### Materials for use in Body - Table 4

<table>
<thead>
<tr>
<th>Materials</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Examples</th>
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<tbody>
<tr>
<td><strong>Polymers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Nylon</td>
<td>Resilient</td>
<td>Not strong</td>
<td>Sutures, blood</td>
</tr>
<tr>
<td>-Silicones</td>
<td>Easy to fabricate</td>
<td>Deform with time</td>
<td>Vessels, hip socket,</td>
</tr>
<tr>
<td>-Teflon</td>
<td></td>
<td>May degrade</td>
<td>Ear, nose, other</td>
</tr>
<tr>
<td>-Dacron</td>
<td></td>
<td></td>
<td>Soft tissues</td>
</tr>
<tr>
<td><strong>Metals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Titanium</td>
<td>Strong, tough</td>
<td>May corrode</td>
<td>Joint replacement,</td>
</tr>
<tr>
<td>-Stainless Steels</td>
<td>Ductile</td>
<td>Dense</td>
<td>Bone plates and</td>
</tr>
<tr>
<td>-Co-Cr alloys</td>
<td></td>
<td></td>
<td>Screws, dental</td>
</tr>
<tr>
<td>-Gold</td>
<td></td>
<td></td>
<td>Root implants</td>
</tr>
<tr>
<td>-Magnesium and alloys</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ceramics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Aluminum Oxide</td>
<td>Very biocompatible,</td>
<td>Brittle</td>
<td>Dental; hip socket</td>
</tr>
<tr>
<td>-Carbon</td>
<td>Inert</td>
<td>Difficult to make</td>
<td></td>
</tr>
<tr>
<td>-Hydroxyapatite</td>
<td>Strong in compression</td>
<td>Not resilient</td>
<td></td>
</tr>
<tr>
<td><strong>Composites</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Carbon-carbon</td>
<td>Strong, tailor made</td>
<td>Difficult to process</td>
<td>Joint implants;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Heart valves</td>
</tr>
</tbody>
</table>
Role of biomaterials is governed by the interaction between the material and the body, in particular, the effect of the body environment on the material, and the effect of the material on the body.

Current applications involve structural functions even in those organs and systems that are not primarily structural in their nature, or very simple chemical or electrical functions. Complex chemical functions such as those of brain and sense organs cannot be performed by biomaterials.
Impact of Multifunctional Materials:
- Several applications in potential key areas
- Tremendous scope for nanostructured materials
Porous sponges of natural polymers

Chitosan

Collagen

Hyaluronic acid
SEM of PLGA microspheres embedded in PLGA scaffolds
Boloampiphiles: Novel protein architectures-building blocks for membranes, fibers, tubes and ribbons
Nanostructured Biocompatible Ceramics
Cell-Materials Surface Interaction
## Applications of Synthetic Materials and Modified Natural Materials in Medicine

<table>
<thead>
<tr>
<th>Application</th>
<th>Types of materials</th>
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<tbody>
<tr>
<td><strong>Skeletal system</strong></td>
<td></td>
</tr>
<tr>
<td>Joint replacements (hip, knee)</td>
<td>Titanium, Ti-Al-V alloy, stainless steel, polyethylene</td>
</tr>
<tr>
<td>Bone plate for fracture fixation</td>
<td>Stainless steel, cobalt-chromium alloy</td>
</tr>
<tr>
<td>Bone cement</td>
<td>Poly(methyl methacrylate)</td>
</tr>
<tr>
<td>Bony defect repair</td>
<td>Hydroxylapatite</td>
</tr>
<tr>
<td>Artificial tendon and ligament</td>
<td>Teflon, Dacron</td>
</tr>
<tr>
<td>Dental implant for tooth fixation</td>
<td>Titanium, Ti-Al-V alloy, stainless steel, polyethylene</td>
</tr>
<tr>
<td></td>
<td>Titanium, alumina, calcium phosphate</td>
</tr>
<tr>
<td><strong>Cardiovascular system</strong></td>
<td></td>
</tr>
<tr>
<td>Blood vessel prosthesis</td>
<td>Dacron, Teflon, polyurethane</td>
</tr>
<tr>
<td>Heart valve</td>
<td>Reprocessed tissue, stainless steel, carbon</td>
</tr>
<tr>
<td>Catheter</td>
<td>Silicone rubber, Teflon, polyurethane</td>
</tr>
<tr>
<td><strong>Organs</strong></td>
<td></td>
</tr>
<tr>
<td>Artificial heart</td>
<td>Polyurethane</td>
</tr>
<tr>
<td>Skin repair template</td>
<td>Silicone-collagen composite</td>
</tr>
<tr>
<td>Artificial kidney (hemodialyzer)</td>
<td>Cellulose, polyacrylonitrile</td>
</tr>
<tr>
<td>Heart-lung machine</td>
<td>Silicone rubber</td>
</tr>
<tr>
<td><strong>Senses</strong></td>
<td></td>
</tr>
<tr>
<td>Cochlear replacement</td>
<td>Platinum electrodes</td>
</tr>
<tr>
<td>Intraocular lens</td>
<td>Poly(methyl methacrylate), silicone rubber, hydrogel</td>
</tr>
<tr>
<td>Contact lens</td>
<td>Silicone-acrylate, hydrogel</td>
</tr>
<tr>
<td>Corneal bandage</td>
<td>Collagen, hydrogel</td>
</tr>
</tbody>
</table>
Biomaterials and Healthcare Market—Facts and Figures (per year) (U.S. numbers—Global numbers are typically 2-3 times the U.S. number)

