Designing soft tissue replacements

Hydrogels as cartilage replacement devices

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**Soft-solids: Natures solution**

- Hydrogels are ubiquitous in the body
  - Mucus and tear films
  - Cartilage
  - Vitreous humor and cornea
  - Tendon
- Microstructure critical function
Gels: the fourth phase of matter

- **Solid**
  - Permanent shape, fixed volume
  - Elastic recovery
- **Liquid**
  - Fixed volume, “conformable” shape
  - No recovery (viscous)
- **Gas**
  - Volume expands to fill container
- **Gel**
  - Properties between solids and liquids
  - Fixed volume and shape (like solids) while static
    - Often turn liquid when agitated
  - Partially elastic, partially viscous (viscoelastic)
**Gel microstructure**

- **Gels and hydrogels**
  - Gel – *gelatus*: frozen, immobile

- **Gels structure continuous solid supporting a discontinuous solvent**
  - Solid is usually a crosslinked or associated network of molecules
  - Liquid is anything compatible with the network

- **Chemistry of network is critical**
  - Solubility of the network “draws in” solvent to “fill” the network
  - Must be balanced by a “restraining” force generated within the network
    - Network can’t expand beyond the length of the chain
Characteristics of hydrogels

- High water content
  - Free water allows diffusion of solutes
  - Viscous damping of mechanical deformation
  - Density “matched” to water
  - Very low solids content
- Network structure
  - Can be static or dynamic
    - Permanent crosslinks (contact lenses)
    - Thermally sensitive (jello)
    - “labile” (hair-gel)
  - Contains and confines water in 3d shape
  - Provides elastic recovery
  - Provides support for attaching active ingredients
Biomedical hydrogels

• Hydrophilic polymers form network
  – Polymeric backbone grown from
    • monomers, oligomers or fully formed polymers
  – Crosslinking
    • During polymerization, post-polymerization
    • Through functional groups, or addition of crosslinker
    • Chemical or physical

• Vast range of performance specifications possible
  • Environmental response (monomeric units)
  • Swellability (crosslink density and monomers)
  • Permeability (pore-size through crosslink density)
  • Viscoelastic response (monomeric units and pore size)
  • Biological interaction (chemistry of monomeric units)
  • Degradability (presence of specific monomeric units)
  • Gelation time (crosslinking mechanism)
  • Injectability (size of initial monomers/oligomers)
Current uses of hydrogels in medicine

- Predominantly as a carrier or protector
  - Drug release
    - e.g. drug eluting stents
  - “smart” gels
    - e.g. enteric coatings (lower stomach targeted delivery)
  - Tissue guides
    - Nerve regeneration guides
  - Vision
    - Contact and intraocular lenses
  - Tissue bulking
    - Soft solid supports tissue
    - Provides fluid motion
    - Flexible and conformable
  - Cartilage replacement
    - Lubricious and water filled*
    - But….
Example: The knee

• Structure of joint drives function
  – “Spherical” femur
  – “Flat” Tibia
  – Mutual translation and rotation
  – Meniscus spreads the load

• Cartilage
  – Biphasic
  – Transitional
  – Lubricious

• Meniscus
  – Reinforced
  – Oriented
  – Lubricious
Disease prevalence

- Symptomatic OA (>45 yrs)
  - Knee 6.7-16.7 per 100,000
  - 253,000 total knees per year
- Cartilage scarring
  - Due to traumatic injury
- Meniscal tears
  - 61 cases per 100,000
  - 850,000 surgeries per year
  - Tears associated with subsequent arthritis
- In 25,000 arthroscopies 60% of patients exhibited cartilage lesions

Date from: The burden of musculoskeletal disease in the US
And: Baker et al. 2011
Cartilage and meniscal repair

• Cartilage
  – Debridement
    • Removal of damaged tissue
  – Microfracture surgery
    • Deliberate generation of fibrocartilage
  – Osteochondral plugs
    • Repair lesion through “patch”
      – Autograft, allograft or synthetic

• Meniscus
  – Debridement
  – Suturing
  – Partial/total menisectomy with/without support
  – Allograft or scaffold
  – Primarily anchored to tibial plateau
**Cartilage properties**

- Cartilage composed of collagen
  - Hyaline cartilage
    - Articular (lubricious)
  - Elastic cartilage
    - Contains elastic fibers (Epiglottis)
  - Fibrocartilage
    - Rough and fibrous (meniscus)

