Structure, microstructure, and magnetism in ferrimagnetic bioceramics

Th. Leventouri\textsuperscript{a,*}, A.C. Kis\textsuperscript{b}, J.R. Thompson\textsuperscript{b,c}, I.M. Anderson\textsuperscript{d}

\textsuperscript{a}Physics Department, Florida Atlantic University, 777 Glades Road, Boca Raton, FL 33431, USA
\textsuperscript{b}Division of Condensed Matter Sciences, Oak Ridge National Laboratory, Oak Ridge, TN 37830-6061, USA
\textsuperscript{c}Department of Physics, University of Tennessee, Knoxville, TN 37996-1200, USA
\textsuperscript{d}Metals and Ceramics Division, Oak Ridge National Laboratory, Oak Ridge, TN 37830, USA

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Abstract

The structural and magnetic properties of ferrimagnetic bioglass ceramics in the system \[0.45(\text{CaO},\text{P}_2\text{O}_5)(0.52-\chi)\text{SiO}_2\times\text{Fe}_2\text{O}_3\times0.03\text{Na}_2\text{O},\] \(\chi=0.05, 0.10, 0.15, 0.20\) and heat-treated at the temperature range 600–1100 °C are assessed. The structure and microstructure of the samples are characterized with X-ray diffraction, scanning electron microscopy, and energy dispersive X-ray spectroscopy. Calcium phosphate and magnetite develop as the two major crystalline phases. For \(\chi=0.10\) and 0.20, calcium phosphate undergoes a gradual transition from the monoclinic to the rhombohedral crystal system (SG P21/a-R3c) as the heat-treatment temperature increases from 800 to 1100 °C. Dendrites of iron oxide with crystallites of various sizes are observed to form within a glassy matrix enriched in calcium, phosphorous, and silicon. Saturation magnetization, remanence, and coercivity are found from dc magnetic measurements. They vary with the specific processing parameters of the composites, and these are correlated with the observed structure and microstructure of the materials.

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1. Introduction

Ferrimagnetic bioglass ceramics (FBC) were introduced [1–3] for hyperthermic treatment of bone cancer. They are complex, multiphasic, biocompatible and bioactive materials that have been fabricated from the original bioglass [4] with the addition of Fe\textsubscript{2}O\textsubscript{3} in the system [SiO\textsubscript{2}, P\textsubscript{2}O\textsubscript{5}, CaO]. Certain compositions of glass-ceramics that develop an adherent interface with tissues have been shown to form a mechanically strong bond to bone and are known as “bioactive ceramics” [5–7]. Bioactivity of the FBC is related to calcium phosphates and calcium silicates that form the generally accepted model compound for bone mineral [8] hydroxyapatite [Ca\textsubscript{5}(PO\textsubscript{4})\textsubscript{3}OH] in a physiological environment. The crystal structure and chemistry of synthetic bioactive materials and bone mineral determine their behavior when used as implanted biomaterials.

The magnetic properties of FBC arise from magnetite [Fe\textsubscript{3}O\textsubscript{4}] that is produced from the Fe\textsubscript{2}O\textsubscript{3} of the starting oxides. FBC have been shown to be bioactive and effective in hyperthermic treatment of animal bone cancer [9–13]. When a FBC material is placed in the region of the tumor and is subjected to an alternating magnetic field, heat is generated by hysteretic ferrimagnetic loss. The tumor is effectively heated and the temperature locally rises to 42–45 °C, even if the tumor is deeply seated because living tissue does not absorb a magnetic field. As a result, the cancerous cells perish while the healthy ones survive.

Current research efforts focus on development of magnetic bioceramics for clinical applications using a variety of compositions and processing methods while it...
is recognized that fundamental studies of physical properties are needed to obtain long-term reliable biomaterials [13–17].

We have undertaken a systematic study of the physical properties of ferrimagnetic bio-ceramics and here we present correlations between processing parameters, crystal structure, microstructure and magnetic properties of these multiphase systems.

