



An accelerated 6-week return to full weight bearing after matrix-induced autologous chondrocyte implantation results in good clinical outcomes to 5 years post-surgery

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Abstract

Purpose To investigate the mid-term outcomes of an accelerated return to full weight bearing (WB) after matrix-induced autologous chondrocyte implantation (MACI).

Methods This randomized study allocated 35 patients (37 knees) to a 6 week ($n = 18$) or 8 week ($n = 19$) return to full WB after MACI. Patients were evaluated pre-operatively and at 1, 2 and minimum 5 years (range 5.5–7 years), using the KOOS, SF-36, visual analogue pain scale, 6-min walk test and active knee range of motion (ROM). Peak isokinetic knee extensor and flexor strength was assessed, with limb symmetry indices (LSIs) calculated. Magnetic resonance imaging (MRI) was undertaken to evaluate the repair tissue, and an MRI composite score was calculated.

Results While no group differences (n.s.) were observed, significant improvement was observed for all patient-reported outcome measures ($p < 0.05$), 6-min walk distance ($p = 0.040$), active knee flexion ($p = 0.002$) and extension ($p < 0.0001$) ROM, and the LSI for peak knee extensor strength ($p < 0.0001$). At final review, 87.5% (6 weeks) and 82.4% (8 weeks) of patients were satisfied overall. A non-significant decline (n.s.) was observed for the MRI composite score from 1-year post-surgery to final review, with no significant MRI-based differences (n.s.) between groups. At final review, two grafts (6-week $n = 1$, 8-week $n = 1$) demonstrated MRI-based graft failure, while an additional patient had progressed toward knee arthroplasty (8.1% failure rate at minimum 5 years).

Conclusions The 6-week return to full WB after MACI provided comparable clinical and MRI-based outcomes beyond 5 years post-surgery, without jeopardizing the graft. This 6-week WB protocol is faster than those previously proposed and studied.

Level of Evidence II.

Keywords Matrix-induced autologous chondrocyte implantation (MACI) · Weight bearing · Rehabilitation · Gait

Introduction

Autologous chondrocyte implantation (ACI) is a regenerative surgical procedure for isolated chondral defects, that involves culturing and re-implanting a patient's own chondrocytes. First and second generations of the surgical technique required suturing of a periosteal [4] or collagen [32] cover to retain the cell-based solution within the chondral defect. However, third-generation techniques (matrix-induced ACI) seed the cells onto a collagen membrane, which is then glued to the subchondral bone, with encouraging mid-term outcomes demonstrated overall [3, 5, 13, 14, 18, 19, 24, 37].

While a range of variables may contribute to the success of ACI, the importance of rehabilitation following ACI has

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been acknowledged and discussed [7, 16, 21, 23, 29–31]. This is important not only for the longer term restoration of strength and functional deficits, but also early post-surgery in the initial graft protective and progressive stimulation stages. Anecdotally, a persistent issue for orthopaedic specialists and patients is the lengthy period on crutches and time required to safely attain full weight bearing (WB) after surgery, together with the additional deconditioning and muscular atrophy this can create. Third-generation MACI has permitted an evolution of early WB pathways as patients transition back toward full WB gait [10], with several studies investigating a progressively accelerated WB regimen, at least compared to traditionally conservative programs [11, 14, 17, 25, 37].

The current study reports the mid-term (minimum 5 year) outcomes of a randomized controlled trial (RCT) that sought to investigate a 6-week (versus 8-week) return to full weight bearing after MACI [11]. It aims to demonstrate that the accelerated 6-week return to full WB, faster than those previously proposed and studied, provides a safe and clinically effective outcome sustained to a minimum 5-years post-surgery. Therefore, it was hypothesized that: (1) patients would demonstrate significantly improved outcomes over the post-operative timeframe to final follow-up, with no significant decline from 2 years to final review (minimum 5 years), and (2) there would be no significant clinical or radiological differences between the two WB pathways.

