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#### WHITE PAPER

### Characterization of Bioceramics for Surgical Implants: Part I - Precursor Qualification

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#### **INTRODUCTION**

Bioceramics are an important subset of biomaterials, employed in medical and orthopedic applications, mainly for the repair and replacement of diseased and damaged parts of the human skeleton, bone, teeth and joints. Based on the common response of tissues to implants, bioceramics are classified into three groups: (1) bioinert ceramics, e.g.,  $Al_2O_3$ , and  $ZrO_2$ ; (2) bioactive ceramics, e.g., hydroxyapatite (HAp); and (3) bioresorbable ceramics such as  $\beta$ - tricalcium phosphate ( $\beta$ -TCP). With the advent of many bioceramic compositions, it has been the primary focus of this field to ensure the safety of newly developed or currently used materials, by proving their biocompatibility and understanding their toxicological profile, at cytotoxic, histotoxic and genotoxic levels. The safety and reliability concerns regarding bioceramics originates from the potential prolonged leaching of ions in the physiological environment, from the integrity of the tissue/implant interface, and from the fatigue fracture and wear behavior of load-bearing implants. HAp,  $\beta$ -TCP, and calcium sulfate hemihydrate and dihydrate have long been recognized as appropriate materials for bones, due to their chemical and biological similarity to human hard tissues. Properly screening bioceramic powders and fabricated implant parts, prior to in vitro and in vivo tests, is appealing in term of safety, and time- and cost-savings. Below are a set of FDA-recognized consensus standards for qualifying these materials for surgical implants:

- ASTM F1185-03 (Reapproved 2014): Standard Specification for Composition of Hydroxyapatite for Surgical Implants
- ASTM F2224-09 (Reapproved 2014): Standard Specification for High Purity Calcium Sulfate Hemihydrate or Dihydrate for Surgical Implants



Figure 1: Modern analytical technique matrix for characterizing bioceramic precursors: X-Ray Photoelectron Spectroscopy (XPS), Transmission Electron Microscopy/Energy Dispersive X-ray Spectroscopy (TEM/EDS), X-ray Diffraction (XRD), High Performance Inductively Coupled Plasma – Optical Emission Spectroscopy (HP-ICP-OES), Inductively Coupled Plasma – Mass Spectroscopy (ICP-MS), and Thermogravimetric Analysis/Differential Scanning Calorimetry – Fourier Transfer Infrared Spectroscopy (TGA/DSC-FTIR).

- ISO 13175-3 1st edition 2012-10-01: Implants for surgery -- Calcium phosphates -- Part 3: Hydroxyapatite and betatricalcium phosphate bone substitutes
- ASTM F1088-18: Standard Specification for Beta-Tricalcium Phosphate for Surgical Implantation
- ISO 13779-2 3rd edition 2018-12: Implants for surgery -Hydroxyapatite - Part 2: Thermally sprayed coatings of hydroxyapatite
- ISO 13779-3 2nd edition 2018-12: Implants for surgery Hydroxyapatite Part 3: Chemical analysis and characterization of crystallinity ratio and phase purity.

This paper will demonstrate how modern analytical tools (Figure 1) can be used for the quality control of hydroxyapatite and  $\beta$ -tricalcium phosphate powders, which are either directly manufactured into bulk parts after proper sintering, or spray coated on load-bearing implants to promote initial osseointegration. Specifically, we will demonstrate EAG's capability in terms of chemical, surface and thermal characterization of bioceramic precursors used for surgical implants (Sigma Aldrich® HAp Lot# 289396, unsintered  $\beta$ -TCP Lot# 13204 and sintered  $\beta$ -TCP Lot#49963).

### CHEMICAL ANALYSIS OF HAP AND $\beta$ -TCP

Accurate determination of Ca/P atomic ratios using HP ICP-OES The mechanical strength of HAp increases as the Ca/P atomic ratio is increased, reaching a maximum value at Ca/P  $\sim 1.67$  (i.e. stoichiometric HAp), and decreases suddenly when Ca/P > 1.67.<sup>1</sup> Unfortunately, producing pure stoichiometric HAp is a challenge, and commercial HAp is often calcium deficient. This calcium deficiency affects lattice parameters, both in crystal orientation and in pairing to a crystallographic system.