2. Experimental

Four series of samples were prepared in the system \[0.45(CaO,P_2O_5) \times \text{SiO}_2 \times \text{Fe}_2\text{O}_3 \times \text{Na}_2\text{CO}_3\] by a standard melting processing method. The Na\textsubscript{2}O was added to reduce viscosity and improve the reactivity of the melting mixture [12,14]. The molar concentrations in \text{Fe}_2\text{O}_3 were maintained at \(x = 0.05, 0.10, 0.15, 0.20\). The Ca/P ratio was maintained at 1.67, which is close to the molar ratio of the mineral phase in human bone [18]. Reagent grade chemicals of Ca\textsubscript{2}P\textsubscript{2}O\textsubscript{7}, Ca(OH)\textsubscript{2}, SiO\textsubscript{2}, Na\textsubscript{2}CO\textsubscript{3}, and Fe\textsubscript{2}O\textsubscript{3} in the appropriate proportions for each system were thoroughly mixed, sieved through a 125 \(\mu\)m sieve, and placed in a corundum crucible for the melting process in an electric furnace. The crucible was held at \(800 ^\circ\text{C}\) for 3 h of calcination. Then the temperature was increased at a rate of \(5 ^\circ\text{C/minute}\) to \(1450 ^\circ\text{C}\) where it was held for the melting process for 30 min. The melt was quenched by pouring onto a stainless steel plate at room temperature. Subsequently, pieces from the four sample series were heat-treated in air for 6 h at temperatures between 600 and 1100 °C. The specimens were labeled according to the starting composition in \text{Fe}_2\text{O}_3 and the heat treatment temperature, as listed in Table 1.

X-ray (XRD) diffraction measurements were performed using a Siemens D5000 powder diffractometer operating at 45 kV and 40 mA with Ni-filtered Cu-K\(\alpha\) radiation and a diffracted beam monochromator. The data bank from the International Center for Diffraction Data (ICDD) was used in a search/match program for phase identification. The Rietveld refinement method [19] in the GSAS program [20] was used for crystal structure determination and quantitative analysis of phase fractions from the diffraction patterns.

Table 1

<table>
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<tr>
<th>Heat treatment temperature (T_A) (°C)</th>
<th>Series 5G ((x = 5))</th>
<th>Series 10G ((x = 10))</th>
<th>Series 15G ((x = 15))</th>
<th>Series 20G ((x = 20))</th>
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<td>As-prepared</td>
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Chemicals: Ca\textsubscript{3}P\textsubscript{2}O\textsubscript{7}, Ca(OH)\textsubscript{2}, \text{SiO}_2, \text{Na}_2\text{CO}_3, \text{Fe}_2\text{O}_3; Molar % of the oxides: 45(CaO·P\textsubscript{2}O\textsubscript{5}) (52–\(x\))\text{SiO}_2·\(x\)\text{Fe}_2\text{O}_3·3\text{Na}_2\text{O}; Ca/P molar ratio: 1.67.

Scanning electron microscopy (SEM) with energy dispersive X-ray spectroscopy (EDX) was used for microstructural and microchemical analysis of the composite specimens. SEM back-scattered electron (BSE) imaging was performed with 15 keV incident electrons in order to acquire images with compositional contrast. EDX was performed on various phases for qualitative analysis of phase compositions and phase identification. Spectra were acquired at lower incident electron energies (e.g. 4 keV) as necessary to achieve improved spatial resolution.

The magnetic response versus applied magnetic field \(H\) was measured primarily at room temperature with \(|H| \leq 20\text{kOe}\) using a Superconducting QUantum Interference Device (SQUID) magnetometer. The mass magnetization \(M\) is defined as the magnetic moment \(m\) per total mass of sample measured. As discussed below, these data have been analyzed to obtain the saturation magnetization, remanence, and coercive field for each material.

