The principles of post-MACI implant rehabilitation**
- **An outline of postoperative rehabilitation guidelines spanning seven phases of repair tissue maturation and patient progress**
- **Additional recommended readings for the treating therapist**

In addition, *Accelerated Rehabilitation Guidelines for the Knee Using MACI®* (matrix-induced autologous chondrocyte implant): *Exercise Companion Guide* has been developed to provide detailed instructions and visual references for each of the gym-based and hydrotherapy exercises listed in the guidelines.

Finally, please note that these guidelines are intended as a guide only, and professional discretion must be applied at all times when prescribing and monitoring exercises for patients. This is by no means the definitive rehabilitation plan for all MACI implant patients; there is great individual variation between patients that must be taken into consideration throughout the rehabilitation process.

I would like to acknowledge the pioneering work in the field of post-MACI implant rehabilitation previously established by Dr. Brett Robertson. Furthermore, both Dr. Robertson and Dr. Helen Gilbey must be acknowledged for their coauthorship of the first edition of these guidelines, while Professors David Wood and Ming Hao Zheng are to be thanked for their ongoing research that led to the evolution of the protocols within the current guidelines.

For more information, please visit our web site at: www.hfrc.com.au.

Thank you.



Dr. Jay R. Ebert, PhD, ESSAM

Acknowledgements

Genzyme would like to thank Dr. Jay R. Ebert, Dr. Brendan Joss, and Professor Timothy Ackland for their pioneering work in MACI implant rehabilitation and for authoring these *Accelerated Rehabilitation Guidelines for the Knee Using MACI® (matrix-induced autologous chondrocyte implant)*. Further, Genzyme thanks the Hollywood Functional Rehabilitation Clinic (HFRC) where the authors conducted the research informing these guidelines. HFRC is located within the Perth Orthopaedic Institute, Perth, Western Australia—a Centre of Excellence within Australia. The facility is committed to peer-reviewed research conducted in association with the School of Surgery and the School of Sport Science, Exercise and Health at The University of Western Australia.

Authors



Dr. Jay R. Ebert is a Clinical Exercise Physiologist (CEP) with a PhD in cartilage repair, biomechanics and exercise rehabilitation. He is a Director and clinician at the Hollywood Functional Rehabilitation Clinic in Perth, Western Australia, and a Lecturer at the School of Sport Science, Exercise and Health, within the University of Western Australia. He has developed a strong clinical and research interest in cartilage repair and rehabilitation following autologous chondrocyte implantation (ACI), and has published and presented on the topic to international audiences.



Dr. Brendan Joss is Managing Director and a Clinical Exercise Physiologist (CEP) at the Hollywood Functional Rehabilitation Clinic in Perth, Western Australia, specialising in orthopaedic rehabilitation and cartilage repair. He obtained his PhD from the University of Western Australia investigating biomechanics following knee replacement, undertook a post-doctoral research fellowship at Queen's University in Canada and has 10 years experience in musculoskeletal rehabilitation.



Professor Timothy Ackland is a Winthrop Professor of Biomechanics within the School of Sport Science, Exercise and Health at the University of Western Australia, and the Director of the Research Institute for Preventive Health and Exercise Science. He has research interests in the mechanics of human movement with themes spanning exercise rehabilitation, high-performance sport and human performance in industry. He has served as a Director of Sports Medicine Australia and chaired the Scientific Program Committee for the 5th IOC World Congress on Sport Sciences for the 2000 Olympics, and was Conference Co-chair for Sports Medicine Australia in Perth, 2001.

Overview of Cartilage Repair and Regeneration Techniques

Articular Cartilage

Articular or hyaline cartilage covers the ends of bone in moveable joints, allowing smooth and near frictionless articulation³, thereby protecting joints from the harsh load-bearing and movement demands of daily activity. Despite these properties, once injury does occur, articular cartilage is unable to regenerate the same hyaline matrix. The knee is the most common site for articular cartilage injury in the lower limb, accounting for about 75% of all osteochondral lesions⁴.

Articular cartilage lacks arterial and lymphatic supply, relying on diffusion of nutrients from the synovial fluid within the joint⁵. This lack of blood supply hampers the healing process⁶, since the vascular system is required to transport specific cells that clear necrotic (damaged) material and synthesise new tissue as well as other molecules that provide the most optimal healing environment⁷ to and from the injured area. Further, the articular cartilage framework contains no nerve supply, thus rendering the tissue insensitive to early injury⁸. Ultimately, damage to the articular cartilage in the knee often results in pain and functional limitation, further leading to reduced activity, muscle atrophy and a downward spiral of joint degradation and debilitation.

Traditional Treatment Options

A number of cartilage repair techniques have been investigated including debridement and lavage, as well as marrow stimulation techniques such as microfracture, subchondral drilling and abrasion arthroplasty. These procedures may temporarily alleviate symptoms such as pain; however, the fibrocartilage formed in response to some of these procedures does not possess the biomechanical or biochemical properties of hyaline articular cartilage⁹. Although it covers the subchondral bone, fibrocartilage repair tissue may still fail to distribute the loads across the articular surface in a manner that avoids pain and further joint degeneration¹⁰⁻¹². Other treatment options include osteochondral autografting (mosaicplasty/OATS), usually used for smaller lesions because of the morbidity of large donor sites¹³ and osteochondral allografts. The use of allografts has been limited because of a low supply of suitable grafts and the risk of disease transmission¹⁴. Consequently, new repair methods have centred on cell regeneration techniques that lead to the long-term regeneration of cartilage.

Cell Regenerative Treatment Options

Therapies using cultured autologous chondrocytes

Autologous Chondrocyte Implantation (P-ACI) — 1st Generation

In autologous chondrocyte implantation (P-ACI), a patient's own cartilage cells (chondrocytes) are isolated and cultured *in vitro*, then re-implanted into the cartilage. A periosteal flap, usually taken from the proximal medial tibia⁹, is cut to fit the defect and sutured around the defect border; this acts as a watertight seal. This repair procedure has demonstrated early clinical success in treating focal articular cartilage defects in the knee^{15,16}, but suffers from complications related to overgrowth of the periosteal flap¹⁶.

Collagen-covered ACI (C-ACI) — 2nd Generation

Collagen-covered ACI (C-ACI) provides surgical advancements to traditional ACI. A biodegradable type I/III collagen membrane contains the implanted chondrocytes, eliminating the drawbacks associated with the use of the periosteal flap. However, problems remain, such as the extensive micro-trauma from suturing, as well as possible cell leakage¹⁷.

MACI® (matrix-induced autologous chondrocyte implant) — 3rd Generation

MACI implant is a third-generation ACI; the chondrocytes are seeded directly onto the biodegradable type I/III collagen membrane during the manufacturing process which enables the attachment of the chondrocytes to the membrane. During the implant procedure the membrane is fixed in place with fibrin glue, which has been shown to support migration and proliferation of human chondrocytes^{18,19}. Therefore, the MACI implant does not suffer the limitations encountered by using the periosteal patch¹⁷: the surgical procedure is less complex and time consuming than 1st or 2nd generation ACI, as periosteal harvest is not required, and a smaller incision is required to obtain defect exposure^{16,17}; there is even an option for arthroscopic implantation²⁰. In addition, the reduced anaesthetic and tourniquet time associated with MACI implant, as opposed to P-ACI and C-ACI, make undertaking concurrent procedures such as anterior cruciate ligament reconstruction more favourable²¹. Five-year studies have been supportive²²⁻²⁴ and long-term studies currently underway are expected to show long-term efficacy.

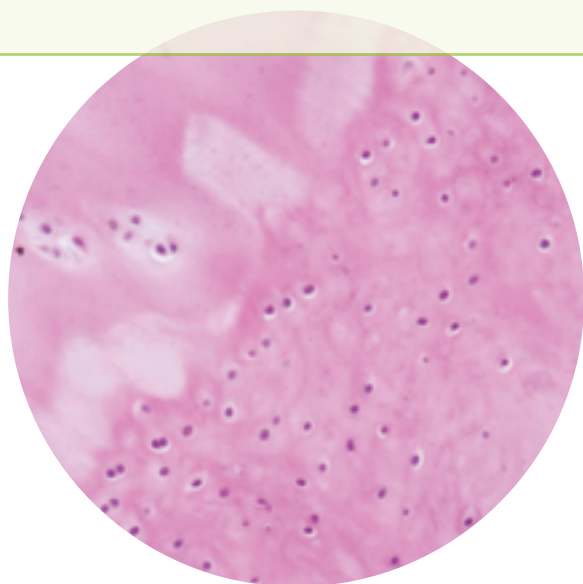
Principles of post-MACI Implant Rehabilitation

Postoperative rehabilitation following MACI implant returns patients to an optimal level of function through a gradual and progressive program that emphasises full motion, progressive partial weight bearing (WB) and controlled exercises²⁵. This progressive program should be tailored to each patient's individual status and needs, the location and size of the defect, and any additional surgical procedures that may have been performed²⁶. Throughout rehabilitation, the focus remains on protecting and progressively stimulating the implanted cells, so that the best development and differentiation of the chondrocytes can occur.

Throughout the MACI implant postoperative timeline, the mechanical environment plays a critical role in chondrocyte re-differentiation and development. In essence, rehabilitation is designed to activate the cell-mediated progression of MACI implant-induced regenerative cartilage into physiologically functional articular cartilage. Articular cartilage responds to mechanical stimuli such as loading and unloading, through altered cell metabolism and matrix synthesis²⁷. The interaction of extracellular proteins (such as collagen and proteoglycan aggregate) strengthen and stiffen articular cartilage, as does resistance to tensile and compressive external stresses²⁸. *In vivo* studies have shown that mechanical exercise of the knee joint increases this protein content in normal articular cartilage, while decreased activity has the reverse effect^{29,30}.