Materials and methods

Ethics approval for this study was obtained from the Hollywood Private Hospital (HPH145) Human Research Ethics Committee (HREC) and the trial was undertaken according to the Declaration of Helsinki. Between January 2010 and April 2014, this RCT allocated 35 patients (37 knees) to a 6-week ($n = 18$) or 8-week ($n = 19$) return to full WB after MACI to the medial or lateral femoral condyle (Table 1). Outcomes were assessed pre-operatively and at 1, 2 and minimum 5 years (range 5.5–7 years) post-surgery. Patients were originally randomized to one of the two WB regimens using a ‘random number generator’ via Microsoft Excel (two

patients underwent MACI on both knees, and on the second knee were allocated to the alternative pathway to which they were randomized on the first knee). Only one investigator had access to the randomization list, and they were not involved in any of the surgical, rehabilitation or assessment components of the study (there was no patient contact). Figure 1 demonstrates the flow of patients throughout the post-operative timeline, while the original study protocol has been provided as a supplement.

The inclusion/exclusion criteria for this prospective RCT have been previously defined [13,23]. Briefly, patients were indicated for MACI if they were 15–65 years of age and had undergone MACI to address full thickness femoral condylar defects in the knee. Patients with ligamentous or meniscal deficiency were included providing it was addressed at the time of MACI. Patients with varus/valgus malalignment ($> 5^\circ$ anatomic tibiofemoral angle), or those that suffered from any ongoing, progressive inflammatory arthritis, osteoarthritis or rheumatoid arthritis, were excluded.

Surgery

The MACI surgical technique(s) has been previously described.^{13, 23} Briefly, an initial arthroscopic cartilage biopsy was undertaken followed by isolation, culturing and seeding of cells onto a type I/III collagen membrane (ACI-Maix Matricel GmbH, Germany). In a second surgery, undertaken via a mini-open (6-week $n = 7$, 8-week $n = 8$) or arthroscopic (6-week $n = 11$, 8-week $n = 11$) approach, the scaffold was glued to the cleaned and prepared subchondral bone.

