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Introduction to Biomedical Materials Research

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Overview

- What are biomedical materials?
- CCMM: Who are we and what do we do?
- Bone and bone replacements
- Spinal disc replacements
- Other research areas

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What is a Biomedical Material?

- Essentially any material that is used in a medical application

"A biomedical material is any material, natural or man-made, that comprises whole or part of a living structure or biomedical device which performs, augments, or replaces a natural function"

Natural materials

- Grafts (auto-, allo-, xeno-)
- Processed (e.g. Collagen)

Man-made materials

- Polymers
- Ceramics
- Metals
- Composites

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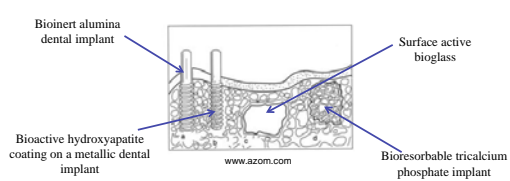
What is a Biomedical Material?

- May be bioinert, bioactive or bioresorbable
- **Bioinert:**
 - Material has minimal interaction with surrounding tissue
 - Examples: stainless steel, titanium, alumina, ultra high molecular weight polyethylene
 - Problems can arise due to fibrous encapsulation of implants
- **Bioactive:**
 - On being placed into the body, these interact with the surrounding bone or soft tissue
 - Examples: Hydroxyapatite, Bioglass, A-W glass ceramic
- **Bioresorbable:**
 - On being placed into the body, these starts to dissolve (resorb) and slowly become replaced by advancing tissue (such as bone)
 - Examples: Tricalcium phosphate, poly(lactic acid), poly(glycolic acid)

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What is a Biomedical Material?






Labels in diagram:

- Bioinert alumina dental implant
- Bioactive hydroxyapatite coating on a metallic dental implant
- Surface active bioglass
- Bioresorbable tricalcium phosphate implant

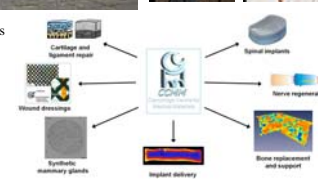
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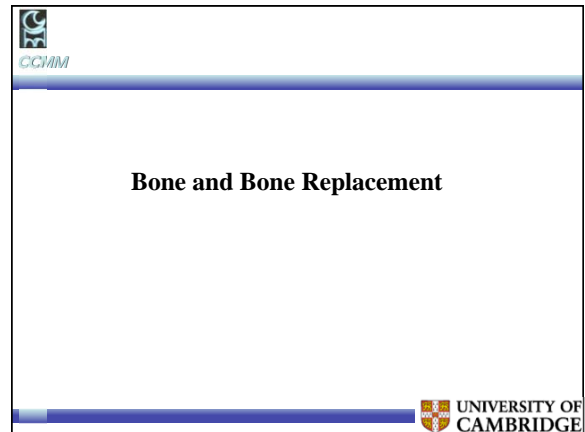
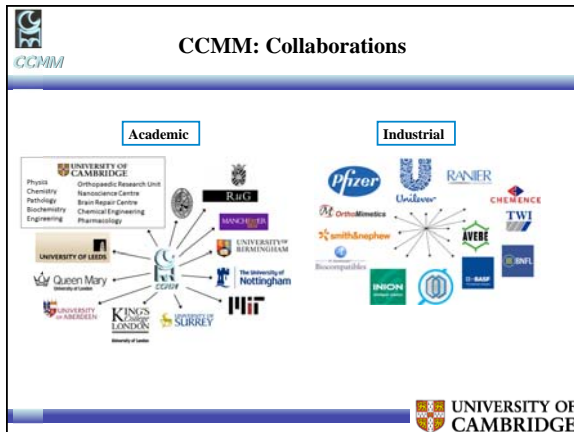
Cambridge Centre for Medical Materials (CCMM)

