The use of biodegradable fixation devices in the treatment of osteochondritis dissecans and osteochondral fractures
Wouters, Diederick Bernard

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Should in the treatment of Osteochondritis Dissecans biodegradable or metallic fixation devices be used? A comparative study in goat knees.

*D.B. Wouters*¹,³
*J.Th.M. De Hosson*²
*R.R.M. Bos*³

¹Department of General and Arthroscopic Surgery and Traumatology, TweeSteden Hospital, Tilburg, The Netherlands,
²Department of Applied Physics, University of Groningen, The Netherlands,
³Department of Oral and Maxillofacial Surgery, University Medical Centre Groningen, The Netherlands.

ABSTRACT

Most of the metallic devices have to be removed, treating osteochondritis dissecans lesions. This animal study describes the biological and mechanical behaviour of screws and pins, made of commercially available PGA/PLA and PLA96 and metallic screws and pins, used for fragment fixation. A sham operation served as control. A tissue reaction with cavity formation was observed around every PGA/PLA screw, beginning at 12 weeks following insertion, in contrast to once around a PLA96 screw (p < 0.001), once around one of the 16 PGA/PLA pins and never around those, made of PLA 96 (no significance). Disintegration of the PGA/PLA devices started 6 weeks following implantation against 34 weeks for the PLA96 implants. The gap between the fragment and the recipient cartilage disappeared only in the sham group. Many fragments of PGA/PLA material were found in the synovia, in contrast with just a few fragments in the PLA96 group, causing a mild cellular reaction. No polymer particles were found in the draining lymph nodes at any interval. In conclusion, the tested biodegradable screws should not be used for fragment fixation in the treatment of Osteochondritis Dissecans. Either an undesirable tissue reaction can be expected (PGAPLA), or, due to the slow degradation (PLLA), a screw might damage the opposite cartilage during weight bearing. Two biodegradable pins provide a safe rotational stability and should be combined with one metallic screw, providing compression. This screw has to be removed before loading the limb to prevent cartilage wear of the opposite tibia plateau.
INTRODUCTION AND OBJECTIVE

The Osteochondritis Dissecans disease should be considered as a pseudarthrosis between the dissecat and its bed and, consequently, the preferred treatment is reposition of the viable and intact fragment and fixation with rotational stability and compression.\textsuperscript{1-10} Several metallic devices, such as Kirschner (K.) wires,\textsuperscript{2,3} pins\textsuperscript{11} or staples\textsuperscript{11} have been used. They are easy to insert, small in diameter, but do not apply the required compression between the fragment and the recipient bone. Obviously, screws are the devices of choice to produce this compression.\textsuperscript{4,5,7-9} However, due to their larger minimal diameter screws cause more damage to the fragment than pins or staples. Moreover, at least two screws have to be used to achieve rotational stability. The combination of one screw and two small pins results in less damage than two screws and yet a rotationally stable fixation with substantial compression.

For several reasons most of the metallic devices have to be removed during a second operation after consolidation of the fragment. When left in place, erosion of the opposite cartilage surface can occur.\textsuperscript{6,7,11} Although deeply imbedded, the implants can still gradually protrude through the cartilage surface and have to be removed after all.\textsuperscript{11,14} They can also interfere with future imaging like Computer Tomography (CT) or Magnetic Resonance Imaging (MRI) and radiation therapy.\textsuperscript{13,14} Finally, some metals, such as chromium, nickel, gold, platinum, cobalt can evoke allergic reactions like eczema or, if implanted in large amounts, an anaphylactic reaction. Chromium, nickel and cobalt are also potent carcinogens in animals.\textsuperscript{15}

Three biodegradable polyesters of the alpha-hydroxy carboxylic acid group, polydioxanon, polyglycolic acid and polylactic acid have been used in humans for the last four decades. Blends and homo- and co-polymer polymers of polylactic and polyglycolic acid were developed to achieve optimal characteristics in terms of mechanical properties and biodegradation. However, tissue reactions like cavity formation or reactive synovitis has been described after the use of pins, screws or plates composed of several of these materials.\textsuperscript{16-19} Application of one biodegradable screw and two biodegradable pins could provide a rotationally stable and compressive fixation in the treatment of the osteochondritis dissecans disease, requiring only one operation, with a minimum of damage to the fragment and avoidance of the above mentioned disadvantages of the metallic devices. But, the implants should last long enough to allow consolidation of the fragments and an undesired local tissue reactions or mechanical damages should not occur.

