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Iron Based Cellular Metals For Degradable Synthetic Bone Replacement

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Abstract

Degrading metal alloys have recently gained substantial scientific and clinical interest for their use as implant materials in bone surgery and cardiovascular surgery. In cardiovascular applications, iron has been used successfully in animal implantation studies and first clinical cases. Iron shows relatively long degradation timeframes, which in particular are needed in bone surgery. The aim of the present study was to investigate the usability of iron and iron based alloys with an open cell structure as degradable bone replacement material, which gives an osteoconductive surface for the stimulation of osseous integration on the one hand, and a degradation rate, which does not overburden the regeneration ability of bone on the other hand. Open cell metal PM foams exhibit a natural bone-like structure, which enables ingrowth of bone tissue and blood vessels. In order to determine the influence of alloying elements on biocompatibility and degradation times, various PM iron alloys were processed and tested in vitro. Observed degradation rates appear to be reasonable for the intended use as bone implant material. Open cell structures with a compressive yield of ~10 MPa were manufactured by a PM replication method and were implanted in the femur condylus of adult merino sheep for 6 and 12 months. This study shows that an open cell iron based bone implant material exhibits good biocompatibility and no inflammatory response. Therefore, iron based implant materials are considered a very promising approach for the design of new load bearing synthetic bone graft substitutes.

Introduction

Metal materials play a key role in the repair or the replacement of bone defects. Due to their mechanically stability there are able to assume the burden of defect bones and have a high damage tolerance. Metals have a high stability, which is higher than the stability of bones. To avoid the resulting problems of stress shielding, cellular metals with low youngs moduli have been proposed [1,2].

The basic idea of the present work is to design implants with a cellular metal structure. Since the majority of manufacturing routes for cellular metals is based on powder metallurgical processes [3], the recent study basically uses powder metallurgical samples.

Degrading metal alloys have recently gained substantial scientific and clinical interest for their use as implant materials in bone surgery and cardiovascular surgery. Degradable iron based implants were approved for cardiovascular surgery. Even though the analysis of cytotoxicity of metal ions shows a low biocompatibility [4] the implanted stents were completely resorbed and did not leave any distinctive inflammatory reactions [5-7]. However, in-vivo tests in the porcine descending aorta indicate, that faster degradation rates are desirable [8].

The aim of the present study was to investigate the usability of iron and iron based alloys with an open cell structure as degradable bone replacement material, which gives an osteoconductive surface for the stimulation of osseous integration on the one hand, and a degradation rate, which does not overburden the regeneration ability of bone on the other hand.

Experimental

To study the influence of various alloying elements (C, P, B, Si, Ag), powder mixtures were pressed into cylinders (Ø 10 mm, h 5 mm) and sintered and their microstructure was analyzed. Therefore, carbonyl iron (BASF, Germany, mean particle size 4 µm) was used. Furthermore, iron based alloys were prepared in order to increase the sintering density and the strength, but also to manupulate the corrosion rates. Thus, steels with phosphorus contents of 0.6 wt.-% respectively 1.6 wt.-%, mixtures of 3.8 % and 10 % Fe_3P and carbonyl iron where realized. Boron-alloyed steels with a boron content of 0.05 wt.-% where synthesized by mixing carbonyl iron powder with commercial available FeB (READE) in a mass ratio of 16.5 : 83.5. Such FeB powders feature particle sizes of 3-5 µm and Boron contents of 16.5 wt.-%. Silver exhibits a large potential difference to iron. Thus, in order to increase the corrosion rates, mixtures with Ag of 1 and 5 wt.-pct were used. Mixtures of iron and silver were prepared by mixing carbonyl iron and fine 100 % pure Ag-powders (Ferro, Germany) with a particle size of 5 µm.

The biodegradation rate was tested by measuring the mass loss in simulated body fluid immersion. Open cell metal structures out of the Fe0.6P-alloy were prepared by a powder metallurgical replication route. The production process involves the metal powder slurry impregnation of open cell polyurethane foams and the subsequent thermal debinding, where the organic material is removed from the structure. In the last step, the residual powder skeleton is sintered. The process is described more in detail in ref. [9]. The resulting material was characterized by microstructural analysis, mechanical tests and degradation tests.

