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Self-reinforced poly-L-lactide screws in the fixation of cortical bone osteotomies in rabbits

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This study was carried out to test absorbable self-reinforced poly-L-lactide (PLLA) screws as lag screws in the fixation of cortical bone osteotomies. A right tibial osteotomy was performed in 72 rabbits, of which 36 were fixed with 4.5 mm in diameter metallic cortical screws and 36 with self-reinforced PLLA screws manufactured by a sintering method. Follow-up times were 6, 12, and 24 weeks. After killing the rabbits all operated and the control tibias were examined macroscopically and radiographed. Sixty pairs of tibias were tested for shear strength; the rest were evaluated histologically, microradiographically and by oxytetracycline fluorescence. Macroscopically, 97% of the metallic and 44% of the PLLA screw-fixed osteotomies healed well. Radiographically, the metallic group healed significantly better and there were less malpositions than in the PLLA group. The shear strengths of the operated tibias were divided by those of the controls to give comparative shear strengths. The mean comparative shear strengths were 52% at 6, 61% at 12 and 76% at 24 weeks in the metallic group and 38, 49 and 61% in the PLLA group, respectively. No statistically significant difference in shear strength was observed between the groups. A mild foreign-body reaction was found in the histological evaluation in both groups, and normal bone healing was noticed in the microradiography and in the fluorescence studies. In conclusion, the sintered self-reinforced PLLA screws were insufficiently strong to be used as a single lag screws in the fixation of tibial cortical bone osteotomies in rabbits.

1. Introduction

Polylactide (PLA) is an absorbable polyester, which has been proved to be well tolerated by tissues [1–6] and which can be manufactured for internal fixation devices [7–10]. The use of PLA implants in fractures of non-weight-bearing bone [7, 8, 11, 12] and even in fractures of weight-bearing cancellous bone [5, 13–16] has shown good results. The fixation of cortical bone osteotomies with PLLA plates has given less satisfactory results [3].

PLLA has better strength properties than racemic poly-DL-lactide (PDLLA) [9, 17]. Törmälä and coworkers [18, 19] have developed self-reinforcing (SR) techniques with which it has been possible to obtain PLLA implants of high strength. In the sintering SR-technique a PLLA device is reinforced with highly oriented PLLA fibres, resulting in an initial bending strength of 250–270 MPa, a bending modulus of 8 GPa and a shear strength of 94–110 MPa [9, 10]. Another SR technique, the fibrillation method, gives even better shear strength properties to SR-PLLA rods than the sintering method [19, 20]. In the fibrillation method the partially crystalline spherulitic structure of a melt-moulded PLLA billet is transformed into a highly oriented fibrillar structure by mechanical deformation in the solid state.

Results for rabbit femoral cortical bone osteotomy fixations with sintered SR-PLLA rods [21] and fibrillated SR-PLLA rods [22] have been encouraging. It is possible to produce SR-PLLA screws, but the initial strength values of the screws are slightly lower than those of rods [10, 15, 23] because of the architecture of the threads. A practical problem with sintered SR-PLLA screws has been their relatively low torsional strength [15, 16, 24]; the maximal torque of 4.5 mm sintered SR-PLLA screws being 0.2 N m [16].

This study was carried out to test sintered SR-PLLA screws as lag screws in the fixation of cortical bone experimental fractures.

2. Materials and methods

2.1. Experimental rabbits and anaesthesia

A right tibial cortical bone osteotomy was performed on 72 rabbits with an average weight of 3.0 kg (range 2.3–4.3 kg). The osteotomy was fixed with metallic AO cortical screws in 36 rabbits and with sintered SR-PLLA screws in 36 rabbits.

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In the metallic group fully threaded AO cortical screws 36–70 mm in length, 3.2 mm in core diameter and 4.5 mm in thread diameter were used. The SR-PLLA screws had the same dimensions but the thread profile was shallower and the tip of the thread was broader than in the metallic screws (Fig. 1). SR-PLLA screws were produced using a sintering reinforcing technique: the molecularly highly oriented PLLA fibres were compression moulded to form the screws [19]. The screws were composed of 35% molecular weight 250 000 PLLA produced by CCA Purac Biochem bv (Gorinchem, The Netherlands) and 65% molecular weight 250 000 PLLA produced by Boehringer Ingelheim (Ingelheim, Germany). The SR-PLLA screws were sterilized with a 2.5 Mrad dose of γ-radiation. After sterilization all SR-PLLA screws were tested with a 0.1 N m torque to eliminate weak screws. In the pilot studies, after sterilization the measured average shear strength of the SR-PLLA screws was 75 MPa and the maximal torque varied from 0.2 to 0.3 N m.

