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Sintering of biphasic calcium phosphates

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Abstract Biphasic calcium phosphate (BCP) discs were fabricated and then sintered using two different sintering programs to establish whether the phases present could be controlled at low and high sintering temperatures. X-ray diffraction (XRD) was used to establish the phases present after sintering and scanning electron microscopy (SEM) determined the microstructure. Sintering program 1 involved a simple heating and cooling schedule and temperatures of 1100, 1250, 1275 and 1300°C. It produced samples containing an additional alpha-tricalcium phosphate (α-TCP) phase at temperatures above 1100°C. The original ratio of hydroxyapatite/beta-tricalcium phosphate (HA/β-TCP) could not be maintained above this temperature. Sintering program 2 combined the heating and cooling schedules of the first program with a 900°C hold stage to allow α-TCP to β-TCP conversion to take place. At temperatures of 1250 and 1275°C, this program was successful in completely removing the α-TCP phase and preserving the HA:β-TCP ratio. The SEM results show that the surface morphology of the discs was not greatly affected by choice of sintering program.

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1 Introduction

Autografts and allografts have long been used to fill bone defects caused by surgery, trauma or disease [1, 2]. Autografts have the advantages of being biocompatible, osteoconductive and osteoinductive, but require additional surgery, which can cause trauma and donor site morbidity and leads to an increase in surgical time and hospital costs [3–5]. Allografts overcome these problems, but can potentially introduce the risk of transmission of infection or provoke an immunogenic response. In both cases, sustainable supply is an issue [2, 3, 6, 7].

Synthetic bone grafts can be used as a substitute or addition to established grafting procedures. The majority of synthetic bone grafts are made from biphasic calcium phosphates (BCPs), combining hydroxyapatite (HA) and beta-tricalcium phosphate (β-TCP) [8]. They exhibit excellent biocompatibility and are osteoconductive [5]. The ideal bone graft should provide strength and support, while allowing gradual resorption and transfer of mechanical loads to the surrounding regenerating tissue. The resorption of the implanted material should not exceed the rate of remodelling and bone ingrowth [9, 10]. An important research challenge is developing bone graft materials with tailored resorption. β-TCP is a resorbing ceramic, while HA does not readily resorb [9–11]. Combining the two calcium phosphates in a biphasic mix allows the rate of resorption to be controlled to an extent [10]. The rate of resorption will be strongly influenced by the material properties and the environment in which they are implanted [12, 13].

Material properties deemed particularly important when designing calcium phosphates with improved resorption are surface characteristics, such as: roughness, grain size and porosity, and chemical properties, in particular phase composition. It is possible to use different sintering regimes

to change surface roughness, grain size and density for example by using high and low temperatures [14], however the use of high sintering temperatures causes unwanted phase changes to occur (e.g. β-TCP to α-TCP) [15].

The present study aimed to establish whether the phases present in biphasic samples could be controlled by altering sintering temperature alone, while maintaining three distinct HA/β-TCP ratios: 20/80, 50/50 and 80/20. This would allow the creation of suitable consistent samples.

2 Materials and methods

2.1 Sample preparation

Biphasic calcium phosphate (BCP) ceramic discs were prepared by mixing dry HA and β-TCP powders (Plasma Biotal Ltd, UK), before pressing and sintering. Three types of BCP discs were made: HA20, HA50 and HA80, having initial HA/β-TCP weight percentage ratios of: 20/80, 50/50 and 80/20, respectively. The powders were turbo blended in a high speed mixer (Rondol Technology Ltd, UK) at 1600 rpm for 30 s, repeated three times. They were then uniaxially pressed at 10 MPa to form the unsintered discs which had a mass of 2 g and a diameter of 19 mm. Sintering was carried out in a furnace (Elite Thermal Systems Ltd, UK) using two sintering programs. Sintering program 1 employed a dwell time of 1 h with temperatures of 1100, 1250, 1275, 1300 or 1350°C and a heating and cooling rate of 4°C/min. Sintering program 2 also employed a dwell time of 1 h and initial temperatures of 1250, 1275 or 1300°C but this was followed by cooling to 900°C with a dwell time of 24 h, and a cooling rate of 1°C/min to room temperature (Fig. 1).

2.2 Characterisation techniques

The phase purity and constitution of the BCP discs were analysed by powder X-ray diffraction (XRD). Three to five discs were pooled to provide sufficient material and ground to a fine powder using a pestle and mortar before being analysed. XRD patterns were recorded using a PANalytical X-Pert Pro X-ray diffractometer system with an X'Celerator X-ray detector (PANalytical Ltd, UK), using Cu Kα radiation generated at 40 kV and 35 mA. Samples were scanned in the range $2\theta = 10$–$70°$ at a step size of 0.02°. X'Pert HighScore Plus software (PANalytical Ltd, UK) and the International Centre for Diffraction Data powder diffraction files were used to determine phases present in the three types of disc post-sintering.

