

Imaging for Design and Evaluation of Tissue Engineered Constructs

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Overview

- Scaffold based Tissue Engineering: Paradigm & Procedure
- Scaffold Design & Fabrication: The need for Structural/Functional Imaging
- Scaffold/Tissue Constructs: The need for Structural/Functional Imaging of Composite Materials
- Ultrasound Elasticity Imaging (UEI): A modality for *in vitro* and *in vivo* Scaffold/Tissue Construct Functional Imaging

Scaffold based Tissue Engineering: Paradigm & Procedure

Tissue Engineering Paradigm

<http://www.cs.cmu.edu/People/tissue/tutorial.html>

- Regenerate tissues using Scaffolds that provide temporary Function while delivering biologics
- Scaffolds degrade over time as tissue grows and assumes function

Time Dependent Scaffold/Tissue Constructs

- Scaffold will lose molecular weight and mechanical properties over time
- Tissue will grow and increase mechanical function over time

Hutmacher, J. Biomaterial Science Polymer Edn., 2001

Scaffold Tissue Engineering Procedures

Scaffold/Tissue Design Input:

1. 3D Tissue Structure
2. Tissue Mechanics
3. Tissue Mass Transport

Scaffold Design/Fabrication:

1. Image-based Design
2. Design Architecture for Mechanics/Mass Transport
3. Scaffold Fabrication by SFF
4. Evaluate Scaffold Structure/Mechanics

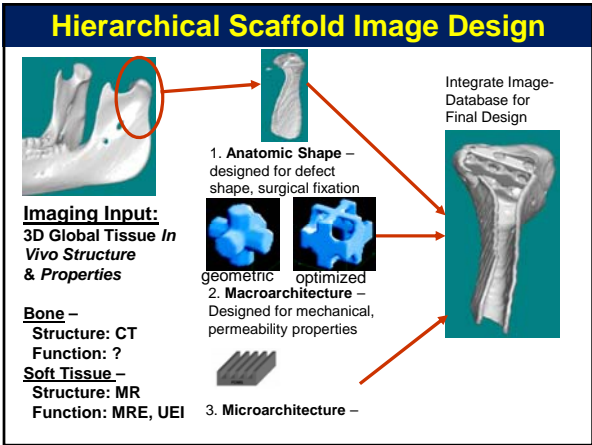
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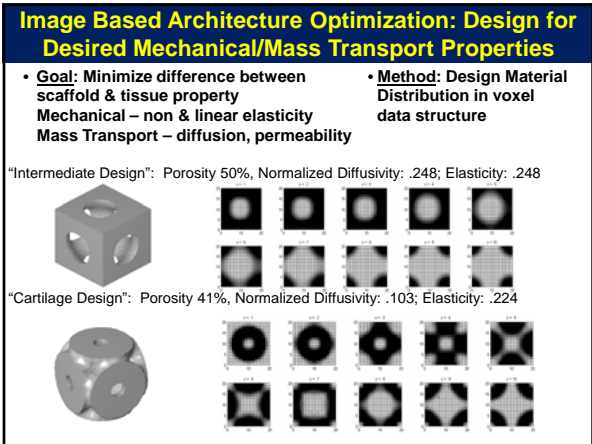
Biologics:
Cells, Proteins, Genes

Scaffold/Tissue Construct Evaluation:

1. Time dependent tissue growth
3D tissue structure
3D tissue mechanical properties
2. Time dependent scaffold degradation
3D scaffold structure
3D scaffold mechanical properties

Scaffold Design & Fabrication: The need for Structural & Functional Imaging





Fabricating Complex Scaffolds

- Complex designed architectures must be built using direct or indirect solid free-form fabrication (SFF)
- Build on layer by layer basis with 250-500 μ m resolution

Direct SFF (Smith et al., 2007, Int J. Med. Robotics & Comp. Assisted Surg)

Indirect SFF (Taboas et al., 2003)

