Using Veterinary Radiation Oncology as Implementation Pathway for New Clinical Technology

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Conflict of Interest

- PI on a UC Davis – SunNuclear agreement for beta testing. This includes their EPID dosimetry software, PerFraction.
- Scientific advisor, MGS research.
- Consultant, NeuroLogica Corporation

Best Friends at Home and Work

Companion animals: Translational scientist's new best friends

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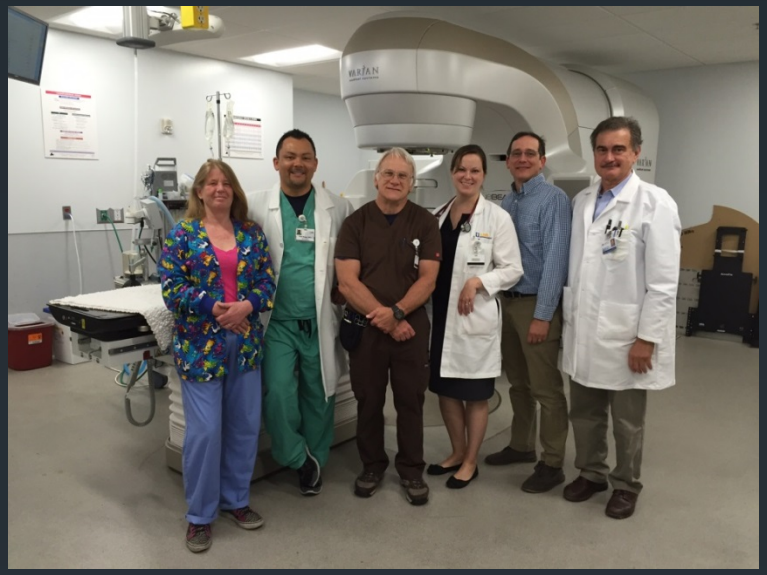
Knowledge and resources derived from veterinary medicine represent an underused resource that could serve as a bridge between data obtained from diseases models in laboratory animals and human clinical trials. Naturally occurring disease in companion animals that display the defining attributes of similar, if not identical, diseases in humans hold promise for providing predictive proof of concept in the evaluation of new therapeutics and devices. Here we outline comparative aspects of naturally occurring diseases in companion animals and discuss their current uses in translational medicine, benefits, and shortcomings. Last, we envision how these natural models of disease might ultimately decrease the failure rate in human clinical trials and accelerate the delivery of effective treatments to the human clinical market.

- Not just for disease models – clinical physics too!

UCD People & Equipment

- People:
  - 3 attending faculty (Tx volume)
  - 1 resident (with physics research project)
  - 3 vet techs
  - Summer research students
- Equipment
  - TrueBeam & Eclipse
  - Phantoms (MapCheck, Red Dog)
  - CT and MR
  - Coming soon – full body PET (mini-EXPLORER)



Reversing directions

FIG. 1. Dog placed in ventral recumbency in a commercially available frameless stereotactic mask system (Brainlab Inc.) with the target positioning device (A) in place. This is composed of a triple layer orthoplast mask (B), attached to the sled (C). This system was modified by replacing the head rest with a MoldCare pillow (Bionix, Inc.) (D) and use of a vacuum-locked deformable bag (E) to hold the body.

1. Studied accuracy and reproducibility of human equipment use in Vet Rad Onc (Hansen et al. 2015) Dieterich et al. 2015)
2. Realized the other way is also valuable!
3. Studied implementation of EPID dosimetry in Vet Clinic first before moving to human clinic (Hsieh et al. 2016)

Benefits

- Clinical workflow exactly like human clinic
- Patient size equivalent to a pediatric population
- IACUC (Institutional Animal Care and Use Committee) serves similar function as IRB
- Less stringent patient privacy issues
  - Bringing in service engineers etc.
- FDA clearance
  - Equipment/drugs generally don’t have specific clearance for animal use
  - Lower barrier for experimental treatments once it clears IACUC

Example 1: Implementing In-Vivo EPID QA

- Issues at UCDMC (the human clinic)
  - Implementing new technology adds workload for RTTs, dosimetrists
  - I can get most things to work on one phantom (Rando)
  - …
- Solution at Vet School:
  - Shorter treatment day: more opportunity to get on machine
  - Availability of cadaver heads for more realistic study
    (Thanks to owners who donate their deceased companion animals for clinical research)

Example 1: Clinical Implementation

- Which QA protocols to use:
  - Gamma?
  - Percent difference?
  - DTA?
  - Same as for DQA measurements?
  - Would these also work for treatment?
- The question of false positives:
  - Root cause analysis for failed QA takes time
  - Learning what cause results in which EPID QA “symptoms”
- What clinical situations should we look for?
  - Exploratory research

Example 1: Figuring out the Basics

Can a commercially available EPID dosimetry system detect small daily patient setup errors for cranial IMRT/SRS?

