


# Continuous Passive Motion, Early Weight Bearing, and Active Motion following Knee Articular Cartilage Repair: Evidence for Clinical Practice

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## Abstract

**Objective:** To systematically review the literature regarding postoperative rehabilitation for articular cartilage repair: (1) does the use of continuous passive motion (CPM) enhance healing, and if so, what parameters should be applied? (2) Can active range of motion (AROM) be used in place of or with CPM? (3) When can individuals safely resume weight bearing (WB) following repair? **Data Sources:** A search using Medline, SportsDiscus, and CINAHL databases was performed with the following keywords: *articular cartilage, AROM, CPM, microfracture, osteochondral allograft, autologous chondrocyte implantation, rehabilitation, weight bearing, and knee.* **Study Selection:** Basic science or clinical outcomes examining the effects of CPM, AROM, or WB on knee articular cartilage healing. **Data Extraction:** Selected articles were rated using the Strength of Recommendation Taxonomy (SORT) to determine evidence for clinical application. **Data Synthesis:** Sixteen articles met selection criteria: 12 were basic science studies; 4 were clinical studies. Basic science evidence supporting CPM exists. However, few patient-oriented outcomes have been documented resulting in a SORT rating of C. Early WB and AROM received a SORT rating of B based on limited clinical research and patient-oriented outcomes. **Conclusions:** Basic science evidence supports CPM to maintain ROM, reduce pain, and promote healing. Patient-oriented research is needed to strengthen CPM's recommendation. Limited evidence exists regarding early WB and AROM post cartilage repair. There is insufficient evidence to confidently address when to begin WB for maximum healing. Appropriate basic science and patient-oriented research are needed for rehabilitation protocols to maximize benefits of cartilage repair procedures.

## Keywords

chondrocyte, microfracture, autologous transplantation, knee surgery, rehabilitation

## Introduction

Treatment of articular cartilage injuries represents a complex and challenging problem for both orthopedic surgeons and rehabilitation specialists. If not treated appropriately, defects to the articular cartilage can become increasingly painful and disabling. This is particularly true for lesions of the knee, where biomechanical stresses result in both shear and compressive forces during normal activities of daily living.

Many of the current rehabilitation protocols following articular cartilage repair are focused predominantly on protection of the repair site with limited attention being given to the surrounding tissues or the stresses needed to ensure functional remodeling of the healing tissues. Similar to early anterior cruciate ligament and meniscal repair rehabilitation practices,<sup>1-3</sup> cartilage repair protocols focus more

on protecting the recent surgical site than providing stress to encourage tissue healing. With limited clinical evidence available, existing postoperative protocols are derived from basic science research examining cellular responses and rely heavily on anecdotal or traditional practices.<sup>4</sup>

Continuous passive motion (CPM) is frequently used following articular cartilage repair to increase synovial fluid movement and joint surface articulation in an attempt to offset the potential complications resulting from being

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non-weight bearing. The concept of motion as therapy is based on the principles that synovial joints are designed to move, that articular cartilage receives nutrition via the movement of synovial fluid, and that prolonged immobilization of joints is detrimental to all involved tissues, including bone and soft tissue structures.<sup>5</sup> In his historical overview of the treatment of orthopedic injury via rest or motion, Salter<sup>5</sup> discusses how evidence in opposition to immobilization prompted the development of a modality that could be used to create continuous joint motion. CPM was initially introduced by Salter on the premise that if some joint motion was good, continuous motion might be even more effective at healing articular cartilage lesions and other damaged tissues.<sup>5,6</sup> In current clinical practice, CPM is conducted using a device that is capable of passively moving the involved joint through variable ranges of motion and speeds. It is common for CPM to be prescribed for at-home use for 6 to 8 hours for 1 to 8 weeks following surgery.<sup>4,7-12</sup>

Active knee flexion and extension can be used in place of or in addition to CPM to regain movement and stimulate circulation of synovial fluid. The application of active motion following articular cartilage repair has not been clearly defined throughout the literature. In many animal models, the term *intermittent active motion* (IAM) has been used to describe unrestricted, voluntary cage activity.<sup>6,13</sup> In these interventions, IAM simply means that motion was not restricted or controlled in any fashion. This is different from investigations in which active motion was regulated either via controlled exercise in an animal model<sup>14</sup> or by verbal instructions to the patient.<sup>15,16</sup> The differences in these interventions are further apparent given investigator reports of little to no voluntary movement of the involved limb during the first week following cartilage injury and/or surgery.<sup>6</sup> The use of structured active motion via the performance of high repetitions of active flexion-extension cycles following articular cartilage repair has not been well studied but has the potential to be more cost-effective and reduce muscle atrophy and inhibition when used in place of or in combination with CPM.