HP ICP-OES is recommended for accurate Ca/P ratio determination.<sup>2</sup> Classical ICP-OES was developed under the assumption that it is sufficiently immune to matrix effects and instrument response nonlinearity. In reality, this is more often than not the case. A key enabler of HP ICP-OES is the development of a drift correction procedure to address what was recognized as the major source of uncertainty observed in classical ICP-OES results, by comparing the transient signal intensity of sample analyte against that of a made-up reference standard (SRM) with composition closely matching the sample.

HP ICP-OES method yields very tight measurement uncertainties typically within 1% relative, at approximately 95% confidence level with coverage factor k of ~ 2 -2.5. Table 1 summarizes the Ca/P ratios of HAp and  $\beta$ -TCP precursors determined by HP ICP-OES, showing calcium deficiency in all samples to various degrees. The measurement uncertainty of HP ICP-OES analysis comprises three major sources: uncertainty from measuring SRM solutions, uncertainty from measuring sample solutions and the uncertainty of the certified values of the SRM used.

Figure 2 illustrates the process of estimating uncertainty for sintered  $\beta$ -TCP, according to A2LA guidelines. For example, the expanded uncertainty U for Ca and P are 0.74% relative and 0.41% relative, respectively. This is not attainable by classical ICP-OES, which typically features expanded uncertainties in the range of 3-5% relative.

Table 1. HP ICP-OES determination of Ca/P ratios of HAp and $\beta$ -TCP ceramics*									
Composition	HAp F	Powder	β-TCP Powder						
Composition	Unsintered	Unsintered Stoichiometry		Sintered	Stoichiometry				
Ca, %mass	38.82	39.89	35.67	37.36	38.76				
Uncertainty, %mass	0.29	-	0.26	0.28	-				
P, %mass	18.66	18.50	18.67	19.72	19.97				
Uncertainly, %mass	0.11	-	0.08	0.08	-				
Ca/P (atom/atom)	1.608	1.667	1.477	1.464	1.500				

\* The measurement uncertainty associated with the reported value represents expanded uncertainty with coverage factor k ~ 2.0 - 2.5 at approximately 95% confidence level.

\*\* HP ICP-OES analysis conditions: PerkinElmer® 7300; Emission lines used: Ca 315.887 nm, P 214.914 nm, Sc (internal standard) 357.634 nm; Reference standards: Inorganic Adventure® single element standard solutions.

Un						
Source	(mg/g)	relativ e	df	coverage factor, <i>k</i>		
SRM Ca-7 Measurements	0.084	0.22%	3			
bioceramic precursor Measurements	0.074	0.20%	3			
Certified Value of SRM Ca-7	0.001	0.11%	61			
Combined Uncertainty	0.119	0.32%	8.00			
Coverage Factor, k				2.31		
Expanded Uncertainty	0.275	0.74%				

Ur	ncertainty	Budget				
Source	(mg/g)	relativ e	df	coverage factor, k		
SRM P-3 Measurements	0.013	0.07%	3			
bioceramic precursor Measurements	0.007	0.04%	3			
Certified Value of SRM P- 3	0.002	0.19%	61			
Combined Uncertainty	0.041	0.21%	62.00			
Coverage Factor, k				2.00		
Expanded Uncertainty	0.081	0.41%				

## Figure 2: Uncertainty estimation of Ca (top) and P (below) during HP ICP-OES composition analysis of sintered $\beta\text{-TCP}$

#### Quantitative analysis of trace metal impurities with ICP-MS

Impurities may affect bioactivity and crystalline structure. For example, anionic substitution of carbonate for phosphate has been shown to increase HAp solubility, while substitution of fluoride for hydroxide increase stability. Moreover, cationic substitution such as Mg<sup>2</sup>+ in place of Ca<sup>2</sup>+ can potentially have a favorable biological effect.<sup>4</sup> Unsubstituted calcium deficient HAp does not exist in biological system. Biological apatites are formed by ion substitution in the presence of water including:

- Ca<sup>2</sup>+ site substitution by Na+, K+, Mg<sup>2</sup>+ and Sr<sup>2</sup>+
- $PO_4^{3}$  and  $HPO_4^{2}$  site substitution by  $CO_3^{2}$ -
- OH- site substitution by F-, Cl-, and CO<sub>3</sub><sup>2</sup>-

In addition, elemental impurities can raise safety concern. These are regulated in ISO13779-3, ISO10993-17, ASTM F1185 and ASTM F1088 standards for  $\beta$ -TCP and HAp. Specifically, As, Cd, Hg, Pb, and other metals such as V, Cr, Ni, Cu, Sb, and noble metals listed in <USP 232> and <ICH Q3D Option 2a> must be controlled to a minimum value.