Furthermore, cytotoxicity test were carried out in order to characterize the effect of alloying elements on the biocompatibility. As a reference, fibroblasts from the five passages were seeded at 1×10^4 cells in 3 ml of the culture medium in 6-well plates (Falcon; BD Biosciences; Germany). They were cultured for 5 days under standard conditions. For the perfusion culture a chamber from the Minucells and Minutissue GmbH (Bad Abbach, Germany) was used. The chamber was connected with the medium bottles and the waste bottles by silicone tubes. The automatic device allows the constant renewal of the culture medium at 1 ml/h within the pulp chamber system. After sub culturing for 4 days, the fibroblasts were seeded at 5×10^3 cells in 400 µl culture medium into the perfusion culture chamber and were cultured for 4 days in the present of the different ferrous alloy materials as indicated above. Finally the cellular metals were implanted in the femur condylus of adult merino sheep for 6 and 12 months.

Results and Discussion

The powder mixture compacts and the pure iron powder compacts were successfully sintered at sintering temperatures between 1050 and 1120 °C, depending on the composition of the mixture. The sintered density of the various alloys is shown in table 1. Sintering densities of 82.7 – 95.3 pct were obtained. In particular, the addition of small amounts of boron leads to the formation of fine distributed small pores (Figure 1). Phosphorus contents of 0.6 and 1.6 pct lead to maximum density, where higher contents of phosphorus give rise to the formation of brittle intermetallic phases (Figure 2). The addition of boron leads lower densities of ~ 90 %.

Table 1: Green densities and sintered densities of various iron based alloy compacts.

material	green density		sintered density	
	specific density [g/cm³]	rel. Density [%]	specific density [g/cm³]	rel. Density [%]
PM iron	4.56	58.5	7.01	89.9
Fe-P 0.6	4.63	59.4	7.43	95.3
Fe-P 1.6	4.68	60.0	7.46	95.6
Fe-B	4.72	60.5	6.84	87.7
Fe-Ag 1.0	4.74	61.6	6.52	83.6
Fe-Ag 5.0	4.81	61.2	6.45	82.7
Fe-Ag-P 1-0.6				

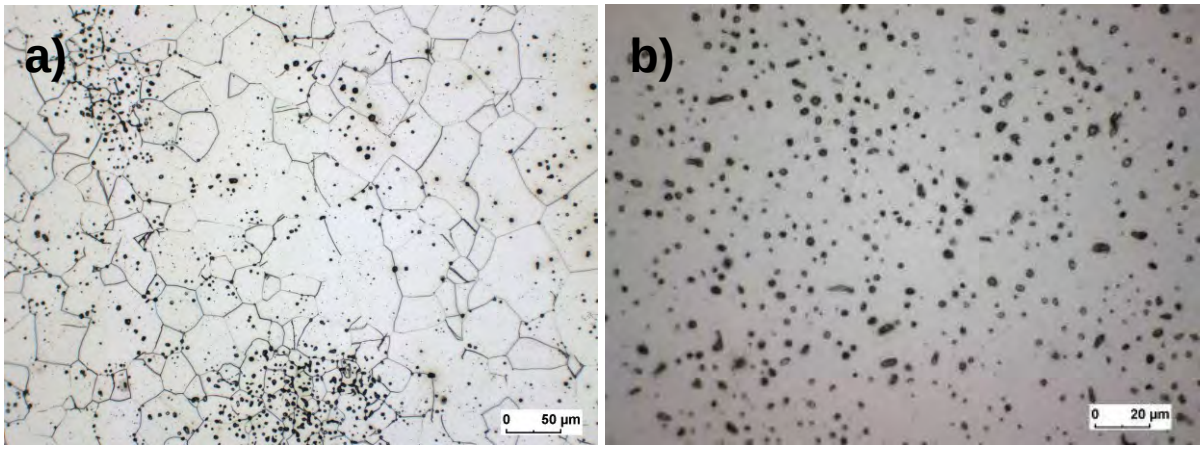

Figure 1: Metallographic cross sections of PM carbonyl iron samples with 0.6 wt.-% phosphorus (left side) and 0.06 % boron. In particular, the boron containing alloy show fine pores with a homogeneous distribution (right side).

