LYon Recherche Innovation contre le CANcer

Dosimetric workflow adapted to a variable number of SPECT/CT acquisitions for ^{177}Lu-DOTATATE treatments

L. Vergnaud[1,2], AL. Giraudet[2], A. Moreau[2], J. Salvadori[3], A. Imperiale[3], T. Baudier[1,2], JN. Badel[1,2] et D. Sarrut[1,2]

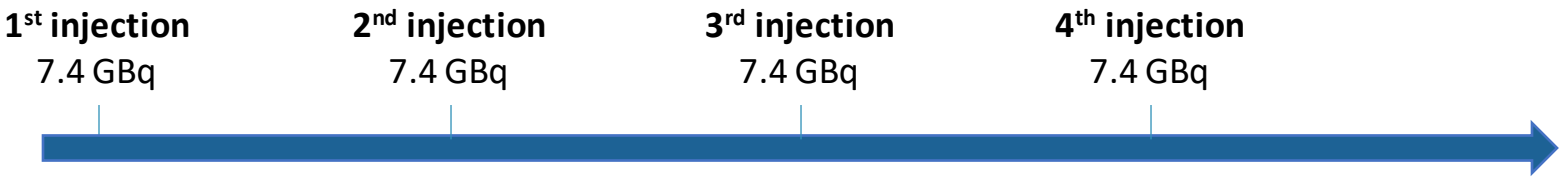
[1]CREATIS, Centre Léon Bérard, CNRS UMR 5220, INSERM U 1044, Université de Lyon; INSA-Lyon; Université Lyon 1, Lyon, France.

[2]Département de Médecine Nucléaire, LUMEN, Centre Léon Bérard, 28 Rue Laennec, 69008, Lyon, France.

[3]ICANS - Institut de cancérologie Strasbourg Europe, 17 Rue Albert Calmette, 67200 Strasbourg, France.

^{177}Lu-DOTATATE therapy

Standardized treatment:



Several SPECT/CT acquisitions are needed to follow the ^{177}Lu biodistribution.

In clinical practice, it is not always possible to have multiple SPECT/CT acquisitions for each cycle.

How to estimate the absorbed doses to organs at risk as a function of the number of acquisitions available?

Single Time-Point methods

- **Reducing the number of acquisitions** by selecting those that result in the lowest possible error [Sundlov and al. 2018, Chicheportiche and al. 2020].

- Dosimetric workflow **based on only one acquisition** [Willowson and al. 2018, Madsen and al. 2019, Hanscheid and al. 2018, Sandstrom and al. 2020, Zhao and al. 2019, Devasia and al. 2020]
  - MIRD formalism (S-values pre-calculated on phantoms)
  - Mono-exponential fitting for the Time Activity Curve

Simplification of the calculation of cumulative activity [Madsen et al. 2019, Hänscheid et al. 2018]

Reuse of patient pharmacokinetics from a previous cure [Willowson et al. 2018, Garske et al. 2012]

Use of average pharmacokinetics of other patients + tri-exponential model [Jackson et al. 2020]

Data available

"Patient cohort"
(Data from Léon Bérard center, Lyon)

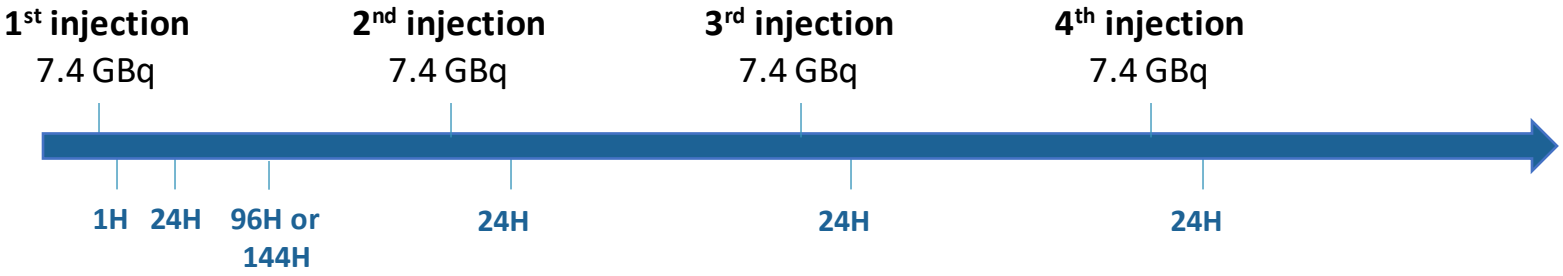
13 patients

Not all SPECT/CT is available for all patients

"Validation cohort"
(Data from ICANS, Strasbourg)