Note the large costs incurred in Diabetes management, Cardiovascular, and Orthopedic-Musculoskeletal Surgery

Heart valves open and close 40 million times a year and can be damaged to be replaced. More than 80,000 replacement valves implanted each year in the U.S. due to damage to natural valve. Made from carbon, metals, elastomers, plastics, fabrics and animal or human tissue.

**Bileaflet tilting-disk** mechanical heart valve. Other valves made from pig valves, cow pericardial tissue. Potentially successful.

**Problems:** blood clots, degeneration, mechanical failure, and infection.
Artificial Hip Joints

Hip joint subjected to large levels of Mechanical stress and is considerably Abused during use. Typically, after 50 years of use, degeneration and rheumatological disease sets leading to wear. Prosthesis are made from: Titanium, SS, high-strength alloys, ceramics, composites, and UHME polyethylene. More than 200,000 humans get hip prosthesis. With replacement ambulatory functions are restored. Major area for healing is the integration between bone and implant before the joint can bear full weight. Typical life: 10-15 years.
Dental Implants

Ti-implants has revolutionized dental implant technology. Form an implanted tooth anchor to which a crown is fixed and implanted in ~ 300,000 people per year. Some patients receive more than 12. Key is to ability to form a tight seal to prevent bacteria invasion where the implant connects to the gingiva. Primary advantages: osseous integration with the bone of the jaw. The bonding is more mechanical fit rather than a true chemical and biological bond. Loss of tissue leading to loosening is still a problem resulting in infection and corrosion coming in due to long term cyclic loads and the pH changes in the oral cavity.
Intraocular lens (IOL)

IOL are made from PMMA, silicone elastomer, soft acrylic polymers, or hydrogels. Replace natural lens when it becomes cloudy due to cataract. By 75 years of age, 50% population suffers from cataracts severe enough to warrant IOL.

i.e. 4 million implantations in the U.S. alone each year. Good vision is restored almost immediately after the lens is inserted.

Healing occurs by inflammatory cells migrating to the surface of the lenses after implantation similar to other materials implanted at other sites in the body.

Complications arise by outgrowth of cells from the posterior lens capsule stimulated by the IOL which can cloud the vision.

FIG. 4. An intraocular lens. (Photograph courtesy of Alcon Laboratories, Inc.)
Historical Perspective

- Biomaterials did not become practical until the advent of aseptic surgical procedures developed by Lister in 1860s.
- Earlier procedures were unsuccessful because of infection which was exacerbated in presence of biomaterials since implant made it inaccessible to body’s immunological competent cells.
- Early success came in light of the skeletal system. Bone plates were introduced in early 1900s to aid in fracture healing.
- Many failed because of poor mechanical design.
- Too thin, stress concentration centers.
- Vanadium steel chosen for good mechanical properties failed because of rapid corrosion.
- Better design soon followed:
  - Introduction of SS
  - Co-Cr in 1930s
  - Success in fracture fixation and joint replacement surgeries performed.
- In WW-II polymers came to rescue of injured pilots. Pilots injured with fragments of PMMA aircraft canopy did not suffer chronic reactions from presence of fragments in the body. PMMA became widely used for corneal replacement and replacement of sections of damaged skull bones.
- Further advances in engineering and technology blood vessel replacements were attempted in 1950s.
- Heart valve replacements and cemented joint replacements in the 1960s.
- In 1980s new materials systems were developed:
  - Bioglass, hydroxyapatite, Carbon-pyrolytic
- In 1990s advent of biodegradable polymers and the concept of tissue engineering resulted in new philosophy and outlook of biomaterials.
Pioneers

