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Degradative and mechanical properties of a novel resorbable plating system during a 3-year follow-up in vivo and in vitro

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Abstract We tested the tissue reactions and mechanical strength of a novel biodegradable craniomaxillofacial plating system, Inion CPS™, in the course of degradation. Plates and screws composed of L-lactide, D-lactide and trimethylene carbonate were implanted to the mandible and dorsal subcutis of 12 sheep. The animals were sacrificed at 6–156 weeks. Histological evaluation was done using paraffin and methylmetacrylate techniques. Degradative and mechanical properties during the follow-up were measured both of in vivo and in vitro implants. In light microscopy, the in vivo implant material began to fragment at 52 weeks and could not be detected at 104 weeks. No significant foreign body reactions were seen in the mandibles. The dorsal subcutis disclosed mild reactions, which were, however, not of clinical significance. The implants in vitro maintained their entire mass for 26 weeks and lost 63–80% of the mass by week 104. The inherent viscosity of the implants in vitro and in vivo diminished uniformly. The screws retained their shear strength for 12–16 weeks. The plates maintained their tensile strength for at least 6 weeks. The maximum capacity of the plates in 3-point bending tests diminished gradually by 87% in 26 weeks. In conclusion, the plates and screws examined maintain adequate strength for the healing period of a bone fracture or osteotomy, producing no harmful foreign body reactions.

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Introduction

The main benefits of biodegradable plates and screws are the avoidance of implant removal, absence of imaging interference and lack of intracranial implant migration [1], while their mechanical durability and possible adverse tissue reactions in the course of degradation have represented the greatest concerns. With more advanced systems becoming available, maxillofacial applications for these resorbable fixation devices have also become more frequent [2].

The optimal polymer or copolymer for facial bone fixation has yet to be determined, although it appears that blends of different polymers or copolymers may be preferred due to the possibility to combine many favourable polymer properties into a single material [1]. Most of the degradable plating systems are based on different copolymers of polylactic acid (PLA) isomers and polyglycolic acid (PGA), with, for instance, trimethylene carbonate (TMC) as a minor constituent. PGA is hydrophilic and

degrades quickly in spite of its highly crystalline structure [3]: it loses virtually all of its strength in 6 weeks and all its mass within 3–12 months [4, 5].

Polylactic acid is hydrophobic and degrades more slowly than PGA. The high stereoregularity of PLA isomer PLLA renders it an easily crystallisable material, however, PLLA implants may exhibit different solid state morphologies based on differences in the manufacturing methods [6, 7]. Moreover, PLA isomers tend to form crystals in the course of degradation [8], which further slows down the process with a complete resorption time for pure PLLA of up to 6 years [3, 9]. The crystallinity of pure PLLA can be significantly lowered by adding small amounts of D-stereoisomer to the L-chain [10]. Copolymerization of L-lactic acid with at least 15 mole-% D-lactic acid gives intrinsically amorphous polylactides (PLDLLA), i.e., materials that are unable to crystallize even during annealing because of irregular distribution of repeating units of L-lactic and D-lactic acid isomers [11, 12]. To tailor resorption times and mechanical behaviour, biodegradable polymers are typically blended or co-polymerised. The mechanical characteristics of the hard and brittle PGA and PLLA can be toughened either by incorporating more flexible TMC units into the polymer backbone, or by blending rubbery copolymers containing TMC.

In addition to polymer structure, the biomechanical strength and degradation characteristics of a plating system depend on, for example, the specific implant design, manufacturing processes and sterilisation methods. Therefore, biomechanics and degradation need to be assessed separately for each new plating system. The biocompatibility and host tissue responses to the polymer implanted need to be explored down to the very late stages of biodegradation. Consequently, long-term in vivo degradation studies are required whenever crucial material characteristics are altered.

A novel plating system, Inion CPS™, for craniomaxillofacial indications is composed of blends of substantially amorphous copolymers incorporating L-lactide, D-lactide and TMC monomers. The present study was designed and conducted to test the mechanical strength and tissue reactions of the system in the course of degradation; these have not been investigated earlier. We hypothesised that the strength of the plates and screws would be almost intact at 6 weeks and nearly nil at 26 weeks, that degradation would be somewhat faster in vivo than in vitro and that tissue reactions observed by histological techniques would be local, mild and of no clinical significance.

Materials and methods

The study protocol was approved by the Tampere University Animal Trial Committee and by the Provincial Administrative Board, according to Finnish law. The trial was documented according to the Good Clinical Practice (GCP) guidelines as applicable.