The surface microstructures of the various BCP discs were examined by scanning electron microscope (SEM, JEOL JSM 6500F) after sputter coating with $\sim$10 nm of gold.

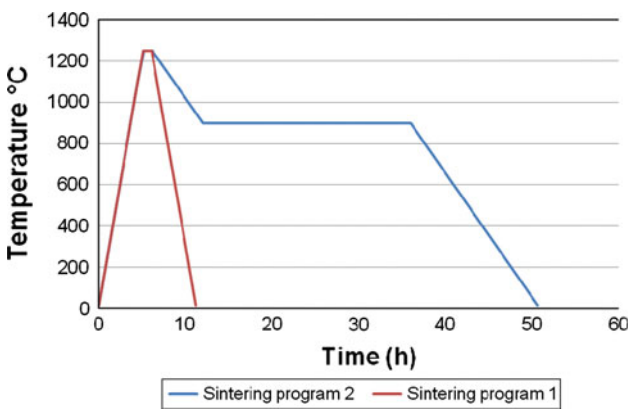

Fig. 1 Sintering programs 1 and 2 represented graphically

3 Results

3.1 Sintering program 1

At 1100°C the BCP sintered discs maintained the pre-sintering HA:β-TCP ratio according to the XRD analysis. At all other temperatures the ratio was altered. An α-TCP phase appeared in all discs at 1250°C and above, increasing with increasing temperature (Fig. 2). α-TCP was also found in higher quantities in the more β-TCP-rich discs (HA20 > HA50 > HA80) (Fig. 2). At higher temperatures β-TCP underwent a larger change the higher the original HA content was (Fig. 4), while at 1250°C there was no discernable trend. No particular trend could be determined for HA (Fig. 3).

In the HA20 discs HA was seen to decrease following sintering to 1250, 1275 and 1300°C (Fig. 3). At the same time β-TCP content decreased with increasing temperature from its original 80 wt% content (Fig. 4). α-TCP was observed to increase with increasing temperature to almost 40 wt% (Fig. 5).

In the HA50 discs HA was seen to remain roughly around the original 50 wt% value, only slightly decreasing with increasing temperature (Fig. 3). β-TCP was again lost from the discs, in a similar pattern to the HA20 discs (Fig. 4). The α-TCP phase increased with increasing temperature to over 30 wt% in the HA50 discs (Fig. 5).

HA content in the HA80 discs increased when sintered at 1250°C and above, the opposite trend to what was observed in the HA20 discs (Fig. 3). β-TCP all but disappeared in the HA80 discs (Fig. 4), while α-TCP again increased with increasing temperature, though to a lesser extent (Fig. 5).

3.2 Sintering program 2

At 1250 and 1275°C α-TCP was eliminated completely (Fig. 6). At 1300°C no α-TCP was present in the HA20

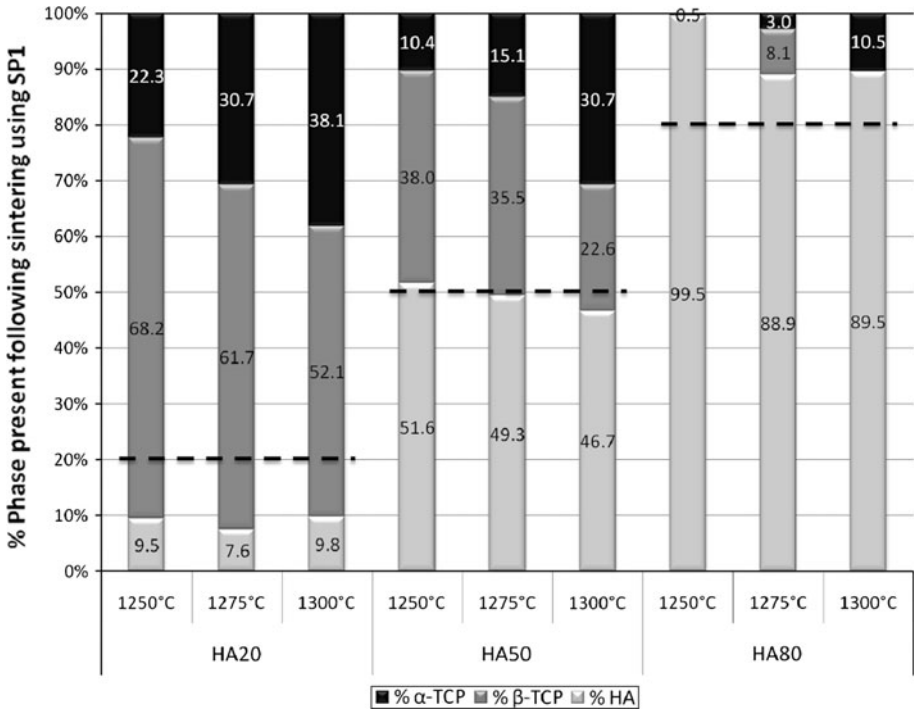

Fig. 2 Percentage of phases present in each composition following sintering to 1250, 1275 and 1300°C under sintering program 1. The *dashed lines* represent the % HA present in the original unsintered discs as a comparison