3. Results and discussion

3.1. Structural studies

Two major phases were identified in all sample series: calcium phosphate, \(\text{Ca}_3(\text{PO}_4)_2\), crystallizing in the hexagonal and monoclinic crystal systems, and magnetite (\(\text{Fe}_3\text{O}_4\)). Calcium silicate (\(\text{CaSiO}_3\)) has been reported [9] as a major phase (wollastonite) in FBC systems of different composition from ours. It was detected within instrumental detection limits with peaks overlapping with those of the major phases. It did not crystallize under the processing conditions and remained in the amorphous matrix of the material. Also, Na\textsubscript{2}O did not form a detectable crystalline phase. \(\text{Fe}_2\text{O}_3\) appears as a secondary phase in the series 20G, while part of the \text{SiO}_2 of the starting chemicals is found as a secondary crystalline phase in some samples of series 10G.

The fractions of the crystalline phases crystallized in each specimen were determined by using standard Rietveld refinement techniques, as implemented by the GSAS program. Scale factors, background parameters,
full-width at half-maximum profile parameters, and lattice parameters of the input phases were refined. The atomic parameters, and temperature factors were not allowed to vary because of the complexity of the diffraction patterns and the models. The data were analyzed solely for the crystalline phases and normalized to 100 wt%, while the amorphous content was ignored. The weight fraction $W_p$ of a phase $p$ in a specimen is given by [21]

$$W_p = \frac{S_p(ZMV)_p}{\sum_i S_i(ZMV)_i},$$

where $S_p$ is the refinable scale factor for the phase $p$ in the specimen; $Z$, $M$ and $V$ are the number of formula units per unit cell, the mass of the formula unit and the unit-cell volume of each phase respectively.

Fig. 1 shows an example of Rietveld refinement of the diffraction pattern of the three-phase sample 15G800. Hexagonal calcium phosphate (SG R3c), monoclinic calcium phosphate (SG P21/a) and orthorhombic magnetite (SG Imma) were introduced in the calculated pattern. The amorphous content was not quantified.

Development of the crystalline phases in the samples series 10, 15 and 20G is presented in Fig. 2 where the refined phase fractions are plotted as a function of the heat-treatment temperature. Results from the series 5G along with detailed crystallographic structural studies of all the sample series are provided elsewhere [22]. Notice that, in the sample series 10G, calcium phosphate crystallizes only in the hexagonal system. The fraction of the minor phase of monoclinic SiO$_2$ (SG Cc) that remains from the starting chemicals in the untreated sample 10G, increases in samples heat-treated at temperatures $\geq$ 1000 °C.

A gradual phase transition of calcium phosphate from P21/a $\rightarrow$ R3c is observed in series 15 and 20G for heat-treatment temperatures above 800 °C. A small fraction of monoclinic phase remains for samples annealed at

Fig. 1. Three-phase Rietveld refinement of the X-ray powder diffraction pattern of the sample 15G800. Crosses show the experimental pattern and solid line marks the calculated one. The first row of tick marks below the profiles shows the calculated Bragg peak positions for magnetite (SG Imma), while the second and third rows mark the ones for monoclinic (SG P21/a) and hexagonal (SG R3c) crystal structures correspondingly. The lowest trace is the difference between the experimental and calculated patterns.

Fig. 2. The refined phase fractions in the samples series 10, 15 and 20G as a function of the heat-treatment temperature. Black columns mark the phase fraction of magnetite; white columns show the hexagonal calcium phosphate; diagonal stripes mark the monoclinic calcium phosphate; horizontally striped columns denote silicon oxide, and diamond stripes mark hematite.
1000 °C or higher. Interestingly, the fraction of monoclinic calcium phosphate increases in samples heat-treated at 600 °C. The effect of such crystallographic phase transition on the bioactivity of the composites will be investigated by exposure of the materials in a simulated body fluid environment.

