Biomaterials: an introduction

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Feb. 2013
What is a Biomaterial?

A material intended to interface with biological systems to evaluate, treat, augment or replace any tissue, organ or function of the body.
BACKGROUND

• Historically, biomaterials consisted of materials common in the labs of physicians, with little consideration of material properties.

• Early biomaterials:
  – Gold: Malleable, inert metal (does not oxidize); used in dentistry by Chinese, Aztecs and Romans--dates 2000 years
  – Iron, brass: high strength metals; rejoin fractured femur (1775)
  – Glass: Hard ceramic; used to replace eye (purely cosmetic)
  – Wood: Natural composite; high strength to weight; used for limb prostheses and artificial teeth
  – Bone: Natural composite; uses: needles, decorative piercings
  – Sausage casing: cellulose membrane used for early dialysis (W Kolff)
  – Other: Ant pincers. Central American Indians used to suture wounds
HISTORY

• Important dates
  – 1860's: Lister develops aseptic surgical technique
  – early 1900's: Bone plates used to fix fractures
  – 1930's: Introduction of stainless steel, cobalt chromium alloys
  – 1938: first total hip prosthesis (P. Wiles)
  – 1940's: Polymers in medicine: PMMA bone repair; cellulose for dialysis; nylon sutures
  – 1952: Mechanical heart valve
  – 1953: Dacron (polymer fiber) vascular grafts
  – 1958: Cemented (PMMA) joint replacement
  – 1960: first commercial heart valves
  – 1970's: PEO (polyethyleneoxide) protein resistant thin film coating
  – 1976: FDA amendment governing testing & production of biomaterials/devices
  – 1976: Artificial heart (W. Kolff)
Evolution of Biomaterial Science & Technology

- 1\textsuperscript{st} generation (since 1950s)
  Goal: Bioinertness
- 2\textsuperscript{nd} generation (since 1980s)
  Goal: Bioactivity
- 3\textsuperscript{rd} generation (since 2000s)
  Goal: Regenerate functional tissue
## Some application of biomaterials

<table>
<thead>
<tr>
<th>Application</th>
<th>Types of Materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal system</td>
<td>Titanium, Stainless steel, PE</td>
</tr>
<tr>
<td>Joint replacement (Hip, knee)</td>
<td>Stainless steel, Co-Cr alloy</td>
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<tr>
<td>Bone plate</td>
<td>PMMA</td>
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<tr>
<td>Bone cement</td>
<td>Hydroxylapatie Teflon, Dacron</td>
</tr>
<tr>
<td>Artificial tendon and ligment</td>
<td>Titanium, alumina, calcium phosphate</td>
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<tr>
<td>Dental implant</td>
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<tr>
<td>Cardiovascular system</td>
<td>Dacron, Teflon, Polyurethane</td>
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<tr>
<td>Blood vessel prosthesis</td>
<td>Reprocessed tissue, Stainless steel, Carbon</td>
</tr>
<tr>
<td>Heart valve</td>
<td>Silicone rubber, teflon, polyurethane</td>
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<tr>
<td>Catheter</td>
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<tr>
<td>Organs</td>
<td>Polyurethane</td>
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<tr>
<td>Artificial heart</td>
<td>Silicone-collage composite</td>
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<tr>
<td>Skin repair template</td>
<td>Cellulose, polyacrylonitrile</td>
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<tr>
<td>Artificial kidney</td>
<td>Silicone rubber</td>
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<td>Heart-lung machine</td>
<td>Platinum electrodes</td>
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<tr>
<td>Senses</td>
<td>PMMA, Silicone rubber, hydrogel</td>
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<tr>
<td>Cochlear replacement</td>
<td>Silicone-acrylate. Hydrogel</td>
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<tr>
<td>Intraocular lens</td>
<td>Collagen, hydrogel</td>
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<tr>
<td>Contact lens</td>
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<td>Corneal bandage</td>
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EXAMPLES OF USES OF BIOMATERIALS

Intraocular Lens

Artificial Hip Joints

Substitute Heart Valves
MOTIVATION

• Improve quality of life...