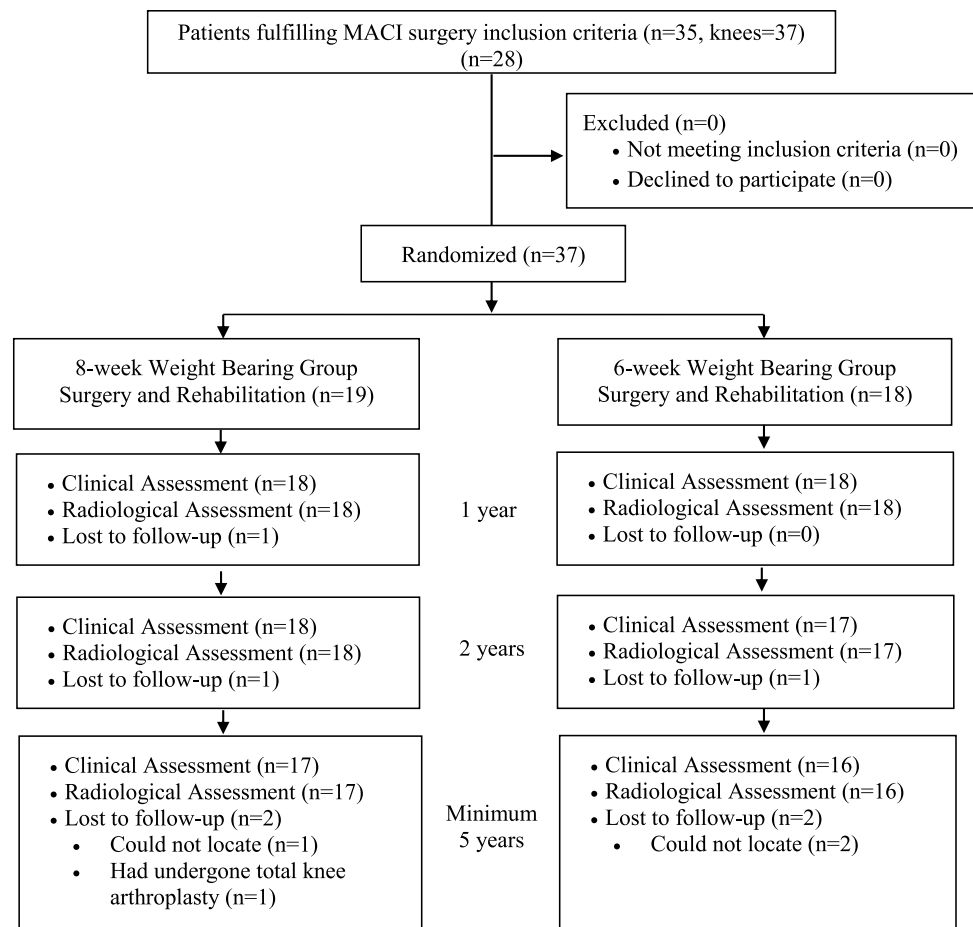
Rehabilitation

In the early in-patient hospital period (1–3 nights), all patients, irrespective of group randomization, underwent continuous passive motion (CPM) within 12–24 h (set at 0–30°) for a minimum of 1 h daily, regular cryotherapy and elevation to control swelling, active ankle plantar- and dorsiflexion to encourage circulation, and isometric contraction of the lower limb muscles to maintain muscle tone. A knee brace was worn for 24 h per day, and all patients underwent

Table 1 The differential weight bearing (WB) gradients that were followed by MACI patients randomized to the 6- or 8-week rehabilitation pathway

6-week group								
Weeks post-surgery	1	2	3	4	5	6	7	8
Weight bearing (%BW)	≤20%		40%	60%	80%	100%		
8-week Group								
Weeks post-surgery	1	2	3	4	5	6	7	8
Weight bearing (%BW)	≤20%		30%	40%	50%	60%	80%	100%

Fig. 1 Flowchart demonstrating recruitment and evaluation over the post-operative period, in patients randomized to the 6-week or 8-week weight bearing rehabilitation pathways



appropriate education on how to ambulate with two crutches permitting $\leq 20\%$ of body weight through the operated limb (which was consistent across both WB rehabilitation groups for the first 2 weeks). All patients then participated in a progressive out-patient rehabilitation program, intensively over the first 12 post-operative weeks, and as required following that time up until 12 months. Apart from the gradient and time to attain full WB (Table 1), all other rehabilitation components were standardized for all patients and have been previously reported [11, 17]. As previously reported [11, 17], WB replication training for all patients was an important component of each rehabilitation session up until the time that full WB was achieved, and WB restrictions were learned via the electronic bathroom scale method [9, 22].

Clinical assessment

All clinical assessments were undertaken by a research assistant blinded to group allocation. Patient-reported outcome measures (PROMs) employed pre- and post-surgery (1, 2 and minimum 5 years) included: (1) a Visual Analogue Pain Scale (VAS) to assess the frequency (VAS-F) and severity (VAS-S) of knee pain on a scale of

0–10, (2) the 36-item Short Form Health Survey (SF-36) [2] to evaluate general health producing a mental (MCS) and physical (PCS) component score, with each subscale reported to the nearest 0.1 point, and (3) the Knee Injury and Osteoarthritis Outcome Score (KOOS) [33]. The KOOS was employed to assess knee pain, symptoms, activities of daily living (ADL), sport and recreation (Sport) and knee related quality of life (QOL), with each subscale reported to the nearest 0.1 point. A satisfaction questionnaire was employed at final follow-up to evaluate overall satisfaction, as well as satisfaction with the MACI surgery to relieve pain, improve the ability to perform daily and work activities, improve the ability to return to recreational activities and improve the ability to participate in sport. Descriptors of ‘Very Satisfied’, ‘Somewhat Satisfied’, ‘Somewhat Dissatisfied’ and ‘Very Dissatisfied’, were employed. The number of patients reporting each response for each domain was reported, as was the percentage of satisfied patients (reported to the nearest 0.1%). At all post-operative time-points, several objective evaluations were undertaken, including 6-min walk capacity (measured and reported to the nearest 1 m), maximal active knee flexion and extension range of motion

(ROM) (measured and reported to the nearest 1 degree), and peak concentric knee extension and flexion isokinetic strength (peak torque, Nm) (measured and reported to the nearest 1 Nm). Strength was assessed using an isokinetic dynamometer (Isosport International, Gepps Cross, South Australia) at a single isokinetic angular velocity of 90°/s.