A fourth phase of Fe₂O₃ (SG R₃c) was introduced in the calculated patterns of the samples in series 20G, except for the one heat-treated at 600 °C. As Fig. 2 shows, while the percentage of magnetite in series 15G is affected by the annealing temperature, the effect becomes dramatic in series 20G: there the magnetite weight fraction decreases by ~50% from its maximum value in samples heat-treated at 1100 °C accompanied by formation of Fe₂O₃. The transformation of ferromagnetic magnetite to non-magnetic Fe₂O₃ is detrimental to the properties of the material.

3.2. Microstructural characterization

SEM images have revealed a strong variation of microstructure with composition and heat treatment. The variation of the as-quenched microstructure with increasing iron oxide concentration is shown in Fig. 3. Apart from the inset in Fig. 3c, the images are of identical magnification. The specimen with the lowest iron concentration (5 wt% Fe₂O₃) is shown in Fig. 3a, which features a bimodal isotropic microstructure. EDX spectra indicate that the coarse primary precipitates shown in the upper right corner are pure silica, the darkly imaging secondary precipitates are calcium phosphates, and the brightly imaging glassy matrix contains all of the elements present in the starting mixtures. The primary silica precipitates are also present as darkly imaging features in Fig. 3b, but at this higher iron concentration (10 wt% Fe₂O₃), brightly imaging iron oxide dendrites also appear. For specimens with 15 wt% Fe₂O₃, the microstructure is featureless at the magnification used to image the specimens, but at higher magnification (inset), a fine-scale homogeneous phase distribution is revealed. The homogeneity of the microstructure is maintained at the highest iron concentration (20 wt% Fe₂O₃), but a more coarse dendritic structure is achieved.

Evolution of the dendritic microstructure shown in Fig. 3d with heat-treatment temperature is illustrated in Fig. 4. The magnification of the images is twice that in Fig. 3. The dendrite grains of the unannealed sample Fig. 4a become longer with oriented domains at 600 °C (Fig. 4b), and 800 °C (Fig. 4c). However, in samples heat-treated at 900 °C or higher, the long dendrite structures start to “break up” and, at 1100 °C, no
well-defined dendritic structure is observed (Fig. 4d), although one can still see a dendrite trace with a distinct phase separation.

3.3. Magnetic properties

Let us now consider the magnetic properties of the materials. Fig. 5 illustrates the compositional dependence of the magnetization of samples that were prepared under similar processing conditions with varying initial molar concentration $x$ of Fe$_2$O$_3$, with $x = 0.05, 0.10, 0.15$, and $0.20$. Room temperature $M$–$H$ curves with applied field up to 4000 G for the as-prepared materials are plotted in this figure. Notice that the magnetization of the samples 15 and 20G appears similar, while the crystalline phase fraction of magnetite in sample 20G is ~28% greater than in the 15G (Fig. 2); this is probably associated with the very fine structure observed in sample series 15G (Fig. 3c) compared with the large dendrites in series 20G (Fig. 3d).

An example of the effect of heat-treatment at elevated temperatures on the magnetic properties of the biomaterial is illustrated in Fig. 6, where magnetization loops for four out of the six samples in series 20G are plotted; two loops are omitted for reasons of clarity. The loop area initially increases with annealing temperature $T_A$ when the untreated sample 20G (marked with open circles) is heat-treated at 600 °C, (20G600, filled circles). The loop area and magnetization decrease to a lower value for $T_A = 1000$ °C (squares); this reflects the
conversion of ferrimagnetic Fe₃O₄ into non-magnetic hematite that is evident in Fig. 2. These magnetic quantities decrease still more in samples heat-treated at 1100 °C (open squares) due to additional conversion of magnetite into hematite.

