

# Tissue engineering using ceramics and polymers

Edited by Aldo R. Boccaccini and Julie E. Gough



R318.08 T599

## Tissue engineering using ceramics and polymers

Edited by Aldo R. Boccaccini and Julie E. Gough





Woodhead Publishing and Maney Publishing on behalf of The Institute of Materials, Minerals & Mining

CRC Press
Boca Raton Boston New York Washington, DC

WOODHEAD PUBLISHING LIMITED

Cambridge England

Woodhead Publishing Limited and Maney Publishing Limited on behalf of The Institute of Materials, Minerals & Mining

Published by Woodhead Publishing Limited, Abington Hall, Abington, Cambridge CB21 6AH, England www.woodheadpublishing.com

Published in North America by CRC Press LLC, 6000 Broken Sound Parkway, NW, Suite 300, Boca Raton, FL 33487, USA

First published 2007, Woodhead Publishing Limited and CRC Press LLC © Woodhead Publishing Limited, 2007
The authors have asserted their moral rights.

Every effort has been made to trace and acknowledge ownership copyright. The publishers will be glad to hear from any copyright holders whom it has not been possible to contact.

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. Reasonable efforts have been made to publish reliable data and information, but the authors and the publishers cannot assume responsibility for the validity of all materials. Neither the authors nor the publishers, nor anyone else associated with this publication, shall be liable for any loss, damage or liability directly or indirectly caused or alleged to be caused by this book.

Neither this book nor any part may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, microfilming and recording, or by any information storage or retrieval system, without permission in writing from Woodhead Publishing Limited.

The consent of Woodhead Publishing Limited does not extend to copying for general distribution, for promotion, for creating new works, or for resale. Specific permission must be obtained in writing from Woodhead Publishing Limited for such copying.

Trademark notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation, without intent to infringe.

British Library Cataloguing in Publication Data A catalogue record for this book is available from the British Library.

Library of Congress Cataloging in Publication Data A catalog record for this book is available from the Library of Congress.

Woodhead Publishing Limited ISBN 978-1-84569-176-9 (book) Woodhead Publishing Limited ISBN 978-1-84569-381-7 (e-book) CRC Press ISBN 978-1-4200-4454-6 CRC Press order number WP4454

The publishers' policy is to use permanent paper from mills that operate a sustainable forestry policy, and which has been manufactured from pulp which is processed using acid-free and elementary chlorine-free practices. Furthermore, the publishers ensure that the text paper and cover board used have met acceptable environmental accreditation standards.

Project managed by Macfarlane Production Services, Dunstable, Bedfordshire, England (macfarl@aol.com)

Typeset by Godiva Publishing Services Limited, Coventry, West Midlands, England Printed by TJ International Limited, Padstow, Cornwall, England

Tissue engineering using ceramics and polymers

### Related titles:

Artificial cells, cell engineering and therapy

(ISBN 978-1-84569-036-6)

This authoritative reference work provides a detailed study of the most up-to-date developments in artificial cells, cell engineering and cell therapy. It covers design, engineering and uses of artificial cells. The clinical relevance of artificial cells and cell engineering is assessed. This is a highly dynamic sector with growing interest in the use of engineered cells in controlled release of active drugs and other therapeutic agents.

Biomedical polymers

(ISBN 978-1-84569-070-0)

This book presents a detailed study of the structure, processing and properties of biomedical polymers and the relationship between them. Emphasis is placed on the various groups of biopolymers including natural polymers, synthetic biodegradable and non-biodegradable polymers.

Molecular interfacial phenomena of polymers and biopolymers (ISBN 978-1-85573-928-4)

This book combines three fundamental areas of interest to the science and engineering community, these being material science, nanotechnology and molecular engineering. Although there have been various results published in this field, there has yet to be a fully comprehensive review. This book covers key research on molecular mechanisms and thermodynamic behaviour of (bio)polymer surfaces and interfaces, from theoretical and experimental perspectives.

Details of these and other Woodhead Publishing materials books, as well as materials books from Maney Publishing, can be obtained by:

- · visiting www.woodheadpublishing.com
- contacting Customer Services (e-mail: sales@woodhead-publishing.com; fax: +44 (0) 1223 893694; tel.: +44 (0) 1223 891358 ext. 130; address: Woodhead Publishing Limited, Abington Hall, Abington, Cambridge CB21 6AH, England)

Maney currently publishes 16 peer-reviewed materials science and engineering journals. For further information visit www.maney.co.uk/journals.

