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Original article

MRI study of bioabsorbable poly-L-lactic acid devices used for fixation of fracture and osteotomies

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Abstract

Background. The overall clinical results of bioabsorbable fixation devices made of poly-L-lactic acid (PLLA) used for fixation of fractures, bone grafting, and osteotomies have been favorable. However, clinical studies demonstrated no sign of normal bony architecture restored after surgery, although implant channels had been filled with fibrous tissue. The purpose of the present retrospective study was to examine the extent of structural changes in PLLA devices (PLLA-Ds) for fixation of rotational acetabular osteotomies and displaced malleolar ankle fractures using magnetic resonance imaging (MRI).

Methods. Altogether, 14 patients with osteoarthritis of hip joints and 15 with displaced malleolar ankle fractures were operated on using PLLA-D (NEOFIX). Of these patients, 22 were finally enrolled in the study, and the period from operation to the time of the study ranged from 17 to 78 months. The postoperative radiographic findings were evaluated for union, and changes around the implant holes were classified as sclerosis, resorption, or no change. MRI was carried out to estimate changes in the PLLA-Ds.

Results. Bone union was obtained in all cases; clinical complications such as infection, joint effusion, soft tissue irritation due to PLLA-D deviation, and motion pain in the joints were not observed. The MRI study suggested that water content in PLLA-D increased mainly due to biodegradation and that implants were not replaced by bony tissue.

Conclusions. The PLLA-Ds were degraded but were not replaced by bony tissue during the observation period. Considering these findings and the assumption that in bony tissues mechanical strength of PLLA-D decreases with time, attention should be paid to mechanical insufficiency, which may occur when the cross-sectional area of a PLLA-D extends beyond the cross-sectional area of the osteosynthesis site.

Introduction

Bioabsorbable fixation devices made of poly-L-lactic acid (PLLA-Ds) have been developed and clinically applied in orthopedic surgery instead of conventional metallic devices, which has some disadvantages: (1) the need for operative removal of the device due to chronic discomfort or allergic reaction; (2) risk of increased osteoporosity due to stress-shielding[1]; (3) long-term implantation-related corrosion[2] or carcinogenicity.[3,4] The overall clinical results of PLLA-Ds used for fixation of fractures, bone grafting and osteotomies have been favorable, and serious adverse reactions were rarely observed. PLLA-Ds contain a large number of degradation-resistant crystals; and as the polymer slowly degrades over several years, these crystals may be released into surrounding tissues and cause a late-stage inflammatory reaction that occurs especially when PLLA-D is applied to subcutaneous tissues. However, such severe adverse reactions have not been reported for intraosseously placed pins and screws made of PLLA.[5–8]

Animal experimental studies on PLLA-D dynamics in vivo showed that almost complete absorption and replacement by bone marrow cells occurred within several years after intramedullar implantation, and only weak residual tissue reaction was observed. However, clinical studies demonstrated that although implant channels had been filled with fibrous tissue there was no sign that the normal bony architecture had been restored after surgery.[7–9]

The purpose of the present retrospective magnetic resonance imaging (MRI) study was to examine struc-

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tural changes of PLLA-D that occurred in patients after successful fixation rotational acetabular osteotomies and displaced malleolar ankle fractures.

Materials and methods

Neofix (Gunze, Kyoto, Japan) was employed as the PLLA-D in this study. Altogether, 14 patients with osteoarthritis of hip joints and 15 with displaced malleolar ankle fractures were operated on using PLLA-D at our hospital from October 1995 to December 2002; bony union was obtained in all patients. Of these patients, 22 were asked to participate and were finally enrolled in the study (76% of the initially operated patients: 7 patients could not be contacted). They were divided into two groups according to the operative method. Informed consent was obtained from all patients.

Rotational acetabular osteotomy group

PLLA-D pins, 4.5 mm in diameter, were used for fixation in rotational acetabular osteotomy in 13 patients (RAO group). The patients' (12 women, 1 man) ages ranged from 20 to 61 years (mean 39.5 years), and the period from their operation to the time of the study ranged from 34 to 78 months (mean 68.1 months).