The type of mechanical loading experienced by the articular surface has the potential to regulate chondrocyte differentiation.

- **Cyclic compressive loading** has been shown to enhance chondrogenesis³¹, as well as matrix synthesis and gene expression in cartilage tissue³²⁻³⁵, dependent on the duration and frequency of dynamic compression³⁶.
- **Shear loading** across the knee articular surface in later stages of rehabilitation has also been shown to result in increased matrix production and improved biomechanical structure³⁷⁻³⁹. Caution: shear loading in early stages may have implications for graft delamination.
- **Static compression**^{34,40-43} and immobilisation during the postoperative period appear detrimental to the development and repair of cartilage⁴⁴.



Of course, favourable proliferative conditions should not be pushed at the expense of potential graft delamination, especially in the early developmental stages. Thus, a structured rehabilitation program is essential to promote an optimal healing environment that is both safe and stimulating for the developing repair tissue.

At present, a progressive increase in dynamic loading is thought to be best provided through a structured exercise and partial WB gait rehabilitation program. Though the postoperative environment is imperative to short-, mid- and long-term clinical and biological graft outcomes, the pre-operative condition of the patient is also important in creating the optimal biomechanical environment at the knee in preparation for surgery and the postoperative progression of graft loading. Therefore, we will discuss both pre- and postoperative patient outcomes.

Above all, it is critical to remember that postoperative regenerative tissue is biomechanically inferior to functional articular cartilage which is capable of withstanding the typical demands placed upon load-bearing joints. Throughout the rehabilitation process, the overarching goal is the best transition from the first to the latter.

At present, a progressive increase in dynamic loading is thought to be best provided through a structured exercise and partial WB gait rehabilitation program.

MACI Implant Pre-operative Rehabilitation

The MACI implant rehabilitation process should begin prior to surgery: Patients need to be physically and mentally prepared for their operative procedure and the associated rehabilitation process. The therapist should focus on improving strength, mobility and function around the affected knee joint, as well as assessing associated musculoskeletal issues spanning the entire kinetic chain. The therapist should also offer the patient theoretical and practical education concerning the postoperative process.

As an ancillary benefit of pre-operative rehabilitation work, when patients return to the clinic postsurgery they are familiar with the clinic protocols, the staff, the environment and the exercise routines. They also receive support and social interaction from other patients and staff.



Specific objectives of the pre-operative program

- 1. Increase bilateral strength**, balance, mobility and function of the muscles and connective tissue of the lower limb
- 2. Increase bilateral active knee** range of motion (ROM) and reduce pre-operative contractures
- 3. Improve muscular strength** of the upper limbs and trunk to assist early postsurgery tasks of bed/chair transfers and crutch ambulation
- 4. Improve cardiovascular fitness** which may aid faster recovery from surgery
- 5. Ensure the patient is proficient** in ambulating and negotiating stairs using two crutches
- 6. Provide appropriate pre-operative education** regarding the surgical procedure and chondrocyte maturation process, thus preparing the patient psychologically for surgery and the lengthy rehabilitation process
- 7. Where appropriate, facilitate weight loss** for normal height-to-weight ratio

MACI Implant Postoperative Rehabilitation

The majority of surgeons and therapists agree that postoperative rehabilitation is a critical factor in achieving best patient outcomes⁴⁵. Robertson et al.⁴⁶ proposed four main factors that influence patient outcome and quality of repair tissue following any MACI implant procedure to the knee:

1. **Successful cell culturing**
2. **Efficiency of the surgical procedure**
3. **Patient cooperation in all aspects of the pre- and postoperative program**
4. **Timely progression of load bearing and postoperative rehabilitation**

Therefore, it is imperative that patients are well supervised throughout the postoperative period, and adhere to a safe, progressive and structured rehabilitation program. Three main components of the postoperative rehabilitation program are clearly established:

1. **A progressive increase in weight-bearing (WB) activities**
2. **A progressive restoration of knee joint range of motion (ROM)**
3. **Appropriate facilitation of muscular control and strengthening⁴⁷**

Thus, therapists experienced in musculoskeletal rehabilitation can treat MACI implant patients safely and with confidence—providing they are well educated in the following four important areas:

1. **Patient demographics, as well as the ability to listen and communicate effectively with the patient**
2. **The wide array of surgical techniques that may be performed in combination with MACI implant, and an ability to adapt the rehabilitation program to incorporate these techniques**
3. **Knee joint biomechanics**
4. **The graft maturation timeline, and how this maturation process facilitates the modality, frequency and intensity of activity permitted throughout the postoperative timeline**

Understanding Patient Individuality

Individual patients undergoing the MACI implant technique vary greatly; variations include age, gender, body mass, physical function, other comorbidities, defect aetiology and the length of time prior to surgery with pain and symptoms. Some of these can dramatically affect outcomes.

- **The age range indicated for MACI implant is typically between 15-55 years**, but may vary due to regional regulatory and therapy licensing requirements. While age and gender have not been shown to significantly affect postoperative clinical outcome⁴⁸, it is well known that as one ages associated regenerative capacity diminishes.
- **The body mass index (BMI) for MACI implant should be < 30^{49,50}**. Studies show that any reduction in body weight results in a four-fold reduction in loads experienced at the knee during normal ambulation and daily activities⁵¹. This highlights the importance of pre-operative weight loss and postoperative weight maintenance so as not to overload postoperative repair tissue.
- **A short (acute injury) history** of trauma, pain and symptoms leading up to the MACI implant procedure are decisive factors in a good clinical outcome, as compared with long-standing trauma or degenerative cartilage defects⁴⁸. However, MACI implant may be used as a secondary treatment following alternative failed cartilage repair procedures⁴⁸; there are often rehabilitative implications associated with a long duration of symptoms⁵². Therefore, it is important to thoroughly document a good patient history; patients with long-standing pain and/or those that have undergone previous surgical procedures may require a more conservative approach.

Of course, in addition to these patient variables, “individuality” remains the overriding variable. Patients progress at different rates and experience different levels of pain, symptoms and joint effusion. Session-to-session treatment plans will be highly dependent upon these factors, as well as individual patient compliance to the program.

Understanding Adjunct Surgical Procedures

MACI implant is not advised in a number of conditions—including uncorrected knee malalignment (tibiofemoral or patellofemoral), ligamentous instability and meniscal deficiency^{53,54}—a variety of adjunct surgical procedures may be performed in combination with the MACI implant surgery.

It is not the purpose of this document to present a thorough outline of rehabilitation variations that may exist between patients who undergo MACI implant versus those with MACI implant in combination with an auxiliary procedure. However, it is the responsibility of the treating clinician to effectively adapt rehabilitation strategies to suit these surgical variations and any unexpected complications.

Understanding Knee Biomechanics

Generally, MACI implant is used for symptomatic lesions located on the femoral condyles or tibial plateau (tibiofemoral joint), and/or the trochlea groove or patella (patellofemoral joint)^{55,56}. To avoid excessive compressive and/or shear loads that may be detrimental to the repair, it is imperative that the treating therapist has a sound knowledge of the individual articulation mechanics of each area, particularly in response to weight-bearing (WB) and knee flexion.

The following brief overview of important biomechanical implications addresses some key elements. Thorough outlines of knee joint biomechanics are readily available⁵⁷⁻⁶⁴ and recommended for further review.

- **Patellofemoral (PF) Joint:** Both WB⁶⁵ and active knee flexion⁶⁶ act to increase contact force through the PF joint; this should be considered particularly in the early protection stage post-implantation. Generally, the inferior pole of the patella does not make contact with the opposing trochlea groove within the first 20-30 degrees of knee flexion⁵⁹. Therefore, upon clearance from the orthopaedic specialist, a well-contained patellar graft may enable a patient to fully weight bear from the



time of surgery, provided they ambulate with a knee brace locked at full extension. As the knee continues to flex, there is an increasing PF contact area. Initially, the inferior patellar facet makes contact with the superior trochlea groove at approximately 30 degrees of knee flexion, followed by the mid patellar facet with the mid trochlea at 60 degrees and the superior patellar facet with the inferior trochlea and femoral condyles at 90 degrees of knee flexion^{59,60}.

- **Tibiofemoral (TF) Joint:** The anterior aspect of the femoral condyles makes contact with the mid surface of the tibial plateau at full knee extension. As the femoral condyles roll posteriorly and slide anteriorly on the tibial plateau with knee flexion, the posterior aspect of the femoral condyles and tibial surface are in contact^{61,62}. Again, this will dictate the exercise modality and range in which activity can be safely performed when working with TF grafts, and further highlights the importance of accumulating a thorough patient history from the referring specialist (e.g., a graft to the anterior femoral condyle may safely permit a range of different exercises, performed in a more flexed knee, when compared to a graft on the posterior aspect).

Understanding Graft Maturation

Titration postoperative rehabilitation to each stage of rehabilitation is of great importance to the outcome of the procedure: over-stimulation may lead to overload and early degeneration of the patch, whereas lack of stimulus may not encourage optimal chondrocyte development⁶⁷. Since the repair process follows typical proliferative, matrix production and remodelling phases, if the mechanical environment provided is both protective and stimulatory of that repair process, then the tissue can continue to remodel and mature⁶⁷ differentiating into the required durable, load-bearing tissue (**Figure 3**).

Clinical studies⁹ identify four stages of tissue maturation.

These stages are:

1. Implantation and Early Protection Stage (0-6 weeks):

Post-implantation the focus rests on restoring knee joint homeostasis and protecting primitive repair tissue.

