Normal Organ Dosimetry to Guide Safe Re-treatment PRRT

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INTRODUCTION

- Re-treatment with PRRT is becoming more common. Historically, 2 cycles were delivered during re-treatment. However, there is limited data surrounding how many additional cycles are safe to deliver.
- Normal organ dosimetry and dose limits may help guide this decision.
- **This study presents dosimetry results for 10 well-differentiated NET patients at our institution. 9 patients received dosimetry with their first cycle of re-treatment, and 1 with their second cycle of re-treatment.**

BACKGROUND

- As agent-specific radiopharmaceutical dose limits are still evolving, normal organ dose limits from external beam radiation therapy (EBRT) and ^{131}I therapy, as well as Biologically Effective Dose (BED) limits were used in this study. Dose limits are defined at the point 5% of the population experiences toxicity within 5 years.
- **Absorbed dose limits** for the **liver, lungs, and bone marrow** were used.
- As dose rate and deposition in PRRT varies markedly from EBRT, **BED limits** were chosen for the **kidneys** to account for biological uptake, clearance, and repair.

METHODS

SPECT/CT-based Dosimetry

- 4-timepoint SPECT/CT-based dosimetry was used.
- Dosimetry calculations were performed with MIM SurePlan MRT.

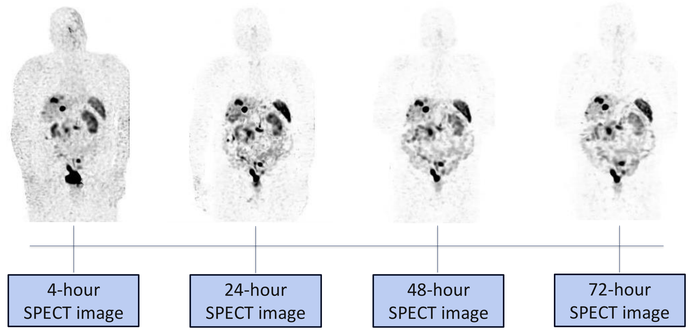


Figure 1: Maximum intensity projections of the 4-, 24-, 48- and 72-hour SPECT images for a PRRT dosimetry patient.

Comparing to Dose Limits & Monitoring Treatment

- Serum creatinine values and CBCs were monitored throughout treatment.
- The dose calculated for the single dosimetry cycle was extrapolated over the initial cycles of PRRT to calculate the cumulative organ dose prior to retreatment.
- The number of additional cycles that could be delivered, beyond the original treatment, without exceeding dose limits was determined.
- The average follow-up time for the patients in the cohort was 1353.4 (SD = 676.6) days, with follow-ups ranging between 241 and 2353 days.

$$\text{Tolerable \# of Re-treatment Cycles} = \frac{\text{Organ Dose Limit} - \text{Organ Dose from Initial Cycles}}{\text{Dosimetry Cycle Organ Dose}}$$

Organ	Dose Limit
Liver	30 Gy
Lungs	17.5 Gy
Bone Marrow	2 Gy
Kidneys	29 Gy (w/comorbidities) 38 Gy (w/o comorbidities)

Normal organ dosimetry, in conjunction with serum creatinine values and CBCs, provides additional information in re-treatment PRRT. Our results demonstrate that the kidneys were the limiting organ for the majority of the patients.

RESULTS

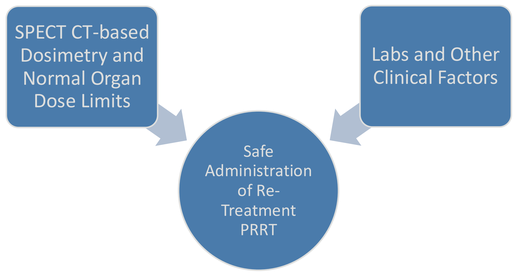
Patient	# Initial Treatment Cycles Administered	# Re-treatment Cycles Administered	Years Between Last Cycle of Initial Treatment and Re-treatment	# Re-treatment Cycles Permitted (Kidneys)	# Re-treatment Cycles Permitted (Bone Marrow)	Limiting Organ	Renal Toxicity	Myelotoxicity
1	4	**2**	1.9	**3**	0**	Bone Marrow	No	No
2	2	**3**	2.9	**4**	5	Kidneys	Yes*	No
3	4	**4**	4 (approx.)	**1**	2	Kidneys	No	No
4	3	**4**	4.5	**2**	3	Kidneys	Yes, recovered	No
5	4	**4**	6 (approx.)	**4**	4	-	Yes*	No
6	4	**2**	3.1	**1**	1	Kidneys	No	No
7	4	**4**	1.5	**4**	4	-	No	No
8	4	**4**	4.2	**0****	0**	Kidneys	No	No
9	4	**4**	3.4	**4**	4	-	No	No
10	4	**1**	4.0	**0****	2	Kidneys	Yes	No

*Multifactorial AKI
**Normal organ dosimetry was completed during the first or second cycle of re-treatment.

DISCUSSION

SPECT/CT-based Dosimetry

- Dosimetry is not an absolute limit and is used in addition to labs and other clinical factors to guide re-treatment with PRRT.
- Many patients received more than 2 re-treatment cycles, indicating that the historical 2 cycle re-treatment protocol may be too conservative.



Renal Dosimetry

- The motivation for renal dosimetry is to warn of potential long-term kidney toxicity.
- The kidneys were the limiting organ for most patients (6/10), however all but 1 chose to continue treatment despite the risk.
- This emphasizes the importance of long-term renal function monitoring, as chronic radiation nephropathy can have a latency period of years (Klaus, Radiat Oncol. 2021).
- While studies have shown an average annual loss in CrCl of 3 – 4 % following PRRT, severe renal injury is infrequent (Bober, J Clin Med 2022).
- However, the relationship between kidney dose and renal toxicity remains undefined, with many confounding factors.
- Because of this, there are many calls for prospective trials exploring dose escalation and kidney toxicity.