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Diaphyseal fractures treated by polylactide and hydroxyapatite pins. Experimental study in rat

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In order to develop a biodegradable interlocking nail for fracture fixation, polylactic acid (PLA) pins and hydoxyapatite pins were implanted in the femoral bone in rats. A distal fracture was performed. The union and the tissue reaction to PLA and hydroxyapatite versus stainless steel rods were studied after 15 days, 1, 2 and 6 months implantation. Metal and PLA pins induced a union. Hydroxyapatite pins (Ossatite®) did not prevent callus formation, but did not lead to consolidation in all cases because of weakness of the gelatin matrix binding the apatite particles together. PLA and stainless steel pins induced the same union and a similar tissue reaction during the studied implantation of 6 months. The biocompatility of Ossatite® is satisfactory and the osteo-inductive properties of hydroxyapatite was confirmed. With injectable Ossatite®, we could not obtain rat femoral fracture consolidation. We can confirm good biomaterial tolerance in bone which contrasts with important soft tissue reactions. Use of such material should be carefully limited to filling intra-osseous cavities.

1. Introduction

Diaphyseal fractures of long bone are frequent at all ages. Their treatment is conservative or surgical depending on the type of fracture and the patient's age. In children, the growth of centromedullary pinning according to Metaizeau's technique [1] has extended the indications for surgical treatment of displaced fractures. This technique has many advantages (preservation of periosteal consolidation, stability of fixation, no need for postoperative plaster, short hospital stay, rapid return to school), but requires a second operation to remove the metallic material. The use of an absorbable material would eliminate the need for this second surgical procedure.

We have tested polylactide pins and hydroxyapatite pins to treat diaphyseal fractures of the femur in rats. Polylactide pins are already used in bone surgery for epiphyseal fractures [2]. Hydroxyapatite is also used to fill bone defects or as material applied on to metallic implants [3–9]. Many experimental studies have been conducted to investigate the reactions and tolerance of these materials [10–14]. We conducted an experimental study in rats to study bone consolidation using this technique and the tolerance of intramedullary implantation of these materials.

2. Material and methods

Absorbable pins were made of polylactide (PLA) or Ossatite®. Polylactide had a molecular weight of 250 000 (PLA 98: 98% of L-lactic units and 2% of D-lactic units) and were manufactured by Phusis (Saint Ismier, France). PLA 98 is absorbed after hydrolysis with metabolization of the degradation products. The pins were sterilized by the cold hydrogen peroxide plasma sterilization technique (STERRAD®).

Ossatite® is synthetic hydroxyapatite, prepared from calcium phosphate, dibasic, proposed by Sharrock [15–17] $[Ca_5(PO_4)_3(OH)]$. The form used consisted of a composite Ossatite® which is a mixture of pure Ossatite® (80%) and pharmaceutical gelatin derived from pig skin and glycerol (20%). This product is manufactured by Medical Calcium Phosphates (Toulouse, France). It is insoluble in water, and its organic phase can be absorbed *in vivo* by digestion. In the composite form, the solid formed is decomposed by dislocation and dissolution of precipitation products to release slowly absorbable hydroxyapatite. These pins were sterilized by gamma radiation (25 000 Gy). The pins were 2 mm in diameter and 70 mm long.

This study was conducted on 64 male Wistar rats, weighing 350 to 374 g (R. Janvier Breeding Center, Le

Genest Saint Isle, France). Experimental conditions complied with current legislation. Rats were housed and fed in the Nice Faculty of Medicine animal house.

The operation was performed under general anaesthesia with ether and ketamine at the dose of 50 mg kg^{-1} (2/3 of the dose of these products was administered by intraperitoneal injection and 1/3 was administered by intramuscular injection). Anaesthesia was maintained with ether. The operative fields were shaved. The rat was placed in the dorsal supine position and the skin was disinfected with iodinated polyvidone. The surgical operation was performed according to the following protocol. Via a median skin incision in the knee, the extensor apparatus was retracted, allowing access to the femoral condyles. A hole was made with a square point in the middle of the trochlea surface and the medullary canal was prepared with trocars of variable calibre (0.7 to 2.2 mm in diameter). The pin was inserted in the prepared medullary canal and sectioned flush with the cartilage. According to the group, a fracture was induced in the lower third of the femoral diaphysis using cutting pliers. The extensor apparatus was sutured by separate sutures using absorbable suture material. The skin was also sutured according to the same technique. The animal was placed in an individual cage without external immobilization with water and food *ad libitum* and was observed until recovery.