Animals and implants

The study animals were 12 skeletally mature female Finnish landrace sheep. The animals were clinically examined by a veterinarian to confirm good health before the study initiation. At the first check, Clostridium vaccination (Heptavac, Intervet Ltd., Milton Keynes, UK) was given to avoid infections caused by Clostridium chauvoei, Cl. perfringens B, C and D as well as Cl. septicum, Cl. tetani and Cl. Novyi—the vaccine does not have any known effects on bone healing or the biodegradation of polymer implants. Two animals were sacrificed at each check point: 6, 12, 26, 52, 104 and 156 weeks postoperatively.

The implants were plates (Figs. 1 and 2) and screws from the Inion CPS™ product range (Inion Ltd., Tampere, Finland), which is CE marked and FDA approved for human use. The implants were manufactured and quality checked according to the standard methods and requirements of the manufacturer. All the implants were sterilised with γ-irradiation (minimum dosage 25 kGy). The exact composition and number of the implants used in the in vivo and in vitro experiments are shown in Tables 1 and 2, respectively. The manufacturer delivered the instruments required—i.e., drill bits and screw drivers sterilised with an autoclave or γ-irradiation.

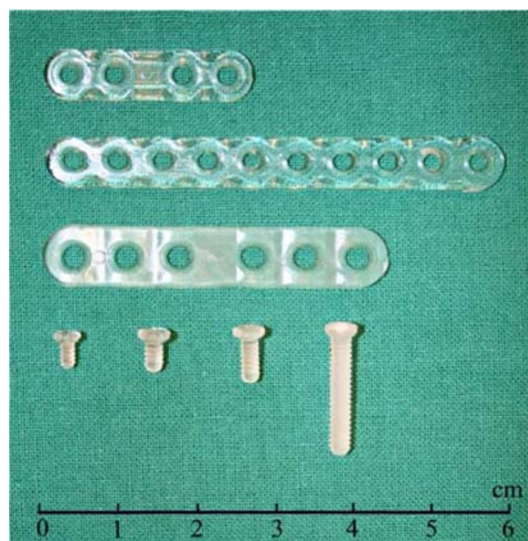

Fig. 1 The implants used in the study: extended 2.0 mm system 4-hole plate (top), 2.0 mm system 10-hole plate, extended 2.5 mm system 6-hole plate, 2.0 mm × 5 mm screw (bottom left); 2.5 mm × 6 mm screw; 2.5 mm × 8 mm screw; and 2.8 mm × 18 mm screw (bottom right)

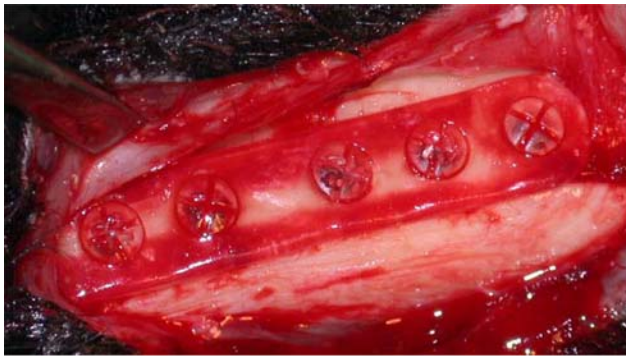

Fig. 2 A plate of the 2.5 mm system implanted on the mandible

Table 1 Proportion of composite monomers in the copolymer blends used to manufacture the implants in the study

Description	Composition %		
	D-lactide	L-lactide	TMC
2.0 mm × 5 mm screw	24	70	6
2.5 mm × 6 mm and 8 mm screws	17	78.5	4.5
2.8 mm × 18 mm screw	17	78.5	4.5
2.0 mm system 4 and 10 hole plates	24	70	6
2.5 mm system 6-hole plate	16	78	6

TMC, trimethylene carbonate

Preoperative procedure

The health status of each animal was observed daily for the preoperative week. Water was given *ad libitum*, while feed was withheld for 24 h prior to the surgery.

Anaesthesia

Preoperatively, the sheep were given 1 mg atropine sc and benzylpenicillin procaine 15 mg/kg sc. The sheep were anaesthetised with medetomidine 0.030 mL/kg im and ketamine hydrochloride 1.5 mg/kg im. Every 30 min, the sheep received 50% of the original dose of medetomidine and ketamine hydrochloride intravenously as necessary. 2% lidocaine/epinephrine was used for local anaesthesia.

Postoperatively, benzylpenicillin procaine 15 mg/kg sc was administered for 5 days and ketoprofen 5 mg/kg im once a day for 3 days.