7 patients

Only cycles 1 and 4



SPECT/CT acquisitions performed at Léon Bérard center

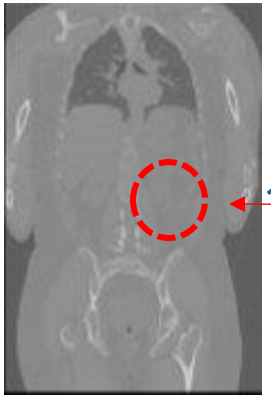
SPECT/CT acquisitions performed at ICANS

Dosimetric workflow (1)

1 - Acquisition

Reconstruction SPECT

CT

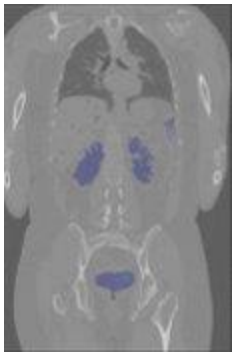


2 - Simulation

Monte Carlo Simulation (GATE)

Source: 1 MBq of ^{177}Lu

Acquisition time: 1s



3 - Segmentation

Left and right kidneys, liver, spleen and three surrogates of bone marrow (L2-L4 [Ferrer and al. 2010], L1-L5 and T9-L5 [Hagmarker and al. 2019])

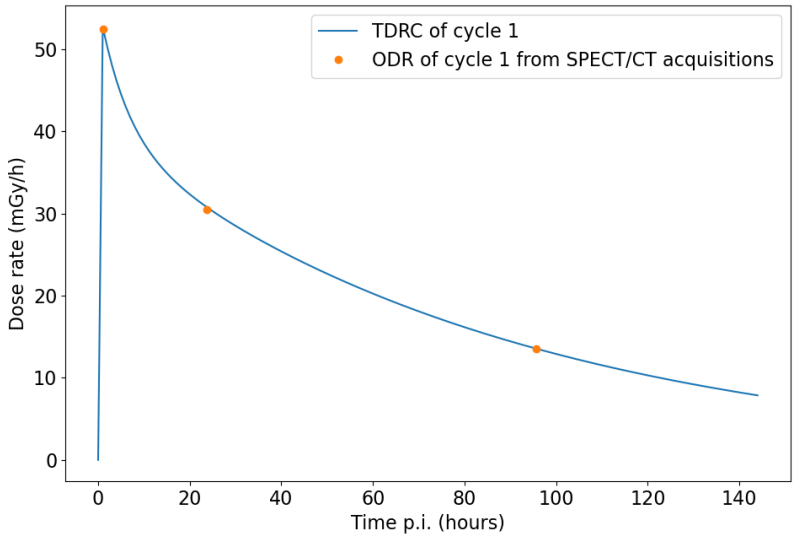
Dosimetric workflow (2)

4 – Dose rate at a specific time

Dose rates at the voxel level (Gy/s)