(\* = main contact)

### **Editors**

Aldo R. Boccaccini Department of Materials Imperial College London Prince Consort Road London SW7 2BP UK

E-mail: a.boccaccini@imperial.ac.uk

Julie E. Gough
Materials Science Centre
School of Materials
University of Manchester
Grosvenor Street
Manchester M1 7HS
UK
E-mail: j.gough@manchester.ac.uk

### Chapter 1

J. Huang\*
Department of Mechanical
Engineering
University College London
Torrington Place
London WC1E 7JE
UK
E-mail: jie.huang@ucl.ac.uk

S. M. Best
Department of Materials Science and Metallurgy
University of Cambridge
Pembroke Street
Cambridge CB2 3QZ
UK
E-mail: smb51@cam.ac.uk

### Chapter 2

Guobao Wei and Peter X. Ma\*
Department of Biologic and
Materials Sciences
Department of Biomedical
Engineering
Macromolecular Science and
Engineering Center
The University of Michigan
Ann Arbor
Michigan 48109-1078
USA
E-mail: mapx@umich.edu

### Chapter 3

J. R. Jones
Department of Materials
Imperial College London
South Kensington Campus
London SW7 2AZ
UK

E-mail: julian.r.jones@imperial.ac.uk

S. K. Misra and A. R. Boccaccini\* Department of Materials Imperial College London Prince Consort Road London SW7 2BP UK

E-mail: a.boccaccini@imperial.ac.uk

### Chapter 5

J. Mansbridge Tecellact LLC 1685 Calle Camille La Jolla USA E-mail: Verajonath@aol.com

JonathanMansbridge@yahoo.com

### Chapter 6

K. Shakesheff\* and G. Tsourpas Division of Drug Delivery and Tissue Engineering School of Pharmacy University of Nottingham Nottingham NG7 2RD UK

E-mail:

Kevin.shakesheff@nottingham.ac.uk

### Chapter 7

N. Tirelli\* and F. Cellesi School of Pharmacy University of Manchester Oxford Road Manchester M13 9PL UK E-mail:

> Nicola.tirelli@manchester.ac.uk f.cellesi@manchester.ac.uk

### Chapter 8

F. Davis and S. P. J. Higson\* Cranfield Health Cranfield University Barton Rd Silsoe MK45 4DT UK

E-mail: f.davis@cranfield.ac.uk s.p.j.higson@cranfield.ac.uk

### Chapter 9

Andrew J. Urquhart and Morgan R. Alexander\* School of Pharmacy University of Nottingham University Park Nottingham NG7 2RD UK

E-mail: Morgan.Alexander@nottingham.ac.uk

### Chapter 10

A. M. Donald Department of Physics Cavendish Laboratory University of Cambridge JJ Thomson Avenue Cambridge CB3 0HE UK

E-mail: amd3@cam.ac.uk

### Chapter 11

E-mail:

S. I. Anderson Advanced Microscopy Unit School of Biomedical Science E Floor Medical School Queens Medical Centre Clifton Boulevard Nottingham NG7 2UH UK

susan.anderson@nottingham.ac.uk

I. Notingher

School of Physics and Astronomy

University of Nottingham

University Park

Nottingham NG7 2RD

UK

E-mail:

ioan.notingher@nottingham.ac.uk

### Chapter 13

A. Atala

Wake Forest Institute for Regenerative Medicine

Wake Forest University Health

Sciences

Medical Center Boulevard

Winston-Salem

NC 27157

**USA** 

E-mail: aatala@wfubmc.edu

### Chapter 14

P. Woźniak\*

Department of Biophysics and Human Physiology

Medical University of Warsaw

Ul. Chalubinskiego 5

02-004 Warsaw

Poland

E-mail: pwozniak@amwaw.edu.pl wozniak\_piotr@yahoo.com

A. J. El Haj

Institute for Science & Technology

in Medicine

Keele University

Thornburrow Drive

Hartshill

Stoke-on-Trent ST4 7QB

UK

E-mail: a.j.el.haj@bemp.keele.ac.uk

### Chapter 15

L. Di Silvio

Senior Lecturer in Biomaterials &

**Biomimetics** 

King's College London Dental

Institute

Biomaterials Science

Floor 17, Guy's Tower

Guy's Campus

St Thomas' Street

London SE1 9RT

UK

E-mail: lucy.di\_silvio@kcl.ac.uk

### Chapter 16

Q. Z. Chen, H. Jawad, A. R.

Boccaccini\*

Department of Materials

Imperial College London

Prince Consort Road

London SW7 2BP

UK

E-mail: a.boccaccini@imperial.ac.uk

S. E. Harding and N. N. Ali

National Heart and Lung Institute

Imperial College London

Dovehouse Street

London SW3 6LY

UK

### Chapter 17

J. Hoyland\* and T. Freemont

Tissue Injury and Repair Group

School of Medicine

Stopford Building

The University of Manchester

Oxford Road

Manchester M13 9PT

UK

E-mail:

