# References – Cartilage Healing

1. Salter, R.B. The Physiologic Basis of Continuous Passive Motion for Articular Cartilage Healing and Regeneration. Hand Clin. 10(2):211, 1994.

**ABSTRACT**
This article historically reviews the limited potential of articular cartilage to heal or regenerate, past emphasis on rest as opposed to motion, and the reasoning that led the author to create the biologic concept of continuous passive motion (CPM) in 1970. The basic premises and hypotheses of CPM are stated. A brief summary is provided of 19 scientific investigations of CPM in rabbits, with particular emphasis on the beneficial short-term and long-term effects of CPM in intra-articular fractures. The conclusions from the basic research are summarized. The clinical applications of CPM to the care of patients are discussed with respect to the indications and the results.

2. Rodrigo, J.J., Steadman, J.R., Silliman, J.F., Fulstone, H.A. Improvement of Full-Thickness Chondral Defect Healing in the Human Knee after Debridement and Microfracture using Continuous Passive Motion. Am. Jo. Knee Surg. 7(3):109, 1994.

3. Shimizu, T., Videman, T., Shimazaki, K., Mooney, V. Experimental Study on the Repair of Full Thickness Articular Cartilage Defects: Effects of Various Periods of Continuous Passive Motion, Cage Activity, and Immobilization. Jo. Orthop. Res. 5(2):187, 1987.

**ABSTRACT**
In order to clarify the dose/response characteristics of continuous passive motion (CPM), the repair response of full thickness articular cartilage defects was studied in a rabbit model. The following combinations of CPM and immobilization (Imm) were utilized: CPM, 24 h/day; CPM, 8 h/day and Imm, 16 h/day; CPM, 2 h/day and Imm 22 h/day; Imm 24 h/day; and normal cage activity. These regimens were used only in the initial week and then all rabbits were permitted to move freely in their cages, except for a sixth Imm-CPM group that was kept immobilized in the initial week and then CPM 24 h/day for another week. The CPM 24 h/day and the CPM 8 h/day groups (groups 1 and 4, respectively) showed better repair than the other groups, i.e., better surface congruity, larger positive Safranin-O staining area, and greater number of chondrocytes in the repair tissue. The CPM 2 h/day group (group 3), however, showed only slightly better repair than the Imm group (group 4). The CPM following immobilization was not effective to overcome the harmful effect of immobilization. We conclude that in the present model, CPM for 8 or 24 h/day is effective for adequate cartilage repair even with some component of immobilization. Its application should be at least 8 h/day. On the contrary, if CPM is delayed for a week following immobilization, the effect of CPM on cartilage will be reduced.

4. O'Driscoll, S.W., Salter, R.B. The repair of major osteochondral defects in joint surfaces by neochondrogenesis with autogenous osteoperiosteal grafts stimulated by continuous passive motion. An experimental investigation in the rabbit. Clin. Orthop. And Relat. Res. 208:131, 1986.

**ABSTRACT**
The purpose of this investigation was to determine the effects of continuous passive motion (CPM) on the chondrogenic potential of autogenous osteoperiosteal grafts to repair major osteochondral defects. A 3.5-mm-wide circular full-thickness defect was drilled in one medial femoral condyle of 55 adolescent New Zealand rabbits. A graft of periosteum from the proximal tibia was wrapped around a disc of bone from the same area (cambium layer of the periosteum facing outward), then press-fitted into the defect. The rabbits were treated by either immobilization (Imm) or intermittent active motion (IAM) for five weeks, or by continuous passive

motion (CPM) for two weeks followed by IAM for three weeks. A control group (no osteoperiosteal graft in the defect) was also treated by CPM for two weeks and IAM for three weeks. At five weeks, hyaline cartilage was the predominant tissue in only 10% of the defects in the Imm, IAM, and control groups, compared with 70% in the CPM group (p less than .025). Bonding of the newly formed tissue to the adjacent cartilage was significantly better in the CPM group.