Open reduction and internal fixation group

In nine patients, PLLA-D screws were used for displaced malleolar ankle fractures treated by open reduction and internal fixation. There were two women and seven men in the group, and their ages ranged from 16 to 67 years (mean 59.4 years). The period from operation to the time of the study ranged from 17 to 79 months (mean 34 months). For fixation of a malleolar fragment, we used eight cancellous screws (4.0 mm diameter) in six cases, four malleolar screws (4.5 mm) in two cases, and two cortical screws (3.5 mm) in one case.

None of the patients reported complications such as infection, breakage of the implant, or aseptic swelling, which could have occurred during the period from their operation to the time of study.

The postoperative radiographic findings were evaluated for union, and changes around the implant holes were classified as sclerosis, resorption, or no change. For all patients, the evaluations were performed with one anteroposterior radiogram in the rotational acetabular osteotomy group; and one anteroposterior, one lateral, and two oblique radiograms in the open reduction and internal fixation (ORIF) group. A routine radiographic checkup was carried out every 2–4 weeks until radiologic union or failure of fixation occurred. Radiologic union was declared when bridging callus or continuity of trabecula was visible on the anteropostrior radiogram or one of four standard radiographs by three orthopedic surgeons. The changes around implant holes were also assessed with one anteroposterior radiogram in both groups by these observers. After an interval of 1 week, the observers repeated the assessments on all sets of radiographs. Inter- and intraobserver reproducibility was assessed using the 95% limits of agreement for radiographic finding assessments.

Magnetic resonance imaging was carried out once in all cases with a Siemens 1.5-T Symphony or Avanto system with a surface coil; T1-weighted (SE 450/16) and T2-weighted (SE 3000/102) coronal images (5 mm thick, 0 mm spacing) were obtained at the time of the study.

Results

None of the patients developed bacterial infection in the surgical wound, late aseptic inflammatory reaction (manifested by painful erythematous and fluctuant swelling that suddenly develops around the healing wound), or motion pain due to joint arthritis. No breakage of the implant or mechanical irritative symptoms caused by the screw head were observed.

Bone union was obtained in all cases over 4–7 months (mean 5.1 months) in the RAO group, and over 3–5 months (mean 3.7 months) in the ORIF group. In the RAO group, the drill channel was detected in 12 cases (92%). No obvious pathological radiographic changes, such as focal ovoid osteolytic lesion or obvious bone resorption around the implant holes, were found in any of the cases of this group. In the ORIF group, the drill channel was detected in all cases. In eight cases (89%), no obvious pathological radiographic changes were found around the implant holes; slight resorption occurred in one patient, and slight to mild resorption around the screw head occurred in two patients. However, osteolytic expansion inside the implant channel was not found in either group (Tables 1, 2).

In the MRI study, the PLLA-D was detected as low signal intensity area on both T1- and T2-weighted images at 34–71 months after operation in the RAO group and at 17–79 months in all cases in the ORIF group (Fig. 1). Low signal intensity on T1-weighted images and high signal intensity areas on the T2-weighted images were seen in three patients (75, 77, and 78 months after operation, respedively) in the RAO group (Fig. 2). These findings suggested that water content in PLLA-D increased mainly due to biodegradation and that implants were not replaced by bony tissue.

Table 1. Patient demographics of the rotational acetabular osteotomy group

Patient	Age (years)	Sex	Bone union (months)	Follow-up (months), at time of MRI study	Implant	Diameter (mm)	No. of pins	Radiographic findings around implant holes
1*	44	M	6	78	NEOF-p	4.5	2	No change
2*	40	F	7	77	NEOF-p	4.5	2	No change
3	42	F	5.5	76	NEOF-p	4.5	2	No change
4	47	F	4.5	76	NEOF-p	4.5	2	No change
5	26	F	4	76	NEOF-p	4.5	2	No change
6*	21	F	4	75	NEOF-p	4.5	2	No change
7	40	F	4.5	75	NEOF-p	4.5	2	No change
8	61	F	6	71	NEOF-p	4.5	2	No change
9	24	F	4.5	71	NEOF-p	4.5	2	No change
10	46	F	4.5	65	NEOF-p	4.5	2	No change
11	56	F	6.5	65	NEOF-p	4.5	2	No change
12	20	F	4.5	46	NEOF-p	4.5	1	No change
13	47	F	5	34	NEOF-p	4.5	2	No change