2. Transition and Proliferation Stage (6-12 weeks):

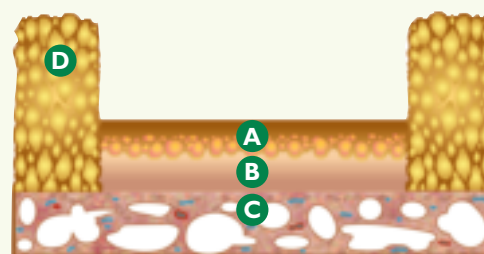
The defect fills with soft, primitive repair tissue.

3. Remodelling Stage (12-26 weeks):

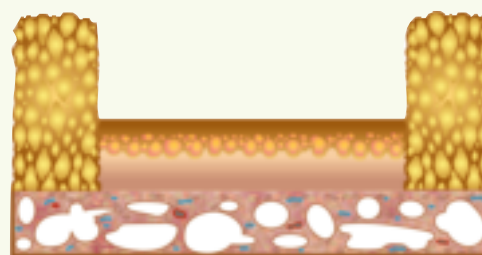
The graft firms as the extracellular matrix expands.

4. Maturation Stage (26 weeks onwards):

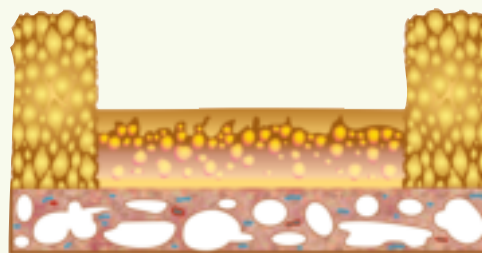
The intercellular matrix further remodels and the repair tissues stiffen. The length of this process consequently has significant implications for the timing and specifics of the rehabilitation plan. Between 12 and 26 weeks postsurgery, repair tissue has a putty-like texture. Though the graft is as firm as normal cartilage by 9 to 18 months⁶⁸, repair tissue continues to develop and remodel up to three years following surgery⁶⁹.



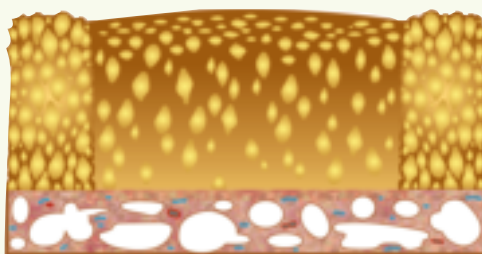
1. **Implantation & Early Protection (0-6 weeks):** The type I/III collagen membrane (A) with seeded chondrocytes is glued onto the subchondral bone (C) using fibrin glue (B). A well-contained defect may be partially protected in the early stages by the walls of the adjacent native cartilage (D).



2. **Transition & Proliferation (6-12 weeks):** Chondrocytes migrate from the membrane through the fibrin sealant, and the defect begins to fill with a soft, primitive repair tissue.



3. **Remodelling (12-26 weeks):** Chondrocytes begin to produce a matrix consisting of type II collagen, aggrecan and other important matrix proteins. The graft begins to firm.



4. **Maturation (26 weeks-3 years):** Cartilage infill is complete, while chondrocytes and matrix reach full maturity. There is good integration of the graft with the adjacent native cartilage and underlying bone. The graft is now firm.

Figure 3. Paradigm of cartilage regeneration following MACI implant. The postoperative timeline of tissue maturation dictates the progression of activity. It is important to note that although graft infill may approximate the height of the adjacent healthy articular cartilage walls at 12-26 weeks postsurgery, this tissue remains immature with a “putty-like” texture; it will continue to develop for up to three years postsurgery⁶⁹.

**Accelerated Rehabilitation
Guidelines for the
Knee Using MACI®**
(matrix-induced autologous
chondrocyte implant)



The Importance of Individualization

Program individualization is one of the most important principles of MACI implant postoperative rehabilitation. While the guidelines outlined within this section document a generic strategy based on clinical experience and good quality research, each patient will have unique circumstances surrounding his or her surgery and a unique response to the surgery itself. When developing and undertaking the rehabilitation plan, the following factors should be considered:

- 1. Patient age and physical function.**
- 2. Patient body weight:** In particular, patients with a body mass index (BMI) > 25 (overweight) to 30 (obese) should be carefully monitored.
- 3. Defect location:** The regional location of the repair will affect the exercise modality and intensity that can be performed throughout the rehabilitation process (e.g., tibiofemoral [TF] grafts will typically require more caution to weight-bearing [WB] status, whilst patellofemoral [PF] grafts will draw caution to the progression of knee range of motion).
- 4. Defect size:** Patients with large defects, in particular those $> 6 \text{ cm}^2$, may require a more conservative approach to rehabilitation.
- 5. Multiple defects:** Patients with multiple implantations, particularly if those grafts span different areas of the knee joint (e.g., primary medial femoral condyle graft within the TF joint in association with a secondary trochlea graft within the PF joint), may require a more conservative approach to rehabilitation.
- 6. Adjunct surgical procedures:** It is important to account for other associated surgical procedures that have been performed to correct joint malalignment (e.g., tibial tubercle transfer to address PF malalignment, or a tibial or femoral osteotomy to address TF malalignment) or instability (e.g., anterior cruciate ligament reconstruction).

Though four primary stages of tissue maturation have been previously outlined (early protection, transition, remodelling and maturation)⁹, we have divided this generic postoperative rehabilitation program into seven phases (**Table 3**), based more specifically upon the progressive physical function of the patient, as well as the graft maturation timeline.

The early postoperative stages are of great importance to the outcome of the procedure⁶⁷; however, repair tissue continues to develop and remodel up to three years following surgery^{9,70}. For this reason, short-, mid- and long-term rehabilitation strategies will combine to produce the most optimal long-term outcome.

Rehabilitation Phases

Maturation

- 1. Phase 1: 0-1 week postsurgery
- 2. Phase 2: 2-3 weeks postsurgery
- 3. Phase 3: 4-6 weeks postsurgery
- 4. Phase 4: 7-12 weeks postsurgery
- 5. Phase 5: 3-6 months postsurgery
- 6. Phase 6: 6-9 months postsurgery
- 7. Phase 7: 9-12 months postsurgery and return to sport

Stages of Repair Tissue

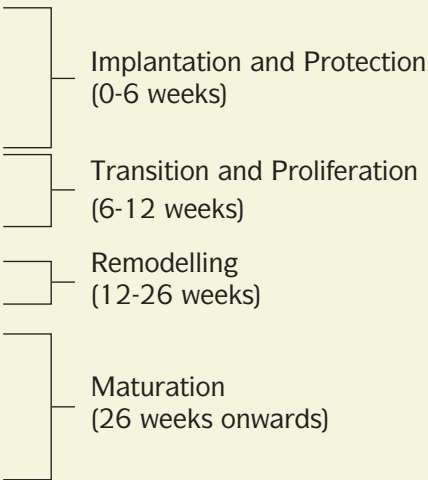


Table 3. Phases of postoperative rehabilitation and the associated graft maturation timeline.

Please reference the *Accelerated Rehabilitation Guidelines for the Knee Using MACI® (matrix-induced autologous chondrocyte implant): Exercise Companion Guide* to find detailed instructions and visual references for each of the gym-based and hydrotherapy exercises described in the following pages.

Phase One: Inpatient hospital stay (0-1 week postsurgery)

During the days immediately following postsurgery, 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.



Time span and dependencies

The postoperative in-patient timeline begins at surgery and may last to postoperative day 7; the time span is highly dependent on what adjunct procedures may have been performed, coinciding patient-specific factors and postoperative complications.

Goals

Maintain joint mobility and muscle tone while adhering to all postoperative precautions.

Rehabilitation plan

Initiate on postoperative day 1 unless otherwise instructed by the operating surgeon.

1. Provide appropriate analgesics for pain control.
2. Commence continuous passive motion (CPM) (0-30° of knee flexion) 12-24 hours postsurgery, for a minimum of 1 hour daily to reduce the chance of intra-articular adhesions⁷¹ and potentially speed up and improve the quality of tissue repair.⁷²⁻⁷⁴
3. Fit a postoperative range of motion (ROM) control brace (initially set at 0-30° of knee flexion); this should be worn 24 hours per day for the first 3 weeks.
4. Apply cryotherapy as standard oedema control (20 minutes with ice, at least 3 times per day).
5. Perform active dorsi-flexion and plantar-flexion exercises of the ankle to encourage lower extremity circulation.
6. Encourage isometric contraction of the quadriceps, hamstrings and gluteal musculature to help maintain muscle tone and minimise muscle loss.^{14,67}
7. Oversee breathing exercises to ensure proper technique during therapeutic exercise.
8. Offer instruction and practice in proficient toe-touch ambulation (using 2 crutches, with ≤ 20% of body weight [BW] through the operated limb, unless otherwise indicated by the operating surgeon), and safety with bed transfers and stairs.
9. Provide detailed verbal and written instruction on how to perform activities of daily living and functional tasks, whilst adhering to postoperative precautions and appropriate weight-bearing (WB) status.