Operative procedure

The right side of the mandible of each sheep was shaved, washed and scrubbed with chlorhexidine gluconate solution. A skin incision was made below the lower border of the mandible in the region of the diastema and carried through the periosteum. The periosteum on the buccal side

Table 2 Total number of implants used for each experiment during the entire course of the study

	Screws			Plates		Total
	2.0 mm	2.5 mm	2.8 mm	2.0 mm	2.5 mm	
Mass loss						
in vitro (7)		21	21	21	21	84
Inherent viscosity						
in vitro (11)		11	11	11	11	44
dorsal subcutis		12[a]	12[a]	12[a]	12[a]	48
mandible	36	48		12	12	108
Shear test						
in vitro (8)		40	40			80
dorsal subcutis		40	20			60
Tensile test						
in vitro (8)				40	40	80
dorsal subcutis				20	20	40
3-point bending						
in vitro (8)				40[b]		40
dorsal subcutis				24[b]		24
Histology						
dorsal subcutis		12	12	12	12	48
mandible	12	24		12[c]	12[c]	60
Total	48	196	104	116	116	580

The number of follow-up points for each in vitro test is shown in parentheses. Two sheep were sacrificed at six different points in time for the in vivo experiments

[a] The same implants were used for mechanical tests

[b] Parts of the plates were also used for tensile test

[c] Parts of plates were analysed for inherent viscosity

of the mandible was elevated. On the left side, a 2.5 mm system 6-hole plate was fitted on the mandible and fastened with six 2.5 mm × 6 mm screws. A 2.0 mm system 4-hole plate was fitted on the right side with four 2.0 mm × 5 mm screws.

A large area of the dorsal skin of the sheep was shaved, washed and scrubbed with chlorhexidine gluconate solution. The implants to the dorsal subcutis (Table 2) were divided into several groups and introduced subcutaneously through stab incisions.

The wounds were closed in layers using absorbable sutures.

Postoperative measures

The sheep were given soft food for three days postoperatively and hay thereafter. The animals were kept in indoor pens for seven days before moving them outdoors. For the first seven postoperative days, the temperature of each animal was measured, and the sheep were observed for neurological symptoms, movement and appetite. The operation sites were scrutinised for infection, inflammation, swelling and wound dehiscence.

In vivo samples

After euthanasia, the mandible was carefully dissected and inspected macroscopically. Two kinds of mandible specimens were obtained for histology. First, the soft tissue on the buccal side of the mandible covering one half of the implanted plates was removed, and the surface towards the implants was marked with tissue dye. After fixation in 4% phosphate-buffered formaldehyde (pH 7.4), the specimens were embedded in paraffin. Paraffin sections were cut at 5 μm and stained with hematoxylin and eosin (HE). Thereafter, the plate sections left exposed on the mandible were removed for testing of inherent viscosity at weeks 6–26.

Secondly, the remaining implant areas and underlying mandibles, still covered by intact soft tissue, were removed and transferred into formaldehyde. After fixation, the specimens were dehydrated and embedded in methylmethacrylate. Sections of 150 μm were cut perpendicularly to the mandible using a low-speed diamond saw (Isomet, Buehler, Inc., Illinois, USA). All samples were ground flat and polished by hand (SiC papers from 800 grit to 4000 grit size). The sections were mounted on objective slides and stained with HE. The tissue-implant interface was investigated with a light microscope to observe tissue reactions and implant degradation.

Implants from the dorsal subcutis were removed with surrounding soft tissue. After fixation in formaldehyde, the specimens were embedded in paraffin. Paraffin sections were cut at 5 μm and stained with HE. At 104 weeks, implants were not detectable macroscopically. For this reason, the areas with more or less macroscopical scar formation were removed and carefully dissected for light microscopic investigation. A subset of the dorsal implants was tested for mechanics and degradation at up to 52 in vivo weeks. Figures 3 and 4 present the histological sections.

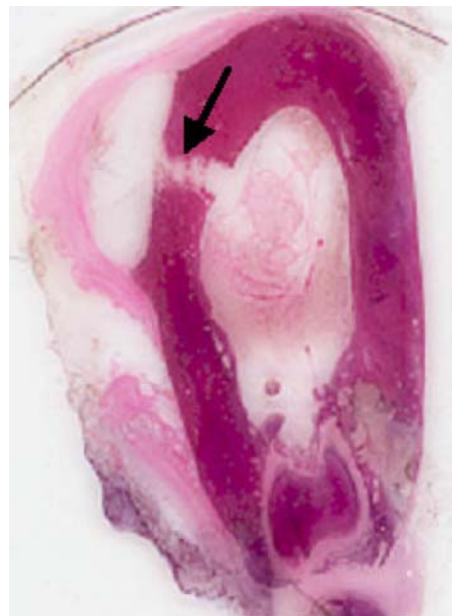

Fig. 3 A 2.0 mm plate on the side of the mandible is in one piece at 24 weeks after implantation. The fastening screw (arrow) and fibrous capsule are clearly visible. Digital scanning of HE-stained methacrylate section

