

New approaches to the treatment of articular cartilage lesions

M. Coviello*, L. Biglieni, M. Fiore, L. Felli

Orthopedic Department, University of Genoa, Largo Rosanna Benzi 10, Padiglione 40, 16132 Genoa, Italy

* coviellomatteo@hotmail.com

KEY WORDS: biomaterial, cartilage, scaffold.

Abstract

Various approaches to the treatment of cartilage defects have been proposed in the literature; reparative and regenerative methods and, more recently, the Maioregen technique are currently available.

Introduction

Articular cartilage has a limited regenerative capacity and cartilage lesions constitute the first stage of osteoarthritis [1]. In the last few decades, numerous *in vivo* and *in vitro* studies have been conducted on the intrinsic features and behavior of the chondrocytes [2,3]. Today, however, novel solutions for the restoration of the physiological micro-architecture of the articular cartilage are emerging in the field of tissue engineering. The aim of the present study was to evaluate the most accredited options currently available for the treatment of cartilage lesions. In addition, we present a project for the implantation of a three-dimensional multilayer scaffold that mimics the entire osteo-cartilaginous anatomical unit.

Materials and methods

A) *Reparative techniques*: the most widely used method is that of micro-fractures, which lead to the formation of a fibro-cartilaginous tissue; the mechanical capabilities of this tissue are markedly inferior to those of the articular hyaline cartilage.

B) *Regenerative techniques*: osteochondral grafts and mosaicoplasty can restore the cartilage of normal tissues; however, their application is limited to minor defects and the problem of the donor site is not negligible. Autologous chondrocyte implantation (ACI) according to Peterson is another regenerative treatment modality; although it yields good long-term results, it is undoubtedly difficult to perform. The creation of new scaffolds has led to the development

of second-generation ACI techniques (Hyalograft and MACI); despite the encouraging early results, however, literature appraisals of these techniques have not been unanimously positive. A new technology (Maioregen) aimed at regenerating the entire osteo-cartilaginous articular surface has now been proposed; this treats the cartilage as part of an anatomical-functional unit and not merely as a surface lining.

The osteochondral nanostructured biomimetic scaffold has a porous three-dimensional tri-layer composite structure. The cartilaginous layer, consisting of type I collagen, has a smooth surface which facilitates joint flow. The intermediate layer (tidemark-like) consists of a combination of type I collagen (60%) and hydroxyapatite (HA) (40%), whereas the lower layer consists of a mineralized blend of type I collagen (30%) and HA (70%), thus reproducing the sub-chondral bone layer. The upper non-mineralized chondral layer is of type I collagen and the intermediate and lower layers are obtained by nucleating bone-like nanostructured non-stoichiometric HA into self-assembling collagen fibers, as occurs in the biological process of neo-ossification. The final construct is obtained by physically combining the layers on a Mylar sheet and finally freeze-drying and gamma sterilizing them.

Results

The Maioregen technique has yielded preliminary results. In a pilot study [4] a total of 15 cartilage lesions of the knee were treated in 13 patients. The lesions varied in size from 1.5 cm² to 5.9 cm², with a mean of 2.8 cm²; the locations were: 4 medial femoral condyle, 2 lateral femoral condyle, 5 patella and 4 trochlea. Five and 25 weeks after surgery, integration of the scaffold was evaluated by means of MRI. After six months, two "second-look" biopsies were performed. Complete integration of the scaffold and restoration of the cartilaginous tissue were observed in 13 of the 15 lesions (86.7%). Partial detachment of the scaffold occurred in two patients (13.3%). Histological analysis of the second-look biopsies showed the formation of subchondral bone and cartilaginous tissue and absence of the scaffold, which had been completely biodegraded.

Discussion

The techniques used so far have not completely satisfied the needs of cartilaginous reconstruction, in that none of them leads to the complete reconstitution of the articular hyaline cartilage. This is especially true of extensive osteochondral defects, in which the support of the subchondral bone is lacking. The advantage of the Maioregen technique lies in its ability to treat large osteochondral defects in their entirety. Its disadvantages lie in the fact that it is an exclusively arthrotomic technique which requires a long postoperative course, the resumption of sporting activity being possible after about 10 months.

References

- [1] Davies-Tuck M.L., Wluka A.E., Wang Y., English D.R., Giles G.G., Cicuttini F. 2009. The natural history of bone marrow lesions in community-based adults with no clinical knee osteoarthritis. *Ann. Rheum. Dis.*, 68(6): 904-908.
- [2] Hattori S., Oxford C., Reddi A.H. 2007. Identification of superficial zone articular chondrocyte stem/progenitor cells. *Biochem. Biophys. Res. Commun.*, 22, 358(1): 99-103.
- [3] Gratz K.R., Wong V.W., Chen A.C., Fortier L.A., Nixon A.J., Sah R.L. 2004. Biomechanical assessment of tissue retrieved after in vivo cartilage defect repair: tensile modulus of repair tissue and integration with host cartilage. *J. Biomech.*, 39(1):138-46.
- [4] Kon E., Delcogliano M., Filardo G., Pressato D., Busacca M., Grigolo B., Desando G., Marcacci M. 2009. A novel nano-composite multi-layered biomaterial for treatment of osteochondral lesions: technique note and an early stability pilot clinical trial. *Injury*, 41(7): 778-786.