

## Tissue engineering using ceramics and polymers

Edited by Aldo R. Boccaccini and Julie E. Gough



## 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 Wet 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
	5	

vi	Contents	
3.4	Glass-ceramics	67
3.5	Conclusions	67
3.6	References	68
4	Biodegradable and bioactive polymer/ceramic	70
	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	100
<i>E E</i>	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 References	105
5.9	References	105
6	Surface modification to tailor the biological	100
	response	108
	K SHAKESHEFF and G TSOURPAS, University of Nottingham, UK	
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	153
	F DAVIS and S P J HIGSON, Cranfield University, UK	
8.1	Introduction	153
8.2	Carrier systems	153
8.3	Commercial systems	161
8.4	Biosensors	162
8.5 8.6	Continuous monitoring	167
8.6 8.7	Future trends Conclusions	169
8.8	References	170 171
0.0	References	1/1
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	•	
10.1	Introduction The instruments a comparison with CCFM	204
10.2	The instrument: a comparison with CSEM	204
10.3 10.4	Static experiments  Dynamic experiments	210
10.4	Dynamic experiments	212

	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

_		
$C \cap$	ntents	IV
-	HUDITUS	1/

	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
	14.7	References	315
	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	200
	1.7.77	IVD degeneration	366
	17.7	Tissue regeneration and the IVD	371

x	Contents	
17.8 17.9	Conclusions Future trends Sources of further information and advice	372 373 374
17.10 17.11	References	375
18	Skin tissue engineering S MACNEIL, University of Sheffield, UK	379
18.1	Why do we need tissue-engineered skin?	379
18.2	Key events in the development of tissue-engineered skin	383
18.3 18.4	Do we need stem cells for tissue engineering of skin?  Key steps in development of tissue-engineered skin for	385
	clinical use	385
18.5	Challenges in converting research into products	386
18.6	Clinical problems in the use of tissue-engineered skin	391
18.7	Unexpected results from using 3D skin models	396
18.8	Future trends References	398 399
18.9	References	399
19	Liver tissue engineering	404
	K SHAKESHEFF, University of Nottingham, UK	
19.1	Introduction	404
19.2	The structure of the liver lobule	405
19.3	Clinical and commercial applications of engineered liver tissue	405
19.4	Approaches to liver tissue engineering	407
19.5	Conclusions	415
19.6	Future trends	416
19.7	References	416
20	Kidney tissue engineering A SAITO, Tokai University, Japan	421
20.1	Introduction	421
20.2	Present status of kidney regeneration	421
20.3	Functional limitation of current haemodialysis as an artificial kidney	423
20.4	System configuration for bioartificial kidneys	423
20.5	Past and current status of development of bioartificial kidneys	426
20.6	Attachment and proliferation of tubular epithelial cells on polymer membranes	429
20.7	Function of tubular epithelial cells on polymer membranes	433
20.8	Evaluation of a long-term function of LLC-PK <sub>1</sub> cell-attached	,,,,
•	hollow fibre membrane	435
20.9	Improvement of the components of a portable bioartificial	
	kidney developed for long-term use	438

	Contents	xi
20.10 20.11	Conclusions and future trends References	441 442
21	Bladder tissue engineering A M TURNER, University of York, UK, R SUBRAMANIAM and D F M THOMAS, St. James's University Hospital, UK, and J SOUTHGATE, University of York, UK	445
21.1	The bladder – structure and function	445
21.2 21.3	The clinical need for bladder reconstruction Concepts and strategies of bladder reconstruction and tissue	447
	engineering	448
21.4	Review of past and current strategies in bladder reconstruction	
21.5	Cell conditioning in an external bioreactor	457 458
21.6 21.7	Future trends Conclusions	459
21.7	References	459
22	Nerve bioengineering	466
	P KINGHAM and G TERENGHI, University of Manchester, V	JK
22.1	Peripheral nerve	466
22.2	Peripheral nerve injury and regeneration	468
22.3	Peripheral nerve repair	468
22.4	Bioengineered nerve conduits	469
22.5	Matrix materials	473
22.6	Cultured cells and nerve constructions	476
22.7 22.8	Conclusions References	484 484
23	Lung tissue engineering	497
	A E BISHOP and H J RIPPON, Imperial College London, UK	ζ.
23.1	Introduction	497
23.2	Lung structure	497
23.3	Sources of cells for lung tissue engineering	499
23.4	Lung tissue constructs	501
23.5	Conclusions	505
23.6	References	505
24	Intestine tissue engineering D A J LLOYD and S M GABE, St Mark's Hospital, UK	508
24.1	Introduction	508
24.2	Approaches to tissue engineering of the small intestine	508
24.3	Artificial scaffolds	510

xii	Contents	
24.4	Intestinal lengthening using artificial scaffolds	514
24.5	Transplantation of intestinal stem cell cultures	516
24.6	Growth factors	523
24.7	Future trends	524
24.8	Conclusions	525
24.9	References	525
25	Micromechanics of hydroxyapatite-based biomaterials and tissue engineering scaffolds A FRITSCH and L DORMIEUX, Ecole Nationale des Ponts et Chaussées (LMSGC-ENPC), France, C HELLMICH, Vienna University of Technology, Austria and J SANAHUJA, Lafarge Research Center, France	529
25.1	Introduction	529
25.2	Fundamentals of continuum micromechanics	535
25.3	Micromechanical representation of mono-porosity biomaterials	
	made of hydroxyapatite - stiffness and strength estimates	538
25.4	Model validation	542
25.5	Continuum micromechanics model for 'hierarchical'	
	hydroxyapatite biomaterials with two pore spaces used for	
25.6	tissue engineering	551
25.6	Conclusions and future trends	557
25.7	Appendix: Homothetic ('cone-type') shape of failure criterion	
25.8	for hydroxyapatite biomaterials – Drucker–Prager approximation Nomenclature	
25.9	References	559 563
23.9	References	303
26	Cartilage tissue engineering	566
	JE GOUGH, University of Manchester, UK	
26.1	Introduction	566
26.2	Structure, cellularity and extracellular matrix	566
26.3	The need for cartilage repair	567
26.4	Current treatments including autologous chondrocyte	
	transplantation	568
26.5	Cell source	569
26.6	Materials	570
26.7	Growth factors and oxygen	576
26.8	Loading	579
26.9	Osteochondral defects	580
26.10	Conclusions and future trends	580
26.11	References	581
	Index	587