The aim of this study in goat knees is to evaluate the clinical reliability, the tissue reactions and cartilage wear of the opposite tibia plateau of a fixation with a combination of one resorbable screw and two resorbable pins, made of two different polymers of an artificially created osteochondral fragment, mimicking an osteochondritis dissecans complex. The outcome is compared with the results of a conventional metallic fixation as well as with a sham operation without implantation of devices.
Chapter 3
MATERIALS AND METHODS

Animal group and study design
Thirty-two knees were operated on 16, apparently, healthy, Saanen goats, with an age between two and three years old. The study was approved by the Ethical Committee for Animal Experiments of the University of Groningen, the Netherlands (nr. 0894-0594/0195).

The procedure was performed under general anaesthesia with 5 mg/kg Nesdonal® (intravenous), 0.6 mg Temgesic® (intramuscular), and 4 ml ampicilline (intramuscular) as pre-anaesthesia, followed by an O₂/N₂O mixture in a ratio of 1:2, combined with Forene® 2% in adequate levels.

Both knees of each goat were operated with an interval of six weeks between the two operations.

The goats were divided into four groups of eight knees each. In the first three groups, the fragment was loosened with a chisel and re-fixed with the centrally placed screw and two pins, made of respectively two different polymers and surgical steel. In the forth, the sham group, only drill holes were made and the outlines of the fragment were cut with the trepan (Table 1).

At the end of the experiment, the goats were sacrificed using 10 ml of intravenous T 61 (Hoechst®) and x-ray photographs were taken of the knees.

The Fisher exact test was used for statistical evaluation of the results.

The devices, inserted in the knees of the goats in the first group were derived from Biomet-USSC (Warsaw, U.S.A.). They were made of a random copolymer composed of 82% poly-L-lactic acid (PLLA) and 18% poly-glycolic acid (PGA) with a glass transition temperature range between 55-60°C and an inherent viscosity between 1.15-1.70 dL/g. (Data obtained from the manufacturer).

DSM-Research (Geleen, The Netherlands) produced the as-polymerized poly(96L4D-lactide) (PLA96) of which the devices used in the second group were made. Polymerisation of the L- and D-lactide (mole ratio 96/4) was performed in bulk under vacuum for 68 hours at 120°C. As a catalyst stannous octoate 0.02 w% was used.

The weight-average molecular weight of the PLA96 was 1.5 x 10⁶ g/mol relative to polystyrene standards, with a residual monomer concentration of 1.8%. The melting temperature was 156.5°C, the heat of fusion was 27.4 J/g.

The devices were sterilized with a special ethylene oxide (EO) gas sterilisation procedure, i.e. 3 h exposure to EO gas with a concentration of 715 mg/l at 40°C under a pressure of 510 mbar. Residual EtO concentration was less than 1 ppm after an aeration time of 3 weeks.

Operation technique
Through a medial parapatellar arthrotomy (Figure 1a), a hole with 2.0mm in diameter (Ø) and 20mm deep was drilled in the centre of the condyle of all knees, perpendicular to the cartilage surface. The outlines of a standardised fragment of 15mm Ø and 5mm deep were created with a trepan (Figure 1b), the drill hole as centre. Subsequently, two holes of 1.0mm Ø were drilled at the lateral and medial side of the central hole, halfway the border of the fragment (Figure 1c). In the central hole,
Biodegradable or metallic fixation devices? A comparative study in goat knees

**Figuur 1a:** the arthrotomy

**b:** the trepan

**c:** drilling of the holes

**d:** tapping of the screw-thread

(see for color image: page 138)

**Figuur 2a:** loosening the fragment with a chisel

**b:** one PGA/PLA screw and 2 pins.

The hexagonal inserting aid breaks off after sufficient torque force applied on the screw

**c:** one PLA 96 screw and 2 pins

**d:** one screw and 2 pins, made of surgical steel
a screw-thread was tapped with a 2.7mm tap (Figure 1d). Subsequently, the fragment, with a bony part of 5mm thick, was loosened with chisel in 3 of the 4 groups (Figure 2a).