An asterisk (*) represents low signal intensity on T1-weighted and high signal intensity on T2-weighted images
NEOF-p: Neofix pin

Table 2. Patient demographics of the ORIF group

Patient	Age (years)	Sex	Bone union (months)	Follow-up (months), at time of MRI study	Implant	Diameter (mm)	No. of screws	Radiographic findings around implant holes or screw head
1	67	M	4	79	NEOF-co	3.5	2	Slight resorption
2	41	M	3.5	52	NEOF-ca	4.5	2	No change
3	46	M	3.5	48	NEOF-ca	4	2	Slight to mild resorption
4	60	M	5	24	NEOF-ma	4.5	2	Slight to mild resorption
5	63	M	3.5	23	NEOF-ca	4	1	No change
6	30	M	3.5	22	NEOF-ca	4	2	No change
7	16	M	3	17	NEOF-ca	4	1	No change
8	61	F	4	22	NEOF-ca	4	1	No change
9	61	F	3.5	19	NEOF-ca	4	1	No change

ORIF, open reduction and internal fixation; co, cortical screw; ca, cancellous screw; ma, malleolar screw
Bone resorption occurred around the screw head, not around implant holes

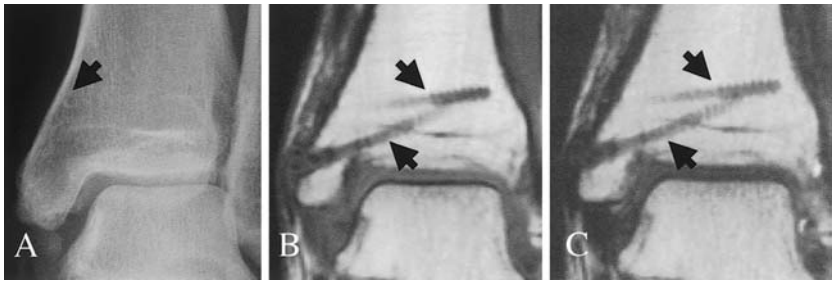

Fig. 1. Patient was a 30-year-old man 22 months after the index operation (case 6). **A** Plain roentgenogram shows a sclerotic area around the screw head (*arrow*) without any osteolytic expansion. **B** Coronal T1-weighted magnetic resonance imaging (MRI) indicates low signal intensity area (*arrows*). **C** Coronal T2-weighted MRI indicates low signal intensity area (*arrows*)

Discussion

The overall clinical results of the PLLA-D used for osteotomies and fractures were favorable in both study groups. Late inflammatory tissue reaction was not observed, although in the ORIF group slight resorption around the implant channel was found in one patient and two patients showed resorption around the screw head. Degradation of the PLLA-Ds tends to be slower in the subcutaneous tissue than in the bone marrow because of weaker cleaning capacity of the surrounding soft tissue.[5] Thus, more stress force may be transmitted to the implant, resulting in a broken screw head, loosening of the screw, or a tissue reaction against an excessive amount of PLLA-D fragments.