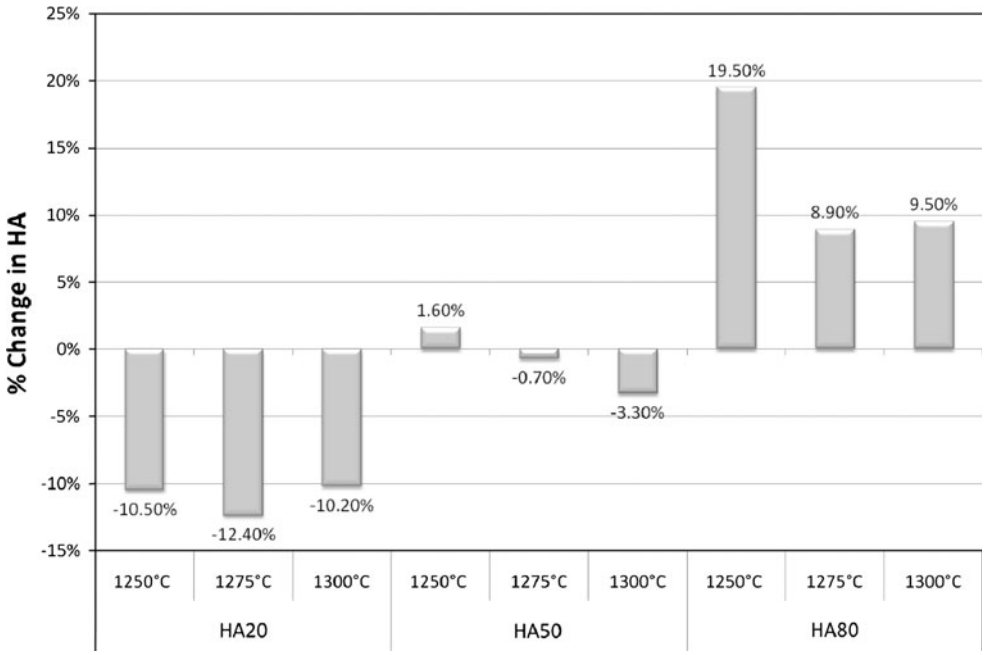

Fig. 3 Percentage change in HA for each composition following sintering to 1250, 1275 and 1300°C under sintering program 1

discs, however small amounts of α-TCP (3–11%) were observed in the HA50 and HA80 discs (Fig. 6).

In the HA20 discs, a decrease in HA content was observed at each temperature (Fig. 7), coupled with an increase of similar magnitude of β-TCP (Fig. 8). No α-TCP was found to be present (Fig. 9).

In the HA50 discs, HA content decreased at 1250 and 1275°C, but increased slightly at 1300°C (Fig. 7). β-TCP increased at 1250 and 1275°C and decreased at 1300°C (Fig. 8), while the α-TCP phase constituted 3.8% of the phases present (Fig. 9).

In the HA80 discs HA increased to a small extent at all temperatures (Fig. 7). β-TCP decreased at all temperatures with the largest decrease occurring after sintering to 1300°C (Fig. 8). α-TCP increased by 10.3% in the HA80 discs (Fig. 9).

At 1250°C the smallest change in phases occurred overall (Table 1) and no α-TCP was present (Fig. 6).