The rats were divided into four groups of 15 rats according to the date of sacrifice (15 days, 1 month, 2 months, 6 months). Each group consisted of three subgroups of 5 rats: subgroup A constituted the control group, as the femoral diaphyseal fracture of these rats was fixed by a stainless steel pin, to study normal consolidation; subgroup B was treated by polylactide pins; subgroup C was treated by Ossatite® pins. An absorbable pin was implanted in the non-fractured right femur of each rat in order to study the tolerance of these pins and a fracture of the left femur was repaired using an identical absorbable pin to study consolidation with an absorbable pin 2 mm in diameter.

At the defined times, the animal was sacrificed (ether and compressive pneumothorax). The thigh was removed and fixed in Bouin's solution. Anteroposterior (AP) and lateral X-rays were performed and interpreted by two examiners. The thigh was sectioned transversely and totally embedded in paraffin after partial decalcification during 8 h in Rapid Bone Decalcifying solution (Eurobio Laboratory, Les Ulis, France). Several sections (one at each extremity and four in the diaphysis) were performed and stained with haematoxylin and eosin. Slides were examined under a Leitz Laborlux 12 light microscope. This histological examination was performed by two pathologists, not informed about the corresponding rat. The radiological examination assessed consolidation with evaluation of the callus (CAL) and bone reaction (REAC) or soft tissue reaction (R) according to several criteria (Table I). The histological examination (Table II) assessed bone consolidation (BC), chondroid metaplasia (CM) and the reaction around the osteosynthesis material in the bone (Rb) and soft tissues (Rst), noting the presence of a polymorphous inflammatory infiltrate (leucocytes, plasmocytes, histiocytes), giant cells in contact with the material or inclusion of the material

TABLE I

CAL 0: absence of callus
CAL 1: bone formation at the seat of fracture with persistence of the fracture line
CAL 2: hypertrophic callus
CAL 3: dense and homogeneous callus
REAC 0: absence of abnormal X-ray signs
REAC 1: cortical or intramedullary bone remodeling
R +: calcifcation or denseness soft tissue
R −: absence of abnormal X-ray signs

TABLE II

BC 0: absence of ossification
BC 1: fibrous hyperplasia and granulation tissue
BC 2: primary fibrillary bone formation
BC 3: secondary ossification
CM 0: absence of chondroid metaplasia
CM 1: less than 50% of chondroid metaplasia of the corresponding section
CM 2: more than 50% of chondroid metaplasia of the corresponding section
Rb 0 and Rst 0: absence of reaction
Rb 1 and Rst 1: reaction

and capillary neogenesis. Phenomena in favor of infection (area of intraosseous or soft tissue suppuration) or the presence of foreign bodies in the soft tissues were recorded.

Statistical analysis was performed using the Chi-square test, completed by two-way analysis of variables. Histological consolidation (BC) and radiological consolidation (CAL) were compared between the various groups and with each other. The same study was conducted for histological and radiological bone reaction (Rb, REAC) and soft tissue reaction (Rst, R). Finally, chondroid metaplasia (CM) was compared between the various groups.

3. Results

The study was conducted in 64 rats, 60 rats distributed into the various groups and four rats which died before or at the end of the operation.

3.1. Results of group 1, sacrificed at 15 days (Table III)

Subgroup A: (rats 4,6,11,16,17). Three rats were classified as BC 1, one as BC 0 and 1 had infection. No bone or soft tissue reaction was observed, except for rat 17, which was infected. Subgroup B: (rats 34,42,44,48,53). All rats were classified as BC 1, with no bone or soft tissue reaction. Subgroup C: (rats 22,23,26,27,28). Four rats were classified as BC 1, one was BC 0 with a bone reaction in five cases and a soft tissue reaction in three cases. Four pins were broken on the fractured side.

3.2. Results of group 2, sacrificed at 1 month (Table IV)

Subgroup A: (rats 9,15,18,19,20). Three rats were classified as BC 1, one was BC 2, but with two

T A B L E I I I Results at 15 days: comparison between metal pins, PLA pins and ossatite pins

