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A strut graft substitute consisting of a metal core and a polymer surface

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Abstract In revision hip replacement surgery cortical strut grafts made of allograft bone are used to augment femoral bone stock and to fix periprosthetic femoral fractures. These struts are made from femoral bone as hemicylinders and are fixed to host bone with cerclage wires. We developed an artificial bone substitute for such strut grafts in order to overcome availability restrictions and potential infectious hazards with allograft bone. The partially biodegradable implant consists of a functionally-graded combination of titanium, polylactide, hydroxyapatite, and calcium carbonate. It is made by manual dip-coating of the metal (after chemical surface treatment) into solutions of polylactide with suspended calcium salts. In this way the titanium core is surrounded by an inner layer of slowly biodegradable poly(L-lactide) with calcium carbonate. The part of the implant that is in contact with the bone consists of rapidly biodegradable poly(D,L-lactide), hydroxyapatite and calcium carbonate. This method leads to an implant which is easily adaptable before the implantation to the geometry of the patient's bone when moderately heated (70 °C), but has a sufficient mechanical strength to serve as support under physiologic temperatures. The implant is mechanically stable, biocompatible, partially biodegradable, and provides a scaffold for growing bone.

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Introduction

Hundreds of thousands of artificial hip joints are successfully implanted worldwide every year. Despite the high clinical success of these implants, problems still remain with their long-time performance, namely, aseptic loosening and loss of bone around the implant. For this bone loss, stress shielding, osteolysis and natural aging are main reasons. This severe condition often requires a revision surgery where onlay strut grafts, nowadays mostly of allogenous bone, are used to restore the damaged bone [1–3]. The preference for such allografts in surgical practice is due to their good mechanical characteristics, their ease of modelling to the patient's bone and the possibility of a connection between the graft and the weakened hard tissue [4]. Unlike autografts, they are not associated with donor site morbidity and can be obtained in larger quantities [3, 5]. However, being transplanted organs, they may cause an immunological response or an infection. This necessitates a thorough sterilization procedure that not only damages the graft's biological and mechanical properties [3, 6], but also makes it expensive.

Reconstruction with a fully synthetic artificial bone graft is another way to provide and create lost bone material. A large variety of different bone substitutes is available for the treatment of acquired bone defects as an alternative to bone grafting. However, these substitutes are not suitable for immediate direct load-bearing as a strut graft: Polymers are too weak and ceramics are too brittle [7–9]. Therefore, a combination of these two classes of materials was sought here to develop an implant which is both elastic (to prevent stress-shielding), mechanically stable (to give mechanical support for weight-bearing bone defects), and offers a biocompatible, partially biodegradable surface as matrix for on-growing bone. This can be used for the mechanical

augmentation of weakened bone structures, e.g. in the femur.

Materials and methods

Chemicals

Two different polymers were obtained from Boehringer Ingelheim (Ingelheim, Germany):

- Poly(L-lactide) (PLLA), RESOMER® L 210, degree of polymerization = 2810 as obtained by viscometry (according to the manufacturer's specification).
- Poly(D,L-lactide) (PDLLA), RESOMER® R 208, degree of polymerization = 1470 as obtained by viscometry (according to the manufacturer's specification).

Titanium plates were obtained from Goodfellow (99.6+ %, thickness: 0.25 mm, annealed). Nanocrystalline hydroxyapatite (HOAp, Merck, for bioceramics; particle size about 1 μm), calcium carbonate ($CaCO_3$, calcite, Fluka, >99%; particle size about 1 μm), potassium hydroxide (KOH, p.a., Merck), hydrogen peroxide (H_2O_2, p.a., 30%, AppliChem), dichloromethane (J. T. Baker, >99.5%), and acetone (Fisher Chemicals, p.a., 99.99%) were used as obtained. The solutions for dip-coating were prepared by dissolving the polymers in the corresponding solvent and suspending the calcium salts in them:

- Solution 1: 0.96 g of PLLA and 0.24 g of PDLLA were dissolved in 20 mL of CH_2Cl_2. 0.40 g of calcium carbonate powder was added to make a dispersion.
- Solution 2: 1.20 g of PDLLA were dissolved in 20 mL of acetone and 0.78 g of hydroxyapatite. 0.42 g of calcium carbonate powder was added to make a dispersion.