Recognized as one of the most important mass spectrometric

techniques, ICP-MS has multi-element capabilities at high sensitivity, which translate to detection limits in the ng/g -  $\mu$ g/g range. To obtain NIST-traceable quantification, an ICP-MS method validation must be established in terms of system suitability, accuracy, precision, limit of quantification, and additional performance parameters according to acceptance criteria specified by the various parties involved. Here we will review some of these key parameters.

The system suitability of an ICP-MS instrument was examined by periodically measuring the drift of a secondary source standard at 1.0 µg/L or 10.0 µg/L (equivalent to 5 and 50 µg/g in a sample, respectively) for a number of key analytes, throughout the course of sample analysis. Figure 3 shows instrument drift, defined as %RSD of readings, over the entire course of analyzing HAp and  $\beta$ -TCP samples. All analytes meet the acceptance criteria specified by the <USP 233> protocol, no more than (NMT) 20%, with majority showing drift RSD% < 2%.

The accuracy of the ICP-MS analysis was validated by spike recovery. Figure 4 shows the spike recovery for some selected analytes. Our ICP-MS method shows spike recovery (%) of analytes ranging from 90-110%, well within the acceptance criteria (75-150%) specified by the <USP 233> protocol.

Table 2 summarizes the ICP-MS analysis results for commercial HAp and  $\beta$ -TCP samples, for the big four impurities, As, Cd, Hg and Pb, and other heavy metals of common concern, with a limit of quantification (LoQ) of 0.5 µg/g, which readily satisfies the



Figure 3: ICP-MS instrument drift. (a) analytes monitored at 10  $\mu$ g/L level, spaced by 10  $\mu$ g/L for clarity; and (b) analytes monitored at 1  $\mu$ g/L level, spaced by 1  $\mu$ g/L for clarity. Acceptance criteria of drift NMT 20% per <USP 233>.

Analysis conditions: PerkinElmer® Nexlon 350D ICP-MS, RF powder - 1.6 kW, Nebulizer - Opalmist, Spray Chamber - Tracey PFA44, Ar Flow - 18.0 L/min, Auxillary Ar Flow - 1.2 L/min, Nebulizer Gas Flow - 0.92 L/min, Integration time - 80s, Scanning mode - Peak hopping, Replicates - 5, Cell gas (NH3) - 0.9 L/min, RPq for Ce as CeO (m/z 156) < 2 %



Figure 4: ICP-MS spike recovery (n=5) for selected analytes at 10  $\mu$ g/g spike level. Acceptance criteria of spike recovery is 75 – 150% per <USP 233>

specification limits set by ASTM F1185 and F1088.

In summary, ICP-MS, as practiced under controlled conditions by EAG, can readily meet the analytical needs for qualifying the purity and trace metal impurity requirements of bioceramic precursors used for surgical implants.

#### Phase identification and content determination by XRD

XRD is a powerful non-destructive technique for characterizing crystalline materials. It provides information on crystal structure, phase, preferred crystal orientation (texture), and other structural parameters, such as average grain size, crystallinity, strain, and crystal defects. According to ASTM F1088 and F1185, crystallinity should be greater than 95% for  $\beta$ -TCP and HAp. Limits should also be given for minor components such as β-TCP, calcium tetraphosphate (TTCP) and lime (CaO) according to ISO 13779-3 - Part 3. Table 3 summarizes the phase content of HAp and B-TCP determined by XRD per ASTM F2024. While HAp and the sintered  $\beta$ -TCP shows the expected HAp and  $\beta$ -TCP phases, the commercial unsintered  $\beta$ -TCP sample was identified to be a mixture of HAp and monetite Ca(PO3)(OH) and does not contain any B-TCP phase, though the bulk Ca/P ratio resembles that of the sintered B-TCP sample. This investigation reveals that how important XRD is as a tool to qualify bioceramic precursors and to verify that the chemicals in the supply chain are correctly identified.