judith.hoyland@manchester.ac.uk tony.freemont@manchester.ac.uk

S. MacNeil

Tissue Engineering Group Kroto Research Institute

University of Sheffield North

Campus

Broad Lane

Sheffield S3 7HQ

UK

E-mail: s.macneil@sheffield.ac.uk

### Chapter 19

K. Shakesheff

Division of Drug Delivery and Tissue

Engineering

School of Pharmacy

University of Nottingham

Nottingham NG7 2RD

UK

E-mail:

kevin.shakesheff@nottingham.ac.uk

### Chapter 20

A. Saito

Division of Nephrology and

Metabolism

Department of Medicine

Tokai University School of Medicine

Bohseidai

Isehara

Kanagawa 259-1193

Japan

E-mail: asait@is.icc.u-tokai.ac.jp

### Chapter 21

A. M. Turner and J. Southgate\*

Jack Birch Unit of Molecular

Carcinogenesis

Department of Biology

University of York

York YO10 5YW

UK

E-mail: js35@york.ac.uk

alexturner64@doctors.org.uk

R. Subramaniam and

D. F. M. Thomas

Department of Paediatric Urology

St James's University Hospital

Leeds LS9 7TF

UK

E-mail: Ramnath.Subramaniam

@leedsth.nhs.uk

D.F.M.Thomas@leeds.ac.uk

### Chapter 22

P. Kingham\* and G. Terenghi

Blond McIndoe Laboratories

Tissue Injury and Repair Group

3.106 Stopford Building

The University of Manchester School

of Medicine

Oxford Road

Manchester M13 9PT

UK

E-mail:

paul.j.kingham@manchester.ac.uk giorgio.terenghi@manchester.ac.uk

### Chapter 23

A. E. Bishop\* and H. J. Rippon

Stem Cells & Regenerative Medicine Section on Experimental Medicine &

Toxicology

Imperial College Faculty of Medicine

Hammersmith Campus

Du Cane Road

London W12 ONN

UK

E-mail: a.e.bishop@imperial.ac.uk

hj.rippon@imperial.ac.uk

D. A. J. Lloyd\* and S. M. Gabe St Mark's Hospital Northwick Park Harrow HA1 3UJ UK

E-mail: dajl@btinternet.com s.gabe@imperial.ac.uk

### Chapter 25

 A. Fritsch and L. Dormieux
 Laboratory for Materials and Structures
 Ecole Nationale des Ponts et Chaussées (LMSGC-ENPC)
 Marne-la-Vallee
 France

C. Hellmich\*
Vienna University of Technology
Karlsplatz 13/E 202
1040 Wien
Austria
E-mail:
christian.hellmich@tuwien.ac.at

J. Sanahuja Lafarge Research Center San-Quentin Fallavier France

### Chapter 26

J. E. Gough
Materials Science Centre
School of Materials
University of Manchester
Grosvenor Street
Manchester M1 7HS
UK

E-mail: j.gough@manchester.ac.uk

J E GOUGH, University of Manchester, UK and A R BOCCACCINI, Imperial College London, UK

The field of tissue engineering has advanced dramatically in the last 10 years, offering the potential for regenerating almost every tissue and organ of the human body. Tissue engineering and the related discipline of regenerative medicine remain a flourishing area of research with potential new treatments for many more disease states. The advances involve researchers in a multitude of disciplines, including cell biology, biomaterials science, imaging and characterisation of surfaces and cell-material interactions. In the field of biomaterials, for example, many additional and novel processing techniques have been developed for the construction of improved porous scaffolds and matrices, including a much wider variety of polymers, ceramics and their composites with tailored micro- and nanostructure, surface topography and chemistry as well as optimised properties for the intended application in tissue engineering strategies. There are in fact many more materials being investigated for potential scaffolds, including novel uses of natural materials, combinations of natural and synthetic materials and new structures designed to mimic extracellular matrix at all relevant scales (macro, micro and nano), which are intended to provide scaffolds that are closer to the in vivo cellular environment. There is also strong emphasis on biomechanics and the effects of mechanical forces on the cell response and subsequent tissue formation, again, aiming to mimic the conditions in vivo. Along with major advances in the design of materials and control of their properties, there have been huge advances in understanding the cell biology of the cell response to artificial environments, substrates and scaffolds, with recent emphasis on the suitability of stem cells for tissue regeneration and the restoration of function.