Emmelyn S. Hsieh [a], Katherine S. Hansen [b], Michael S. Kent [b], Sanjeev Saini [c], Sonja Dieterich [d,*]

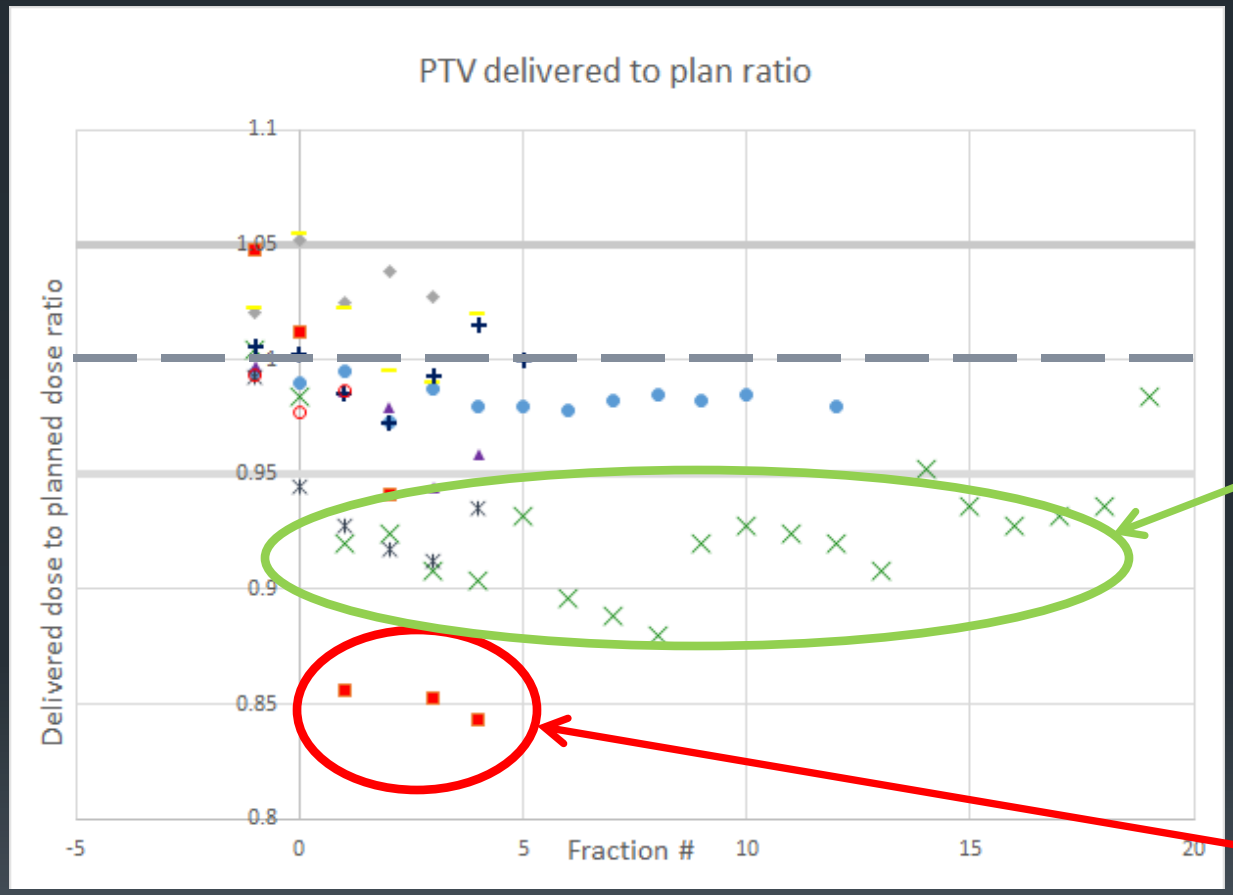
- Red Dog phantom and 5 cadaver heads
- Gamma was not useful
  - 5 mm shifts undetected
- % Difference was much more sensitive parameter

Table 3 Matrix listing recommended clinical parameter settings for detecting shifts using the 2D EPID dosimetry function in PerFRACTION

Desired shift detection level	1 mm	3 mm	5 mm	5° yaw
3% difference	Not advised	97%	96%	73%
1% difference	89%	63%	62%	37%

2D, 2-dimensional; EPID, electronic portal imager device.
Columns indicate the desired shift detection level; the rows list the % difference setting in PerFRACTION. Each cell indicates which pass rate tolerance setting would be required to flag at least 1 field for each of the 5 cadaver heads and the solid water phantom as failing.

