Knee Replacement Therapy

Primary Problem:
- Damaged cartilage leads to various forms of arthritis
- Osteoarthritis: 20.7 million Americans

Symptoms:
- hard, bony swelling of the joints
- gritty feeling
- Immobility
Introduction - Background

Solution: *Total Knee Replacement (TKR)*

- Nearly 250,000 Americans receive knee implants each year

Results:
- Stops or greatly reduces joint pain
- Improves the strength of the leg
- Increases quality of life and comfort
Four Primary Components:
1. Femoral Component
2. Tibial Component
3. Plastic Insert
4. Patellar Component
**Current TKR Design - Components**

**Femoral Component**
- **Materials:** Cobalt-chromium-molybdenum, Ti-6Al-4V ELI Titanium Alloy
- **Interface:** Press fit, biological fixation, PMMA

**Patellar Component**
- **Materials:** Polyethylene, Cobalt-chromium-molybdenum (Ti Alloy)
- **Interface:** Press fit, biological fixation, PMMA

*Modular or singular design*
Current TKR Design - Components

**Tibial Component**

Materials: Cobalt-chromium-molybdenum (cast)
            Ti-6Al-4V ELI Titanium Alloy

Interface: Press Fit, Biological Fixation, PMMA

**Plastic Insert**

Materials: Polyethylene

Interface: Press Fit
Current TKR Design - Problems

#1 Polyethylene “The Weak Link”
- Articulation wear produces particulates
- Leading to osteolysis and bone resorption at the implant interface.
- Loosening and eventual malfunction of the implant will occur.

Figure 2.3 Examples of worn UHMWPE components for total hip and knee replacements.
Current TKR Design - Problems

#1 Polyethylene “The Weak Link”
- Articulation wear produces particulates
- Leading to osteolysis and bone resorption at the implant interface.
- Loosening and eventual malfunction of the implant will occur.

#2 Metal-Bone Interface
- Stress-shielding leads to bone degeneration

Average lifespan of 10-20 years
Total Artificial Hip
The surgical procedure
The surgical procedure

Traditional Incision Site

Approximately 12"

Mini Incision Hip Replacement
Preparation of the acetabulum is obtained using specially designed acetabular reamers (like cheese graters).
Preparation of Femoral Canal

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Bone Cement

- a mixture of PMMA particles, the liquid monomer MMA (methyl methacrylate), a radio-opaque barium salt, and initiator (organic peroxide) to start the polymerization reaction of the MMA to PMMA.
Mini-Incision total hip Replacement
HIP ARTHROPLASTY: Alignment and Stem Position
Stem Position
A Number of Components to Choose from:
Polyethylene and porous acetabular cups, back and front views
Metal acetabular cup with polyethylene liner, disassembled and assembled
Metal acetabular cup with metal liner, disassembled and assembled
Metal acetabular cup with polyethylene liner disassembled, with various ceramic and metallic femoral component heads
Acetabular cups—ceramic, metal and polyethylene, and porous ingrowth
Porous ingrowth femoral stem with various metal and ceramic heads
Porous ingrowth total hip replacement with polyethylene cup line
Major factors causing failure of total joint replacements include:

1. Infection during orthopedic surgery;
2. Fracture of the implants;
3. Fixation problem of the implants;
4. Wear of the implant materials; and,
5. Osteolysis induced by wear particles.
Figure 2.3  Examples of worn UHMWPE components for total hip and knee replacements.

Worn UHMWPE cup of total hip replacement.

