Veterinary Clinical Trials as Stepping Stone to Human Trials
Tokihiro Yamamoto, Ph.D.

Learning Objectives
- To understand how the canine can be used as a model for medical physics research.
- To understand advantages and challenges associated with canine clinical trials.
- To learn about practical considerations for canine trials.

Outline
- Rationale for imaging research with dogs
- Examples of canine imaging trials
  - Multiple CT scans to investigate single-energy CT pulmonary functional imaging
  - Repeat PET and CT scans to evaluate tumor hypoxia
- Advantages and challenges
- Summary

Rationale for Imaging Research with Dogs
- Anatomical and physiological similarities between dogs and humans
- Common features between naturally occurring cancers in pet dogs and in humans
  - e.g., histological appearance, tumor genetics, and treatment response

Vet Care to Pet Animals
Paoloni and Khanna (Nat Rev Cancer 2008)
Imaging Studies with Dogs

- Studies of tissue pharmacokinetics and pharmacodynamics
  
  Nguyen et al. (Proc Natl Acad Sci USA 2009)

- Assessment of tumor response to therapy
  
  Bradshaw et al. (IJROBP 2015)

- Studies of pulmonary physiology
  
  Hoffman et al. (J Appl Physiol 1985); Marcucci et al. (J Appl Physiol 2001)

Outline

- Rationale for imaging research with dogs

- Examples of canine imaging trials
  
  - Multiple CT scans to investigate single-energy CT pulmonary functional imaging
  - Repeat PET and CT scans to evaluate tumor hypoxia

- Advantages and challenges

- Summary

Multiple CT and PET Scans with Different Radiotracers

- Single-energy CT Pulmonary Functional Imaging

  - Study-related interventions
    
    - 4 breath-hold CT scans
    - Anesthesia
    - IV line for contrast agent injection

  - 17 dogs with normal or diseased lungs studied

  - Owner informed consent obtained

  - Protocol approved by the institutional clinical trials review board and the institutional animal care and use committee (IACUC)
CT for Anesthetized/Intubated Dog with Peripheral IV Line

Outline
- Rationale for imaging research with dogs
- Examples of canine imaging trials
  - Multiple CT scans to investigate single-energy CT pulmonary functional imaging
  - Repeat PET and CT scans to evaluate tumor hypoxia
- Advantages and challenges
- Summary

Advantages
- Flexibility in study designs and study-related interventions
  - e.g., serial imaging for longitudinal studies
- Similar genetic diversity to human can be obtained by including dogs of different breeds
  - Lindblad-Toh et al. (Nature 2005)

Challenges
- Animal welfare issues
  - Imaging is not completely non-invasive
  - Possible pharmacological effects of contrast agents
- Costs
  - Pet owners are not responsible for study-related costs
- Cancer prevalence
  - Common: sarcomas and lymphomas
  - Less common: breast, lung, GI and prostate tumors – common cancers in humans

Outline
- Rationale for imaging research with dogs
- Examples of canine imaging trials
  - Multiple CT scans to investigate single-energy CT pulmonary functional imaging
  - Repeat PET and CT scans to evaluate tumor hypoxia
- Advantages and challenges
- Summary

Summary
- The canine model has features similar to humans, and can effectively and uniquely contribute to medical physics research.
- One major advantage is the flexibility in study designs and study-related interventions.
- Risks associated with interventions should still be evaluated to protect the welfare of dogs.
Acknowledgments
John Boone, Ph.D.
Simon Cherry, Ph.D.
Yukio Fujita, Ph.D.
Michael Kent, DVM
Guobao Wang, Ph.D.
Erik Wisner, DVM
Allison Zwingenberger, DVM
UCD Interdepartmental Collaborative Research Grant