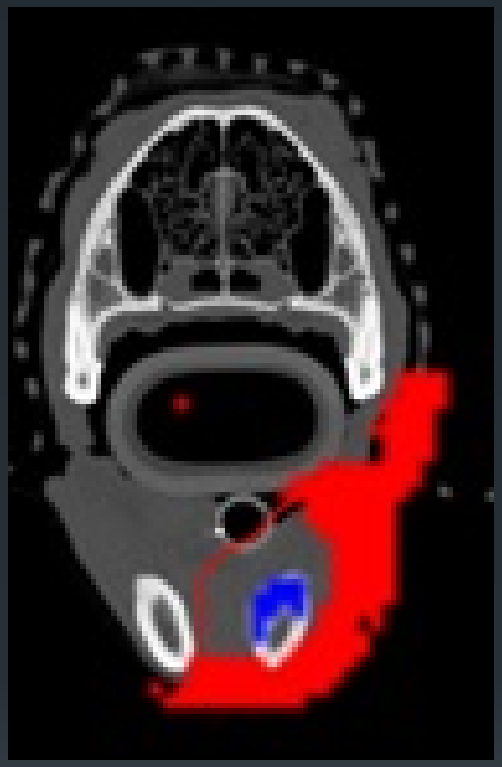
Example 1: Root Cause Analysis



- Looks ok
- What is going on here?
- Definitely not ok

Example 1: Definitely Not OK

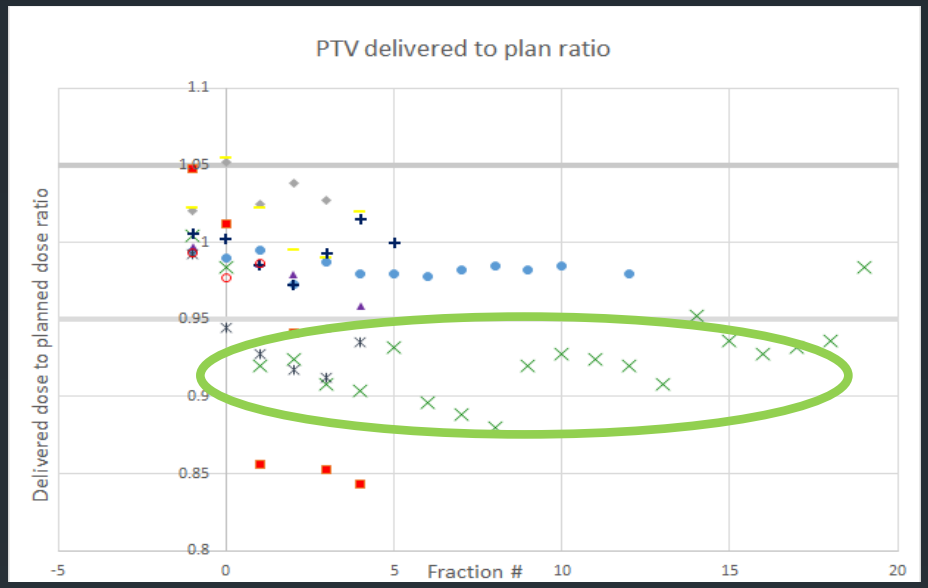
Eclipse

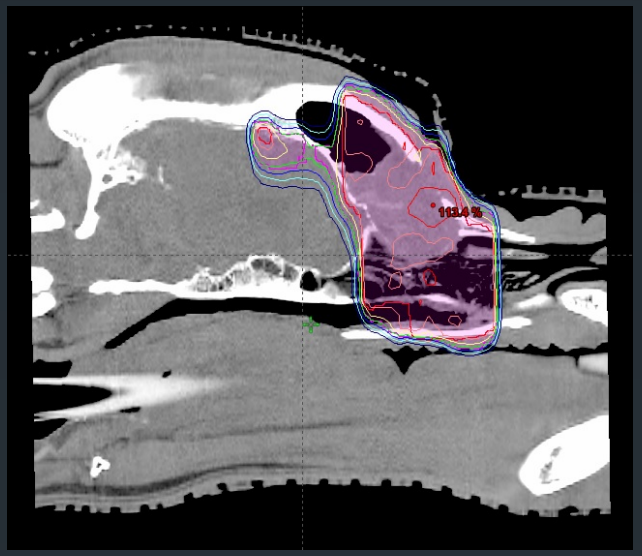


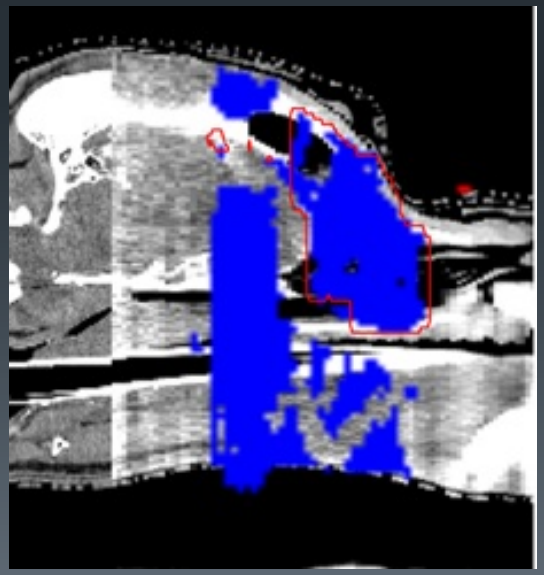
DoseCheck

Root Cause: User error.
