The use of high-resolution magnetic resonance imaging for monitoring interbody fusion and bioabsorbable cages: an ex vivo pilot study

MATTHIJIS R. KRIJNEN, M.D., THEO H. SMIT, PH.D., GUSTAV J. STRIJKERS, PH.D.,
KLAAS NICOLAY, PH.D., PETRA J. W. POWELS, PH.D.,
AND PAUL I. J. M. WUISMAN, M.D., PH.D.

Skeletal Tissue Engineering Group Amsterdam, Departments of Orthopedic Surgery and Physics and Medical Technology, Vrije Universiteit Medical Center Medical Center, Amsterdam; and Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

Object. Interbody fusion is a gradual process of graft resorption and tissue formation, ideally resulting in a bone bridge between two adjacent vertebral bodies. Initially, fibrous tissue and cartilage are formed, which subsequently are replaced by bone through the process of endochondral ossification. When cages and/or their contents are made of resorbable polymers like lactic or glycolic acids, there is a simultaneous process of implant degradation, which is eventually accompanied by reactions in the surrounding tissues. The purpose of this study was to explore the use of high-resolution magnetic resonance (MR) imaging for monitoring tissue differentiation, spinal fusion, cage degradation, and eventually tissue reactions as a function of time.

Methods. Lumbar vertebral segments obtained in 14 goats with 3, 6, and 12 months of follow up (three, four, and seven animals, respectively) were available from a study of the feasibility of poly(L,D-lactic acid) cages for spinal fusion. Plain x-ray films, MR images, and histological sections were used to evaluate spinal fusion and cage resorption. The first follow-up tests revealed that MR imaging noninvasively provided three-dimensional information on cage placement, cage degradation and bone formation, and that it has potential to differentiate between the various soft tissues.

Conclusions. Although the magnetic field strength and thus the resolution used were higher than normal in clinical practice, MR imaging appears to be a promising modality for the noninvasive clinical follow up of patients who undergo fusion with resorbable cages. Tissue reactions were not encountered in this study, and thus could not be evaluated.

KEY WORDS • interbody fusion • bioabsorbable cage • magnetic resonance imaging • poly-(L,D-lactic acid)

Spondylosyndesis is a surgical procedure that aims to correct spinal deformities, decompress the nerves, and fix unstable vertebral segments resulting from disc degeneration, fracture, spondylolysis, and/or spondylolisthesis. Ideally, a biological and mechanical environment is created that results in an osseous fusion of adjacent VBs. Interbody fusion is essentially a biological process of tissue differentiation, involving (among others) mesenchymal stem cells and directed by (among others) growth factors, vascularization, and oxygen.^{7,19,22} The mechanical environment is involved in two different ways. First, as in fracture repair, mechanical stability is a prerequisite for bone formation: excessive motion leads to cartilaginous or fibrous tissues (pseudarthrosis).^{2,6,8,9,23} Second, connective tissues need mechanical deformation to transport nutrients and waste products to and from the cells through the extracellular matrix,^{16,21,24} and probably also to proliferate and differentiate; stiff implants relieve the load on living tissues and thus may retard or even inhibit interbody fusion (stress shielding).^{14,28,34–36,40} Therefore, the design and material of the spinal instrumentation largely determine clinical success.

The introduction of the intervertebral cage revolutionized the surgical treatment of degenerative spinal distortions with excellent clinical results.^{3–5} The cage allowed surgeons to restore the sagittal plane alignment and the load-bearing capacity of the anterior column accurately, and introduced proper mechanical stability into the treated segment.^{10,39,41} With the relatively small size of the cages, minimally invasive techniques could be applied, thus limiting soft-tissue damage and the risk of infections.^{13,15} As a result, patients could be mobilized earlier, which shortened the rehabilitation process. The first-generation cages, however, had important disadvantages. First, the metal cages were much stiffer than the surrounding tissues, thus retarding or even inhibiting interbody fusion.^{28,34–36,40} Second, the metal cages obscured the intervertebral space on neuroimaging examination; it be-

Abbreviations used in this paper: MR = magnetic resonance; PLLa = 70:30 poly-(L,D-lactic acid); ROI = region of interest; VB = vertebral body; 3D = three-dimensional.

came practically impossible to determine if interbody fusion had occurred. Third, the cages are foreign bodies within the bone bed; if infection or immune rejection occurs, removal of the device is almost impossible. Newer cage materials like carbon fibers or polyethylethylketone reduced the first two problems but did not solve the third.