In the first group of eight knees, screws made of PGA/PLA with a thread of 2.7mm Ø, a core of 2mm Ø and 15mm in length and pins with 1.5mm Ø and a length of 15mm were inserted (Figure 2b). In the second group of eight knees, the screws and pins with the same sizes, were composed of the PLA96 (Figure 2c).

In the third group, metallic screws and Kirschner wires of corresponding sizes (Synthes, Switzerland) were used, sterilized in the standard way for metal implants (Figure 2d).

Finally, in the fourth group, the three holes were drilled in the femoral condyle, the thread in the central hole was cut and the outlines of the fragment were created with the trepan. The fragment however, was not loosened nor were devices implanted.

All the operations were completed by closure of the wound in layers with Vicryl® 3.0 (Johnson & Johnson, Warsaw, USA).

Postoperatively, the goats were allowed to load their knees and were observed daily.

Six, 12, 18 and 46-52 weeks following the second operation, four goats, representing two knees of each different group, were sacrificed (Table 1).

**Table 1. Operation schedule**

<table>
<thead>
<tr>
<th>goat nr</th>
<th>first operation: t = 0 implants left knee</th>
<th>second operation: t + 6 wks implants right knee</th>
<th>Survival time after first operation</th>
<th>total insertion time biodegradables</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>metal</td>
<td>PLA96</td>
<td>12 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>2</td>
<td>PLA96</td>
<td>PLA96</td>
<td>12 weeks</td>
<td>6 weeks + 12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>PLA96</td>
<td>sham</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>4</td>
<td>PLA96</td>
<td>metal</td>
<td>18 weeks</td>
<td>18 weeks</td>
</tr>
<tr>
<td>5</td>
<td>PLA96</td>
<td>metal</td>
<td>18 weeks</td>
<td>18 weeks</td>
</tr>
<tr>
<td>6</td>
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<td>PLA96</td>
<td>40 weeks</td>
<td>34 weeks*</td>
</tr>
<tr>
<td>7</td>
<td>sham</td>
<td>PLA96</td>
<td>52 weeks</td>
<td>46 weeks</td>
</tr>
<tr>
<td>8</td>
<td>PLA96</td>
<td>sham</td>
<td>18 weeks</td>
<td>18 weeks</td>
</tr>
<tr>
<td>9</td>
<td>PGA/PLA</td>
<td>metal</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>10</td>
<td>metal</td>
<td>PGA/PLA</td>
<td>12 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>11</td>
<td>PGA/PLA</td>
<td>sham</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>12</td>
<td>PGA/PLA</td>
<td>metal</td>
<td>18 weeks</td>
<td>18 weeks</td>
</tr>
<tr>
<td>13</td>
<td>sham</td>
<td>PGA/PLA</td>
<td>12 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>14</td>
<td>PGA/PLA</td>
<td>sham</td>
<td>18 weeks</td>
<td>18 weeks</td>
</tr>
<tr>
<td>15</td>
<td>metal</td>
<td>PGA/PLA</td>
<td>52 weeks</td>
<td>46 weeks</td>
</tr>
<tr>
<td>16</td>
<td>sham</td>
<td>PGA/PLA</td>
<td>52 weeks</td>
<td>46 weeks</td>
</tr>
</tbody>
</table>

* Died premature due to goat paratuberculosis or CAE. The knees were uneffected
Evaluation
Clinical follow up, radiological examination of the knees and histological evaluation of the knees, the synovia and regional lymph nodes were performed.
The samples of the knees, synovia and lymph nodes were fixed at 4°C in 2% glutaraldehyde in 0.1M phosphate-buffer of pH 7.4 (University Medical Centre, Groningen, the Netherlands) for one week. Two millimetre-thick slices were cut by means of a microtome (Jung 1140/autocut). In the bony samples, the direction was as much as possible through the screw and the two pins, parallel to the long axis of the implants. In the soft tissues, the direction of the cuts was perpendicular through the long axis of the excised tissue. Dehydration followed in graded series of ethanol. The explants were embedded in 2-hydroxyethyl-methacrylate (“GMA”; Technovit 7100, Heraus-Kulzer, Wehrheim, Germany). Sections (2 μm) were cut by the same microtome and stained with toluidine blue or toluidine bleu-basic fuchsine. Light microscopical identification, localisation and evaluation of the polymeric material were carried out with polarised light, induced by crossed Nicol prisms.