Settings in DoseCheck were causing bolus to be handled incorrectly!

Example 1: What is Going On Here?



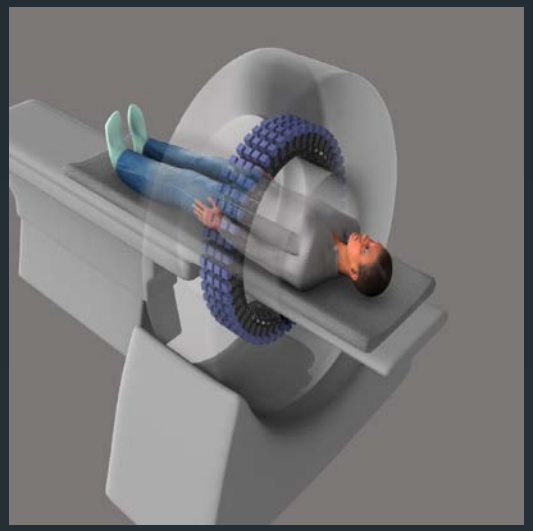




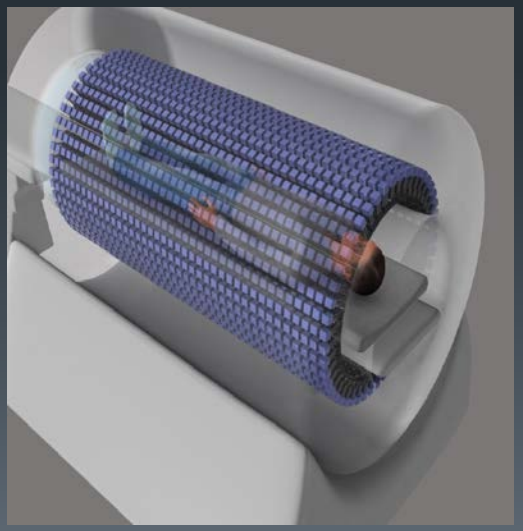
Root Cause: Residual Setup Error!

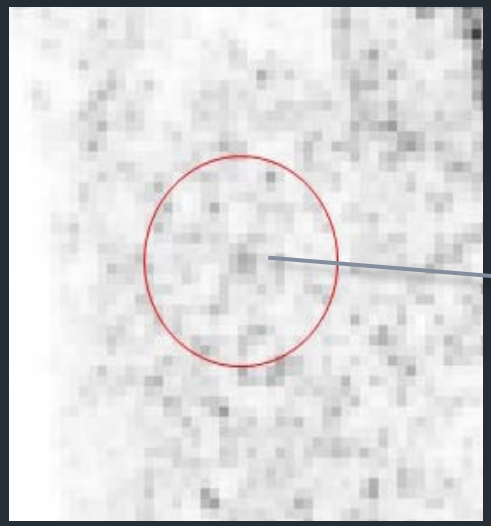
- CBCT alignment systematically shifted in high gradient region
- Solution: focus alignment on region
- Learning