The concept of motion in rehabilitation following articular cartilage repair is important due to the restrictions in weight bearing placed on patients postoperatively. Following articular cartilage repair or restoration procedures, it is currently recommended that weight bearing be limited for 4 to 12 weeks following surgery.<sup>4,8-11,17</sup> Restriction of weight bearing ensures that patients avoid shear stresses that are known to cause chondrocyte apoptosis.<sup>18,19</sup> However, it is also possible that no stress to the tissue is detrimental to the health of not just the repair site but also the surrounding bone, ligament, and cartilage structures.<sup>20</sup> In addition, if it can be done safely, early full or partial weight bearing may have the potential to enhance patient quality of life by allowing them to return to work and other regular activities sooner.

The purpose of this article is to review the literature addressing the use of CPM, active range of motion (AROM), and early weight bearing following knee articular cartilage repair. We examine the following questions: (1) does the use of CPM enhance cartilage healing following repair, and if so, what parameters should be applied? (2) Can AROM be used safely and effectively in place of or in addition to CPM? and (3) When can individuals safely resume weight bearing following articular cartilage repair? This review focuses on literature related to articular cartilage repair and restoration of the knee in order to identify what clinical practices are supported by current evidence and where further research is needed.

## Methods

A search of the literature using the databases of Medline, SportsDiscus, and CINAHL was performed. The keywords and resulting hits from that search can be seen in **Table 1**. Additional articles were also identified from the references of articles discovered during this initial search. Criteria for inclusion in this review were basic science studies examining the effects of continuous passive motion, active range of motion, or weight bearing on articular cartilage or knee joint health or inflammation. Clinical outcomes studies comparing these variables in knee articular cartilage repair patients were also included. All studies were required to be published in English and available in full manuscript form as of August 1, 2009. Exclusion criteria were clinical studies involving joints other than the knee or total knee arthroplasty patients and studies examining surgical practices not indicated for clinical treatment of articular cartilage damage. Summary articles that failed to present original research or concepts and nonsystematic reviews were also excluded from review.

All selected articles were rated using the Strength of Recommendation Taxonomy (SORT) (**Tables 2 and 3**).<sup>21</sup> This evaluation system was selected for use in this review because of its focus on patient-oriented outcomes as the strongest evidence for clinical application. The use of the SORT grading system allows for the evaluation of individual articles on a scale of 1, 2, or 3 and the evaluation of the overall body of evidence in support of a particular treatment on a scale of A, B, or C. The SORT system is in agreement with the primary goals of this article to identify evidence from which clinical practice can be based.

## Results

From the initial 689 hits, 16 articles met all inclusion and exclusion criteria (**Tables 4 and 5**). Of the articles excluded, many were articles regarding surgical techniques without investigation of rehabilitation methods, involved total knee

**Table 1.** Search Words and Resulting Literature Hits

Terms	Hits
articular cartilage AND active range of motion	0
articular cartilage AND continuous passive motion	39
articular cartilage AND early weight bearing	3
articular cartilage AND weight bearing AND rehabilitation	45
autologous chondrocyte implantation AND continuous passive motion	2
autologous chondrocyte implantation AND weight bearing	25
continuous passive motion AND knee AND rehabilitation	161
continuous passive motion AND knee AND rehabilitation AND cartilage	15
microfracture AND continuous passive motion	4
microfracture AND rehabilitation	56
microfracture AND weight bearing	31
osteochondral allograft AND continuous passive motion	0
osteochondral allograft AND rehabilitation	6
osteochondral allograft AND weight bearing	7
weight bearing AND articular cartilage AND knee	295
Total	689

Databases searched were Medline, SportDiscus, and CINAHL.

arthroplasty, or were “nonsystematically reviewed” summary articles of existing research. Of the articles selected for inclusion, 12 were basic science studies involving animal models of articular cartilage healing. All basic science studies received a SORT rating of 3 because the use of animal models alone requires significantly more research before these findings can be translated into direct clinical practice.<sup>21</sup> The remaining 4 were clinical studies, with 2 being case series study designs, 1 being a prospective randomized controlled trial, and 1 a single-subject case report. The 2 case series reports received a rating of 2 for their clinical applicability despite having weak experimental designs. The prospective randomized controlled trial warranted a rating of 1 based on a high-level prospective study design that included both disease- and patient-oriented outcome measures. Finally, the case study received a 3 based on its limited evidence for broad clinical application.

