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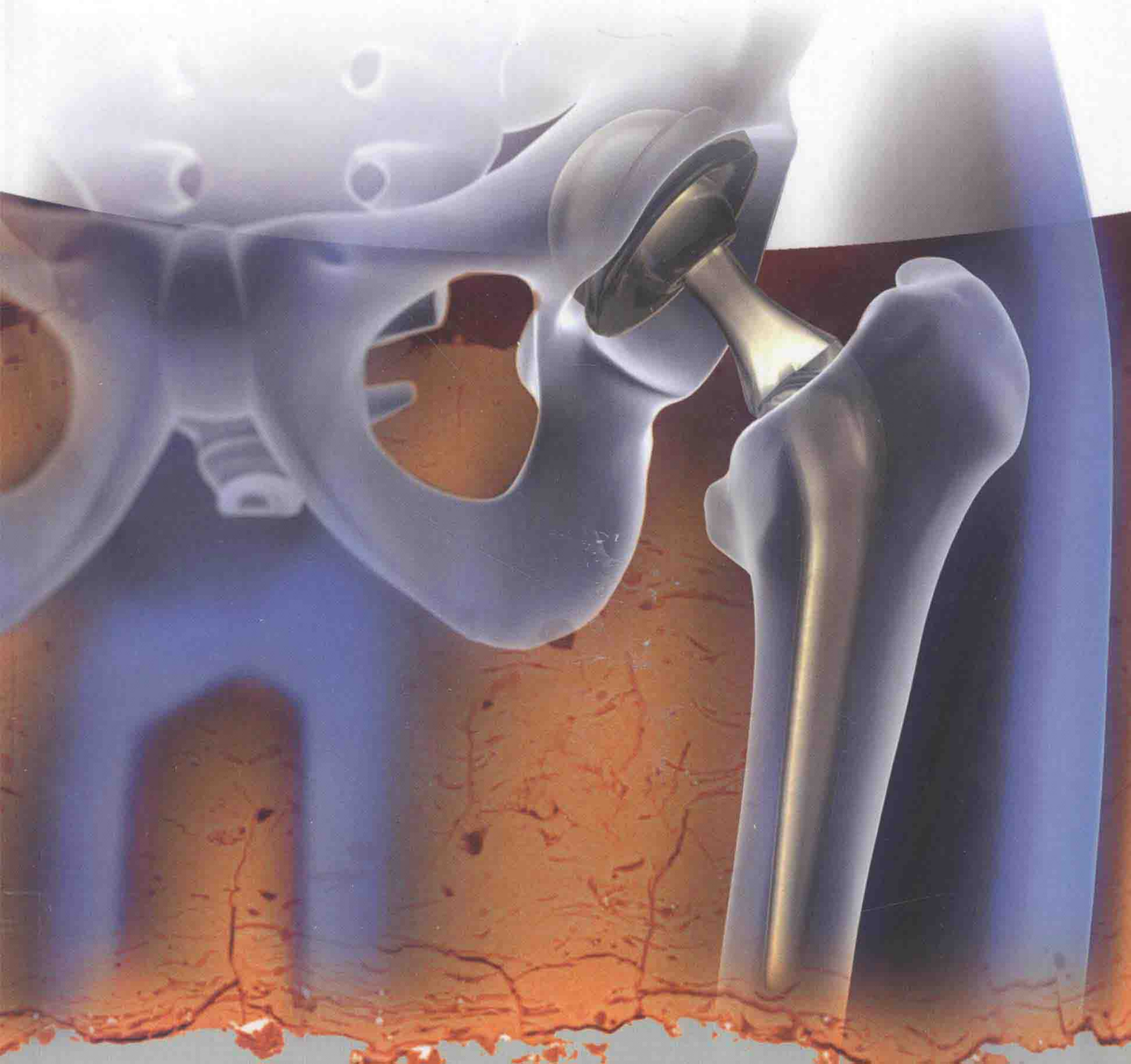
Bioceramic Coatings for Medical Implants