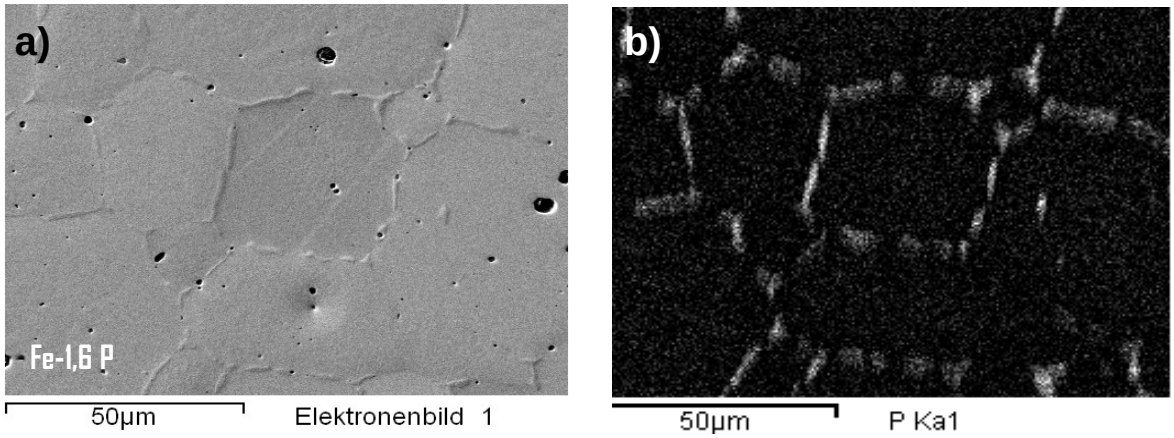

Figure 2: REM-picture (Figure a) and EDX-mapping of the Ka-line (Figure b) of pressed and sintered mixtures of carbonyl iron and 1.6 % phosphorus show a distinct phosporus enrichment at the grain boundary.

However, the degradation tests give no significant decreased degradation rates irrespective of the used alloy; despite e.g. phosphorus is known to lower the corrosion rate of steels. On the

other hand, phosphorus is known to increase mechanical strength. Therefore, a powder mixture of carbonyl iron and 3.8 % Fe_3P was prepared to give a Fe0.6P alloy. Water, PVA binder and further rheological additives were than mixed and impregnation of the PU foams was carried out by a double roller coating machine. Thus, open cell metal structures as depicted in Figure 3 were synthezised. The cell size of the templates was 45 ppi, which correlates with cell diameters of the large cell of approx. 1 mm. Such foams exhibit highly homogeneous cell structures, showing a density of 1.4 g/cm³.

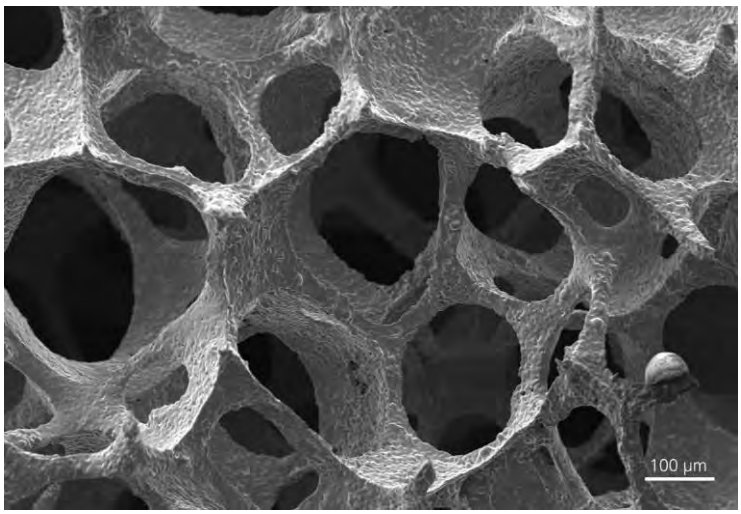

Figure 3. Electron microscopy picture of a metal foam made by a Fe0.6P alloy.

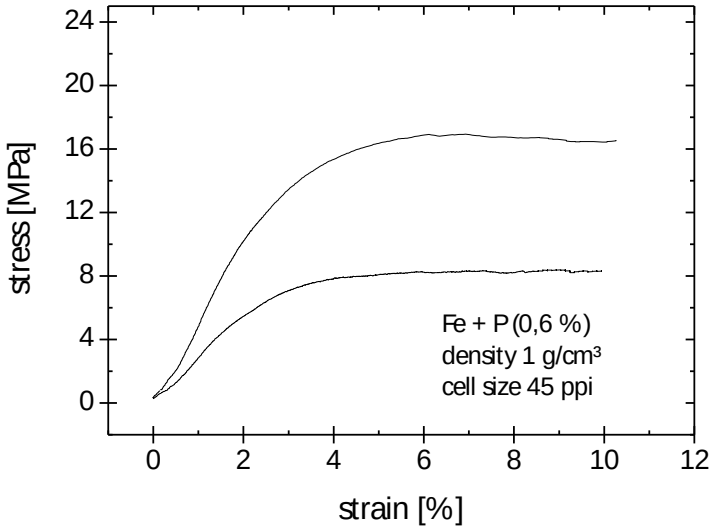

Figure 4: Compression-strain curves of a typical Fe0.6P open cell metal foam with a density of 1 g/cm^3. The curves give the upper and the lower maximum of the compressive yield point. The medium compressive yield point is 10.9 ± 5.5 MPa.