## Discussion

The purpose of this review was to examine the evidence regarding use of continuous passive motion, active range of motion, and early weight bearing following articular cartilage repair to the knee. Only 16 studies were identified as meeting our inclusion criteria, with only 4 of those studies being clinical. Overall, these studies were low in quality with few subjects and only 1 was a prospective controlled study evaluating patient-oriented outcomes.<sup>17</sup>

## Continuous Passive Motion

Significant basic science evidence using animal models supports the use of CPM in the treatment of articular cartilage defects.<sup>6,13,22-27</sup> In the first published experimental investigation of CPM, Salter *et al.*<sup>6</sup> used a rabbit model to compare the effect of CPM to immobilization and IAM. In this study, articular cartilage defects were created in both adolescent and adult rabbits. The rabbits were assigned to 3 groups. Group 1 was immobilized in a cast. Group 2 was permitted unrestricted cage activity, and the final group was placed in CPM continuously for durations varying from 1 to 4 weeks. Use of CPM resulted in better defect healing as evaluated by gross inspection, increased formation of hyaline repair tissue, and the degree of metachromasia in the surrounding matrix. Both the intermittent cage activity group and the CPM group had greater joint mobility than the immobilized group. An additional important observation by the investigators was the tolerance of the rabbits to CPM. The investigators suggested that CPM may in some way block the perception of pain, a concept that is apparent clinically and has subsequently undergone further evaluation.<sup>22</sup> It is important to note that the effects of treatment on subchondral bone and other surrounding tissues were not evaluated in this study. Similarly, the authors stress that this study did not evaluate the ability of the healed cartilage in the CPM group to tolerate the stresses of regular weight-bearing activity.<sup>6</sup>

Despite being excluded from our results due to the use of a treatment that is not common to clinical practice, additional historical work by Salter, O’Driscoll, and colleagues provides significant support for the use of CPM. O’Driscoll *et al.*<sup>25,26,28</sup> further investigated the beneficial effect of early mobilization and CPM in a series of studies in rabbits following periosteal autograft coverage of a trochlear cartilage defect. In these studies, comparisons were made between groups undergoing autologous periosteal grafting, followed by either CPM or IAM, and a control group that was also allowed free intermittent cage activity but did not receive a periosteal graft. Among this research was the first report on the long-term effect (1 year) of CPM on a tissue engineering-based treatment approach.<sup>25</sup> The authors reported that CPM reduced the presence of gross degenerative changes from 77% to 22%. CPM overall allowed for better defect fill and better histological scores than the IAM group. Of particular importance may be the fact that concomitant erosions of the defect edges observed in the IAM group (40%) were not present in the CPM group.<sup>25</sup> These findings were also corroborated in the patella with similar results.<sup>24</sup>

In another early study supporting the use of CPM for tissue-engineered cartilage constructs, O’Driscoll and Salter<sup>27</sup> actually created periosteum-wrapped autologous bone grafts to fill deep osteocartilaginous defects in the

**Table 2.** Strength of Recommendation Taxonomy (SORT) Level of Study Quality<sup>21</sup>

Study Quality	Type of Studies		
	Diagnosis	Treatment/Prevention/Screening	Prognosis
Level 1: Good quality patient-oriented evidence	Validated clinical decision rule	Systematic review (SR)/meta-analysis of randomized controlled trials (RCTs) with consistent findings	SR/meta-analysis of good quality cohort studies
	SR/meta-analysis of high-quality studies	High-quality individual RCT	Prospective cohort study with good follow-up
	High-quality diagnostic cohort study	All or none study	
Level 2: Limited quality patient-oriented evidence	Unvalidated clinical decision rule	SR/meta-analysis of lower quality clinical trials or of studies with inconsistent findings	SR/meta-analysis of lower quality cohort studies or with inconsistent results
	SR/meta-analysis of lower quality studies or studies with inconsistent findings	Lower quality clinical trial	Retrospective cohort study or prospective cohort study or prospective cohort study with poor follow-up
	Lower quality diagnostic cohort study or diagnostic case control study	Cohort study Case control study	Case control study Case series
Level 3: Other evidence	Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), and case series for studies of diagnosis, treatment, prevention, or screening		

medial femoral condyle. Animals receiving CPM showed a higher percentage of hyaline cartilage than animals in the other groups. These animal experiments therefore have shown that CPM seems to be beneficial in different anatomic locations in the rabbit knee joint. Furthermore, O'Driscoll and Salter's groundbreaking work has shown that CPM is consistently beneficial for articular cartilage treatments compared to immobilization or IAM across a variety of graft techniques.<sup>6,24-28</sup>

Further research has also used a rabbit model to explore the dosing effect of CPM and immobilization.<sup>13</sup> Full-thickness articular cartilage defects were created surgically in each rabbit. The defects were then treated with 1 of 6 potential protocols of varying combinations of CPM and immobilization. All treatments except for the combined 1-week immobilization followed by 1 week of 24-hour per day CPM were only administered for the initial week following inducement of the defect. The animals were sacrificed 6 weeks postoperatively for evaluation of mobility and gross and histological healing. The group immobilized for 24 hours per day exhibited reduced ROM and the poorest cartilage repair both macro- and microscopically compared to the other groups. It was also observed that the initiation of CPM following 1 week of immobilization was not sufficient to recover from the detrimental aspects of immobilization, including loss of ROM and tissue degradation. The groups that received CPM for either 8 or 24 hours per day had a significantly better histological appearance with more densely distributed