Magnetic resonance imaging (MRI) assessment

High-resolution MRI employing a Siemens Symphony 1.5 or 3 T scanner (Siemens, Erlangen, Germany; Philips, Best, the Netherlands; General Electric, Milwaukee, WI, USA) was undertaken to assess graft repair at all post-operative time-points. Standardized proton density and T2-weighted fat-saturated images were obtained in coronal and sagittal planes (slice thickness 3 mm, field of view 14–15 cm, 512 matrix in at least one axis for proton density images with a minimum 256 matrix in one axis for T2-weighted images). Axial proton density fat-saturated images were obtained (slice thickness 3–4 mm, field of view 14–15 cm, minimum 224 matrix in at least one axis). Pertinent parameters of graft repair (graft infill, signal intensity, border integration, surface contour, tissue structure, effusion, subchondral lamina and bone) were assessed [28], following the magnetic resonance observation of cartilage repair tissue (MOCART) scoring tool [27, 32, 35, 36]. Each variable was scored from 1 to 4 (1 = poor; 2 = fair; 3 = good; 4 = excellent) in comparison to the adjacent native cartilage, and an MRI composite score was calculated by weighting each variable [32], and summing the scores. MRI evaluation was performed by an independent, experienced radiologist, blinded to group allocation.

Data and statistical analyses

The mean (SD, range) of all measures were calculated pre-surgery (for PROMs), 1 and 2 years post-surgery, and final follow-up (minimum 5 years). Limb Symmetry Indices (LSIs) were calculated for strength measures (by dividing the peak values on the operated limb by that on the non-operated limb, reported to the nearest 0.1%). While analysis of variance (ANOVA) was used to investigate changes in clinical and MRI-based scores over the entire period, and between the two WB groups, *t* tests were specifically employed to evaluate change from 2 years to final review. To assess intra-observer reliability, 20 randomly selected MRI images were re-assessed a second time by the radiologist. For the morphological MRI scores, the kappa coefficient was employed, while the intra-class correlation coefficient was employed for the MRI composite score. Statistical analysis was performed using SPSS software (SPSS, Version 23.0, SPSS Inc., USA). Statistical significance was determined at $p < 0.05$. Prior to study onset, a priori power calculation was performed using G-Power (Dusseldorf, Germany) for the primary outcome variable (KOOS Pain), demonstrating that 28 knees (14 in each group) were required to reveal differences at the 5% significance level, with 90% power and employing a large effect size (1.1) as reported by previous research [38].

Results

No significant differences (n.s.) were observed between the two WB groups in pertinent patient demographics (age, body mass index), or prior injury or surgery history (duration of symptoms, number of prior procedures) (Table 2).

Table 2 Pre-operative patient demographics and injury/surgery parameters for the two weight bearing (6- and 8-week) rehabilitation groups

Variable	6-week	8-week	<i>p</i> value
Number of patients (knees)	17 (18)	18 (19)	N/A
Gender (male/female)	9/9	12/7	N/A
Age (years)	36.4 (21.0–55.0)	36.4 (23.0–53.0)	n.s
Body mass index	26.2 (18.4–32.1)	25.2 (19.1–33.1)	n.s
Defect location (MFC/LFC)	13/5	14/5	N/A
Prior procedures	1.1 (0–4)	1.0 (0–4)	n.s
Duration of symptoms (years)	7.5 (1.0–25.0)	6.8 (1.0–25.0)	n.s
Defect size (cm ²)	3.2 (1.0–6.3)	2.9 (1.0–7.7)	n.s
≤2.0	7	8	N/A
2.1–3.0	4	5	
3.1–4.0	4	2	
4.1–5.0	1	2	
≥5.1	2	2	