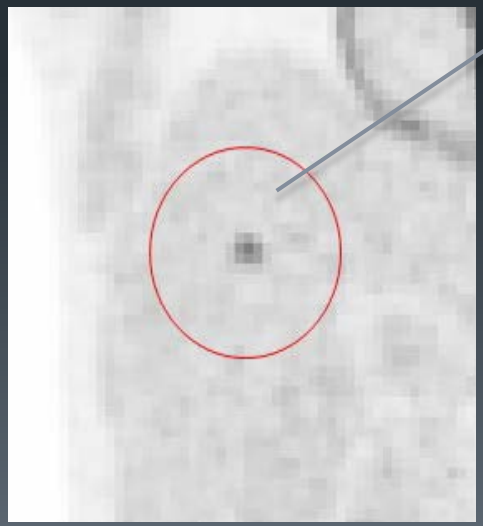
EXPLORER @ UC Davis:
The World's First Total Body PET scanner



vs.





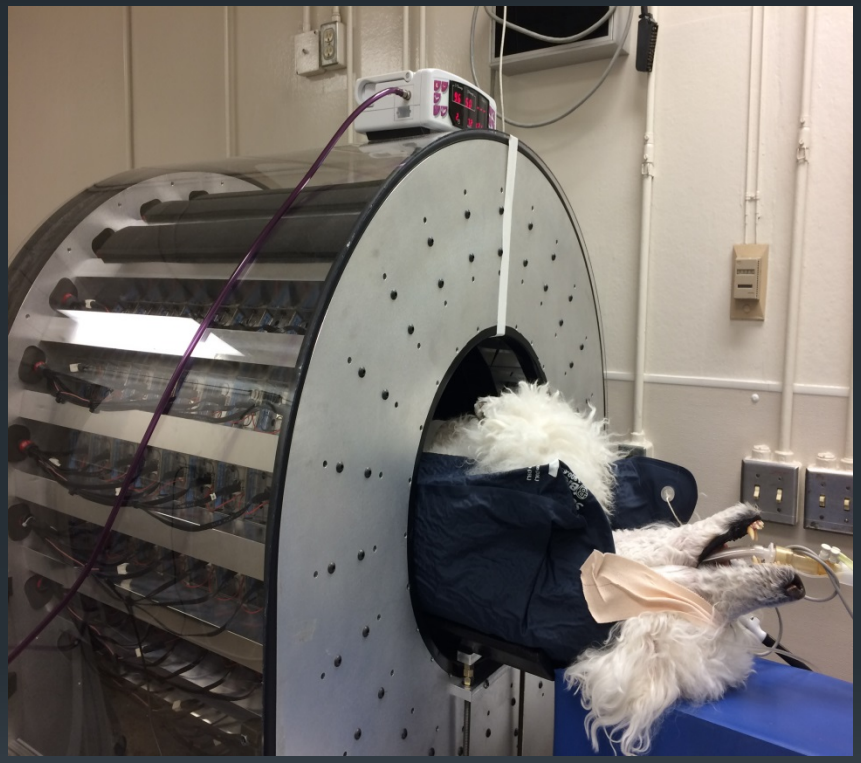


Simulation by Dr. Xuezhu Zhang

Conventional PET

EXPLORER

mini-EXPLORER:
^{18}F-FDG Canine Cancer Patient



11-yo female standard poodle; 17.4 kg
Osteosarcoma of the forelimb

2.5 mCi ^{18}F-FDG
2 beds, 20 mins each, 2 hours post injection

Courtesy of :