chondrocytes and improved Safranin-O staining than either of the immobilization groups or a group permitted cage activity. These results demonstrate the importance of CPM in the first week of cartilage healing, suggesting that treatment with either 8 hours of CPM per day or the use of CPM for 24 hours per day results in superior cartilage healing with better surface congruity and more densely distributed chondrocytes than immobilization or free activity. It is important to note that like the previous study, these investigators examined only the natural healing response of cartilage to injury and not the healing response following an attempted cartilage repair with currently used clinical techniques. This article is an important source of evidence for many of the current rehabilitation protocols recommending CPM for 6 to 8 hours per day following surgery. However, it does not address whether shorter or longer treatment doses are effective or for how long postoperative CPM should be used.

The anti-inflammatory effects of CPM have also been examined with a rabbit model of antigen-induced arthritis.<sup>22</sup> Symptomatic rabbits were either placed immediately in CPM for 24 to 48 hours or immobilized for the same time period. Following sacrifice, the menisci were cultured to determine the presence of inflammatory mediators and glycosaminoglycans. Significant differences between groups in the expression of inflammatory factors were seen as early as 24 hours following the initiation of treatment. The differences were larger following 48 hours, whereby the CPM group had a decrease in the proinflammatory



**Table 3.** Strength of Recommendation Taxonomy<sup>21</sup>

Strength of Recommendation	Definition
A	Recommendation based on consistent and good quality patient-oriented evidence
B	Recommendation based on inconsistent or limited quality patient-oriented evidence
C	Recommendation based on consensus, usual practice, opinion, disease-oriented evidence, and case series for studies of diagnosis, treatment, prevention, or screening

mediators compared to the immobilization group. There was an increase in the anti-inflammatory interleukin-10 and a reduction in glycosaminoglycan loss in the CPM group as compared to the immobilized group.<sup>22</sup> It is possible that this increase in anti-inflammatory mediators is a possible mechanism for the reduction in pain that is often clinically reported with the use of CPM. In addition to pain reduction, the decrease in matrix metalloproteinases represents a significant decrease in a major matrix-degrading enzyme.<sup>22</sup> These data suggest that CPM may have a significant effect on reducing generalized inflammation within the knee as a whole; however, the results are only compared to immobilized limbs as there was no control group.

The positive effect of CPM is further supported by the work of Nugent-Derfus *et al.*<sup>29</sup> Their work demonstrated that CPM stimulates the metabolism of the gene product of the proteoglycan-4 gene, a chondroprotective molecule (lubricin/superficial zone protein).<sup>29</sup> Using an *in vitro* bovine model, it was observed that variations in metabolism were different throughout the joint surface. CPM was particularly effective in stimulating biosynthesis in the areas experiencing the greatest shear force.

CPM has also demonstrated a similarly protective effect on proteoglycans following chemically induced cartilage degradation in a rabbit model.<sup>23</sup> When rabbits were permitted 2 days of free cage activity before a random group began CPM for up to 21 days, those rabbits participating in free cage activity throughout the study showed surface defects in the loaded region of the joint after 21 days. By comparison, those in the CPM group demonstrated an intact articular surface and a replenishment of proteoglycans. The authors concluded that CPM served to prevent the proteoglycan breakdown and subsequent joint destruction that was observed in the cage activity group. It is interesting to note that the authors' decision to allow 2 days of free cage activity for all subjects was based on initial pilot testing, which demonstrated that if CPM was introduced immediately following injection, early cartilage damage was observed.<sup>23</sup> The influence of motion on cellular transport may play a key role in the findings of this study. Unfortunately, the chemical means by which cartilage degradation was initiated in this study greatly limits its translation to clinical practice.

It has been previously reported that CPM creates a cyclic pressure gradient within the knee.<sup>30</sup> In appropriate dosages, these pressure gradients may improve chondrogenesis.<sup>31</sup> It has also been suggested that CPM may affect the nutritional transport system of the knee as well.<sup>32</sup> Similarly, CPM has been observed to reduce the cartilage degradation associated with immobilization in a rat model.<sup>33</sup> In this study, only 30 minutes of CPM 6 days per week demonstrated significant improvements in joint health as compared to immobilization with histological findings similar to those observed in a control group. This protective benefit of CPM may be related to a reduction in articular hypoxia resulting from poor circulation of synovial fluid associated with immobilization.<sup>33</sup> These physiologic effects of CPM may be key to understanding its observed benefits on cellular synthesis during cartilage healing and to determine ideal dosing parameters following cartilage repair.