Polymer-based bioabsorbable materials like polylactic acids have recently been shown to be promising cage materials for spinal fusion: they have demonstrated strength and resorption characteristics commensurate with the physiological and biomechanical requirements of the human spine.^{31–33} Histological analysis has also demonstrated successful and timely resorption, accompanied by bone replacement and remodeling in an animal model.^{34,40} The radiolucent nature of these materials improves image assessment of spinal fusion, and their resorption characteristics allow controlled dynamization. Over time, the devices are resorbed through natural pathways, thereby reducing load sharing and consequently stress shielding of the surrounding tissues.^{34,40} Nevertheless, the composition of polymers is very diverse, showing a wide variety of resorption characteristics and evoking tissue reactions of various grades of severity.¹¹ Also, the polymer degradation rate depends on the implant dimensions, sterilization procedure, implant site, mechanical loading conditions, and host tissue.^{11,32}

To follow the process of interbody fusion, as well as the degradation of the bioabsorbable material, a noninvasive tool for clinical evaluation is required. We think that MR may be ideal for this purpose, because it has been shown to be sensitive to changes in tissues over time, for example, during differentiation, inflammation, and edema.^{1,18,20,26,29} Moreover, MR images are able to demonstrate the infiltration of tissues into the implants as well as the materials' degradation over time *in vivo*.¹⁷ Specifically, MR imaging can be helpful for the evaluation of the fusion zone within the cage and for the assessment of a sentinel sign at the anterior side of the segment. The 3D coverage can provide information on the position of the cage after surgery. There is an additional advantage in the analysis of specimens in animal models: whereas histological and histomorphomic studies will be limited to one or more sections of a specimen at one point in time (after planned death), MR imaging can be used to evaluate the complete 3D content of a cage in a longitudinal follow-up study.

To explore the potential benefits of high-resolution MR imaging, without incurring the practical problems that arise when testing large animals *in vivo*, we performed an *ex vivo* investigation by using specimens originating from a related study on resorbable cages in goats. Qualitative and selected quantitative analyses were performed on treated vertebral segments obtained in goats at 3 to 12 months of follow up. The focus of the research was on placement and degradation of the cage, tissue differentiation within the cage, tissue reaction, and assessment of the sentinel sign.

MATERIALS AND METHODS

Experimental Animals

The surgical procedures and animal care were performed in compliance with the regulations specified in the Dutch legislation

regarding animal research. The protocol was approved by review boards of the Vrije Universiteit Medical Center for animal experiments. For this study we used 14 skeletally mature female Dutch milk goats. Animals were killed at 3, 6, and 12 months postsurgery (three, four, and seven goats, respectively). During this period, they were allowed to move freely in an open field with access to a spacious stable. The surgical procedure has been described in detail elsewhere.³⁴

Surgical Procedure

Via a left retroperitoneal approach, the L3–4 intervertebral disc was identified and transversely penetrated by a 2-mm guidewire. An 8-mm drill bit was positioned over the guidewire, and a round channel was drilled through the intervertebral disc and adjacent vertebral endplates, leaving the anterior and posterior longitudinal ligaments intact. This was repeated with a 10-mm drill bit. The intervertebral disc and approximately 2 mm of endplate and subchondral bone of both adjacent VBs within the transverse rectangular defect were then removed in a standardized way by using a custom-made box gauge (10 × 10 mm).

Cage Description and Implantation

Custom-made interbody cages (MacroPore Biosurgery, Inc., San Diego, CA) with a vertical and rectangular configuration were used (10 × 10 × 18 mm; wall thickness 1.5 mm). The implants were made of a radiolucent PLA and had an axial compression strength of 6546 ± 188 N (mean ± standard deviation, six implants). All cages were packed with autologous bone graft from the iliac crest.

Specimen Preparation

After the animals were killed, a gross pathological examination was performed. Subsequently, the surgically treated motion segment was excised and trimmed of residual musculature. The transverse and spinous processes were removed. The segment was kept at 0°C and immediately transported to an MR unit.