15 Days rat	Pin	Radiology		Macroscopic appearance		Histology	
		L	R Fracture	L	R Fracture	L	R Fracture
4	Metal		CAL 1 REAC 0 R –				BC 1 CM 1 Rb 1 Rst 1
6	Metal		CAL 0 REAC 0 R –		Expelled pin		BC 1 CM 2 Rb 1 Rst 1
11	Metal		CAL 1 REAC 0 R –				BC 1 CM 1 Rb 1 Rst 1
16	Metal		CAL 3 REAC 0 R – FALSE PASSAGE		False passage		BC 0 CM 0 Rb 0 Rst 1
17	Metal		CAL 1 REAC 0 R –				BC 0 CM 0 Rb 0 Rst 0 INFECTION
34	Polylactide	REAC 0 R –	CAL 0 REAC 0 R –			Rb 1 Rst 0	BC 1 CM 1 Rb 1 Rst 0
42	Polylactide	REAC 0 R –	CAL 0 REAC 0 R – Overlapping	Granuloma at entry site	Prominent pin	Rb 1 Rst 0	BC 1 CM 2 Rb 0 Rst 1
44	Polylactide	REAC 0 R +	CAL 1 REAC 0 R –	Haematoma		Rb 0 Rst 0	BC 1 CM 1 Rb 1 Rst 1
48	Polylactide	REAC 0 R –	CAL 1 REAC 0 R – False passage		Mobile	Rb 0 Rst 0	BC 1 CM 2 Rb 1 Rst 1
53	Polylactide	REAC 0 R –	CAL 1 REAC 1 R –		Granuloma at entry site	Rb 0 Rst 0	BC 1 CM 2 Rb 1 Rst 1
		Fracture	No fracture	Fracture	No Fracture	Fracture	No Fracture
22	Ossatite	CAL 0 REAC 0 R – FRACTURED PIN	REAC 0 R –	Heamatoma	Granuloma	BC 1 CM 1 Rb 1 Rst 0	Rb1 Rst –
23	Ossatite	CAL 0 REAC 0 R – FRACTURED PIN	REAC 0 R –	Overlapping		BC 1 CM 1 Rb 1 Rst 1	Rb 1 Rst –
26	Ossatite	CAL 1 REAC 0 R – FRACTURED PIN	REAC 1 R –	Misalignement	Haematoma	BC 1 CM 1 Rb 1 Rst 1	Rb 1 Rst –
27	Ossatite	CAL 1 REAC 0 R –	REAC 0 R –			BC 1 CM 2 Rb 1 Rst 0	Rb 1 Rst –
28	Ossatite	CAL 0 REAC 1 R – FRACTURED PIN	REAC 0 R –			BC 0 CM 1 Rb 1 Rst 1	Rb 1 Rst –

radiological non-union and one rat (rat 19) had a bone and soft tissue infection. No bone or soft tissue reaction. The metal pin was partially expelled in two of the five cases. Subgroup B: (rats 37,39,40,49,50). Four rats were classified as BC 2, one was BC 1, with no bone or soft tissue reaction. Two rats had also consolidated, two had forming callus and one had not consolidated because the fracture had not been reduced with a pin lying outside of the femur (rat 40). Subgroup C: (rats 29,30,31,33,54). Three rats were classified as BC 2, two were BC 1, with a bone reaction, but no soft tissue reaction. Misalignment of the fracture site with rupture or curvature of the material was observed in four cases.

3.3. Results of group 3, sacrificed at 2 months (Table V)

Subgroup A: (rats 8,10,12,13,14). Three rats were classified as BC 3, one was BC 2 and one was BC 1, with one infection (rat 10). No reaction; subgroup B: (rats 35,43,45,51,52). All five rats were classified as BC 2, with no reaction. Subgroup C: (rats 55,56,57,58,59). Three rats were classified as BC 2, one was BC 1 and one was BC 3. A bone reaction was observed in four out of five cases and one rat presented angulation of the fracture site.

3.4. Results of group 4, sacrificed at 6 months (Table VI)

Subgroup A: (rats 1,2,3,5,7). All five rats were classified as BC 3 (Fig. 1a) and one of them was CM 2 (rat 2) due to the presence of pseudarthrosis, without reaction. Two rats (rats 2 and 7) died several days before the 6-months was over and one of them (rat 7) presented an external haemorrhage from the right ear. They were included in the study, as samples were able to be obtained. Subgroup B: (rats 36,38,41,46,47). Five rats were classified as BC 3, CM 0 or 1, with no bone or soft tissue reaction (Fig. 1b; Fig. 2a); subgroup C: (rats 60,61,62,63,64). Three rats were classified as BC 3 (Fig. 1c; Fig. 2b), one as BC 1 and one as BC 0 with a bone reaction in three out of five cases. The two non-consolidated cases showed misalignment with fracture of one of the pins. Overall, fracture consolidation was obtained in 12 out of 15 cases. Absence of consolidation (rat 2) was observed in a femur in which the metal pin was only inserted into the distal fragment, and in two out of five cases with the

TABLE IV Results at 1 month. Comparison between metal pins, PLA pins and ossatite pins