5. Mukherjee, M., Saris, D.B., Schultz, F.M., Berglund, L.J., An, K.N., O'Driscoll, S.W. The enhancement of periosteal chondrogenesis in organ culture by dynamic fluid pressure. J. Orthop. Res. 19(4):524, 2001.

**ABSTRACT**

Cartilage repair by autologous periosteal arthroplasty is enhanced by continuous passive motion (CPM) of the joint after transplantation of the periosteal graft. However, the mechanisms by which CPM stimulate chondrogenesis are unknown. Based on the observation that an oscillating intra-synovial pressure fluctuation has been reported to occur during CPM (0.6-10 kPa), it was hypothesized that the oscillating pressure experienced by the periosteal graft as a result of CPM has a beneficial effect on the chondrogenic response of the graft. We have developed an in vitro model with which dynamic fluid pressures (DFP) that mimic those during CPM can be applied to periosteal explants while they are cultured in agarose gel suspension. In this study periosteal explants were treated with or without DFP during suspension culture in agarose, which is conducive to chondrogenesis. Different DFP application times (30 min, 4 h, 24 h/day) and pressure magnitudes (13, 103 kPa or stepwise 13 to 54 to 103 kPa) were compared for their effects on periosteal chondrogenesis. Low levels of DFP (13 kPa at 0.3 Hz) significantly enhanced chondrogenesis over controls (34 ± 7% vs 14 ± 5%; $P < 0.05$), while higher pressures (103 kPa at 0.3 Hz) completely inhibited chondrogenesis, as determined from the percentage of tissue that was determined to be cartilage by histomorphometry. Application of low levels of DFP to periosteal explants also resulted in significantly increased concentrations of Collagen Type II protein (43 ± 8% vs 10 ± 5%; $P < 0.05$). New proteoglycan synthesis, as measured by $^{35}$S-sulphate uptake was increased by 30% in periosteal explants stimulated with DFP (350 ± 50 DPM vs 250 ± 75 DPM of $^{35}$S-sulphate uptake/μg total protein), when compared to controls though this difference was not statistically significant. The DFP effect at low levels was dose-dependant for time of application as well, with 4 h/day stimulation causing significantly higher chondrogenesis than just 30 min/day (34 ± 7 vs 12 ± 4% cartilage; $P < 0.05$) and not significantly less than that obtained with 24 h/day of DFP (48 ± 9% cartilage, $P < 0.05$). These observations may partially explain the beneficial effect on cartilage repair by CPM. They also validate an in vitro model permitting studies aimed at elucidating the mechanisms of action of mechanical factors regulating chondrogenesis. The fact that these tissues were successfully cultured in a mechanical environment for six weeks makes it possible to study the actions of mechanical factors on the entire chondrogenic pathway, from induction to maturation. Finally, these data support the theoretical predictions regarding the role of hydrostatic compression in fracture healing.

6. Steadman, J.R., Rodrigo, J.J., Briggs, K.K., Rodkey, W.G., Silliman, J., Sink, E. Debridement and microfracture, ("Pick Technique") for full-thickness articular cartilage defects. Insall, J.N., Scott, W.N. Surgery of the Knee. Churchill Livingstone, New York, p. 361, 2001.

7. Alfredson, H., Lorentzon, R. Superior results with continuous passive motion after periosteal transplantation. A retrospective study of human patella cartilage defect treatment. Knee Surg. Sports Traumatol Arthrosc. 7(4):232, 1999.