• $$$ Biomaterials is a $100 billion + market, increasing at 5-7% / yr

  – Consider diabetes, which afflicts over 15 million Americans (5.9% of population)
    • An artificial pancreas, if it existed, and were given to 10% of diabetics would generate over 2.3 billion/yr
## Devices currently on the market$^2$

<table>
<thead>
<tr>
<th>Device</th>
<th>patient cost</th>
<th>cost of biomaterial</th>
<th>annual revenue (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>hemodialyzer</td>
<td>$18</td>
<td>$6</td>
<td>$110M</td>
</tr>
<tr>
<td>pacemaker</td>
<td>$6,000</td>
<td>$75</td>
<td>$6.75M</td>
</tr>
<tr>
<td>hip</td>
<td>$3,000</td>
<td>$100</td>
<td>$0.5M</td>
</tr>
<tr>
<td>stent and catheter</td>
<td>$3,000</td>
<td>$30</td>
<td>$1.75M</td>
</tr>
</tbody>
</table>

Biomaterials

• Polymeric biomaterials
• Bioceramics
• Metallic biomaterials
• Biocomposite
• Biologically based (derived) biomaterials
Biocompatibility

- Biocompatibility: The ability of a material to perform with an appropriate host response in a specific application.
- Host response: the reaction of a living system to the presence of a material
Biocompatibility

• $B = f(X_1, X_2, \ldots, X_n)$

• Where $X$: material, design, application etc.
Polymeric Biomaterials: Adv & Disadv

- Easy to make complicated items
- Tailorable physical & mechanical properties
- Surface modification
- Immobilize cell etc.
- Biodegradable

- Leachable compounds
- Absorb water & proteins etc.
- Surface contamination
- Wear & breakdown
- Biodegradation
- Difficult to sterilize
Polymeric Biomaterials

- PMMA
- PVC
- PLA/PGA
- PE
- PP
- PA
- PTFE
- PET
- PUR
- Silicones
Bioceramic: Advantages and disadvantage

- High compression strength
- Wear & corrosion resistance
- Can be highly polished
- Bioactive/inert
- High modulus (mismatched with bone)
- Low strength in tension
- Low fracture toughness
- Difficult to fabricate
Bioceramics

- Alumina
- Zirconia (partially stabilized)
- Silicate glass
- Calcium phosphate (apatite)
- Calcium carbonate
Metallic Biomaterials: Advantages & Disadvantages

- High strength
- Fatigue resistance
- Wear resistance
- Easy fabrication
- Easy to sterilize
- Shape memory

- High moduls
- Corrosion
- Metal ion sensitivity and toxicity
- Metallic looking
Metallic biomaterials

- Stainless steel (316L)
- Co-Cr alloys
- Ti$_6$Al$_4$V
- Au-Ag-Cu-Pd alloys
- Amalgam (AgSnCuZnHg)
- Ni-Ti
- Titanium
Surface modification (treatment)

• Physical and mechanical treatment
• Chemical treatment
• Biological treatment
Surface Properties of Materials

- Contact angle (Hydrophilic & Hydrophobic)
- ESCA & SIMS (surface chemical analysis)
- SEM (Surface morphology)
Deterioration of Biomaterials

- Corrosion
- Degradation
- Calcification
- Mechanical loading
- Combined
General Criteria for materials selection

• Mechanical and chemicals properties
• No undesirable biological effects carcinogenic, toxic, allergenic or immunogenic
• Possible to process, fabricate and sterilize with a good reproducibility
• Acceptable cost/benefit ratio
Material Properties

- Compressive strength
- Tensile strength
- Bending strength
- E-Modulus
- Coefficient of thermal expansion
- Coefficient of thermal conductivity
- Surface tension
- Hardness and density
- Hydrophobic/philic
- Water sorption/solubility
- Surface friction
- Creep
- Bonding properties
Cell/tissue reaction to implant

- Soft tissue
- Hard tissue
- Blood cells
The biological milieu

- Atomic scale
- Molecular scale
- Cellular level
- Tissue
- Organ
- System
- Organism
pH in humans

- Gastric content: 1.0
- Urine: 4.5-6.0
- Intracellular: 6.8
- Interstitial: 7.0
- Blood: 7.17-7.35
Sequence of local events following implantation in soft tissue

- Injury
- Acute inflammation
- Granulation tissue
- Foreign body reaction
- Fibrosis
Standards