Worn UHMWPE component of total knee replacement.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample source</th>
<th>Particle isolation</th>
<th>Material analysis</th>
<th>Particle analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campbell et al. [36] JBMR, vol. 29, pp. 127-131 (1995) *LA orthopedic hospital</td>
<td>Tissues (THR)</td>
<td>NaOH digestion, density gradient ultracentrifugation, sucrose density gradient centrifugation</td>
<td>FTIR, DSC</td>
<td>SEM * Rounded (0.3 µm) * Elongated (1.9 µm) * Fibrils with rounded heads at one end, thin taper at the other</td>
</tr>
<tr>
<td>Shambhag et al. [37] JBJS, vol. 76-B, pp. 60-67 (1994) *Rush-Presbyterian-St Luke’s medical center</td>
<td>Tissues, interfacial membranes (THR)</td>
<td>KOH digestion, centrifugation, hexane-ethanol fractions</td>
<td>FTIR, EDX</td>
<td>SEM * Spheres: 0.1 µm to 0.2 µm * Fibrils: 0.2 µm to 0.3 µm wide, up to 10 µm long. * 92 % particles are smaller than 1 µm</td>
</tr>
<tr>
<td>Hailey et al. [38] PIME, vol. 210, pp. 3-10 *U. of Leeds, UK</td>
<td>Tissue (THR)</td>
<td>KOH digestion, centrifugation, 0.2 µm filtration</td>
<td>N/A</td>
<td>SEM 0.3 µm up to 3 mm</td>
</tr>
<tr>
<td>Maloney et al. [40] JBJS, vol. 77-A, pp. 1301-1310 (1995) *Stanford U.</td>
<td>Tissues (THR)</td>
<td>Papain digestion</td>
<td>X-ray</td>
<td>SEM, Coulter multisizer II * Fixed cup: 0.4 µm * Bipolar: 0.7 µm</td>
</tr>
<tr>
<td>Schmizled et al. [41] JBMR, vol. 38, pp. 203-210 (1997) *LA orthopaedic hospital</td>
<td>Tissues (THR, TKR)</td>
<td>NaOH digestion, sucrose ultracentrifugation, isopropanol density gradient ultracentrifugation</td>
<td>FTIR, DSC</td>
<td>SEM * Granules: sub-micron * Beads: 1 µm to 2 µm * Fibrils: up to 5 µm * Shreds: 10 µm to 20 µm long, up to several microns wide.</td>
</tr>
<tr>
<td>Hirakawa et al. [42] JBMR, vol. 31, pp. 257-263 (1996) *The Cleveland clinic foundation</td>
<td>Tissues (THR, TKR)</td>
<td>70 % Nitric acid digestion, centrifugation, 0.4 µm filtration</td>
<td>EDX</td>
<td>SEM, Coulter multisizer II * &lt;10 µm particles: 0.72 µm (hip), 0.74 (knee) * &gt;10 µm particles: 81 µm (hip), 283 µm (knee)</td>
</tr>
</tbody>
</table>
Figure 2.4 Examples of UHMWPE particles retrieved from total knee replacement.
Wear particle induced osteolysis

Figure 2.5 Osteolysis taking place around the total hip replacements which is detected by X-ray diagnosis.
<table>
<thead>
<tr>
<th>Terms</th>
<th>Definition</th>
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<tr>
<td>Osteolysis</td>
<td>Dissolution of bone through disease, commonly due to infection or by loss of blood supply to the bone.</td>
</tr>
<tr>
<td>Necrosis</td>
<td>The death of some of all the cells in an organ or tissue, caused by disease, physical or chemical injury, or interference with the blood supply.</td>
</tr>
<tr>
<td>Phagocytosis</td>
<td>The engulfment and digestion of bacteria and other foreign particles by a cell.</td>
</tr>
<tr>
<td>Macrophage</td>
<td>A large scavenger cell (a phagocyte) present in connective tissue and many major organs and tissues, including the bone marrow, spleen, lymph nodes, liver, and the central nervous system.</td>
</tr>
<tr>
<td>Osteoblast</td>
<td>A cell, originating in the mesoderm of the embryo that is responsible for the formation of bone.</td>
</tr>
<tr>
<td>Osteoclast</td>
<td>A large multinucleate cell that resorbs calcified bone. Osteoclasts are only found when bone is being resorbed and may be seen in small depressions on the bone surface.</td>
</tr>
<tr>
<td>Cytokine</td>
<td>Soluble mediators secreted by macrophages, controlling many critical interactions among cells of the immune system.</td>
</tr>
<tr>
<td>IL-1β, IL-6</td>
<td>Cytokine, interleukins mediators</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Cytokine, tumor necrosis factor α</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>Cytokine, colony-stimulating factors</td>
</tr>
<tr>
<td>PGE-2</td>
<td>Cytokine, prostaglandins</td>
</tr>
</tbody>
</table>
Hip Implant

Osteointegration
The leap

- 1952 - Per Ingvar Branemark,
- Discovered the titanium screw.
- Introduced the concept of Osseointegration

All existing designs based on Branemark Titanium Screw
Osseointegration – The Divine Mantra

A fixture is osseointegrated if it provides a stable and apparently immobile support of prosthesis under functional loads, without pain, inflammation, or loosening.
Ceramics and Glasses
Definitions

Ceramic: an inorganic, nonmetallic, typically crystalline solid that is prepared from powdered materials and is fabricated into products through the application of heat.