Contraindications

1. Excessive load bearing (>20% of patient BW) especially in combination with knee flexion
2. Ambulation without crutches and a protective knee brace
3. Generation of shear forces within the knee
4. Knee flexion beyond 30°
5. Active knee extension (especially against resistance)

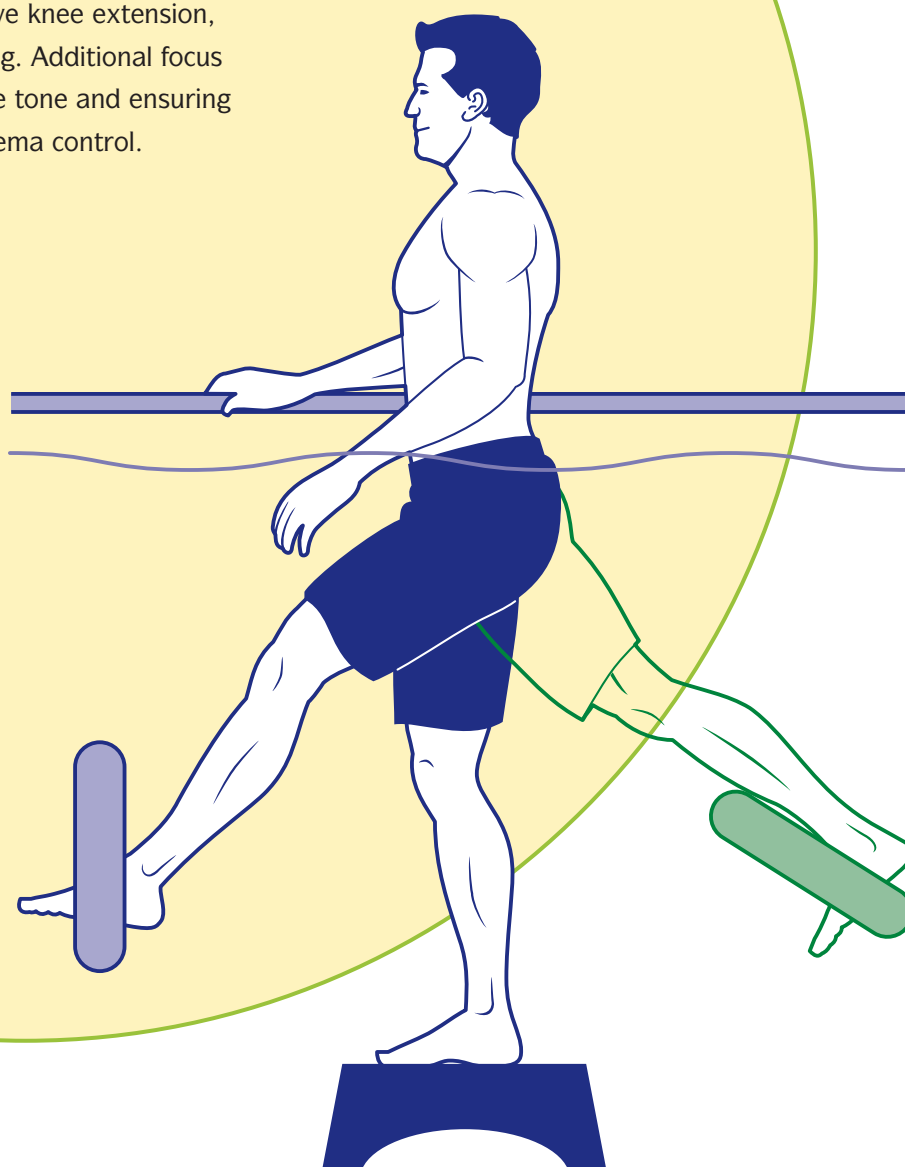
Prior to discharge

1. Ensure that the patient has an initial appointment (or appropriate contacts) for out-patient functional rehabilitation.
2. Ensure that the patient is aware that the next postoperative appointment with the orthopaedic surgeon normally occurs within 4-6 weeks postsurgery.
3. If required, ensure that patient has an appointment for the removal of stitches/staples, or is aware when they must be removed (generally within 8-10 days postsurgery).
4. Instruct and educate the patient on the importance of following the RICE (rest, ice, compression and elevation) guidelines for oedema control.
5. Reinforce WB constraints and brace guidelines.
6. Review the home exercise regimen, ensuring the patient is proficient in safely performing these activities.
7. Review (and educate on) techniques for performing functional activities (e.g., stairs, bed transfers, showering, etc.), ensuring the patient is proficient in safely performing these activities.
8. Ensure the patient is educated in wound healing, and how to assess changes in the wound and surrounding soft tissue that may indicate infection.

PLEASE REFER TO PHASE ONE IN THE EXERCISE COMPANION GUIDE FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Phase Two: Weeks 2-3 postsurgery

During these first weeks, the patient should achieve pain-free and full passive knee extension, as well as limited weight bearing. Additional focus is placed on maintaining muscle tone and ensuring proper wound healing and oedema control.



The initial postoperative out-patient session

1. Review the patient's level of pain and medication use.
2. Review the patient's swelling and provide appropriate education on the RICE (rest, ice, compression and elevation) guidelines for oedema control.
3. Review the patient's wound and reinforce education on wound monitoring, cleanliness and infection control.
4. Ensure the appropriate knee brace is obtained, correctly fitted and adjusted appropriately (0-30° of knee flexion, or as directed by the orthopaedic specialist).
5. Ensure proficiency with crutches, both during normal ambulation and negotiating stairs.
6. Provide appropriate education, training and proficiency with the desired level of partial weight-bearing (WB) ($\leq 20\%$, or as directed by the orthopaedic specialist)⁷⁵.
7. Reiterate instructions and movement contraindications outlined by the orthopaedic specialist and the hospital rehabilitation therapists.
8. Review and progress the home exercise program, based on the current postoperative timeline and status of the patient.

Goals

By week 3 postsurgery, patients are expected to achieve:

1. Pain-free knee flexion of 90° for tibiofemoral (TF) grafts and 60° for patellofemoral (PF) grafts.
2. Pain-free and full passive knee extension.
3. Proficient heel-to-toe gait with 30% body weight (BW) for TF grafts or 50% BW for PF grafts, using 2 crutches and a knee brace.
4. Reduced (and/or well controlled) postoperative pain and oedema.
5. Ability to generate an active, isometric quadriceps contraction.
6. Proficiency with home-exercise program.

Rehabilitation plan

WEIGHT BEARING

Electronic scales should be used as a means to train, educate and provide practice to patients in attaining the desired levels of partial WB^{75,76}, calculated as a percentage of the patient's BW, throughout the postoperative timeline.

- TF joint: progress from $\leq 20\%$ BW (week 1-2) to 30% BW (week 3)
- PF joint: progress from 20-30% BW (week 1-2) to 50% BW (week 3)

AMBULATORY AIDS

- TF joint: 2 crutches
- PF joint: 2 crutches

RANGE OF MOTION (ROM)

- TF joint: progress active ROM from 30° (week 2) to 90° (week 3)
- PF joint: progress active ROM from 30° (week 2) to 60° (week 3)

PROTECTIVE KNEE BRACING

- TF joint: progress brace from 0-30° (week 1-2) to 0-45° (week 3)
- PF joint: lock brace at full knee extension

RANGE OF MOTION AND FLEXIBILITY EXERCISES

- Use continuous passive motion (CPM) at the end of each session for 20-30 minutes to reduce the chance of intra-articular adhesions⁷¹ and potentially speed up and improve the quality of tissue repair⁷²⁻⁷⁴
- TF joint: progress from 30° (week 2) to 90° (week 3)
- PF joint: progress from 30° (week 2) to 90° (week 3)
- Passive and active heel slides
- Passive knee extension
- Careful patellar mobilisation in all directions

STRENGTHENING EXERCISES

- Isometric quadriceps contraction and co-contraction activities (aided with the use of neuromuscular electrical muscle stimulation to stimulate voluntary muscular contraction)
- Isometric gluteal, hamstrings, adductor and calf contractions
- Straight-leg-raise activities (hip flexion, abduction, adduction and extension)

HYDROTHERAPY EXERCISES

- Deep-water walking (forwards, backwards and sideways)
- Deep-water calf raises
- Straight-leg hip flexion, extension, abduction and circumduction (with or without floatation devices for additional resistance)
- Passive knee flexion
- Stretching of hamstring and calf musculature

ADJUNCT MODALITIES

- Perform clearance and lymphatic remedial massage as needed to assist in the reduction of soft tissue oedema
- Perform cryotherapy, compression and elevation regularly to assist in the reduction of soft tissue oedema

PLEASE REFER TO PHASE TWO IN THE EXERCISE COMPANION GUIDE FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Phase Three: Weeks 4-6 postsurgery

During Phase Three, the patient increases weight-bearing and range-of-motion activities, as appropriate, while augmenting strengthening exercises.



Goals

By week 6 postsurgery, patients are expected to achieve:

1. Pain-free active knee flexion to 125°.
2. Proficiency in performing home exercises, including a straight-leg raise.
3. Pain-free gait using 1-2 crutches (dependent on weight-bearing [WB] status), a knee brace and 60% body weight (BW) pressure for tibiofemoral (TF) grafts. Patients with patellofemoral (PF) grafts may be progressed to full WB as tolerated, following clearance from the orthopaedic specialist.

