Multimodality Imaging Possibilities of Therapeutic Isotopes in the Preclinical Setting

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1. Introduction

Therapeutic radionuclides are not easily visualised and are paired with positron (β+) or gamma-emitting radionuclides for imaging purposes.

Popular theranostic pairs include:

^{68}Ga/^{177}Lu; ^{68}Ga/^{255}Ac; ^{64}Cu/^{67}Cu; ^{188}Re/^{99m}Tc

Single Photon Emission Tomography (SPECT) advances increases feasibility of imaging of therapeutic radionuclides.

Cerenkov-derived luminescence imaging (CLI) detects light emitted because of charged particles from radioactive decay moving faster than light in a medium; therefore, CLI is suitable to directly visualise beta-emitting therapeutic radionuclides.

This dual imaging capability presents an opportunity to be utilised to support clinically relevant questions.

This study evaluates the SPECT and CLI capabilities of three relatively unused therapeutic nuclides in comparison to known theranostic radionuclides:

186Re; 188Re; 109Pd

2. Methods

2.1 microSPECT

- Isotopes calibrated on nanoSPECT/CT according to manufacturer specifications using the appropriate multipinhole collimator
- Activity calibration (8-10MBq in 2-3ml syringe) and uniformity assessment performed for each isotope
- Images acquired using Derenzo or PET Nema phantom according to in-house developed acquisition parameters
- All Images reconstructed with iterative reconstruction and using CT attenuation correction and assessed for:
  - Sensitivity (cps/MBq)
  - Resolution (visual assessment ^{188}Re and ^{186}Re)
  - Uniformity (NEMA NU 1-2012 2.4)

2.2 CLI

- Stock solution of each isotope prepared in 1mL saline and activity measured
- Activity (± 1 – ±9 kBq/µl) pipetted (in triplicate) into 4 descending wells to create a 1:2 dilution series with saline (Total volume/well = 1 mL)
- Average activity per well (t = 0): A = 7.8 ± 1.1 kBq/µl; B = 3.9 ± 0.6 kBq/µl; C = 2.0 ± 0.3 kBq/µl; D = 1.0 ± 0.1 kBq/µl
- Imaging done at t = 0, 1 and 2 half-lives using IVIS Lumina (PerkinElmer) with following parameters:
- Open filter; F/stop 1; Binning 8
- FOV 12.5; 180s or 300s exposure
- Radionuclides were compared with respect to activity concentration (kBq/µl) and average radiance (p/s/cm²/sr)

3. Results

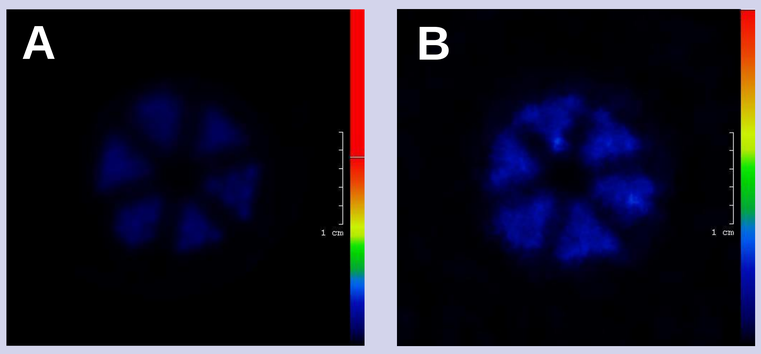
Table 1: SPECT Sensitivity Summary

Isotope	Activity (MBq)	Count Rate System	CPS/MBQ
^{109}Pd	11.1	142	12.8
^{186}Re	10.5	553	52.8
^{188}Re	42.6	5495	129.0
^{177}Lu	22.0	4226	191.9
^{99m}Tc	245.0	115838	472.8