#### SURFACE CHARACTERIZATION

#### Surface chemistry with XPS

XPS is used to determine atomic composition and chemistry. It is

Table 2: ICP-MS quantification of key trace metal impurities in HAp and β-TCP									
		HAp, μ	g/g	β-TCP, μ <b>g/g</b>					
Impurities	LoQ, µg/g	ASTM F1185	Unsintered	ASTM F1088	Unsintered	Sintered			
		Spec Limit <sup>a</sup>	(n=3)	Spec Limit <sup>a</sup>	(n=3)	(n=3)			
As	0.5	3	<0.5	3	<0.5	<0.5			
Cd	0.5	5	<0.5	5	<0.5	<0.5			
Hg	0.5	5	<0.5	5	<0.5	<0.5			
Pb	0.5	30	<0.5	30	<0.5	<0.5			
V	0.5		<0.5		0.54±0.03	4.5 ± 0.1			
Cr	0.5		<0.5		<0.5	1.8 ± 0.2			
Ni	0.5		<0.5		<0.5	2.7 ± 1.1 <sup>b</sup>			
Cu	0.5		<0.5		<0.5	<0.5			
Мо	0.5		<0.5		<0.5	3.0 ± 0.2			
Ru	0.5	50 -	<0.5	50 -	<0.5	<0.5			
Rh	0.5	$\Sigma$ [As,Cd,Hg,Pb]	<0.5	$\Sigma$ [As,Cd,Hg,Pb]	<0.5	<0.5			
Pd	0.5		<0.5		<0.5	<0.5			
Sb	0.5		<0.5		<0.5	<0.5			
Os	0.5		<0.5		<0.5	<0.5			
lr	0.5		<0.5		<0.5	<0.5			
Pt	0.5		<0.5		<0.5	<0.5			
a Total heavy metals	a Total heavy metals as lead (Pb) NMT 50 ug/g; b increased variation likely due to inherent sample heterogeneity.								

Table 3: Phase identification, crystallite size/strain and quantification results per ASTM F2024								
Sample ID	Phases Identified	Concentration (± 5 wt%)	Crystallite Size (nm)	Microstrain (%)				
НАр	Ca <sub>10</sub> (PO <sub>4</sub> ) <sub>6</sub> (OH) <sub>2</sub> – Hydoxylapatite Hexagonal, S.G.: P63/m (176) PDF #00-066-0738	100.00	248.6 (13.3)	0.039 (0.002)				
β-TCP, unsintered	Ca <sub>10</sub> (PO <sub>4</sub> ) <sub>6</sub> (OH) <sub>2</sub> – Hydoxylapatite Hexagonal, S.G.: P63/m (176) PDF #00-066-0738	95	17.3 (0.2)	ND				
	Ca(PO <sub>3</sub> )(OH) – Monetite Triclinic, S.G.: P-1 (2) PDF #00-009-0080	5.0	25.6 (2.0)	ND				
β-TCP, sintered	Ca <sub>3</sub> (PO <sub>4</sub> ) <sub>2</sub> – β-TCP (Tuite) Hexagonal, S.G.: R3c (161) PDF #04-008-8714	100.0	>1000	0.088 (0.002)				

ND – Not determined. XRD data was collected by a coupled theta: two-theta scan on a Rigaku Ultima-III diffractometer equipped with copper X-ray tube with double Ni beta filters, parafocusing (Bragg-Brentano) optics, computer-controlled slits, and a 1D strip detector.

a surface analysis technique with a sampling volume that extends from the surface to a depth of approximately 5 -10 nm. As an elemental analysis technique, XPS is unique in also providing chemical state information for the detected elements.

All the three powders contained C, O, P, Ca, and traces of Cl on their surfaces (see Table 4 and Figure 5). Sample  $\beta$ -TCP, sintered, also had a low level of Si in the state of SiO<sub>2</sub>. No other contaminants were detected, within the expected XPS detection limit of ~0.1 atom%.

Table 4: Atomic concentrations (in atom%) <sup>a, b</sup>									
Sample	C <sub>1S</sub>	0 <sub>1S</sub>	Si <sub>2P</sub>	P <sub>2P</sub>	CL <sub>2P</sub>	Ca <sub>2P</sub>			
HAp	15.0	53.3	-	13.6	0.4	17.6			
β-TCP, unsintered	5.0	60.0	-	15.6	0.3	19.2			
β-TCP, sintered	17.7	51.5	2.2	11.9	0.7	16.0			

a Normalized to 100% of all the elements detected. XPS does not detect  ${\rm H}$  or He.

b "-" indicates the element is not detected.



Figure 5: XPS survey spectra

The O1s spectra were dominated by a lower binding energy peak associated with Ca phosphates and had a higher binding energy shoulder indicating the presence of organically bonded O (Table 5 and Figure 6).