The MR Imaging Protocol

The MR imaging experiments were performed using a 6.3-tesla MR imaging scanner with a 9.5-cm diameter horizontal bore, equipped with a VXR-S imaging console (Varian Associates, Palo Alto, CA). The MR imaging studies were started approximately 3 hours after killing the animals, and were performed at room temperature. The segments were wrapped in plastic and inserted into a 5.5-cm diameter linear driven birdcage radio frequency coil. Two plastic tubes containing standard solutions of 0.15 and 0.3 mM MnCl₂ were put next to the segments as a reference.

Depending on the size of the specimen, 21 to 35 slices were recorded; the slice thickness was 1 mm and there was no gap between them. The in-plane field of view for all images was 5.5 × 5.5 cm². High-resolution MR images were acquired in the transverse and sagittal planes by using a standard spin echo sequence with a repetition time of 4 seconds, an echo time of 15 msec, and 12 signal averages. The matrix size was 256 × 256, zero-filled to 512 × 512, yielding an in-plane resolution of 200 and 100 μm in the original and interpolated images, respectively.

The T₁-weighted MR images were acquired in the transverse planes by using a standard spin echo sequence (TE 15 msec, four or eight signal averages, and varying TRs: 0.5, 0.76, 1.14, 1.73, 2.26, 4, and 6 seconds). The matrix size was 256 × 128. This repetition time array was used to calculate corresponding T₁-weighted maps. The T₂-weighted MR images were recorded in the transverse planes by using a standard spin echo sequence (TR 4 seconds, four signal averages, and varying TEs: 15, 21, 28, 37.5, 53, 73, and 100 msec). The matrix size for these images was 256 × 128. This echo time array was used to calculate corresponding T₂-weighted maps. The MR images were analyzed using Mathematica software (Wolfram Research, Inc., Champaign, IL); the total scan time was approximately 16 hours per specimen.

Magnetic resonance imaging for monitoring interbody fusion

Analysis of Fusion

After MR imaging, the segment was sectioned in a standardized manner by using a water-cooled band saw (EXAKT, Norderstedt, Germany), creating parasagittal sections 3 and 5 mm thick. Lateral radiographs of the sectioned specimens were used to estimate interbody fusion within the cage devices according to a validated three-point radiographic score,³⁶ as follows: radiographic Score 0, no ingrowth of bone into the cage; radiographic Score 1, ingrowth of bone with the cage securely fixed to vertebral bone above and below, but with a radiolucent discontinuity in the fusion mass; and radiographic Score 2, spondylosyndesis with solid bone bridging the fusion area. Similarly, the interbody fusion stage was determined on MR images, according to the same scoring range, but now expressed as MR Scores 0, 1, and 2.

Undecalcified Histological Sections

The 5-mm sections were dehydrated and embedded without decalcification in methyl methacrylate.³⁰ After polymerization, PLA specimens were cut into 7- μ m sections with a microtome (Jung-K R; Jung, Heidelberg, Germany). All sections were stained with Goldner trichrome, H & E, and toluidine blue for transmitted light microscopy.

RESULTS

All animals recovered uneventfully from the surgical procedure, and normal ambulatory and social activities were regained at approximately the 2nd postoperative day. The MR findings on cage resorption, fusion, and the formation of a sentinel sign for each goat are listed in Table 1.

The Bioabsorbable PLA

The cages themselves produced no detectable MR signal at 3 and 6 months (Fig. 1 *left* and *center*). At 3 months the cages showed small cracks and at 6 months they all showed considerable plastic deformation. At 12 months the cages demonstrated a moderate signal intensity, indicating the presence of free water or tissue within the device (Fig. 1 *right*). Some parts of the cages were resorbed and the parts that were still visible demonstrated an increase in thickness of up to 50%. At 3 and 6 months, a thin line of high signal intensity was found on the surface of the cage. At 12 months this thin line had disappeared, but the cage itself had a higher intensity. Also during histological examination, the cages with 3 and 6 months of follow up revealed tiny fractures. All cages were surrounded by a thin layer of fibrous tissue, which changed into fibrocartilage in the fusion zone and on the loaded edges of the cage (Fig. 2 *upper* and *lower left*). No inflammatory reaction was observed at 3 and 6 months. Results of the 12-month histological evaluation were not available at the time of this writing.