- Biomaterials knowledge dates back to 9000 years when a spear point embedded in a hip healed in the active person.
- Dental implants first work dates back to 600 A.D. related to use of sea shells and achieved bone integration.
- Sutures known for over 32,000 years. Linen used by Egyptians and Catgut used in the middle ages in Europe. Metallic sutures mentioned by the Greeks; silver wire, lead and gold.
Pioneers

**FIG. 2.** Sir Harold Ridley, inventor of the intraocular lens.

**FIG. 3.** Sir John Charnley.

Inventor of the hip-joint protheses.
Dr. Willem Kolff: inventor of the dialysis machine and the artificial heart in 1943 and in 1957.
-dialysis membrane made from cellulose.
- artificial heart from PVC
Pioneers

Pacemakers: Earl E. Bakken, founder of Medtronic, Inc. developed the first wearable pacemaker.

John Hopps in 1949 discovered the early cardiac pacemaker.

FIG. 6. Dr. Julio Palmaz, inventor of the coronary artery stent.
Synthetic Materials

- Silicones: In 1940 by Eugene Rochow of GE by reacting methyl chloride and silicon.
- Polyurethanes: Otto Bayer in Germany by the reaction of diisocyanates and diamines.
- Teflon: Roy Plunkett from DuPont discovered PTFE.
- Hydrogels: Wichterle and Lim published in Nature about polyHEMA.
- PEG: Friedman in 1944.
- PLA-PGA: first identified in 1966 but later developed by Langer and Vacanti in 1993 for Tissue Engineering.
- HA: First applications as biomaterial by Levit in 1969.
- Titanium: As early as 1791 by William Gregor later in 1932 by William Kroll identified the extraction of Ti from mineral sources.
Performance of Biomaterials

• Success of biomaterial depends on factors:
  – Materials properties, design, and biocompatibility of the material used, other factors not in control of the engineer
    • Techniques used by surgeon
    • The qualification of the surgeon
    • Health of the patient
    • Activities of patient
Performance of Biomaterials

• We can assign a numerical value of ‘f’ to probability of failure of an implant.
• The reliability can be expressed as:
  \[ r = 1 - f \]
If there are multiple modes of failure the total reliability, \( r_t \) can be expressed as:
Product of individual reliabilities:
\[ r_1 = (1 - f_1), \text{ etc.} \]
Thus \( r_t = r_1 r_2 r_3 \ldots r_n \)
Performance of Biomaterials

- Thus if one failure mode such as implant fracture is perfectly controlled so that the corresponding reliability is unity, other failure modes such as infection could severely limit the utility represented by the total reliability of the implant.

- One common and important failure mode is the attack by the body’s immune system on implant. Another failure mode is an unwanted effect of the implant on the body, e.g. toxicity, inducing an inflammation, or causing cancer.

- Biocompatibility is thus an important criteria.

- Biocompatible materials do not irritate the surrounding structures, do not provoke an antiinflammatory response, do not incite allergic reactions, and are not carcinogenic.

- Other functions for device that are important:
  - Mechanical properties, strength, stiffness, and fatigue properties; optical properties for eye, skin, tooth; density, manufacturing ease and engineering design.

- Failure modes may differ in importance as time passes following implant surgery. Ex. Consider the case of a total joint replacement in which infection is most likely soon after surgery, while loosening and implant fracture becomes progressively more important with passage of time as seen in Figure 1. Failure also depends on type of implant and its location, environment in the site and the type of function in the body.

- Example, artificial blood vessel is more likely to cause clots and become clogged with thrombus than by breaking or failing mechanically.
Figure 1-1. Schematic diagram of role of various failure modes as they depend on time for a joint replacement prosthesis. Not to scale. Failure modes of small probability, such as surgical error, allergic reaction to metal, not shown.
Magnitude of the Need

- Magnitude is tremendous: Compared to the cost, the potential for providing a better life is the key.
- Contact lens-$100; hip joint and a hydrocephalous shunt to prevent brain damage-$1000-$4000.
- In a year, 75 million contact lenses, 275,000 heart valves, 5000 hydrocephalous shunts, and 500,000 total artificial hip and knee prostheses required.
- Issues: 1. number of devices, 2. medical significance, and 3. commercial potential-who will make it and why?
Magnitude of the Need

- In 2000, more than 20 million patient lives were supported and improved.
- Cost of organ replacement and prostheses exceeds $300 billion per year and represents between 7% and 8% of total worldwide health-care spending.
- Cost of substitute heart valve is ~ $4000. Surgery to implant the device results in a hospital bill and first year follow up costs of ~$60,000. Reoperation for replacing a failed valve will have the same costs. Reoperations for failed valves now exceed 10% of all valve replacements.
Successes and Failure