RESULTS

Overall
The postoperative course was uneventful in every goat. No limping was observed in the follow up period.
In the fourth group, intended to be sacrificed after 52 weeks, one goat died prematurely 34 weeks following implantation of PLA96 screws and pins in one knee and 40 weeks following a sham operation of the other knee. The cause of death was pulmonary goat paratuberculosis; the knee joints, however, were unaffected. The retrieval of the specimens took place instantly after death and this goat was included in the series, accepting the slightly shortened implantation time (Table 1). Cavities around all the screws, composed of PGA/PLA were found after an implantation time of more than 12 weeks. Only once a similar cavity was found around a screw, made of PLA96. This difference is significant (p < 0.001).

Only once a cavity was found around a pin, composed of PGA/PLA. No cavities were observed around the 15 other pins of this group and neither around all the 16 pins, made of PLA96. This is not significant (p > 0.995).
Table 2 shows an overview of the microscopical evaluation, which reflects the foreign body response to the polymers. Details are given below in time.

Macroscopy at 6 weeks. No fracture line was seen anymore on the x-rays and the fragments were all clinically consolidated at autopsy. No synovitis was found macroscopically in any of the groups. All goats started walking within a few days following surgery and could bear full weight within a few weeks.
Table 2. Tissue response to the (biodegradable) material

<table>
<thead>
<tr>
<th>Implantation time</th>
<th>Material</th>
<th>Disintegration</th>
<th>Fibroblasts</th>
<th>Macrophages</th>
<th>Giant cells</th>
<th>Osteoblasts</th>
<th>Vascularization</th>
<th>Synovia</th>
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<td>6 weeks</td>
<td>PGAPLA</td>
<td>++</td>
<td>+</td>
<td>±</td>
<td>+</td>
<td>+++</td>
<td>± +</td>
<td>+++</td>
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<tr>
<td></td>
<td>PLA 96</td>
<td>+</td>
<td>± + ++</td>
<td>+</td>
<td>± +</td>
<td>++</td>
<td>+ ++</td>
<td>0 - ±</td>
</tr>
<tr>
<td></td>
<td>Metal</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0 - ±</td>
<td>++</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Sham</td>
<td>0</td>
<td>0 - ±</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>±</td>
<td>0</td>
</tr>
<tr>
<td>12 weeks</td>
<td>PGAPLA</td>
<td>+++</td>
<td>- ++</td>
<td>± - +</td>
<td>± +</td>
<td>+++</td>
<td>+ ++</td>
<td>+++</td>
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<tr>
<td></td>
<td>PLA 96</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>+ - +</td>
<td>+++</td>
<td>+ + - ++</td>
<td>+ - ++</td>
</tr>
<tr>
<td></td>
<td>Metal</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>± + +</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Sham</td>
<td>0</td>
<td>±</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>±</td>
<td>0</td>
</tr>
<tr>
<td>18 weeks</td>
<td>PGAPLA</td>
<td>+++</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>++ - +++</td>
<td>+ - - ++</td>
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<tr>
<td></td>
<td>PLA 96</td>
<td>± - ±</td>
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<tr>
<td></td>
<td>Metal</td>
<td>0</td>
<td>±</td>
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<td>0</td>
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<td>+</td>
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<tr>
<td></td>
<td>Sham</td>
<td>0</td>
<td>±</td>
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<td>0</td>
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<td>- +</td>
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<tr>
<td>46 weeks</td>
<td>PGAPLA</td>
<td>++ - +++</td>
<td>0</td>
<td>±</td>
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<td>++ - +++</td>
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<tr>
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<td>±</td>
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<td>+</td>
<td>++</td>
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<tr>
<td>46 weeks</td>
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<tr>
<td>52 weeks</td>
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</tr>
<tr>
<td>52 weeks</td>
<td>Sham</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
</tbody>
</table>