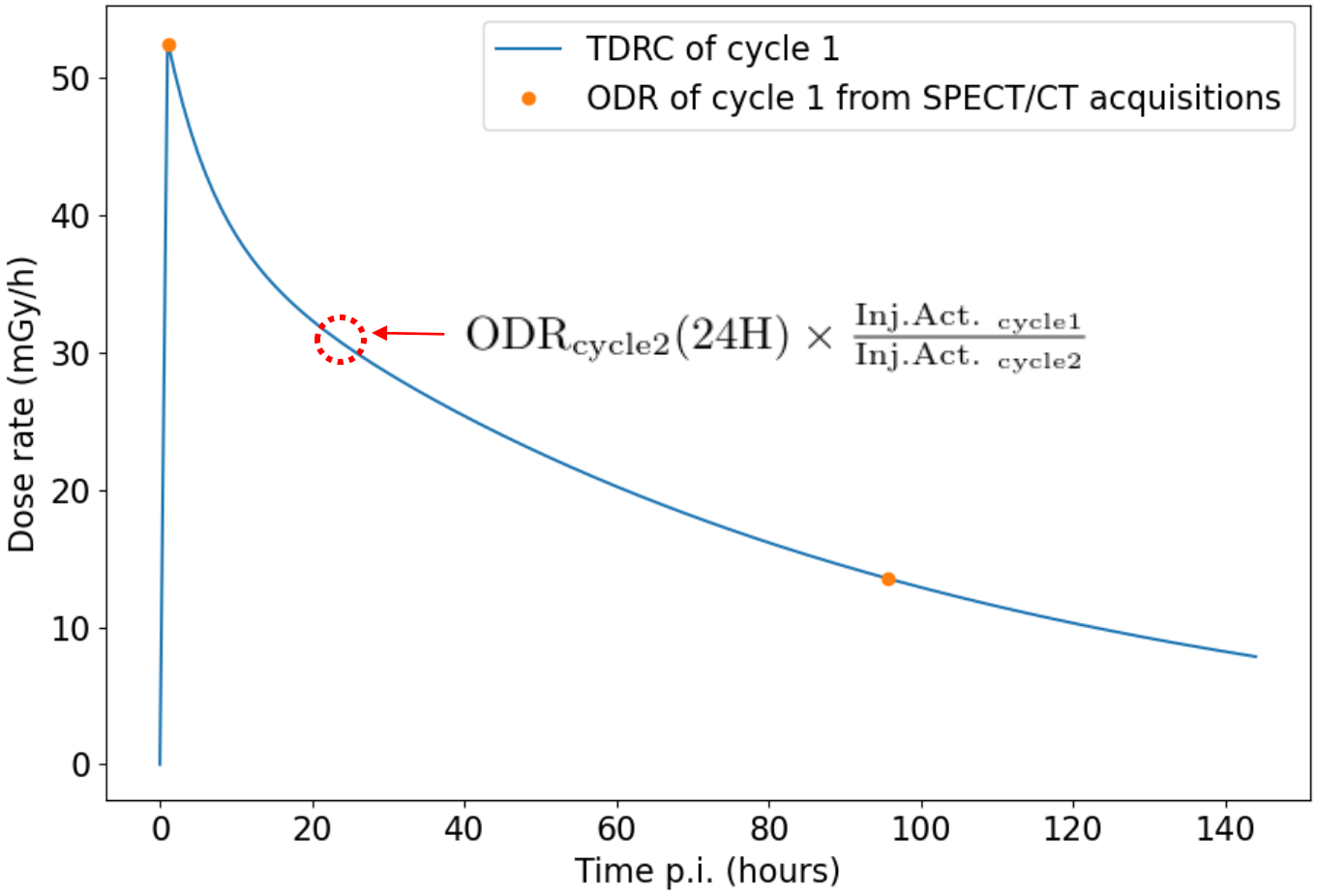
Average Organ Dose Rate: ODR (Gy/s)
+
Dose rate scaling (1MBq simulated only)

5 – Fit and integration of the Time Dose Rate Curve (TDRC)



