Investigation of Cherenkov Imaging Using IVIS Bioluminescence Scanner

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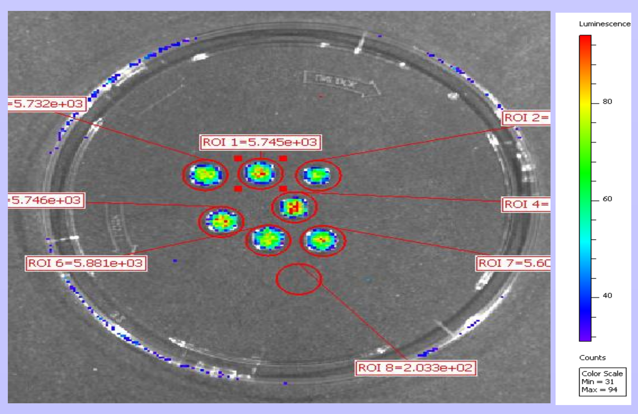
Introduction

Cerenkov luminescence imaging (CLI) is a methodology that uses the light emanated from numerous regularly utilized therapeutic and diagnostic particle emitting isotopes. Cherenkov radiation (CR) is created when charged particles go through a dielectric medium faster than the speed of light in that medium. Numerous PET isotopes and nuclear medicine isotopes have particle that produce Cherenkov of radiation such as18F, 68Ga and 177Lu. These isotopes were investigated in IVIS system to assess its utility to image these radioisotopes. In Cherenkov imaging, it is possible to image injected radiopharmaceuticals in small animals at low costs. In addition, multiple subjects might be imaged simultaneously, which has the advantage of saving both cost and time. Moreover, CLI can image both emitted β+ and β- particles.

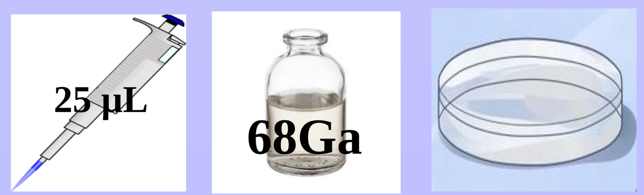
Methods

Linearity with time, activity and sensitivity across the field of view



•Increasing number of activity for 18F.

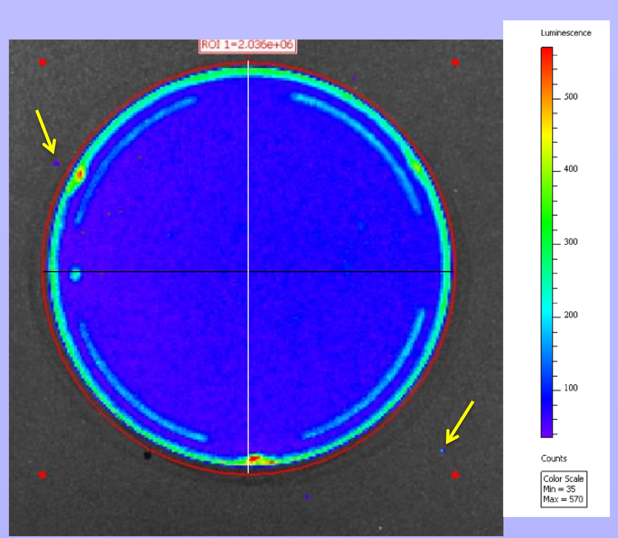
Linearity with dilution



•Mixed with several drops of water.
•Mixed with salt and sugar solution.

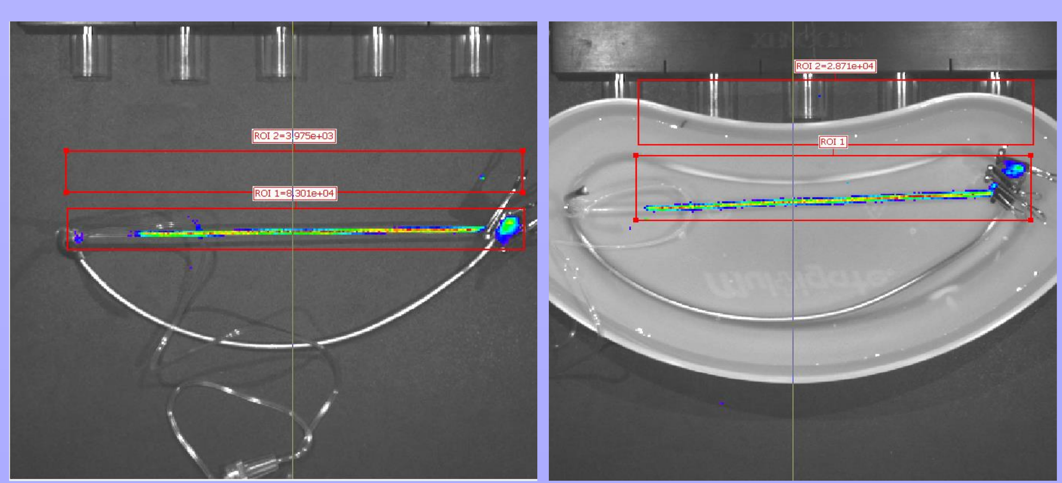
Uniformity

At high activities there may be gamma stimulation of CCD pixels, yellow arrows.