Shown are means (range)

MFC medial femoral condyle, LFC lateral femoral condyle

All PROMs significantly improved ($p < 0.05$) over time (Table 3), though there were no group differences (n.s.) (Table 3). T tests indicated that there was no significant change (n.s.) in PROMs from 2 years post-surgery to final follow-up, apart from the KOOS Sport which significantly improved ($p = 0.032$) over that period. At final review, both groups demonstrated a similar percentage of patients that were satisfied with the ability of MACI to relieve their knee pain, though a greater percentage of patients that underwent the 6-week protocol appeared satisfied with their overall outcome (Table 4).

All objective measures (apart from the peak isokinetic flexor strength LSI) significantly improved ($p < 0.05$) over the post-operative timeline (Table 5), with no group differences (n.s.) (Table 5). While a significant improvement in the peak knee extensor strength LSI ($p = 0.015$) and significant increase in active knee extension ROM ($p = 0.048$) was observed from 2 years post-surgery to final follow-up (minimum 5 years), no other differences were observed.

No significant change (n.s.) was observed in the overall MRI composite score, or any other MRI-based variable, from 1 year to final follow-up (minimum 5 years) (Table 6). While there were no group differences (Table 6), when grouped together a non-significant decline was observed in tissue structure, subchondral lamina and bone, as well as the overall MRI composite score, from 2 years post-surgery to final review. Intra-observer reliability assessment indicated a significant correlation between MRI-based scores within each of the scoring variables (MRI composite score $\rho = 0.811$; graft infill $\rho = 0.949$; signal intensity $\rho = 1.00$; border integration $\rho = 0.982$; surface contour $\rho = 1.00$; structure $\rho = 0.840$; subchondral lamina $\rho = 1.00$; subchondral bone $\rho = 0.920$ and; effusion $\rho = 0.993$).

At final review, two grafts (6-week $n = 1$, 8-week $n = 1$) demonstrated graft failure on MRI, defined by de-lamination or a graft bed devoid of repair tissue. Of these, the first patient (8-week WB protocol) displayed no graft tissue on 1-, 2- and minimum 5-year MRI, despite displaying early tissue infill on 3-month MRI (scored via the MOCART scoring tool as ‘fair’, $< 50\%$ infill). The second patient who underwent the 6-week WB protocol displayed viable tissue infill at 2-years post-surgery (scored via the MOCART scoring tool as ‘good’, $> 50\%$ infill), despite having failed on MRI at minimum 5-year follow-up. Both of these patients remained relatively asymptomatic within their ADLs. An additional patient in the 8-week WB group had demonstrated failure on MRI by 2 years post-surgery, though was not reviewed at final follow-up given he had already progressed toward total knee arthroplasty (TKA). However, this patient had also displayed no discernible tissue infill on MRI at either 3-month, 1- or 2-year MRI. Therefore, a graft failure rate of 8.1% was observed at final review (minimum 5 years).

Table 3 Patient-reported outcome measures (PROMs) throughout the pre- and post-operative timeline for the two weight bearing rehabilitation groups