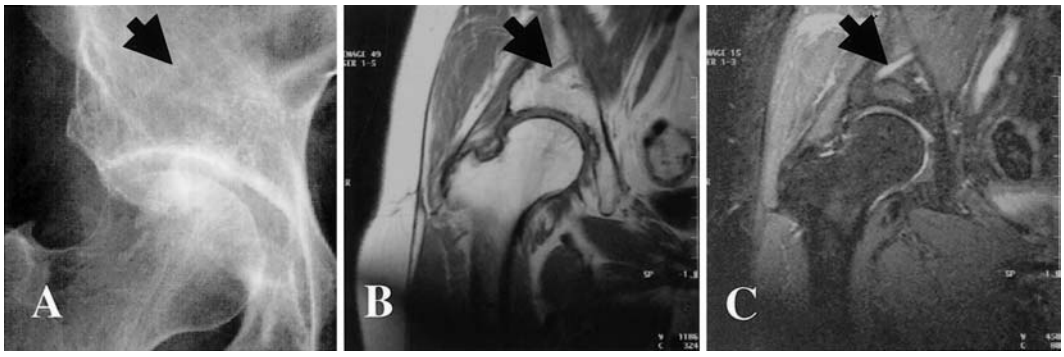

Fig. 2. Patient was a 44-year-old woman 88 months after the index operation (case 2). **A** Plain roentgenogram shows a sclerotic area around the implant hole (*arrow*) without any osteolytic expansion. **B** Coronal T1-weighted MRI indicates low signal intensity area (*arrow*). **C** Coronal T2-weighted MRI indicates high signal intensity area (*arrow*)

Osteolytic expansion in the implant channel and severe inflammatory reactions seen occasionally with self-reinforced polyglycolide devices (SR-PGA-Ds)[10–14] or self-reinforced PLLA devices (SR-PLLA-Ds),[15] especially when used near or in the joint, were also not observed in this study. SR-PGA-Ds have been used extensively in Scandinavia for fixation of ankle fractures.[16,17] However, late drainage, a disturbing complication, has been reported mainly as a result of a late, noninfectious inflammatory tissue response to polyglycolide. Because of the comparatively rapid rate of polyglycolide (SR-PGA-D) degradation, the resulting acidic product decreases the pH around the device and evokes local inflammation.[18] The hydrophilic polyglycolide characteristics may be also responsible for cavity formation and bone resorption because of increased osmotic pressure in the implant channels. They can also explain earlier onset of late inflammatory tissue reaction with SR-PGA-D that is manifested by histological findings of specimens obtained during débridement of the sinus tracts: a nonspecific foreign-body reaction with abundant giant cells phagocytosing the polymer debris.[10,19,20]

Although SR-PLLA-Ds have attracted interest because of their good mechanical properties, tissue reactions develop more frequently in patients treated with these devices (compared to PLLA-Ds), especially when used for repairs in osteochondritis dissecans.[15,21] Large particles produced by degradation of self-reinforced or highly oriented biodegradable polymers may stimulate macrophages and evoke a foreign body-related giant cell reaction at the final stages of the degradation process. This may initiate inflammatory tissue responses such as late aseptic swelling and sinus formation.[5,22] On the other hand, because PLLA-Ds do not contain fibrils in their structure[23,24] and because of their relatively low crystallinity, small PLLA-D particles may induce phagocytosis mainly via histiocytes, not giant cells, resulting in fewer adverse tissue reactions.[7,9,25]

Although determining the precise time course of structural changes in the PLLA-Ds was not the purpose of this study, MRI findings suggested that biodegradation of PLLA-Ds might have occurred in the ORIF group, but tissue replacement in the implant channel was never assumed up to at least 79 months after surgery. In the RAO group, however, MRI studies indicated that biodegradation and tissue replacement by scar or fibrous tissue occurred postoperatively after more than 75 months. In general, the degree of polymer degradation varies among interosseous PLLA-Ds and histological reaction induced by the implants may also vary. A general hypothesis, based on the experience of several research groups, is that the tissue response to the degrading polymer is the result of factors originating from the relation between local accumulation of polymer debris and the ability of surrounding tissues to eliminate it, and between host buffer capacity and osmotic pressure in the implant channel.[20,26] The degradation rate differences between polymers may also be caused by a varying local mechanical stress load, the type and size of an implant, manufacturing procedures, the blood supply, or the water content around intraosseously placed PLLA-Ds. Most probably, these were the reasons why various PLLA-D patterns were observed in the present MRI study, although the possibility that the differences were caused by limitations of the MRI technique (various screw/pin angles, mallow structures) or the small numbers of patients, cannot be fully excluded.