For use as load bearing implants a sufficient mechanical strength of the foams is required. Therefore the axial compression tests were carried out, considering 8 samples for each value.

The compressive yield point was than calculated as defined in DIN 50134. As a result, metal foams made by pure carbonyl iron show a compressive yield of 2.4 MPa at maximum. The compressive yield point σ_c, the relative density ρ_{rel}, and the yield strength σ_{ys} of the matrix material may be described analytical as follows [10]

$$\sigma_c = \sigma_{ys} \cdot 0.3 \cdot \rho_{rel} \ .$$

Thus, the compressive yield is mainly controlled by the relative foam density as well as the strength of the matrix material. Since the yield strength of the phosphorus alloyed matrix material is considerably higher, a distinct effect on the cellular metal structures is observed. Here, the compressive yield point is 9.4 ± 2.7 MPa at a density of 1 g/cm³ and 10.9 ± 5.5 MPa at 1.4 g/cm³ (Figure 4). The young's modulus of the Fe-P foams measured by acoustic impedance spectroscopy is 2.3 GPa. This is comparable to the typical bone stiffness. E.g., characteristic stiffness of the vertebra is 0.3 – 1.5 GPa, the strength is 3.4 – 4.2 MPa, dependend on the age of the patient [11].

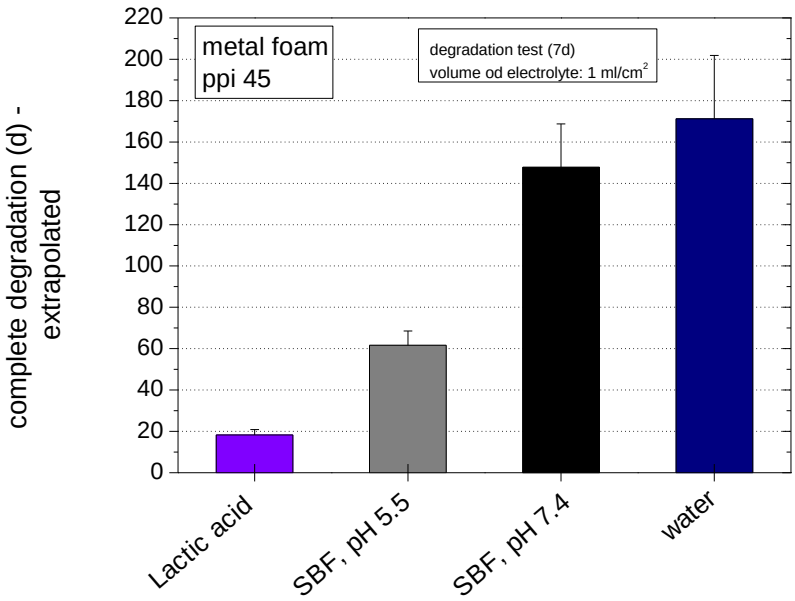

Figure 5: Degradation of iron foams in lactic aicd, SBF and in water at 37 °C.

The degradation rate of the Fe-P foams was analyzed in simulated body fluid (pH 7.4) for 7 days. The results are depicted in figure 5. Extrapolated, the total degradation time amounts 120 days at maximum. Further tests with a duration of 31 days revealed the same results. However, since a large discrepancy between in-vitro tests and in-vivo corrosion is to be expected due to former publications [8] the in-vitro degradation only gives indications of the tendency of corrosion rates in-vivo. In SBF with pH 5.5, which simulates inflammatory reactions in the body tissue, the degradation is decreased significantly. The analysis of the degradation rate of the various alloys (Figure 6) demonstrates that neither the addition of boron, nor the addition of phosphorus results in a significant change of the corrosion rate in vitro. Since phosphorus typically is known to retard the corrosion of steels (which would be detrimental in the present application), this is an im-

port fact, because from the powder metallurgical viewpoint, phosphorus has beneficial effects on the microstructure as demonstrated above.