1 Month rat	Pin	Radiology		Macroscopic appearance		Histology	
		L	R Fracture	L	R Fracture	L	R Fracture
9	Metal		CAL 3 REAC 0 R –				BC 1 CM 0 Rb 1 Rst 0
15	Metal		CAL 3 REAC 0 R –				BC 1 CM 1 Rb 1 Rst 0
18	Metal		CAL 0 REAC 0 R – Pin expelled		Pin expelled		BC 1 CM 1 Rb 0 Rst 1
19	Metal		CAL 0 REAC 1 R – Pin expelled		Osteitis		BC 0 CM 0 Rb 1 Rst 1
20	Metal		CAL 0 REAC 0 R – Pin expelled		Pin expelled		BC 2 CM 1 Rb 1 Rst 0
37	Polylactide	REAC 0 R –	CAL 1 REAC 0 R –			Rb 1 Rst 0	BC 2 CM 1 Rb 1 Rst 0
39	Polylactide	REAC 1 R – False passage	CAL 1 REAC 0 R –		Skin dehiscence	Rb 0 Rst 0	BC 2 CM 1 Rb 1 Rst 0
40	Polylactide	REAC 0 R –	CAL 0 REAC 0 R –		False passage	Rb 0 Rst 0	BC 1 CM 1 Rb 1 Rst 1
49	Polylactide	REAC 0 R –	CAL 1 REAC 0 R –			Rb 1 Rst 0	BC 2 CM 1 Rb 1 Rst 1
50	Polylactide	REAC 0 R –	CAL 1 REAC 0 R –			Rb 1 Rst 0	BC 2 CM 2 Rb 1 Rst 1
		Fracture	No fracture	Fracture	No Fracture	Fracture	No Fracture
29	Ossatite	CAL 1 REAC 1 R – Misalignment	REAC 0 R –			BC 2 CM 1 Rb 1 Rst 0	Rb 1 Rst 0
30	Ossatite	CAL 0 REAC 1 R – Misalignment	REAC 1 R –	Granuloma		BC 2 CM 0 Rb 1 Rst 0	Rb 1 Rst 0
31	Ossatite	CAL 0 REAC 1 R –	REAC 0 R –	Granuloma		BC 1 CM 1 Rb 1 Rst 0	Rb 1 Rst 0
33	Ossatite	CAL 0 REAC 1 R – Misalignment	REAC 1 R –			BC 2 CM 1 Rb 1 Rst 0	Rb 1 Rst 0
54	Ossatite	CAL 0 REAC 1 R – Misalignment	REAC 1 R –			BC 1 CM 1 Rb 1 Rst 0	Rb 1 Rst 0

Ossatite® pin. The polylactide pin did not induce any reactions on the non-fractured femur, while the Ossatite® pin induced a reaction in three out of five cases.

3.5. Statistical analysis

Statistical analysis demonstrated the absence of any significant difference ($P < 0.19$) between metal pins and polylactide pins in terms of histological consolidation (BC), at each sacrifice date. Similar results were observed for radiological consolidation ($P = 0.34$). However, comparison of groups, independently of the type of pin, demonstrated a highly significant difference ($P < 0.0001$) for histological (BC) or radiological consolidation (CAL) as a function of time, from D 15 to D 180. A good correlation was also observed between histological consolidation and radiological callus ($P = 0.0016$) with a Cramer V of 0.47 (knowledge of one of the two parameters predicted 47% of the variation of the other parameter).

No significant difference in the course of chondroid metaplasia (CM) was observed between D 15 and D 180, regardless of the group ($P = 0.08$) or the type of pin ($P = 0.06$). A significant reduction of histological bone reaction (Rb) was observed between D 15 and D 180, regardless of the type of pin ($P = 0.036$), but no significant difference ($P = 0.09$) was observed between the group of rats in which the fracture was osteosynthesized by an absorbable pin and the control group. In contrast, a highly significant difference ($P = 0.002$) was observed in rats treated with an absorbable pin according to the presence or absence of fracture. A significant difference ($P = 0.011$) was also observed when all rats with a fracture were compared to those without a fracture. No significant difference ($P = 0.99$) was observed for radiological bone reaction (REAC) as a function of the type of pin and according to the presence or absence of fracture. Similar results were observed for histological soft tissue reaction (Rst) ($P = 0.20$). No significant difference ($P = 0.15$) was observed for radiological soft tissue reaction (R) as a function of the type of pin used for osteosynthesis of the fracture.

4. Discussion

The use of absorbable material such as polylactide or Ossatite® pins to treat diaphyseal fractures would eliminate the second phase of the surgical procedure for removal of osteosynthesis material. Apart from the human benefit, Juutilainen *et al.* [18], in a comparative study on 140 patients, found that the treatment of ankle fractures cost £3503 with PGA screws and £3906 with PLLA screws versus £4514 with metal screws, corresponding to a cost saving of between £608 and £1011.