Fusion Zone

The results of the evaluation with x-ray films are summarized in Table 2. They show that there was always bone ingrowth into the cage, but complete fusion was found only in two of four specimens at 6 months, and in two of seven specimens at 12 months. One sentinel sign was found after 6 months with a radiographic score of

TABLE 1
Findings on MR images obtained in goats treated with bioabsorbable devices*

Goat No.	Cage			Fusion Zone		SS
	Geometry	Signal	Interface	MR Score	Comments	
3-mo FU						
13	fx, little deformation	none	little reaction	1†	very irregular	yes
15	fx, little deformation	none	little reaction	1†	irregular	yes
17	fx, little deformation	none	no obvious reaction	1†	very irregular	no
6-mo FU						
10	deformation	none	HS, thin line	1		yes
19	deformation	none	HS, thin line	2 (radiographic Score 1)	central HS	no
22	fx	none	HS, thin line	2		no
23	fx	none	HS, thin line	2	thin line, LS in cage	no
12-mo FU						
1	PR, thick wall, bowing	moderate	little HS, thin line	2	very irregular, no continuity in trabecular bone	no
3	PR, collapsed	moderate	no HS, reaction (signal) in bone	1 (radiographic Score 0)	collapsed cage	no
5	several parts, thick wall	moderate	no difference around cage	1	HS near disc height	no
8	PR, thick wall	moderate	no reaction	2	much trabecular bone in zone	yes
12	PR, collapsed	moderate	no reaction	2 (radiographic Score 1)	little fusion	no
25	PR, collapsed	moderate	no reaction	1	LS line near disc	?
27	PR, collapsed	moderate	no reaction	1	near fusion	no

* FU = follow up; fx = fracture; HS = high signal; LS = low signal; PR = partial resorption; SS = sentinel sign; ? = MR not conclusive.

† Recorded in the transverse plane.

Fig. 1. Transverse T₁-weighted high-resolution MR images of the fusion zone after different follow-up periods: 3 months (*left*); 6 months (*center*); and 12 months (*right*). See text for explanation. The central nerves were sometimes lost during killing, and therefore are not visible in the *left* panel.

1 and two sentinel signs were found after 12 months (one with radiographic Score 1 and one with radiographic Score 2). The MR score, as shown in Table 1, confirms the radiographic score for most specimens, but not for all: the radiographic Score 1 (ingrowth) of Goat No. 19 (6-month follow-up review), for example, appears to be an MR Score 2 (fusion). The reason for this finding is that the

radiographic score is based on an x-ray film of a 5-mm midsagittal section and the MR imaging score is based on a total evaluation of the fusion zone. Histological investigation of the 5-mm section in the nonfused area, as well as the corresponding MR imaging slice, confirms the radiographic score of 1 (Fig. 2 *upper left* and *right*), but MR images reveal a fusion in another location within the

Fig. 2. *Upper and Lower Left*: Midsagittal slices of a specimen obtained at 6-month follow-up review, showing bone ingrowth but no fusion (radiographic Score 1). *Upper Left*: Photomicrograph of a histological section showing bone (green), fibrocartilage (rose), and fibrous tissue (gray). On the left side in the fusion zone is a spot of hyaline cartilage (light green). The thick red band on the right is muscle tissue. Goldner stain, original magnification $\times 4$. *Lower Left*: Photomicrograph of a histological section showing the presence of fibrocartilage (dark purple) in the fusion zone and the intervertebral discs; hyaline cartilage shows as a bright spot on the left side in the fusion zone. Fibrous tissue (blue/gray) appears at the cage interface and in the longitudinal ligaments (left and right at the cortex). Trabecular bone (bright purple) enters into the fusion zone from both VBs. Toluidine blue, original magnification $\times 4$. *Upper Right*: An MR image of the same sagittal slice discriminates between cage, bone, fibrous tissue, and cartilage, but not between fibrocartilage and hyaline cartilage. *Lower Right*: An MR image obtained elsewhere in the specimen indicates that fusion has been achieved at some locations within the cage.