Mathieu Spriet,

Allison Zwingenberger,

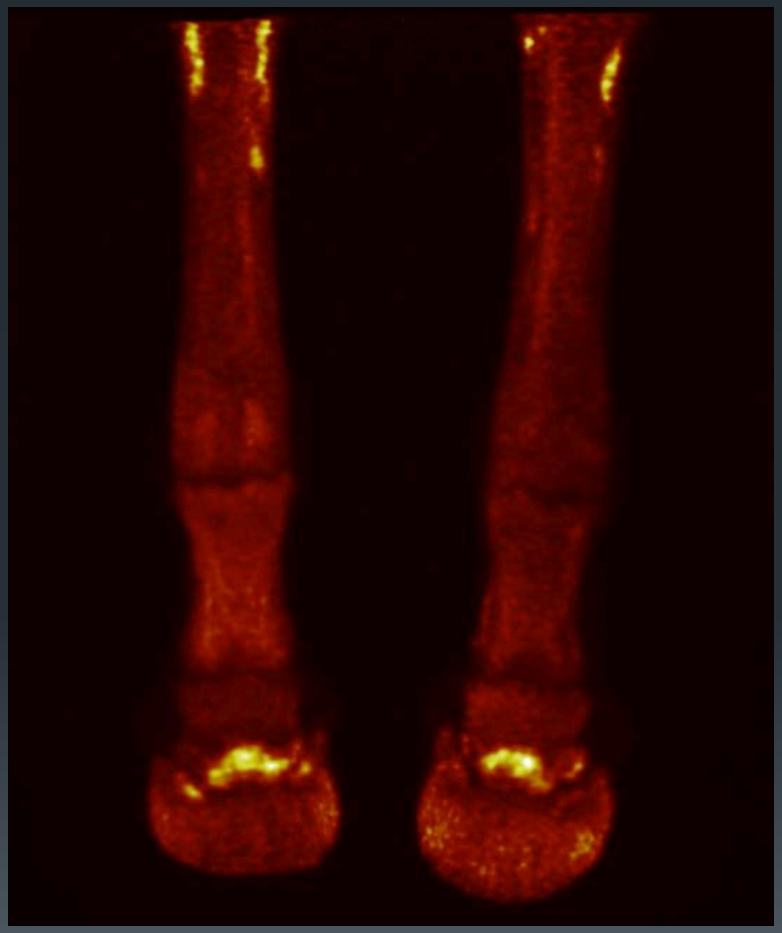
Eric Berg,

Xuezhu Zhang

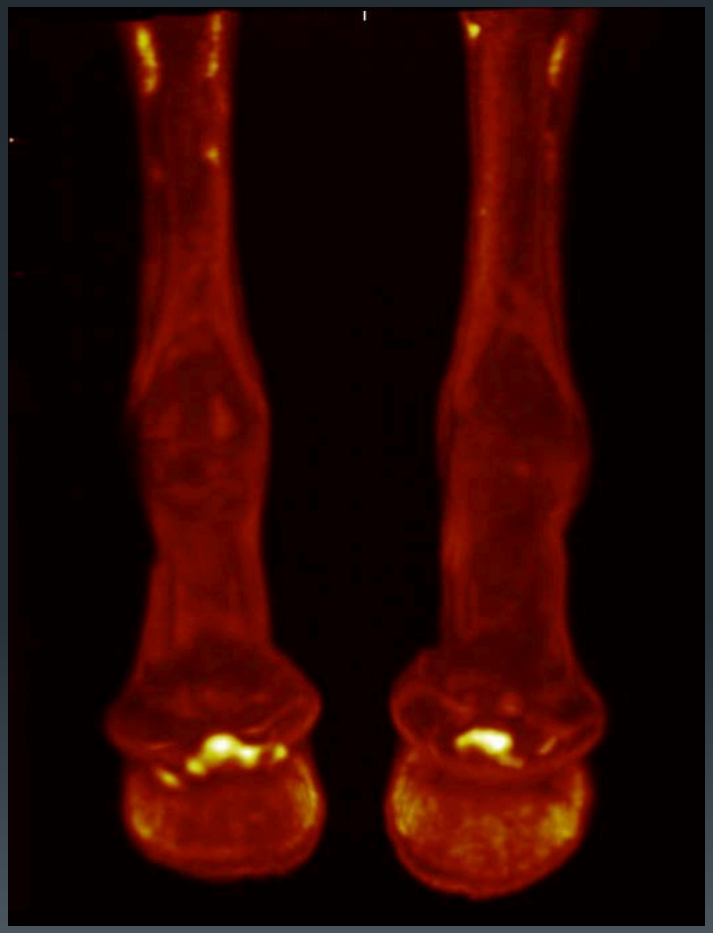
Horse in Mini-Explorer (1st ever PET in a horse!)