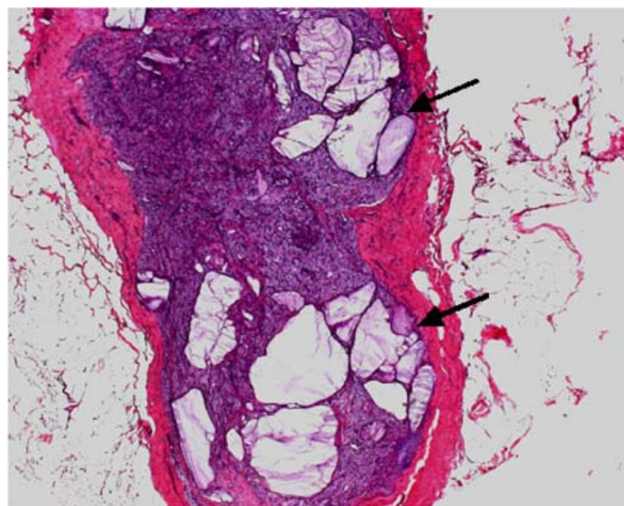

Fig. 4 Fragmented and globular implant material (arrows) in the dorsal subcutis 52 weeks after implantation of a 2 mm plate. The implant material is surrounded by a fibrous capsule, and granulomatous foreign body reaction is visible. Original magnification was 40×

In vitro samples

The in vitro samples of equal products, as in the in vivo implantation, were placed in plastic vials with approximately 10 mL phosphate-buffered saline of pH 7.4 ± 0.2. The weights of the implant samples were the following: 2.0 mm system 10-hole plate 0.49 g, 2.5 mm system 6-hole plate 0.54 g, 2.5 mm × 8 mm screw 0.05 g and 2.8 mm × 18 mm screw 0.13 g. The samples were subjected to aging in an incubator at 37 ± 1 °C for up to 104 weeks. The phosphate-buffered saline was changed every 2 weeks, with the pH of the solution being checked every time.

The follow-up of the in vitro samples comprised of 10 checkpoints: 0, 3, 6, 9, 12, 16, 20, 26, 52 and 104 weeks; however, not all of these were used for each experiment (Table 2). The baseline (0 weeks) measurements were performed after keeping the samples in water for 24 h. Degradation of polymer devices was analysed by measuring the inherent viscosity of the polymer, the remaining mass and the mechanical strength of the devices, according to the in vitro experiment recommendations by FDA.

Remaining mass was assessed at weeks 0–104. Three samples of each product were vacuum dried at each follow-up point, and mean ± standard deviation (SD) of the remaining mass (%) was calculated as a comparison to the initial mass (Fig. 5).

Inherent viscosity, a measure of molecular weight, was assessed with Lauda viscometer (Lauda, Lauda-Königshofen, Germany) using Schott Ubbelohde capillary viscometer tubes at weeks 0–52. The samples were prepared by dissolving 20.0 mg of the polymer sample in 20.0 mL of chloroform. The measurements were performed at 25 °C. A calibrated viscometer tube was chosen according to ISO 3105/DIN51562. The apparatus measured three

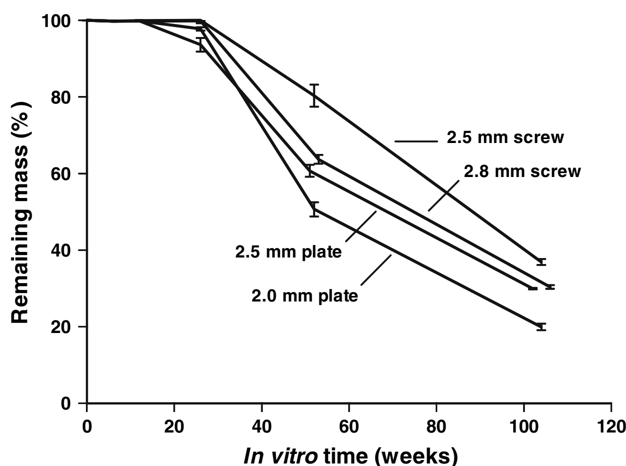

Fig. 5 Remaining mass (mean ± SD) of the plates and screws in vitro as a function of time. The implants were immersed in phosphate-buffered saline for the entire follow-up period at pH 7.4, 37 °C

inherent viscosity values (mean is shown) for each implant type at each checkpoint (Fig. 6).

Mechanical tests

The plates were subjected to tensile and three-point bending tests and the screws to shear strength testing in a calibrated Zwick Z020/TH2A, class 1 universal materials testing machine (Table 2). The shear tests were carried out according to the guidelines of the standard BS 2782: Method 340B. A shear test determines the maximum shear load capacity of the screws. The screw samples were loaded with a constant speed of 5 mm/min in a shear fixture until fracture. Mean ± SD of maximum load (in Newtons, N) were calculated (Fig. 7a).