Table 2: SPECT Uniformity Summary according to NEMA NY 1-2012 2.4

		UFOV		CFOV	
Isotope		Detector 1	Detector 2	Detector 1	Detector 2
^{99m}Tc	Integral Uniformity	1.10	0.90	0.80	0.90
	Differential	1.90	1.70	1.50	1.60
^{131}I	Integral Uniformity	1.10	1.10	0.80	0.80
	Differential	1.80	1.60	1.50	1.60
^{188}Re	Integral Uniformity	1.40	1.10	1.00	1.00
	Differential	1.90	1.70	1.40	1.50
^{186}Re	Integral Uniformity	1.00	1.00	0.90	0.90
	Differential	1.80	2.00	1.60	1.50
^{109}Pd	Integral Uniformity	1.10	1.10	0.90	0.90
	Differential	2.20	2.10	1.50	1.60
^{177}Lu	Integral Uniformity	1.50	1.40	0.90	1.00
	Differential	2.10	2.10	1.70	1.80

Figure 1: Derenzo Phantom Cross-section of A)) 186Re and B) 188Re



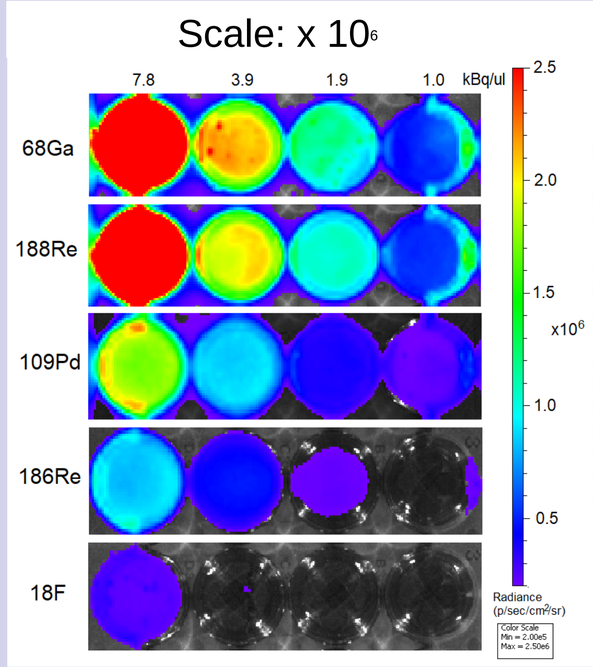


Figure 2: Representative CL images (t = 0) of therapeutic 188Re-, 186Re- and 109Pd-nuclides in comparison to imaging 68Ga- and 18F-nuclides. Average Radiance (x106)(p/s/cm²/sr) determined from mean radiance for triplicate dilution with background correction. Activity concentration (kBq/µl) calculated as mean ± SD for all nuclides.