Trends and Techniques



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Preface

This introductory text deals predominately with calcium phosphate-based bioceramic materials that are now ubiquitously used in clinical applications to coat the surfaces of metallic endoprosthetic and dental implants that aim at replacing lost body parts or restoring functions to diseased or damaged tissues of the human body. The authors have written the text from a materials scientist's point of view. Hence, its main subject matter concerns the technology of coating deposition as well as the description of properties of bioceramic coatings including their *in vitro* alteration and testing in contact with simulated body fluids. We will also provide some salient information on *in vivo* coating–tissue interactions within the natural environment of the living body. Relevant information gained from experimental animal models will be described, without diving too deeply into the biomedical, physiological and endocrinological background.

Calcium phosphates are harbingers of life. They play a paramount role on Earth as one of the essential basic building blocks of living matter. Hydroxyapatite–collagen composite scaffolds provide the mechanical supporting strength and resilience of the gravity-defying bony skeletons of all vertebrates. The dentine and enamel of teeth are likewise based on these materials. However, natural biological apatite–collagen composites provide not only strength but also flexibility, their porous structure allowing exchange of essential nutrients, and a biologically compatible resorption and precipitation behaviour under appropriate physical and chemical conditions that control the build-up by osteoblasts and resorption by osteoclasts within bony matter. Hence, the calcium-deficient defect hydroxyapatite in bone is a reservoir of phosphorus that can be delivered to the body on demand (Pasteris, Wopenka and Valsami-Jones, 2008).

Nevertheless, if one considers the low abundance of phosphorus in the Earth's crust of slightly less than 0.1 mass%, it is a remarkably odd and puzzling choice of Nature to construct many critical pathways of both plant photosynthesis and animal metabolism around this exceedingly rare element (Westheimer, 1987; Filippelli, 2008). Apart from building up the skeleton of vertebrates, biological phosphate compounds are engaged in fuelling the energetic requirements of the photosynthetic pathway of plants called the Calvin–Benson cycle as well as the intercellular energy transfer within the mitochondria of animals that both rely on adenosine triphosphate (ATP). ATP releases the energy needed to sustain the metabolic processes when reduced to adenosine diphosphate (ADP). Hence, this unique energetic contribution of the phosphate groups is central to the functioning of ATP, arguably the most abundant biological molecule in Nature. Furthermore, deoxyribonucleic acid (DNA) as the carrier of the genetic information code owes its double helical structure to phosphate ester bridges that link the two strands of the helix, and are composed of the four nucleobases, the purine-based adenine and guanine, and the pyrimidine-based thymine and cytosine. Lastly, phospholipid bilayers are the main structural components of all cellular membranes that isolate the cell interior from its surrounding, potentially hostile environment. Most phospholipids contain a glycerol-derived diglyceride, a phosphate group, and a simple organic molecule such as choline, a quaternary 2-hydroxy-*N*,*N*,*N*-trimethylethanammonium salt.

The inorganic calcium phosphate minerals most ubiquitously occurring in Nature belong to the apatite group in its many crystal chemical expressions such as hydroxyapatite, fluorapatite and chlorapatite as well as other calcium orthophosphates such as monetite, brushite and whitlockite. While in the past there has been general agreement that these calcium phosphate-based minerals are the most important reservoirs supplying life on Earth with essential phosphorus, more recently feldspars came into focus as a hidden source of phosphorus. It happens that in feldspars P^{5+} is able to replace tetrahedrally coordinated Si^{4+} by coupled substitution with Al^{3+} to maintain charge balance, that is $2\ Si^{4+} \leftrightarrow Al^{3+} + P^{5+}$ (London *et al.*, 1990; Manning, 2008). Considering the abundance of feldspars in the Earth's crust, and the easy accessibility for plants and soil biota of their P-containing weathering products, predominately clays, feldspars may indeed be a much more significant source of phosphorus than apatites (Parsons, Lee and Smith, 1998).