• Most devices perform satisfactorily. No manmade material is perfect. All devices have a failure rate. Humans differ, body chemistries differ, environments are also vastly different, combined with the level of activity.
• Physicians’ skill is also variable.
• Central issues: 1. what represents a good design?; 2. who should be responsible when devices perform with an inappropriate host response; and 3. What is the cost/risk or cost/benefit ratios for the implant or therapy?
Successes and Failure

• Examples to illustrate the magnitude of what success and failure mean.
• Heart valve disease is a serious problem. Patients with diseased aortic valve have a 50% death rate in 3 years. Surgical intervention and replacement can increase life by 10 years in 70% of the cases. However, 60% of the people whose life has been improved will suffer a serious heart valve related complications within 10 years after the surgery.
Important Characteristics of Biomaterials Science

- Multidisciplinarity
- Multimaterial
- Need-driven
- Considerable market potential
- Risk-benefit
Other Aspects of Biomaterials Science

- Toxicology: Materials need to be non-toxic, not lead to any adverse immune and cancerous response that can lead to death.

- Many polymers elicit leachable products that exhibit cell toxicity.

- Metallic systems elicit wear debris and soluble corrosion products that can exhibit toxicity.

- Toxicology evaluates the safety of the design criteria.
Other Aspects of Biomaterials Science

- Tissue structure and pathobiology: structure of normal and abnormal cells and tissues, organs, the techniques to study the structure and functions of normal and abnormal tissues. Fundamental mechanisms of disease processes are important considerations.
- Healing: Foreign body reactions, normal response of the body to a solid implant. How a foreign object alters the normal inflammatory reaction sequence is an important concern.
Other Aspects of Biomaterials Science

• Specific Anatomical Sites of Implantation: Considerations are required for proper design, size, geometry, mechanical properties and response depending on the device and the site of implantation. Ex. IOL goes into the lens capsule or the anterior chamber of the eye; hip joint will be implanted in bone across an articulating joint space; heart valve will be sutured to a cardiac muscle and will contact both soft tissue and blood.

• Mechanical and Performance Requirements: 1. mechanical performance, mechanical durability and physical properties. Ex. A hip prosthesis must be strong and rigid; heart valve must be flexible and tough; a dialysis membrane must be strong and flexible but not elastomeric. Durability: catheter need to perform 3 days, a bone plate for 6 months or longer. A heart valve must flex 60 times per minute without tearing for life, at least 10 or more years. Hip joint must not fail for at least 10 years.

• Physical properties vary from structure, mechanical properties, permeability, optical properties etc. Thus requiring expertise from multiple disciplines: physics, chemistry, mechanical engineering, chemical engineering and materials science and engineering.
Ethical Concerns

• A wide range of ethical considerations impact biomaterials science. Considerable debate exists over many issues.

Is the use of animals justified? Specifically, is the experiment well designed and important so that the data obtained will justify the suffering and sacrifice of the life of a living creature?

How should research using humans be conducted to minimize risk to the patient and offer a reasonable risk-to-benefit ratio? How can we best ensure informed consent?

Companies fund much biomaterials research and own proprietary biomaterials. How can the needs of the patient be best balanced with the financial goals of a company? Consider that someone must manufacture devices—these would not be available if a company did not choose to manufacture them.

Since researchers often stand to benefit financially from a successful biomedical device and sometimes even have devices named after them, how can investigator bias be minimized in biomaterials research?

For life-sustaining devices, what is the trade-off between sustaining life and the quality of life with the device for the patient? Should the patient be permitted to “pull the plug” if the quality of life is not satisfactory?

With so many unanswered questions about the basic science of biomaterials, do government regulatory agencies have sufficient information to define adequate tests for materials and devices and to properly regulate biomaterials?

Should the government or other “third-party payors” of medical costs pay for the health care of patients receiving devices that have not yet been formally approved for general use by the FDA and other regulatory bodies?

Should the CEO of a successful multimillion dollar company that is the sole manufacturer a polymer material (that is a minor but crucial component of the sewing ring of nearly all heart valves) yield to the stockholders’ demands that he/she terminate the sale of this material because of litigation concerning one model of heart valve with a large cohort of failures? The company sells 32 pounds of this material annually, yielding revenue of approximately $40,000?

Should an orthopedic appliance company manufacture two models of hip joint prostheses: one with an expected “lifetime” of 20 years (for young, active recipients) and another that costs one-fourth as much with an expected lifetime of 7 years (for elderly individuals), with the goal of saving resources so that more individuals can receive the appropriate care?