Introduction: The natural repair process of osteochondral defects can be enhanced through the use of biocompatible, biodegradable materials to serve as scaffolding for the regeneration process. These materials provide structural and mechanical support for the reparative activity of mesenchymal progenitor cells recruited into the damaged area, presumably from the underlying bone marrow. The failure or success of the reparative process can be determined by the rate of acquisition of mechanical stability in the damaged area through synthesis of extracellular matrix by the cells recruited into the defect. We hypothesize that impregnation of the implant material with autologous bone marrow at the time of surgery will provide additional progenitor cells and/or bioactive factors required for the regeneration process. This addition of bone marrow is thought to accelerate the sequence of events that occur in the initial stages of the healing response and, therefore, was expected to improve the quality of the repair.

Methods: Following an IACUC-approved protocol, 27 four month-old rabbits received bilateral, 3-mm diameter x 3-mm deep osteochondral defects on the medial femoral condyle. Defects on one knee were filled with ACP™ sponge, a hyaluronic acid-based polymer generously provided by Fidia Advanced Biopolymers srl (Abano Terme, Italy), and the contralateral defects received ACP™ sponge loaded with fresh autologous bone marrow aspirated from the proximal tibia during the same surgical procedure. Both treatment groups were matched in every animal. Rabbits were sacrificed at 4, 12 and 24 weeks after surgery. The condyles were fixed in formalin, decalcified, embedded in paraffin, cut and stained with Toluidine blue or Safranin O for histologic evaluation. All defects were scored with a semi-quantitative twenty-nine point scale. Scores were compared with a Wilcoxon signed rank test.

Results: Four weeks after surgery, the repair tissue found in defects treated with ACP™ sponge did not fill the defect area up to the level of the surrounding cartilage. Most of the defects presented new bone filling the defect with a layer of hyaline cartilage on top that integrated well with the adjacent cartilage. In some cases, hypertrophic cartilage was present at the interface between the bone and the hyaline cartilage (Figure 1A). The defects treated with bone marrow-loaded sponges presented a very similar appearance to those of the control group (Figure 1D).

Discussion: The early sequence of events that take place in the repair of an osteochondral defect has not been studied in depth. In very young animals complete regeneration can be observed; older animals do not exhibit this regenerative capacity. The partial ability of osteochondral defects for self-repair in young adults indicates the presence of natural mechanisms that respond to the injury. Mesenchymal progenitor cells present in the bone marrow are believed to migrate into the defect and differentiate to provide a repair tissue. The introduction of a hyaluronic acid-based polymer to serve as scaffolding for the regeneration process improves both short-term and medium-term outcome of this natural healing response.

ACP™ sponge is a polymer of cross-linked hyaluronic acid obtained by condensation. This polymer is hydrophilic and expands when hydrated. These physical characteristics account for a rapid infiltration of the implant with bone marrow even in the control defects, which may partially explain the lack of significant differences between the groups. It is noteworthy that the quality of the repair tissue does not decrease with time up to 24 weeks after surgery. Both the overall appearance of the defects and the values of the histologic scores remained unchanged between 12 and 24 weeks.

The results presented here indicate that impregnation of this polymer with autologous bone marrow, prior to its implantation into an osteochondral defect, may contribute to the improvement of the quality of the repair tissue since, although not at significant levels, the defects treated with bone marrow-loaded implants consistently presented slightly higher scores than those treated with the ACP™ sponge alone. The small differences found in this study may also be due to the age of the animals. Four-month-old rabbits are still relatively young with a very active bone marrow. The effect of pre-loading of these implants with fresh autologous bone marrow may be more significant in more mature animals.

We are currently conducting a new series of experiments to analyze the regeneration of osteochondral defects in mature rabbits when treated with hyaluronic acid-based delivery vehicles loaded or not with autologous bone marrow.

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References:

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