Treatment of Articular Cartilage Lesions Using Two Polymer Scaffolds

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The challenge of the chondral lesions treatment has been considerably answered with the development of non-cellular scaffolds. Among the most frequently used, the scaffolds based on Hyaluronic Acid and, respectively, collagen derived polymers are the subject of our comparative research. The present paper highlights some particularities related to their intrinsic physical properties such as adhesiveness, microstructure and cellular permeability and concludes that the two alternatives present qualitatively similar outcome and effectiveness.

Keyword: hyaluronic acid polymer scaffold, collagen scaffold, chondral lesions, osteoarthritis

The articular cartilage damage (fig. 1) represents an important challenge for both the patient and the orthopaedic surgeon. On one hand, the patient has to cope with aggravating symptoms like pain and impelled physical activity. On the other hand, the surgeon confronts with the limited healing capacity of avascular articular cartilage [1-4].

Among the various treatments, one of the most frequently applied has been the procedure of microfracture surgery, which involves creating 3-4 mm deep micro-holes throughout the damaged cartilage (3-4 microfractures per squared cm). The therapeutically induced bleeding of the subchondral bone spontaneously activates the healing process as the later blood clot formation generates the development of a fibrous type of cartilage tissue, whose properties remain, yet, qualitatively inferior to the articular cartilage [5-9].

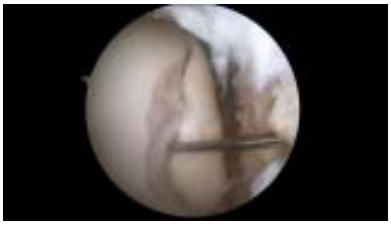

Fig. 1. Chondral lesion on femoral condyle

Another alternative treatment is the in-vitro cultivation of condrocyte cells that can later be reimplanted into the patient. Unfortunately, the growing medium allows only one-layer cell reproduction, which may render a small part of the native tissue complexity. Moreover these cells shortly lose the capacity to secrete key specific extracellular matrix components, such as aggrecan, decorin, bigylcan and fibromodulin, collagen types II, IX, XI, cartilage oligometric matrix protein (COMP), etc. After several days in the culture medium, the condrocytes become functionally similar to fibroblasts [10].

In response to the above mentioned disadvantages, another procedure has been developed, the Matrix-assisted Autologous Chondrocyte Transplantation (MACT). It provides a tridimensional matrix as a culture medium for chondral cells drawn from the patient. After three days, these would be reimplanted at the damaged cartilage site. Yet, despite encouraging results acknowledged in many experimental studies [11](current and future), the costs associated with cell culture, the treatment in two-stages and the morbidity following culture cell extraction have rendered this procedure not very popular (current and future).

Therefore, the development of an effective non-cellular tridimensional matrix has become timely. It needed to be concurrently biocompatible, non-cytotoxic, resorbable, elastic and porous in order to allow cellular proliferation. It also should support the adhesion and migration of cells, to present volume stability and structural anisotropy.

The main advantage of a scaffold implantation is that chondrocytes migrate and form a cartilage similar in structure and form with normal cartilage, as opposed to the cartilage that appears after microfractures that has a fibrous structure.

Experimental part

In our research, we used two types of scaffolds for chondral lesion treatment, Condro-Guide® (produced by Geistlich Biometrials, Switzerland) and, respectively, Hyalofast® (produced by Fidia Advanced Biopolymers, Abano Terme, Italy) which partially meet the above mentioned requirements.

Condro-Guide® is a double layered membrane formed of collagen type II and III extracted from pig tissue. The two layers present different consistency. The lower bed is relatively lax and porous, allowing the chondral cells to penetrate, settle on the matrix fibers and proliferate. The collagen matrix spurs the chondrocytes to secrete type II collagen and glycosaminoglycans. The outer layer, in direct contact with the synovial liquid, presents higher density and a smooth surface. Its functions refer to mechanical resistence, to the obstruction of the exit of inward chondral cells [12,13], as well as to averting the inflow of exterior fibroblastic and sinoviocite cells that would convert the

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healing process into a fibrous one. Both layers are resorbed within 6 -24 weeks [14].

The Hyalofast® scaffold is a semisynthetic derivative of hyaluronic acid, esterified with benzyl alcohol whose sulfonate form has a molecular weight of approx. 200kDa. A very important attribute of the hyaluronic acid is that it stimulates the chondrocyte differentiation pathway for the mesenchymal stem cells. The final product is a non-cross-linked linear water insoluble polymer developed into two forms [15]: sodium hyaluronat benzyl ester and sulfonat-hyaluronat benzyl ester. The tridimensional structure is formed of 10-15μm thick fibres at 40μm away from each other, ensuring enough space in between them, necessary for the formation of cell clusters and for the storage of fibrotic material that eventually would be part of the extracellular matrix [16, 17].