From a clinical perspective, only 2 studies have examined the effects of CPM in patients following a microfracture procedure for the treatment of chondral defects.<sup>12,15</sup> Rodrigo *et al.*<sup>12</sup> performed second-look arthroscopies that were medically indicated in 77 patients, 6 months to 2 years following microfracture. Of these patients, 46 had received CPM therapy postoperatively for an average of 7.83 weeks, and 31 patients did not have access to a CPM machine. Each treated defect was scored both at the initial surgery and at follow-up based on visual inspection. On average, patients who received CPM had significantly greater improvement in lesion scores when compared to those who did not. However, between-group comparisons for age, lesion location, and lesion size were statistically significant. Those in the non-CPM group were older (37 vs. 30 years of age) and experienced nearly twice as many patellofemoral defects (14 vs. 8) as compared to the CPM group, whereas the CPM group was observed to have greater average defect size (322 vs. 210 mm<sup>2</sup>). All of these variables have been thought to influence success following cartilage repair. It is likely that the retrospective nature of this study resulted in this poor matching between groups, lowering the clinical strength of the study. It is also important to note that no patient-oriented outcome measures of objective or subjective function were documented in this study.

**Table 4.** Selected Basic Science Articles

Author	Model	Comparison	Key Finding	Strength of Recommendation Taxonomy
Chang <i>et al.</i> <sup>36</sup>	Rat with surgically induced full-thickness articular cartilage lesion	Resected NWB limb vs. intact limb permitted FWB	No difference in macroscopic exam of cartilage quantity; FWB demonstrated significantly greater cartilage quality under microscopic exam.	3
Dowdy <i>et al.</i> <sup>35</sup>	Adult dogs undergoing meniscal repair	Immobilized weight bearing vs. weight bearing with motion	Fewer articular cartilage lesions when motion and weight bearing combined.	3
Ferretti <i>et al.</i> <sup>22</sup>	Rabbits with antigen-induced arthritis (AIA) immobilized and CPM vs. non-AIA controls compared AIA using t tests at 24 and 48 hours	Immobilized vs. CPM	CPM shown to have anti-inflammatory effects as early as 24 hours compared to immobilization.	3
French <i>et al.</i> <sup>14</sup>	Horses with a surgically induced cartilage lesion into the intercarpal joint and third carpal bone	Rest vs. gradual return to exercise at 4 days post-op	Found no significant differences in defect repair quality, but active horses did show increased repair thickness.	3
Klein <i>et al.</i> <sup>20</sup>	Healthy dogs	FWB active motion vs. NWB active motion	NWB active motion prevented soft tissue atrophy but did not prevent bone atrophy.	3
Nugent-Derfus <i>et al.</i> <sup>29</sup>	Bovine in vitro	Effect of 24-hour CPM on proteoglycan 4 (PRG4) metabolism	CPM stimulates chondrocyte PRG4 synthesis.	3
Palmoski <i>et al.</i> <sup>37</sup>	Healthy dogs	Resected NWB limb vs. intact limb permitted FWB	Resected limbs demonstrated thinning of articular cartilage and other changes similar to immobilization.	3
Sakamoto <i>et al.</i> <sup>33</sup>	Healthy rats	Immobilized vs. CPM (30 minutes 6 days/week) vs. control	CPM reduced cartilage thinning, occurrence of subchondral bone resorption pits, and irregularity at the osteochondral junction when compared to immobilization.	3
Salter <i>et al.</i> <sup>6</sup>	Rabbit with surgically induced full-thickness articular cartilage lesion	CPM 24 hours per day vs. immobilization vs. free cage activity	CPM 24 hours per day resulted in better defect healing.	3
Shimizu <i>et al.</i> <sup>13</sup>	Rabbit with surgically induced full-thickness articular cartilage lesion	CPM 24 hours per day vs. CPM 8 hours per day, CPM 2 hours per day, 24-hour immobilization, or free cage activity	Significantly better healing in CPM 24-hour and CPM 8-hour groups. CPM could not overcome negative effects of 1-week immobilization prior to CPM.	3
Williams <i>et al.</i> <sup>23</sup>	Rabbit with chemically induced proteoglycan loss	48 hours. Free cage activity and 19 days CPM vs. 21 days free cage activity	Cage activity group developed surface defects after 21 days while CPM group did not.	3
van de Lest <i>et al.</i> <sup>38</sup>	Shetland pony synovial fluid (SF) on <i>ex vivo</i> samples of articular cartilage from the same ponies	Box rest vs. mild to moderate exercise	SF from exercise group enhanced chondrocyte synthesis and reduced breakdown.	3

CPM = continuous passive motion; FWB = full weight bearing; NWB = non-weight bearing.