Rehabilitation plan

WEIGHT BEARING

- TF joint: progress from 40% BW (week 4) to 60% BW (week 6)
- PF joint: progress from 75% BW (week 4) to full WB (week 6)

AMBULATORY AIDS

- TF joint: 1-2 crutches
- PF joint: 1-2 crutches (weeks 4 and 5); 1 crutch as required (beginning at week 6)

RANGE OF MOTION (ROM)

- TF joint: progress active ROM from 110° (week 4) to 125° (week 6)
- PF joint: progress active ROM from 90° (week 4) to 125° (week 6)

PROTECTIVE KNEE BRACING

- TF joint: progress brace from 0-60° (week 4) to full flexion (week 6)
- PF joint: use brace as required (beginning at week 6)

RANGE OF MOTION AND FLEXIBILITY EXERCISES

- Continue Phase 1 and 2 flexibility/stretching exercises
- Stretch hamstrings and calf musculature
- Carefully mobilise patella in all directions
- Use continuous passive motion (CPM) to maximum comfortable range as required

STRENGTHENING EXERCISES

- Continue Phase 1 and 2 strengthening exercises
- Progress straight-leg-raise activities (i.e., supine straight-leg hip flexion half-seated and/or with externally rotated foot)
- Introduce side-lying gluteal exercises with a flexed knee
- Introduce standing-calf raises (dependent on WB status)
- Introduce seated or standing weighted-hip adduction and abduction
- Introduce trunk strengthening exercises
 - Supine sit-ups
 - Weight-supported trunk flexion
- Introduce recumbent cycling (modified knee flexion; 90°) (weeks 5-6)

HYDROTHERAPY EXERCISES

- Continue Phase 2 hydrotherapy exercises
- Introduce active knee flexion (with floatation devices for additional resistance)
- Introduce shallow water walking (waist depth, dependent on WB status)
- Introduce shallow-water calf raises
- Introduce deep-water squatting activities
- Introduce pool cycling (full knee ROM)

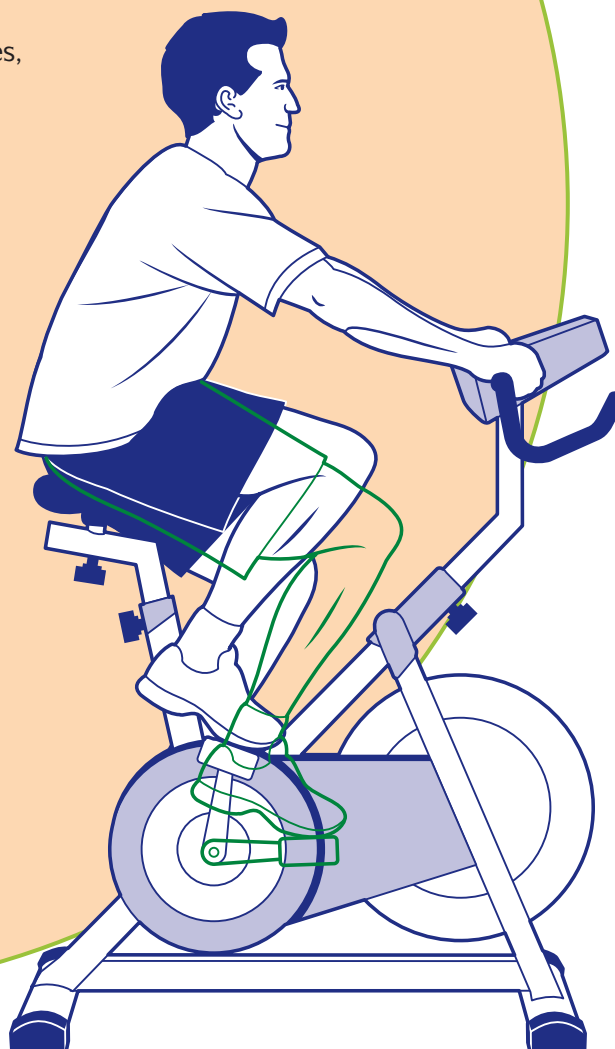
ADJUNCT MODALITIES

- Perform clearance and lymphatic remedial massage as required
- Perform cryotherapy, compression and elevation as required

PLEASE REFER TO PHASE THREE IN THE *EXERCISE COMPANION GUIDE* FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Phase Four: Weeks 7-12 postsurgery

In Phase Four, the patient works towards movement independent of ambulation devices and knee braces. Focus is also placed on becoming thoroughly proficient with the rehabilitation exercises, as clinic visits become less frequent.



Goals

By week 12 postsurgery, patients are expected to achieve:

1. Pain-free active knee range of motion (ROM) within anatomical limits (0° to 130-160°).
2. Pain-free six-minute walk test^{76,77} without the use of walking aids.
3. Pain-free upright cycle ergometry, without the protective knee brace.
4. Proficiency in performing home and gym-based exercises, for continuation of rehabilitation following clinic discharge.

Following the completion of Phase Four, patients generally undergo a 3-month postsurgery assessment, and a written report is sent to the orthopaedic specialist to coincide with the patient's review.

Rehabilitation plan

WEIGHT BEARING

- Tibiofemoral (TF) joint: progress from 80% body weight (BW) (week 7) to full weight bearing (WB) (weeks 8-10)
- Patellofemoral (PF) joint: full WB

AMBULATORY AIDS

Upon clearance from the orthopaedic specialist, patients with TF are generally permitted to fully weight bear indoors without crutches, though a single crutch outdoors and in unfamiliar areas is encouraged.

- TF joint: 1 crutch as required in outdoor/unfamiliar areas (beginning week 8)
- PF joint: no crutches

RANGE OF MOTION (ROM)

- TF joint: progress to full active knee ROM (weeks 7-8)
- PF joint: progress to full active knee ROM (weeks 7-8)

PROTECTIVE KNEE BRACING

- TF joint: allow full knee flexion within brace
- PF joint: no brace

RANGE OF MOTION AND FLEXIBILITY EXERCISES

- Continue Phase 2-3 flexibility/stretching exercises
- Stretch quadriceps musculature (weeks 9-10)
- Introduce passive knee ROM on rowing ergometer (weeks 9-10)
- Carefully mobilize patella in all directions
- Conduct continuous passive motion (CPM) to maximum comfortable range as required

STRENGTHENING EXERCISES

- Continue Phase 2-3 strengthening exercises
- Introduce standing weighted hip adduction and abduction
- Introduce weighted knee flexion (week 8)
- Introduce upright (knee flexion; 105-110°) cycling (weeks 9-12)

HYDROTHERAPY EXERCISES

- Continue Phase 2-3 hydrotherapy exercises
- Stretch quadriceps musculature
- Progress water squatting activities
- Introduce weight-supported lunge activities
- Introduce weight-supported "step up and down" activities
- Introduce "patter" kick (week 12)

ADJUNCT MODALITIES

- Perform clearance and lymphatic remedial massage as required
- Perform cryotherapy, compression and elevation as required

PROPRIOCEPTION EXERCISES

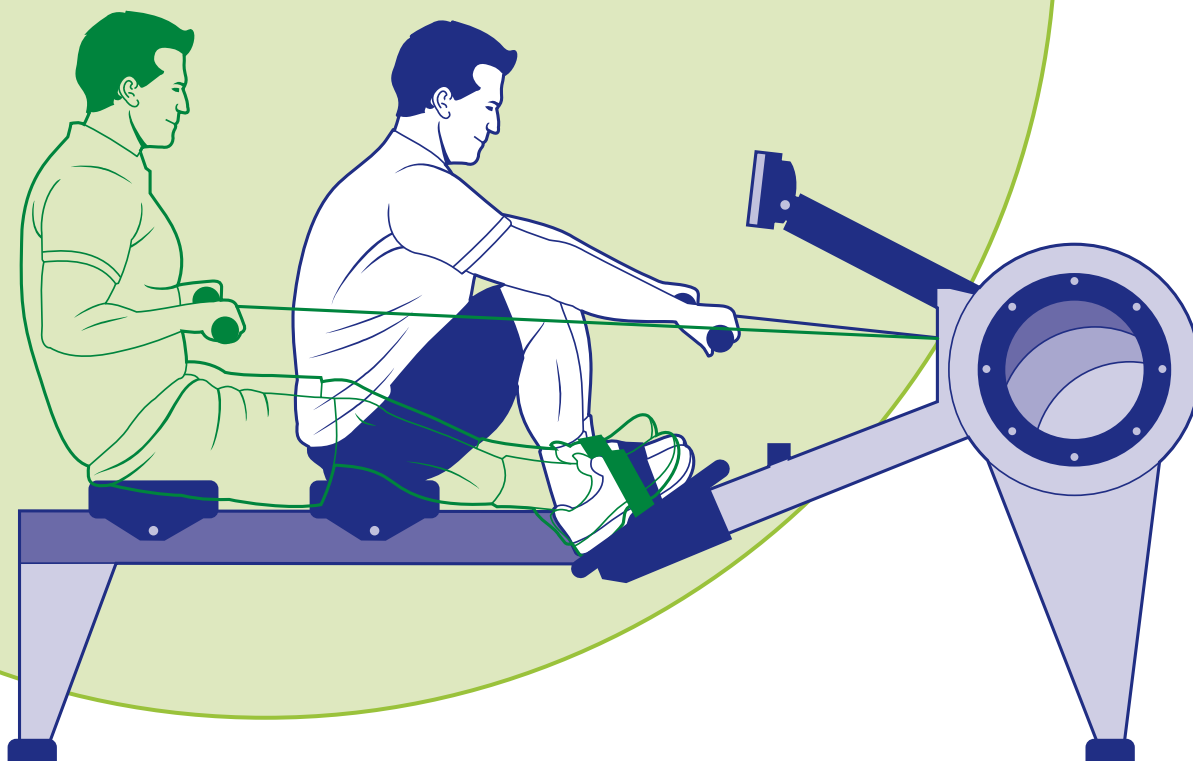
Introduced following the return to full WB, both within the hydrotherapy pool and the clinic setting, these activities should be undertaken on both the affected and non-affected leg. Slowly progress proprioceptive activities from partial to full WB positions by altering:

1. The patient's postural position (i.e., seated to standing).
2. The environment in which the activity is to be undertaken (i.e., gym- or pool-based).
3. Proprioceptive input mechanisms (i.e., eyes open or closed).
4. The speed of movement.
5. The magnitude of the base of support (i.e., 2-legged to 1-legged).
6. The stability of the base of support (i.e., introduction of unstable surfaces including a soft mat or pillow, wobble board, dura disc, theraball or mini trampoline).
7. Introducing "weight transfer" and/or "sport-specific drills" with other equipment.