- Most ceramics are made up of two or more elements.
- Inorganic compounds that contain metallic and non-metallic elements, for which inter-atomic bonding is ionic and covalent, and which are generally formed at high temperatures.

Glass: (i) An inorganic product of fusion that has cooled to a rigid condition without crystallization; (ii) An amorphous solid.
Various microstructures

*Amorphous:* (i) Lacking detectable crystallinity; (ii) possessing only short-range atomic order; also *glassy* or *vitreous*

*Bioactive material:* A material that elicits a specific biological response at the interface of the material, resulting in the formation of a bond between the tissues and the material.
Crystalline versus Glassy Ceramics

- Crystalline ceramics have long-range order, with components composed of many individually oriented grains.
- Glassy materials possess only short-range order, and generally do not form individual grains.
- The distinction is based on x-ray diffraction characteristics.
- Most of the structural ceramics are crystalline and oxides.
**Metal-Ceramic Comparison**

<table>
<thead>
<tr>
<th>Property</th>
<th>Units</th>
<th>Ti 6Al 4V</th>
<th>316 SS</th>
<th>CoCr Alloy</th>
<th>TZP</th>
<th>Alumina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young's modulus</td>
<td>GPa</td>
<td>110</td>
<td>200</td>
<td>230</td>
<td>210</td>
<td>380</td>
</tr>
<tr>
<td>Strength</td>
<td>MPa</td>
<td>800</td>
<td>650</td>
<td>700</td>
<td>900–1200</td>
<td>&gt; 500</td>
</tr>
<tr>
<td>Hardness</td>
<td>HV</td>
<td>100</td>
<td>190</td>
<td>300</td>
<td>1200</td>
<td>2200</td>
</tr>
</tbody>
</table>

- Stiffness is comparable to the metal alloys
- The biggest problem is fracture toughness (sensitivity to flaws).
- Rigid plastics < Metals < ceramics
- Metals are ductile, whereas ceramics are brittle
Advantages:

- inert in body (or bioactive in body); Chemically inert in many environments
- high wear resistance (orthopedic & dental applications)
- high modulus (stiffness) & compressive strength
- esthetic for dental applications
Disadvantages

- brittle (low fracture resistance, flaw tolerance)
- low tensile strength (fibers are exception)
- poor fatigue resistance (relates to flaw tolerance)
Basic Applications:

Orthopedics:
- bone plates and screws
- total & partial hip components (femoral head)
- coatings (of metal prostheses) for controlled implant/tissue interfacial response
- space filling of diseased bone
- vertebral prostheses, vertebra spacers, iliac crest prostheses
Dentistry:

- dental restorations (crown and bridge)
- implant applications (implants, implant coatings, ridge maintenance)
- orthodontics (brackets)
- glass ionomer cements and adhesives
Veneers

Before

1. Etch
2. Epoxy; Bond or Veneer
3. Ultraviolet Light

After

Bonding & Veneer
Before and after
Other:

- inner ear implants (cochlear implants)
- drug delivery devices
- ocular implants
- heart valves
Ceramics

- Alumina, Zirconium, Hydroxyapatite, Calcium phosphates.
- Porous ceramic materials exhibit much lower strengths but have been found extremely useful as coatings for metallic implants.
- The coating aids in tissue fixation of the implant by providing a porous surface for the surrounding tissue to grow into and mechanically interlock.
- Certain ceramics are considered bioactive ceramics if they establish bonds with bone tissue.
Types of Bioceramic-Tissue Interactions:

Dense, inert, nonporous ceramics attach to bone (or tissue) growth into surface irregularities by press fitting into a defect as a type of adhesive bond (termed “morphological fixation”) - Al$_2$O$_3$

Porous inert ceramics attach by bone resulting from ingrowth (into pores) resulting in mechanical attachment of bone to material (termed “biological fixation”) - Al$_2$O$_3$

Dense, nonporous surface-reactive ceramics attach directly by chemical bonding with bone (termed “bioactive fixation”) - bioactive glasses & Hydroxyapatite.
Processing of Ceramics

1. **Compounding**
   - Mix and homogenize ingredients into a water based suspension = slurry
     or, into a solid plastic material containing water called a clay

2. **Forming**
   - The clay or slurry is made into parts by pressing into mold (sintering). The fine particulates are often fine grained crystals.