Immediately before the operation, 50 000 IU kg^{-1} subcutaneous benzylpenicillin procaine (Procapen, Orion, Espoo, Finland) and subcutaneous atropin (Atropin, Orion) 0.5 mg kg^{-1} were given to the rabbits. They were anaesthetised with subcutaneous ketamine (Ketalar, Parke-Davis, Barcelona, Spain) 30–40 mg kg^{-1}, subcutaneous medetomidine (Domitor, Lääkefarmos, Turku, Finland) 0.2–0.3 mg kg^{-1} and subcutaneous diazepam (Diapam, Orion) 1.0 mg kg^{-1}.

2.2. Operation technique

The right knee was shaved and scrubbed with chlorhexidine gluconate (Klorheksidos, 5 mg ml^{-1}, Lääkefarmos). A medial parapatellar arthrotomy was made and the patella was dislocated laterally. After excision of the retropatellar fat, a 3.2 mm hole was drilled into the tibial medullary cavity. When a resistance of narrowing cavity was felt, the drilling was discontinued. The drill hole was carefully tapped with a 4.5 mm AO tap in the metallic group and with a special 4.5 mm tap made for Biofix absorbable screws (Bioscience, Tampere, Finland) in the SR-PLLA group. The proximal part of the tibial hole was widened to a 4.5 mm gliding hole and a depression for the head of the screw was created. After exposing the tibial shaft distally from a tibial tuberosity, a perpendicular cortical bone osteotomy was performed with a circular diamond saw (Fig. 2a). The fibula was broken so that the right leg of the rabbit was totally unstable. The thread hole and the proximal gliding hole were thoroughly flushed. The osteotomy was fixed with an AO cortical or an SR-PLLA screw. The wound was sutured in layers with absorbable 3-0 polyglycolide sutures (Dexon, Davis and Geck, Gosport, UK).

The SR-PLLA screws were more demanding to handle than the metallic screws; one SR-PLLA screw broke peroperatively and was impossible to remove, and the rabbit had to be killed. In five metallic and one SR-PLLA fixations either the proximal or the distal fragment of tibia fractured longitudinally and they were stabilized with two 1-0 polyglycolide cerclages (Dexon). All metal (100%) and 23 of 36 (64%) SR-PLLA fixations were peroperatively firm, the rest having slight torsional instability.

2.3. Postoperative care and specimens

Postoperatively no external support was used and the rabbits were allowed to move freely in their cages. Food and water were freely available. Follow-up times were 6, 12, and 24 weeks (Table I). Rabbits were killed,