The titanium was cut into plates of adequate size ($25 \times 9 \times 0.25$ mm^3 for the small test samples, $35 \times 200 \times 0.25$ mm^3 for the real size implant) and washed for 10 min in an ultrasonic bath, first with acetone and then with ethanol. The surface of the titanium was activated with a boiling solution of KOH/H_2O_2 (five parts of 5 M KOH and one part of 30% H_2O_2) for 15 min. After activation, the titanium was washed several times with water in an ultrasonic bath.

The inner layer of polymer was applied on the surface of the activated titanium by manually dipping the metal 24 times into solution 1 at room temperature (speed of dipping and retrieving: about 1 mm s^{-1}), and allowing each layer to dry in air (drying time between two layers: 40–60 min). After all the layers had been applied, the samples were dried for four days at 70 °C to remove the solvent dichloromethane. The outer layer was then applied by manual dipping into solution 2, using the same procedure. In order to avoid the formation of wrinkles in the outer layer, the partially dried but still moldable implant was mechanically flattened between two plates of PTFE if necessary.

For degradation studies, one coated sample ($25 \times 9 \times 0.25$ mm^3) was immersed in 100 mL of continuously stirred deionised water at 37 °C for 50 days in a closed vessel. The immersion medium was not exchanged. The pH was measured every 7 days with a calibrated pH electrode.

Instruments

Dynamic mechanical analysis was performed on coated samples ($25 \times 9 \times 0.25$ mm^3) with a Netzsch DMA 242 instrument in penetration mode (1 mm^2) with a frequency of 5 Hz in the temperature range of –10 °C to 80 °C with a heating rate of 1 °C min^{-1}, using the software of the manufacturer for evaluation. Thermogravimetry was performed with a Netzsch STA 409 PC instrument (40–50 mg; 30–1000 °C; 3 °C min^{-1}; dynamic oxygen atmosphere; 50 mL min^{-1}; Al_2O_3 crucibles), connected to a Bruker Vertex 70 infrared spectrometer for in-situ gas analysis. Scanning electron microscopy (SEM) was performed with an ESEM Quanta 400FEG instrument on gold-sputtered samples. Synchrotron radiation-based microtomography (SRμCT) was performed at beamline BW2 at HASYLAB DESY using a monochromatic X-ray photon energy of 18 keV. Images were recorded at different sample rotations between 0° and 180°, with steps of 0.25°. The 3D reconstruction work was done at HASYLAB [10] and images were created with the program VGStudio MAX 1.2. The voxel size was 1.9 μm^3 and the reconstructed data set comprised $1535 \times 1535 \times 1023$ voxel within a volume of $2.9 \times 2.9 \times 1.9$ mm^3.

Results and discussion

In order to serve its purpose as a strut graft, the artificial implant must have sufficient mechanical strength and stability to serve as support while the bone regenerates and re-builds. Furthermore, it should have a high plasticity so that it can be fixed into tight contact with the bone. Biocompatibility and ease of sterilization are essential properties, and the matrix should provide a scaffold for new bone ingrowth.

To fulfil these requirements, we used a combination of titanium, poly(L-lactide), and poly(D,L-lactide) organized in different layers (Fig. 1). The implant has an outer elastic

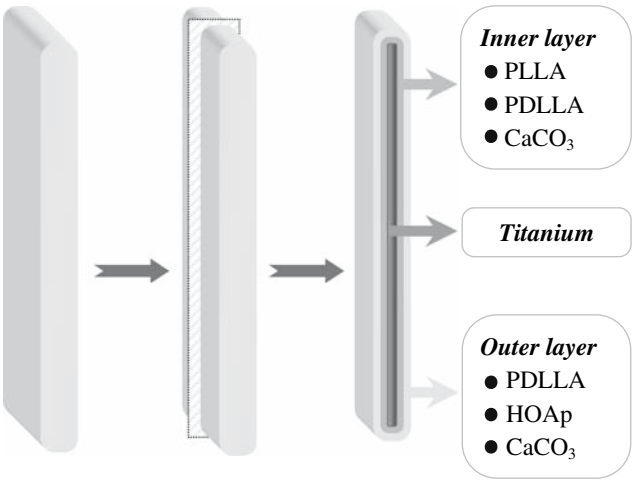

Fig. 1 Schematic view of the implant with a longitudinal section. The outer layer consists of PDLLA/HOAp/$CaCO_3$ (50/32.5/17.5 wt%). The inner layer consists of PLLA/PDLLA/$CaCO_3$ (60/15/25 wt%). The core consists of titanium

