Metal Foam - Biocement Composites: mechanical and biological properties and perspectives for bone implant design

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1 Introduction

Several approaches for the development of highly porous metal structures with the intended application as bone implant materials have been published in recent years and some of them have reached the stage of commercial products [1, 2]. There is however always a conflict of interests between highly open pore structures and sufficient mechanical strength in order to be applicable in loaded bone defect sites. The aspect of stress shielding remains a still unsolved issue if the bone implant retains a constant strength over time. In our developmental approach we therefore combined highly open porous metal foams with high strength resorbable mineral bone cements in order to obtain metal/mineral composite materials with very high initial load bearing capability. As the selected mineral bone cements are bioactive and resorbable, they are considered to support bony integration. By gradual replacement of the cement matrix with newly formed bone the implant shall be finally converted into a biohybrid composite of metal foam and bone.

2 Materials and Methods

Powder metallurgy processes were applied for the fabrication of metal foams. Briefly, shaped parts of PU-foam were coated with metal powder suspension, dried, pyrolyzed and finally the remaining metal foam was sintered to reach final strength. The metal foams had an open porosity of 85 % and a pore size of 45 pores per inch, the pore structure was 100 % interconnecting. In the present study metal foams of titanium alloy (Ti6Al4V, in the following Ti), stainless steel (316L) and iron alloyed with 3.8 % Fe_3P (Fe) were used for investigation. Metal foams had the dimensions of 10 mm in diameter and 20 mm in height for mechanical testing and 10 mm in diameter and 5 mm in height for biological investigations.

The metal foams were either coated with a brushite ($CaHPO_4 \times 2\ H_2O$) layer or filled completely with mineral bone cement. The latter was either a calcium phosphate cement (CPC) prepared from α-TCP, $CaHPO_4$, $CaCO_3$ and precipitated hydroxyapatite (pHA) with Na_2HPO_4 as setting accelerator or magnesium calcium phosphate cement (MgCPC) with $(NH_4)_2HPO_4$ solution as setting liquid. Cement slurry was infiltrated into the foams and cured.

Complete filling was monitored by weighing all samples and by inspecting cross sections of selected samples by electron and stereo microscopy.
Compressive strengths of samples were measured on an universal testing machine (Instron 5566) at a cross head speed of 1 mm/min.
For cytobiological characterization, *in vitro* cell culture experiments with human mesenchymal stem cells (hMSC) were performed. Therefore, gamma sterilized samples (25 kGy) were preincubated in cell culture media (DMEM with 10% fetal calf serum) for 24 h. Preincubated media (stored at +4 °C) were added twice a week to adherent hMSC in well plates. Cell proliferation (by quantifying the LDH enzyme) and the corrosion relevant parameters iron release, oxygen saturation and hydrogen peroxide concentration were measured.

3 Results and Discussion

3.1 Mechanical properties

Compressive strength values are lowest for 316L, significantly higher for Fe and highest for Ti samples (Table 1). However, all unmodified metal foams showed characteristic elastic-plastic deformation behavior (Figure 1) whereas the mineral bone cements have a very brittle fracture behavior once the compressive strength is exceeded (Figure 1). The MgCPC is much more stable than CPC.

The composite materials show higher compressive strength than the respective mineral bone cements and are stable over broad range of deformation (exemplary shown for Fe+MgCPC in Figure 1). For titanium and iron based composites, the maximum compression strength resulted in values even higher than the sum of both single components (Table 1).