In contrast, Marder *et al.*<sup>15</sup> reported no differences between subjects using CPM 6 to 8 hours per day for 6 weeks combined with toe touch weight bearing when

compared to subjects not using CPM who were permitted to bear weight as tolerated. Both disease- and patient-oriented measures were used to retrospectively classify outcomes

**Table 5.** Selected Clinical Research Articles

Author	Model	Comparison	Key Finding	Strength of Recommendation Taxonomy
Allen <i>et al.</i> <sup>7</sup>	Single-subject case report following autologous chondrocyte implantation	Accelerated weight bearing vs. nil	No detrimental effects of early weight bearing were observed.	3
Ebert <i>et al.</i> <sup>17</sup>	Postoperative MACI Patients	TTWB for 5 weeks progressing to FWB at 11 weeks vs. immediate progression to FWB at 8 weeks	Only the accelerated group reported a significant improvement in pain at 3 months. The accelerated group also had significantly greater 6-minute walk test distance and higher activity levels. Neither group experienced graft delamination or failure.	1
Marder <i>et al.</i> <sup>15</sup>	Retrospective case comparison series among femoral condyle microfracture patients	CPM and TTWB ( <i>n</i> = 23) vs. AROM and WBAT ( <i>n</i> = 20)	No differences between groups in clinical or functional outcomes with an average follow-up of 4.2 years.	2
Rodrigo <i>et al.</i> <sup>12</sup>	Case series of microfracture patients undergoing medically necessary second-look arthroscopy	CPM post-op of initial surgery ( <i>n</i> = 46) vs. no CPM ( <i>n</i> = 31)	The CPM group had greater improvements in lesion grading than the non-CPM group following initial microfracture.	2

TTWB = toe-touch weight bearing; FWB = full weight bearing; AROM = active range of motion; WBAT = weight bearing as tolerated; MACI = matrix-induced autologous chondrocyte implantation.

for 43 patients. These measures included the Lyshom knee rating scale, the Tegner activity scale, radiographs, range of motion, ligamentous stability testing, and patient reports of pain, swelling, instability, and return to activities. Only subjects with lesions of less than 2 cm<sup>2</sup> on the femoral condyle were included in this study, and there were no significant differences between groups for age or complication rate. Unfortunately, the retrospective and poorly controlled nature of this study limits the ability to reach clear conclusions regarding CPM and partial weight bearing following cartilage repair.

There exists significant basic science and limited clinical evidence to support the use of continuous passive motion therapy following surgery to maintain range of motion, reduce inflammation, and promote healing. Due to this large body of basic science evidence, CPM has become a standard of postsurgical knee rehabilitation. Research by Shimizu *et al.*<sup>13</sup> in an animal model supports the current dosing level of 6 to 8 hours per day. However, no evidence exists regarding how long postoperative CPM should be used. No clear evidence opposing the use of CPM was identified during this review. Unfortunately, much of the evidence in favor of CPM has been focused on what are considered disease-centered outcomes,<sup>21</sup> such as histological or biochemical markers. In the SORT system, these results are less preferable than patient-centered outcomes such as clinical measures of function and health-related

quality of life.<sup>21</sup> As a result, the strength of recommendation for CPM following articular cartilage repair is a C.<sup>21</sup>

### Early Active Range of Motion and Weight Bearing

In contrast to immobilization,<sup>34</sup> active motion has been shown to have several benefits to joint health. In a study that failed to meet the inclusion criteria for this review due to its patient population, Friemert *et al.*<sup>16</sup> documented increased joint position sense in patients using a continuous active motion (CAM) device compared to CPM. Both therapies were used for 1 week following surgery, and joint position sense was tested using an angle reproduction test. Significant improvements were seen in the CAM group at the angle combination of 10°/15° while no significant differences were seen at 30°/35° and 50°/60°. No long-term outcomes were provided to suggest how these differences may affect function over time.

In a canine model permitting weight bearing and range of motion, fewer articular cartilage lesions and greater cartilage formation were reported compared to immobilization following meniscal repair.<sup>35</sup> Although these significant differences were observed at 10 weeks post repair, no differences in cartilage health were observed between groups at 2 or 4 weeks. The absence of differences at these early time points, combined with positive findings at later follow-up, suggests that early ROM and weight bearing

were not detrimental and over time were protective for joint health.

Active motion has also been shown to prevent disuse atrophy of soft tissues, including the meniscus and ligaments.<sup>20</sup> In this early study by Klein *et al.*,<sup>20</sup> active motion was permitted in the absence of weight bearing, yet osteopenic changes were observed in the bone. These results demonstrate that although active motion was protective of soft tissue structures, weight bearing is necessary to stimulate bone growth and maintenance. Although articular cartilage was not evaluated in this study, the failure of active motion alone to prevent osteopenia suggests that some loading may be necessary to properly stimulate healing in the knee.

