Applications of Contrast-enhanced MicroCT Imaging in MSK Tissues

Simon Tang, Ph.D.
Assistant Professor
Orthopaedic Surgery

Associate Director, Structure and Strength Core

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Adipocyte imaging

Intervertebral Disc Imaging

- Commonly done by Magnetic Resonance Imaging
- Resolution on the order of hundreds of microns to mm
- Structural and biochemical characteristics
- Discerns between degenerate and healthy discs

MicroCT imaging of soft tissues

- Single to tens of micron resolution
- Highly attenuating tissues (i.e., mineralized)
- Can be combined with contrast agents improved attenuation and specificity

- Can we do this for the rodent intervertebral disc?

loversol: a hydrophilic nonionic contrast agent

- Low cytotoxicity
- Low nephrotoxicity
- Approved for human use

Objective: Validate loversol for contrast-enhanced microCT imaging of the rodent IVD *ex vivo, in vitro, and in vivo*; and develop quantitative metrics for characterizing the rodent IVD
Experimental Design

Rat IVDs (ex vivo)

Control - CON
Trypsin-injected - TRYP
Vehicle - VEH
Stab
Collagenase

Day 0
n = 3 SCAN
Histo/Biochem

Day 2
n = 3 SCAN
Histo/Biochem

Day 5
n = 3 SCAN
Histo/Biochem

Day 7
n = 3 SCAN
Histo/Biochem

Mouse IVDs (Organ culture)

Alamarblue and uCT

Alamarblue, uCT, and sent to Histo
Longitudinal Monitoring of Rat IVD degeneration

Day 0  Day 2  Day 5  Day 7

Sham

PBS

Trypsin

Collagenase

2.5mm
4.7T MRI Assessment of Degeneration Models
(Sagittal views)

- 2 Day
- 5 Day
- 7 Day

- Nothing
- Stab
- Trypsin
- Collagenase

3 mm

100 µm Isotropic resolution
T2 Maps of Rat IVD

4.7 T Magnet, Custom coil

13 minute scan (for map), 75 x 75 x 500 µm Resolution
Map from Multi-Echo Spin Echo Sequence  (Jim Quirk, Ph.D.)
Structural changes can be quantified

Changes in Disc Height Measured by Contrast-enhanced microCT

(a = p < 0.001 day 7 compared with the day 0; b p < 0.001 = day 5 compared with day 0)
NV/DV to Quantify IVD Structural Changes

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\frac{NV}{DV} = \frac{\text{Voxels}_{\text{NP}}}{\text{Voxels}_{\text{disc}}}
\]
NI/DI nondestructively quantitates sGAG
NI/DI to Quantify Biochemical Changes

\[
\frac{NI}{DI} = \frac{\text{Average Intensity}_{NP}}{\text{Average Intensity}_{disc}}
\]
In vitro longitudinal Monitoring of Rat IVD degeneration in organ culture
In vitro longitudinal Monitoring of Rat IVD degeneration in organ culture
Discussion

• Ioversol discriminates the compartments of the IVD
• Nuanced changes quantitatively captured by contrast-enhanced CT
• Structural and biochemical changes with excellent correspondence to histology and DMMB assays
• No adverse biological effects observed
• Potential to leverage the power of rodent and transgenic models for understanding disc degeneration
Future Work

- Apply *in vivo*
- Apply in genetically modified animals
- Automated segmentation
Contrast-enhanced Cartilage Imaging: in development
How to get started?

• What is the tissue of interest?
• What are the defining features?
• How does it change with maturation, aging, disease, or treatment?
• How to leverage the composition-structure-function?
• Encourage investigator-driven projects to develop new approaches and applications.

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Questions