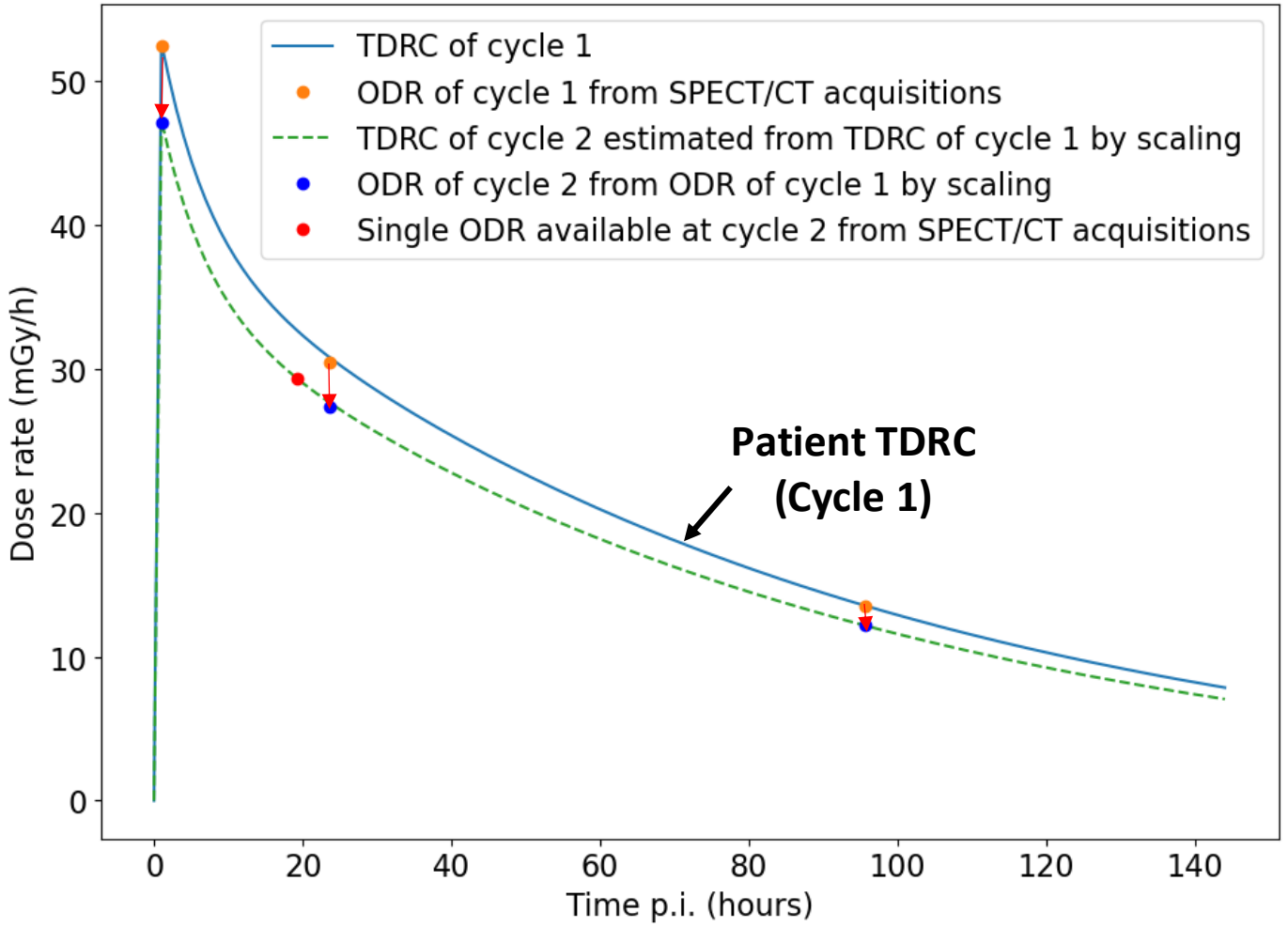
= Reference method
(tri-exponential function [Jackson and al. 2020])

Missing Time-Point method (M1)