The importance of joint loading for cartilage health is further supported by the work of Chang *et al.*<sup>36</sup> In this study of Long-Evans rats, full-thickness defects were induced bilaterally, and then one limb was resected to permit full motion but restrict weight bearing, whereas the other limb was left intact. Following 6 weeks of unrestricted cage activity, no significant differences were observed in macroscopic healing of the defects. However, microscopic evaluation demonstrated higher quality repair tissue in the intact, weight-bearing limbs. The authors concluded that compressive loading significantly accelerated the metaplasia of the repaired tissue.<sup>36</sup> These findings are in agreement with a similar study by Palmoski *et al.*<sup>37</sup> involving a transected limb model in dogs. Both studies support the need for some degree of compressive loading in addition to joint motion for successful cartilage healing.

Activity has also been observed to influence the presence of chemical mediators in synovial fluid. van de Lest *et al.*<sup>38</sup> placed ponies on box rest for 1 month after which a sample of synovial fluid was taken. The animals then participated in mild to moderate exercise daily for 1 week. Following treadmill exercise on the eighth day, synovial samples were taken again. Cartilage explant cultures were then treated with the different synovial fluids to see if physical activity altered synovial fluid's influence on chondrocyte metabolism. Postactivity synovial fluid was observed to have a positive effect on proteoglycan content, increasing proteoglycan synthesis and decreasing breakdown. The cultures treated with the postactivity synovial fluid also showed enhanced glycosaminoglycan synthesis compared to those treated with the synovial fluid sampled following an extended period of rest. This study demonstrates that in addition to any benefits occurring from the direct mechanical loading of cartilage surfaces, physical activity also affects the chemical mediators within the synovial fluid that may influence chondrocyte activity.

The effect of gradual loading and activity on chondral healing in 12 horses was investigated by French *et al.*<sup>14</sup> The studied protocol was similar to an accelerated rehabilitation program following cartilage injury. Although no actual

treatment was performed in this study, a cartilage lesion was induced in the horses. Following the surgery, all horses were rested in a small paddock for 5 days. After 5 days, half of the horses were started on a gradual progressive exercise program over a course of 13 weeks, while the other horses remained confined. After 13 weeks, the lesion sites underwent macroscopic and histological evaluation. No significant differences in the quality of repair were detected between groups with a combination of fibrous tissue and fibrocartilage filling and covering the defect. However, those in the exercise group did display significantly thicker repair tissue. These results suggest that an accelerated return of less than 7 days to weight bearing and active motion following cartilage repair may be reasonable. However, these results should be taken with caution as the authors report a higher number of complications among the physically active group.

An accelerated rehabilitation somewhat similar to that used by French *et al.*<sup>14</sup> has been reported in a successful case report by Allen *et al.*<sup>7</sup> as well as a larger randomized controlled trial by Ebert *et al.*<sup>17</sup> Allen *et al.* permitted full weight bearing as tolerated at 1 week following autologous chondrocyte implantation (ACI). It is important to note that although the patient was permitted to bear weight as tolerated, 2 crutches were used postoperatively for 3 weeks and the use of a single crutch continued through week 5. Active knee motion began in week 3, and a locked knee brace was worn for ambulation until week 6. The author reports that part of the rationale for continued brace locking was a quadriceps extensor lag. Future clinical studies using this protocol may consider investigating whether earlier active motion could be useful in reducing this lag.

In a larger controlled trial, Ebert *et al.*<sup>17</sup> prospectively randomized 62 patients into either a traditional or an accelerated weight-bearing protocol following matrix-induced autologous chondrocyte implantation (MACI). Those in the traditional protocol were limited to toe-touch weight bearing for 5 weeks and then progressed to full weight bearing at week 11. The accelerated group was permitted to bear weight as tolerated and gradually progressed to full weight bearing by 8 weeks post surgery. This study included disease-oriented outcomes (magnetic resonance imaging [MRI] and gait analysis), patient-reported outcomes (Knee Injury and Osteoarthritis Outcome Score [KOOS], visual analog scale [VAS], and SF-36), and performance-based outcomes (6-minute walk test, 3-repetition maximum strength straight leg raise, activity level, and active range of motion) evaluated at 3 months post surgery. The results of this study supported the safe use of the accelerated protocol with decreased pain scores and improved 6-minute walk distances and activity levels in the accelerated group at 3 months. No patients in either group experienced graft failure or delamination during the 3-month time period.



Although both of these clinical studies offer support for the use of accelerated weight bearing following cartilage repair, further clinical research is needed to determine long-term outcomes and what degree of weight bearing is appropriate throughout rehabilitation.

Clear practical benefits to the use of early weight bearing and active motion following articular cartilage repair exist. Ambulating without crutches or with limited crutch dependence can greatly improve a patient's quality of life and ability to return to activities of daily living. In addition to the return to work, there are economic benefits by reducing rehabilitation costs related to rental of the CPM unit. Despite these benefits, there is only limited evidence supporting early weight bearing and active motion post cartilage repair. This evidence consists of basic science using animal models,<sup>14,16,20,35-38</sup> a single clinical case series,<sup>15</sup> and one randomized controlled trial.<sup>17</sup> Based on these findings, the use of early weight bearing and active motion following cartilage repair can be given a strength of recommendation of B using the SORT system.<sup>21</sup> However, due to the variation in what is considered "accelerated," the variations in criteria to progress weight bearing, and the short-term nature of the outcomes that have been reported, no clear recommendations for implementing accelerated weight bearing and early active motion into clinical practice can be made at this time.