Evaluating Fabricated Scaffolds

- **Ultimate goal:** determine how scaffold design affects *in vivo* function/tissue regeneration; FDA Quality – must know fidelity of scaffold to design
- **Imaging Need 1:** Evaluate how closely scaffold pore structure matches design – currently μ CT
- **Imaging Need 2:** Evaluate how closely scaffold function matches designed function – currently mechanical testing, future: ultrasound/MR elasticity imaging, other functional imaging

Slice from Image Design File
Registered Volume data to quantify design vs. fab
 μ CT Slice fabricated Cage

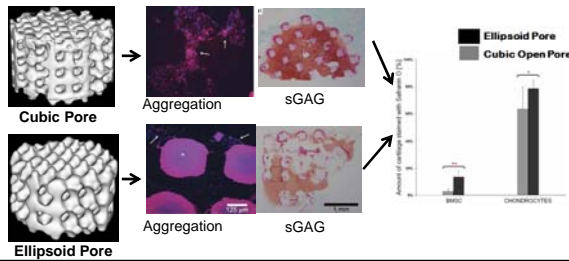
Scaffold/Tissue Constructs: The need for Structural/Functional Imaging of Composite Materials

Evaluating Scaffold/Tissue Constructs

- **Ultimate goal:** Need to evaluate time dependent evolution of cell/tissue and scaffold structural & functional properties to assess efficacy of tissue engineering therapy
- **Imaging Need 1:** Evaluate time dependent tissue morphology and function (mechanical & mass transport) *in vivo* and *in vitro*
- **Imaging Need 2:** Evaluate degradation in scaffold structure and function *in vivo* and *in vitro*
- Need to evaluate 3D non-destructively *in vivo* (ideal for both animal studies and human clinical trials) but *in vitro* (specimen retrieved from animal) would be significant advance
- Complete 3D quantitative structural imaging (μ CT) widely done only for bone

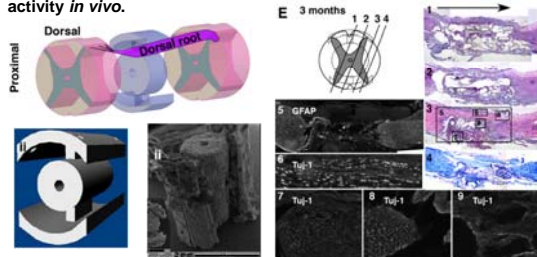
Scaffold Architecture & Cartilage Growth

- **Goal:** determine how scaffold pore design (ellipsoid vs. cubic) affects *in vivo* function and cartilage regeneration
- **Current Evaluation:** Histological/Immunohistochemical for GAG, type II collagen; mechanical confined compression test
- **Imaging Need:** Non-destructively quantify 3D GAG distribution, collagen I vs. collagen II content; UEI, MR Elastography of poroelastic properties