CEH Array of an Omen, March 6 2017
Horse slides courtesy of Mathieu Spriet, UC Davis

Mini-Explorer Horse Limb

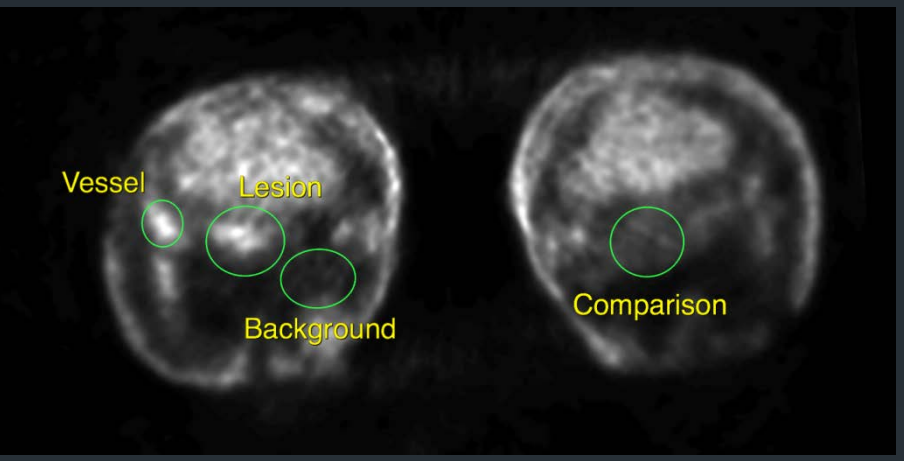


NaF

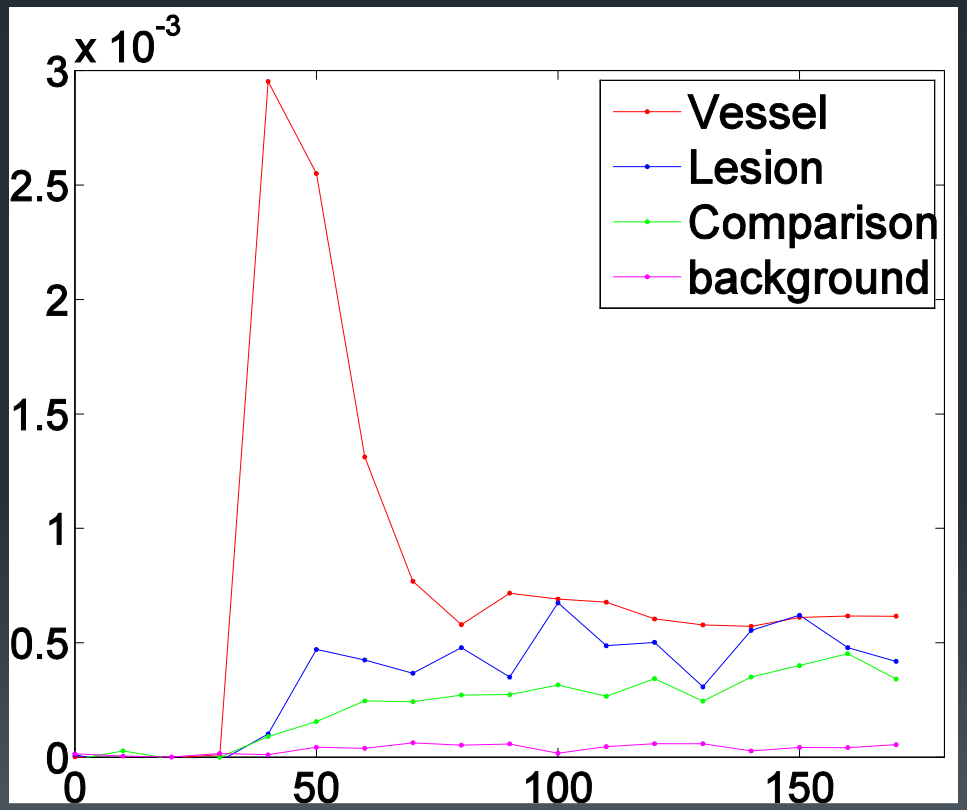


NaF + FDG

Time Activity Curve – FDG Injection



Early Phase
180 seconds
10 s / frame



The Next Steps …

- Studying musculoskeletal disease
  - Effectiveness of interventions
    - RICE regiments
    - Anti-inflammatories
    - Stem cell interventions
    - …
- Radiation Oncology:
  - Dose painting
  - Treatment response over time
  - High time resolution radiomics
- Immunology

In Conclusion

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- Synergy of companion animal and human health research
- New discoveries benefit both
- Effective bridge from lab to human