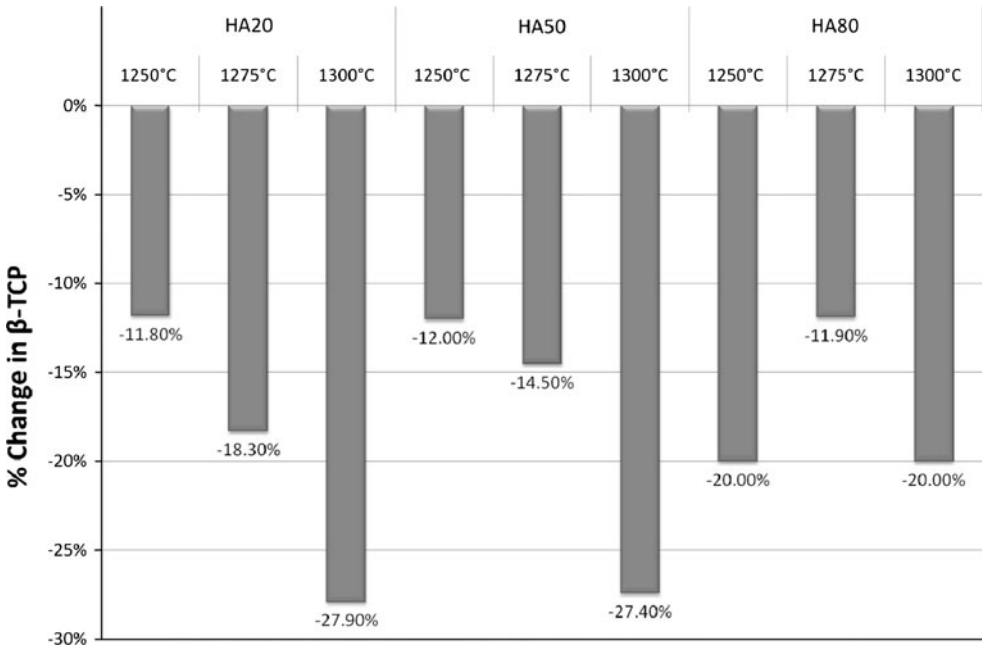

Fig. 4 Percentage change in β-TCP for each composition following sintering to 1250, 1275 and 1300°C under sintering program 1

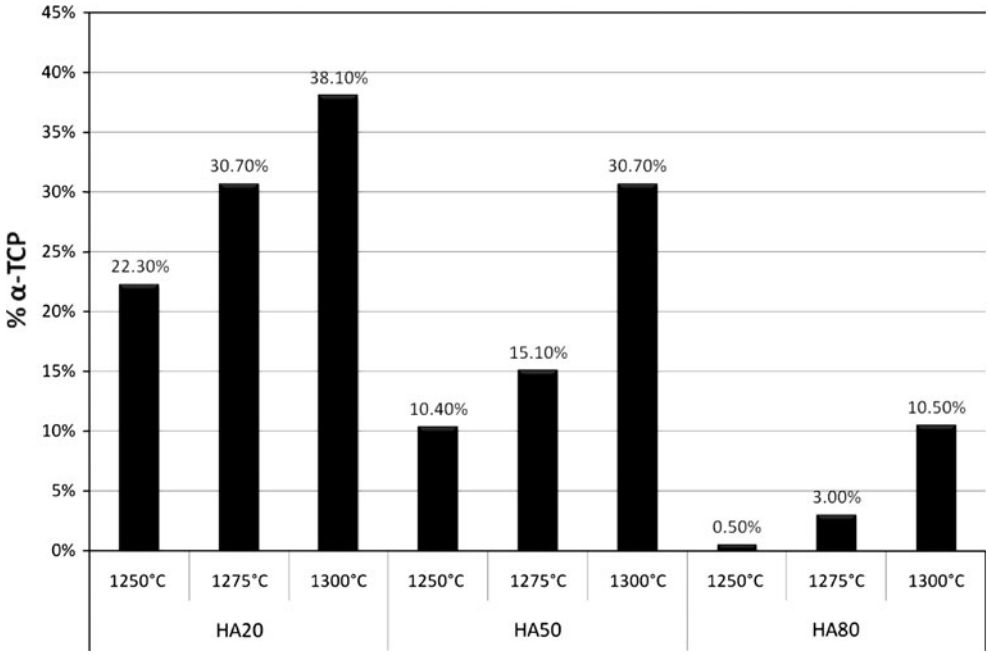

Fig. 5 Percentage α-TCP for each composition following sintering to 1250, 1275 and 1300°C under sintering program 1

3.3 Microstructure

3.3.1 Sintering program 1

At 1100°C the surface is porous, with necking between particles visible (Fig. 10a). At 1250°C the HA20 surfaces were smoother with little porosity (Fig. 10b). The HA80 surfaces, by comparison were also smoother at 1250°C than at 1100°C, but still exhibited some porosity and had smaller grains (Fig. 10c). At 1275 and 1300°C, a similar microstructure was observed with more smoothing and densification of the surface occurring as temperature increased.

3.3.2 Sintering program 2

The microstructure of the samples sintered under sintering program 2, with the 900°C dwell stage, was similar to that of the samples sintered under sintering program 1 at the same temperature, as can be seen by comparing Fig. 10b and d. A smoother microstructure evolved as the sintering temperature was increased.

