


# Veterinary Clinical Trials as Stepping Stone to Human Trials

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COMPREHENSIVE  
CANCER CENTER  
Radiation Oncology

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## 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



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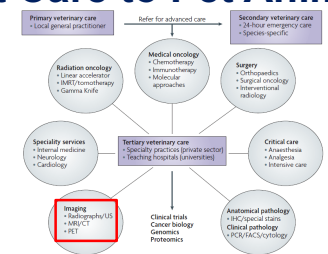
## Rationale for Imaging Research with Dogs

- 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


Paoloni and Khanna (*Nat Rev Cancer* 2008)



## Vet Care to Pet Animals



Paoloni and Khanna (*Nat Rev Cancer* 2008)



### Vet Imaging Resources at UCD

Digital fluoro   Scintigraphy   Ultrasound   PACS

Multislice CT   PET   1.5 T MRI

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### 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. (JROBP 2015)
- Studies of pulmonary physiology  
Hoffman et al. (J Appl Physiol 1985);  
Marcucci et al. (J Appl Physiol 2001)

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### Multiple CT and PET Scans with Different Radiotracers

Pretreatment   Hypofractionated IMRT   Posttreatment

Day -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

Fraction 1 2 3 4

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Bradshaw et al. (JROBP 2015)

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### Single-energy CT Pulmonary Functional Imaging

IV contrast

Time

End-expiratory breath-hold CT   Mid-expiratory breath-hold CT   End-inspiratory breath-hold CT (pre-contrast)   End-inspiratory breath-hold CT (post-contrast)

Ventilation   Perfusion

Yamamoto et al. (Med Phys 2016)  
 Fujita et al. (Wed 4:30-6pm, Rm 201)

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### Canine Trial to Investigate 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)

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## CT for Anesthetized/Intubated Dog with Peripheral IV Line

The left photograph shows a dog lying on a CT table, with a red box labeled 'Intubator' pointing to the dog's mouth and another red box labeled 'IV line' pointing to a tube on the dog's side. The right photograph shows the dog in the CT scanner with a blue ventilator connected to its airway.

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## 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)

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## 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

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## 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.

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