



 biospace lab

μ imager

Application Notes

Simultaneous dual-isotope imaging of Technetium-99m and Thallium-201 using the μ-Imager™

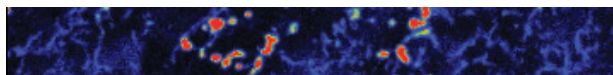
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Goal :

The development of new radiolabeled tracers requires the comparison of the newly proposed compound with the gold-standard molecule. ^{201}Tl is the reference myocardial blood flow tracer and is being widely used for the diagnosis of coronary artery disease in patients. $^{99\text{m}}\text{Tc}$ -labelled tracers have been synthesized and proposed as substitutes for ^{201}Tl because of the better physical characteristics offered by $^{99\text{m}}\text{Tc}$ (shorter half-life [6.02 hrs vs. 72 hrs for ^{201}Tl] and better suited emission energy [140 vs. 69 keV for ^{201}Tl]).

The development of high-resolution imaging systems now allows the assessment of the myocardial uptake of a given flow tracer on small animal models such as the rat or the mouse. Specifically, the μ IMAGER™ provides a resolution of ~20 μm and a field-of-view compatible with rat or mouse *ex vivo* imaging of myocardial slices. μ IMAGER™ is a radioactive disintegration imaging/counting system that allows the recording of data in the list mode. This record include spatial coordinates but also the time at which each disintegration occurs.

The objective of this study was to evaluate the potential of the time information recorded by the μ IMAGER™ for the simultaneous dual-isotope imaging of a $^{99\text{m}}\text{Tc}$ labeled perfusion tracer ($^{99\text{m}}\text{TcN-NOET}$) and of ^{201}Tl in rat myocardium. Such a capability would provide perfect image registration and excellent resolution for the quantitative comparison of *ex vivo* images obtained with 2 different radiolabeled tracers in an organ of interest.



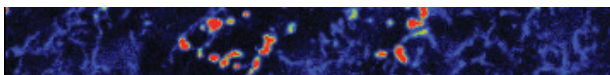
Material and methods :

$^{99m}\text{TcN-NOET}$ (2 mCi) and ^{201}Tl (0.25 mCi) were intravenously coinjected to male Sprague-Dawley rats subjected to a permanent left anterior descending coronary artery occlusion 1 week prior to the administration of both tracers. The animals were euthanized 15 min following $^{99m}\text{TcN-NOET}$ and ^{201}Tl injection, and the hearts were excised, rinsed, and immersed into embedding medium before being frozen using liquid nitrogen. 40 μm -thick myocardial slices were then obtained and deposited on pre-coated microscope slides for simultaneous dual-isotope *ex vivo* myocardial imaging of ^{99m}Tc and ^{201}Tl using the μ IMAGERTM.

Slides were exposed 12 hours starting at time T_0 , 5 hours after injection. The resulting image (Fig 1a) is the sum of the detected electrons originating from the ^{99m}Tc and ^{201}Tl disintegrations. These two populations of particles were separated based on the decay time difference of the two tracers (6.02 hrs for ^{99m}Tc vs. 72 hrs for ^{201}Tl) as follows : activity versus time is calculated at each pixel using time information recorded in the list file. With a least square criterion, this curve is compared to a weighted sum of two decay curves which half periods are, in this case, 6.02 hrs and 72 hrs. The two weights obtained correspond to the number of disintegration of each isotope at the corresponding pixel. Once this calculation has been made, two new list files are generated by adding to the already existing information (coordinates, times) the probability for each disintegration to be issued from Technetium (first file) or Thallium (second file). The time decays of these two new files follow exactly the natural decay curves of the corresponding isotopes.

Results :

The count rates for ^{99m}Tc and ^{201}Tl were approximately 20 and 35 dpm/mm², respectively, i.e. well within the detection range of the μ IMAGERTM (0.4 – 4.103 dpm/mm²). Representative short-axis images of $^{99m}\text{TcN-NOET}$ and ^{201}Tl myocardial uptakes are shown in Figure 1b) and 1c) respectively. The infarcted area can be readily identified as the anteroseptal area with $^{99m}\text{TcN-NOET}$ and ^{201}Tl uptake defects on these images. Quantitative image analysis was performed using the β -vision + software Mean $^{99m}\text{TcN-NOET}$ and ^{201}Tl defect magnitudes (minimal-to-maximal tracer activity ratio) were not statistically different (0.12 \pm 0.01 vs. 0.14 \pm 0.00, respectively). The extent of $^{99m}\text{TcN-NOET}$ and ^{201}Tl defects (defect area-to-total LV area ratio) was also similar (0.24 \pm 0.05 vs. 0.21 \pm 0.05). A pure Technetium drop has been spotted on the slide in order to control the quality of the isotope separation. The amount of parasitic ^{99m}Tc in the image is measured at a level lower than one percent of the total amount of Technetium.



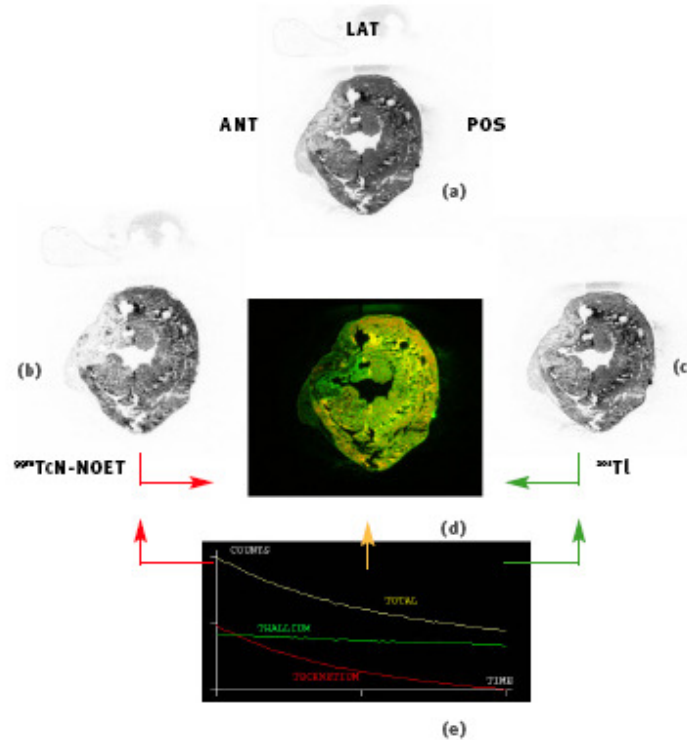


Figure 1

a : Simultaneously acquired ex vivo images of ^{201}Tl and $^{99m}\text{Tc-NOET}$ uptake in $40\ \mu\text{m}$ -thick short-axis myocardial slices (ANT indicates anterior; LAT, lateral; and POS, posterior).

b : $^{99m}\text{Tc-NOET}$ image.

c : ^{201}Tl image. Isotope separation was performed from image a) as described in Methods.

d : Fused ^{201}Tl (green) and $^{99m}\text{Tc-NOET}$ (red) images obtained from images c) and d).

e : Decay curves of ^{201}Tl (green), ^{99m}Tc (red) and total image count time decay (yellow) as obtained from the total list file.

Conclusion :

Simultaneous dual-isotope imaging of ^{99m}Tc and ^{201}Tl using the $\mu\text{IMAGER}^{\text{TM}}$ and local time analysis of the raw image led to separate ^{99m}Tc and ^{201}Tl images with excellent resolution and allowed the ex vivo comparison of the organ uptake of 2 different tracers. The technique is currently extended to imaging with three tracers including a positron emitter.



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