- Around 30 students and post-docs
- Co-directors: Ruth Cameron and Serena Best



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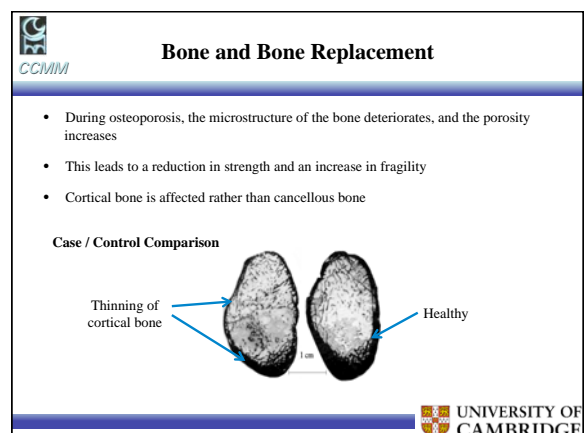
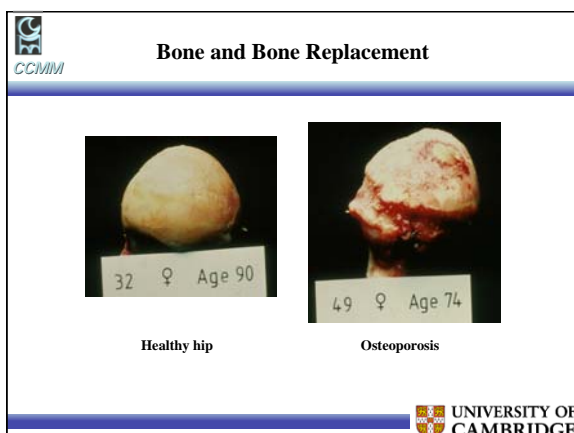
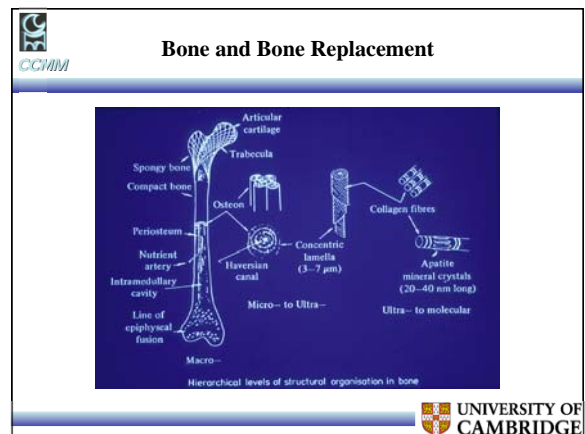


Bone and Bone Replacement

Bone is...

- A living tissue
 - Complex hierarchical structure
 - Constantly changing and adapting to loading environment

BUT...
Suffers from a number of degenerative diseases



Bone and Bone Replacement

- An ageing population means that increasing numbers of surgical procedures will be necessary
- Current solutions for bone replacement:
 - 60% allografts (material from another patient)
 - 35% autografts (material from the same patient but a different site)
 - 5% synthetic materials
- However:
 - Autografts – two surgical procedures required, leading to more pain and increased risk of infection
 - Allografts – possible risk of implant rejection and infection, and possible degradation of mechanical properties (due to sterilisation)
 - Limited availability is a problem for both autograft and allograft materials
- Therefore there is an increasing need for synthetic bone graft alternatives**

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Bone and Bone Replacement

Which inorganic materials can we use to replace bone?

- The inorganic (mineral) phase in bone is similar in chemical composition to hydroxyapatite (HA)

$$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$$
- In its synthetic form, HA can be prepared using conventional ceramic processing techniques
- HA is bioactive
- But how can we make it more bioactive?**

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Bone and Bone Replacement

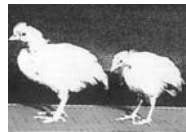
- In reality, bone mineral contains many ions in addition to calcium, phosphorous, oxygen and hydrogen, including:
 - Carbonate ions
 - Sodium ions
 - Magnesium ions
 - Zinc ions
 - Silicon ions
- Therefore, we need to produce apatites with physiologically relevant ionic substitutions
- Current work in our group includes silicon, zinc and carbonate substitutions

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Bone and Bone Replacement

Silicon-substituted hydroxyapatite

- Silicon ions have been shown to be important in early bone formation
- In vivo* studies by Carlisle (published in *Science* in 1970) indicated the importance of silicon to bone formation and mineralisation
- However, the mechanism by which Si increases the *in vivo* bioactivity of HA is still unresolved