Time-point	Group	KOOS (pain)	KOOS (symptoms)	KOOS (ADL)	KOOS (sport)	KOOS (QOL)	SF-36 (PCS)	SF-36 (MCS)	VAS-F	VAS-S
Pre-surgery	6-week	63.2 (13.2)	64.0 (17.0)	73.8 (15.9)	26.8 (16.7)	31.7 (14.7)	35.1 (9.0)	51.1 (9.3)	6 (2)	6 (2)
	8-week	66.9 (9.3)	73.1 (11.2)	80.6 (9.4)	36.2 (25.1)	35.6 (11.4)	39.6 (5.8)	51.5 (10.2)	7 (2)	5 (2)
1 year	6-week	86.8 (6.6)	85.8 (9.7)	92.5 (5.9)	60.7 (19.6)	70.8 (9.6)	46.7 (7.8)	59.3 (5.6)	2 (1)	2 (1)
	8-week	88.3 (6.3)	88.7 (8.5)	95.4 (5.1)	64.8 (24.1)	59.1 (16.1)	49.6 (5.5)	57.1 (5.1)	1 (1)	2 (2)
2 years	6-week	88.0 (13.5)	86.1 (10.6)	92.3 (9.2)	69.0 (24.7)	71.5 (19.0)	49.1 (8.5)	54.9 (6.5)	2 (2)	2 (2)
	8-week	90.2 (10.6)	88.8 (7.7)	95.4 (9.1)	69.4 (25.1)	67.3 (22.9)	50.2 (8.6)	58.0 (4.3)	1 (2)	2 (2)
Minimum 5 years	6-week	87.4 (19.7)	83.5 (18.9)	93.4 (17.7)	80 (29.8)	73.1 (30.0)	50.3 (11.6)	55.6 (7.1)	2 (3)	2 (2)
	8-week	90.1 (10.8)	88.4 (9.3)	91.7 (11.4)	75.6 (26.6)	70.3 (24.2)	52.6 (4.7)	55.1 (9.3)	2 (2)	2 (2)
Time Effect (p value)		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.045	< 0.0001	< 0.0001
Group Effect (p value)		n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Interaction Effect (p value)		n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

Shown are means (SD)

KOOSKnee Injury and Osteoarthritis Outcome Score, ADLsActivities of Daily Living, QOLQuality of Life, PCSPhysical Component Score, MCSMental Component Score, VAS-FVisual Analogue Pain Scale (frequency of pain), VAS-SVisual Analogue Pain Scale (severity of pain)

Table 4 The number of patients within each of the four satisfaction gradings (very satisfied, somewhat satisfied, somewhat dissatisfied, very dissatisfied) for each of the five satisfaction items, within the two

weight bearing rehabilitation groups, specifically at the final post-operative follow-up

Group	Satisfaction item	Pain relief	Improving ability to undertake ADLs	Improving ability to participate in recreational activities	Improving ability to participate in sport	Overall satisfaction
6-week (<i>n</i> = 16)	Very satisfied	10	12	10	9	10
	Satisfied	4	2	4	3	4
	Dissatisfied	2	1	1	2	1
	Very dissatisfied	0	1	1	2	1
	Satisfied overall, <i>n</i> (%)	14 (87.5)	14 (87.5)	14 (87.5)	12 (75.0)	14 (87.5)
8-week (<i>n</i> = 17)	Very satisfied	9	9	9	6	8
	Satisfied	6	6	5	7	5
	Dissatisfied	1	1	1	1	2
	Very dissatisfied	1	1	2	3	2
	Satisfied overall, <i>n</i> (%)	15 (88.2)	15 (88.2)	14 (82.4)	13 (76.5)	13 (76.5)

Table 5 Clinical outcome measures throughout the pre- and post-operative timeline for the two weight bearing rehabilitation groups

Time-point	Variable	Six-minute walk distance (m)	Maximal knee flexion (deg)	Maximal knee extension (deg)	Knee extensor strength LSI	Knee flexor strength LSI
1 year	6-week	634 (91)	141 (7)	-1 (2)	82.1 (14.9)	107.8 (14.1)
	8-week	626 (60)	145 (6)	-2 (2)	83.5 (17.9)	108.8 (16.1)
2 years	6-week	656 (90)	144 (8)	-2 (2)	93.7 (14.7)	101.1 (8.5)
	8-week	664 (88)	145 (6)	-2 (2)	87.5 (11.8)	101.2 (9.1)
Minimum 5 years	6-week	651 (93)	145 (9)	-1 (1)	99.8 (12.4)	104.5 (9.0)
	8-week	660 (77)	148 (6)	-1 (2)	97.8 (12.4)	105.1 (10.5)
Time effect (<i>p</i> value)		0.040	0.002	<0.0001	<0.0001	n.s
Group effect (<i>p</i> value)		n.s	n.s	n.s	n.s	n.s
Interaction effect (<i>p</i> value)		n.s	n.s	n.s	n.s	n.s

Shown are means (SD)

Discussion

Previous studies have demonstrated safety and efficacy in a rehabilitation program that reduced the time required to attain full WB after MACI surgery, from 12 to 8 weeks [12, 14]. The most important finding from the current study was that further acceleration of this WB timeframe, namely 8–6 weeks, provided good patient outcomes without any adverse clinical or radiological outcomes up until and including 5 years post-surgery.