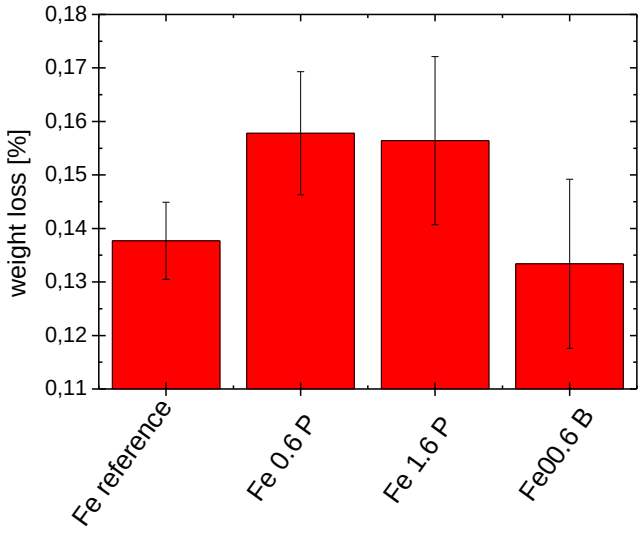

Figure 6: Degradation of pure iron, Fe-0.6P, Fe-1.6P, and Fe-0.06B.

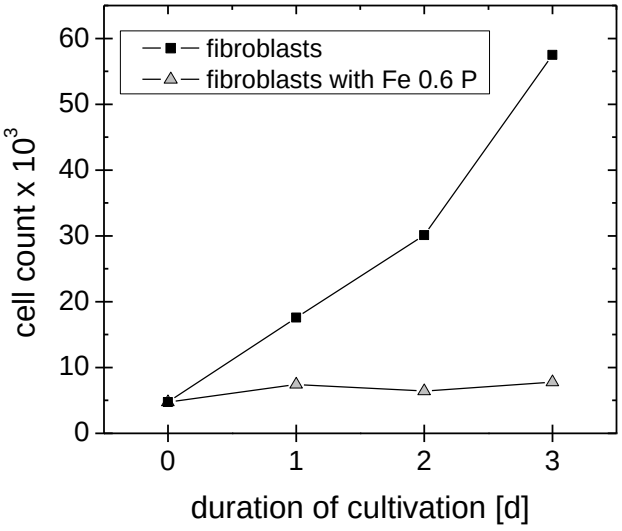

Figure 7: Cytotoxicity tests of fibroblasts in a dynamic perfusion chamber. Cells in contact to iron based alloys with 0.6 wt.-% phosphorus show a slight increase of the cell population.

In order to characterize the iron based alloys in vitro, cell toxicity tests were carried out using a perfusion chamber system to simulate the dynamic body environment. Fibroblasts were maintained successfully for the duration of the experiment. The results are shown in Figure 7 and Figure 8, respectively. In comparison, cell proliferation of cells in contact to iron or iron alloys is

significantly decreased. However, the comparison of the different alloys shows, that cell counts on the iron and alloyed iron discs show proliferation with highest proliferation rate on 1.6 wt.-% phosphorus containing alloys. At phosphorus contents of 0.6 wt.-% the proliferation is slightly decreased.

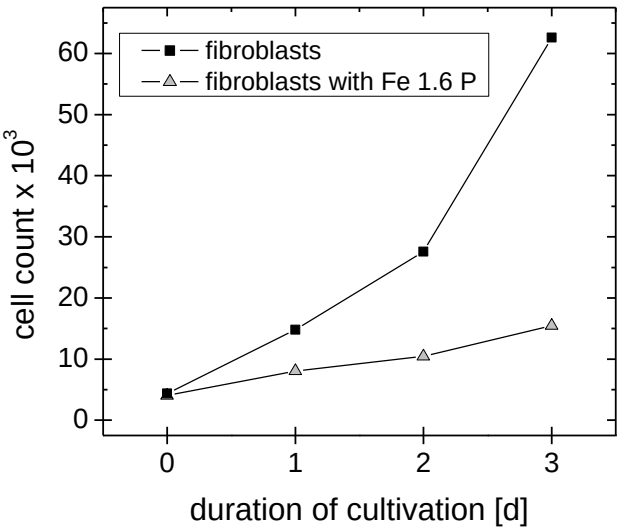

Figure 8: Cytotoxicity tests of fibroblasts in a dynamic perfusion chamber. The cell activity on iron based alloys with 1.6 wt.-% phosphorus show a significant increase.

Finally, the implant study revealed a large fraction of residual implant material even after implantation time of 12 months, thus showing, that the in vitro tests only give indications for the degradation time in vivo. Further work has to be done to increase the degradation rates of the iron alloys. On the other hand, no inflammatory response of the surrounding bone tissue was detected, giving rise to the good biocompatibility of iron as biomaterial.

Conclusions

The study shows that open cell metal foams can be strengthened by the use of phosphorus without the risk of decreasing the degradation rates. Such materials show mechanical properties comparable to bone properties. Thus stress shielding may be prevented. Therefore, iron based implant materials are considered a very promising approach for the design of new load bearing synthetic bone graft substitutes. Nevertheless, further work on increasing the biocorrosion has to be done.

Acknowledgments

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