We conducted an experimental study in rats to assess

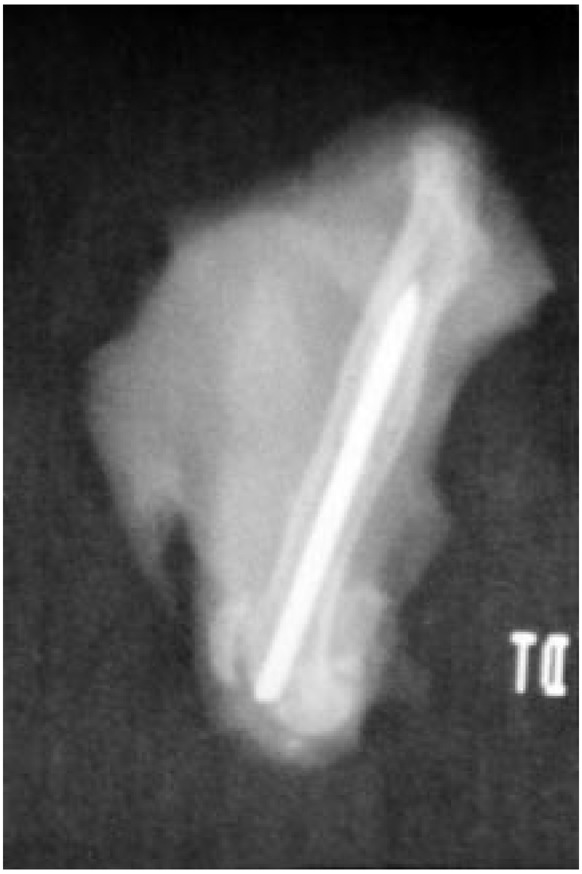
TABLE V Results at 2 months. Comparison between metal pins, PLA pins and ossatite pins

2 Months rat	Pin	Radiology		Macroscopic Appearance		Histology	
		L	R Fracture	L	R Fracture	L	R Fracture
8	Metal		CAL 3 REAC 0 R –		Haematoma		BC 3 CM 0 Rb 1 Rst 1
10	Metal		CAL 1 REAC 0 R –				BC 1 CM 1 Rb 1 Rst 1 INFECTION
12	Metal		CAL 3 REAC 0 R +				BC 2 CM 1 Rb 1 Rst 0
13	Metal		CAL 3 REAC 0 R +		Haematoma		BC 2 CM 1 Rb 1 Rst 1
14	Metal		CAL 3 REAC 0 R –				BC 3 CM 1 Rb 1 Rst 1
35	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –			Rb 0 Rst 0	BC 2 CM 1 Rb 1 Rst 0
43	Polylactide	REAC 0 R –	CAL 1 REAC 0 R –			Rb 1 Rst 0	BC 2 CM 2 Rb 1 Rst 1
45	Polylactide	REAC 0 R –	CAL 1 REAC 0 R –			Rb 0 Rst 0	BC 2 CM 1 Rb 1 Rst 1
51	Polylactide	REAC 0 R –	CAL 1 REAC 0 R –			Rb 0 Rst 0	BC 2 CM 1 Rb 1 Rst 1
52	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –			Rb 0 Rst 0	BC 2 CM 1 Rb 1 Rst 1
		Fracture	No fracture	Fracture	No Fracture	Fracture	No Fracture
55	Ossatite	CAL 3 REAC 0 R –	REAC 1 R –			BC 2 CM 1 Rb 1 Rst 0	Rb 1 Rst 0
56	Ossatite	CAL 1 REAC 1 R –	REAC 0 R –			BC 2 CM 1 Rb 1 Rst 1	Rb 1 Rst 0
57	Ossatite	CAL 1 REAC 1 R –	REAC 1 R –	Angulation granuloma of knee		BC 2 CM 1 Rb 1 Rst 0	Rb 1 Rst 0
58	Ossatite	CAL 1 REAC 0 R –	REAC 1 R –	Angulation		BC 1 CM 2 Rb 0 Rst 1	Rb 1 Rst 0
59	Ossatite	CAL 3 REAC 1 R –	REAC 1 R –		Granuloma	BC 3 CM 1 Rb 1 Rst 0	Rb 1 Rst 0