Considering the importance of the structure of bone as a biocomposite of Ca-deficient defect hydroxyapatite and triple helical strands of collagen I, it is not surprising that as early as about 40 years ago synthetic hydroxyapatite was suggested as a biocompatible artificial material for incorporation in the human body. Hydroxyapatite was used in the form of densified implants for dental root replacement (Denissen and de Groot, 1979) and as a suitable material for filling bone cavities, for fashioning skeletal prostheses (Hulbert *et al.*, 1970) and for coatings hip endoprosthetic devices (Ducheyne *et al.*, 1980; León and Jansen, 2009). Since then research into the biomedical application of calcium phosphate as osseoconductive coatings has virtually exploded. Many deposition methods were experimentally and some, eventually, clinically evaluated that range from biomimetical processing routes intended to mimic Nature's low temperature, template-mediated biomineralisation pathways (Bryksin *et al.*, 2014) to surface-induced mineralisation (SIM), to electrochemical and electrophoretic deposition, to plasma-assisted metal–organic chemical vapour deposition (PA-MOCVD), to atmospheric plasma spraying (APS) or suspension plasma spraying (SPS) (Campbell, 2003). This treatise will review many of these deposition techniques and will thus provide up-to-date information on the resulting bioceramic coatings, their structure, composition and biomedical functions (see Heness and Ben-Nissan, 2004; Sarkar and Banerjee, 2010; Ducheyne *et al.*, 2011; Heimann, 2012; Dorozhkin, 2012; Zhang, 2013; Surmenev, Surmeneva and Ivanova, 2014). In short, the present book intends to act as a primer to introduce non-specialists to the wide-reaching field of bioceramic coatings that are being designed, developed and tested with the aim to alleviate medical deficiencies and the associated suffering of millions of people afflicted with joint and dental maladies.

During the last several decades, research into bulk bioceramics and bioceramic coatings has emerged as a hot topic among materials scientists. Virtually thousands of papers can now be found in relevant journals (see Appendix) and on the Internet. Attempting to treat this vast field in an encyclopaedic fashion is clearly impossible as each day new contributions are being published with ever-increasing speed and regularity. Hence, trying to keep abreast with these developments is akin to shooting at a very fast moving target. The best that one can do is to provide snapshots of currently available information and attempting to separate the wheat from the chaff whenever possible. To paraphrase the resigning comment by the great German poet Johann Wolfgang von Goethe, uttered in his autobiography 'Out of my Life: Poetry and Truth': 'Such (...) work will never be finished; one has to declare it finished when one has done the utmost in terms of time and circumstances'.

As a parting glance, it should be mentioned that during the preparation of the text, three imaginary readers have intently looked over our shoulder: an interested layperson, a professional working in the area of the subject matter of this treatise, and a diligent student whose interest and knowledge are located somewhere in-between. The layperson may not be conversant with many of the subtleties expounded throughout our text but may be eager to penetrate deeper into the subject of bioceramic coatings. Hence, to somewhat relieve this potential reader from the burden of looking up non-familiar analytical techniques and special scientific terms in other textbooks or encyclopaedias, we have provided in the Chapters 5 and 7 short explanations that precede the more detailed descriptions of coating deposition techniques, and characterisation and testing procedures.

Our second imaginary reader is the professional who may look into specific chapters to extract expert knowledge. He or she will act as a thorough if not harsh critic of our endeavour, and will undoubtedly castigate us for having left out crucial aspects of the subject matter treated in this book. This expert may also criticise us for having used inappropriate terms and faulty connections among materials science and biomedical facts. Alas, we used such possibly scientifically shaky explanations to satisfy the limited level of understanding of imaginary reader #1. The expert may also accuse us of having skimmed over the deep subtleties of the subject, and, in particular, not having given due consideration to those aspects in which he or she has earned scientific standing and international acclaim. However, during the vast progress made in developing increasingly sophisticated techniques to design and engineer bioceramic materials including coatings, many unexplored vestiges and nooks and crannies have been left behind the speedily advancing battle lines that require additional and more detailed studies. Some of the content of this book has been devoted to 'mopping up' such neglected research topics. These topics notwithstanding, we are much aware of deficiencies in our approach and hence ask imaginary reader #2 for understanding and kind forgiveness.