Table 5: Oxygen Chemical States (in % of Total O <sup>a</sup> )								
Sampla	Binding E	Energy, eV	%Area					
Sample	CaPO <sub>x</sub>	C-0	CaPO <sub>x</sub>	C-0				
НАр	531.16	532.61	81	19				
$\beta$ -TCP, unsintered	531.49	533.26	88	12				
β-TCP, sintered	531.04	532.77	80	20				
a Values in this table are	nercentages	of the total at	tomic concent	ration of the				

a Values in this table are percentages of the total atomic concentration of the corresponding elements in Table 4;

Table 6 includes a number of concentration ratios for all the samples. The Ca/P and O/Ca ratios were calculated using the total concentrations of these elements from Table 4. The O/Ca<sub>adj</sub> ratio was calculated using the total Ca concentration and the CaPO<sub>x</sub> portion of the O concentration. The Ca/P ratios appear to be lower than the theoretical bulk values, indicating that the surface was Ca deficient. The O/Ca<sub>adj</sub> ratio for HAp was slightly lower than its theoretical value of 2.6. The O/Ca<sub>adj</sub> ratios for β-TCP were slightly above for unsintered and slightly below for sintered powders than the theoretical value of 2.67.

Also included in Table 6 are peak intensity ratios of the O shakeup satellite 2 (at binding energy of 567.5 eV) to the total O1s peak (which includes the regular photoelectron O1s line and both satellite 1 and satellite 2) in Figure 7. For the adjusted ratio, only the phosphate portion of the O1s peak is used. This procedure follows a published article by Ratner et al<sup>5</sup>, although other approaches are possible. The O1s-Sat 2/O1s ratios for HAp and  $\beta$ -TCP unsintered, are very similar to previously published data, consistent with a conclusion that these could be used as an identifying parameter for specific phosphate materials.

The substantial surface calcium deficiency discovered by XPS is insightful. It not only reveals how drastically the surface chemistry can differ from the bulk, for example, by ion exchange of surface calcium ions with protons in synthesis media of varied pH, but it could also provide insight into process used to tune surface/



Figure 6: XPS high resolution O1s spectra and their curve fit model



Figure 7: XPS high resolution O1s spectra with shake-up satellites

interface sensitive physical properties, such as sintering of bioceramic precursors and the bioactivity of formed parts and ceramic coatings.

#### Structural and compositional characterization using TEM-EDS

HA in bone is nanocrystalline. Nanoparticles (NPs) of HA crystals smaller than 100 nm have the highest reported efficacy with respect to cellular integration. It has been suggested that these NPs induce responses different from larger structures, implying that NPs could more easily form biocompatible surfaces that integrate well with bone tissue. Nanoscale HA has superior functional properties over its microscale counterpart, particularly

Table 6: Atomic Concentrations and Intensity ratios									
		Atomic Ratios							
Sample ID	Ca/P, Theoretical	Ca/P	O/Ca, Theoretical	0/Ca	O/Ca <sub>adj</sub>	0 <sub>1s-Sat 2</sub> /0 <sub>1s</sub>	$O_{1s-Sat 2}/O_{1s adj}$		
НАр	1.67	1.29	2.6	3.03	2.46	0.065	0.077		
β-TCP, unsintered	1.5	1.23	2.67	3.13	2.76	0.073	0.081		
β-TCP, sintered	1.5	1.34	2.67	3.23	2.58	0.051	0.061		

in regards to surface reactivity and ultrafine structure, which are the most relevant properties for tissue-graft interaction upon implantation. Its high surface area-volume ratio, superior chemical homogeneity, and microstructural uniformity result in enhanced bone integration and more desirable mechanical properties.

While ICPMS, XRD and XPS are optimal for assessing the overall structure and composition of bulk materials, electron microscopy is necessary to provide spatially resolved morphological information of small groups of or even individual particles. Scanning Electron Microscopy (SEM) Energy Dispersive X-Ray Spectroscopy (EDS) can provide detailed information regarding particle shape and composition for particle sizes down to ~ 1um, but for smaller particles, such as the ones presented in this work, we must rely on transmission electron microscopy (TEM). Figure 8 shows a comparison of Scanning Transmission Electron Microscope (STEM) High Angle Annular Dark Field (HAADF) images of the three different particle types in this work. (HAADF) images have contrast related to the average atomic number (Z) of the sample. Unlike SEM, where secondary electron signals are collected above the sample, STEM utilizes detectors below a sample to collect information from incident electrons that have travelled through the sufficiently thin electron-transparent sample. As the beam is scanned over the sample, we can treat the acquisition of information at each pixel like a small individual scattering experiment, collecting signals from a variety of detectors simultaneously. This acquisition strategy provides structural details with atomic scale spatial resolution. When combined with EDS, the structure can then be correlated to composition with ~1 nm spatial resolution.

