User project report

Dedicated phantom measurements to develop and validate quantitative 225Ac-(micro)SPECT imaging

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Report on dedicated phantom measurements to develop and validate quantitative ^{225}Ac-(micro)SPECT imaging

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The main objective of this proposal is to perform phantom measurements on currently available clinical and preclinical SPECT/CT systems:

1. To evaluate and select the optimal state-of-the-art acquisition and reconstruction protocols for quantitative ^{225}Ac-(micro)SPECT imaging
2. To evaluate whether a redistribution of free ^{213}Bi can be differentiated from ^{225}Ac and accurately quantified in-vivo using these state-of-the-art SPECT acquisition and reconstruction protocols. This will be combined with the design of optimal gamma counter measurement protocols to quantify ^{225}Ac and excess ^{213}Bi activity concentrations in solutions using the ^{213}Bi (and ^{221}Fr) photopeak window to anticipate the analysis of blood samples of patients undergoing ^{225}Ac-TAT
3. To provide reference data for the development of a new spectral SPECT image reconstruction using multiple energy windows to surpass the current state of the art in terms of ^{225}Ac-SPECT reconstruction and image quality

We evaluate the performance of quantitative ^{225}Ac-SPECT imaging for the following SPECT-CT systems:

- clinical Siemens Intevo T16 SPECT/CT system
- preclinical Molecubes γ/X-CUBE SPECT/CT system

^{225}Ac-activities

Source	Activity	Time	Form	site
A	**95.8 kBq in 500 µl of 4M HNO3**	**19.06.2023 @ 15h**	**Liquid**	**JRC**
B	**10 MBq**	**19.06.2023 @ 15h**	**Dry**	**JRC**
C	**9.26 MBq Ac-225 with 24.2 MBq Ra-225 producing Ac-225**	**20.06.2023 @ 9am**	**Liquid**	**MEDICIS**

From these activities, a concentration was made from source B and C resulting in 15 MBq in 250 ml volume or 60 kBq/ml (22.06.2023 @ 17h Source B: 7.33 MBq - 7.5% residual activity and Source C: 7.68 MBq - 24% residual activity).

Radionuclide calibrators

We confirm Ac-225 settings for Capintec CRC-55t which was Cal # 775 with a multiplication factor of 5.

Gamma well counter

We also checked the calibration factors for the gamma well counter for a Wizard 1480 and compared it to Wizard 2480 system available at SCK using the same energy window settings.

	SCK		KUL	
Bismuth peak	6.1	cpm/Bq	6.32	cpm/Bq
Francium peak	7.4	cpm/Bq	7.73	cpm/Bq

We could demonstrate that calibration factors are well in line with each other.

Clinical Siemens Intevo T16 SPECT/CT system

For the Siemens Intevo system, the NEMA IEC image quality phantom (Data Spectrum Ltd) will be used. This image quality phantom contains 6 spheres of different diameters: 6.0, 3.7, 2.8, 2.2, 1.7, and 1.3 cm corresponding to a volume of 160 ml. Each sphere will be filled with the same activity concentration while the main cavity (9800 ml) will be filled with non-radioactive water, simulating a cold background. To optimize settings, peaking of the energy spectrum was performed with source A (see Figure 1).

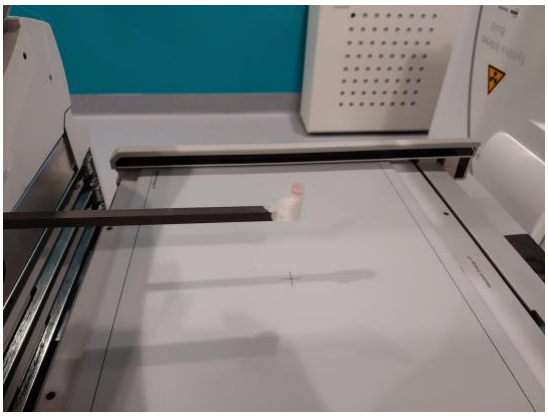
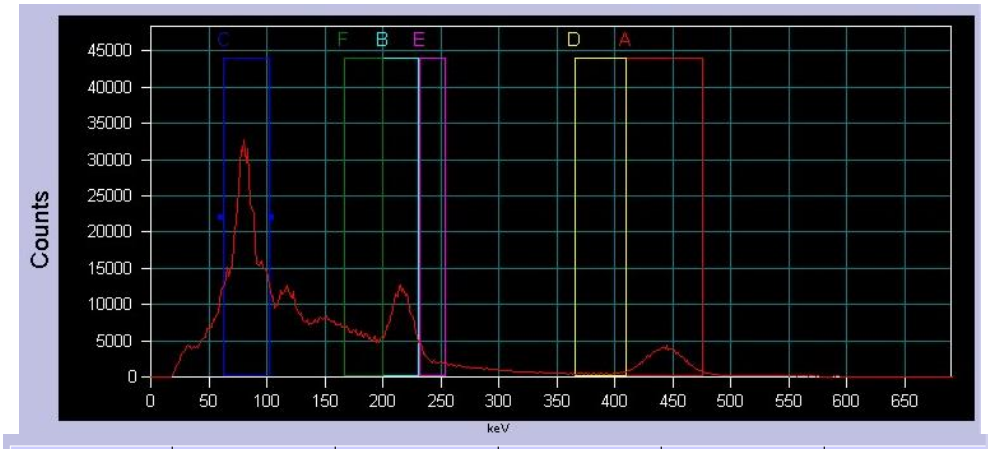