Our third imaginary reader is a student who may want to inform himself/herself quickly on the general subject of bioceramic coatings, their preparation technology, materials science, uses, properties, as well as analytical characterisation, and *in vitro* and *in vivo* testing. We are hopeful that our treatise will provide the information sought by this student without forcing him/her to delve into the abyss of specialised literature. Hence, imaginary reader #3 may benefit from our concise and condensed approach in as much as it will provide relief from ploughing through piles of original papers scattered over dozens of scientific journals.

The dangers of attempting to satisfy both the curiosity and the need for knowledge of these three imaginary readers are obvious. The only thing we can hope for is, on the one hand, to have avoided to be over the head of the layperson, and on the other hand, to have provided enough scientific 'meat', limited as it may be, to earn the approval of the expert and the appreciation of the student as well. Readers trained in the realm of medical and biological sciences will likely appreciate the materials science aspects of bioceramic coatings whereas those educated in materials science may find the biomedical content of the book enlightening and useful. To satisfy both types of our potential audience is intrinsically difficult, and should we have failed here and there in this endeavour, we beg the gentle reader for pardon.

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Glossary

AAGR	average annual growth rate
AAS	atomic absorption spectroscopy
a.c.	alternating current
ACP	amorphous calcium phosphate
ADP	adenosine diphosphate
AFM	atomic force microscopy
ALP	alkaline phosphatase
ANOVA	analysis of variance
AO	acridine orange
APS	atmospheric plasma spraying
ATP	adenosine triphosphate
A/W	apatite/wollastonite
ATZ	alumina-toughened zirconia
BCA	bone-like carbonated apatite
BCP	biphasic calcium phosphate
bFGF	basic fibroblast growth factor
BIC	countries Brasil, India, China
BIR	bone ingrowth rate
BMD	bone mineral density
BMP	bone morphogenetic protein
BMSC	bone marrow stromal cell
BP	bisphosphonate
BRIC	countries Brasil, Russia, India, China
BSA	bovine serum albumin
BSE	back-scattered electron
BSP	bone sialoprotein
CAGR	compound annual growth rate
calcein-AM	acetoxymethyl-ester of calcein
CaP	calcium phosphate (in a general sense)
Ca-PSZ	calcia-partially stabilised zirconia
CCC	carbon–carbon composite
CCD	charge-coupled device
CCDS	computer-controlled detonation spraying

CCVD	combustion chemical vapour deposition
CDHAp	calcium-deficient hydroxyapatite
CEC	Fédération Europèene des Fabricants de Carreaux Ceramiques
Ce-TZP	ceria-stabilised tetragonal zirconia polycrystal
CFD	computational fluid dynamics
CFRP	carbon fibre-reinforced polymer
CGDS	cold gas dynamic spraying
CHAp	carbonated hydroxyapatite
CiA	citric acid
CL	cathodoluminescence
ClAp	chlorapatite
CMP	calcium metaphosphate
CNS Glasses	calciumoxide-sodiumoxide-siliciumdioxide glasses, see also NCS
CNT	carbon nanotubes
CP	cross polarisation (in NMR)
CPM	calcium dihydrogenphosphate monohydrate
CPP	calcium pyrophosphate
CPPD	calcium pyrophosphate dihydrate
cp-titanium	commercially pure titanium
CR	corrosion rate
CRM	confocal Raman microscopy
CTE	coefficient of thermal expansion
CTO	calcium titanate, CaTiO3, perovskite
CVD	chemical vapour deposition
d.c.	direct current
DCPA	dicalcium phosphate anhydrate
DCPD	dicalcium phosphate dihydrate
DDA	degree of deacylation
DFT-LDA	density-functional theory with local-density approximation
DGS	detonation gun spraying
DIPS	diffusion-induced phase separation
DLC	diamond-like carbon
DMEM	Dulbecco's modified eagle's medium
DNA	deoxyribonucleic acid
DOE	design of experiment
DS	detonation spraying
DTA	differential thermal analysis
EBAD	electron beam assisted deposition
EBPVD	electron beam physical vapour deposition
EBSD	electron back-scattered diffraction
ECD	electrochemical deposition
ECF	extracellular fluid
ECM	extracellular matrix
ED	electron diffraction
EDS	energy dispersive spectroscopy

