Technical Note

# Particulated Autologous Chondral–Platelet-Rich Plasma Matrix Implantation (PACI) for Treatment of Full-Thickness Cartilage Osteochondral Defects

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**Abstract:** Articular hyaline cartilage injuries can occur as a result of either traumatic of progressive degeneration. When the articular cartilage in a joint is damaged, it can cause joint pain and dysfunction, predisposing patients for the development of early-onset osteoarthritis. There are many restoration procedures available to treat these injuries, such as bone marrow–stimulation techniques, osteoarticular auto/allograft transplants, and autologous chondrocyte implantation. Each of these techniques has its own limitations, which led researchers to explore new regenerative and repair techniques to produce normal hyaline cartilage. The purpose of this Technical Note is to describe in detail the particulated autologous chondral–platelet-rich plasma matrix implantation (PACI) technique that could be used as a single-stage cartilage restoration procedure for treatment of full-thickness cartilage and osteochondral defects.

Articular hyaline cartilage injuries can occur as a result of either traumatic of progressive degeneration. When the articular cartilage in a joint is damaged, it can cause joint pain and dysfunction, predisposing patients for the development of early-onset osteoarthritis. These lesions present a challenging clinical problem due to the inherent poor healing and regenerative potential of hyaline cartilage. Currently, several restoration procedures for chondral defects have been used, including bone marrow stimulation technique aimed at intrinsic reparative mechanisms, cell-based techniques such as autologous chondrocyte implantation (ACI), and osteoarticular auto/allografts to fill and restore cartilage defects.[1] Each of these repair procedures has its own shortcomings, including fibrocartilage formation, necessity for two surgical procedures, long recovery time, or high variability in time to return-to-play and durability of repair tissues.[2,3] These limitations have led researchers to explore new regenerative and repair techniques to produce normal hyaline cartilage in the chondral and osteochondral defects.

ACI is an established and well-accepted procedure for the treatment of localized full-thickness cartilage defects of the knee. ACI results in a greater proportion of hyaline-like tissue in histologic, mechanical, and clinical aspects. It has a beneficial effect on durability and appears to be effective in larger lesions.[3] ACI relies on the in vitro expansion of patient's chondrocytes, a 3- to 4-week process, which is associated with cellular dedifferentiation, impairing the quality of regenerated tissue.[4] Disadvantages of ACI include multiple interventions, longer time to return-to-activity, high cell-producing cost, and lack of availability in various countries.[5]

Recently, many researchers looked into applying particulated juvenile allograft cartilage (PJAC).

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Immature chondrocytes have stronger ability to regenerate hyaline-like tissue, which is crucial for the repair of cartilage defects. DeNovo NT (Zimmer Biomet, Warsaw, IN) is a prepackaged PJAC containing 30 to 200 PJAC pieces from only one donor 2 to 12 years old.[6] In an animal study in 2019, Ao et al.[6] compared the repair effect of autologous cartilage chips and PJAC on cartilage defects in 30 Guizhou minipigs and reported autologous cartilage chip was better than that of PJAC at 1 and 3 months postoperatively but demonstrated no statistical difference at 6 months. A comparative study of patients who received DeNovo NT graft for treatment of osteochondral lesions of the talus with those of patients who underwent microfracture reported postoperative functional outcomes and quality of repair on MRI were similar with no significant differences in outcome scores between the 2 groups.[7]

The use of minced or particulated cartilage chips has attracted wide attention, as it could overcome the limitations of ACI. This technique was first described by Albrecht et al.[8] in 1982 and many authors have contributed to its development in the following years.[9,10] Studies in animal models by Lu et al.[10] have shown that the use of minced cartilage without cell cultures resulted in uniform chondrocyte outgrowth by 6 weeks with formation of new extracellular matrix. The ability of cells to outgrow is characterized by their ability to deposit new extracellular matrix (ECM). These promising results are due to the ability of particulated articular chondrocytes to migrate into a biomaterial and synthesize new ECM.[11]

Researchers have looked into parameters that could influence chondrocytes to deposit extracellular matrix. The degree of chondral fragmentation is believed to be an important parameter for the amount of ECM production in vitro.[12] If the cartilage chips are too large, the surface is too small for the chondrocytes to become active. Bonasia et al.[13] reported that a paste-like appearance provides optimal circumstances for the generation of high-quality repair tissue. Levinson et al.[14] conducted an in vitro study using device-minced human cartilage, and their findings reported similar results to hand-minced cartilage, with >50% of the cells being alive enough to observe outgrowth from tissue, while providing a faster and more efficient clinical procedure.