Figure 1: setup for peaking the energy spectrum for ^{225}Ac

Based on the spectrum, we defined six energy windows (max number possible) including the three photopeak windows at 440 keV (^{213}Bi), 218 keV (^{221}Fr), both with a width of 15% for both peaks and a lower X-ray peak at 80 keV with a width of 50%. A lower scatter window of 10% was defined for the 440 keV photopeak and both a upper (10%) and lower (15%) scatter window for the 218 keV photopeak.



Window Number	Center (keV)	Width (%)	Shift (%)	Type	Parent
A1	440	15	0	Photopeak	
B2	217	15	0	Photopeak	
C3	80	50	0	Photopeak	
D4		10		Lower Scatter	A1
E5		10		Upper Scatter	B2
F6		15		Lower Scatter	B2

Figure 2: Photopeak and scatter window settings for ^{225}Ac

After acquisition, data were reconstructed according to the following acquisition and reconstruction protocol. We acquired both a uniform phantom (vial with a volume of 250 ml) for calibration as well as the IEC phantom for image quality evaluation (see Figure 4).

Acquisition and reconstruction parameters	
Orbit	Body contour
Matrix	256 x 256
Pixel size	2.4 x 2.4
# projections	60/32
Time per projection	40 sec
Reconstruction	OSEM
Iterations/subsets	50/2
Attenuation map	CT based
Scatter correction	scatter windows
Filter	No filter

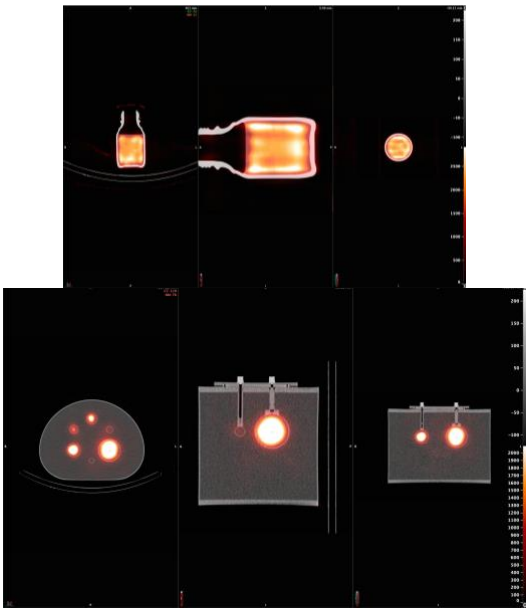


Figure 3: Acquisition and reconstruction protocol for the Clinical Siemens Intevo T16 SPECT/CT system with a representative reconstruction of the

These acquisitions allowed us to implement and validate a clinical acquisition and reconstruction protocol on the Siemens Intevo T16 SPECT/CT system such that this system is ready for supporting clinical trials.
In addition, we used both medium and high energy collimators for the measurements such that collected data can be used to support research on new reconstruction methods with an improved scatter model and using multiple energy windows.

Molecubes γ/X-CUBE SPECT/CT system

We also explored ^{225}Ac-microSPECT imaging with the preclinical Molecubes γ/X-CUBE SPECT/CT system equipped with low energy collimators and a detector with a 3/8" crystal thickness. For these measurements, we used a 20ml syringe filled with 19.73 ml ^{225}Ac solution of 60 kBq/ml with the photopeak energy window centred on 440 keV ± 10%. Data were reconstructed with a voxel size of 500µm using MLEM and 30 iterations (cfr Figure 4).