Tensile testing (standard ASTM D638M) was carried out to determine the yield load (N, mean ± SD in Fig. 7b) of the plates. The yield load was determined as the load at the first point on the stress–strain curve at which an increase in strain occurs without an increase in stress. The 2.5 mm plates were tested in one piece. The 2.0 mm plates were cut to pieces of 4 and 6 holes. The former piece was used in the three-point bending test, and the latter one for tensile testing. The plates were fixed to the stainless steel testing fixture with three metal pins through the holes of the plate at both ends of the plate. The plates were loaded with a constant speed of 5 mm/min until failure.

The three-point bending test was performed to determine the load-carrying capacity of the plates as advised in standards ISO 178:2001 and ASTM D790M. The yield load was determined as the load at the first point at which the load does not increase with an increase in deflection. Only the 10-hole 2.0 mm system plates were tested, since the 6-hole 2.5 mm system plates used in the study were too short to take samples for both tensile and 3-point bending tests. The plates were laid on the lower supports and loaded with the loading nose in the middle of the supports with a constant speed of 5 mm/min. The support span was 12 mm and the radii of the supports and the loading nose 2 mm. Maximum load (N) was recorded, and mean ± SD are shown in Fig. 7c.

Results

All the 12 animals recovered well from the operations, and all the wounds healed with no infections. The sheep remained healthy for the entire course of the study.

Macroscopical inspection

Upon macroscopical examination after euthanasia, the wounds were barely visible at 6 weeks and could not be detected thereafter. No signs of inflammation or discharge in the operation sites were observed at any of the follow-up

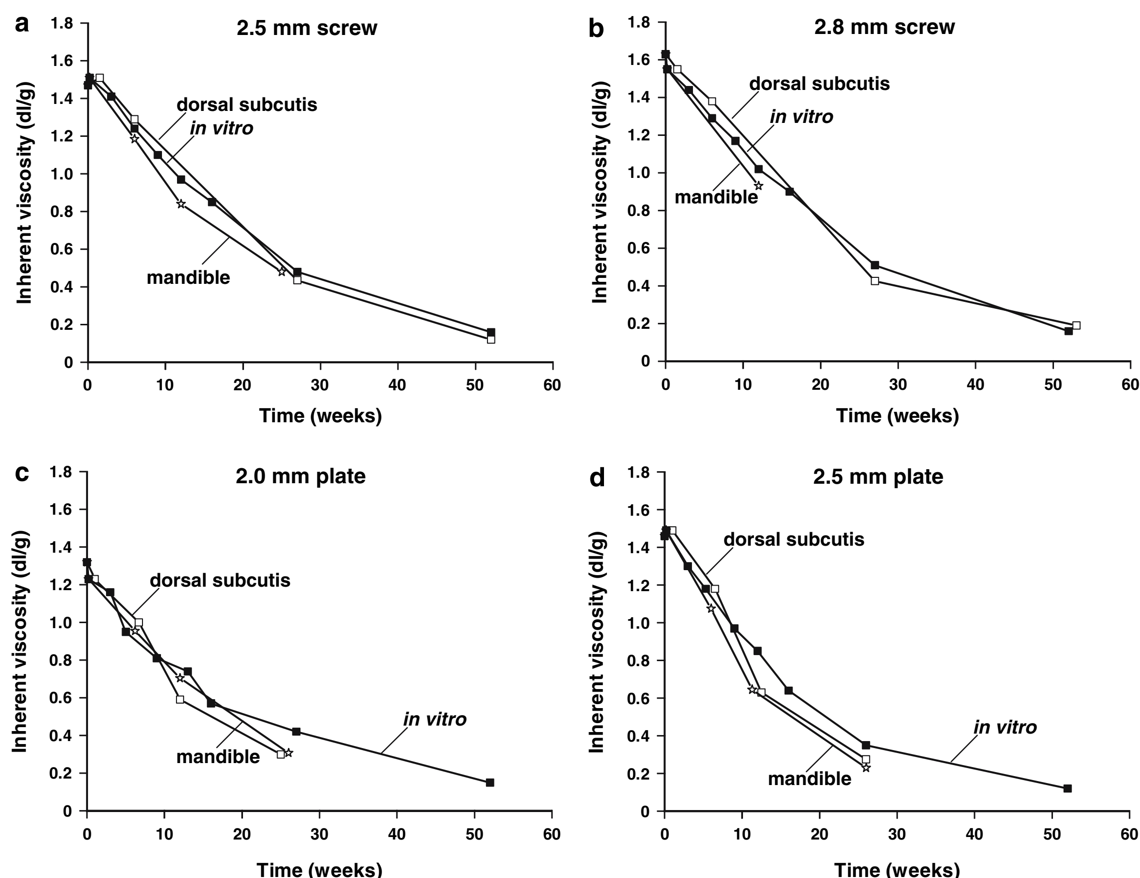

Fig. 6 Inherent viscosity of the polymers of the (**a**) 2.5 mm screws, (**b**) 2.8 mm screws, (**c**) 2.0 mm system plates and (**d**) 2.5 mm system plates in the course of the follow-up weeks. The data points for implants in vitro (phosphate-buffered saline at pH 7.4, 37 °C), in dorsal subcutis and on the mandible are shown