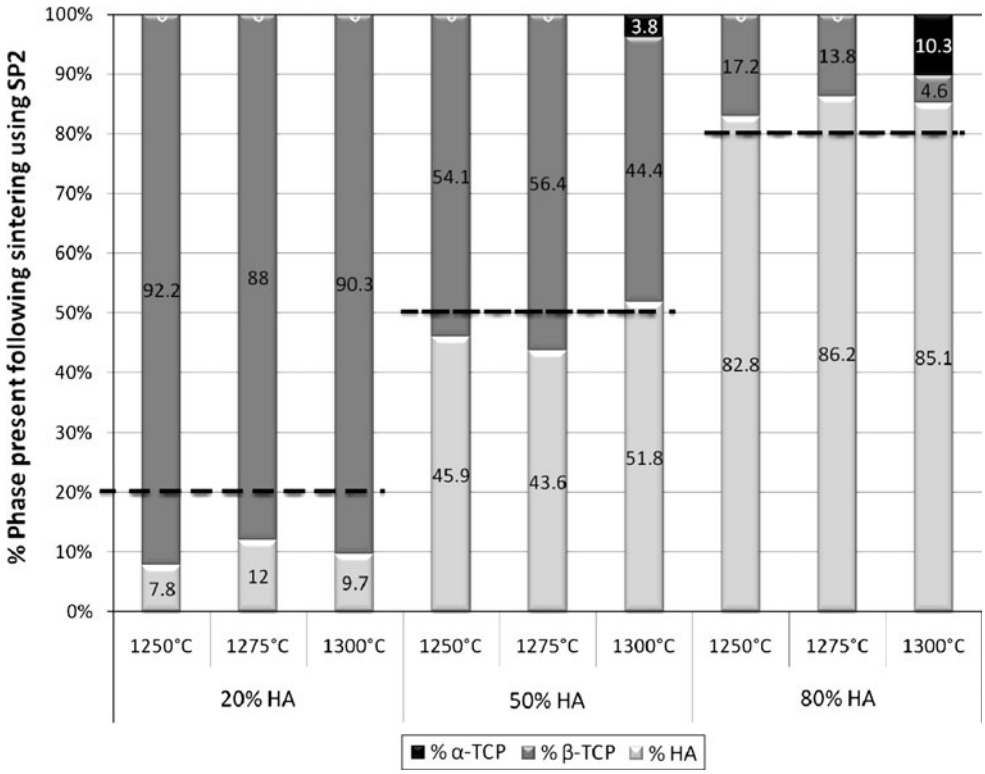

Fig. 6 Percentage of phases present in each composition following sintering to 1250, 1275 and 1300°C under sintering program 2. The *dashed lines* represent the % HA present in the original unsintered discs as a comparison

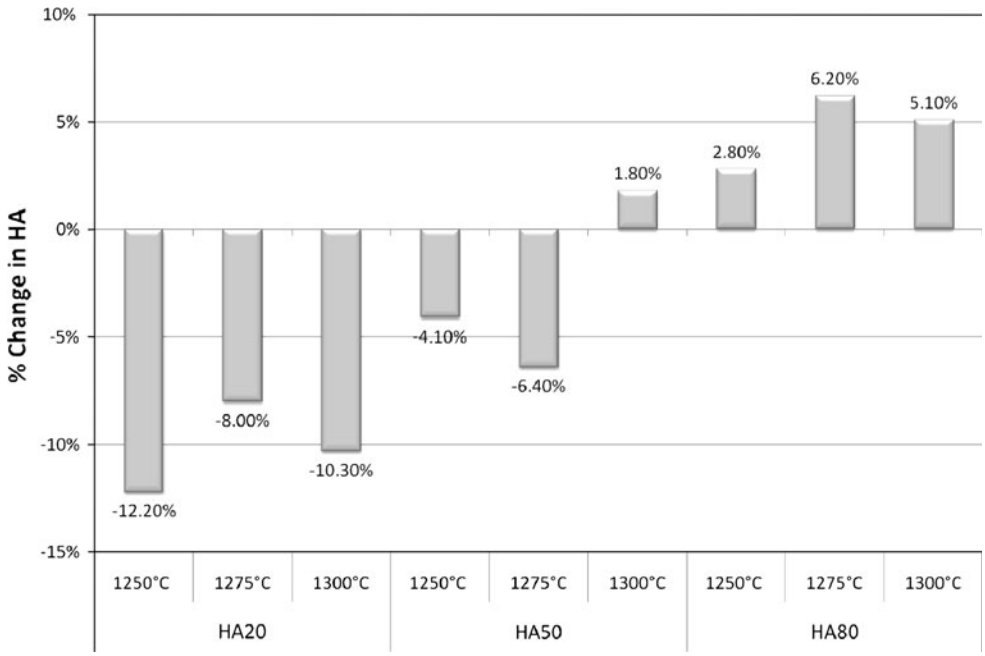

Fig. 7 Percentage change in HA for each composition following sintering to 1250, 1275 and 1300°C under sintering program 2

Figure 10d shows HA20 sintered to 1250 with a 900°C hold temperature.

