Choosing the best animal model – preclinical cartilage and meniscal studies.

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Disclosures: Kensey Nash Board of Scientific Advisors, Arthrex consultant

Choosing an Animal Model - Cartilage

- Drug, neutaceutical
  - Rat, mouse, rabbit, dog
- Device or product to repair/replace cartilage

Foundation

- Products intended to repair or replace knee cartilage
- Pre-clinical animal models
  - excluding non-human primates
  - excluding models for OA

FDA Guidelines

- Goats, sheep, horses are most frequently used
- Choose after consideration of clinical use
  - Dimensions of product
  - Delivery of product
  - Number of outcome measures desired
    - balance of n and $

Challenges and goals

- All animal models are challenging and expensive
- Ideal animal model should include:
  - Represent intended human clinical use
  - Low cost
  - Assessable outcome measures
    - Known clinical entity, antibodies, probes

Courtesy, MD Markel. From Lu et al, 2005

Anatomic comparisons

Cartilage and subchondral bone – between species comparison

Bone attributes – similarities between animals and humans

Location within location
Biphasic scaffold

- Kensey Nash - Bioresorbable biphasic scaffold
  - β-TCP/PLA - collagen
  - Soak in bone marrow aspirate
  - Advantages: off the shelf, bone + cartilage
  - Disadvantages: increase defect size, few cells

Conclusions

- Small animal species typically perform better than large animal species
- Full thickness defects perform better than partial thickness defects
- Partial thickness defects may be a better model for OA than full thickness defects

Meniscus - sheep as a model

- Anatomic size, cellularity, vascularity, collagen structure
  - sheep, rabbit, human
  - Chevrier JOR 2009
- Compressive biomechanical properties
  - human, bovine, monkey, canine, sheep, and porcine
- Goat?

Considerations for approach

- Medial vs. lateral
- What are you trying to model?
Lateral meniscal approach

- takedown and repair of the LCL

Kelly et al, AJSM, 2006
Kelly et al, AJSM 2007
Rodeo, HSS

Excise and Replace the lateral meniscus

Rodeo, HSS

Going medial - what NOT to do

- Bone block approach if you need to suture meniscus
- Transect MFPL
- Bilateral
- ? Epidural

Going medial - what NOT to do

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1. Medial skin incision
2. Lateral parapatellar arthrotomy, patella luxated medially

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Practice, practice, practice

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Many Species. One Medicine.™
Thoughts for all animal models

• Age of skeletal maturity is critical
  – >2 years of age is general guideline
• Dimensions of critical size defect must be known
• Choice of full or partial thickness defects
• Importance of validating that subchondral has not been penetrated
  – very difficult for smaller animals
• Difficult to ensure removal of calcified cartilage

Equine cartilage structure with age

7 months  18 months  24 months

IGF-I


Relative disadvantages

• Goats
  • Caseous Lymphadenitis – Coryne pseudotB
  • Behavior
  • Low cartilage thickness

• Sheep
  • Scrapie (TSE)
  • Shoulder ramming
  • Lowest cartilage thickness

• Horses
  • Cost
  • Immediate loading (MFC)
  • Emotive