This book aims to combine some of the most recent innovative research with reviews of specific aspects of tissue engineering to provide an up-to-date source for undergraduate, postgraduate, academic and industrial readers. Advances in the related areas of biomaterial science, cell biology and characterisation techniques are reported, and the relevance of the chosen biomaterial (polymer, ceramic) is highlighted.

Part I of this book contains chapters concerning the materials of choice for tissue engineering – polymers, ceramics, bioactive ceramics and glasses and

### Introduction

composites. It contains some general issues related to novel tissue engineering strategies with emphasis on transplantation of engineered tissues, surface modification of scaffolds and combined tissue engineering and drug delivery approaches. Specific chapters on state-of-the-art characterisation techniques are also included with particular reference to those techniques of major relevance to tissue engineering: X-ray photoelectron spectroscopy and secondary ion mass spectrometry, environmental scanning electron microscopy, confocal microscopy and Raman spectroscopy.

Part II of this book focuses on some specific examples of organ and tissue regeneration. It covers some of the highly challenging, more recent advances in tissue engineering such as liver, kidney, bladder, intervertebral disc, lung, cardiac tissue and intestine and also recent advances in nerve bioengineering. Some of the largest, longer-standing areas of tissue engineering research (including bone, skin and cartilage) which require new innovative approaches are covered. There has been a great deal of activity in determining and optimising new cell sources for tissue engineering which is mentioned in various areas of the book.

We hope this book will be a valuable source of information and an inspiration to new and existing researchers in the field.

## Contents

	Contributor contact details	xiii
	Introduction	xix
Part I	General issues	
1	Ceramic biomaterials J HUANG, University College London, UK and S M BEST, University of Cambridge, UK	3
1.1	Introduction	3
1.2	Characteristics of ceramics	9
1.3	Microstructure of ceramics	12
1.4	Properties of ceramics	16
1.5	Processing of ceramics	22
1.6	Conclusions	26
1.7	Future trends	26
1.8	References	27
2	Polymeric biomaterials G WEI and P X MA, The University of Michigan, USA	32
2.1	Introduction	32
2.2	Polymeric scaffolds for tissue engineering	33
2.3	Polymeric scaffolds with controlled release capacity	43
2.4	Conclusions	47
2.5	References	47
3	Bioactive ceramics and glasses J R JONES, Imperial College, London, UK	52
3.1	Introduction	52
3.2	Synthetic hydroxyapatite	54
3.3	Bioactive glass	58

vi	Contents	
3.4 3.5 3.6	Glass-ceramics Conclusions References	67 67 68
4	Biodegradable and bioactive polymer/ceramic composite scaffolds S K MISRA and A R BOCCACCINI, Imperial College London, UK	72
4.1	Introduction	72
4.2	Biodegradable polymers and bioactive ceramics	74
4.3	Composite material approach	78
4.4	Materials processing strategies for composite scaffolds	80
4.5	Case studies	83
4.6	Conclusions and future trends	87
4.7	References and further reading	89
5	Transplantation of engineered cells and tissues J MANSBRIDGE, Tecellact LLC, USA	93
5.1	Introduction	93
5.2	Rejection of tissue-engineered products	95
5.3	Testing and regulatory consequences	102
5.4	Generality of the resistance of tissue-engineered products to immune rejection	102
5.5	Manufacturing consequences	103
5.6	Conclusions and future trends	104
5.7	Sources of further information and advice	105
5.8	Acknowledgements	105
5.9	References	105
6	Surface modification to tailor the biological response K SHAKESHEFF and G TSOURPAS, University of Nottingham, UK	108
6.1	Introduction	108
6.2	The biochemistry of cell interactions with the ECM	108
6.3	The need for surface modification of scaffolds	114
6.4	General strategies for surface modification	115
6.5	Examples from the literature	116
6.6	Future trends	123
6.7	References	124