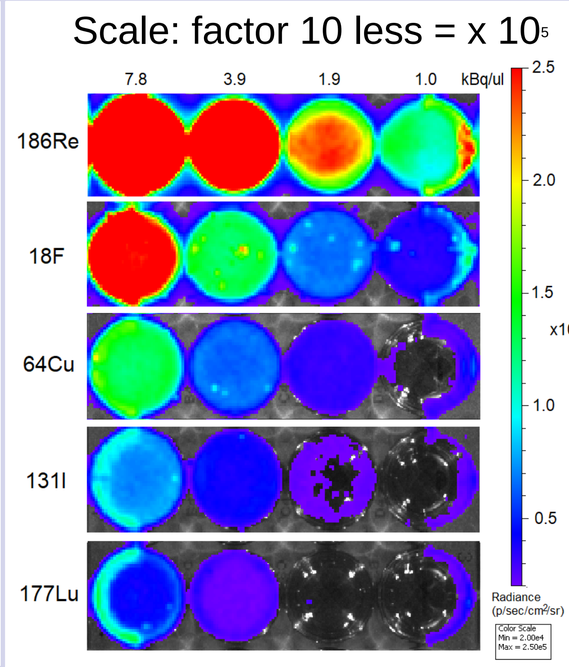
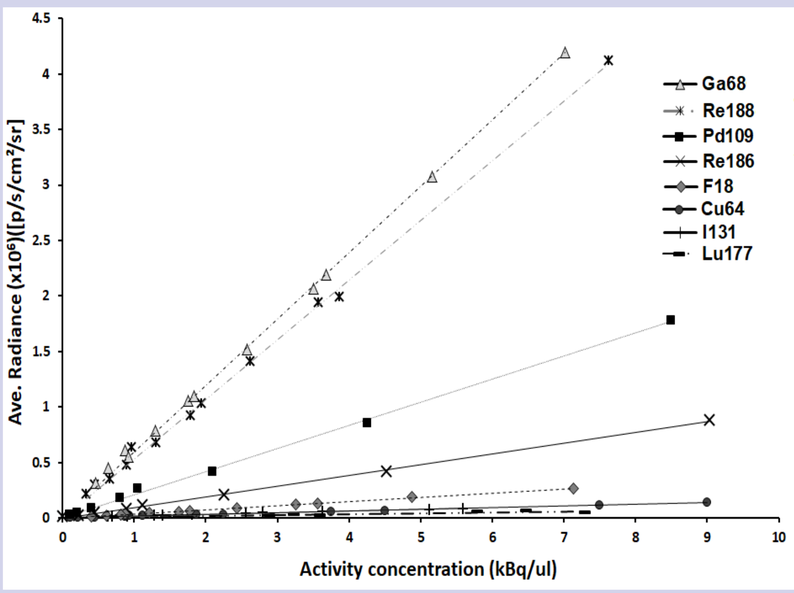


Figure 3: Representative CL images (t = 0) of therapeutic 186Re-, 131I- and 177Lu-nuclides in comparison to imaging 64Cu- and 18F-nuclides. Average Radiance (x105)(p/s/cm²/sr) determined from mean radiance for triplicate dilution with background correction. Activity concentration (kBq/µl) calculated as mean ± SD for all nuclides.

Graph 1: Comparison of Cherenkov Luminescence between new therapeutic isotopes (**186Re, 188Re, 109Pd**), evaluated therapeutic isotopes (**177Lu,131I**) and imaging isotopes (**68Ga, 64Cu, 18F**)



4. Discussion

- SPECT and CL Imaging of all three investigatory radionuclides is possible in a preclinical setting
- *SPECT*

  ^{109}Pd - lowest sensitivity
  - requires longer acquisition times
  - uniformity is in line with Lu-177 (Table 1 and 2)

  ^{188}Re and ^{186}Re - high sensitivity
  - Uniformity measurements correlated with each other as well as other known isotopes (Table 2)
  - Better visual resolution of ^{186}Re (Figure 1) but can be optimised by improving acquisition parameters

- *Cherenkov Luminescence*
  - Radiance$_{(Ave)}$ of nuclides correlates with E(max)MeV of particle emissions including additional influence by %abundance of the particle emissions.
  - Radiance$_{(Ave)}$ of ^{188}Re (2.1 MeV, 70% abundance) is similar to 68Ga (1.89 MeV, 87% abundance) (Figure 2 and Graph 1)
  - ^{109}Pd (1.02 MeV) has double the Radiance$_{(Ave)}$ of ^{186}Re (1.07 MeV) as result of higher % abundance
  - At half the E(max) of ^{188}Re, the ^{109}Pd and ^{186}Re radiance is 2.5 and 5 fold lower (Graph 1)
  - CL of ^{188}Re, ^{109}Pd and ^{186}Re is much higher than 131I- and 177Lu-nuclides which have very low E(ave) and therefore average radiance almost too low for suitable detection (Figure 2 and 3)

5. Conclusion

In the preclinical setting Rhenium-186/-188 exhibits superior SPECT imaging capabilities over 131I- and 177Lu-radionuclides. 109Pd has lower sensitivity but still provides suitable SPECT images for diagnostic application. All three therapeutic isotopes have excellent CLI properties comparable to other therapeutic-/PET-isotopes. The SPECT- and CLI imaging capabilities of these therapeutic radionuclides allow for further research into applications for disease targeting.

6. References

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