No consensus exists on the nature of the biomaterial to be used to promote chondrocyte migration. Protein-based scaffolds, such as collagen and fibrin, serve as adhesion sites for chondrocytes to achieve fibrocartilage repair. In vivo evaluation of autologous cartilage fragments incorporated with platelet-rich plasma (PRP) scaffolds promoted not only cell migration but also served as a bioactive scaffold in promoting chondrocyte viability, proliferation, and differentiation.[15] PRP scaffold acts as a reservoir of growth factors and cytokines and is more bioactive than collagen membrane or synthetic meshes.

Platelet products have been well studied due to their intrinsic capacity to induce endogenous reparative and regenerative mechanisms when administered both in vitro and in vivo. PRP preparation augment the 3 phases of tissue healing: inflammation, cell proliferation, and remodeling. Unlike single targeted biological therapies, PRP is one of the few therapies that contains several bioactive factors that are able to induce cell migration and recovery.[16] Although treatments based on PRP have been shown to produce favorable results, there are still controversies of its clinical application. Various compositions, production methods, status of platelet activation, and administration of these factors (loaded in a scaffold or soluble in the culture medium) have been reported in literature, which can explain the variable efficiency of PRP use.[14-16] It is therefore imperative to develop a consistent method that can ensure standardized PRP preparations for expected biological responses.

This Technical Note details a single-stage particulated autologous matrix-enhanced chondral transplantation for treatment of cases with chondral and osteochondral defects (Table 1), especially grades 3 to 4 regarding the classification of the International Cartilage Repair Society (Table 2). This technique harvests cartilage tissue from the chondral defect and combines it with PRP scaffolds. PRP scaffold serves as a bioactive component to interact with embedded cartilage fragments, which induces migration, proliferation, and differentiation of chondrocytes to facilitate cartilage repair. We entitle this technique as particulated autologous chondral−PRP matrix implantation (PACI).

## Surgical Technique (With Video Illustration)

The PACI surgical technique uses particulated cartilage mixed with PRP, getting a malleable scaffold that was implanted to cover the chondral defects. The procedure is performed using a combination of arthroscopy and mini-open arthrotomy (Video 1).

**Table 1.** Indications and Contraindications for the Particulated Autologous Chondral-PRP Matrix Implantation (PACI) Technique

| Indications | Contraindications |
|---|---|
| • Younger patients, up to 40 years of age<br>• Full-thickness chondral or osteochondral defects<br>• Medium (10-15 mm) to large (>15 mm) chondral defect size with preserved cartilage<br>• International Cartilage Repair Society grades 3 to 4 lesions | • Active infection at surgical site<br>• Diffuse osteoarthritis<br>• Malalignment<br>• Morbid obesity<br>• Patient noncompliance |

PRP, platelet-rich plasma.

**Table 2.** International Cartilage Repair Society Classification for Osteochondral Lesions

| Grade | Criteria |
|---|---|
| Grade I | Stable, superficial lesions |
| Grade II | Stable on probing, partial discontinuity, <50% cartilage depth |
| Grade III | Complete discontinuity, nondislocated, >50% cartilage depth |
| Grade IV | Dislocated fragment, loose within bed or empty defect, through the subchondral bone |

Samples of healthy hyaline cartilage are harvested from defect edges using a shaver and curette, and prepared at the back table (Fig 1A). A BTI System IV (BTI Biotechnology Institute, Vitoria-Gasteiz, Spain) is used to centrifugate eight 9-mL tubes containing the patient's blood extracted before surgery. The centrifugation process lasts 8 minutes at 580*g*, obtaining the sedimentation of red and white cells at the bottom and platelets with plasma on the top part of the tubes.[17] The centrifugation process created 2 fractions: fraction 1 is the upper part of the supernatant and is the plasma poor in platelets (PPP), which is placed in BTI 9-mL, sterile-fractionation tubes; fraction 2 is the plasma rich in platelets (i.e., PRP), which is obtained by extracting the layer just over the white cells and placed in other BTI 9-mL, sterile-fractionation tubes. It is paramount to avoid aspiration of white cells when obtaining fraction 2, so that no inflammatory reaction is elicited.

Other pearls and pitfalls should be taken into account for the PACI technique (Table 3).

