EFFICACY OF BONE MORPHOGENIC PROTEIN-2 TO PROMOTE GAP FILLING AND INGROWTH ACROSS THE GAP IN A CANINE TOTAL HIP REPLACEMENT MODEL

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Introduction: The capacity to augment bony ingrowth in the fixation of porous total joint replacement components would be of great value. Even in instances in which clinical success is achieved with porous coated implants used in total joint replacements, the extent of the bony ingrowth may be marginal, particularly in revision operations. The recent advances in molecular biology techniques using proteins, which stimulate bone growth such as TGF beta introduced locally into the surgical site, have shown enhanced bone ingrowth into non-loaded porous implants in dogs. BMP-2 made by recombinant techniques by Genetics Institute also has the demonstrated capacity to stimulate bone growth. This material has been intensively studied in many animal experiments and has been shown to form bone in the subcutaneous tissue and across large segmental bone defects leading to union. In this study, we evaluated the capacity of this BMP-2 to enhance bone ingrowth into the porous coated canine total hip replacement implants both with a) intimate contact with adjacent bone and b) across a gap between the porous coating and surrounding bone by using BMP-2 in conjunction with two types of delivery carriers.

Materials and Methods: Institutional approval was received to perform this study using twenty-one adult male hunting hounds, which received right total hip replacements using a 29mm titanium acetabular component with a beaded porous surface fixed to the pelvis initially using four screws through the shell. A polyethylene insert with a 16mm I.D. served as the articulating surface. The titanium femoral component consisted of a straight, proximally porous coated collared component having a proximal medial/lateral flare. The diameter of the cylindrical, non-porous coated distal stem was 10mm. A hemispherical gap 1 mm in length was created external to the cup using a specially fabricated reamer. Ten dogs received acetabular implants coated with a thin layer of hydroxyapatite; in five of these there was no added BMP. Three animals received acetabular components with “thin coat” plus 200 µg of BMP-2, and two received acetabular components with “thin coat” plus 200µg of BMP-2 dried onto the surface. In five others the gap and the porous region were filled with a calcium phosphate paste and 200µg of BMP-2 mixed throughout the material, called BSM/BMP-2. In addition, in this group the BSM/BMP-2 material was applied as a paste to the superior lateral region of the acetabular component which remained exposed, i.e., not covered by bone. Finally, six animals received standard implants without creation of a gap and without carrier or biologically active agent to serve as controls.

All animals were radiographed prior to surgery and at 2 weeks, 6 weeks, 12 weeks, and 24 weeks postoperatively. The animals were euthanized at 24 weeks postoperatively. The right acetabular and femoral heads were harvested. Contact radiographs were obtained in several views of the explanted constructs.

All specimens were dehydrated in alcohol, embedded in methylmethacrylate, and serially sectioned using a water-cooled diamond wheel. Contact radiographs were obtained of all sections. All acetabular sections were gold coated for SEM analysis with a backscatter detector. Bone ingrowth into the porous surface was quantified from contiguous fields at a magnification of 30X using an imaging analysis system. The sections were divided into regions of the gap and regions of intimate bone contact. Bone ingrowth was reported as an average percentage of the total area of the porous layer occupied by new bone (area fraction) and as a percentage of the void space within the porous layer.

Results: All animals recovered from surgery and ambulated well, except one with deep sepsis in the BSM group. This animal was excluded.

Examination of the contact radiographs of the explanted constructs revealed extensive filling of the gaps with new bone in the BSM/BMP-2 treated constructs. The gaps were completely bridged with cancellous bone. In contrast, the thin coat and thin coat/BMP-2 treated components showed less trabecular bone bridging the gap.

Table 1- Bone Ingrowth Values for Each Group

<table>
<thead>
<tr>
<th>Gap Region</th>
<th>Non-Gap</th>
<th>Gap Region</th>
<th>Non-Gap</th>
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<tbody>
<tr>
<td>Area Fraction of Bone Ingrowth</td>
<td></td>
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<tr>
<td>Thin Coat/ 80 µg</td>
<td>2.5 ± 1</td>
<td>5.8 ± 0.7</td>
<td>6.3 ± 2.4</td>
</tr>
<tr>
<td>Thin Coat/ 200 µg</td>
<td>5.5 ± 3.4</td>
<td>7.3 ± 0.4</td>
<td>12.2 ± 8.3</td>
</tr>
<tr>
<td>BSM/ 200 µg</td>
<td>7.0 ± 3.4</td>
<td>8.5 ± 3.0</td>
<td>17.8 ± 8.3</td>
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The average amount of bone ingrowth into the porous layer of each group is listed in Table 1. While average bone ingrowth into the porous surface under the gap region of the implants receiving thin coat alone was only 2.2% and with the thin coat plus 80 µg BMP-2 was about 2.5%, bone ingrowth under the gap region of the thin coat and 200 µg BMP-2 measured 5.5%. In contrast, the porous region under the gap in dogs which received the BSM/BMP-2, averaged 7.0% bone ingrowth. This was similar to the amount of bone ingrowth achieved in the areas of the porous surface in direct contact with the host bone.

Histology confirmed these findings. The sections from the BSM/BMP-2 treated implants showed intra-trabecular new bone formation distant from the implant interface, robust bone formation within the gap region, bone surrounding remnants of the carrier, and extensive bone formation throughout the porous surface. In addition, new bone formation had replaced the BSM/BMP-2 material in the superior lateral, exposed region of the acetabular component and had fused to the existing surrounding bone, Figure 1.

Figure 1-Contact Section X-Rays Showing Lack of Gap Filling With the Thin Coat and Complete Gap Filling With the BSM/200 µg BMP-2

Conclusion: For the first time, this study has demonstrated the ability of a biological agent to promote bone bridging of a periprosthetic gap plus bone ingrowth into the porous surface adjacent to the gap in a weight bearing implant. The efficacy of BMP-2 to promote bone formation in this THR model appears to be dependent on both the total applied dose and the release kinetics of the carrier.

Although the amount of bone ingrowth in those regions of intimate host bone contact at 12 weeks was not higher than the control animals using this porous implant without a biologically active agent, a shorter duration study is required to determine if this agent increases the rate of bone formation within the porous surface in areas of intimate contact.

1. ETEx Corp. Boston, Massachusetts