points. None of the plates or screws implanted on mandibles had migrated from the implantation sites. The plates retained visual transparency for up to 6 weeks, after which they appeared matt. At weeks 6–52, the implants were covered with soft tissue capsules. At 26 weeks, the 2.5 mm plates were partly fragmented, while the 2.0 mm plates were still unbroken. At 52 weeks, the plates on the mandible of one of the sheep were fragmented and soft, while the plates of the other sheep were covered by bone. At 52 weeks, the dorsal screws were soft and bent, the 2.0 mm plates were soft but mostly unbroken, and the 2.5 mm plates were completely fragmented. At 104 weeks and 156 weeks, no implant material was found either on the mandibles or dorsal subcutis. On mandibles, there was bone on the former locations of the implants. One of the sheep presented scar tissue in the implantation site in the dorsal subcutis at 104 weeks.

Histology

In methylmethacrylate-embedded specimens, the HE staining disclosed the implants, covered by soft tissue capsules, on the buccal side of the mandibles from 6 weeks to 26 weeks (Fig. 3). At 52 weeks, the implant material became fragmented and formed more or less globular structures surrounded by a fibrous capsule. In some areas, the fibroblasts and connective tissue fibres invaded the surface of the implant. Slight infiltration of inflammatory cells was present in one animal, but in other animals no signs of inflammation or foreign body granulomatous reactions were seen at any point. At 104 weeks, the implants on mandibles were not detectable. In the corresponding paraffin-embedded tissue samples, separated from the buccal side of the implants, tissue reactions were stronger (Table 3). From 6 weeks to 26 weeks, scarce or moderate bone formation was seen in the vicinity of the implants of a few animals (Table 3).

In the dorsal subcutis, the implants were first surrounded by a quite uniform fibrous layer. Mild to moderate inflammatory reactions were found around the implants. At 26 weeks, the implants became fragmented, and from 52 weeks onwards, fibroblasts and connective tissue fibres invaded the implants. At 52 weeks, the implant material was completely fragmented and formed globular structures