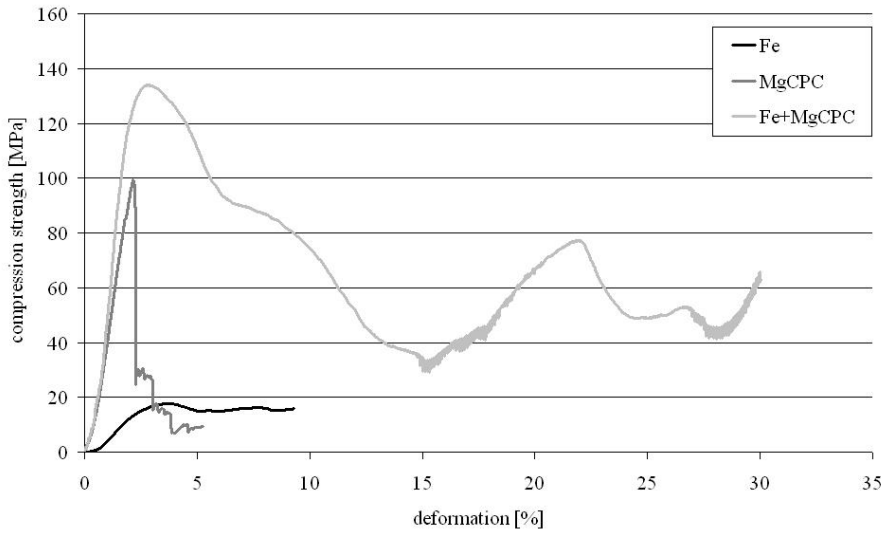


Figure 1: Exemplary stress–strain curve of an iron/MgCPC composite and the constituent materials thereof.

Table 1: Maximum compression strength and compression strength at 10 % deformation of metal/mineral composites and the constituent materials thereof.

	maximum compression strength [MPa]			compression strength at 10 % deformation [MPa]	
metal/mineral	*none*	*CPC*	*MgCPC*	*CPC*	*MgCPC*
none	---	30,3 ± 5,6	97,4 ± 13,6	---	---
316L	3,2 ± 1,6	24,5 ± 2,1	n.a.	~ 22	n.a.
Fe	14,5 ± 3,0	64,9 ± 8,4	140,3 ± 4,6	~ 50	50-70
Ti	50,2 ± 4,5	n.a.	157,6 ± 23,6	n.a.	60-85

3.2 Biological properties

Due to intensive studies on titanium based materials for medical implants it is well known that bioactive coatings with biomimetic calcium phosphates markedly increases biocompatibility of titanium based materials [3-5]. Iron-based materials are however intended to corrode over time and corrosion products of untreated iron occur in highest concentrations early after incubation/implantation. During this phase potential cytotoxic effects of corrosion products would be most detrimental for bony integration of an implant material. For iron-based implants a bioactive coating would therefore serve its purpose best, if it temporarily reduces the rate of corrosion and simultaneously provides a surface for bone cell attachment.

In Figure 2, results of *in vitro* cultivation of hMSc on unmodified (Fe), brushite coated (Fe-B) and MgCPC filled iron foams (Fe+MgCPC) are presented. The incubation of unmodified Fe foams (Fe) led - as expected - to a high release of iron ions. During corrosion of iron, oxygen saturation decreased and hydrogen peroxide concentration increased in the surrounding medium and therefore, an inhibited cell proliferation over the cultivation period was observed. Corrosion of iron foam could be diminished almost completely by brushite coating. For MgCPC filled iron foams comparable corrosion behaviour to Fe-B with less released iron and less iron oxidation by-products could be observed and high cell proliferation was observed too.

Biocompatibility of CPC or MgCPC filled Ti- or 316L-metal foams would be affected mainly by the cement matrix which almost completely shields the surface of the metal foam. Therefore, it can be assumed that biocompatibility of 316L+MgCPC or Ti+MgCPC is at least as good as for Fe+MgCPC and for 316L+CPC or Ti+CPC it will most likely be comparable or even better than for Fe+CPC.

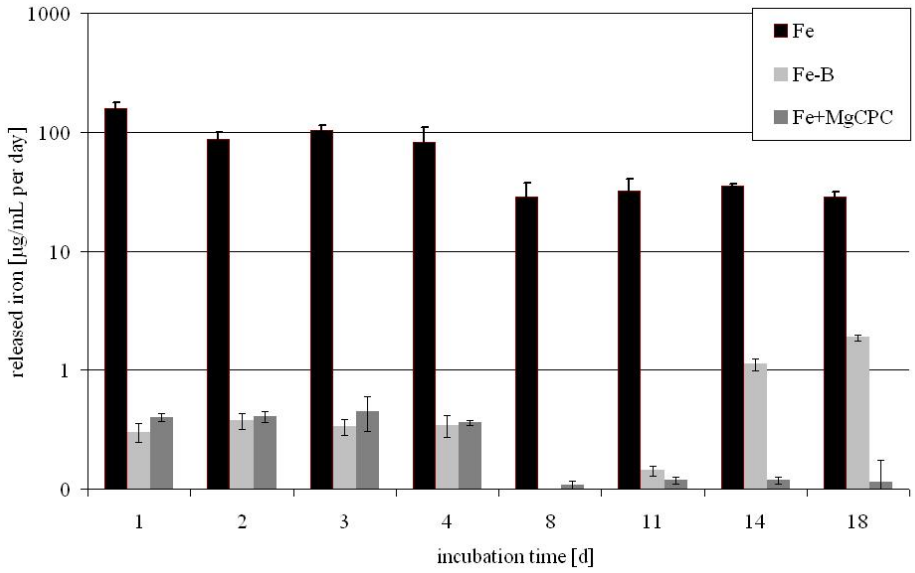
Combination of open celled metal foams with high strength mineral bone cements opens new opportunities for design of bone implants. The tested metal/mineral composites provided very high initial compression strengths, largely contributed by the respective mineral bone cements. At deformation rates destructive for the pure cements the composites retain much of their strengths, thus suggesting the application of these composites for applications with high load bearing.