4 Discussion

At temperatures above 1100°C a phase change from β-TCP to α-TCP and possibly also from HA to α-TCP was observed. The conversion of β-TCP to α-TCP is a well-documented phenomenon, known to occur at around 1125°C [16, 17]. HA has also been shown to convert to β-TCP at temperatures below 1200°C and to α-TCP at temperatures above 1200°C [17]. There is some discrepancy over the degree of phase changes which occur in biphasic calcium phosphates, which can be attributed to the

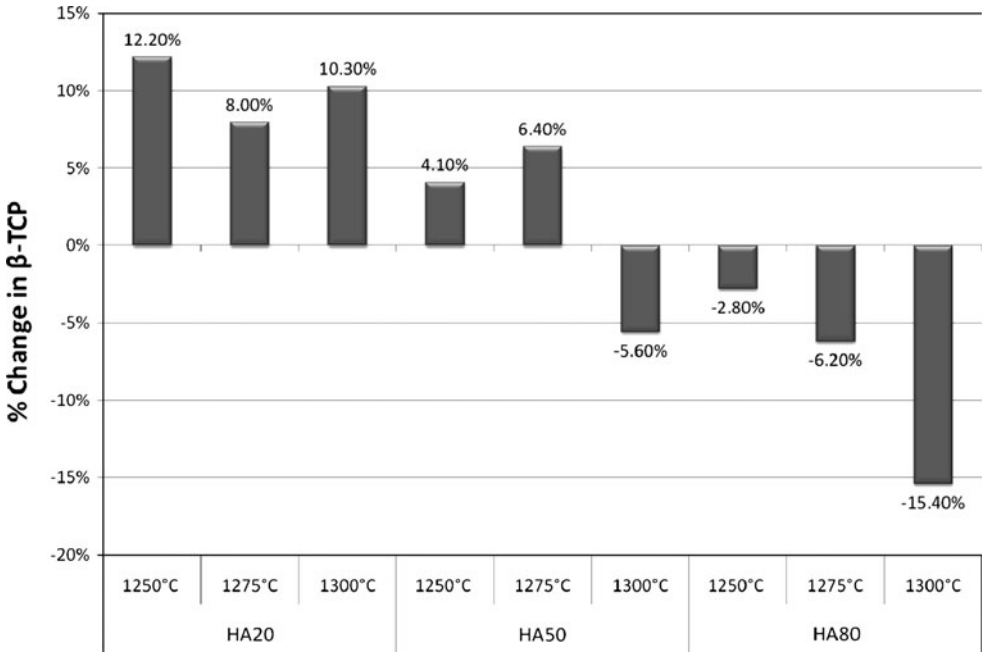

Fig. 8 Percentage change in β-TCP for each composition following sintering to 1250, 1275 and 1300°C under sintering program 2

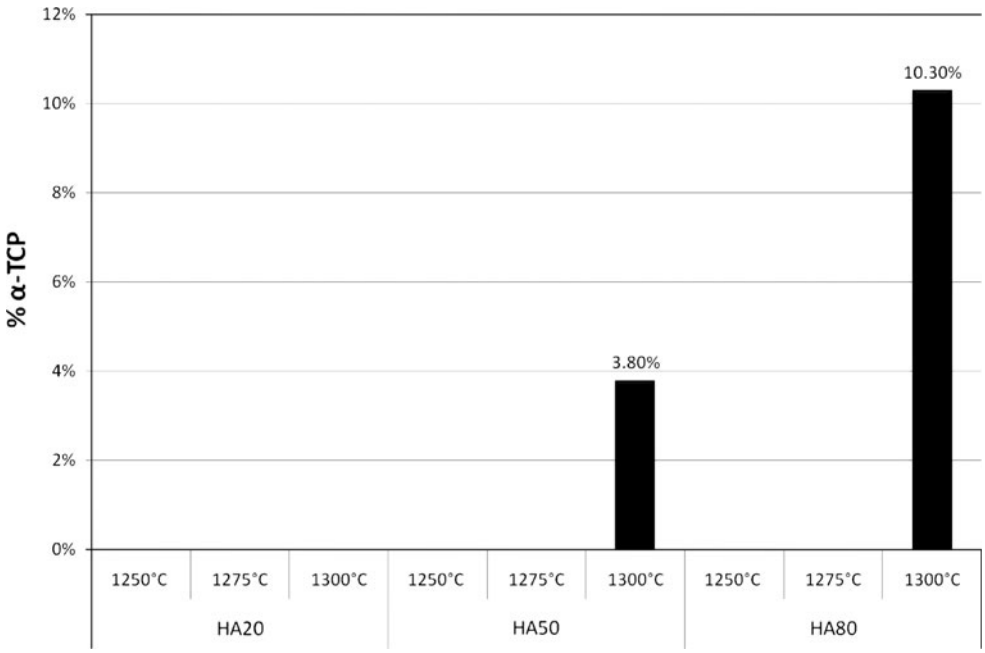

Fig. 9 Percentage α-TCP for each composition following sintering to 1250, 1275 and 1300°C under sintering program 2