Methods and materials

Our research was performed on a lot of 40 subjects with damaged articular cartilage that were treated in our clinic between 2011-2013. The average age was 31. The inclusion criteria were:

- chondral lesions larger than 1squared cm;
- stable knee;
- good axial alignment;
- if present, meniscal lesions were arthroscopically treated , concurrently with the cartilage lesion.

The surgical technique involves a first stage of preparing the affected area, through detaching all injured cartilage and rendering a relatively oval shaped area with healthy walls perpendicular to the bone tissue (fig. 2a). The underneath bone is also carefully debrided of all cartilage residue (fig. 2b). In the next phase, we made the microfractures that penetrate the subchondral bone (fig. 2c). The newly formed defect is covered with a scaffold film– either Chondro-Guide® or Hyalofast® (fig. 3) – perfectly fitting the area and submerged for several minutes into Ringer solution. Aftewards, in case of Chondro-Guide® the sides of the scaffold are attached to the cartilaginous tissue through suturing or sealing with a fibrin glues.(fig. 2c, 2d).

The lesions were treated arthroscopically, except for the retropatellar lesions which were treated through medial parapatellar arthrotomy.

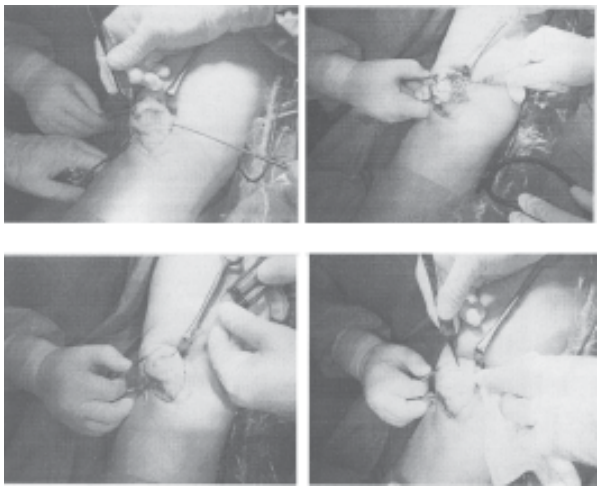


Fig. 2. Images of Chondo-Guide® implantation on Patella

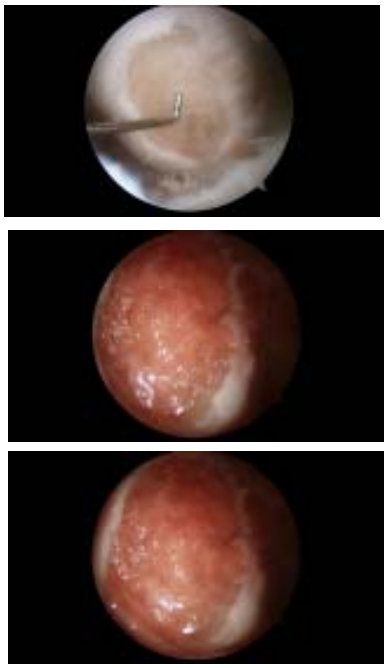


Fig. 3 Hyalofast implantation on femoral condyle

Results and discussion

27 of the subjects were treated with Condro-Guide® scaffold, while in 13 of the 40 interventions we used Hyalofast®. The summary of the interventions are displayed in the table below.

One year postoperatively, only 3 of 40 subjects presented pain, the others were asymptomatic and the average time for pain receding was about 7 weeks for both products. The patients that still accused pain – two treated with Condro-Guide® and one with Hyalofast® - had Visual Analogue Scale for pain (VAS) scores of 4 and 5 and Knee injury and Osteoarthritis Outcome Score for pain (KOOS for pain) with values between 34-70. The 1 year post operative MRI also showed satisfactory integration of the scaffolds.

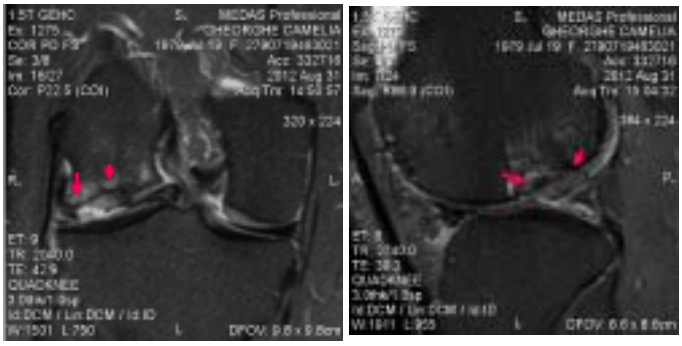
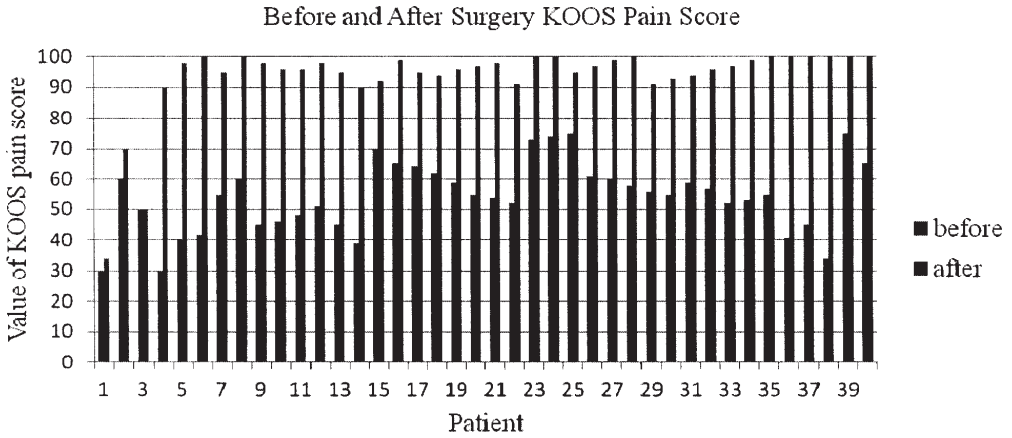