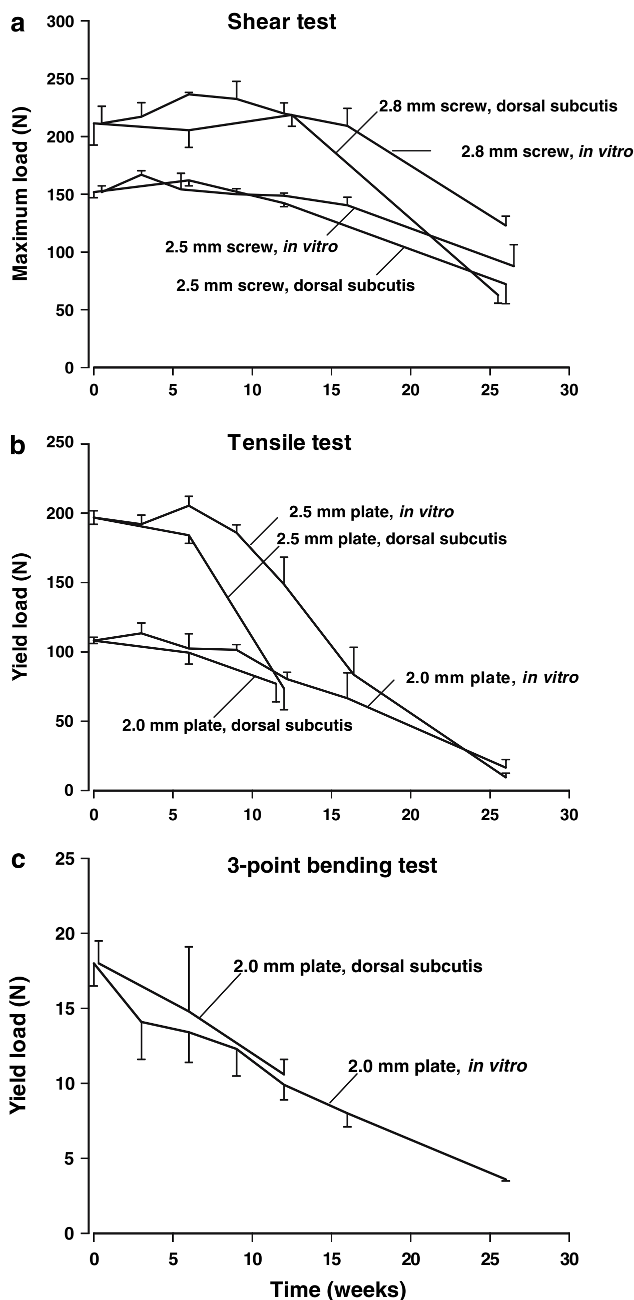

Fig. 7 (**a**) Shear strength (N, mean ± SD) of 2.5 mm and 2.8 mm screws in vitro (phosphate-buffered saline at pH 7.4, 37 °C) and in dorsal subcutis as a function of weeks. (**b**) Tensile yield load (N, mean ± SD) of 2.0 mm and 2.5 mm plates in vitro and in dorsal subcutis. (**c**) The yield load (N, mean ± SD) of 2.0 mm plates kept in vitro and in dorsal subcutis in three-point bending test

(Fig. 4). At 104 weeks and 156 weeks, implants could not be found macroscopically, but in the areas of scar formation, implant material could be seen microscopically at 104 weeks.

Degradation

All the four implant types essentially maintained their entire mass for the first 26 weeks in vitro (Fig. 5). Thereafter, the implants lost mass more or less linearly down to 20–37% of the original mass by week 104.

The inherent viscosity of the implants in vitro, on the mandible and in dorsal subcutis diminished relatively uniformly for each product (Fig. 6). The screws showed a rather linear initial decrease in inherent viscosity; the trend was cut at week 26. Thereafter, another linear period of decline with a flatter slope followed until the end of the follow-up. For the plates, the corresponding change in the slope occurred between weeks 12 and 26.

Mechanical tests

The screws in vitro retained their initial shear strength (Fig. 7a) for 16 weeks, but had lost 42% at 26 weeks. The screws in vivo lost 52–70% of their original shear strength between weeks 12 and 26; this parameter was not assessed at 16 weeks.

The tensile strength of the 2.5 mm plates decreased rapidly after 6 weeks, particularly in vivo (Fig. 7b). The 2.0 mm plates, on the contrary, lost their tensile rigidity at a slower pace: the initial tensile strength of 2.0 mm plates was about half of the values for 2.5 mm plates, while the difference was already negligible at 12–16 weeks.

Three-point bending data is only available for 2.0 mm plates (Fig. 7c); the strength in vitro weakened gradually by 87% in 26 weeks, and the in vivo data at 6 weeks and 12 weeks coincided well with the corresponding values in vitro.

Discussion

The histological responses induced by the implants on the mandibles were mild during the entire degradation process, with some variation between concurrent animals (Table 3). The tissue reactions in the dorsal subcutis were also mild, but stronger than those seen on the mandibles. These results agree with recent studies [13–16]. The previously reported sterile sinus formation, prolonged degradation, osteolysis or other considerable adverse reactions—not observed in the present study—have almost solely been connected with older-generation implants with high PGA content, bulky size or high initial degree of crystallinity in the polylactide-based devices [17, 18].

The degradation of biodegradable polymers starts with hydrolysis cutting the molecular chains into shorter fragments. This decreases the molecular weight of the implants

Table 3 Histological findings (paraffin embedded samples) in the mandible for control locations as well as for Inion CPS™ 2.5 mm and 2.0 mm systems at 6–104 weeks

Sample	Inflammation	Foreign body reaction	Macrophages	Giant cells	PMNs	Eosinophils	Bone formation
Control							
6 weeks	0/0	0/0	0/0	0/0	0/0	0/0	0/0
12 weeks	0/0	0/0	0/0	0/0	0/0	0/0	0/0
26 weeks	0/0	0/0	0/0	0/0	0/0	0/0	0/0
52 weeks	0/0	0/0	0/0	0/0	0/0	0/0	0/0
104 weeks	0/0	0/1	1/2	0/1	0/0	0/0	0/0
CPS 2.5 mm plate and screws							
6 weeks	0/1	0/1	1/1	0/1	0/0	0/0	0/0
12 weeks	0/0	0/0	0/1	0/0	0/0	0/0	0/*
26 weeks	0/1	0/1	0/1	0/0	0/0	0/0	0/*
52 weeks	0/1	0/3	0/0	0/0	0/0	0/0	0/0
104 weeks	0/1	0/1	0/3	0/1	0/0	0/0	0/0
CPS 2.0 mm plate and screws							
6 weeks	0/0	0/0	0/1	0/0	0/0	0/0	0/*
12 weeks	0/0	0/0	0/1	0/0	0/0	0/0	*/0
26 weeks	0/1	0/2	1/2	0/2	0/0	0/1	*/0
52 weeks	0/0	0/0	0/0	0/0	0/0	0/0	0/0
104 weeks	0/0	0/0	0/0	0/0	0/0	0/0	0/0