layer in contact with the bone, consisting of PDLLA, HOAp and $CaCO_3$. PDLLA is biocompatible [11–14] and rapidly biodegradable and will give bone the opportunity for on- and ingrowth when it degrades. The inner layer consists of PLLA, PDLLA and $CaCO_3$. Poly(L-lactide) has a slow degradation rate and will provide a biocompatible interface between the living tissue and the bioinert metal while the bone consolidates. Its low elasticity is increased by adding the more elastic PDLLA. The inner core of the implant is titanium which will give mechanical stability to the artificial strut graft.

The implant was made by manual dip-coating from the appropriate polymer solutions as described in the experimental section and as summarized in Fig. 2. The composition chosen for the two layers was based on the results of previous studies on the pH buffering capacity of materials with different polylactide/hydroxyapatite/calcium carbonate compositions [15]. The thickness of the inner layer and the outer layer was about 500 µm, respectively.

Thermogravimetry was applied to analyze both layers. First of all, no traces of the potentially harmful solvents used were detected (Fig. 3). This included the absence of any evolved gases below 200 °C by gas-phase infrared-spectroscopic analysis (data not shown). The results of thermogravimetry also showed that the composition of the layers corresponds to the composition of the solutions used to apply them: 76 wt% of polymer in the inner layer (expected: 75 wt%) and 66 wt% in both layers combined (expected: 62.5 wt%).

Both layers contain well-dispersed calcium salts (Figs. 4 and 5), and can be easily distinguished. The inner layer contains pores of approximately 10 µm in diameter whereas the outer layer is compact and richer in inorganic salts. This difference in porosity is due to the different