	Contents	vii
7	Combining tissue engineering and drug delivery N TIRELLI and F CELLESI, University of Manchester, UK	129
7.1	Introduction	129
7.2	Growth factor (GF) delivery	131
7.3	Signalling molecules in solution (parenteral administration)	135
7.4	Signalling molecules physically entrapped in a matrix	136
7.5	Signalling molecules released from a bound state	147
7.6	References	149
8	Carrier systems and biosensors for biomedical applications F DAVIS and S P J HIGSON, Cranfield University, UK	153
	F DAVIS and S F J HIGSON, Claimed University, OK	
8.1	Introduction	153
8.2	Carrier systems	153
8.3	Commercial systems	161
8.4	Biosensors	162
8.5	Continuous monitoring	167
8.6	Future trends	169
8.7	Conclusions	170
8.8	References	171
9	Characterisation using X-ray photoelectron spectroscopy (XPS) and secondary ion mass spectrometry (SIMS) A J URQUHART and M R ALEXANDER, University of Nottingham, UK	175
9.1	Introduction	175
9.2	X-ray photoelectron spectroscopy (XPS)	177
9.3	Static secondary ion mass spectrometry (SIMS)	187
9.4	Specific sample preparation and acquisition procedures	193
9.5	Conclusions	197
9.6	Future trends	198
9.7	Acknowledgement	199
9.8	References	199
10	Characterisation using environmental scanning electron microscopy (ESEM) A M DONALD, University of Cambridge, UK	204
10.1	Introduction	204
10.2	The instrument: a comparison with CSEM	204
10.3	Static experiments	210
10.4	Dynamic experiments	212
seminant 1550	* · · · · · · · · · · · · · · · · · · ·	

viii	Contents	
10.5	Dual beam instruments – an emerging technique	218
10.6	Potential and limitations	219
10.7	Conclusions	221
10.8	References	221
11	Characterisation of cells on tissue engineered construsts using imaging techniques/microscopy S I ANDERSON, University of Nottingham, UK	226
11.1	Introduction	226
11.2	General considerations and experimental design	226
11.3	CLSM	228
11.4	Combining techniques	241
11.5	Future trends	244
11.6	References	245
12	Characterisation using Raman micro-spectroscopy I NOTINGHER, University of Nottingham, UK	248
12.1	Introduction	248
12.2	Principles of Raman spectroscopy	251
12.3	Characterisation of living cells	254
12.4	Characterisation of tissue engineering scaffolds	259
12.5	Conclusions and future trends	263
12.6	References	264
Part II	Tissue and organ generation	
13	Engineering of tissues and organs A ATALA, Wake Forest University, USA	269
13.1	Introduction	269
13.2	Native cells	270
13.3	Biomaterials	271
13.4	Alternate cell sources: stem cells and nuclear transfer	273
13.5	Tissue engineering of specific structures	277
13.6	Cellular therapies	284
13.6	Conclusions and future trends	288
13.7	References	289

14	Bone regeneration and repair using tissue engineering P WOŹNIAK, Medical University of Warsaw, Poland and A J EL HAJ, Keele University Medical School, UK	294
14.1	Introduction	294
14.2	Principles of bone biology	294
14.3	Basics of bone remodelling	299
14.4	Skeletal tissue reconstruction – a tissue engineering approach	304
14.5	Conclusions	314
14.6	Acknowledgements	315 315
14.7	References	313
15	Bone tissue engineering and biomineralization L DI SILVIO, Kings College London, UK	319
15.1	Introduction	319
15.2	Tissue engineering	320
15.3	Scaffolds and biomineralization	327
15.4	Conclusions and future trends	330
15.5	References	331
16	Cardiac tissue engineering Q Z CHEN, S E HARDING, N N ALI, H JAWAD and A R BOCCACCINI, Imperial College London, UK	335
16.1	Introduction	335
16.2	Cell sources	336
16.3	Construct-based strategies in myocardial tissue engineering	343
16.4	Conclusions and future trends	350
16.5	Acknowledgement	352
16.6	References and further reading	352
17	Intervertebral disc tissue engineering J HOYLAND and T FREEMONT, University of Manchester, UK	357
17.1	Introduction	357
17.2	The impact of disorders of the intervertebral disc (IVD) on	
	modern society	357
17.3	The normal anatomy, function and cell biology of the IVD	358
17.4	The pathobiology of IVD degeneration	359
17.5	Treatment of degeneration of the IVD	364
17.6	The place of biomaterials in proposed strategies for managing	366
177	IVD degeneration Tissue regeneration and the IVD	371
17.7	1155uc regeneration and the 14D	5 1 1