•A Petri dish with activity approximately 3 mL was filled with 2 cm of depth .

Resolution of 68Ga in air and water

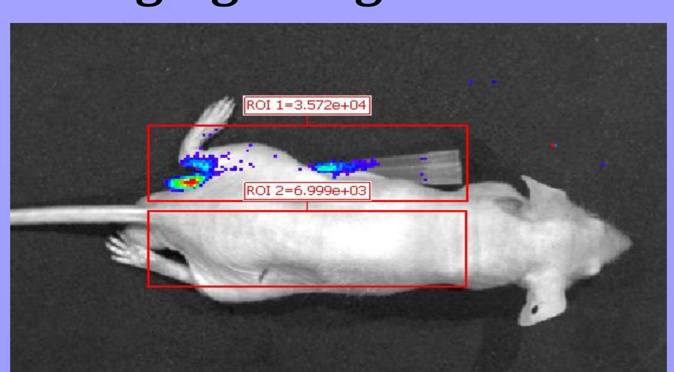


•Extension line tube was filled with 68Ga in air and water in a kidney dish.

Sensitivity

•Different concentrations with addition volumes of 175 µL of water were added, mixed .

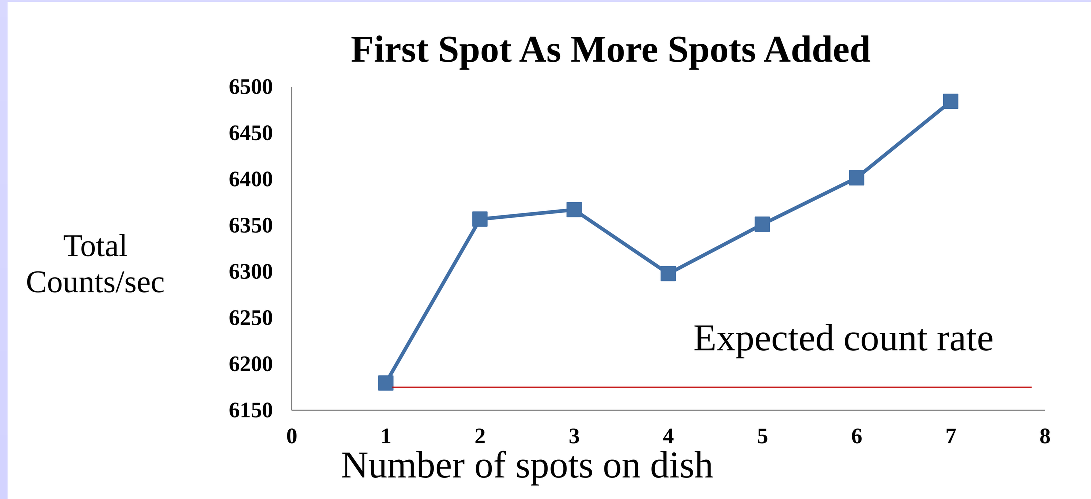
In Vivo imaging using Cerenkov radiation



•Small Eppendorf tubes and pipette tips containing18F and 68Ga were imaged through mouse tissue to investigate attenuation.