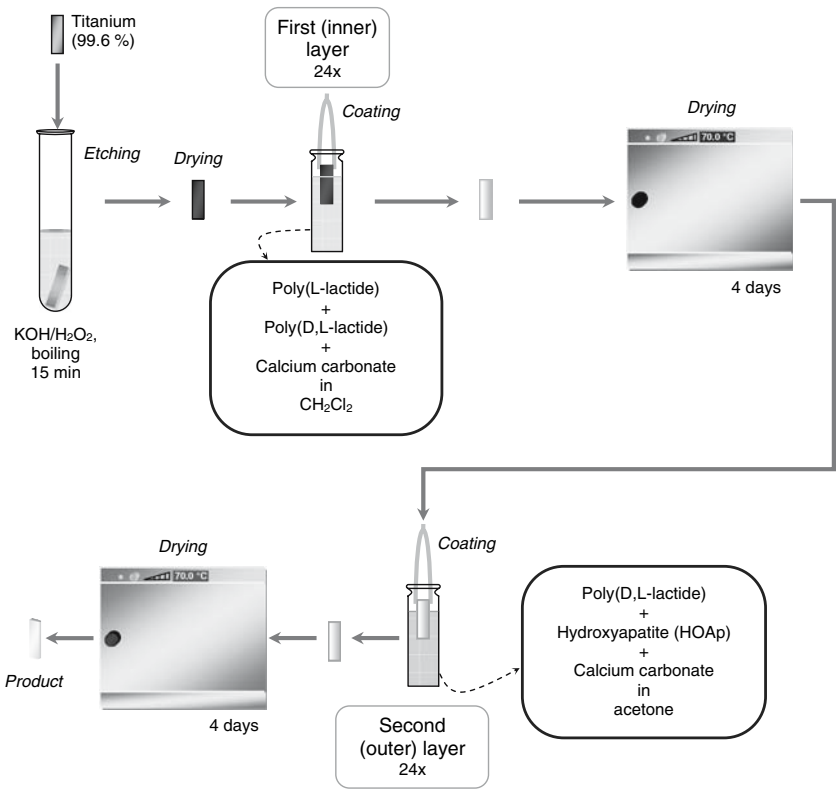

Fig. 2 Manufacture of the implant: First, the surface of the titanium plate is activated with KOH/H_2O_2; after washing it is manually dipped into solution 1 to apply the inner layer of PLLA/PDLLA/$CaCO_3$; after applying 24 layers, the implant is dried at 70 °C for four days; after that, the outer layer of polymer of PDLLA/HOAp/$CaCO_3$ is applied (also 24 layers). Then the implant was dried at 70 °C, resulting in the final product

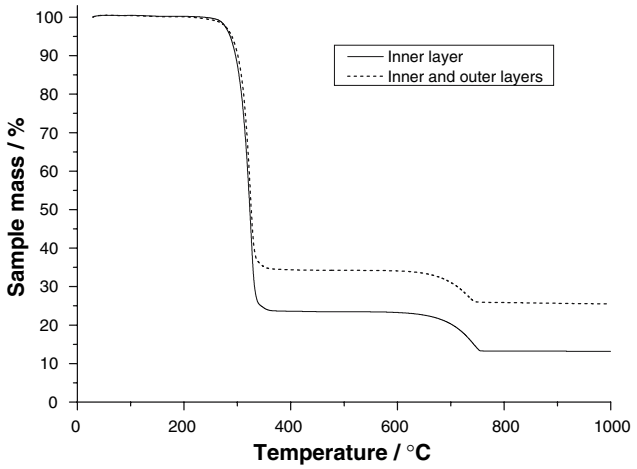

Fig. 3 Thermogravimetric analysis of samples of inner and both layers (without the titanium inner core). Around 200 °C the combustion of polylactide begins and at around 620 °C calcium carbonate decarboxylates to CaO. There is no residual solvent in the sample, as evident from the absence of a mass loss below 200 °C, also supported by the absence of gas-phase infrared absorption of evolved gases (data not shown)

solvents and not an intrinsic property of the different polymers.

Although the implant presents no open porosity capable of allowing the ingrowth of cells into its structure directly after surgery, it is expected that bone will still be able to attach when the polymer degrades, taking advantage of the irregularities formed on the surface during this procedure (see Figs. 6 and 7), and of the presence of nanocrystalline hydroxyapatite and calcium carbonate. The inner layer consists mainly of the slowly degrading PLLA whereas the outer layer consists mainly of the faster degrading PDLLA [16–19]. These calcium salts have an important function in the biological characteristics of the implant, increasing its biocompatibility. Nanocrystalline hydroxyapatite is similar to the inorganic part of the bone and well accepted by the body [20–23]. Calcium carbonate, besides being biocompatible, acts as a pH-buffer during the resorption of the polylactides [15], to avoid inflammatory reactions caused by the decrease in pH in the vicinity of the implant during polymer degradation [11, 24–27]. This buffering effect is shown in Fig. 8, where the pH was followed when the implant was immersed in deionized water. There was no pH drop observed as it usually is observed with polylactides upon long-term immersion (see Ref. [15, 24, 28] for extensive studies). At the end of the experiment, the plates showed no major swelling (Fig. 9), preserving their original shape.

The implant is hard and impossible to be manually bent at room temperature. However, its elasticity increases above 43 °C, as shown by the results of the penetration experiments (Fig. 10), a temperature which lies outside the physiological temperature range of the human body. After