The growth factors are activated using $CaCl_2$ at a rate of 0.02 mL per milliliter of plasma, maintaining the tubes at room temperature. The activated PPP-PRP at a 50/50 ratio is combined with the minced hyaline cartilage chips acquired from the patient and left for 30 minutes until the semisolid CN-Biomatrix is formed (Fig 1B). The time needed to form the Biomatrix varies according to the room temperature and patients' blood. Next, the chondral defect is debrided and measured (Figs 2A and 3A), and the autologous chondral PRP scaffold is adjusted to defect size. Once the arthrotomy is performed, the autologous combined chondral PRP matrix is applied to fill in the patient's chondral defect (Fig 2B and 3, B and C). The biomatrix is evenly distributed along the defect and left in place for 5 - minutes for adequate adhesion. After setting, the knee is passively ranged under direct dry arthroscopic visualization to assess for graft adherence and stability. Next, the arthrotomy and portals are closed and the remaining of the fraction 2 was intra-articularly injected after activation with $CaCl_2$.

**Table 3.** Pearls and Pitfalls of the Particulated Autologous Chondral–PRP Matrix Implantation (PACI) Technique

| Pearls | Pitfalls |
|---|---|
| • Create a vertical rim on the cartilage defect<br>• In case of osteochondral defects use a thin layer of minced autologous bone graft before implanting the CN-Biomatrix<br>• In femoral or tibial loading areas, extend the knee to create compression once the graft has been placed | • Using minimal amount of cartilage to generate the CN-Biomatrix<br>• When obtaining the PRP fraction 2 extract the layer just over the white cells avoiding aspiration of those<br>• Wait at least 5 minutes for the Biomatrix to seal the defect and prevent early detachment |

PRP, platelet-rich plasma.

## Complications

Complications may include failure of graft incorporation, graft hypertrophy, and graft delamination as well as the standard risks usually associated with arthroscopy and arthrotomy techniques.

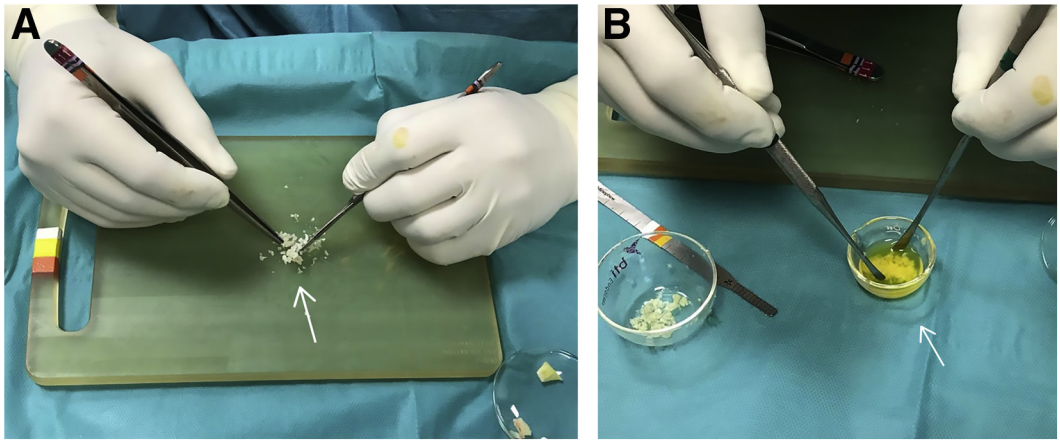


**Fig 1.** Left knee. Parapatellar open lateral approach. Patient in supine position. Preparation method of the CN-Biomatrix. (A) The healthy hyaline cartilage harvested from the edges of the defect are particulated with a blade or directly obtained with a shaver connected to an aspiration filter. (B) The platelet-rich growth factors preparation is mixed with the hyaline cartilage chips. The mixture is left at room temperature for about 30 minutes until the semisolid state is reached.