* Amount of material present: 0 = absent, ± = sporadically present, + = present, ++ = ample present, +++ = abundantly present
* FBR: foreign body reaction: 0 = absent, ± = minimal, + = mild, ++ moderate,
  * NR: non retrieved

**Microscopy at 6 weeks.** At six weeks no area of osteolysis or any inflammatory reaction was observed around the screws and pins of both biodegradable polymers (Figure 3a,3b) and the synovia had a normal morphology. In some cases, the fibrous membrane with fibroblasts and macrophages around the PGA/PLA and to a lesser extent around the PLA96 material was thickened and some giant cells were found in these regions (3c,d). To some extent, polymeric debris was present between the PGA/PLA screws and the original bone. Free erythrocytes were seen in all groups, but most predominantly in those with PGA/PLA and the metal implants, especially in the region of the screw-head. A slight increase of the vascularisation in the surrounding bone, mostly sub-chondral and adjacent to the implant, was found. The PGA/PLA material was already cracking and disintegrating and many fragments appeared in the surrounding tissue (Figure 4a).

In contrast, the PLA96 screws and pins seemed to be still intact. Infrequently, small polymer fragments were found adjacent to the polymer devices (Figure 4b).

In the synovia of the knees with PGA/PLA devices several small fragments of degraded material were found. The particles were surrounded or phagocytosed by giant cells (Figure 4c). In the surrounding
**Figuur 3:** aspect at 6 weeks following implantation  
(see for color image: page139)  
- a: the PGA/PLA devices  
- b: the PLA 96 devices, with some PLA 96 particles (p)  
- c: PGA/PLA material with adjacent fibrous capsule and giant cells (g) and fibrous tissue (fb)  
- d: giant cells (g) surrounding the fragments of PGA/PLA (p)  

**Figuur 4:** disintegration of the materials at 6 weeks:  
(see for color image: page 139)  
- a: extensive of the PGA/PLA material surrounded by many particles (p)  
- b: minimal of the PLA 96 material with scarcely a particle (p) found  
- c: PGAPLA particles (p) in the synovia (birefringent).  
- d: the one fragment of PLA 96 material (p), found in the synovia
tissue, capillaries as a result of an increase of angiogenesis were observed. Only once in the reviewed synovia samples in the PLA96 group, a particle of degraded material, surrounded by giant cells, was observed (Figure 4d).
No sign of polymer particles or an inflammatory reaction was found in the regional inguinal lymph nodes in any case and at any later interval.
Around the metal devices fibroblasts, premature bone formation and an increased vascularisation, but no inflammatory cells were observed.
In the sham operation group many osteoblasts and young bone formation with some increase of vascularisation had filled the drill holes. The cleft between the cartilage of the fragment and the condyle persisted in all groups except in this sham group.

**Macroscopy at 12 weeks.** A mild chondropathy of the femoral condyles was seen at autopsy in some animals with metal implants (Figure 2d). The synovia had a normal aspect in all groups.

**Microscopy at 12 weeks.** The PGA/PLA material showed progressive fragmentation and a decrease of birefringency in the centre of the material (Figure 5a). A zone of a sack-like osteolysis with polymeric debris around the screws of PGA/PLA adjoined a fibrous capsule (Figure 5b).
Small particles of PGA/PLA material were dispersed in the neighbouring bone, surrounded by phagocytic cells (Figure 6a). Some vascularisation adjacent to the screw-head and some osteoblast activity was noted. Compact fibrous tissue gradually shaded into in newly-formed bone with fields of cartilage-like material. The PLA96 screws and pins, as contrasted with the PGA/PLA devices, seemed to be still intact and fully birefringent at this stage. A thin fibrous capsule separated them from the contiguous surrounding bone. This bone contained only a few polymer fragments (Figure 6b).

**Figuur 5a:** loss of birefringence in the PGA/PLA material at 12 weeks after implantation. (see for color image: page 140)
In the synovia samples of the PGA/PLA group, many polymer particles were observed, encapsulated by giant cells and surrounded by a macrophage infiltrate (Figure 6c).

In the PLA96 group, several fragments were found in the synovia as well, surrounded by only a few giant cells (g) (Figure 6d).

