



Quantifying Radiopharmaceutical Uptake *In Vivo* Using Small-Animal SPECT/CT

B. Gershman¹, J.W. Hoppin², C. Lackas², J.Y. Hesterman², N.U. Schramm³, T. Anderson¹, J. Howard¹, L. Sklar¹, J.P. Norenberg¹

¹ University of New Mexico Health Sciences Center, Albuquerque, NM ² Bioscan, Inc., Washington, DC ³ Research Center Jülich, Jülich, Germany



INTRODUCTION

Multi-pinhole SPECT provides the necessary sensitivity, resolution, and quantification capability needed to facilitate non-invasive, longitudinal, *in vivo* studies. We present the methodology by which our small-animal SPECT system is calibrated for absolute quantification along with the results of longitudinal, *in vivo* tumor studies. In our laboratory, imaging studies performed with the small-animal SPECT/CT facilitate high-resolution. Quantification *in vivo* of radiopharmaceutical uptake under conditions which allow for multiple observations within the same animal.

METHODS AND MATERIALS

Imaging System The small-animal SPECT/CT system (1) was calibrated for absolute quantification using a custom-made quantification phantom (2). Physical characteristics of the phantom were selected to simulate attenuation properties of mice. SPECT acquisitions were conducted using a small-animal SPECT/CT with 4 detectors (215 x 230 mm² NaI, 33 PMT's). Each detector is fitted with a 9-pinhole aperture, $\varnothing = 1.4$ mm, as the image-forming element (3).

Quantification Calibration of source radioactivity was performed with a Capintec CRC-12 dose calibrator. The CRC-12 uses an Argon filled ionization chamber measuring 406 mm tall with an 168 mm inner diameter. A region of interest (ROI) was created in the reconstructed volume using the InVivoScope post-processing suite. The ROI estimated radioactivity was compared to the known radioactivity level as measured with the CRC-12. The ratio between the known value and the estimated value was used to generate a correction factor or 'quantification factor.'

***In vivo* Studies** Small-animal studies were performed on nude, tumor-bearing mice using ^{99m}Tc-Glucurate. Pancreatic (KP1-N) and colorectal (HCT-116) tumor models were investigated. Body temperature has been shown to have a strong correlation with uptake of radiopharmaceutical in mice¹. A pronounced decrease in uptake is seen as body temperature decreases. To combat this effect, mice were kept at or near normal body temperature before injection and during imaging. The mice were kept in at 34° C for one hour prior to injection. The animal bed (4) on the small-animal SPECT/CT system was heated to 35° C for all acquisitions. Imaging time points were chosen within the first 90 minutes post-injection based on published ^{99m}Tc-Glucurate data². The NanoSPECT/CT was employed to acquire small-animal SPECT and CT data.

Image Segmentation Absolute quantification of radiopharmaceutical uptake was based on ROI estimates of the reconstructed SPECT data. ROIs were estimated using a probabilistic seeded segmentation algorithm that works in both 2D and 3D. Results of the segmentation routine were verified both qualitatively as well as quantitatively by comparing 3D volume estimates to reported organ weights². The quantified ROI data was used to generate time-activity curves showing the time-varying radiopharmaceutical uptake within each region of interest.

1. Tseng JR, Dandekar M, Subbarayan M, et al. Reproducibility of 3'-deoxy-3'-(18)F-fluorothymidine microPET studies in tumor xenografts in mice. *J Nucl Med* 2005; 46 (11): 1851-7.
2. Liu Z, Stevenson GD, Barrett HH, et al. ^{99m}Tc glucurate high-resolution imaging of drug sensitive and drug resistant human breast cancer xenografts in SCID mice. *Nucl Med Commun* 2004; 25 (7): 711-20.
3. Iwaki T, Yamashita H, Hayakawa T (eds.). *A Color Atlas of Sectional Anatomy of the Mouse*. Braintree, Massachusetts: Braintree Scientific Publishers, 2001.



1 Small-animal SPECT/CT system



2 Quantification phantom for mice

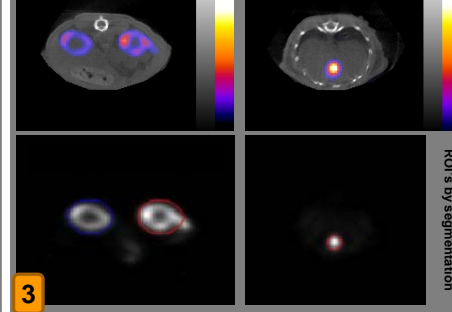
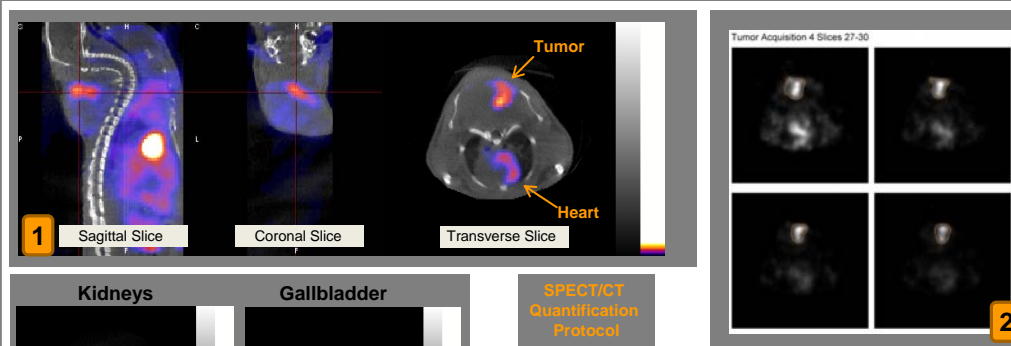


3 9-pinhole aperture

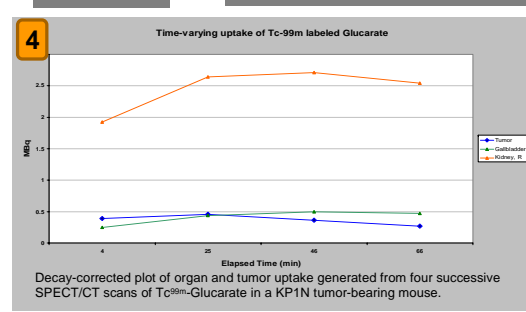


4 Animal bed w/integrated heating & gas

RESULTS



SPECT/CT Quantification Protocol



Imaging Results: KP1-N tumor-bearing nude mouse injected with 1.42 mCi ^{99m}Tc-Glucurate; 18 min. SPECT acquisition taken 26 min. post-injection (PI). 24 projections, 60 sec/projection (1). SPECT images with contours generated with automated segmentation algorithm (2), multiple slices are shown in order to display 3D capabilities of the algorithm. Transverse slices of SPECT/CT images as well as segmentation protocol of kidneys and gallbladder (3) from images 66 minutes PI. Note that the algorithm returns an array of different colored contours allowing the user to select the preferred curve based on qualitative assessment. Quantification results of dynamic scan presented in (4). ROI and quantification results were compared to reported organ weights and *ex vivo* gamma well-counter results (not shown) respectively.

DISCUSSION and CONCLUSION

- Absolute quantification *in vivo* is possible using the NanoSPECT/CT.
- We have employed a probabilistic seeded segmentation algorithm to automate ROI selection in 3D.
- Combining properly quantified data sets with segmentation algorithm in turn enables generation of time-activity curves in a wide array of units, e.g., %ID/g vs. time, activity vs. time, activity/vol vs. time, mole vs. time, mole/vol vs. time, etc.

ACKNOWLEDGEMENTS

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