Some animal experimental studies demonstrated that biodegradation and tissue replacement with bony tissue occurs eventually even if a longer period is required for this to happen.[19,25,27] In a rabbit study using SR-PGA-D, Böstman et al.[19] indicated that at 36 weeks the average trabecular bone restoration in the central area in the examined samples reaches one-third of the normal trabecular bone volume, although polyglycolide screws disappear by the end of this period. In another rabbit

study, Matsusue et al.[25] also demonstrated that PLLA-D are almost completely resorbed and replaced by bone marrow cells, with only a small amount of residual tissue reaction 62 months after intramedullar implantation. On the other hand, clinical studies have shown that PLLA-Ds are degraded longer and are never replaced by bony tissue.[7] Taking into consideration these findings and the assumption that mechanical strength of PLLA-D decreases in bony tissues with time, attention should be paid to the mechanical insufficiency of the devices that may occur when the cross sectional area of a PLLA-D extends well beyond the cross sectional area of the osteosynthesis site. Long follow-up or postmortem histological studies, however, may show some bony tissue formation in the implant sites.

Recently, to achieve good osteoconductivity and to induce better ingrowth of the bony tissue, bioresorbable devices made of forged composites of hydroxyapatite particles and poly-L-lactide has been clinically applied. Although osteoconductive bone formation on the composites may enhance the stability of the bone–implant relation during osteosynthesis, the degradation rate of the composites is slow and normal bone marrow does not grow into spaces surrounded by the implant composite.[28,29] A long-term in vivo study is needed to evaluate degradation patterns of the composites and tissue reaction to them.