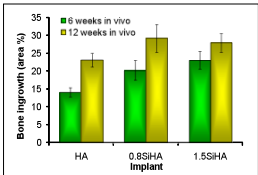


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Bone and Bone Replacement

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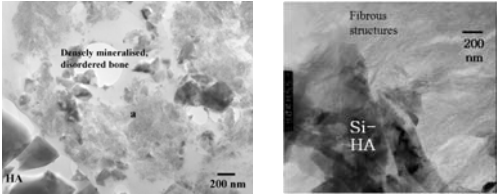


Material	6 weeks in vivo	12 weeks in vivo
HA	~15%	~22%
0.8SiHA Implant	~20%	~28%
1.5SiHA	~22%	~28%

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Bone and Bone Replacement

Mineral arrangement: HA vs Si-HA



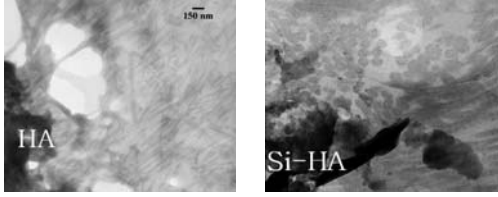
Pure HA - Densely mineralised disordered bone

Si-HA - Densely mineralised ordered bone

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Bone and Bone Replacement

Collagen arrangement: HA vs Si-HA



Pure HA - at 6 weeks, disarray of the collagen fibrils in the vicinity of the implant

1.5 wt% Si-HA - at 6 weeks, organised pattern of collagen fibrils

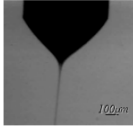
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Bone and Bone Replacement

HA and substituted HA coatings

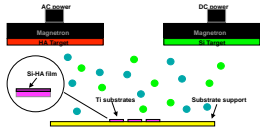
- Bioactive coatings often added to implants (e.g. hip replacements) to encourage better bonding to the surrounding bone
- Deposition methods include:

Electrostatic atomisation



Allows 2D and 3D surface patterning

R-F magnetron sputtering



Allows formation of very thin films

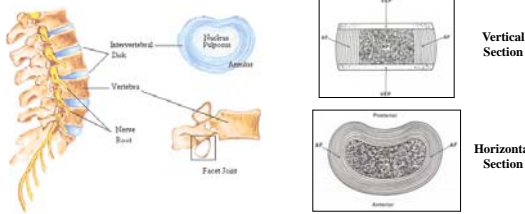
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Spinal Disc Replacement

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Spinal Disc Replacement


- The main function of a natural spinal disc is to maintain the stability of the spinal column whilst providing shock absorption



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Spinal Disc Replacement

- The degeneration of lumbar intervertebral discs is a major cause of lower back pain
- Traditional surgical method is spinal fusion, which has severe limitations
- Currently available designs aim to preserve motion but do not reproduce compliance of natural discs

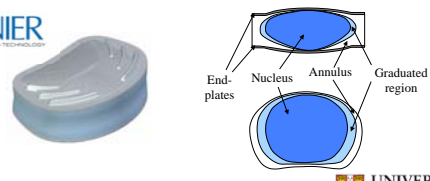


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Spinal Disc Replacement

Compliant Artificial Disc - CAdisc

- PU disc consisting of lower modulus nucleus and higher modulus annulus regions separated by graduated modulus region
- Annulus and nucleus materials made from the same chemical components but in different relative proportions



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Spinal Disc Replacement

Experimental Work


- Interested in the variation of properties across the graduated region between the annulus and nucleus and how the bulk properties are affected
- Main techniques used:
 - Small Angle X-ray Scattering (SAXS)
 - Variation in chemistry/morphology
 - Nanoindentation
 - Variation in mechanical properties
 - Photoelasticity
 - Effect on bulk properties

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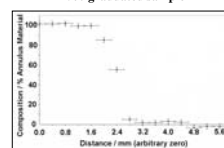
Spinal Disc Replacement

SAXS - Linescans

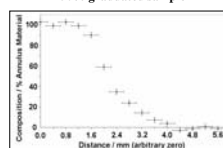
Data acquired at regular intervals across samples



0% graduated sample



50% graduated sample



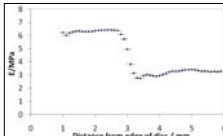
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Spinal Disc Replacement