In cell culture experiments with human mesenchymal stem cells (hMSC) all metal/mineral composite samples showed results comparable to the respective mineral bone cements. Iron

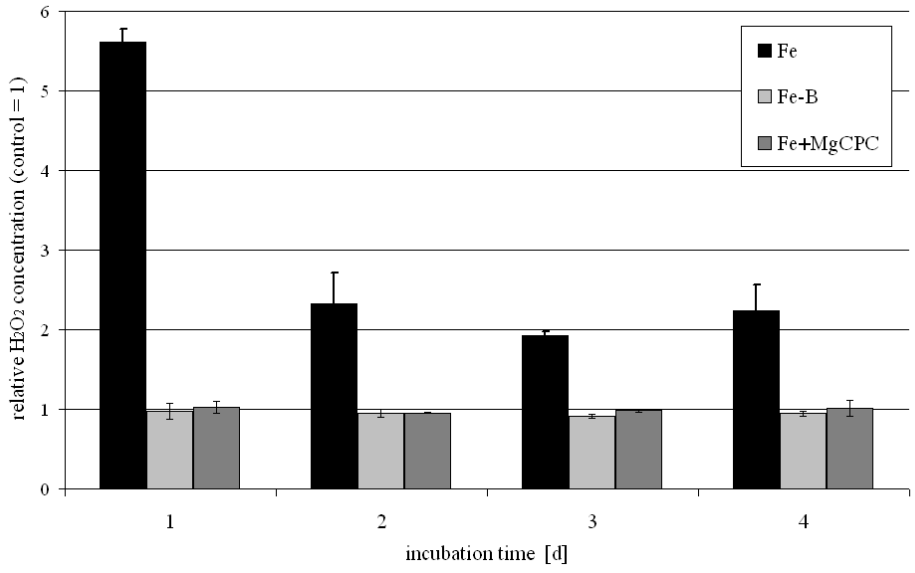
foams without cement filling showed reduced cell viability. This cytotoxic effect could be completely avoided by coating the iron foams with a brushite layer.

The osteoconductivity of the mineral phase may allow cracks in the cement structure to be repaired by ingrowing bone, while the structure is protected from falling apart by the metal reinforcement. After complete resorption of the cement phase the assumed resultant bone/metal composite will be much less prone to stress shielding than any porous metal implant that has more or less constant strength and stiffness over its life time. The use of the iron based metal foam and its calcium phosphate coated bioactivated derivative additionally may open the opportunity to combine a bioresorbable cement matrix with a biocorrodable reinforcement. According to initial experimental data the iron component will only start to corrode after the mineral matrix gets removed.