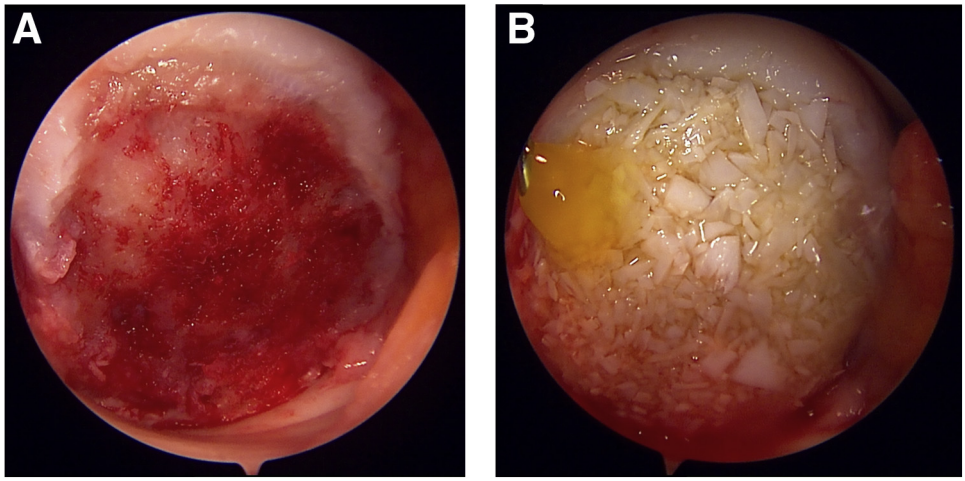


**Fig 2.** Filling of osteochondral defect using CN-Biomatrix surgical technique. (A) Dry arthroscopy view of an osteochondral defect in lateral femoral condyle after the lesion is debrided up to the subchondral bone and the edges of the surrounding cartilage are perpendicularly created. (B) Dry arthroscopy view of the osteochondral defect after it has been filled with the semisolid CN-Biomatrix preparation. Note the needle at the top of the image is used to create a film above the defect using the supernatant obtained from the platelet-rich plasma.

### Rehabilitation Protocol

Postoperatively, the patient is kept in a nonweight-bearing regimen for 4 weeks, followed by a transition to full weight-bearing at approximatively 6 to 8 weeks. Gentle passive flexion−extension exercises are conducted once a day to avoid stiffness for 1 week, progressing to twice a day for the following 2 weeks. Aquatic-based exercises are allowed as soon as skin incisions are healed. Stationary bicycle is typically allowed after 2 to 3 months, running at 4 to 5 months, and return-to-sports no earlier than 7 months, depending on the type of sport, injury, characteristics, and status of the patient.

## Discussion

This current surgical Technical Note details the use of PACI for chondral and osteochondral defects. This method is different from other studies in cartilage repair because it relies on the ability of particulate cartilage to migrate and deposit newly synthesized ECM and the use of bioactive processes of PRP scaffold to attract and nourish chondrocytes via growth factors.

Cugat et al.[15] published first 2 cases of full-thickness knee cartilage injuries treated with CN-Biomatrix, an autologous-made scaffold consisting of hyaline cartilage chips combined with a clot of mixed platelet-rich growth factors in a semisolid state. They reported successful outcomes with excellent knee function, pain relief, and return to high-level soccer at preinjury level, and follow-up MRI showed adequate filling of the defect and absence of significant bone edema. The same group confirmed the clinical, functional, and MRI-based based (cartilage repair quality and quantity) outcomes in a first clinical study on 15 patients using PACI.[2] A histologic and immunohistochemical study of this technique on sheep by Dominguez-Perez et al.[17] demonstrated at 6 months nearly normal hyaline cartilage, consisting of 75% type II collagen and 8% type I collagen. The original technique used in animal studies led to a too rigid matrix that could not be easily

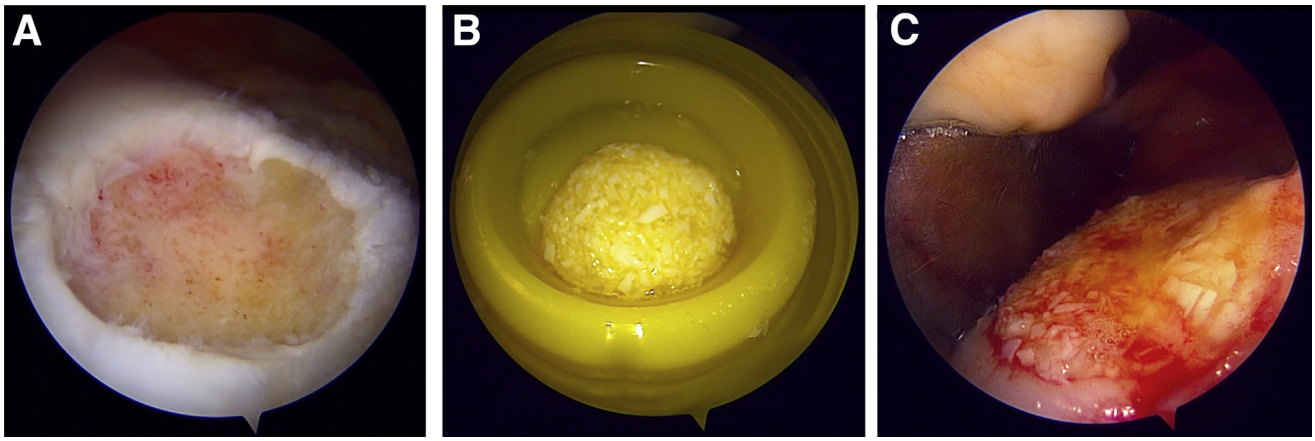


**Fig 3.** Right knee. Parapatellar open lateral approach. Patient in supine position. (A) Dry arthroscopy view of an osteochondral defect in trochlea after debridement (B) Demonstration of the semisolid CN-Biomatrix state before the intra-articular placement using a mini-arthrotomy. (C) Dry arthroscopy view of the filled osteochondral defect once the CN-Biomatrix has been placed.