EDTA	ethylenediaminetetraacetic acid (sequestrant)
EDX	energy-dispersive X-ray spectroscopy
EELS	electron energy loss spectroscopy
EIS	electrochemical impedance spectroscopy
ELISA	enzyme-linked immunosorbent assay
EPD	electrophoretic deposition
EPMA	electronic probe microanalysis
EPR	electron paramagnetic resonance (spectroscopy), see also ESR
ESEM	environmental scanning electron microscopy
ESR	electron spin resonance (spectroscopy), see also EPR
EtBr	ethidium bromide
EXAFS	extended X-Ray absorption fine structure
EXSY	exchange spectroscopy (in NMR)
FA-CVD	flame-assisted chemical vapour deposition
FE-SEM	field emission scanning electron microscopy
FFT	fast Fourier transform
FGC	functional gradient composites
FGHA	functionally graded hydroxyapatite
FGM	functionally graded material
FHAp	fluorine-doped hydroxyapatite
FIB	focused ion beam
FTIR	Fourier transform infrared spectroscopy
FTRS	Fourier transform Raman spectroscopy
GD	glow discharge
GN	graphene nanosheet
HA, HAp	hydroxyapatite
HAV	hyaluronic acid visco-supplementation
HBDC	human bone-derived cell
hBMSC	human bone marrow stromal cell
HBSS	Hank's balanced salt solution
HCA	hydroxycarbonate apatite
HCP	heptacalcium phosphate
HDPE	high-density poly(ethylene)
hECF	human extracellular fluid
HEPES	2-(4-(2-**h**ydroxy**e**thyl)-1-**p**iperazinyl)-**e**than**s**ulfonic acid (buffer)
HETCOR	heteronuclear correlation
hICF	human intracellular fluid
hISF	human interstitial fluid
hMSC	human mesenchymal stem cell
HRTEM	high resolution transmission electron microscopy
HSTC	hierarchical-structured titanium coating
hUVEC	human umbilical vein endothelial cell
HVOF	high velocity oxyfuel spraying
HVSFS	high velocity suspension flame spraying
IBAD	ion beam assisted deposition

IBSD	ion beam sputtering deposition
ICP/MS	inductively coupled plasma/mass spectroscopy
ICPS	inductively coupled plasma spraying
IGF	insulin-like growth factor
IPS	induction plasma spraying
IR	infrared (spectroscopy)
ISE	indentation size effect
ISQ	implant stability quotient
KDR	kinase insert domain receptor
LASAT	laser shock adhesion test
LEPS	low-energy plasma spraying
LGN	laser gas nitriding
LPCVD	low pressure chemical vapour deposition
LPPS	low pressure plasma spraying
LRS	laser Raman spectroscopy
MAO	micro-arc oxidation
MAPLE	matrix-assisted pulsed laser evaporation
MAS	magic angle spinning (technique in NMR)
MCSF	macrophage colony-stimulating factor
MEMS	microelectromechanical system
Mg-PSZ	magnesia-partially stabilised zirconia
M(I)PS	micro-plasma spraying
MRI	magnetic resonance imaging
MSC	marrow stem cell
MTT	3-(4,5-di**m**ethyl**t**hiazol-2-yl)-2,5-diphenyl**t**etrazolium bromide (dye)
MWCNT	multi-walled carbon nanotubes
NAD	nicotinamide adenine dinucleotide
NCS	sodiumoxide calciumoxide silicate glasses, see also CNS
NASICON	sodium super ionic conductor (structural family)
NMR	nuclear magnetic resonance (spectroscopy)
NZP	sodium zirconium phosphate
OAp	oxyapatite
OC	osteocalcin
OCP	octacalcium phosphate
OES	optical emission spectroscopy
OHAp	oxyhydroxyapatite
OP	osteopontin
OPG	osteoprotegerin
PA	polyamid
PAA	poly(acrylic acid)
PA-MOCVD	plasma-assisted metal-organic chemical vapour deposition
PBC	periodic bond chain
PBTCA	2-phosphonobutane-1,2,4-tricarboxylic acid (dispersant)
PC	pulsed current