3. **Drying**
   - The formed object is dried, usually at room temperature to the so-called "green" or leathery state.

4. **Firing**
   - Heat in furnace to drive off remaining water. Typically produces shrinkage, so producing parts that must have tight mechanical tolerance requires care.
   - Porous parts are formed by adding a second phase that decomposes at high temperatures forming the porous structure.
Alumina (Al$_2$O$_3$) and Zirconia (ZrO$_2$)

The two most commonly used structural bioceramics.

- Primarily used as modular heads on femoral stem hip components.
- Wear less than metal components, and the wear particles are generally better tolerated.
Femoral Component
Alumina (Al$_2$O$_3$):

- single crystal alumina referred to as “Sapphire”
- “Ruby” is alumina with about 1% of Al$^{3+}$ replaced by Cr$^{3+}$; yields red color
- “Blue sapphire” is alumina with impurities of Fe and Ti; various shades of blue
Structure and Properties:

- most widely used form is polycrystalline
- unique, complex crystal structure
- strength increases with decreasing grain size
- elastic modulus (E) = 360-380 GPa
Fabrication of Biomedical devices from Al$_2$O$_3$ & (ZrO$_2$):

- devices are produced by pressing and sintering fine powders at temperatures between 1600 to 1700ºC.
- Additives such as MgO added (<0.5%) to limit grain growth
Dental Porcelain:

- ternary Composition = Mixture of $\text{K}_2\text{O}-\text{Al}_2\text{O}_3-\text{SiO}_2$
  made by mixing *clays, feldspars, and quartz*
  
  **CLAY** = Hydrated alumino silicate
  
  **FELDSPAR** = Anhydrous alumino silicate
  
  **QUARTZ** = Anydrous Silicate
Calcium Phosphates

- Calcium phosphate compounds are abundant in nature and in living systems.
- Biologic apatites which constitute the principal inorganic phase in normal calcified tissues (e.g., enamel, dentin, bone) are carbonate hydroxyapatite, CHA.
- In some pathological calcifications (e.g., urinary stones, dental tartar or calculus, calcified soft tissues – heart, lung, joint cartilage)
Calcium hydroxyapatite
\((\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2)\): HA

- Hydroxyapatite is the primary structural component of bone. As its formula suggests, it consists of Ca\(^{2+}\) ions surrounded by PO\(_4^{2-}\) and OH\(^{-}\) ions.
Calcium hydroxyapatite
\( \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \): HA
Calcium hydroxyapatite (Ca$_{10}$(PO$_4$)$_6$(OH)$_2$): HA

- gained acceptance as bone substitute
- repair of bony defects, repair of periodontal defects, maintenance or augmentation of alveolar ridge, ear implant, eye implant, spine fusion, adjuvant to uncoated implants.
HA is:
\[ \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \]

- Since collagen is closely associated with HA in normal bone, it is a logical candidate for induction of a host response. In some cases bone growth in or near implanted HA is more rapid than what is found with control implants. In the literature HA is sometimes referred to as an "osteoinductive" material. However, HA does not seem to induce bone growth in the same way as, say, BMP.
Bioceramic Coatings

- Coatings of hydroxyapatite are often applied to metallic implants (most commonly titanium/titanium alloys and stainless steels) to alter the surface properties.
- In this manner the body sees hydroxyapatite-type material which it appears more willing to accept.
- Without the coating the body would see a foreign body and work in such a way as to isolate it from surrounding tissues.
- To date, the only commercially accepted method of applying hydroxyapatite coatings to metallic implants is plasma spraying.
Bone Fillers

- Hydroxyapatite may be employed in forms such as powders, porous blocks or beads to fill bone defects or voids.
- These may arise when large sections of bone have had to be removed (e.g. bone cancers) or when bone augmentations are required (e.g. maxillofacial reconstructions or dental applications).
- The bone filler will provide a scaffold and encourage the rapid filling of the void by naturally forming bone and provides an alternative to bone grafts.
- It will also become part of the bone structure and will reduce healing times compared to the situation, if no