TABLE 2
Radiographic scores of fusion in the retrieved spinal segments

FU (mos)	No. of Goats	Radiographic Score			
		0	1	2	SS
3	3	none	3 of 3	none	0 of 3
6	4	none	2 of 4	2 of 4	1 of 4
12	7	none	5 of 7	2 of 7	2 of 7

cage (Fig. 2 lower right). Similarly, the MR image of Goat No. 12 (12-month follow-up review) demonstrates fusion, whereas the radiographic score is 1. The reason for this discrepancy is a small fusion zone that is visible on MR images but not on x-ray films.

Tissue Identification

Qualitatively, high-resolution T₁-weighted MR images reveal many details of the composition of the tissues within and around the fusion zone (Fig. 3). Bone, for instance, always has a low signal, whereas fibrous tissue yields high-intensity signals (see also Fig. 1). With the high resolution used here, individual trabeculae are visible; these have a thickness of approximately 200 μm. The thickness of the fibrous cartilage layer is also in this order of magnitude. Another remarkable finding is that yellow marrow has a bright appearance on the MR images, whereas red marrow can hardly be distinguished from bone (Fig. 3). Apart from the bright and dark areas, several levels of gray can be seen, which are sometimes difficult to discriminate among. Most of the gray area in the fusion zone can be identified as cartilage (compare Fig. 2 upper and lower left and upper right). Nevertheless, cartilage can be either the fibrous or the hyaline type; these are different types of tissue, indicating also different phases of fusion. At first glance, it is difficult to tell whether one or the other is present from the MR images.

One possibility for overcoming this problem is to take a more quantitative approach and focus on T₁ and T₂ relaxation times, which may be tissue specific. Figure 4 upper left is a high-resolution transverse slice of the fusion zone in a specimen obtained at 6-month follow-up review. The buckled cage has almost no signal intensity, and the bright line of fibrous tissue is clearly visible. Within the cage, there is a broad spectrum of gray values. The T₁ map (Fig. 4 upper right) shows less variation of T₁ values within the cage, but in the T₂ map a brighter spot can be seen at the lower edge of the cage (Fig. 4 lower left). We chose three ROIs (Fig. 4 lower right), and determined the regional values of the T₁ and T₂ relaxation times (Table 3). The ROI with the much longer T₂ relaxation time (the bright spot in Fig. 4 lower left) also has a somewhat longer T₁ relaxation time. This indicates higher water content in the tissue, presumably an area of fibrous tissue embedded within more cartilage-like ones, or an area with relatively high blood volume (for example, blood vessel).

Three-Dimensional Information

An important feature of MR imaging is that a volume of interest is displayed, not just one or two single slices; in this volume, one can evaluate the alignment of the cage within the intervertebral disc. Ideally, the cage is placed symmetrically in the frontal plane (Fig. 1 left), entering the endplates of both VBs. Cages are sometimes more shallowly placed (Fig. 1 center), and Fig. 1 right shows that the lateral approach is sometimes difficult, presumably because of the rounded edge of the VBs, which forces the surgeon to choose a more anterolateral angle. The placement of the implant through both endplates appears to be less difficult but still problematic. Because of the low signal intensity of the cage, it is easy to evaluate eventual damage to the nerve tissues.

The 3D information is also helpful in determining whether fusion is achieved. Figure 2 shows that one sagittal section may present a nonunion, although fusion can be

Fig. 3. Photograph showing a macroscopic view (left) and MR image (right) of the midsagittal slice of a specimen obtained at 12-month follow-up review. The cage has clearly thickened, and the gray appearance points to an advanced stage of degradation. Note the difference between the yellow marrow, which appears bright on the MR image, in contrast to the red marrow, which appears dark in this image.

Fig. 4. *Upper Left*: Transverse section of a specimen obtained at 6-month follow-up review. *Upper Right*: Quantitative T_1 -weighted map of the same slice. *Lower Left*: Quantitative T_2 -weighted map of the same slice. *Lower Right*: Red circles designating the location of the ROIs: ROI 1 is on the lower left; ROI 2 is on the lower right; and ROI 3 is enclosed by the uppermost circle.

found elsewhere within the cage. The radiographic score used in earlier studies appears to be reliable (that is, specific), but sometimes underestimates the level of fusion because it is based only on a midsagittal slice of 5-mm thickness.