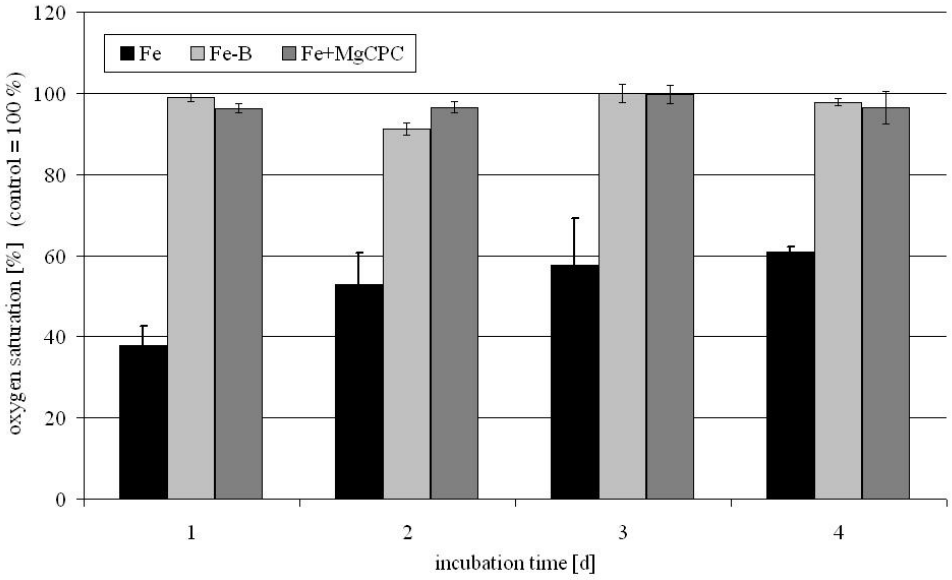
(a)



(b)



(c)



(d)

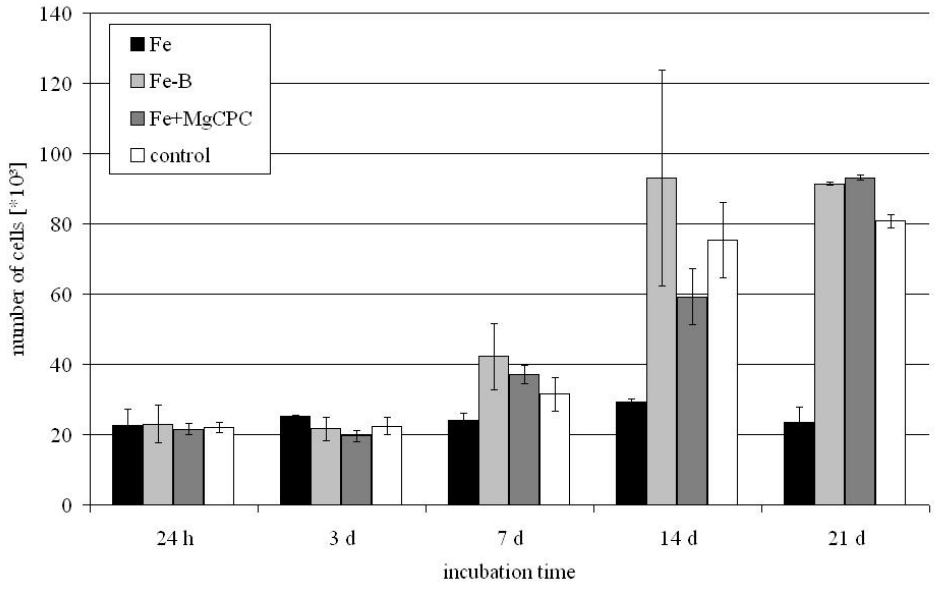


Figure 2: *(a) – (c)* Incubation of unmodified (Fe), brushite coated (Fe-B) and MgCPC filled iron foams (Fe+MgCPC) in cell culture media: iron release *(a)*, hydrogen peroxide *(b)* and oxygen saturation *(c)*. *(d)* Cell proliferation of hMSC cultured with supernatant of pre-incubated media of unmodified (Fe), brushite coated (Fe-B), MgCPC filled iron foams (Fe+MgCPC foams (Fe+MgCPC) or pure cell culture medium (control).

5 Conclusion

Combination of open celled metal foams with high strength mineral bone cements opens new opportunities for design of bone implants. The tested metal/mineral composites provided not

only very high initial compression strengths but furthermore a suitable mechanical stability over a broad range of deformation. Excellent biocompatibility of the investigated composites was prevalently caused by the mineral matrix. Filling with resorbable bone cement completely protected cultured bone cells from detrimental effects of corrosion products of iron metal matrices. Similarly, cytotoxic effects of corroding iron could be completely avoided by coating the iron foams with a brushite layer.

We conclude that development of metal foam/biocement composites for application as bone implant materials deserves further efforts and especially testing in implantation studies that are predictive for performance in clinical use. In the long run bioactivation and control over corrosion may enable us to apply biocorrodable metals for implants with temporary function.

6 Acknowledgment

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7 References

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