Scoring of reactions is on the scale 0–3. An asterisk (*) denotes scarce to moderate bone formation alongside the implants. The two sheep sacrificed at each point in time are separated by "/"

PMN = polymorphonuclear neutrophil

directly after either implantation or submerging in phosphate buffer solution [19], as is also clearly seen in our data. In an amorphous polymer, water penetrates the entire structure and shortens the molecular chains all over the device. The mechanical properties of an amorphous polymer remain almost intact as long as the molecular weight exceeds certain critical values yielding a sufficient amount of entanglement points between molecular chains. As the molecular weight is reduced sufficiently, chains start slipping past each other more freely and polymer strength diminishes [3, 19]. In the present plates and screws, a marked decrease in mechanical properties commenced only after some 19–44% of the molecular weight had been lost 6 weeks to 16 weeks into the follow-up.

The screws appeared to retain inherent viscosity longer than the plates, even though the difference was not tested statistically due to the small number of samples. At 12 weeks, the values for screws ranged from 0.84 to 1.02, and for plates from 0.59 to 0.85. This may be explained by slightly differing polymer compositions, but partly also by different geometries: the rounded screws have a smaller surface area to mass ratio than the plates, thus being less exposed to hydrolyzing water.

The total mass of a polymeric device starts declining only after the molecular chains are shortened sufficiently to diffuse out as water-soluble monomers and oligomers. This phase of degradation is primarily due to simple hydrolysis. As the polymer is further hydrolysed, it is eventually fragmented into tiny debris particles, which may be phagocytised by macrophages and histiocytes [3, 19]. The mass of the present plates and screws started to diminish only after 26 weeks in vitro, when the molecular weight had already dropped by roughly 67–76%. Thereafter, the implants lost mass more or less linearly down to 20–37% of the original mass by the week 104.

The present plates seemed to lose mass at a more rapid pace than screws. Again, these differences are probably due to different compositions and geometries. The sequence of losing first molecular mass, then mechanical properties and only thereafter the mass of the device is in concordance with earlier reports [3, 19, 20].

In vivo, the monomers are metabolised in the citric acid cycle to carbon dioxide and water that are secreted from the body via respiration and urine. The role of this enzymatic degradation alongside with passive hydrolysis has been a subject of constant dispute, since the previous data on the degradation differences between in vivo and in vitro is somewhat inconsistent [4, 21–23]. In those two of the present study sheep which were sacrificed at 2 years, particles of implants were not observed microscopically,

except in the dorsal subcutis of one of the sheep. At the same follow-up point, the in vitro plates and screws had 20–37% of the original mass left. It seems that the degradation of these plates and screws occurs similarly in vivo and in vitro during the first year, thereafter, enzymatic reactions expedite the breakdown in vivo in comparison to in vitro. In the present study, histiocytic reaction could not be seen in the thick methylmethacrylate sections, but infiltration of histiocytes came clearly visible in the corresponding paraffin sections (Table 3).

The plates and screws examined retained 70% of their strength for 6–12 weeks in vivo. Since a bone fracture or osteotomy typically heals within 6–9 weeks in the craniomaxillofacial area of adults, the strength retention of these implants is adequate for bone healing. The present evidence affirms the safety and mechanical adequacy of biodegradable devices in low-load-bearing applications, such as in reconstructive procedures performed on the craniofacial skeleton, mid-face, maxilla and mandible.

If a plate is implanted next to a bone, or a screw is fastened inside a bone, it is fairly impossible to extract the implant after a few weeks in situ without tampering with its mechanical properties. On the other hand, the implants located in soft tissue, such as dorsal subcutis, can be removed and tested mechanically. In our data, the implants in dorsal subcutis and on the mandible degraded in a strikingly similar manner, even though the subcutaneous tissue reactions were slightly stronger possibly due to mechanical irritation of loose implants. This gives justification to mechanical testing of only subcutaneous implants. Furthermore, even the in vitro implants lost their molecular mass similarly to in vivo implants, thus supporting the use of the present laboratory model as a surrogate for in vivo degradation analysis.

The fact that merely two sheep were used at each follow-up point is a limitation of the present study. However, this may not distort the data appreciably, since the current in vivo findings form consistent time series.

Conclusions

The biodegradable plates and screws examined maintain adequate strength for the healing period of a bone fracture or osteotomy. No harmful inflammation or foreign body reactions were observed during the degradation process of 3 years.

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