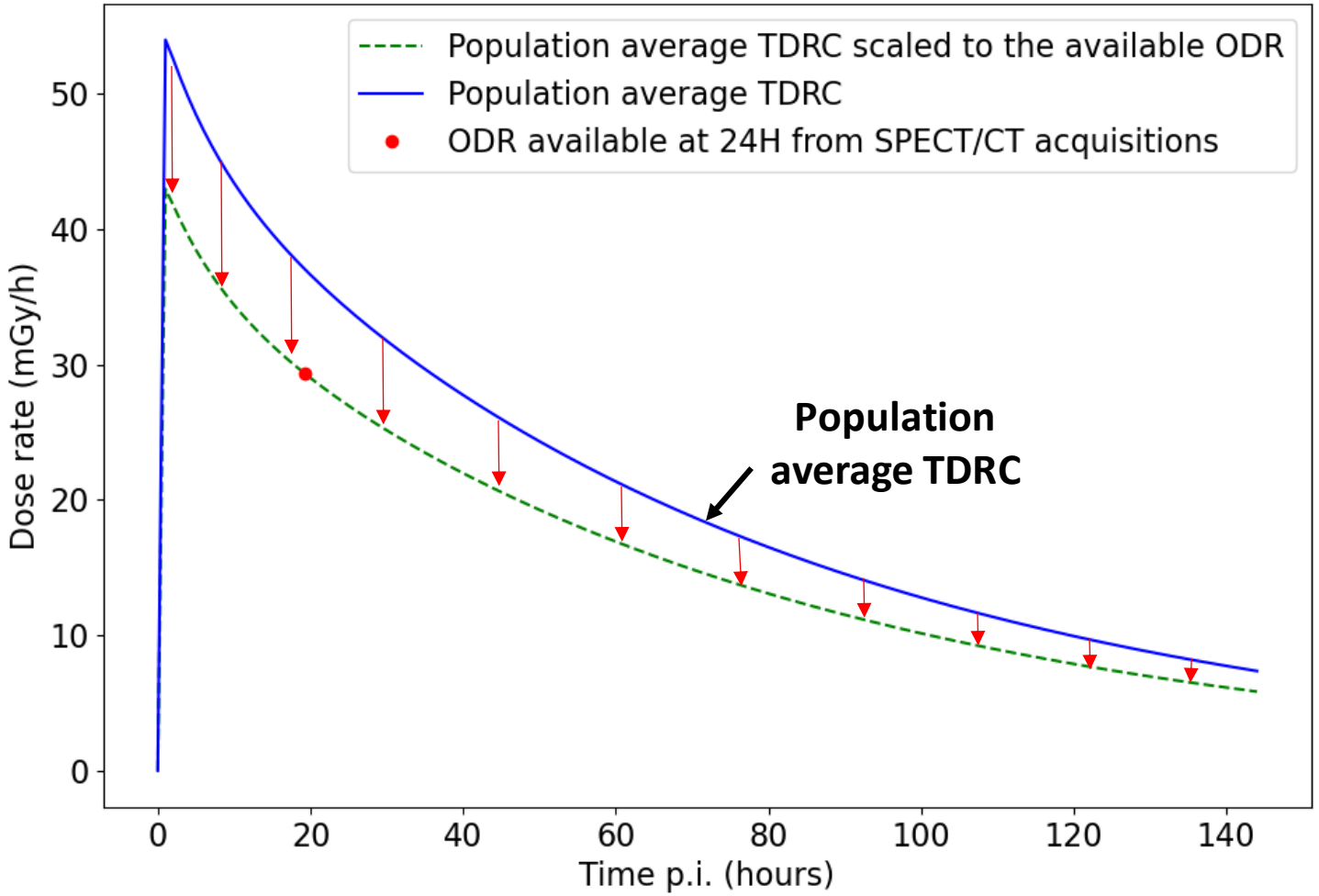
Approximation of the ODR missing at 24H to use a tri-exponential fitting at the first cycle.

Single Time-Point Intra method (M2)



Reuse pharmacokinetic parameters estimated at cycle 1 for following cycles.

Single Time-Point Inter method (M3)



Use pharmacokinetic parameters of a population average TDRC

[Jackson and al. 2020].

Comparison simplified method vs reference method

- We compare simplified methods (M1, M2 and M3) to the reference method (three SPECT/CT acquisitions + tri-exponential function).
- We computed the percentage of dose difference (PDD):

$$PDD = \frac{(D_{Method} - D_{Reference}) \times 100}{D_{Reference}}$$

- For the M3 method, we use the leave-one-out method independently to each cohort.
- We use only cycles with three SPECT/CT acquisitions.

Validation results

- **M1 method vs Reference method (acquisition at 24H)**

	Left kidney	Right kidney	Liver	Spleen	L2 - L4	L1 - L5	T9 - L5
Mean ± Std	2.0 ± 14.0 %	1.5 ± 11.8 %	2.7 ± 9.9 %	9.0 ± 18.9 %	0.4 ± 4.8 %	-0.1 ± 5.6 %	0.2 ± 3.8 %

- **M2 method vs Reference method (acquisition at 24H)**

	Left kidney	Right kidney	Liver	Spleen	L2 - L4	L1 - L5	T9 - L5
Mean ± Std	0.7 ± 17.3 %	19.4 ± 32.3 %	2.1 ± 25.2 %	4.9 ± 20.7 %	9.4 ± 23.6 %	9.3 ± 21.1 %	4.1 ± 21.9 %

Validation results

- **M3 method vs Reference method (acquisition at 1H)**

	Left kidney	Right kidney	Liver	Spleen	L2 - L4	L1 - L5	T9 - L5
Mean ± Std	4.5 ± 21.6 %	7.7 ± 29.0 %	8.8 ± 33.0 %	9.0 ± 36.9 %	7.3 ± 27.4 %	4.3 ± 21.1 %	2.9 ± 19.9 %