Around the metallic devices, osteolysis was absent. Only a thin fibrous capsule, with many dispersed erythrocytes was formed at the outermost edge of the screw thread. Active new bone formation separated this layer from the original bone.

In the sham knees the aspect was similar to that at 6 weeks. The drill holes were filled up with bone with a few fibroblasts and some blood vessel formation. The clefts in the cartilage, demarcating the fragment, had disappeared. In contrast, they were still visible in both polymer groups and in the metal group.
Chapter 3

Macroscopy at 18 weeks. The mild chondropathy of the condyles was found in the group with the metallic implants, as was seen at 6 weeks. This was also noted in the PGA/PLA and the PLA96 group. In the sham group, the condyles had a normal aspect. No apparent synovitis was encountered.

Microscopy at 18 weeks. The PGA/PLA material was extensively fragmented. Under crossed Nicol prisms, the centre of the devices showed still decreased birefringency. Around the screws, a sack-like defect, comparable with the 12-week specimens, was filled with a fine network of septae (Figure 7a). This cavity was surrounded by newly-formed bone.

The PLA96 devices showed some central cracking, but were still fully birefringent. Immature bone with slightly increased vascularization enclosed the devices. The interface showed a few macrophages, giant cells, and osteoblasts. In one knee, however, the screw lay in a sack-like hole similar to the cavity around the PGA/PLA screws at both 12 and 18 weeks with a small amount of erythrocytes at the interface with the bone (Figure 7b).

Figuur 7a: at 18 weeks, the sack-like defect (d) around the devices of PGA/PLA (p), filled with a fine network of septae (s)

b: at 18 weeks, in 1 specimen, the PLA 96 device is lying in a sack-like defect (d), similar to the cavity around the PGA/PLA devices at 12 weeks and 18 weeks

c: at 46 weeks, the PGA/PLA implant (p) can clearly be identified, enveloped by a thin capsule (ca), directly adjacent to trabeculae of mature bone. The surrounding space is filled with fine septae (s)

d: in all the specimens of the longest surviving group, except in the sham operation group, the inter-fragmentary cleft (arrow) is, with some reaction of the cartilage at acceptor side, still visible. Specimen after removal of the metal implant

(see for color image: page 141)
In the metallic implant group newly-formed bone enclosed the implant cavity. Many erythrocytes filled the space around the screw-head.
In the sham group, the operation sites showed a slight increase in vascularisation and number of osteoblasts. The drill-holes were filled with bone formation.

**Macroscopy at 46 (34) and 52 weeks.** The chondropathy of the condyles was slightly more pronounced, the aspect of the synovia was the same as at 18 weeks.

**Microscopy at 46 (34) and 52 weeks.** At 46 weeks following insertion, the PGA/PLA implant site had the same aspect as at 12 weeks and 18 weeks.
The PLA96 devices showed now progressively disintegration. The PLA96 screw, 34-weeks following implantation in knee of the goat, that prematurely died, had the same aspect as the PGA/PLA material at 12 weeks and it was surrounded by young bone with a thin fibrous capsule and some macrophages (7c).
The implant cavity in the knee, 46-weeks post implantation of PLA 96 screw and pins, showed a lining of immature bone and a fibrous capsule. Some polymer debris, with macrophages and giant cells, was noticed.
No birefringent particles were found anymore in the synovia at the 34-week and 46-week interval of all groups.
In the metallic implants group, the subchondral bone structure in the knees had healed. Locally, still a small number of erythrocytes surrounded the devices. The gap between the transplant and the recipient cartilage is still visible (7d).
In the sham operation group only an irregularity in the bone structure, indicating the place of the drill holes, was seen at the tide mark region with still some enhanced vascularity.