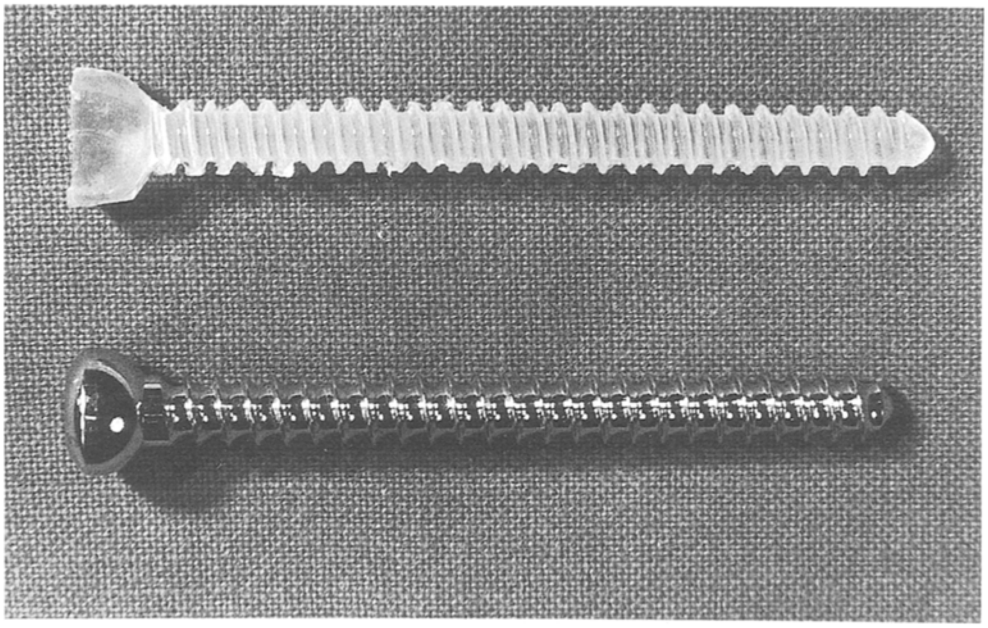

Figure 1 The screws used in the study. A metallic AO cortical screw (left) and (right) a sintered self-reinforced PLLA screw, both 4.5 mm thread diameter and 50 mm length. Note the smoother thread profile of the SR-PLLA screw.