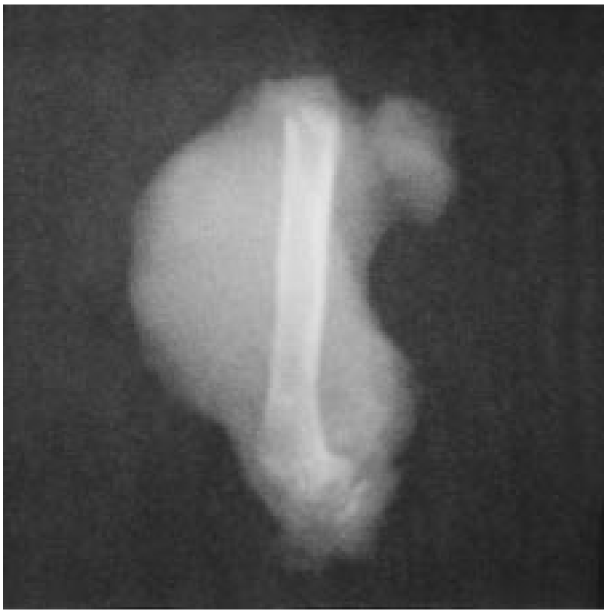
bone consolidation of a diaphyseal fracture osteosynthesized by a polylactide or hydroxyapatite pin and the tolerance of intramedullary implantation of these materials. The rats were grouped as a function of the time of death. At autopsy, we studied the macroscopic appearance, recording all lower limb or distant abnormalities. We observed four cases of pin expulsion, metal in every case, fracture of Ossatite® pins (nine cases), infection (one case), haematoma (three cases) and inflammatory granuloma at the site of entry of the pin (twice with the polylactide pin, four times with the Ossatite® pin). Two rats died 2 and 4 days before the planned date of death, but their thighs were able to be removed under the same conditions as for the other rats, allowing them to be included in the study.

We observed progressive consolidation of femoral fractures osteosynthesized by a metal pin. This consolidation was obtained between 2 and 6 months. Similar results were obtained with polylactide pins. However, in 10 rats, the Ossatite® pin fractured or bent, causing misalignment. Callus formation nevertheless occurred normally, but remained of poor quality. Only one rat had consolidated at 2 months and three rats had consolidated at 5 to 6 months. Chondroid metaplasia was frequent and severe, confirming pseudarthrosis in the non-consolidated cases. It is reasonable to suppose that better quality callus was obtained when a PLA pin was used, as chondroid metaplasia, which reflects the persistently cartilaginous part of the callus, was absent at 6 months with PLA pins, but was more frequent and more severe after the same time when a metal pin was used. This is in line with the study by Viljanen [19], who demonstrated the superiority of poly-L-lactid acid (PLLA) screws over metal screws in a study in rabbits comparing these two types of osteosynthesis. Based on analysis of computed tomography and magnetic resonance images, he found that PLLA screws induced less reaction around the material than metal screws. This reaction was due to the rigidity of metal screws which induced more constraints on bone, while the less rigid PLA screws allowed better adaptation. A similar explanation can be proposed for our results. Three cases of infection and four cases of expulsion of metal pins from the proximal fragment were observed in the series of 20 control rats, while, in the group treated with PLA pins, there was no infection and only one PLA pin had been expelled by 2 mm at 6 months. Resistance to infection was satisfactory, in line with the studies by Williams [20, 21] and Pavan *et al.* [22].

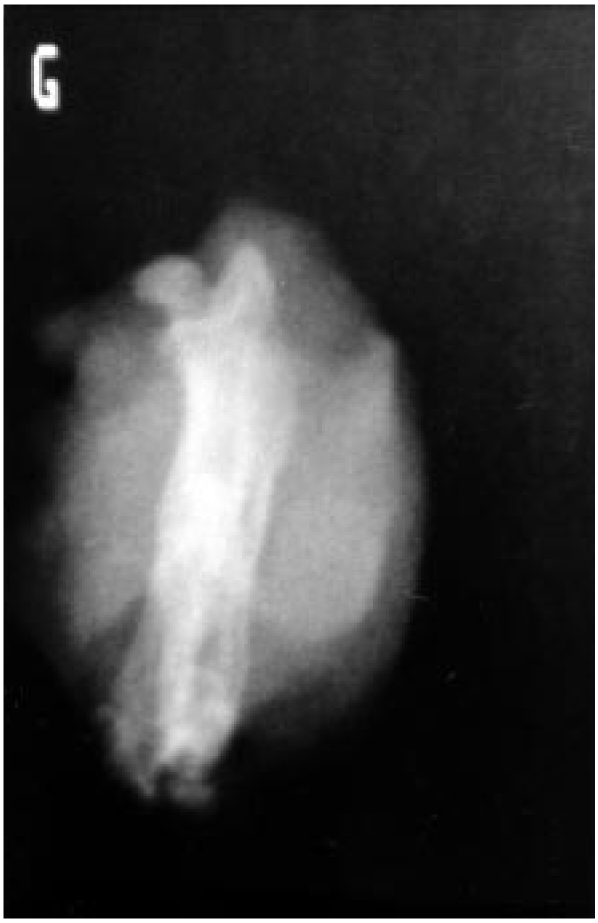
Many experimental studies have been conducted to test polyglycolide or polylactide pins, screws or plates. Kulkarni *et al.* [23] used PLLA pins in mandibular fractures in dogs. Consolidation was equivalent to that observed in the control group, treated with metal pins. Tunc *et al.* [24] also obtained consolidation of calcaneus osteotomy in Beagle dogs using PLA screws. PLA