PLEASE REFER TO PHASE FOUR IN THE EXERCISE COMPANION GUIDE FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Phase Five: Months 3-6 postsurgery

During these months, the majority of patients return to work either on a part-time or full-time basis. Therefore, patients either continue to attend the outpatient clinic once or twice per week independently (though group supervised), or should continue with their prescribed gym and home rehabilitation program independently.



Goals

By 6 months postsurgery, patients are expected to achieve:

1. Normal gait pattern without pain, walking aids or a knee brace.
2. Ability to negotiate stairs and mild gradients.
3. A return to work, depending on the demands of the job.
4. Proficiency in performing a weighted-leg press through 60-90° of knee flexion, and with up to (though no more than) 50% of body weight (BW) pressure.
5. Proficiency in performing full weight-bearing (WB) proprioception activities.

Rehabilitation plan

WEIGHT BEARING

- Tibiofemoral (TF) and patellofemoral (PF) joint: full WB

AMBULATORY AIDS

- TF and PF joint: no crutches

RANGE OF MOTION (ROM)

- TF and PF joint: full and pain-free active knee ROM

PROTECTIVE KNEE BRACING

- TF and PF joint: no brace

RANGE OF MOTION AND FLEXIBILITY EXERCISES

- Continue Phase 3-4 flexibility/stretching exercises

STRENGTHENING EXERCISES

- Continue Phase 3-4 strengthening exercises
- Introduce bridging exercises
- Introduce standing single-leg calf raises
- Introduce modified open kinetic-chain (OKC) exercises (e.g., terminal leg extension, with appropriate use based on lesion location and knee joint biomechanics)
- Introduce modified closed kinetic-chain (CKC) exercises (e.g., inner range quadriceps and leg press activities)
- Progress upright stationary and outdoor road cycling
- Introduce rowing ergometry as tolerated

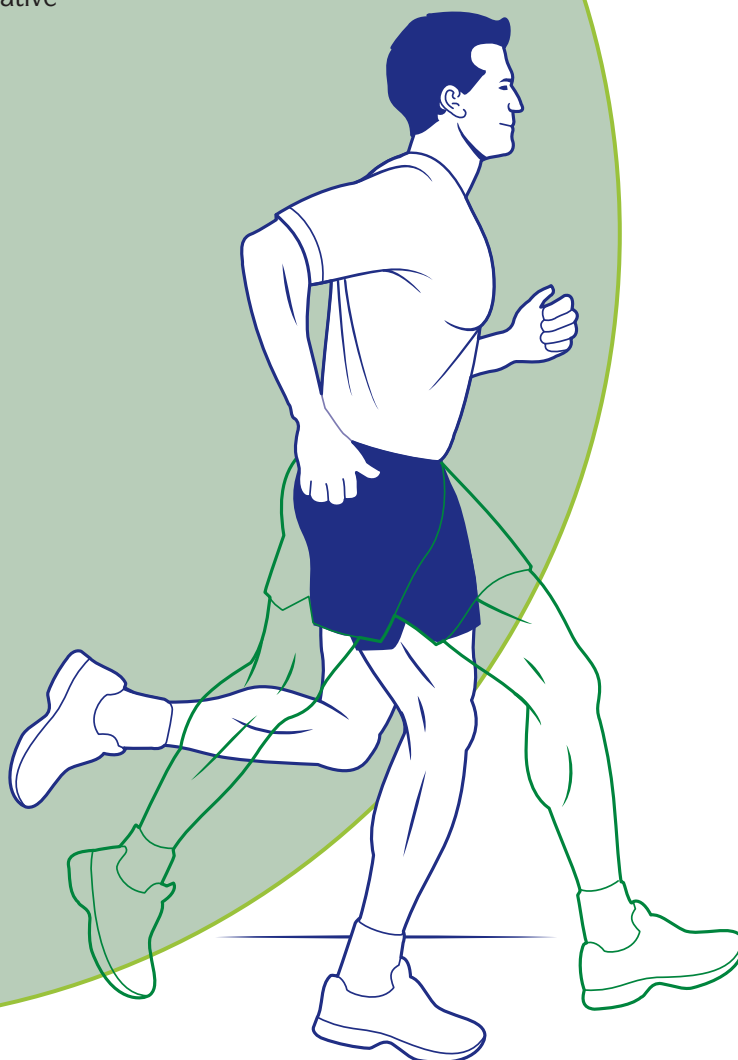
HYDROTHERAPY EXERCISES

- Generally not required from week 12, though the pool may be used for ongoing cardiovascular exercise

PLEASE REFER TO PHASE FIVE IN THE *EXERCISE COMPANION GUIDE* FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Phase Six: Months 6-9 postsurgery

In this phase, gradually increasing the difficulty of the exercises, the patient returns to pre-operative low-impact recreational activities.



Goals

By 9 months postsurgery, patients are expected to achieve:

1. Hamstring and calf strength within 80-90% of the contralateral leg.
2. Ability to tolerate walking distances of more than 5-10 km.
3. Ability to effectively negotiate uneven ground, including soft sand.
4. Ability to return to pre-operative low-impact recreational activities.

Rehabilitation plan

RANGE OF MOTION AND FLEXIBILITY EXERCISES

- Continuation of Phase 3-4 flexibility/stretching exercises

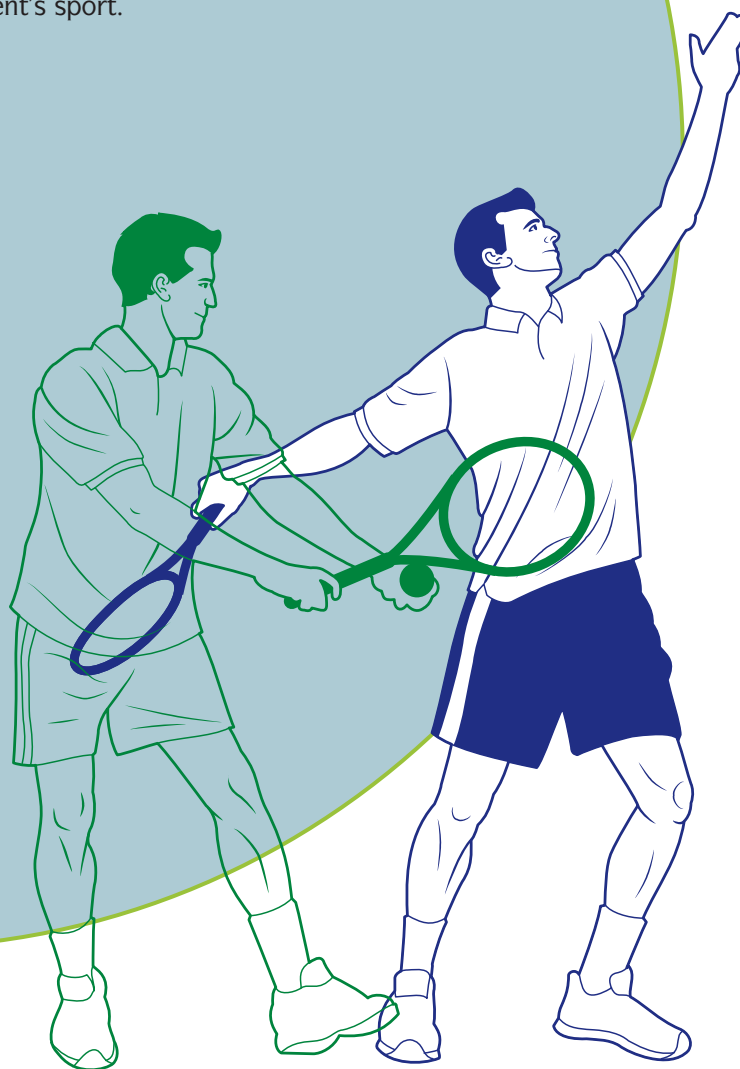
STRENGTHENING EXERCISES

- Continuation of Phase 3-5 strengthening exercises
- Progression and increased difficulty of open kinetic-chain (OKC) exercises
- Progression and increased difficulty of closed kinetic-chain (CKC) exercises (i.e., step ups/downs, modified squat activities)
- Introduction of controlled running on a mini trampoline

PLEASE REFER TO PHASE SIX IN THE *EXERCISE COMPANION GUIDE* FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Phase Seven: Months 9-12 and Return to Sports

In the final phase, the patient is able to resume all normal functionality, as well as low-compression recreational activities. Sport-specific agility drills lay the foundation for a full return to the patient's sport.



Goals

- By 12 months postsurgery, patients are expected to achieve:
1. Ability to perform all activities of daily living.
 2. Ability to commence a return to a running program, for example: walk/jog, jog/run, run on soft surface (grass or soft sand only).
 3. Resumption of dynamic recreational activities (however, sports that generate high compression, shear and rotational loads are to be avoided until 12-18 months, or as directed by the orthopaedic surgeon).

Rehabilitation plan

- RANGE OF MOTION AND FLEXIBILITY EXERCISES**
- Continuation of Phase 3-4 flexibility/stretching exercises

- STRENGTHENING EXERCISES**
- Continuation of Phase 3-6 strengthening exercises
 - Progression and increased difficulty of close kinetic-chain (CKC) exercises (i.e., lunge and squat activities on unstable surfaces)
 - Introduction of agility drills relevant to the patient's sport

PLEASE REFER TO PHASE SEVEN IN THE *EXERCISE COMPANION GUIDE* FOR MORE DETAILED INSTRUCTIONS ON THE EXERCISES.

Return to Sports

At this stage patients are gradually re-introduced to the functional activities that form the basis for their particular sport, augmented by relevant agility drills on grass. These activities are initially performed in isolation, and then with the appropriate sport-specific equipment.