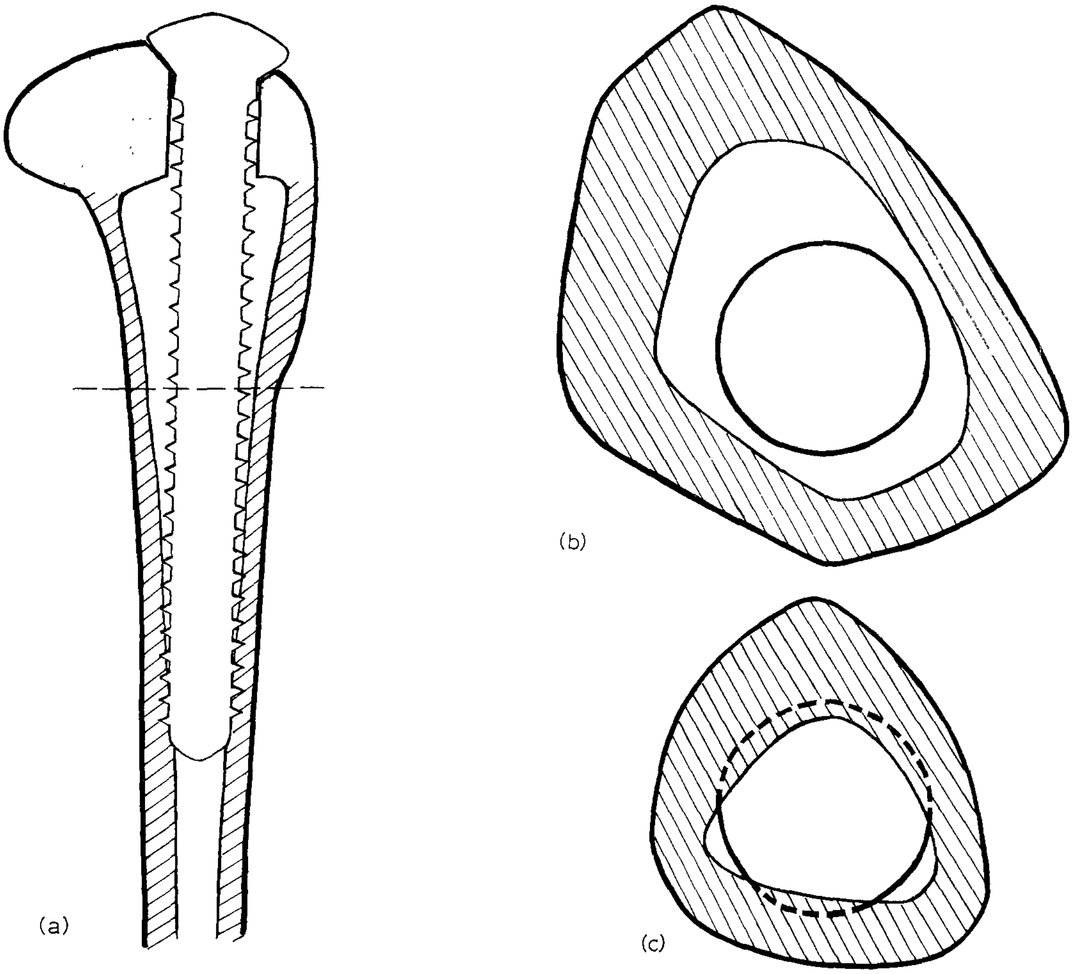

Figure 2 Osteotomy and fixation. (a) Lateral view of sagittal cross-section of the rabbit's right tibia After drilling and tapping the medullary cavity, an osteotomy was made (broken line); fibula, which is not drawn, was broken, and the osteotomy was fixed with metallic or SR-PLLA screw Note the gliding hole in proximal fragment. (b) Horizontal cross-section of the fixed tibia at the level of osteotomy Note the wide medullary cavity, which allowed some movement of the fixation if the compression was not sufficiently good. (c) Horizontal cross-section of the tibia at the distal part of the screw, where the thread–bone connections could be seen

and both tibias were exarticulated, dissected and radiographed. Fibulas and metallic screws were removed. The stability of the tibias was checked and the angulation of the healed osteotomy was measured. Sixty pairs of tibias were tested for shear strength and 12 pairs were taken for microradiographic, oxytetracycline (OTC) fluorescence and histological analysis. Two days before killing, the 12 rabbits in the histological group were injected with intramuscular OTC (Terramycin, Pfizer, Brussels, Belgium) 50 mg kg^{-1}, for OTC fluorescence studies.

2.4. Examination methods

Radiographs of both tibias were taken in the anteroposterior and lateral projections (target–tube distance 120 cm, exposure factors 40 kV, 12 mA s, 0.03 s). The visibility of the osteotomy, callus formation, malpositions and radiographic healing of the osteotomy at the end of the follow-up period were evaluated of all 72 pairs of femurs.

For microradiographic, OTC fluorescence and histological analysis, the proximal thirds of tibias of 12 rabbits were fixed in 70% ethanol and embedded in methylmethacrylate. For microradiographic and OTC fluorescence studies longitudinal sections 80 μm thick were cut with a Leitz 1600 saw microtome (Ernst Leitz Wetzlar GmbH, Wetzlar, Germany). For histological analysis sections 5 μm thick were cut with a Jung Polycut S-microtome (R. Jung GmbH, Nußloch, Germany) and stained using the method of Masson–Goldner. The microradiographs were taken with a Faxitron 43855A cabinet X-ray system (Hewlett–Packard Corporation, McMinnville, Oregon, USA) on Kodak Spectroscopic Plates, type 649-0 (Eastman Kodak Co., Rochester, New York, USA). The technical values were 50 kV, 9 mA, 12 min exposure and a 22 cm film–focus distance. Histological, OTC fluorescence and microradiographic samples were studied with a Leitz Diaplan microscope (Ernst Leitz Wetzlar GmbH), and the fluorescence microscopy was performed using an HBO 220 ultraviolet lamp and a BG 812/6 primary filter.

The shear strength was measured within 30 h from killing and the specimens were retained at room temperature (22–23 °C) in 0.9% saline solution. The distal ends of the bone specimens were embedded in Acryfix SQ (Struers, Rødovre/Copenhagen, Denmark) cold-mounting acrylic resin to the level of osteotomy. The shear forces (F) of the tibias were measured using a JJ 5003 tensile testing equipment (J. J. Lloyd Instruments, Southampton, UK) with a testing speed of

TABLE I Examination groups, macroscopic and radiographic results and number of rabbits. Met, metallic; SR-PLLA, self-reinforced PLLA; shear, shear strength study; and histologic, histological, microradiographic and OTC fluorescence analysis. Malposition points in the radiographic evaluation were used to describe the extent of deformation of the malpositions; ante-, recurvatum, varus- and valgus deformities were measured in degrees and every 10° gave one point, 1 mm displacement in AP-projection and in lateral projection gave both one point, and 1 mm shortening of bone gave also one point The sum of the points gave the degree of the malposition