PROMs significantly improved, without any significant decline from 2 years to final review. Several other studies have demonstrated clinical improvement at mid-term follow-up after MACI [3, 5, 13, 14, 18, 19, 24]. Interestingly, the KOOS Sport was significantly better at final review when compared to 2-year outcomes, suggesting a longer period required to obtain the full benefit of MACI and

of importance when counselling patients on expectations. This is also supported by the continued improvement in objective measures beyond 1-year, as well as the improvement from 2-years to final review in the LSI for peak knee extensor strength. This lengthy recovery period may be affected by the more conservative nature of rehabilitation overall, combined with other factors such as the long duration of pre-operative symptoms.

No significant change was observed from 1- and 2-years post-surgery through to final review (minimum 5 years) in any MRI-based scoring parameter, nor were there any group differences. Therefore, the 6-week return to full WB was well tolerated and did not affect graft status. Some mild (though non-significant) deterioration was observed from 2-years to final follow-up (tissue structure, subchondral lamina and bone), and ongoing review is required to see whether these changes may pre-dispose to subsequent graft failure. In particular, the subchondral bone, inclusive of

Table 6 Post-operative magnetic resonance imaging (MRI) assessment of grafts over the post-operative timeline for the two weight bearing rehabilitation groups

Post-operative time point	Group	Graft infill	Signal intensity	Border integration	Surface contour	Structure	Subchondral lamina	Subchondral bone	Effusion	MRI Score
1 year	6-week (n = 18)	3.5 (0.5)	3.0 (1.0)	3.2 (0.8)	3.2 (1.2)	3.2 (0.8)	3.5 (0.6)	3.4 (0.7)	3.7 (0.6)	3.3 (0.6)
	8-week (n = 18)	3.2 (0.9)	2.7 (0.8)	2.8 (1.2)	2.6 (1.1)	3.2 (1.1)	3.3 (0.7)	3.0 (1.0)	4.0 (0.3)	3.0 (0.8)
2 years	6-week (n = 17)	3.5 (0.4)	3.3 (0.6)	3.3 (0.6)	3.7 (0.5)	3.6 (0.7)	3.6 (0.5)	3.4 (0.8)	3.9 (0.4)	3.5 (0.3)
	8-week (n = 18)	3.2 (0.9)	2.6 (0.8)	2.8 (0.9)	2.8 (0.9)	3.2 (0.9)	3.4 (0.5)	3.1 (1.0)	3.9 (0.3)	3.0 (0.8)
Minimum 5 years	6-week (n = 16)	3.4 (0.3)	3.2 (0.3)	3.0 (1.1)	3.1 (1.2)	3.0 (1.1)	3.2 (0.6)	3.1 (1.2)	3.8 (0.5)	3.2 (0.4)
	8-week (n = 17)	3.3 (0.5)	2.8 (0.2)	2.9 (1.4)	3.0 (1.5)	3.1 (1.2)	3.5 (0.5)	3.0 (1.4)	3.7 (0.5)	3.1 (0.6)
Time effect (p value)		n.s	n.s	n.s	n.s	n.s	n.s	n.s	n.s	n.s
Group effect (p value)		n.s	n.s	n.s	n.s	n.s	n.s	n.s	n.s	n.s
Interaction effect (p value)		n.s	n.s	n.s	n.s	n.s	n.s	n.s	n.s	n.s

Shown are means (SD)

both the subchondral bone plate and trabecular bone [20], is intimately associated with the cartilage [1]. The subchondral bone may be important for supplying nutrition to the cartilage [6], and the association between any ongoing adverse changes and overall graft status should be monitored closely. In the current study, three graft failures were observed, two of which were observed on MRI at (or before) 2-years post-surgery and both in the 8-week WB group. Of these, one was not reviewed at final follow-up given he had progressed toward TKA due to further knee deterioration. A third patient (6-week group) demonstrated repair tissue at 2-year review and, despite being relatively asymptomatic at final follow-up, demonstrated a graft bed devoid of repair tissue on MRI at 5-year review.