Table 1 Total change in phase for each material at each temperature as determined by XRD

	1250°C	1275°C	1300°C
HA20 (%)	24.4	16.0	20.6
HA50 (%)	8.2	12.8	7.4
HA80 (%)	5.6	12.4	20.5
Total (%)	38.2	41.2	48.5

initial phases present and their purity. For example, it seems that the greater the incidence of β-TCP in a biphasic sample, the larger the quantity of HA that decomposes, which is corroborated by the results found in this study. The presence of ions, such as magnesium, can also affect transition temperatures of phases [18]. Examining the results from sintering program 1, it was surprising that the α-TCP did not reconvert to the more stable β-TCP upon

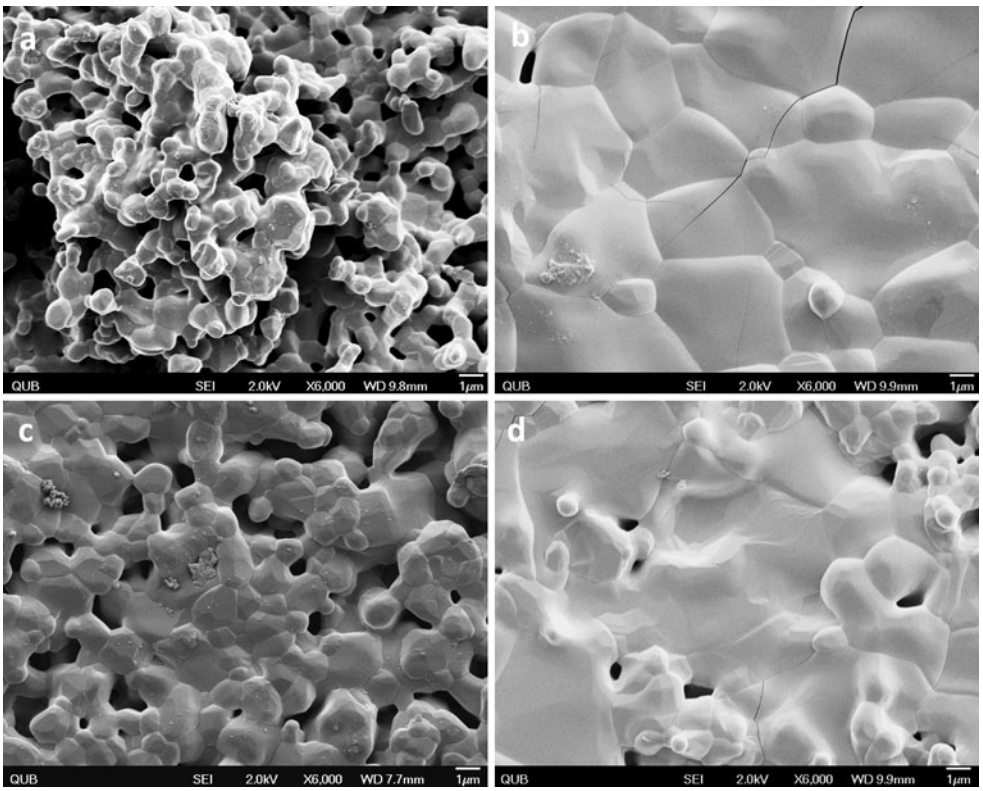

Fig. 10 **a** HA20 sample sintered to 1100°C (sintering program 1) ×6000 **b** HA20 sample sintered to 1250°C (sintering program 1) ×6000 **c** HA80 sample sintered to 1250°C (sintering program 1) ×6000 **d** HA20 sample sintered to 1250°C (sintering program 2) ×6000