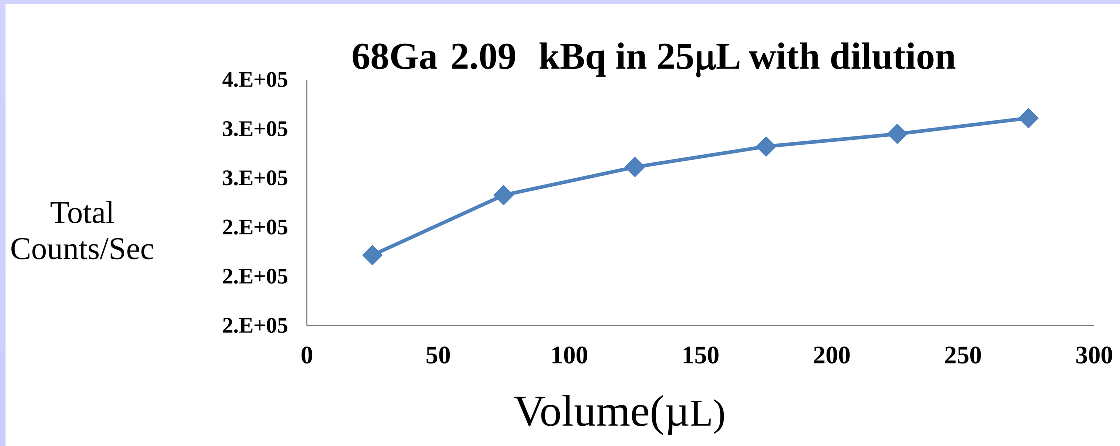
Results

Change sample count with additional samples and with time



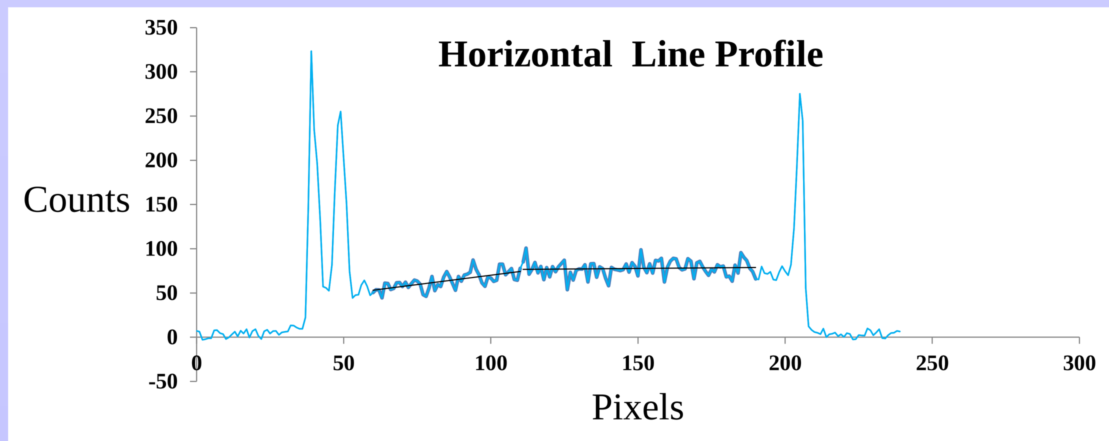
The IVIS was linear with time and activity when assessed for the full field of view. There was significant change in counts from a single sample as other samples were placed nearby. See graph. Reduction in light output was also observed as the sources evaporated with time but this was less than the increase from near by samples. Users need to consider cross talk between samples when imaging multiple samples.

Linearity with dilution in 68Ga



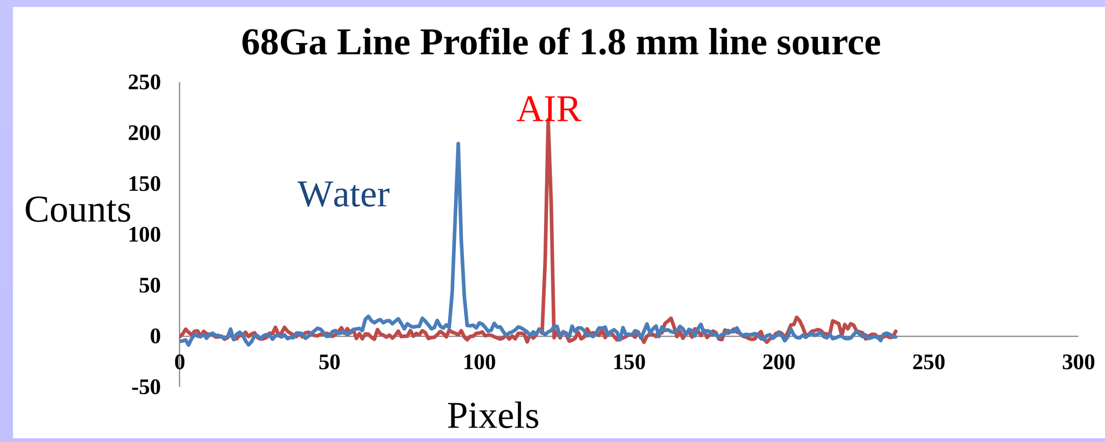
When sample size (25 µL is approx 4 mm round) is small with respect to positron range (4 mm in water for 68Ga) sensitivity increased with diliution due to less positrons leaving the sample. The sensitivity plateaus then falls as the sample size is further increased. This may significantly under estimate activity when imaging small samples e.g. of dissected tissue.