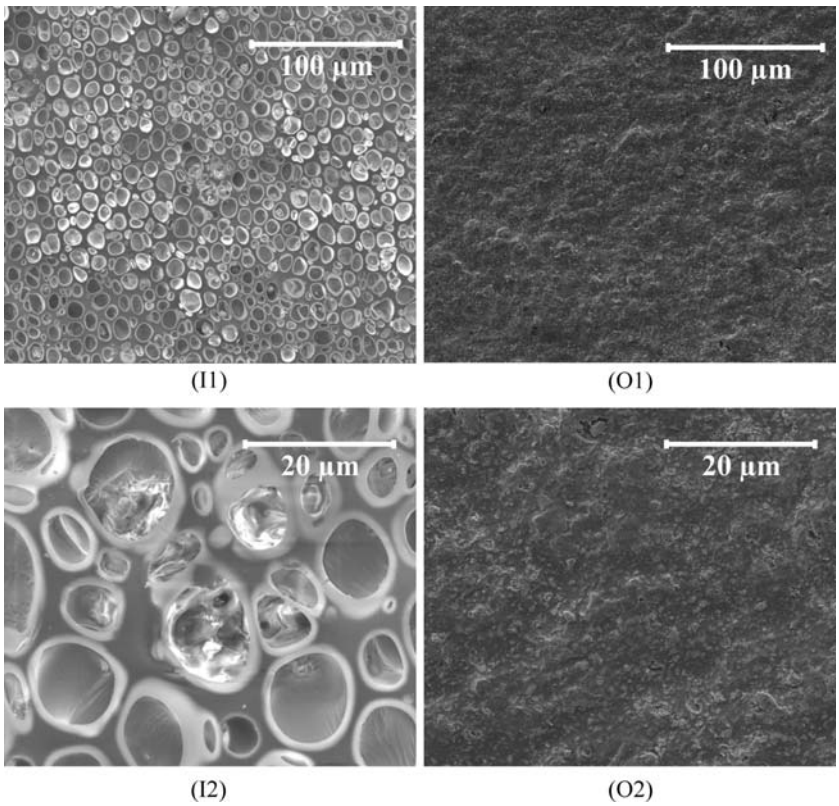

Fig. 4 SEM pictures of the inner layer on titanium, i.e. before application of the outer layer (**I1** and **I2**), and of the outer layer of the final implant (**O1** and **O2**). A porous structure can be seen in the inner layer of the polymer, but it is absent in the outer layer. In both cases the calcium salts are well dispersed within the polymer, i.e. no crystals can be seen

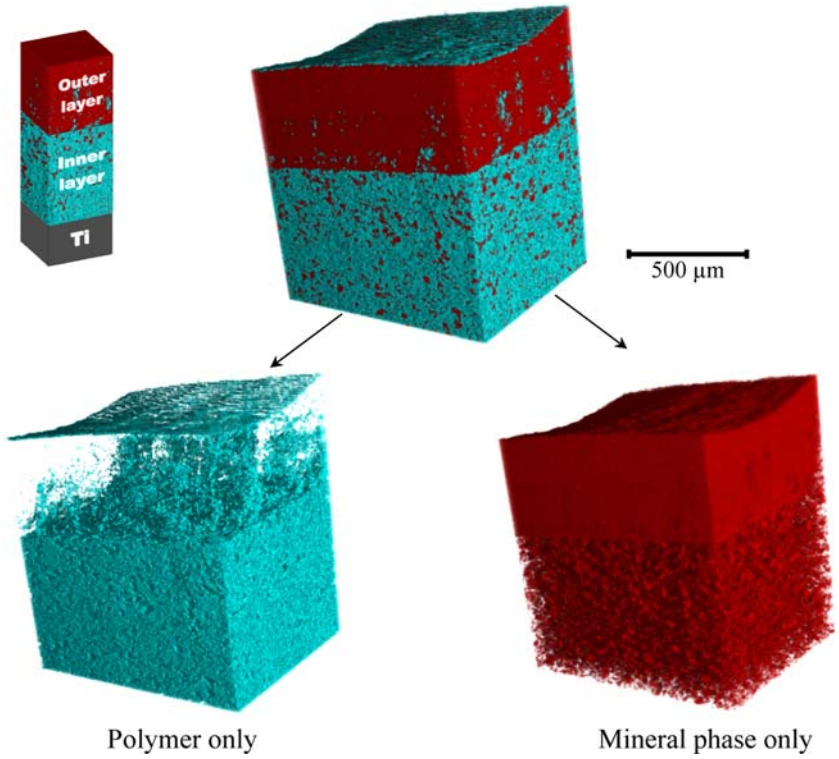

Fig. 5 Synchrotron radiation micro computer tomography (SRμCT) of the two layers of polymer. Calcium salts (i.e. the mineral phase) are coloured in red and the polymer is coloured in cyan, as distinguished by the different X-ray density. The two layers can be easily identified because the outermost layer (top layer) contains a higher amount of the mineral phase. In the Figures at the bottom either only the polymer (left) or only the mineral phase (right) are shown