adapted to chondral defects and reached a semisolid state quicker. The modified and improved technique has been used in Cugat et al.[2,15] case reports and studies. A study by Delman et al.[11] reported promising initial results using PACI technique in 8 patients with acute osteochondral lesion of talus. The postoperative imaging of a 15-year-old female patient showed graft incorporation, resolution of bony edema, and restoration of articular contour. Sullivan et al.[18] reported the use of a similar autologous cartilage technique in a professional rugby player with return to play at 23 weeks postoperatively and imaging at 16 months showing subchondral plate restoration.

The MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) scoring system remains the most accepted standardized method for postoperative evaluation of cartilage repair with MRI. Recent studies used a MOCART scoring system and reported average MOCART scores of 59.5 ± 17.2 points and 64 ± 14 points.[19,20] Cugat et al.[2] reported a mean MOCART score of 70 (a score of 100 represents completely healthy cartilage) at 12 months using PACI technique , which was greater when compared with microfracture and collagen membrane matrix, microfracture, and chitosan-based polymer scaffolding biomaterial, mesenchymal stem cells, and cell-free scaffold with collagen and hydroxyapatite.[21-23] Massen et al.[9] reported a mean MOCART score of 40.6 ± 21.1 at 6 months, and similar results were reported by Christensen et al.[24] observed a MOCART score of 52.5 at 1 year after a particulate cartilage procedure, and Niemeyer et al.[25] observed a long-term (follow-up of 10.9 years) MOCART score of 44.9 ± 23.6 after first-generation ACI.

Christensen et al.[24] used a different technique of application of platelet-rich growth factors, suggesting the application of growth factors may make a significant difference in the quality of the cartilage repair tissue. Trattnig et al.[26] reported greater MOCART scores at 24 months (84.4) after applying a cell-free biosynthetic, biodegradable hydrogel implant. It is important to note that cartilage repair process is a lengthy process (>2 years) to generate the final tissue morphology and that MOCART score continuously improves over time. This is supported by studies showing a lower MOCART score at 6 months to 1 year postoperatively as compared with follow-up at 2 years.

We have been applying PACI in more than 150 active patients with full chondral defects for approximatively 5 years. We have encountered good clinical, functional, and MRI-based outcomes. This procedure is performed as a single-stage procedure, is safe and cost effective, and has shown histologic and immunohistochemical similarity to healthy articulate cartilage in previous and ongoing animal studies.[11] Osteochondral injuries also can be treated applying the same technique and concepts, combining cancelled bone, PRP matrix and chondral matrix as it was the case for these osteochondritis dissecans lesions in the medial talus.

The clinical outcomes of the patients after treatment with the autologous particulate cartilage procedure are comparable with published results after ACI.[25,27,28] The advantage of PACI is that it can be applied as a one-stage procedure and is a more economical option when compared with ACI. Our technique allows for harvesting donor cartilage from the edge of existing lesion during debridement, and since the cartilage chips expand and create extracellular matrix, it is possible to treat large lesions without increasing the donor site morbidity. The PACI technique may be suited for younger patients, up to the age of 40 years, given that juvenile chondrocytes sustain their reparative potential and retain intrinsic mechanical and structural properties of hyaline cartilage.

A limitation to the published studies is the short clinical follow-up and the results are not entirely comparable with those of previous studies on ACI or microfracture with long-term follow-up of more than 10 years.[27] The goal of our study is to present a safe, efficient, low-cost alternative to ACI and other cartilage repair techniques. Our intention is to analyze and describe the outcomes of patients who underwent this surgical procedure. Another limitation to our study is the potential variation of PRP content existing among different preparations. Platelet content and growth factor concentrations, which vary among individuals, may influence therapeutic effects and is an inevitable limitation in using platelet derivatives. It is imperative that future clinical research be conducted in a more standardized manner, minimizing study-to-study variability and ensuring a reproducible methodology.

The risks of this technique include failure of graft to incorporate, necessitating a second cartilage operation, being a technically challenging procedure, and increased operative time.

In conclusion, PACI is a safe and efficient surgical procedure in young, active individuals with full-thickness cartilage or osteochondral defects. It could represent an alternative to ACI or other cartilage repair options. Nevertheless, longer follow-up and comparative trials are needed to further provide evidence and potentially enlarge the scope of application of PACI.

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