The 3D information also appeared to be helpful in analyzing so-called sentinel signs. A sentinel sign is defined as a bone bridge, occurring outside the fusion zone, mostly at the anterolateral edge of the intervertebral discs. At 6 (one goat) and 12 months (two goats), sentinel signs were observed on radiographic evaluation of the midsagittal slice. An MR image evaluation allowed us to confirm the sentinel sign at 6 months (Goat No. 10) and the one at 12 months (Goat No. 8), but led us to question the second

sentinel sign (Goat No. 3). On the other hand, MR images revealed two sentinel signs at 3 months (Goat Nos. 13 and 15) that were not scored on x-ray films because of the lateral position of the bone bridge.

DISCUSSION

The purpose of this ex vivo study was to explore the potential benefits of high-resolution MR imaging in monitoring spinal fusion by using bioabsorbable cages. It was found that bone, fibrous tissue, cartilage, and red and yellow marrow were well visualized on MR images. An analysis of T_1 - and T_2 -weighted maps shows that a more quantitative approach could be helpful for further tissue identification. The bioabsorbable cages were clearly visible at 3 and 6 months, because of the marked contrast between the low signal intensity of the cage and higher signal intensity of surrounding tissue. Hydrolysis became visible after 12 months, when the cage showed a grayer appearance. Possibly, the dynamics of hydrolysis of the cage could be followed over time by using ultrashort echo time imaging, which will reveal water at a very short T_2 relaxation time.^{25,38} The 3D nature of MR imaging and the possibility of obtaining images in all directions reveals

TABLE 3

*The T_1 - and T_2 -weighted relaxation times (mean $\pm$ SD) in three ROIs**

Relaxation Time	ROI 1	ROI 2	ROI 3
T_1 -weighted (secs)	1.9 ± 0.1	1.6 ± 0.2	1.4 ± 0.2
T_2 -weighted (msec)	30.0 ± 4.0	16.0 ± 5.0	17.0 ± 4.0

* Standard deviations are based on the variance of intensities within each ROI. Abbreviation: SD = standard deviation.

much information of interest compared with the single-slice approach of radiographs and histological sections.

It was interesting to find that the cages had fractured already after 3 months, and that they were covered with a thin layer of fibrous tissue; these findings were confirmed histologically. The cracks in the cage seem at least to be of some clinical value, because they affect the mechanical integrity of the implant and thus of the treated segment. The fact that less than half the specimens of the 6- and 12-month groups showed fusion is an indication that the fusion process is hindered by a reduced mechanical stability. The PLA cages apparently were mechanically overloaded in this stand-alone configuration. It has been determined that the spinal load in the goat is comparable to that in an adult human, despite the smaller body size and the horizontal position of its spine.²⁷ Clinically, cages are routinely applied in conjunction with internal fixation.

It should be emphasized that the resolution of the MR images used in this study was quite high (~0.1 mm) compared with what is used routinely in the clinic (~1 mm). This was made possible by using both a high field strength and long measuring times. High-resolution images are of very high quality but have the disadvantage of longer scanning times. This is not problematic in the evaluation of explanted segments such as those used in this goat study, but it is less than optimal for clinical application. Intervertebral cages for humans are larger than the ones used in this goat model, but only by a factor of two or three, not 10. Microcracks will not be detected as easily on clinical MR images, but there is still plenty of information of interest that will be visible. The cage itself, for example, is clearly identified, and its placement and resorption can be evaluated at follow-up review. Because polylactic acid provides no artifacts on MR images, all tissues are clearly visible, which allows us to determine whether fusion through the cage has been achieved and/or a sentinel sign has been formed. Quantitative analyses may allow more accurate tissue identification, but that is a subject for further study. It is interesting to note that yellow and red marrow can be distinguished so well from one another and from cartilage, as pointed out earlier by others.^{12,37} In previous studies investigators have shown that the fusion zone contains yellow marrow shortly after fusion, whereas red marrow is found only at later stages.³⁴ This indicates that the color of the marrow can be indicative of the "maturity" of the newly formed bone. Whether this has any clinical relevance is as yet unclear.