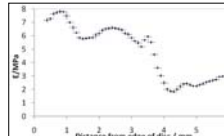
Nanoindentation - Linescans

- Indents carried out at regular intervals across disc samples

0% graduated sample



40% graduated sample



- More features highlighted than by using SAXS
- These can be explained by considering the way in which the polymer flows into the mould during manufacture


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Spinal Disc Replacement

Photoelasticity

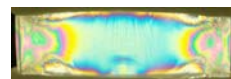
- Lateral sections cut and compressed between crossed polars
- Regions of constant colour represent regions of constant stress

20% graduated



Stress discontinuities at interface

50% graduated



Much smoother interface

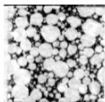
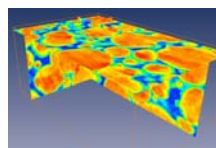
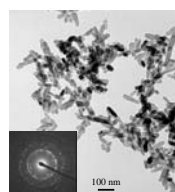
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Other Research Areas

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Resorbable Bioactive Composites

- Manufactured using a polymeric component and a ceramic component
 - Poly(glycolic acid), poly(lactic acid), copolymers
 - HA and other calcium phosphates (may be nanoscale)

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Drug Delivery

- Resorbable polymers with tailored degradation rates

- Fullerenes and the blood-brain barrier

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Cartilage and Ligament Repair

- A cartilage repair product was developed by a PhD student in the CCMM group
- After finishing his PhD, he started a spin-out company called Orthomimetics, which received £5M venture capital funding in December 2006

- Their Chondromimetic product is a 2-layer porous collagen-based scaffold containing mineralised and unmineralised layers

- To repair the cartilage, the damaged area is removed and a hole is drilled into the bone below
- The mineralised layer fits into the hole and enhances bone in-growth whereas the unmineralised layer allows cartilage regeneration

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Cartilage and Ligament Repair

- Orthomimetics are now branching out into other areas:
 - Ligament repair/regeneration
 - Meniscus repair
- These have additional challenges since high tensile and compressive strengths are required respectively

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Synthetic Mammary Gland

- Synthetic mammary gland being developed in collaboration with the pathology dept
- Collagen-based scaffold using a similar method to Chondromimetic
- Designed to allow new drugs to be tested in order to reduce the amount of animal testing that needs to be done

<http://www.path.cam.ac.uk/pages/watson/image/>

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Carbon Nanotubes

- Rolled up single sheets of graphite with interesting electrical and mechanical properties

Can be used as fibre reinforcement of HA

Or with peptide attachment for controlled cell adhesion

www.lces.utexas.edu

Or for nerve cell guidance: their structure can guide the cells and their electrical properties can be used to stimulate growth

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Neuroelectronic Interfaces

Natural Nerve Repair

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Neuroelectronic Interfaces

The diagram illustrates a neuroelectronic interface. The top part shows a cross-section of a 'Damaged nerve' being repaired by a 'Neuroelectronic implant' which contains 'Regenerating axons'. The bottom part shows a detailed view of the interface, including 'Chemical guidance paths for neurons', an 'Unrolled polymer sheet', an 'Electrode for detecting electrical behaviour of axon', and an 'Electrode in contact with axon'.

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Magneto-Mechanical Stimulation of Bone Growth

- Work being carried out in the Composite Materials and Coatings group (led by Prof. Clyne)
- Development of ferromagnetic fibre network layers on prostheses, into which bone tissue growth can be promoted *via* magnetically-induced straining of the network

The diagram shows a ferromagnetic fibre network positioned between a South (S) and North (N) magnetic pole. A magnetic field (B) is applied across the network. A magnified view on the right shows the 'Structure of fibre network'.

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The diagram shows a hip prosthesis with a magnified view of the 'Porous Magneto-Active Layer (Ferritic Stainless Steel)' and the 'Dense Core of Prosthesis (Austenitic Stainless Steel)'. It also indicates 'In-growing Cortical Bone'.

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Magneto-Mechanical Stimulation of Bone Growth

Fibre Biocompatibility & Topography

The images show the topography of a stainless steel fibre network and cells cultured on it. The bottom image is labeled 'Cells cultured on a stainless steel fibre network'.

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