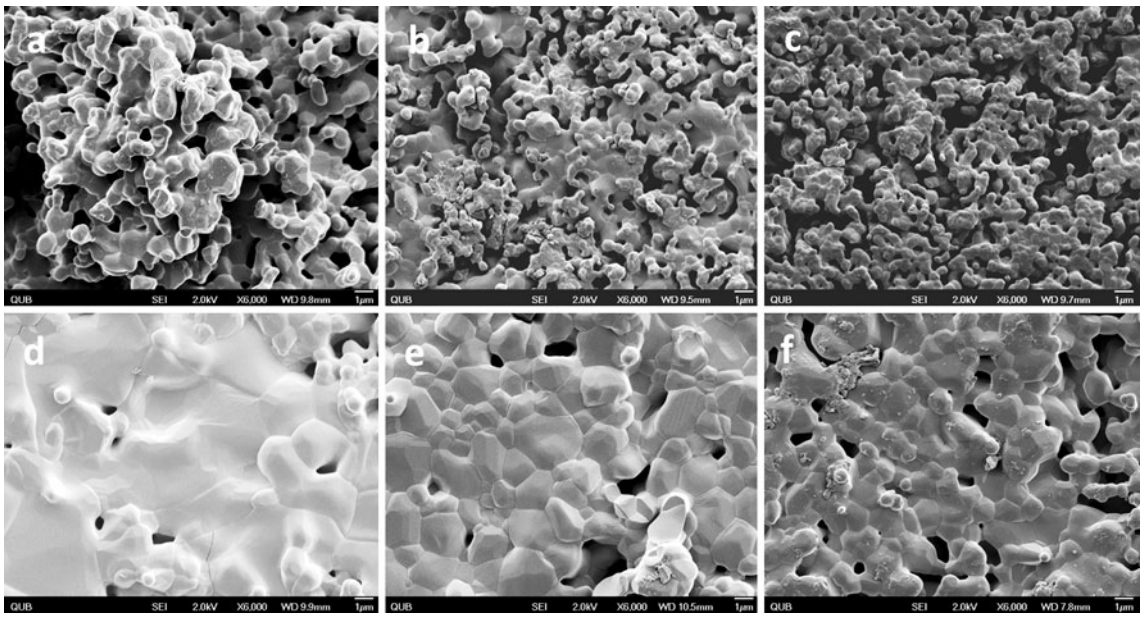

Fig. 11 **a** HA20 sample sintered to 1100°C (sintering program 1) ×6000 **b** HA50 sample sintered to 1100°C (sintering program 1) ×6000 **c** HA80 sample sintered to 1100°C (sintering program 1) ×6000 **d** HA20 sample sintered to 1250°C (sintering program 2) ×6000 **e** HA50 sample sintered to 1250°C (sintering program 2) ×6000 **f** HA80 sample sintered to 1250°C (sintering program 2) ×6000

slow cooling (4°C/min), as air quenching has been reported to be necessary for the retention of α-TCP upon cooling to room temperature [19]. Instead, large quantities of α-TCP were present in most of the samples, in particular those with high initial β-TCP quantities.

To allow production of biphasic samples which maintain the prescribed HA:β-TCP ratio after sintering it is necessary to alter the sintering conditions or employ substitute ions such as magnesium to stabilise the β-TCP. Multistage sintering, whereby the heating and cooling stages of sintering are controlled, is often used as a technique to achieve specific features, such as microstructure or phase composition [14]. Sintering program 2 was investigated as a possibility for controlling the phases present as it has been noted that a holding temperature of around 900°C facilitates the conversion of α-TCP to β-TCP. It was thought that including a 900°C step after the sintering stage could allow the reaction to take place. It would appear from the results, Fig. 6 in particular, that the addition of this cooling stage has indeed provided a facility for α-TCP to reconvert to β-TCP.

Using sintering program 1, at 1100°C only a small amount of sintering has taken place, with more sintering occurring in the HA20 samples (Fig. 10a) than in the HA80 samples. This is in agreement with what Yang et al. [20] found when sintering biphasic ceramic filaments where β-TCP was reported to sinter sooner than the HA phase. At 1250°C further sintering has left the HA20 surfaces smoother and almost completely free from pores, as was expected. The HA80 surfaces, by comparison are also smoother, but sintering has not taken place to the same extent. The HA20 samples have larger grains than the HA80 samples, due to enhanced sintering and more coarsening. At 1275 and 1300°C, the same trend exists with more sintering and densification occurring, while porosity continues to decrease.

Under sintering program 2 the same microstructure can be seen as the samples sintered under sintering program 1. As the temperature was increased, more sintering took place. Again, greater sintering occurred in samples with higher β-TCP content. The differences in microstructure caused by using two sintering temperatures (1100 and 1250°C) create materials with very different surface areas (Fig. 11). As it is the surface which will be first exposed to either the dissolution media, in the case of dissolution testing, or the cells in the case of an in vitro or in vivo situation, this will have a huge effect on the speed of dissolution or resorption.

5 Conclusions

The present study has established a sintering program which maintains the original HA/β-TCP ratio of a biphasic disc, even when sintered at temperatures above 1100°C. The control of phases in biphasic calcium phosphates is important not only for producing consistent samples for testing, but also for implantable bone graft substitutes in general. The sintering program identified by this study has allowed the complete removal of the α-TCP phase from discs sintered up to 1275°C.

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