XPS analysis indicated the likely presence of an SiO2 surface layer on the  $\beta$ -TCP sintered particles, which is clearly observable in the STEM-EDS Maps (Figure 9). STEM HAADF combined with EDS shows a non-uniform, ~23 nm thick layer, of mainly Si and O at the surface of the particle. Having such clear evidence of a Si surface layer is of great importance to the overall performance of the resulting films that are formed using these precursor materials and may be indicative of a contamination present in the production of the powder in the sintering step.

#### Thermal characterization with simultaneous TGA/DSC

Bioceramic precursors are fabricated into bulk parts, scaffolds and coatings on metal implants via high temperature sintering. In previous sections, we have discussed the suitable analytical techniques and corresponding testing methods that are applicable for systematic quality control of HAp and  $\beta$ -TCP precursors, including Ca/P ratios, impurities, crystalline structure, powder size, shape, and surface characteristics, etc. All of these factors can affect the sintering behavior and final microstructure of the parts.

Simultaneous TGA/DSC directly evaluates the thermal behavior of precursors, including thermal decomposition kinetics and phase transition events relevant to outgassing and sintering behavior as temperature goes up. TGA/DSC instrumentation can have



Figure 8: HAADF STEM images of HAp (A),  $\beta$ -TCP unsintered (B),  $\beta$ -TCP sintered (C) to show differences in individual particle morphology.



Figure 9: STEM-EDS of a  $\beta$ -TCP sintered particle showing a non-uniform SiO2 layer, primarily on the surface of the particles.

a temperature range of up to 1500 °C, which is sufficient to cover the sintering temperature range of  $\beta$ -TCP. It can also be coupled to a long optical pathlength FTIR cell, thus enabling the measurement and identification of any evolved gas simultaneously with respect to temperature.

Figure 10A shows the TGA analysis of unsintered  $\beta$ -TCP in air. Various mass loss stages can clearly be identified and quantified. Figure 10B shows the simultaneous TGA/DSC profiles of HAp, unsintered and sintered  $\beta$ -TCP precursors. In this particular case, the unsintered  $\beta$ -TCP exhibits a mass loss pattern similar to the HAp sample. This further confirms the XRD finding that the unsintered  $\beta$ -TCP in fact contained a large fraction of HAp (Table 3). Also, it is clear that HAp and unsintered  $\beta$ -TCP exhibited multiple endothermic events up to 1000 °C, all related to thermal decomposition. On the other hand, the sintered  $\beta$ -TCP did not register any detectable mass loss or endo-/exothermal events, with practically no outgassing and no detectable low melting point phase impurities when heated up to 1000 °C, consistent with the XRD data (Table 3).



Figure 10: TGA and first derivative of TGA of β-TCP unsintered (A), and simultaneous TGA/DSC (B) of β-TCP unsintered, β-TCP sintered and HAp. Solid line – TGA signal, Dashed line – DSC signal. Experimental parameters: TA® SQ600, ceramic pans, 10 °C/min, air, 40 – 50 mg sample.particles.

#### SUMMARY

Full qualification of bioceramic precursors requires various characterization:

- from composition to trace level impurities (elements and phases)
- from macroscopic to microscopic structure
- from surface to bulk structures
- from specification/regulatory compliance to investigative analysis
- thermal properties pertinent to ceramic sintering

This paper demonstrates EAG's comprehensive capability in qualifying bioceramics, such as HAp and B-TCP for surgical implant applications in meeting these requirements. Specifically, we have detailed our advanced chemical analysis capabilities for determination of Ca/P ratio, impurity type and level, and phase content with high accuracy and precision, using HP ICP-OES, ICP-MS, XRD and TGA/DSC techniques. We also demonstrated our advanced surface chemical characterization and imaging techniques such as XPS and AC-STEM-EDS, to study surface chemistry and nanostructures in great detail. This paper also demonstrates that a multi-technique approach is essential to fully characterize these materials and that no single measurement, whilst providing lots of specific detail, is sufficient to address all relevant characteristics of importance. Coupled with EAG's robust quality system and an even broader materials science expertise far beyond the measurements details here, EAG's analytical service is well suited for qualifying virtually all types of bioceramic precursors including HAp, β-TCP,

calcium sulfate hemihydrides and dihydrides, and corresponding manufactured bioceramic coatings.

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