PCA	percentage of coated area
PCL	poly(ε-caprolactone)
PDA	post deposition annealing
PDGF	platelet-derived growth factor
PDOP	poly(dopamine)
PE	poly(ethylene)
PECVD	plasma-enhanced chemical vapour deposition
PEEK	poly(etheretherketone)
PEG	poly(ethyleneglycol)
PEI	poly(ethylene imine)
PEO	plasma electrolytic oxidation
PE-UHMW	poly(ethylene) ultra-high molecular weight
PGA	poly(glutamic acid)
PIXE	particle- or proton-induced X-ray emission
PLA	poly(lactic acid)
PLD	pulsed laser deposition
PLGA	poly(lactic-*co*-glycolic acid)
PMMA	poly(methylmethacrylate)
PSZ	partially-stabilised zirconia
PVD	physical vapour deposition
RANK(L)	receptor activator of nuclear factor kappa (ligand)
REE	rare earth elements
RF, r.f.	radio frequency
RFA	resonance frequency analysis
rhBMP	recombinant human bone morphogenetic protein
RIPS	reaction-induced phase separation
RNA	ribonucleic acid
ROS	reactive oxygen species
r-SBF	revised simulated body fluid (see also: SBF-H, Table 7.8)
RT-PCR	reverse transcription polymerase chain reaction
RTQ	removal torque
$RUNX_2$	runt-related transcription factor 2
SAED	selected area electron diffraction
SAM	self-assembled monolayer
SAXS	small-angle X-ray scattering
SBF	simulated body fluid
SCE	standard calomel electrode
SDE	statistical design of experiments
SEM	scanning electron microscopy
Si-HAp	silicate-doped hydroxyapatite
SIM	surface-induced mineralisation
SIMS	secondary ion mass spectrometry
SOFC	solid oxide fuel cell
SPC	statistical process control
SPM	scanning probe microscopy

SPPS	solution precursor plasma spraying
SPS	suspension plasma spraying
Sr-HAp	strontium-doped hydroxyapatite
SRO	short range order
SS	stainless steel
STEM	scanning transmission electron microscopy
SZS	strontium-zinc-silicium ceramic
TCP	tricalcium phosphate
TCPS	tissue culture-grade polystyrene
TDHP	tetracalcium dihydrogenhexaphosphate
TEM	transmission electron microscopy
TERS	tip-enhanced Raman spectroscopy
TGA	thermogravimetric analysis
TGF	transforming growth factor
THA	total hip arthroplasty
THR	total hip replacement
TiCN	titanium carbonitride
TiN	titanium nitride
TIPS	temperature-induced phase separation
TKA	total knee arthroplasty
TL	thermoluminescence
TLR	toll-like receptor
TMCP	transition metal-substituted calcium phosphate
TNF	tumor necrosis factor
ToF-SIMS	time-of-flight secondary ion mass spectrometry
TRAP	tartrate-resisting acid phosphatase
TRIS	tris(hydroxymethyl)-aminomethan (buffer solution)
TTCP, TetrCP	tetracalcium phosphate
TZP	tetragonal zirconia polycrystal
UHMWPE	ultra-high molecular weight poly(ethylene)
UV	ultraviolet
VCS	vacuum/reduced pressure cold spraying
VEGF	vascular endothelial growth factor
VPS	vacuum plasma spraying
XANES	X-ray absorption near-edge structure
XPS	X-ray photoelectron spectroscopy
XRD	X-ray diffraction
Y-PSZ	yttrium-partially stabilised zirconia
YSZ	yttria-stabilised zirconia
Y-TZP	yttria-stabilised tetragonal zirconia polycrystal
ZA	zoledronic acid
ZTA	zirconia-toughened alumina
μCT	micro computed tomography