The important role of rehabilitation following ACI has been acknowledged [7, 16, 21, 23, 29–31]. Given the early requirement for graft protection, with respect to the third-generation technique (MACI) though more so its first- (periosteal-covered ACI) and second (collagen-covered ACI)-generation predecessors, rehabilitation and WB pathways have been conservative. Even upon initiation of the current study an 8-week return to full WB was considered ‘accelerated’ [14], though encouraging mid-term outcomes after a 6-week (versus 10-week) WB approach have since been published [37]. The current study supports these outcomes, suggesting the 6-week pathway is well tolerated and, while it did not demonstrate any further clinical benefit, it also did not jeopardize graft integrity. The earlier return to full WB may be of benefit anecdotally to the frustration often reported by patients seeking transition off their crutches, while improving early physical function and QOL [17].

The current study acknowledges some limitations. First, we acknowledge the relatively small patient cohort (n = 35) and the limited conclusions that may be drawn from the study, despite the positive outcomes across the majority of patients embarking on the 6-week WB protocol and the pre-study power calculation undertaken and being fulfilled. Second, it is acknowledged that only a 2-week period existed between groups with respect to their time to full WB. At the time of initiating the study it had been reported that an 8-week return to full WB (which was accelerated at that time) had demonstrated success in patients after MACI [14, 15], hence this was chosen as the control arm. While the study aimed to ascertain whether patients could be safely accelerated toward full WB, the research group was hesitant at that time to take patients off their crutches before 6 weeks, hence that time-point was chosen. Nonetheless, clinically, the 2-week delay remains burdensome and an anecdotally reported issue in considering surgery, together with the additional deconditioning and time off work that is often required when crutches are required.

Third, an issue that must be considered is the confidence in patients adhering to the WB protocols and being

able to follow the WB restrictions. While the bathroom scale method was employed to teach WB restrictions and this still remains the most practical and widely used WB modality [9, 22], prior research has demonstrated improved accuracy with more practice [9]. This was an important part of every rehabilitation session. Furthermore, it should be acknowledged that the current study investigated the time to full WB in addition to the WB gradient, whereby full WB was ensured in each group at the designated time by cessation of crutch use. This guaranteed that the time to full WB was true across each group. Finally, the current study sought to investigate the morphological outcome of the graft as per the MRI-based scoring method employed, and acknowledge that other MRI-based imaging modalities can evaluate the biochemical characteristics of the repair tissue [8, 26, 34].

As the clinical relevance, this study demonstrated that an accelerated 6-week return to full WB after MACI results in encouraging and sustained post-operative clinical and radiological outcomes, without jeopardizing the integrity of the developing cartilage tissue. Anecdotally, this traditionally conservative early post-operative period is burdensome to the patient, promotes further physical deconditioning, often enforces a delayed period on crutches and away from work, and is a concern to patients considering MACI as a treatment pathway.

Conclusion

This study demonstrated sustained clinical outcomes beyond 5 years after MACI, with safety and efficacy demonstrated in the 6-week return to full WB. While the 6-week WB pathway provided no additional clinical benefit beyond the early post-operative stages [17], it was well tolerated by patients without adverse features and remains a protocol faster than those previously proposed and studied [12, 14].

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Compliance with ethical standards

Conflict of interest No benefits in any form have been received or will be received from a commercial party related to the subject of this article.

Ethical approval This research was approved by the Hollywood Private Hospital (HPH145) Human Research Ethics Committee (HREC).

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