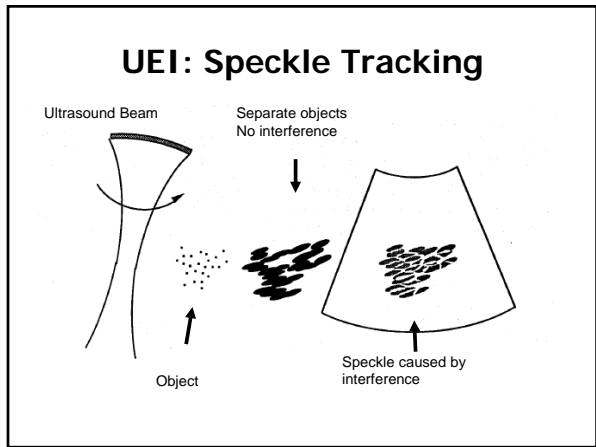


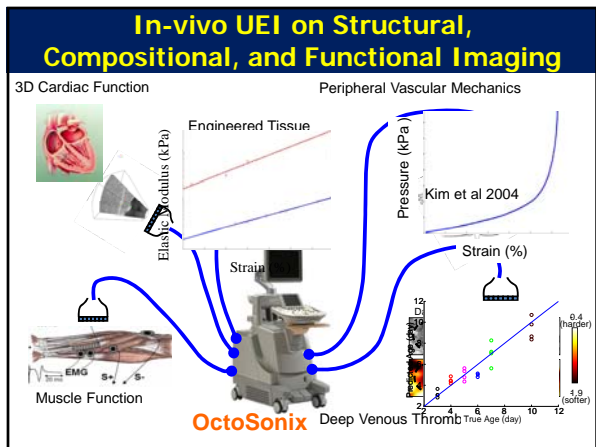
Scaffold Architecture & Spinal Cord Regeneration

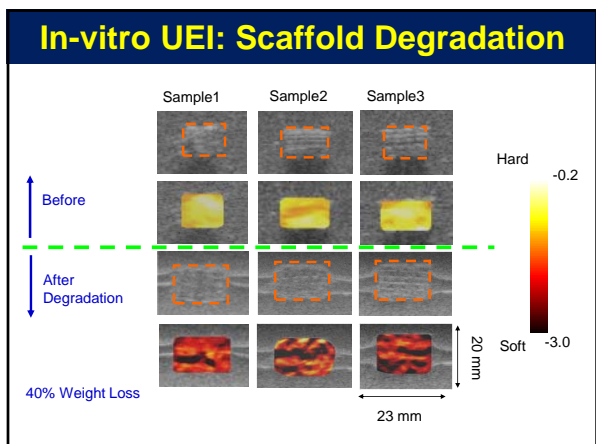
- **Goal:** determine how scaffold design affects neural tissue growth in rat spinal cord transection model
- **Current Evaluation:** Histological/Immunohistochemical staining for Tuj-1, Nestin, β -tubulin, Glial Fibrillary Acidic Protein (GFAP)
- **Imaging Need:** Non-destructively track axon growth and electrical activity *in vivo*.

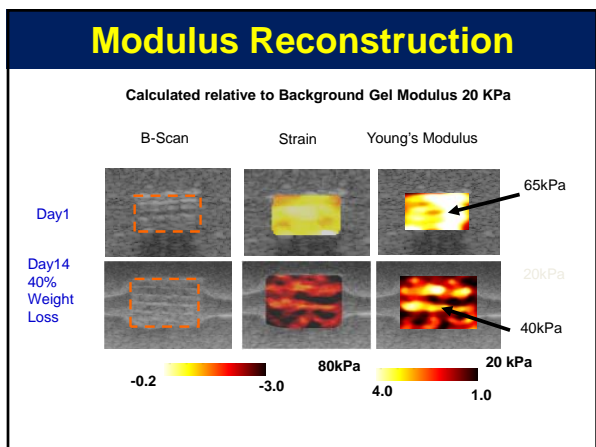


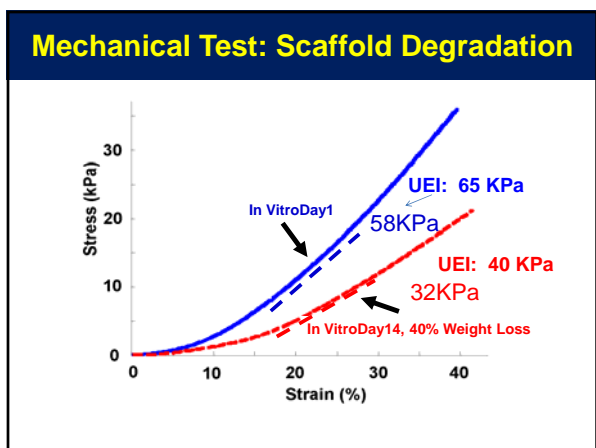
**Ultrasound Elasticity Imaging (UEI):
A modality for *In Vivo/In Vitro*
Scaffold/Tissue Construct
Structural/Functional Imaging**