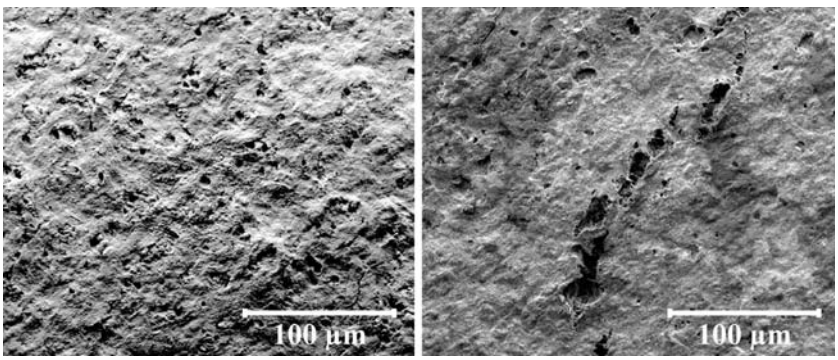

Fig. 6 Surface of the outer layer after immersion in deionized water at 37 °C for 50 days (in vitro degradation). When compared to Fig. 4, the increase in porosity as the polymer begins to degrade becomes clear (two views of the same sample are shown)

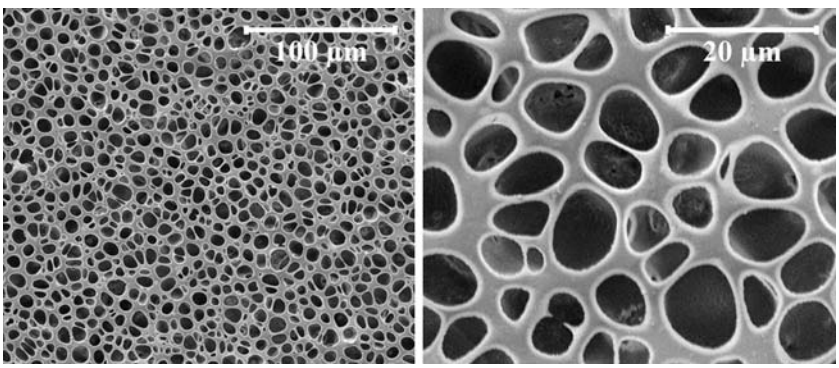

Fig. 7 Surface of the inner layer on titanium after immersion in deionized water at 37 °C for 50 days (in vitro degradation). The immersion in water caused no significant changes in the surface structure, demonstrating its substantially smaller rate of degradation

implantation and subsequent resorption of the outer layer, the elasticity of the implant will increase in the long run. This will help to prevent stress shielding of the femoral bone. This increase in elasticity of the implant at higher temperatures allows it to be manually adapted to the patient's bone during surgery. Figure 11 illustrates the

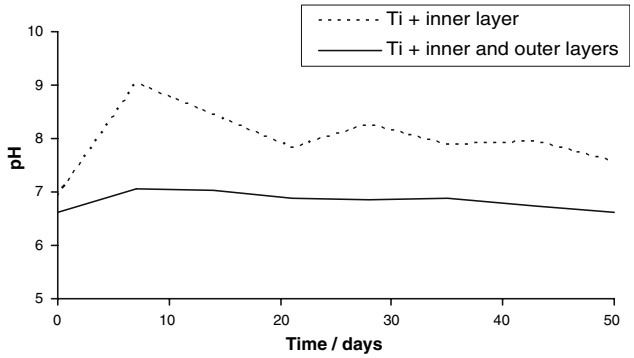

Fig. 8 Representative pH curves of the samples immersed in deionized water (non-buffered) at 37 °C for 50 days (in vitro degradation)

procedure: after immersion in water at 70 °C for 5 min, the implant becomes highly elastic and can be modelled into the desired shape, recovering its hardness as it cools down again. Although this bending causes small fissures on the surface (Fig. 12), it does not disturb the general stability of the polymer layer and the temperature used does not damage the living tissue. So far, we did not yet consider the question of fixation of the implant to the bone. Cerclage wiring or screws may lead to additional stresses which interfere with the surface integrity of the implant.