<table>
<thead>
<tr>
<th></th>
<th>Cartilage</th>
<th>Meniscus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water content [%]</td>
<td>68-85</td>
<td>60-70</td>
</tr>
<tr>
<td>Collagen [%]</td>
<td>10-20</td>
<td>15-25</td>
</tr>
<tr>
<td>Proteoglycan [%]</td>
<td>5-10</td>
<td>1-2</td>
</tr>
<tr>
<td>Young’s modulus [MPa]</td>
<td>5-10</td>
<td></td>
</tr>
<tr>
<td>Tensile modulus [MPa]</td>
<td>~10</td>
<td>100-200</td>
</tr>
<tr>
<td>UTS [MPa]</td>
<td>2/5</td>
<td></td>
</tr>
<tr>
<td>Aggregate modulus [MPa]</td>
<td>~0.7</td>
<td>~0.4</td>
</tr>
<tr>
<td>Permeability x 10^{15} [m^4/N.s]</td>
<td>~4</td>
<td>~1</td>
</tr>
<tr>
<td>Friction Coeff [ ]</td>
<td>0.1</td>
<td>0.08</td>
</tr>
<tr>
<td>Thickness [mm]</td>
<td>0.5-5</td>
<td>0-10</td>
</tr>
</tbody>
</table>
The importance of the meniscus

- Meniscus protects cartilage
  - Distributes and cushions loads
- Cartilage does not bear full load
  - Tension in meniscus
- Cartilage fails through
  - Trauma, arthritis, overuse
- Meniscus fails through
  - Trauma, age

Why is this important?

• Joint replacement materials with physiological properties
  – Less invasive
    • thinner, conformable
  – Preserve biomechanics
    • similar anchoring, protects existing cartilage
• But biomechanical mimic requires similar properties
  – Cartilage friendly
    • Hydrophilic, lubricious and viscoelastic
  – Anisotropic
    • Meniscus tensile properties different from compressive
  – Compound structure
    • Meniscus and cartilage work together
• Design, and testing must take this into account
**Compression testing**

- Conventional approach
  - Compressive Modulus (e.g. ASTM D1621)
- Porous viscoelastic solid
  - Rate, total strain and fluid component matters
- Compression using different rates
- Creep and recovery
- Aggregate Modulus

\[ E = \frac{\text{stress}}{\text{strain}} = \frac{\sigma}{\varepsilon} = \frac{F}{A_1} = \frac{F L_0}{A_1 L} \]
Example data (PVA hydrogels)

- 15-28 control
- 15-28 2L coarse nylon
- 15-28 5L coarse nylon
- 15-28 10L coarse nylon
- 15-28 14L coarse nylon

1 hr. load, 0.5 MPa
0.5 hr. load, 0.05 MPa

14 layers of unspaced coarse nylon mesh

Elastomer
**Tensile testing**

- Conventional approach
  - Compressive Modulus (e.g. ASTM D1621)
- Porous viscoelastic solid
  - Gripping soft solids virtually impossible
    - Make materials with grips attached
  - Materials anisotropic
    - Must test $\parallel$ and $\perp$
Example data (PVA hydrogels)

Stress vs. Strain

- 15-28 AG 1
- 15-28 AG 2
- 15-28 AG 3
- 15-28 DP 1
- 15-28 DP 2
- 15-28 DP 3
- 25-28 AG 1
- 25-28 AG 2
- 25-28 AG 3
- 25-28 DP 1
- 25-28 DP 2
- 25-28 DP 3

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**Coefficient of Friction**

- Various ASTM standards
- More important for partial joint replacements
- Measures sliding friction as a function of normal force
- Sensitive to media and counterface

![Graph showing Coefficient of Friction](image)

**Legend:**
- ▲ LB on CoCr in DI
- ● LB on CoCr in BS
- ▲ non-LB on CoCr in DI
- ○ non-LB on CoCr in BS

LB=“load-bearing”
Example data (PVA hydrogels)
Design strategies

- Total replacement of the articular cartilage (TKR)
  - Invasive, relieves demands on materials, engineering problem
  - Removes meniscus
- Partial replacement/repair (osteochondral plug)
  - Stress-shielding an issue
  - Fixation and wear a concern
- Meniscus replacement
  - Concerns with “intersection” line and modulus matching
  - Does not directly protect cartilage surface
- Meniscus replacement with bearing zone
  - More forgiving design criteria
  - Requirements
    - Anistropy
    - Lubricious
    - Hard wearing
    - Modulus close to meniscus
    - Biocompatible
    - Hydrated
Possible design structure

- What would this look like?

- Femoral head cartilage
- Tibial plateau
- Anchor point
- Fiber mats or hoops
- Contact zone

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Soft-solids require novel designs and testing

• Designs that utilize hydrogels are closest to the natural solution
  – Like the natural tissue, can only work in composite design
    • Nucleus replacement, relies on annulus
      – Too hard, results in end-plate failure
      – Too soft, device failure (extrusion)
    • Cartilage repair, needs reliable fixation method
      – Hydrogels rarely have good tensile properties
      – Discontinuities in designs poorly tolerated
      – Wear is difficult to predict

• Tests have to take in to account the use of the material
  – “simple” engineering tests no longer relevant
    • stress-strain, fatigue crack, tensile etc
  – Design new tests that mimic conditions likely to be encountered
Thank you

Cambridge Polymer Group is a contract research laboratory specializing in polymers and their applications. We provide outsourced research and development, consultation and failure analysis as well as routine analytical testing and custom test and instrumentation design.

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