Examination groups							
Material of the screw	Met	SR-PLLA	Met	SR-PLLA	Met	SR-PLLA	Total
Follow-up time (weeks)	6	6	12	12	24	24	
Shear	10	10	10	10	10	10	60
Histologic	2	2	2	2	2	2	12
Total	12	12	12	12	12	12	72
Macroscopical result							
Good	11	3	12	5	12	8	51
< 45° angulation	1	7		3		3	14
> 45° angulation		1		4		1	6
Unstable		1					1
Radiographic results							
Visibility of osteotomy							
Not visible	1		10	4	12	6	33
Slightly visible	7	4	1	2		4	18
Visible	4	8	1	6		2	21
Callus formation							
None	3		2		5	1	11
Slight	7	4	10	6	7	8	42
Moderate	1	2		4		1	8
Abundant	1	6		2		2	11
Malposition points							
0–5	11	5	12	6	12	9	55
6–10	1	2		1		1	5
11–15		4		2			6
> 15		1		3		2	6
Final radiographic healing							
Good	9	3	11	6	12	9	50
Satisfactory	2	3	1	5		1	12
Poor	1	6		1		2	10
Failure							

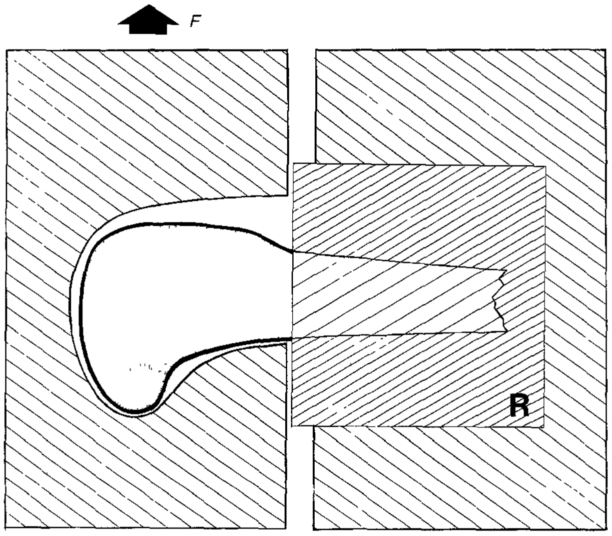

Figure 3 Measurement of shear load-carrying capacity. A distal fragment of the bone specimen was embedded in cold-mounting acrylic resin (R) and the bone was sheared through the osteotomy line to investigate the strength of the bone. *F*, force.

10 mm min^{-1}, at room temperature. The osteotomized tibias were tested through the osteotomy line. The left control bones were tested in a same way (Fig. 3).

The shear strength (τ) is given by

$$\tau = F/A$$

where F is the shear force at fracture and A is the cross-sectional area of the tested bone. A was determined from a drawing of the shearing surface. In the metallic group the area of empty medullary cavity was excluded from A, but in the SR-PLLA group the cross-sectional area of broken screw was included.

For statistical analysis, correlation coefficiencies were calculated and the Wilcoxon rank test was used for the non-parametric ranked variables.

3. Results

3.1. Macroscopic and radiographical results

Macroscopically 35 of 36 (97%) of the metallic and 16 of 36 (44%) of the SR-PLLA fixed osteotomies were well healed (Wilcoxon test 23.8; $P < 0.0001$, Table I).

In the radiographical evaluation (Table I and Fig. 4) the osteotomy line was better seen (Wilcoxon test 11.4; $P < 0.001$), the external callus formation was more