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References

1. Cochran GVB. Effects of internal fixation plates on mechanical deformation of bone. Surg Form 1969;20:469–71.
2. Cohen J, Wulff J. Clinical failure caused by corrosion of a vitallium plate. J Bone Joint Surg Am 1972;54:617–28.
3. Dodion P, Putz P, Amiri-Lamraski MH, Efira A, de Martelaere E, Heimann R. Immunoblastic lymphoma at the site of an infected vitallium bone plate. Histopathology 1982;6:807–13.
4. Ward JJ, Thornbury DD, Lemons JE, Dunham WK. Metal-induced sarcoma: a case report and literature review. Clin Orthop 1990;252:299–306.
5. Böstman OM, Pihlajamäki HK, Partio EK, Rokkanen PU. Clinical biocompatibility and degradation of polylevolactide screws in the ankle. Clin Orthop 1995;320:101–9.
6. Bucholz RW, Henly S, Henry MB. Fixation with bioabsorbable screws for the treatment of fractures of the ankle. J Bone Joint Surg Am 1994;76:319–24.
7. Matsusue Y, Nakamura T, Iida H, Shomizu K. A long-term clinical study on drawn poly-L-lactide implants in orthopaedic surgery. J Long Term Eff Med Implants 1997;7:119–37.
8. Pihlajamäki H, Böstman O, Hirvensalo E, Törmälä P, Rokkanen P. Absorbable pins of self-reinforced poly-L-lactic acid for fixation of fractures and osteotomies. J Bone Joint Surg Br 1992;74:853–7.
9. Matsusue Y, Nakamura T, Suzuki S, Iwasaki R. Biodegradable pin fixation of osteochondral fragments of the knee. Clin Orthop 1996;322:166–73.
10. Böstman O, Hirvensalo E, Mäkinen J, Rokkanen P. Foreign-body reactions to fracture fixation implants of biodegradable synthetic polymers. J Bone Joint Surg Br 1990;72:592–6.
11. Böstman OM. Intense granulomatous inflammatory lesions associated with absorbable internal fixation devices made of polyglycolide in ankle fractures. Clin Orthop 1992;278:193–9.
12. Böstman OM. Osteoarthritis of the ankle after foreign-body reaction to absorbable pins and screws. J Bone Joint Surg Br 1998;80:333–8.
13. Fridén T, Rydholm U. Severe aseptic synovitis of the knee after biodegradable internal fixation: a case report. Acta Orthop Scand 1992;63:94–7.
14. Frøkjær J, Møller BN. Biodegradable fixation of ankle fractures: complications in a prospective study of 25 cases. Acta Orthop Scand 1992;63:434–6.
15. Tegnander A, Engebretsen L, Bergh K, Eide E, Holen KJ, Iversen OJ. Activation of the complement system and adverse effects of biodegradable pins of polylactic acid (Biofix®) in osteochondritis dissecans. Acta Orthop Scand 1994;65:472–5.
16. Hirvensalo E. Fracture fixation with biodegradable rods: forty-one cases of severe ankle fractures. Acta Orthop Scand 1989; 60:601–6.
17. Törmälä P, Vasenius J, Vainionpää, Laiho T, Pohjonen T, Rokkanen P. Ultra-high-strength absorbable self-reinforced polyglycolide (SR-PGA) composite rods for internal fixation of bone fracture: in vitro and in vivo study. J Biomed Mater Res 1991;25:1–22.
18. Kobayashi H, Shiraki K, Ikeda Y. Toxicity test of biodegradable polymers by implantation in rabbit cornea. J Biomed Mater Res 1992;26:1463–76.
19. Böstman O, Päivärinta U, Partio E, Vasenius J, Manninen M, Rokkanen P. Degradation and tissue replacement of an absorabable polyglycolide screw in the fixation of rabbit femoral osteotomies. J Bone Joint Surg Am 1992;74:1021–31.
20. Suuronen R, Pobjonen T, Hietanen J, Lindqvist C. A 5-year in vitro and in vivo study of the biodegradation of polylactide plates. J Oral Maxillofac Surg 1988;56:604–14.
21. Barfod G, Svendsen RN. Synovitis of the knee after intraarticular fracture fixation with Biofix®: report of two cases. Acta Orthop Scand 1992;63:680–1.
22. Bergsma EJ, Rozema FR, Bos RRM, de Bruijin WC. Foreign body reactions to resorbable poly (L-lactide) bone plates and screws used for the fixation of unstable zygomatic fractures. J Oral Maxillofac Surg 1993;51:666–70.
23. Matsusita T, Nakamura K, Shiro R, Takazawa H, Tsuji K, Kurokawa T. Initial strength of highpressed extrusion poly-L-lactide screw. Biomed Mater Eng 2000;10:199–204.
24. Matsusue Y, Yamamuro T, Yoshii S, Oka M, Ikeda Y, Hyon SH, et al. Biodegradable screw fixation of rabbit tibia proximal osteotomies. J Appl Biomater 1991;2:1–12.
25. Matsusue Y, Hanafusa S, Yamamuro T, Shikinami Y, Ikeda Y. Tissue reaction of bioabsorbable ultra high strength poly (L-lactide) rod: a long-term study in rabbits. Clin Orthop 1995; 317:246–53.
26. Pistner H, Bendix DR, Mühling J, Reuther JF. Poly (L-lactide): a long-term degradation study in vivo 1993. Part III. Analytical characterization. Biomaterials 1993;14:291–8.
27. Majola A, Vainionpää S, Vihtonen K, Mero M, Vasenius J, Törmälä P, et al. Absorption, biocompatibility, and fixation properties of polylactic acid in bone tissue: an experimental study in rats. Clin Orthop 1991;268:260–9.
28. Furukawa T, Matsusue Y, Yasunaga T, Nakagawa Y, Okada Y, Shikinami Y, et al. Histomorphometric study on high-strength hydroxyapatite/poly (L-lactide) composite rods for internal fixation of bone fractures. J Biomed Mater Res 2000;50:410–9.
29. Ishii S, Tamura J, Furukawa T, Nakamura T, Matsusue Y, Shikinami Y, et al. Long-term study of high-strength hydroxyapatite/poly (L-lactide) composite rods for internal fixation of bone fractures: a 2–4-year follow-up study in rabbits. J Biomed Mater Res B Appl Biomater 2003;66:539–47.