INTRODUCTION:
The number of spinal fusion operations has increased tremendously during the last decennium. In current practice, cages of various designs and materials are used to provide stability and to maintain segment height until bony fusion is formed. The use of autologous bone for grafting material inside the cages is regarded as the golden standard. Autologous bone graft is generally taken from the iliac crest. However, disadvantages are pain, donor site morbidity, and the risk of infection at the donor site. Within the last few years, bone morphogenetic proteins (BMPs) have been introduced in spinal fusion surgery to stimulate bone healing. BMPs are a family of proteins regulating cartilage and bone formation. Recombinant human BMP-7, also known as osteogenic protein 1 (OP-1) has been proven safe and efficacious in bone healing procedures. Without the use of interbody cages, rhOP-1 was shown to improve spinal fusion in dogs and sheep.

In this study we address the question if rhOP-1 delivered via a carrier biomaterial (OPCMC device) is a suitable alternative grafting material for spinal fusion. Lumbar spinal fusion using bioresorbable PLLA cages were performed in a goat model. The use of autologous bone graft was compared with the OPCMC device. The carrier material consisted of bovine-derived type I collagen, stabilized with the water soluble, non-toxic polymer carboxymethylcellulose (CMC). The OPCMC device was shown previously to improve bone healing in critical sized bone defects.

METHODS:
The study was performed in compliance with the regulations of the Dutch legislation for animal research and approved by the University Animal Ethics Committee. Interbody fusions were performed at L3-L4 level in 17 skeletally mature Dutch milk goats. Custom made resorbable PLLA cages (Stryker Orthopedics) were implanted as stand alone cages. In ten goats the cage was filled with autologous bone graft from the iliac crest. In seven goats, cages were filled with 1.1-1.4 cc of the OPCMC putty. The putty consisted of 3.5 mg rhOP-1, 1 g bovine bone-derived Type I collagen and 200 mg carboxymethylcellulose (CMC). The components were mixed by adding saline (2 cc) according to the manufacturer’s instructions (Stryker Biotech). The goats were sacrificed after three or six months. Radiographical and histological analyses were performed on the retrieved segments.

RESULTS:
Radiographs were evaluated according to a validated 3-point radiographic score. The results are summarized in Table 1.

Table 1: Analysis of fusion using a radiographic score

<table>
<thead>
<tr>
<th>Graft material</th>
<th>Follow up (months)</th>
<th>no bone ingrowth</th>
<th>bone ingrowth, no fusion</th>
<th>fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autograft</td>
<td>3</td>
<td>5/5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autograft</td>
<td>6</td>
<td>1/5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPCMC</td>
<td>3</td>
<td>2/3</td>
<td>1/3</td>
<td></td>
</tr>
<tr>
<td>OPCMC</td>
<td>6</td>
<td>2/4</td>
<td>2/4</td>
<td></td>
</tr>
</tbody>
</table>

Histological evaluation showed creeping substitution of the bone graft in the autograft specimens at 3 months and active bone formation and remodeling at 6 months, with the bioresorbable PLLA cages still present. Cages filled with OPCMC showed diverse results (Figure 2). At 3 months, remnants of the CMC material were still present. Three out of the total seven cages showed intramembranous bone formation, but no fusion. In the other cages bone forming activity was small or absent.

DISCUSSION:
Resorbable PLLA cages in combination with autologous bone graft showed good results with regard to bone ingrowth and fusion. These cages all showed advanced bone ingrowth and ongoing bone formation. Four out of five cages were fused at 6 months. Cages filled with the alternative grafting material, OPCMC, did not achieve fusion. Histology revealed retarded ingrowth of bone. In previous studies it was shown that OP-1 without the use of the carrier material can stimulate fusion. However, the CMC appeared to inhibit the invasion of the cage by ingrowing tissue. Furthermore, different tissue types, such as fibrous and fat tissue formed in some of the cages. The OPCMC putty, as used in the current study, showed inferior results as compared to autologous bone graft to achieve spinal fusion in this goat model. The retardation of the fusion process was most likely due to an inhibition of invasion by host cells, which delayed and altered new tissue formation.

NOTES:

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Figure 2: Radiographs, macroscopic, and histological images for the best and worst results are shown for the OPCMC graft material at 3 and 6 months post-operatively.

REFERENCES:
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