**DISCUSSION**

The removal operation for metallic fixation devices can be avoided using biodegradable devices. However, the optimal device and its composition is still not found.
The mechanical properties of the different biodegradable polymers differ widely, from a sheer strength of 179 – 250 MPa for self-reinforced polyglycolide (PGA) rods, to 92 MPa for polydioxanone pins.20 This is one of the reasons that devices, made of polydioxanone and larger than pins or sutures, have only been applied experimentally.21,22
Because of superior mechanical properties of as-polymerised poly (L-lactide) (PLLA), plates and screws of this material were used to fix unstable zygomatic fractures in 10 patients by Bos et al.23,24
However, three years after implantation, a swelling at the implantation site was observed, corresponding with the presence of cavities. In these sack-like defects, densely packed needle-like PLLA remnants with high crystallinity were found.24 To find material with less residue, the
application of other polylactic copolymers like poly (96L/4D-lactide, PLA96), was explored. Disks of PLA96 and disks of PLLA, subcutaneously implanted in rats, degraded into comparable debris, both evoking a granulomatous inflammatory reaction as well and semi-crystalline PLA96 disks were, even after 101 weeks, still not fully resorbed. The PLLA induced a clinically detectable swelling of the overlying soft tissue after 16 weeks and the PLA96 after 101 weeks. In contrast, fully amorphous poly (50L/50D-lactide) (PLA50) disks of 80 mg, subcutaneously implanted in rats, seemed to be totally resorbed after 32 weeks. But, they induced a considerable tissue reaction as well. However, intramedullary implanted rods of PLLA and PLA96 in tibiae of rabbits caused no osteolytic changes to the bone and only a mild histological reaction, as Bergsma showed.27

The PGA/PLA has the theoretical advantage of a faster resorption, leading to less damage to the opposite cartilage of the tibia plateau, if used for the indication as in our study. Miller et al. found, that the half life of the 50/50 PGA/PLA copolymer was one week, of the 25/75 PGA/PLA copolymer about 3 weeks, rapidly increasing to 5 months for 100% pure PGA and 6.1 months for 100% pure PLLA.28 Theoretically, the 18/82 PGA/PLA copolymer would keep long enough its mechanical strength to provide consolidation of the fragment, but degrades fast enough to limit the damage to the opposite cartilage. The above mentioned considerations led to the choice of the materials in our study. The difference in degradation time between devices of 18/82 PGA/PLA and those made of PLA96, was also confirmed in our experiment. But, as found in the literature as well, a remarkable higher soft tissue reaction at six weeks and 12 weeks was found the in the synovia samples of the knees with the PGA/PLA material, compared to those with the PLA96 material (Table 2). A plausible explanation for this phenomenon is that the amount of degraded material, released during the faster degradation process, is more than the tissue can absorb and digest. So, during the decomposition of the implant, as long as the particles are still too large to be ingested by phagocytic cells, they will be found in the surrounding tissues as was shown in the experiments of Bos et al.24 and Bergsma et al [see also Ref. 25 pp 95 – 111, 113 – 135]. The slower degradation of PLA96 loads the surrounding tissues less and evokes less reaction.

The aspect of the PGA/PLA at 6 weeks following implantation suggests that the mechanical strength is far less than PLA96, which seems still to be intact at that moment. This is confirmed by laboratory studies.16,20,23,25,28 Consequently, the first onset of consolidation of the fixed fragments should have taken place considerably earlier than 6 weeks, if PGA/PLA devices are used. The partial loss of birefringence at 12 weeks, not mentioned in the literature before, as far as we know, suggests also a local decomposition of the material. The persistence of the gap between the transplanted fragment and the host cartilage in all the knees, except in those of the sham operation group is probably caused by a minimum of instability in the first weeks following operation, not enough to hamper bony consolidation, but interfering with early cartilage healing in those three groups of animals in our study. In the sham group the fragment remains stable postoperatively. The phenomenon of failure of integration of the transplanted
cartilage to the recipient surrounding is also described after osteochondral transplantations.\textsuperscript{25-31} and during the natural cartilage repair process.\textsuperscript{32,33} The influence of the stability of the graft is plausible, but not yet proven. Local collagenase VII treatment could improve the integration of the cartilage edges.\textsuperscript{34}

Though reported in one study,\textsuperscript{35} no polymer particles were found, in our experiment in the excised lymph nodes at all time intervals during light microscopically examination under crossed Nicol prisms.