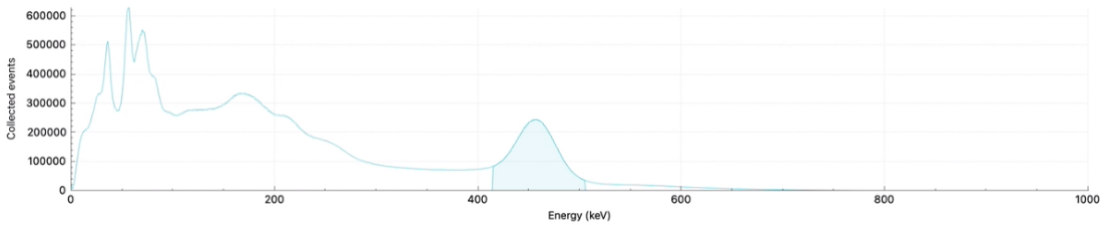
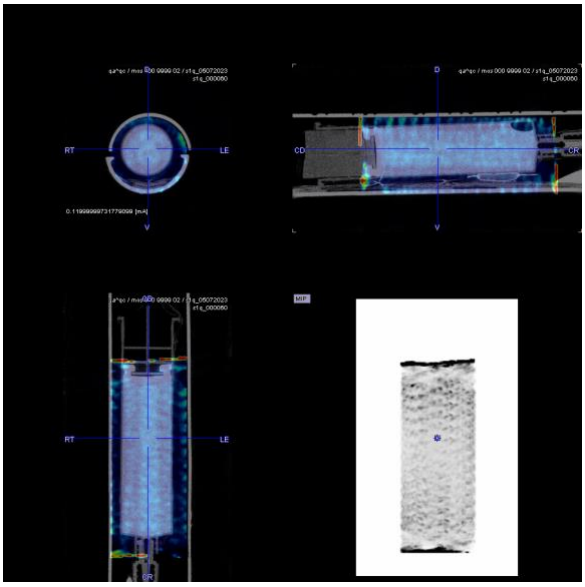


Figure 4: ^{225}Ac energy spectrum measured with the Molecubes gamma-cube scanner together with the 440 keV energy window that was used for the reconstruction.

Even an overnight scan of the uniformly filled syringe didn't prove feasibility of quantitative with the current configuration of Molecubes gamma-cube system (see Figure 5). As an alternative, we used the Perkin Elmer IVIS Spectrum system to perform Cerenkov Luminescence imaging (CLI) where we filled an Eppendorf with the same activity concentration and used a 5 min exposure to acquire the image with a Field of View (FOV) of 3 cm.



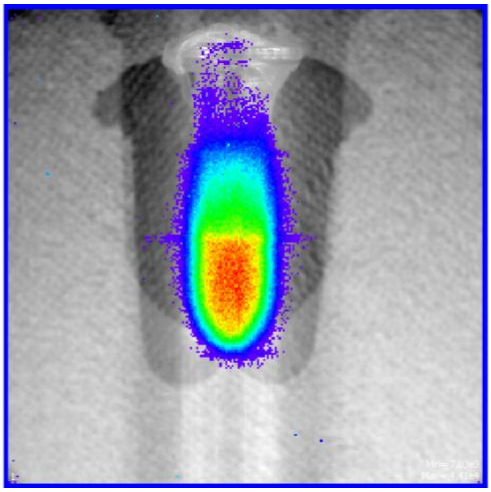


Figure 5: 16 hour scan of a syringe filled with 60 kBq/ml ^{225}Ac using the Molecubes gamma-cube system equipped with low energy collimators and a 3/8" crystal. As alternative, we used an Eppendorf with the same activity concentration to demonstrate the potential of Cerenkov Luminescence imaging (CLI) as an alternative to microSPECT imaging.

Conclusion

Radionuclide calibrator and gamma counter settings for ^{225}Ac measurements could be confirmed. Meanwhile a series of calibration and image quality measurements with the clinical SPECT system could be performed to implement and validate a quantitative clinical ^{225}Ac-SPECT protocol. Finally, initial experiments showed that the available preclinical SPECT system in current configuration would not suitable for quantitative ^{225}Ac-SPECT imaging Cerenkov imaging feasible