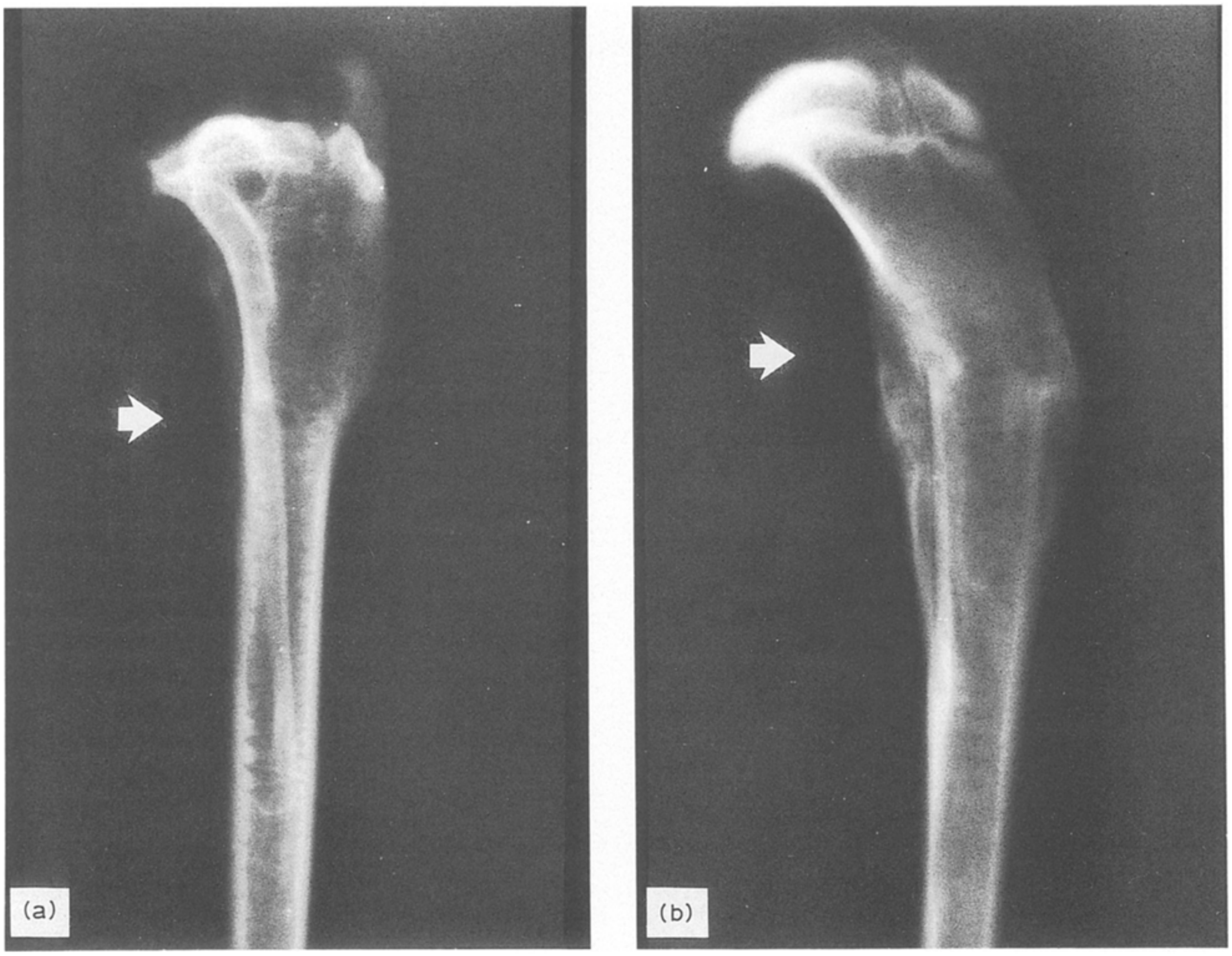

Figure 4 Lateral radiographs of typical (a) metallic screw- and (b) SR-PLLA screw-fixed right tibias of rabbits at 6 weeks. The locations of osteotomies are indicated by arrows.

TABLE II Mean shear load-carrying capacities and strengths with standard deviations (SD). Met, metallic, and SR-PLLA, self-reinforced PLLA

Material of the screw Follow-up time (weeks)	Met 6	SR-PLLA 6	Met 12	SR-PLLA 12	Met 24	SR-PLLA 24
Mean shear load-carrying capacity, operated tibia (N)	420	300	330	520	440	470
SD	200	180	120	260	130	270
Mean shear load-carrying capacity, control tibia (N)	430	400	450	470	500	500
SD	90	190	100	140	120	150
Mean shear strength, operated tibia (MPa)	8.3	3.8	7.9	8.9	12.6	9.5
SD	3.6	2.0	3.7	5.6	3.6	5.6
Mean shear strength, control tibia (MPa)	17.3	13.4	13.6	18.6	17.6	15.7
SD	5.6	6.7	4.0	6.5	5.0	5.5

abundant (19.5; $P < 0.0001$) and the final healing was worse (13.1; $P < 0.001$) in the SR-PLLA group than in the metallic group. The malpositions were more abundant in the SR-PLLA group (correlation coefficiency 0.46; $P < 0.001$).