Sack-like cavities in the bone were found around all the screws in the PGA/PLA group starting at 12 weeks and only once around a pin of the same material. In the PLA96 group, these cavities were found only once around a screw, 18 weeks following implantation and not around the pins. During the disintegrative hydrolysis process, the intra-osseous pressure increases due to the uptake of water by the polymer. If the orifices of the drill holes become blocked, the only way the debris can be expelled is into the surrounding spongy bone, leading to the formation of cavities.\textsuperscript{22,32,33,36}

This is in contrast to intramedullary placed rods, of which the degradation products can be more easily abducted by the osseous vascular and lymph drainage system. In their study, Böstman et al. found these sack-like cavities in five out of 20 animals in a biodegradable screw fixation experiment and in one out of four rabbits with a biodegradable pin as implanted device. Bergsma et al. found a well-defined swelling and identical sack-like cavities at the implantation site in every one of the nine patients in this group.

Our experiment shows, that even when small fragment screws of PGA/PLA are inserted, sack-like cavities developed in all six cases after 12 weeks of implantation time. Far less, only once out of six specimens and later following implantation, this occurred around a similar screw of PLA96. In contrast, only once a cavity was found around one out of the 16, smaller, pins of PGA/PLA and never around the 16 pins, made of PLA96. This indicates that the amount of biodegradable material of very small implants, like the used pins, is mostly below the local tissue tolerance level, as described by Sevastjanova et al.\textsuperscript{37} Using the larger screws, this level can be exceeded, as found in our experiment and in the literature as well, leading to sack-like defects in the bone.\textsuperscript{22,25,27,32,33,36}

Recently, also the second disadvantage has been demonstrated in the literature as well. Due to the relatively long degradation time of PLLA screws, the cartilage in patients, opposite to the screw, was damaged when the limb in question was loaded before total degradation of the screw.\textsuperscript{38,39}

Several means are applied to sterilize devices, made of PLLA or its co-polymers, i.e. plasma and ethylene oxide (EtO), gamma radiation and electron beams. Potentially, they can influence the mechanical properties by accelerate the degradation and increase the crystallinity. The biodegradable material used in this study was sterilized with EtO and several authors demonstrate, that this sterilisation method did not alter markedly the properties during in vitro degradation.\textsuperscript{42,43}

Moreover, during the sterilisation according to the method, developed by Griffith Microscience in cooperation with the department of Polymer Science and Maxillofacial Surgery of the University of Groningen, the temperature of the gas is 40° Celsius. Analysis of the as-polymerized PLA96 revealed
no significant (p>0.05) changes in the initial material properties (Table III). In contrast, steam sterilisation or annealing at 120º C at 4 hours prior to sterilisation by ethylene oxide can influence the properties substantially. Therefore, according to these biodegradation characteristics, the application of thin pins as biodegradable fixation devices, sterilized with ethylene oxide, seems to be more safe than the use of the, more bulky, biodegradable screws. At the other hand, the use of a faster resorbing material like PLA50 or 75/25 PGA/PLA as raw material will compromise the mechanical demands.

Metal implants induce, biologically seen, far less tissue reaction. Screws are easy to remove in the same way as they are inserted, i.e in open as well as in arthroscopic procedures. In contrast, small metallic pins are much more difficult to remove, due to the lack of hold, when grasping these headless tiny implants. Unsuccessful as well as successful attempts will both lead to considerable local cartilage damage.

The combination of a metal small fragment screw and two biodegradable pins is in our opinion the way of fixation of choice in the treatment of osteochondritis dissecans at this moment.

CONCLUSIONS

Reviewing the results of this study and the available literature, the best way to fix the fragments in the treatment of Osteochondritis Dissecans is, in our opinion, the insertion of one, easy to remove, centrally placed, metallic small fragment screw, in combination with two biodegradable pins made of one of the tested materials. This combination provides compression as well as rotational stability during the process of consolidation. If a pin, made of PGA/PLA, is used, the risk of damage to the opposite cartilage of the tibia plateau is less, due to the faster degradation, compared to a pin, made of PLA96.

The metallic screw should be removed after full consolidation of the fragment and before loading the limb.

The use of a biodegradable screw of PGA/PLA results in a significant risk for an undesirable tissue reaction. A PLLA screw will lead to damage of the opposite cartilage surface due to a too slow degradation of the polymeric material.

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