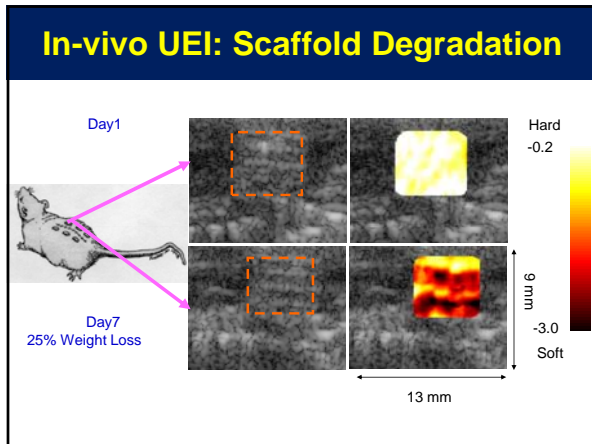


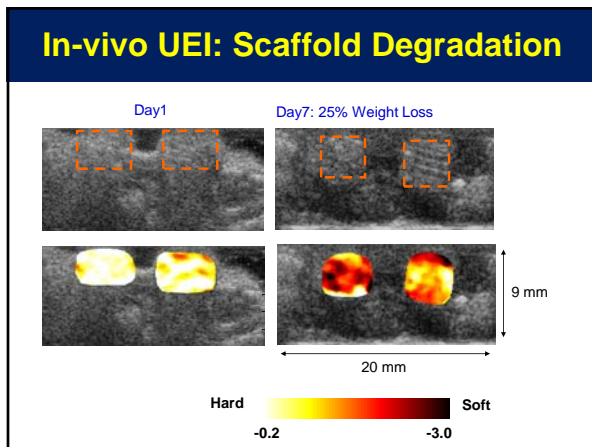


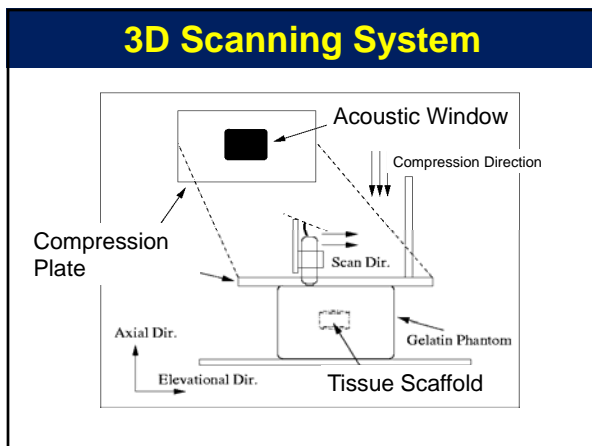




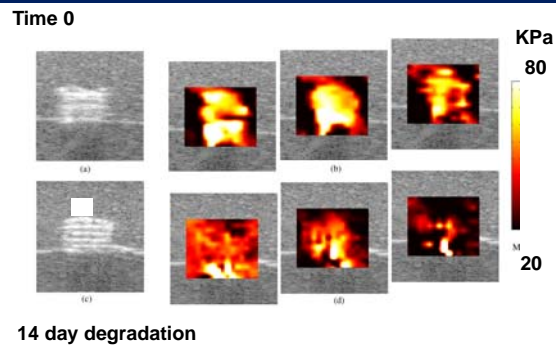








3D Elastic Modulus Reconstruction



Conclusion/Questions?

- What technologies would help you understand critical aspects of tissue architecture and microenvironments?
 - 3D structural and functional soft tissue imaging
 - Composite 3D imaging of scaffold degradation and tissue structure/function *in vivo*, including nonlinear elastic and viscoelastic mechanical properties
 - Something akin to the information μ CT gives for bone but for soft tissue
- Is spatial resolution an issue? The higher the resolution the better, but resolution on the order of 100-300 microns is a good start
- What would you need to extend design concepts to soft tissues? (see first answer)