It is not the purpose of this document to outline a protocol of sport-specific exercises and drills; moreover, both the patient and therapist must use their own discretion. Not only the graft maturation process, but the mental preparedness of the patient and the general physical function and level of specific knee strength, stability and support, among other individual patient variations, must be evaluated when considering a patient's long-term outcome and ability to return to competitive activity. Specific considerations include whether:

1. The patient's graft has matured to the point at which it is able to withstand the specific demands of the chosen activity.
2. The patient has been appropriately rehabilitated to the point at which he or she is able to physically undertake the demands of the chosen activity.
3. The overall value of the patient as a player.
4. The commitment and psychological profile of the patient.
5. The patient has undergone appropriate clinical assessment with an orthopaedic specialist experienced with the results of a MACI implant.

Cellular regeneration, matrix production and adaptation of the regenerating tissue to natural function take time, and it is unrealistic and impractical to expect patients to return to competitive sport within the first postoperative year. High-impact sports such as tennis, badminton, ice hockey, basketball, football, rugby and field hockey should not be performed until 12-18 months postsurgery.

Recommended Readings

Ebert JR, Robertson WB, Lloyd DG, Zheng MH, Wood DJ, Ackland T. A prospective, randomized comparison of traditional and accelerated approaches of postoperative rehabilitation following autologous chondrocyte implantation: 2-year clinical outcomes. *Cartilage*. 2010;1:180-187.

Ebert JR, Fallon M, Robertson WB, Lloyd DG, Zheng MH, Wood DJ, Ackland T. Radiological assessment of accelerated versus traditional approaches to postoperative rehabilitation following matrix-induced autologous chondrocyte implantation. [published online ahead of print October 18, 2010]. *Cartilage*. doi:10.1177/1947603510380902.

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

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

Hambly K, Bobic V, Wondrasch B, Van Assche D, Marlovits S. Autologous Chondrocyte Implantation Postoperative Care and Rehabilitation: Science and Practice. *Am J Sports Med*. 2006;34:1-19.

Reinold MM, Wilk KE, Macrina LC, Dugas JR, Cain EL. Current concepts in the rehabilitation following articular cartilage repair procedures in the knee. *J Orthop Sports Phys Ther*. 2006;36(10):774-94.

Riegger-Krugh CL, McCarty EC, Robinson MS, Wegzyn DA. Autologous chondrocyte implantation: current surgery and rehabilitation. *Med Sci Sports Exerc*. 2008;40(2):206-14.

Wondrasch B, Zak L, Welsch G, Marlovits S. Effect of Accelerated Weightbearing After Matrix-Associated Autologous Chondrocyte Implantation on the Femoral Condyle on Radiographic and Clinical Outcome After 2 Years. A Prospective, Randomized Controlled Pilot Study. *Am J Sports Med*. 2009.

References

- Ebert JR, Robertson WB, Lloyd DG, Zheng MH, Wood DJ, Ackland T. A prospective, randomized comparison of traditional and accelerated approaches to postoperative rehabilitation following autologous chondrocyte implantation: 2-year clinical outcomes. *Cartilage*. 2010;1:180-187.
- Ebert JR, Fallon M, Robertson WB, Lloyd DG, Zheng MH, Wood DJ, Ackland T. Radiological assessment of accelerated versus traditional approaches to postoperative rehabilitation following matrix-induced autologous chondrocyte implantation. [published online ahead of print October 18, 2010]. *Cartilage*. doi:10.1177/1947603510380902.
- Mainil-Varlet P, Aigner T, Brittberg M, Bullough P, Hollander A, Hunziker E, Kandel R, Nehrer S, Pritzker K, Roberts S and others. Histological assessment of cartilage repair: a report by the Histology Endpoint Committee of the International Cartilage Repair Society (ICRS). *Journal of Bone & Joint Surgery*. American Volume 2003;85-A Suppl 2:45-57.
- Birk GT, DeLee JC. Osteochondral injuries. Clinical findings. *Clinics in Sports Medicine*. 2001;20(2):279-86.
- Peterson L. Articular cartilage injuries treated with autologous chondrocyte transplantation in the human knee. *Acta Orthop Belg*. 1996;62 Suppl 1:196-200.
- Minas T, Nehrer S. Current concepts in the treatment of articular cartilage defects. *Orthopedics*. 1997;20(6):525-38.
- Newman AP. Articular cartilage repair. *Am J Sports Med*. 1998;26(2):309-24.
- Bentley G, Minas T. Treating joint damage in young people. *BMJ*. 2000;320(7249):1585-8.
- Minas T, Peterson L. Advanced techniques in autologous chondrocyte transplantation. *Clinics in Sports Medicine*. 1999;18(1):13-44.
- Kreuz PC, Steinwachs M, Erggelet C, et al. Results after microfracture of full-thickness chondral defects in different compartments in the knee. *Osteoarthritis Cartilage*. 2006;14:1119-1125.
- Mithöfer K, McAdams T, Williams RJ, Kreuz PC, Mandelbaum BR. Clinical efficacy of the microfracture technique for articular cartilage repair in the knee: an evidence-based systematic analysis. *Am J Sports Med*. 2009;37(10):2053-2063.
- Henderson I, Lavigne P, Valenzuela H, Oakes B. Autologous chondrocyte implantation superior biologic properties of hyaline cartilage repairs. *Clinical Orthopaedics Related Research*. 2006;455:253-261.
- Iwasaki N, Kato H, Kamishima T, Suenaga N, Minami A. Donor site evaluation after autologous osteochondral mosaicplasty for cartilaginous lesions of the elbow joint. *Am J Sports Med*. 2007;35:2096-2100.
- 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.
- Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med*. 1994;331(14):889-95.
- Peterson L, Minas T, Brittberg M, Nilsson A, Sjogren-Jansson E, Lindahl A. Two- to 9-year outcome after autologous chondrocyte transplantation of the knee. *Clinical Orthopaedics & Related Research*. 2000(374):212-34.
- Willers C, Zheng MH. Osteochondral Injury of the Knee. Perth, Australia: University of Western Australia; 2003.
- Gille J, Meisner U, Ehlers EM, Muller A, Russlies M, Behrens P. Migration pattern, morphology and viability of cells suspended in or sealed with fibrin glue: a histomorphologic study. *Tissue Cell*. 2005;37(5):339-48.
- Kirilak Y, Pavlos NJ, Willers CR, Han R, Feng H, Xu J, Asokanathan N, Stewart GA, Henry P, Wood D and others. Fibrin sealant promotes migration and proliferation of human articular chondrocytes: possible involvement of thrombin and protease-activated receptors. *Int J Mol Med*. 2006;17(4):551-8.
- Abelow S, Guillen P, Ramos T. Arthroscopic technique for matrix-induced autologous chondrocyte implantation for the treatment of large chondral defects in the knee and ankle. *Operative Techniques in Orthopaedics*. 2006;16:257-261.
- Amin A, Bartlett W, Gooding CR, Sood M, Skinner JA, Carrington RW, Briggs TW, Bentley G. The use of autologous chondrocyte implantation following and combined with anterior cruciate ligament reconstruction. *Int Orthop*. 2005;1-6.
- Bartlett W, Skinner JA, Gooding CR, Carrington RW, Flanagan AM, Briggs TW, Bentley G. Autologous chondrocyte implantation versus matrix-induced autologous chondrocyte implantation for osteochondral defects of the knee: a prospective, randomised study. *J Bone Joint Surg Br*. 2005;87(5):640-5.
- Behrens P, Bitter T, Kurz B, Russlies M. Matrix-associated autologous chondrocyte transplantation /implantation (MACT/MACI)—5-year follow-up. *The Knee*. 2006;13:194-202.
- Jagiello MJ, Rogers B, Briggs TWR. Sequential outcome improvement following autologous chondrocyte implantation; 7-year follow-up, abstract (No: 182) presented American Academy of Orthopaedic Surgeons (AAOS) annual meeting, San Diego, February 2007.
- Gillogly SD, Voight M, Blackburn T. Treatment of articular cartilage defects of the knee with autologous chondrocyte implantation. *J Orthop Sports Phys Ther*. 1998;28(4):241-51.
- Brittberg M, Peterson L, Sjogren-Jansson E, Tallheden T, Lindahl A. Articular cartilage engineering with autologous chondrocyte transplantation. A review of recent developments. *Journal of Bone & Joint Surgery*. American Volume 2003;85-A Suppl 3:109-15.