### Limitations

Substantial research concerning cartilage healing using animal models exists. Unfortunately, the conclusions that can be reached from this evidence are limited, not only due to translation from animal experimentation but also because the majority of these studies only examine the natural healing response to injury, not the healing response after currently accepted repair treatments. Furthermore, many comparisons in the reviewed studies are between an intervention therapy (CPM or active motion) and total joint immobilization. Immobilization is an inaccurate comparator because postoperative immobilization alone has not been an accepted clinical practice following articular cartilage repair for many years. The conclusions of this review are also limited secondary to the paucity and limited quality of clinical studies comparing rehabilitation protocols following cartilage repair. Finally, it should also be noted that this is not an exhaustive review of basic science research concerning immobilization or CPM. As stated in the methods, only those clinical studies specifically concerning the healing of articular cartilage in the knee were selected for inclusion. Additional literature concerning CPM in other joints or as a modality for other treatments such as total knee arthroplasty and anterior cruciate ligament reconstruction was beyond the scope of this review.

### Future Research

Two key areas concerning rehabilitation following articular cartilage repair need further research. First, it is imperative that basic science research explore cartilage healing following current operative repair techniques. This research needs to go beyond comparing procedures to one another and explore how rehabilitation techniques can be used to augment and ensure success of effective procedures. The vast majority of existing research compares a motion-based intervention to total joint immobilization, a practice that is rarely if ever used. It is also important that when animal models are used, the appropriate species are used for the given cartilage pathology. As demonstrated by Athanasiou *et al.*<sup>39</sup> and others, there is significant variation in the mechanical properties of articular cartilage between both species and locations on the femur. For translation between basic science and clinical practice to occur, appropriate modeling of repair and intervention is essential.

Second, it is clear that clinical research has lagged behind that of basic science. Significantly more patient-centered outcomes research is needed in the area of articular cartilage rehabilitation. Although ideal, blinded, and randomized trials are not always compatible with good clinical practice (GCP), GCP-guided cohort studies comparing various rehabilitation protocols are feasible. Although existing basic science evidence supports the use of CPM initially following surgery, clinical research is needed to understand what volume of CPM is necessary or if CPM can be replaced in part or entirely by active range of motion. Similarly, the benefits versus risks of early weight bearing have gone largely unexplored. Finally, rehabilitation specialists must continue to strive to practice evidence-based medicine and not become complacent in accepting traditional rehabilitation protocols as the best that can be done—particularly when little to no quality evidence exists to support those protocols.

### Conclusions

At the beginning of this study, we set out to answer 3 questions: (1) does the use of CPM enhance healing, and if so, with what parameters should it be applied? (2) Can AROM be used in place of or with CPM? and (3) When can individuals safely resume weight bearing following repair? This systematic review of the literature unfortunately falls short of answering these questions, clearly indicating the need for better evidence.

We can summarize that CPM has become a staple of knee rehabilitation protocols, and several animal models have documented its efficacy in reducing the problems associated with joint immobilization.<sup>6,13,22-28,33</sup> At least one clinical study reports improved cartilage healing among

those using CPM when compared to those who did not.<sup>12</sup> Existing basic science research supports current CPM dosages of 6 to 8 hours per day,<sup>13</sup> yet there is no evidence regarding how long postoperatively CPM is beneficial. Regarding early active motion, no detrimental effect has been reported in basic science or clinical reports. Allowing weight bearing as tolerated immediately following cartilage repair with a gradual increase to full weight bearing at 8 weeks has been reported to safely improve pain, function, and activity compared to a more conservative progression in one prospective controlled trial, with no increase in complications as of 3 months post operation.<sup>17</sup> Other case series that have documented accelerated rehabilitation following articular cartilage repair have also reported positive outcomes.<sup>7,15</sup> The short length of follow-up, low number of subjects, and limited quality of existing research prevent clear recommendations for a timeline for weight bearing at present. However, there is evidence to suggest that future clinical guidelines for weight bearing following cartilage repair may be less restrictive, with greater emphasis on patient-reported outcomes than standardized time periods.

The reported clinical results, combined with the existing basic science evidence, suggest that there may be an ideal combination of all 3 treatments—CPM, AROM, and early weight bearing—that is most advantageous for both quality of life and quality of healing. Appropriate basic science research and focused clinical research are needed to generate postoperative rehabilitative protocols that will maximize benefits of articular cartilage repair and restorative procedures as they continue to advance and gain popularity.

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