**ABSTRACT**

Fifty-seven consecutive patients (33 men and 24 women), with a mean age of 32 years (range 16-53 years), who suffered from an isolated full-thickness cartilage defect of the patella and disabling knee pain of long duration, were treated by autologous periosteal transplantation to the cartilage defect. The first 38 consecutive patients (group A) were postoperatively treated with continuous passive motion (CPM), and the next 19 consecutive patients (group B) were treated with active motion for the first 5 days postoperatively. In both groups, the initial regimens were followed by active motion, slowly progressive strength training, and slowly progressive weight bearing. In group A, after a mean follow-up of 51 months (range 33-92 months), 29 patients (76%) were graded as excellent or good, 7 patients (19%) were graded as fair, and 2 patients (5%) were graded as poor. In group B, after a mean follow-up of 21 months (range 14-28 months), 10 patients (53%) were graded as excellent or good, 6 patients (32%) were graded as fair, and 3 patients (15%) were graded as poor. Altogether, nine of the fair or poor cases (50%) were diagnosed with chondromalacia of the patella. Our results, after performing autologous periosteal transplantation in patients with full-thickness cartilage defects of the patella and disabling knee pain, are good if CPM is used postoperatively. The clinical results using active motion postoperatively are not acceptable, especially not in patients with chondromalacia of the patella.

8. Deszczynski, J., Slynarski, K. Rehabilitation after cell transplantation for cartilage defects. Transplant Proc. 38(1):314, 2006.

**ABSTRACT**

Rehabilitation is a key element of successful treatment of cartilage defects with cell transplantation. The process of graft maturation takes approximately 18 months and cannot be accelerated, but requires carefully introduced steps leading to early recovery of joint function. Rehabilitation starts at 8 hours after surgery with the continuous passive motion (CPM) exercises and physiotherapy. For the first 6 weeks, patients continue with CPM in the range of 0 degrees to 45 degrees for femoral and tibial defects and 0 degrees to 30 degrees for patellofemoral joint reconstruction. Isometric muscle training and scar manual therapy are introduced. Patients are allowed to weight-bear as tolerated from the second week after surgery. After this initial phase, from 6 to 8 weeks after surgery, rehabilitation is accelerated with increased load-bearing and progressive range of motion to full flexion. Usually patients are able to walk without crutches in this time. Proprioceptive training is introduced with the advance of pain-free full range of motion and no discomfort with full weight-bearing. At 6 months after surgery, most patients recover joint function, making it possible for them to return to daily living activities. However, they need to continue with muscle, proprioceptive, and sports-specific rehabilitation exercises. The rehabilitation process is complicated, requiring close cooperation between the patient and surgeon-physiotherapist team to understand the symptoms and address them in a timely fashion.

9. Delaney, J.P., O'Driscoll, S.W., Salter, R.B. Neochondrogenesis in free intraarticular periosteal autografts in an immobilized and paralyzed limb. An experimental investigation in the rabbit. Clin. Orthop. Rel. Res. 248:278, 1989.

**ABSTRACT**

The purpose of this investigation was to determine whether neochondrogenesis can be induced in free intraarticular autografts of periosteum in the complete absence of motion. In 17 adolescent rabbits, a rectangular graft of periosteum was elevated from the medial aspect of each proximal tibia and folded back on itself so that its deep (cambium) layer was facing outward on both sides. The grafts were transplanted into both ipsilateral knee joints that had been paralyzed by section of the femoral and sciatic nerves, and a cast was applied to one hind limb to provide immobilization. The opposite knee joint of each animal was then placed in the continuous passive motion (CPM) apparatus. At the time of death (21 days postoperatively), some degree of neochondrogenesis was evident in 69% of the grafts in the group with casts and in 100% of the grafts in the CPM group. Hyaline cartilage was the predominant tissue in 13% of the grafts in the group with casts compared to 63% of the grafts in the CPM group. Although this investigation has confirmed the chondrogenic potential of free periosteal grafts in a synovial fluid environment (and the significantly stimulating effect of CPM), the results have also demonstrated that at least some hyaline cartilage can be formed by periosteal grafts even with paralysis of the limb plus immobilization of the joint (presumably complete immobilization). Thus, other factors capable of stimulating neochondrogenesis warrant investigation.