3.2. Shear strength studies

No statistically significant differences were found between the metallic and the SR-PLLA groups in shear test values (Table II and Fig. 5). The absolute shear strength of the osteotomized tibias and the comparative shear strength increased from 6 to 24 weeks significantly (correlation coefficiency 0.42; $P < 0.001$ and 0.28; $P < 0.05$, respectively). The mean shear load-carrying capacity of the control tibias was 460 N (range 150–790 N) and of the osteotomized tibias 410 N (40–880 N). The mean shear strength of the controls was 16.0 MPa (3.9–32.9 MPa) and of the osteotomized bones 8.5 MPa (0.8–18.5 MPa).

3.3. Histology, microradiography and OTC fluorescence

No inflammation reaction was found in the qualitative histological evaluation. Foreign-body giant cells were

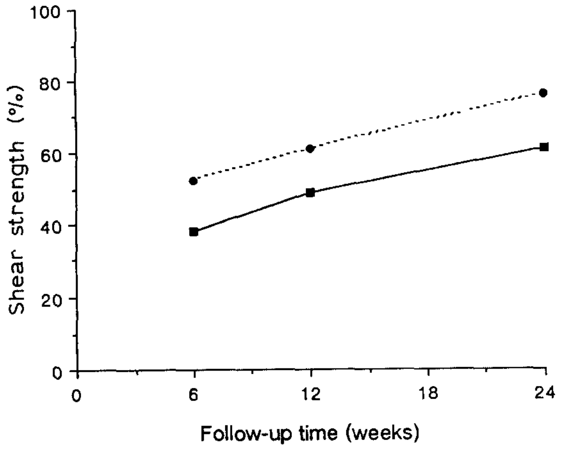

Figure 5 Mean comparative shear strengths (%) of the tibias. The strength of the operated tibia was divided by that of the control tibia, giving the comparative shear strength. (●) Metallic and (■) self-reinforced PLLA screw-fixed groups.

observed around the metallic and the SR-PLLA screws, where foamy macrophages were also seen. New bone was surrounding the threads in both groups; in SR-PLLA samples there was a thin layer of connective tissue between the screws and the bone. Callus bone formation was more intensive in the SR-PLLA group than in the metallic group; the external callus was poorly organized trabecular bone at 6 weeks and in later samples it was observed that the bone remodelled and became organized along the outer layer of the callus bone. In both 6 week histological SR-PLLA samples the screws were broken, the fibre structure was delaminated and connective tissue and foam cells were intruding between the fibres (Fig. 6).

External callus and new bone formation were more abundant in SR-PLLA fixed samples than in the metallic samples in the microradiographic and the OTC fluorescence evaluation. In both groups the callus bone was trabecular at 6 weeks and a more-organized cortical callus structure was observed at 12 and 24 weeks. The intake of OTC was strong at 6 weeks in external callus bone, in the osteotomy line and around the screw in both groups. Thereafter the intake of OTC decreased except for the region around the screw, where the high level was maintained throughout the follow-up period.

4. Discussion

PLA screws have been used in the fixation of cancellous bone osteotomies with satisfactory results. Tunc *et al.* [25] fixed nine calcaneus osteotomies in beagles with high-strength PLA screws, and they all healed well after fixation with a cast treatment. Räihä *et al.* [24] used SR-PLLA/PDLLA screws to fix six trochanteric osteotomies in beagles. Five healed well and there was one non-union. The cause of the non-union was faulty reduction. Majola [13] used SR-PLLA/PDLLA and SR-PLLA screws in the fixations of the distal femoral cancellous bone osteotomies of 72 rabbits; 31 of 36 and 34 of 36 of them healed well.