Large values of remanence $M_r$ and coercivity $H_c$ are desirable for the FBC, since the hysteretic ferrimagnetic loss determines the hyperthermic properties of the biomaterial. A correlation of the parameters $M_s$, $H_c$ and $M_r$ with the molar composition of the reacting oxides and heat-treatment temperature is illustrated in Fig. 7 for all the samples studied. The saturation magnetization $M_s$ in samples of series 15G (marked with open circles) remains almost unaffected by heat-treatment. It is reduced in series 10G (triangles) by annealing above 900 °C, while it is reduced to ~55% of its maximum value in samples of series 20G that were heat-treated at 1100 °C (diamonds). As the plot of the coercivity $H_c$ versus heat-treatment temperature shows, materials with the highest magnetite fraction and $M_s$ values (system 20G) become demagnetized ($M = 0$) at the lowest values of reverse applied magnetic field. For the 20G series, only a small effect of temperature $T_A$ on $H_c$ is observed. On the other hand, the system 15G attains higher values of $H_c$, which increases with annealing temperature. A similar, but even more pronounced trend for the $H_c$ is revealed in the system 10G, which attains the largest coercivity. In general, the relatively large values of magnetite coercivity, 100–350 Oe, compared with bulk materials, can be associated with the small particle size [23] of fine and/or “broken” dendrites of Fe₃O₄. Magnetite particles that are roughly equiaxed are expected to be single magnetic domains for sizes less than ~0.3–2 μm [24]. For Fe₂O₄ particles in this size range, which were once considered for magnetic recording purposes, the values of $H_c$ are comparable with those observed here [24]. Furthermore, an elongated particle geometry typically enhances magnetic hysteresis, and this may explain why $H_c$ is larger in the series 10 and 15G than in the 20G
The results of the present studies show that the effect of synthesis variables on the structure and magnetism of FBC are bound to the specific parameters of the sample series. For instance, while the saturation magnetization $M_s$ is clearly determined by the concentration of the reacting oxides in Fe$_2$O$_3$ up to 15%, heat-treatment temperature takes over in sample series 20G as demonstrated in Fig. 7. As the SEM image of Fig. 4d illustrates, the breaking of the ferrimagnetic dendrites above 800 °C correlates with the large changes in the magnetic properties of the material. These changes also correlate with a progressive conversion of magnetite into Fe$_2$O$_3$, whose (crystalline) weight fraction increases from 0 in the sample 20G600 to 0.17 in the 20G1100 (Fig. 2). Notice in the same figure that only the sample heat-treated at 600 °C contains no Fe$_2$O$_3$, while Fig. 6 reveals that the maximum magnetic hysteresis loop develops in this specimen.

4. Conclusions

The present studies have shown that the relation between the processing parameters and the physical properties of the FBC is complex, but they provide some conclusions about the trends.

(1) Two major phases develop in the bulk material: calcium phosphate crystallizing in monoclinic and rhombohedral structures and magnetite in an orthorhombic structure. In series 15 and 20G, calcium phosphate undergoes a phase transition from P21/a to R3c in fractions increasing as the heat-treatment temperature increases from 900 to 1100 °C, while it forms only in the rhombohedral structure in series 10G.

(2) Sample microstructure is determined by the specific processing parameters of each system. Iron oxide phases are resolved in most sample series with dendrite structures of various sizes forming within a glassy matrix enriched in silicon, calcium, and phosphorous.

(3) Magnetic properties are determined by the synthesis parameters of each system. A trend of increased magnetic hysteretic loss with the concentration in Fe$_2$O$_3$ in the system of reacting oxides is reversed in samples heat-treated above 900 °C in the series 20 G, related to the observed breaking of the magnetic dendrites and progressive conversion to non-magnetic Fe$_2$O$_3$.

Extended investigation of the composites is needed in additional samples series and with concentrations in Fe$_2$O$_3$ higher than 20% in order to obtain predictable and universal relations between processing parameters and physical properties of the biomaterial. Furthermore,
research on the effect of simulated body fluid on structure and magnetism of FBC can be expected to lead to a designed material with tailored properties for bone cancer treatment.

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References