Conclusions

In this study we present a new artificial structural elastic, partially degradable bone graft for supporting weak bone in the proximal femur. The mechanical properties of this artificial implant are similar to bone, with sufficient strength and stability at 37 °C and a high plasticity above 43 °C which makes it possible to fix the implant tightly on the host bone. Only well-established biomaterials (polylactide, calcium phosphate, calcium carbonate) were used, therefore there are no concerns about the biocompatibility of the implant.

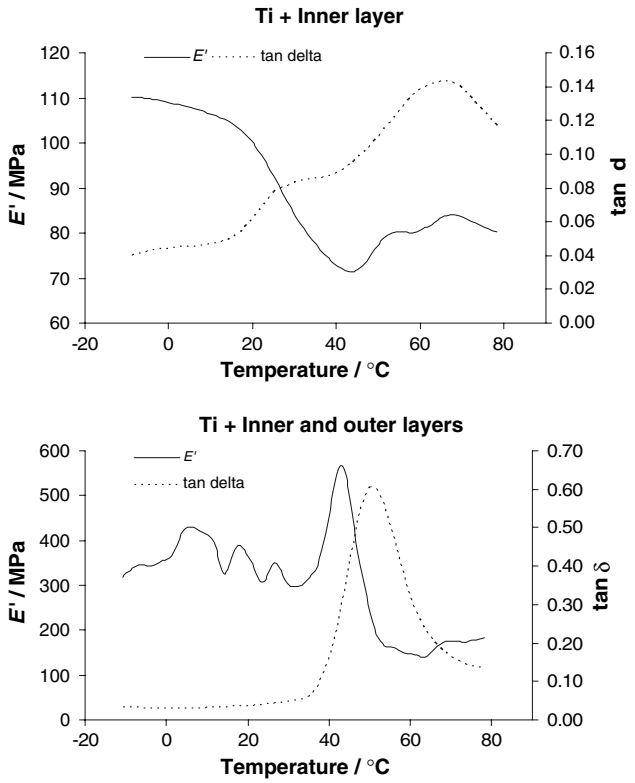

Fig. 10 Results of the penetration experiments on samples of titanium with only the inner layer of polymer (top) and with both polymer layers (bottom). The implant increases its elasticity above 43 °C and after implantation and resorption of the outer layer, the sample is elastic. Note that the presented numerical data are only semi-quantitative for the investigated layered material

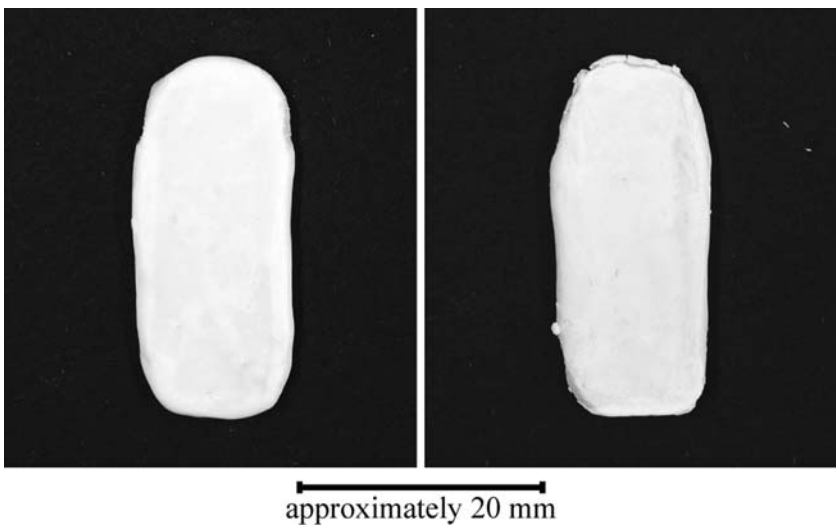

Fig. 9 Photographs of a PLA-coated titanium sample before (left) and after (right) immersion in deionized water at 37 °C for 50 days (in vitro degradation). No swelling is seen after the immersion in water