- Test methods
- Materials standards
- Device standards
- Procedure standards
ISO 10993 and EN 30993

- ISO 10993-1: guidance on selection of tests
- ISO 10993-2: Animal welfare requirements
- ISO 10993-3: Test for genotoxicity, carcinogenicity and reproductive toxicity
- ISO 10993-4: Selection of tests for interactions with blood
- ISO 10993-5: Tests for cytotoxicity: In vitro methods
- ISO 10993-6: Test for local effects after implantation
- ISO 10993-7: Ethylene oxide sterilization residuals
- ISO 10993-8: Clinical investigation
- ISO 10993-9: Degradation of materials related to biological testing
- ISO 10993-10: Tests for irritation and sensitization
- ISO 10993-11: Tests for systemic toxicity
- ISO 10993-12: Sample preparation and reference materials
- .......
Testing of Biomaterials

- Physical and mechanical
- Biological
  - In vitro assessment
  - In vivo assessment
  - Functional assessment
  - Clinical assessment
Biomaterials applications

- Dental implant
- Tooth fillings
- Vascular implants
- Drug delivery, bone fixing pine, suture
- Bone defect fillings
- Hip joint prosthesis bone plate
- Scaffolds for tissue engineering
- Contact lens
3-principles in dental implant design

- Initial retention
- Anti-rotation mechanics
- No sharp-edges
Tooth fillings materials

- Amalgam
- Dental composite
- Ceramics
- Other metals
General criteria for tooth filling materials

- Non-irritation to pulp and gingival
- Low systemic toxicity
- Cariostatic
- Bonding to tooth substance without marginal leakage (20 u)
- Not dissolved or erode in saliva
- Mechanical strength, wear resistance, modules matching.
- Good aesthetic properties
- Thermal properties (expansion & conductivity)
- Minimal dimensional changes on setting and adequate working time and radio opacity
Textile structure and vascular implant

- Weaving
- Braiding
- knitting
Calcium phosphate-based bioceramic

- Bone (ACP, DCPD, OCP & HA)
- Ca-P compounds
- Applications:

  Bone fillers/HA-coatings/HA-PLA/In situ setting cement/tooth paste/drug tablets
Hip joint prosthesis

- Ceramic head
- Metallic stem
- Polymeric socket
- Composite bone cement
Tissue engineering

• The application of engineering disciplines to either maintain existing tissue structures or to enable tissue growth.

• From a material engineering point of view, tissues are considered to be cellular composites representing multiphase system:

Three main structural components:

1. Cells organised into functional units
2. The extracellular matrix
3. Scaffolding architecture
Polymer concepts in tissue engineering

• Fabrication procedures of a porous polymer 3D scaffold:
  PLGA dissolved in chloroform and mixed with NaCl particles, evaporation of the chloroform, dissolution of NaCl in water, resulting a polymer sponge with over 96% porosity.
Requirements for Soft Tissue Adhesive

- Biodegradable
- Fast spread on wet (wound) surface
- Adequate working time
- Adequate bonding strength
- Hemostasis
- Biocompatible
Contact lens

- Optical properties
- Chemical stability
- Oxygen transmissibility
- Tear film wettability
- Resistance to lipid/protein deposition
- Easy to clean
Drug delivery (Slow/Controlled release)

- Most effective and low toxic dose
- A constant dosage over a long period
- Local treatment
- Easy to handle and cost-effective
Classification of slow release system

- Diffusion controlled
- Water penetration controlled
- Chemically controlled
- Pendant chain systems
- Regulated system (Magnetic or ultrasound)
Sterilization Methods

- Moist heat (121-125°C, 15-30 min)
- EO (CH₂CH₂O)
- Radiation (⁶⁰Co & Electron Beam)
- Dry heat > 140°C
- Others (UV, Ozone X-ray etc)
Leading medical device company

- Johnson & Johnson (www.jnj.com)
- Biomet INC (www.biomed.com)
- Strycker Howmedica Osteonics (www.osteonis.com)
- Sulzer Orthopedics Ltd (www.sulzerortho.com)
- Zimmer (www.zimmer.com)
- Merck & Co Inc (www.merck.com)
- Nobel biocare/AstraZeneca/Pacesetter AB/Q-med/Artimplant/Doxa
References:

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& some others.