(a)



(b)



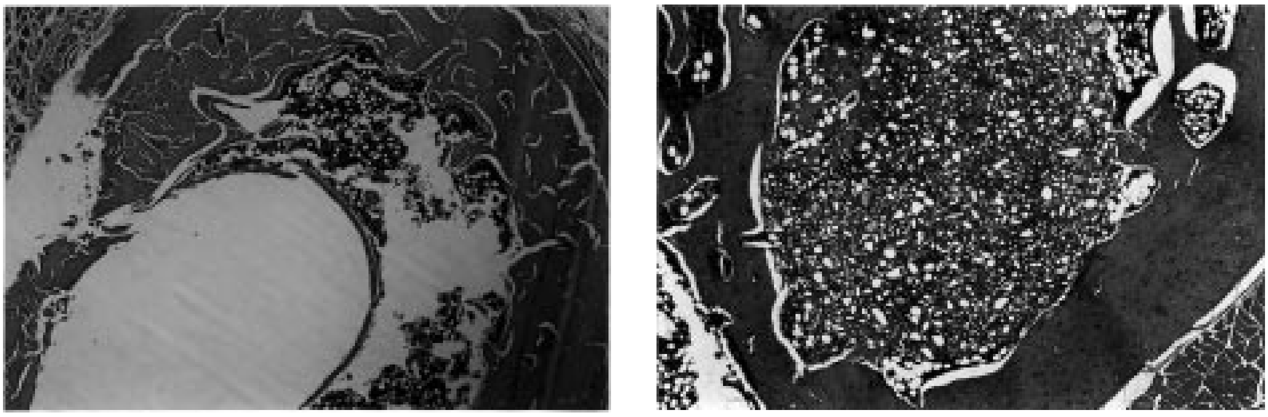
(c)

Figure 1 (a) X-ray at 6 months: the union is obtained with metal pin. (b) X-ray at 6 months: union by PLA pin. (c) X-ray at 6 months: union by Ossatite® pin.

screwed plates ensured consolidation of mandibular fractures in dogs and sheep [25, 26]. Other studies on consolidation of distal femoral osteotomy in rabbits confirmed these good results with polyglycolide pins [27] or poly-D-L-lactid acid (PDLLA) or PDLLA/PLLA screws [28]. Pihlajamäki *et al.* [29] conducted the same study in 20 rats with a follow-up of 24 weeks and obtained consolidation and good biocompatibility in 15 cases. Getter *et al.* [14] used PLA screws and plates to treat mandibular fractures in six dogs and obtained consolidation in 4 to 6 weeks.

Implantation of polyglycolide pins through the growth caltilage demonstrated the good tolerance of these pins and the absence of epiphysiodesis. Donigian [30] did not find any significant difference between PLA screws and PDS pins in the treatment of Salter IV fracture of the lower extremity of the femur in goats. This suggests the possibility of a diaphyseal fracture osteosynthesis technique by centromedullary pinning through the growth cartilage in children. The operative technique would therefore be facilitated for absorbable pins which are not sufficiently elastic to be introduced via the metaphysis without breaking.

Clinical trials mainly report the results of treatment of



(a) (b)

Figure 2 (a) Histological overview of bone–pin interface. This sample shows the intramedullary PLA pin and the callus at 6 months. (b) Histological overview. This sample shows the intramedullary Ossatite® pin and the new ossification into the hydroxyapatite and the callus at 6 months.