Fig. 4. Image of chondra; lesion on internal femurral condyle

Lesion	No of patients	The average affected area	Condro-Guide® ®	Hyalofast® ®
External femoral condyle	2	1.8cm^2	2	0
Internal femoral condyle	9	2.4 cm^2	6	3
External tibial plateau	3	1.9 cm^2	2	1
Internal tibial plateau	11	2.7 cm^2	6	5
Patella	15	2.8 cm^2	11	4

Table 1
SUMMARY OF PATIENTS AND LESIONS

At the last follow-up, the knee mobility was normal for all subjects, irrespective of scaffold type, with a recovery period of 6 months, on average. 85% of the patients were able to return to intensive physical activity one year after surgery. There have been reported no adverse reactions to the matrix implant nor failures. Two cases of superficial infections existed, both in patients with chondral lesions on the patella, they were successfully treated with antibiotics.



The main objective of this study was to identify and analyze important particularities of the two types of scaffold, emphasizing some practical aspects of their utilization. Overall, our research presents similar qualitative results for both scaffolds, thus lining up with the findings of other studies in the literature.

A 7 years postoperative study performed by Filardo G. et al [18] on 62 subjects treated with Hyalofast®, showed improvement of IKDC score (International Knee Documentation Committee) and a failure rate of only 11%.

Also, in a study published in 2013, Sven Andres et al. [19] noticed, after a randomized control trial, a significant improvement of the symptomatology for the subjects treated with Chondro-Guide®. Also they observed that using Fibrin Glue in the fixation of the scaffold improves chondrogenesis when compared to suture fixation. Fibrin glue plays two important roles: to bond the Chondro-Guide® film to the edges of the cartilaginous tissue and to seal the boundaries, blocking the entrance of fibroblasts and sinoviocites that may shift the differentiation pathway from chondrocytes towards fibroblasts, altering the healing process.

As mentioned before, collagen type I as well as hyaluronic acid fibers stimulate the migration and proliferation of chondrocytes. Yet, the Hyaluronic Acid presents additional adhesive attributes that allow its utilization without supplementary glue that the collagen matrix requires. Therefore, we would emphasize that the intervention time and cost are lower in case of Hyaluronic Acid based scaffold, as compared to collagen scaffold. The authors also notice the difficulties encountered when using any of the scaffolds in arthroscopic treatment of retropatellar chondropathy, as the procedure requires parapatellar open approach that increases the risk of infection.

With respect to the level of porosity, we refer to a study [20] that aimed at assessing the impact of the pore dimension on the chondrocyte proliferation by using the same scaffold of poly e-caprolactone with pores of different sizes (100, 200, 300 and respectively 400 μm). The authors argued that the 200 and 400 μm pores seemed the most appropriate for cartilage regeneration.

The chondrocytes are small cells (5-15μm). It has been noticed [21] that, when entering a 200-400 μm wide space, they tend to form colonies and then secrete substances specific to the chondral matrix. Nevertheless, when entering a space smaller than 100 μm, there is a tendency for the chondrocytes to incapsulate and become functionally inactive. Hyalofast® producers specified an aprox. 40 μm porosity. Yet, our clinic and MRI results suggest a satisfactory integration of the scaffold, requiring, in our opinion, further research on the topic. To our knowledge, there are no values published for the Condro-Guide® scaffold porosity.

Conclusions

It seems that, at present time, non-cellular scaffolds – either of collagen or hyaluronic acid fibers – remain the best alternative for the chondral lesion treatment, as they avoid the aforementioned risks and disadvantages associated to autologous grafting. The scaffolds present similar qualitative results. Yet, from the surgeons point of view, an alternative form of a gel structure instead of film, with adhesive properties would considerably facilitate the scaffold application.

Given the short follow-up, the relevance of our conclusions is somewhat limited. The paper presents only partial and intermediary results of an on-going comparative study that involves gathering follow-up information for 7-10 years after intervention.

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