CONCLUSIONS

Magnetic resonance imaging has great potential as a noninvasive tool for the evaluation of spinal fusion after placement of bioabsorbable cages. The degradation of the cages can be visualized, although only long after they lose mechanical integrity. The broad coverage of MR images allows us to evaluate cage placement and bone formation both within and outside (sentinel sign) the cage; cartilage and fibrous tissue can also be identified. Quantitative analyses may allow more detailed tissue identification, but this must be investigated further.

Acknowledgments

The specimens analyzed in this study originate from an animal

study supported by Medtronic Sofamor Danek. We thank Paulien Holzmann of the Laboratory of Oral Cell Biology, Academic Center of Dentistry, Amsterdam, for preparing the histological slices.

References

1. Alikacem N, Stroman PW, Marois Y, et al: Noninvasive follow-up of tissue encapsulation of foreign materials. Are magnetic resonance imaging and spectroscopy breakthroughs? **ASAIO J** **41**:M617–M624, 1995
2. Augat P, Burger J, Schorlemmer S, et al: Shear movement at the fracture site delays healing in a diaphyseal fracture model. **J Orthop Res** **21**:1011–1017, 2003
3. Bagby GW: Arthrodesis by the distraction-compression method using a stainless steel implant. **Orthopedics** **11**:931–934, 1988
4. Blumenthal SL, Ohnmeiss DD: Intervertebral cages for degenerative spinal diseases. **Spine J** **3**:301–309, 2003
5. Brislin B, Vaccaro AR: Advances in posterior lumbar interbody fusion. **Orthop Clin North Am** **33**:367–374, 2002
6. Carter DR, Beaupre GS, Giori NJ, et al: Mechanobiology of skeletal regeneration. **Clin Orthop** **355** (Suppl):S41–S55, 1998
7. Chen WJ, Lai PL, Chang CH, et al: The effect of hyperbaric oxygen therapy on spinal fusion: using the model of posterolateral intertransverse fusion in rabbits. **J Trauma** **52**:333–338, 2002
8. Claes L, Wolf S, Augat P: Mechanische Einflüsse auf die Callusheilung. **Chirurg** **71**:989–994, 2000
9. Claes LE, Heigele CA, Neidlinger-Wilke C, et al: Effects of mechanical factors on the fracture healing process. **Clin Orthop** **355** (Suppl):S132–S147, 1998
10. Cunningham BW, Polly DW Jr: The use of interbody cage devices for spinal deformity: a biomechanical perspective. **Clin Orthop** **394**:73–83, 2002
11. Gogolewski S: Bioresorbable polymers in trauma and bone surgery. **Injury** **31** (Suppl 4):28–32, 2000
12. Hall TR, Kangaroo H: Magnetic resonance imaging of the musculoskeletal system in children. **Clin Orthop** **244**:119–130, 1989
13. Heim SE, Altamari A: Laparoscopic approaches to fusion of the lumbosacral spine: latest techniques. **Orthop Clin North Am** **33**:413–420, 2002
14. Kandziora F, Schollmeier G, Scholz M, et al: Influence of cage design on interbody fusion in a sheep cervical spine model. **J Neurosurg (Spine)** **96**:321–332, 2002
15. Kim DH, Jaikumar S, Kam AC: Minimally invasive spine instrumentation. **Neurosurgery** **51** (Suppl 5):15–25, 2002
16. Knothe Tate ML: "Whither flows the fluid in bone?" An osteocyte's perspective. **J Biomech** **36**:1409–1424, 2003
17. Liem MD, Zegel HG, Balduini FC, et al: Repair of Achilles tendon ruptures with a polylactic acid implant: assessment with MR imaging. **AJR** **156**:769–773, 1991
18. Ling CR, Foster MA: Changes in NMR relaxation time associated with local inflammatory response. **Phys Med Biol** **27**:853–860, 1982
19. Liu Z, Luyten FP, Lammens J, et al: Molecular signaling in bone fracture healing and distraction osteogenesis. **Histol Histopathol** **14**:587–595, 1999
20. McCully K, Shellock FG, Bank WJ, et al: The use of nuclear magnetic resonance to evaluate muscle injury. **Med Sci Sports Exerc** **24**:537–542, 1992
21. Mow VC, Holmes MH, Lai WM: Fluid transport and mechanical properties of articular cartilage: a review. **J Biomech** **17**:377–394, 1984
22. Murphy CL, Sambanis A: Effect of oxygen tension and alginate encapsulation on restoration of the differentiated phenotype of passaged chondrocytes. **Tissue Eng** **7**:791–803, 2001
23. Perren SM: Evolution of the internal fixation of long bone fractures. The scientific basis of biological internal fixation: choos-