TABLE VI Results at 6 months. Comparison between metal pins, PLA pins and ossatite pins

6 Months rat	Pin	Radiology		Macroscopic Appearance		Histology	
		L	R Fracture	L	R Fracture	L	R Fracture
1	Metal		CAL 3 REAC 0 R –				BC 3 CM 1 Rb 1 Rst 0
2	Metal		CAL 2 REAC 0 R –		Death		BC 3 CM 2 Rb 0 Rst 0
3	Metal		CAL 3 REAC 0 R –				BC 3 CM 0 Rb 0 Rst 0
5	Metal		CAL 3 REAC 0 R –				BC 3 CM 0 Rb 0 Rst 0
7	Metal		CAL 3 REAC 0 R –		Death (haemorrhage right ear)		BC 3 CM 1 Rb 0 Rst 0
36	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –			Rb 1 Rst 0	BC 3 CM 0 Rb 1 Rst 0
38	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –			Rb 0 Rst 0	BC 3 CM 1 Rb 1 Rst 1
41	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –			Rb 0 Rst 0	BC 3 CM 0 Rb 0 Rst 0
46	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –			Rb 0 Rst 0	BC 3 CM 0 Rb 1 Rst 1
47	Polylactide	REAC 0 R –	CAL 3 REAC 0 R –		Pin expelled by 2 mm	Rb 0 Rst 0	BC 3 CM 0 Rb 0 Rst 0
		Fracture	No fracture	Fracture	No fracture	Fracture	No Fracture
60	Ossatite	CAL 0 REAC 1 R –	REAC 0 R –			BC 0 CM 2 Rb 1 Rst 1	Rb 0 Rst 0
61	Ossatite	CAL 3 REAC 0 R –	REAC 0 R –			BC 3 CM 0 Rb 0 Rst 0	Rb 0 Rst 0
62	Ossatite	CAL 3 REAC 0 R –	REAC 0 R –			BC 3 CM 0 Rb 1 Rst 0	Rb 0 Rst 0
63	Ossatite	CAL 3 REAC 0 R –	REAC 0 R –			BC 3 CM 0 Rb 1 Rst 0	Rb 0 Rst 0
64	Ossatite	CAL 0 REAC 1 R – Misalignment	REAC 0 R –			BC 1 CM 1 Rb 0 Rst 1	Rb 0 Rst 0

epiphyseal fractures [11, 24, 31–37] or facial bones in adults, using polylactide or polyglycolide implants. However, we did not find any published studies using hydroxyapatite pins. Böstman [11] used PGA pins in 286 patients with ankle fractures and reported 18 inflammatory reactions, corresponding to a nonspecific histological foreign body reaction. In another study [31] in 516 patients with wrist or patella fractures, he reported a 1.7% infection rate and a 1.2% reoperation rate. Only Benz *et al.* [2] used polyglycolide pins in children to treat epiphyseal fractures with good results. Several studies concerning hydroxyapatite used blocks or granules [4, 7, 9] to fill bone defects. Other studies evaluated the use of hydroxyapatite to cover metal material in order to improve its bone anchorage [3, 38].

The excellent biocompatibility of PLA pins has already been reported in the literature [27, 33, 36, 39–44]. Our study confirms this good tolerance of polylactide pins, even in the case of intramedullary implantation, as demonstrated by the absence of reaction in rats with or without a fracture, for 15 days to 6 months. A fibrous reaction occurs around the pin which gradually becomes organized into a ''neocapsule'' around the pin, as described by Vert *et al.* [45]. No soft tissue radiological reaction was observed in the absence of fracture and in only three out of 40 cases in the presence of fracture. The tolerance of PLA was always excellent, and much better than that of PGA, as foreign body reactions were observed with PGA pins in sheep by Weiler *et al.* [46] and with PGA pins and screws in rabbits by Päivärinta *et al.* [34]. Resorption of PLA is also better. Getter *et al.* [14] observed degradation of PLA screws and plates in 32 to 40 weeks, while the pins that we used had not been absorbed at 6 months.

A marked bone reaction was observed with Ossatite® pins with reorganization of cortical bone, which had a thinned appearance on X-ray, particularly in the group of rats sacrificed at the first month. This reaction subsequently faded and only persisted in the non-consolidated rats at the sixth month, at which time bone formation was observed inside the pin.

5. Conclusions

Polylactide pins allowed consolidation within the same time interval as metal pins. The callus appeared to be of better quality and tolerance was excellent. These results encourage us to propose this material for osteosynthesis of diaphyseal fractures of the upper limb in children, but the material and instrumentation has yet to be designed.

In contrast, hydroxyapatite in the form of Ossatite® did not achieve satisfactory consolidation of femoral fractures in rats. This was due to the solvent, which failed to ensure sufficiently prolonged rigidity of the material. Further research is required to develop a new composition. Ossatite® has good biocompatibility with bone. Its use must therefore be reserved for the repair of bone defects.

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