27. Hunter CJ, Imler SM, Malaviya P, Nerem RM, Levenston ME. Mechanical compression alters gene expression and extracellular matrix synthesis by chondrocytes cultured in collagen I gels. *Biomaterials*. 2002;23(4):1249-59.
28. Buckwalter J. Articular cartilage injuries. *Clinical Orthopaedics & Related Research*. 2002(402):21-37.
29. Behrens F, Kraft EL, Oegema TR, Jr. Biochemical changes in articular cartilage after joint immobilization by casting or external fixation. *J Orthop Res*. 1989;7(3):335-43.
30. Saamamen AM, Kiviranta I, Jurvelin J, Helminen HJ, Tammi M. Proteoglycan and collagen alterations in canine knee articular cartilage following 20 km daily running exercise for 15 weeks. *Connect Tissue Res*. 1994;30(3):191-201.
31. Elder SH, Kimura JH, Soslowky LJ, Lavagnino M, Goldstein SA. Effect of compressive loading on chondrocyte differentiation in agarose cultures of chick limb-bud cells. *J Orthop Res*. 2000;18(1):78-86.
32. Sah RL, Kim YJ, Doong JY, Grodzinsky AJ, Plaas AH, Sandy JD. Biosynthetic response of cartilage explants to dynamic compression. *J Orthop Res*. 1989;7(5):619-36.
33. Burton-Wurster N, Vernier-Singer M, Farquhar T, Lust G. Effect of compressive loading and unloading on the synthesis of total protein, proteoglycan, and fibronectin by canine cartilage explants. *J Orthop Res*. 1993;11(5):717-29.
34. Quinn TM, Grodzinsky AJ, Buschmann MD, Kim YJ, Hunziker EB. Mechanical compression alters proteoglycan deposition and matrix deformation around individual cells in cartilage explants. *J Cell Science*. 1998;111(Pt 5):573-83.
35. Buschmann MD, Kim YJ, Wong M, Frank E, Hunziker EB, Grodzinsky AJ. Stimulation of aggrecan synthesis in cartilage explants by cyclic loading is localized to regions of high interstitial fluid flow. *Arch Biochem Biophys*. 1999;366(1):1-7.
36. Elder SH, Goldstein SA, Kimura JH, Soslowky LJ, Spengler DM. Chondrocyte differentiation is modulated by frequency and duration of cyclic compressive loading. *Annals of Biomedical Engineering*. 2001;29(6):476-82.
37. Vunjak-Novakovic G, Martin I, Obradovic B, Treppo S, Grodzinsky AJ, Langer R, Freed LE. Bioreactor cultivation conditions modulate the composition and mechanical properties of tissue-engineered cartilage. *J Orthop Res*. 1999;17(1):130-8.
38. Martin I, Obradovic B, Treppo S, Grodzinsky AJ, Langer R, Freed LE, Vunjak-Novakovic G. Modulation of the mechanical properties of tissue engineered cartilage. *Biorheology*. 2000;37(1-2):141-7.
39. Gooch KJ, Blunk T, Courter DL, Sieminski AL, Bursac PM, Vunjak-Novakovic G, Freed LE. IGF-I and mechanical environment interact to modulate engineered cartilage development. *Biochemical & Biophysical Research Communications*. 2001;286(5):909-15.
40. Fitzgerald JB, Jin M, Dean D, Wood DJ, Zheng MH, Grodzinsky AJ. Mechanical compression of cartilage explants induces multiple time-dependent gene expression patterns and involves intracellular calcium and cyclic AMP. *Journal of Biological Chemistry*. 2004;279(19):19502-11.
41. Ragan PM, Chin VI, Hung HH, Masuda K, Thonar EJ, Arner EC, Grodzinsky AJ, Sandy JD. Chondrocyte extracellular matrix synthesis and turnover are influenced by static compression in a new alginate disk culture system. *Arch Biochem Biophys*. 2000;383(2):256-64.
42. Buschmann MD, Gluzband YA, Grodzinsky AJ, Hunziker EB. Mechanical compression modulates matrix biosynthesis in chondrocyte/agarose culture. *J Cell Sci*. 1995;108 (Pt 4):1497-508.
43. Lee DA, Bader DL. Compressive strains at physiological frequencies influence the metabolism of chondrocytes seeded in agarose. *J Orthop Res*. 1997;15(2):181-8.
44. Grumbles RM, Howell DS, Howard GA, Roos BA, Setton LA, Mow VC, Ratcliffe A, Muller FJ, Altman RD. Cartilage metalloproteinases in disuse atrophy. *J Rheumatol Suppl*. 1995;43:146-8.
45. Rehabilitation after Cartilage Repair. International Cartilage Repair Society Survey. 2006.
46. Robertson WB, Gilbey H, Ackland T, editors. Standard practice exercise rehabilitation protocols for Matrix Induced Autologous Chondrocyte Implantation Femoral Condyles: Published by the Hollywood Functional Rehabilitation Clinic, Perth, Western Australia, 2004.
47. Hamby K, Bobic V, Wondrasch B, Van Assche D, Marlovits S. Autologous Chondrocyte Implantation Postoperative Care and Rehabilitation: Science and Practice. *Am J Sports Med*. 2006;34:1-19.
48. Pietschmann MF, Horng A, Niethammer T, Pagenstert I, Sievers B, Jansson V, Glaser C, Muller PE. Cell quality affects clinical outcome after MACI procedure for cartilage injury of the knee. *Knee Surg Sports Traumatol Arthrosc*. 2009.
49. Jones DG, Peterson L. Autologous chondrocyte implantation. *J Bone Joint Surg Am*. 2006;88(11):2502-20.
50. Peterson L. Chondrocyte transplantation. In: Jackson DW, ed. *Master Techniques in Orthopaedic Surgery: Reconstructive Knee Surgery*. Philadelphia, PA: Lippincott, Williams, and Wilkins; 2003:353-74.
51. Messier SP, Gutekunst DJ, Davis C, DeVita P. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum*. 2005;52(7):2026-32.
52. Mithöfer K, Peterson L, et al. Articular cartilage repair in soccer players with autologous chondrocyte transplantation: functional outcome and return to competition. *Am J Sports Med*. 2005;33(11):1639-1646. Med Info Ref No: 1903.
53. Gillingly SD, Myers TH, Reinold MM. Treatment of full-thickness chondral defects in the knee with autologous chondrocyte implantation. *J Orthop Sports Phys Ther*. 2006;36(10):751-64.
54. Lewis PB, McCarty LP, 3rd, Kang RW, Cole BJ. Basic science and treatment options for articular cartilage injuries. *J Orthop Sports Phys Ther*. 2006;36(10):717-27.
55. Brittberg M. Cell carriers as the next generation of cell therapy for cartilage repair: a review of the matrix-induced autologous chondrocyte implantation procedure. *Am J Sports Med*. 2010;38(6):1259-1271.
56. Ronga M, Grassi FA, Bulgheroni P. Arthroscopic autologous chondrocyte implantation for the treatment of a chondral defect in the tibial plateau of the knee. *Arthroscopy*. 2004;20(1):79-84.
57. Grelsamer RP, Klein JR. The biomechanics of the patellofemoral joint. *J Orthop Sports Phys Ther*. 1998;28(5):286-98.
58. Grelsamer RP, Weinstein CH. Applied biomechanics of the patella. *Clin Orthop Relat Res*. 2001(389):9-14.
59. Hungerford DS, Barry M. Biomechanics of the patellofemoral joint. *Clin Orthop Relat Res*. 1979(144):9-15.
60. Hungerford DS, Lennox DW. Rehabilitation of the knee in disorders of the patellofemoral joint: relevant biomechanics. *Orthop Clin North Am*. 1983;14(2):397-402.
61. Iwaki H, Pinskeroova V, Freeman MA. Tibiofemoral movement 1: the shapes and relative movements of the femur and tibia in the unloaded cadaver knee. *J Bone Joint Surg Br*. 2000;82(8):1189-95.
62. Martelli S, Pinskeroova V. The shapes of the tibial and femoral articular surfaces in relation to tibiofemoral movement. *J Bone Joint Surg Br*. 2002;84(4):607-13.
63. McGinty G, Irrgang JJ, Pezzullo D. Biomechanical considerations for rehabilitation of the knee. *Clin Biomech*. (Bristol, Avon) 2000;15(3):160-6.
64. Steinkamp LA, Dillingham MF, Markel MD, Hill JA, Kaufman KR. Biomechanical considerations in patellofemoral joint rehabilitation. *Am J Sports Med*. 1993;21(3):438-44.
65. Besier TF, Draper CE, Gold GE, Beaupre GS, Delp SL. Patellofemoral joint contact area increases with knee flexion and weight-bearing. *J Orthop Res*. 2005;23(2):345-50.
66. Nakagawa S, Kadoya Y, Kobayashi A, Tatsumi I, Nishida N, Yamano Y. Kinematics of the patella in deep flexion. Analysis with magnetic resonance imaging. *J Bone Joint Surg Am*. 2003;85-A(7):1238-42.
67. Minas T. The role of cartilage repair techniques, including chondrocyte transplantation, in focal chondral knee damage. *Instructional Course Lectures*. 1999;48:629-43.
68. Alparslan L, Minas T, Winalski CS. Magnetic resonance imaging of autologous chondrocyte implantation. *Semin Ultrasound CT MR*. 2001;22(4):341-51.
69. Ebert JR, Joss B, Ackland T. HFRC standard practice exercise rehabilitation protocols for matrix-induced autologous chondrocyte implantation (MACI)-the knee. Hollywood Functional Rehabilitation Clinic & Verdun Physiotherapy. © 2009.
70. King PJ, Bryant T, Minas T. Autologous chondrocyte implantation for chondral defects of the knee: indications and technique. *J Knee Surg*. 2002;15(3):177-84.
71. Minas T, Peterson L. Autologous chondrocyte implantation. *Op Tech in Orth*. 1997;7(4):323-333.
72. O'Driscoll S, Keeley F, Salter R. Durability of regenerated articular cartilage produced by free autogenous 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.
73. 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.
74. Salter RB. The physiologic basis of continuous passive motion for articular cartilage healing and regeneration. *Hand Clin*. 1994;10(2):211-9.
75. 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.
76. 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.
77. Enright PL. The six-minute walk test. *Respir Care*. 2003;48(8):783-5.



Genzyme Corporation
55 Cambridge Parkway
Cambridge, MA 02142

www.MACI.com

MACI and Genzyme are registered trademarks of Genzyme Corporation.
©2010 Genzyme Corporation. All rights reserved.
M-00004a /1011EUMARE02V1 12/2010



HOLLYWOOD FUNCTIONAL REHABILITATION CLINIC
VERDUN PHYSIOTHERAPY
Tomorrow's Treatment Today

Hollywood Functional
Rehabilitation Clinic &
Verdun Physiotherapy
Gate 3, Verdun St.
Nedlands, WA 6009
Australia

www.hfrc.com.au