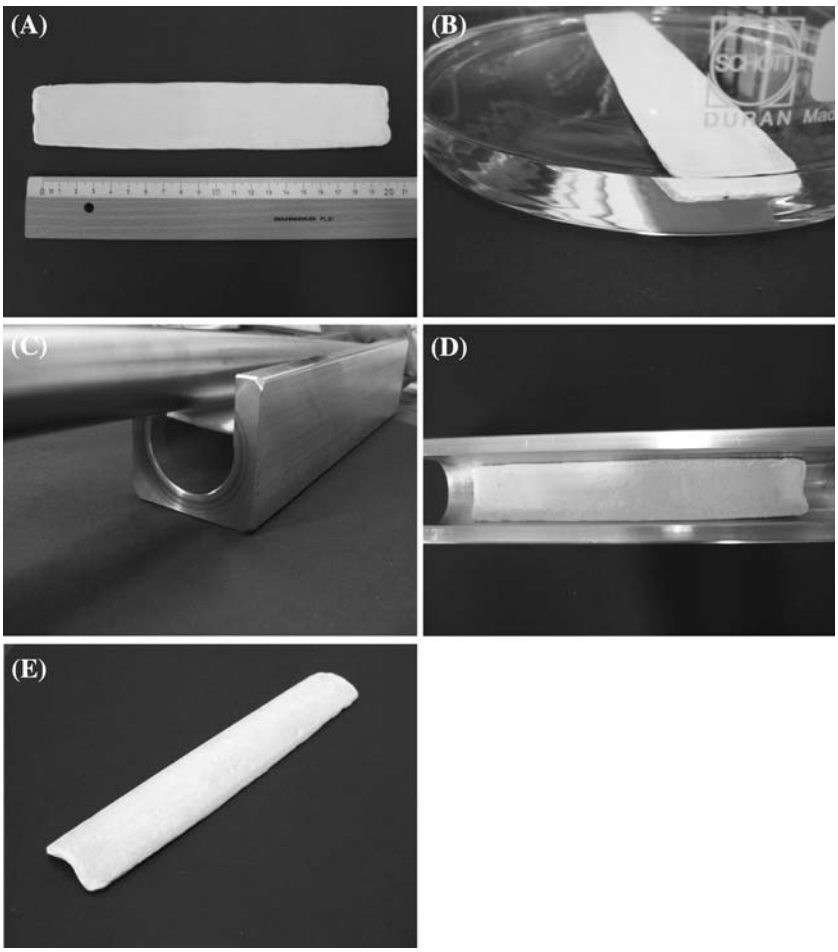

Fig. 11 Details of the tentative shaping procedure before or during the operation. The implant (**A**) is immersed in water at 70 °C for 5 min (**B**) and rapidly shaped, e.g. by an appropriate mould (**C**). Pictures (**D**) and (**E**) show the implant after shaping. The degree of bending can be changed by variation of the mould (**C**)

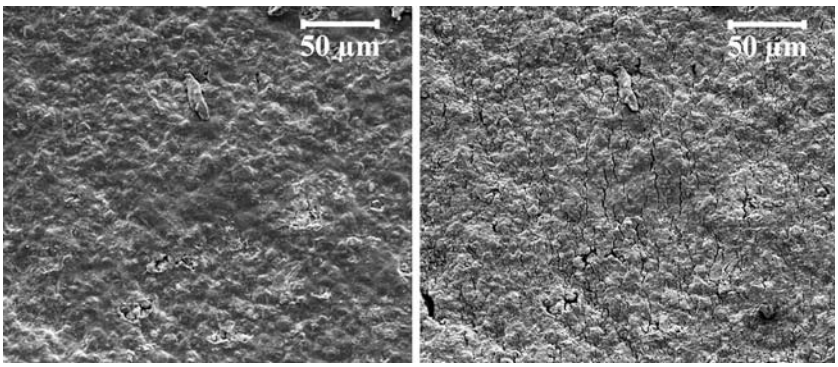

Fig. 12 Surface of a sample before (left) and after (right) bending at 70 °C. The bending process causes small fissures on the surface, but the overall stability of the implant is not affected

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