Horizontal line profile of mixed activity



The horizontal line profile shows clear deviation in linearity. It appears to be less sensitive in the left side of Petri dish and became uniformity sensitive at the middle of the imaging. Several faulty or hot pixels were observed outside the sample area but these were unlikely to be the reason of the non-linear uniformity.

Vertical line profile of 68Ga in the air and water



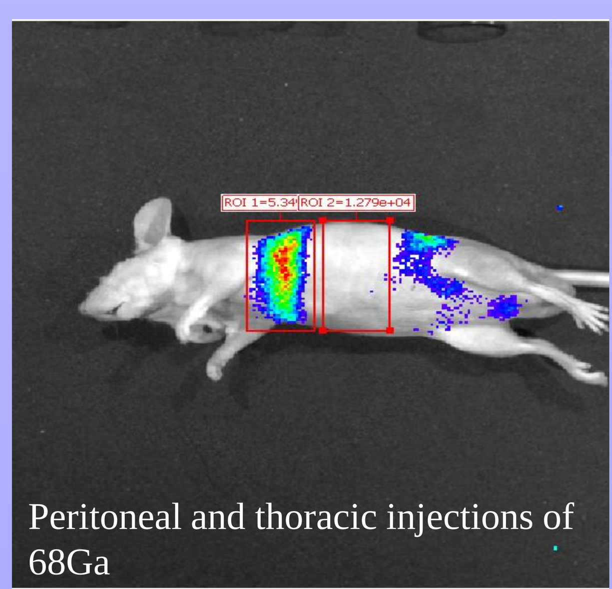
The optical resolution of the system is very high. The ability to image the radioisotope distribution depends on where the CR is generated. This is shown by the full width half maximum increasing from 1.86 in air to 2.29 when the line source was placed in water which allowed addition light to be generated outside the line source.

Sensitivity of different concentrations of 177Lu

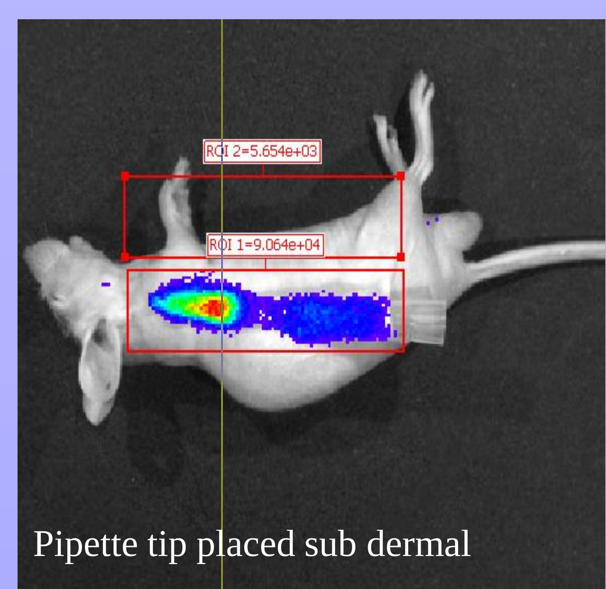
Radioactive Source	Activity(kBq)	Sensitivity (counts/kBq)
Weak 177Lu in 25 µL	4.6	15.34
Add 175 µL of water	4.4	3.38
Strong 177Lu in 25 µL	86.5	27.00
Add 175 µL of water	86.5	25.28

The technique allows imaging of non PET isotopes which are difficult to image without micro SPECT systems providing a method to image therapeutic radio isotopes.

The dead mouse injected by 68Ga in the thorax mainly near the lung



Mouse tissue strongly attenuated CR. CR was not visible through the mouse body or even a mouse leg. Activity in the peritoneal cavity was hard to see although less so for the thoracic cavity. CR shows the most clinical use for sub dermal applications.



Conclusion

- The IVIS system has suitable linearity and uniformity for Cherenkov imaging of radio nuclides.
- The sensitivity for Lu177 requires that activity concentrations greater than 4.6kBq/ 25 µL for in vitro sample.
- CR imaging is sensitive to sample size when dealing with small sample sizes with respect to the particle range. This is show in decreasing count data when small samples evaporate and increased sensitivity with dilution when starting with small sample sizes.
- CR imaging is an optical technique for secondary detection of particle emitting radio isotopes and as such effects from light reflection between samples and light propagation through objects in the field of view need to be considered.
- CR is significantly attenuated by tissue with the best application likely to be in sub dermal imaging.
- The use of CR in whole animals is likely to be semi quantitative. CR for imaging of dissected tissue may be subject to underestimation when sample size is small with respect to particle range.
- CR provide an effective preliminary method to image distribution of particle emitting radioisotopes, including therapy isotopes not easily imaged with microPET.