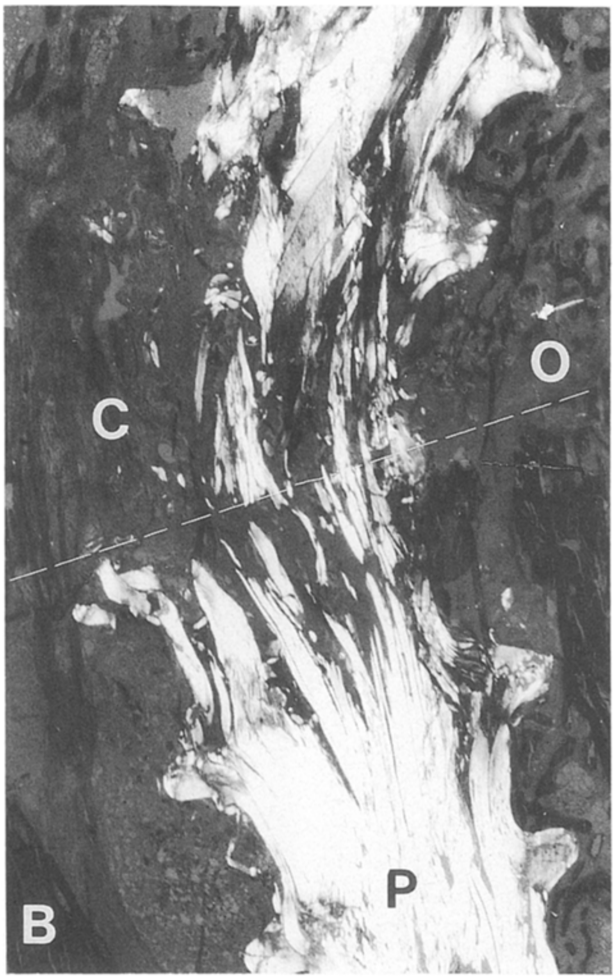

Figure 6 Failed SR-PLLA screw in the tibial medullary cavity at the level of the osteotomy at 6 weeks, threads 4.5 mm in diameter. Polarized light was used to get PLLA bright. P, PLLA; B, bone; C, connective tissue; and O, osteotomy (broken line). Note the connective tissue intruding between the delaminated PLLA fibres.

Suuronen [16] fixed nine experimental osteotomies on the necks of a sheep's mandibular condyles with sintered SR-PLLA screws, and the consolidation of the osteotomies seemed to be faster in the PLLA group than in the metallic group. We used sintered SR-PLLA screws [15] in the fixations of the olecranon osteotomies in ten sheep, and two of the fixations broke at the first week and eight healed well; the strength of healed bone was better in the PLLA screw-fixed group than in the control metallic screw group at 12 weeks. In all of these studies the contact between the screw and the thread hole has been good. Therefore, straight bending forces could not act on the screw, only shear and tensile stresses.

Even though the results of the femoral cortical bone osteotomy fixations in rabbits with SR-PLLA rods have been excellent in previous studies [21, 22], the results of SR-PLLA screw fixations in this study were not promising. The wide medullary cavity of the rabbit's tibia allowed some movement of the fixation if the compression was insufficiently good (Fig. 2a and b). Due to the modest torsional stability (0.2–0.3 N m) and the rough surface structure of the SR-PLLA screws, it was difficult to create sufficient compression between the fragments. Even if the primary fixation had been excellent, the possible relaxation of the tensiled screw could possibly stretch it, thus making the fixation unstable. When the fixation became unstable, the wide medullary cavity allowed torsional and bending forces to act on the screw. This caused unfastening of the reinforcing PLLA fibres from the screw matrix (Fig. 6); the screw then bent and the fixation failed.

The thread profile of SR-PLLA screws was shallower and less sharp than that of the metallic screws (Fig. 1) and the cross-section of the narrowing tibial medullary cavity was triangular rather than circular (Fig. 2c). These facts resulted in a smaller contact area between the screw and the bone in the SR-PLLA group than in the metallic group, thus making the threads more likely to break.

Qualitative histological, microradiographical and OTC fluorescence studies gave only suggestive results, so no exact conclusions could be drawn from them. The two failed fixations in the SR-PLLA 6 week group gave some material-related information; the screw delaminated when it bent and the fibres were seen well in the place of osteotomy (Fig. 6). Histological results with few foreign-body cells and foam cells support the findings reported earlier [1–3, 5]. The radiographical and microradiographical findings of more-abundant callus bone formation in the SR-PLLA group are in line with the greater instability of these fixations.

Moderate torsional strength and possible elasticity and thus stretching of the SR-PLLA screws caused incomplete compression between the fixed bone fragments. These, together with lack of intimate bone–screw contact at the osteotomy site, led to the non-rigid fixations and failing in 56% of the cases in the SR-PLLA group. Therefore, it can be concluded that sintered SR-PLLA screws are not yet sufficiently strong to be used as single lag screws in the fixation of tibial cortical bone osteotomies in rabbits.

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