- ing a new balance between stability and biology. **J Bone Joint Surg Br** 84:1093–1110, 2002
24. Piekarski K, Munro M: Transport mechanism operating between blood supply and osteocytes in long bones. **Nature** 269: 80–82, 1977
 25. Robson MD, Gatehouse PD, Bydder M, et al: Magnetic resonance: an introduction to ultrashort TE (UTE) imaging. **J Comput Assist Tomogr** 27:825–846, 2003
 26. Saryan LA, Hollis DP, Economou JS, et al: Nuclear magnetic resonance studies of cancer. IV. Correlation of water content with tissue relaxation times. **J Natl Cancer Inst** 52:599–602, 1974
 27. Smit TH: The use of a quadruped as an in vivo model for the study of the spine—biomechanical considerations. **Eur Spine J** 11:137–144, 2002
 28. Smit TH, Muller R, van Dijk M, et al: Changes in bone architecture during spinal fusion: three years follow-up and the role of cage stiffness. **Spine** 28:1802–1809, 2003
 29. Stroman PW, Dorvil JC, Marois Y, et al: In vivo time course studies of the tissue responses to resorbable polylactic acid implants by means of MRI. **Magn Reson Med** 42:210–214, 1999
 30. Theuns HM, Bekker H, Fokkenrood H, et al: Methyl-methacrylate embedding of undecalcified rat bone and simultaneous staining for alkaline and tartrate resistant acid phosphatase. **Bone** 14:545–550, 1993
 31. Vaccaro AR, Madigan L: Spinal applications of bioabsorbable implants. **J Neurosurg (Spine)** 97:407–412, 2002
 32. Vaccaro AR, Singh K, Haid R, et al: The use of bioabsorbable implants in the spine. **Spine J** 3:227–237, 2003
 33. van Dijk M, Smit TH, Burger EH, et al: Bioabsorbable poly-L-lactic acid cages for lumbar interbody fusion: three-year follow-up radiographic, histologic, and histomorphometric analysis in goats. **Spine** 27:2706–2714, 2002
 34. van Dijk M, Smit TH, Burger EH, et al: Bone histomorphometric evaluation of a clinically fused titanium tumor cage in a child. **Eur Spine J** 11:507–511, 2002
 35. van Dijk M, Smit TH, Sugihara S, et al: The effect of cage stiffness on the rate of lumbar interbody fusion: an in vivo model using poly(l-lactic acid) and titanium cages. **Spine** 27:682–688, 2002
 36. van Dijk M, Tunc DC, Smit TH, et al: In vitro and in vivo degradation of bioabsorbable PLLA spinal fusion cages. **J Biomed Mater Res** 63:752–759, 2002
 37. vande Berg BC, Galant C, Lecouvet FE, et al: The lumbar vertebral body and diskovertebral junction. Radio MR imaging anatomic correlations. **Radiol Clin North Am** 38:1153–1175, 2000
 38. Waldman A, Rees JH, Brock CS, et al: MRI of the brain with ultra-short echo-time pulse sequences. **Neuroradiology** 45: 887–892, 2003
 39. Weiner BK, Fraser RD: Spine update lumbar interbody cages. **Spine** 23:634–640, 1998
 40. Wuisman PJ, van Dijk M, Smit TH: Resorbable cages for spinal fusion: an experimental goat model. **Orthopedics** 25 (Suppl 10):S1141–S1148, 2002
 41. Zdeblick TA, Phillips FM: Interbody cage devices. **Spine** 28: S2–S7, 2003

Manuscript received January 15, 2004.

Accepted in final form February 11, 2004.

Address reprint requests to: Paul I. J. M. Wuisman, M.D., Ph.D., Department of Orthopaedic Surgery, Vrije Universiteit Medical Center, Postbox 7057, 1007 MB Amsterdam, The Netherlands. email: orthop@vumc.nl.