Introduction: The natural repair process of osteochondral defects can be enhanced through the use of biodegradable, biocompatible polymers that serve as a scaffolding for the regenerative process. These polymers 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 rapid acquisition of mechanical stability in the damaged area by synthesis of extracellular matrix by the cells recruited into the defect is one of the early events that can determine the failure or success of the reparative process. We hypothesize that the impregnation of the implant material with autologous bone marrow at surgery will provide the progenitor cells and/or bioactive factors required for the regeneration process; this addition of whole 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 overall quality of the repair process.

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

Results: Both types of implants stayed in the defects as revealed by the presence of a non-calcified layer that was slightly thicker in the ACP™ sponge + bone marrow-treated defects, and it also exhibited a staining pattern more similar to that of the adjacent normal cartilage. The integration of the regenerative tissue with the surrounding normal cartilage was also superior in the the ACP™ sponge + bone marrow-treated group.

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 with small defects, complete regeneration can be observed, older animals do not exhibit this regeneration capacity. The partial ability of osteochondral defects for self-repair in young adults indicates the presence of natural mechanisms that respond to the damage. Mesenchymal progenitor cells present in the bone marrow are believed to enter the defect and differentiate into bone endochondrally in the natural repair process. The introduction of a hyaluronic acid-based polymer that serves as scaffolding for the regeneration process improves the outcome, both short-term and medium-term, 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 characteristics account for a rapid infiltration of the implant with bone marrow in the control group and allows complete saturation of the implant loaded with autologous bone marrow. The results presented here indicate that the impregnation of these polymers with autologous bone marrow, prior to their implantation in an osteochondral defect, may contribute to the improvement of the quality of the repair tissue.

A composite implant (carrier + bone marrow) presents several advantages over the carrier alone. With the marrow already present in the implant, there is not a delay in the response due to the time required for the reparative cells to migrate into and populate the polymer. The cytokines and growth factors present in the marrow-impregnated implant may act as chemotactant agents for the reparative cells as well as to regulate and to produce their differentiation into the appropriate phenotypes. At the minimum, the HA carrier insures that the healing response is more homogeneous throughout the volume of the implant, independent of the accessibility to the bone marrow in different areas of the defect.

The small differences found may be due, in part, to the small sample size of this study as well as to the nature of the material used as carrier for the marrow. Further work is in progress to increase the sample size and to elucidate the contribution of the impregnation of this unique tissue engineering material with bone marrow and study the long-term outcome of osteochondral defects treated with these composites.

References:

Table I. Histologic scoring system used to grade the specimens

<table>
<thead>
<tr>
<th>Group</th>
<th>Score</th>
<th>n</th>
<th>Score</th>
<th>n</th>
</tr>
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<tbody>
<tr>
<td>ACP</td>
<td>16.3 ± 7.12</td>
<td>6</td>
<td>19.8 ± 3.54</td>
<td>6</td>
</tr>
<tr>
<td>ACP + BM</td>
<td>20.2 ± 5.19</td>
<td>6</td>
<td>21.2 ± 6.0</td>
<td>6</td>
</tr>
</tbody>
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Figure 1. Histologic appearance of an ACP™ sponge-treated defect (A) and 12 (B) weeks after surgery, Toluidine Blue staining.

Figure 2. Histologic appearance of an ACP™ sponge + bone marrow-treated defect (A) and 12 (B) weeks after surgery, Toluidine Blue staining.

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