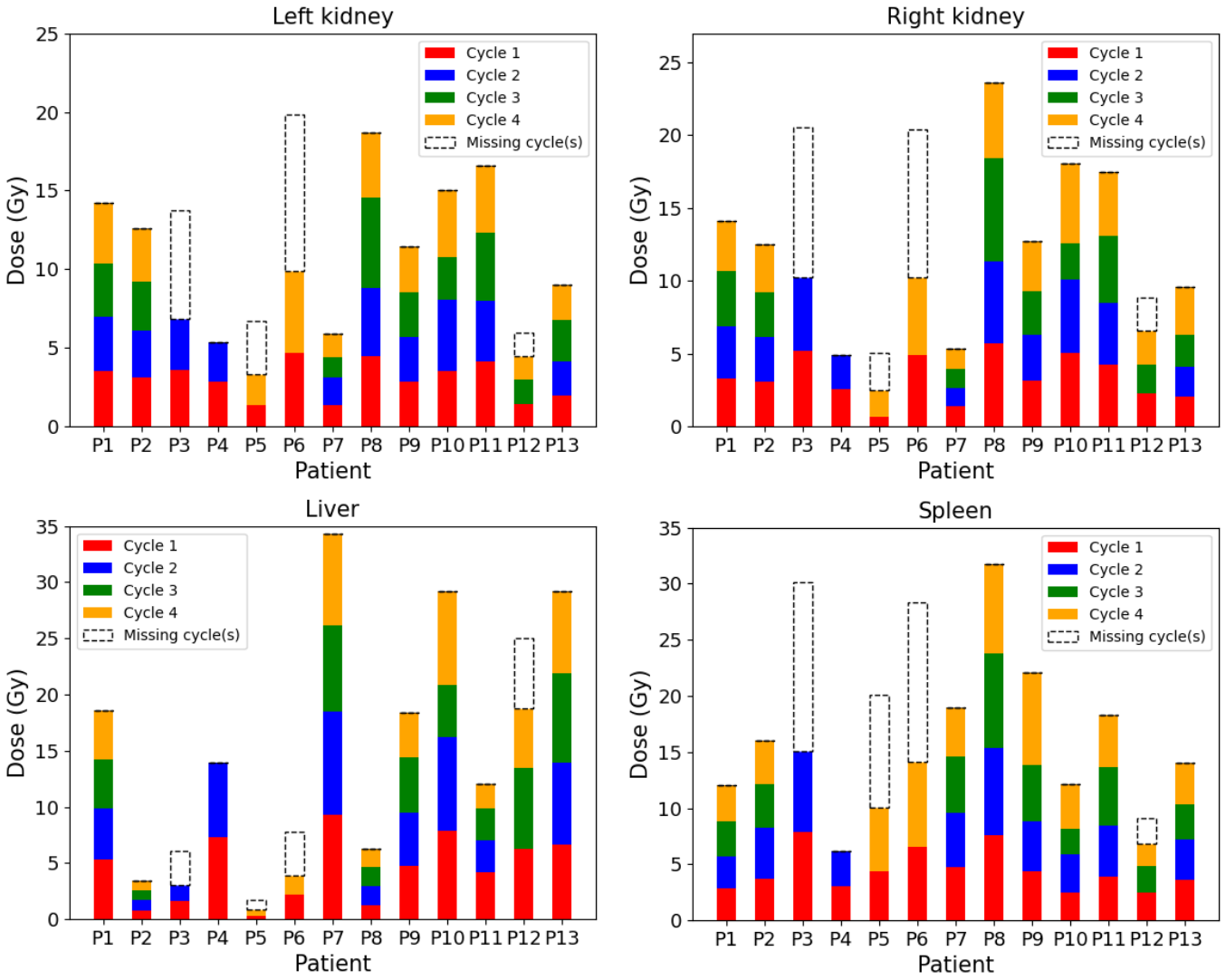
- **M3 method vs Reference method (acquisition at 24H)**

	Left kidney	Right kidney	Liver	Spleen	L2 - L4	L1 - L5	T9 - L5
Mean ± Std	1.3 ± 14.9 %	2.0 ± 15.8 %	3.9 ± 25.9 %	3.2 ± 20.9 %	-9.9 ± 23.3 %	-7.5 ± 19.8 %	-7.0 ± 20.0 %

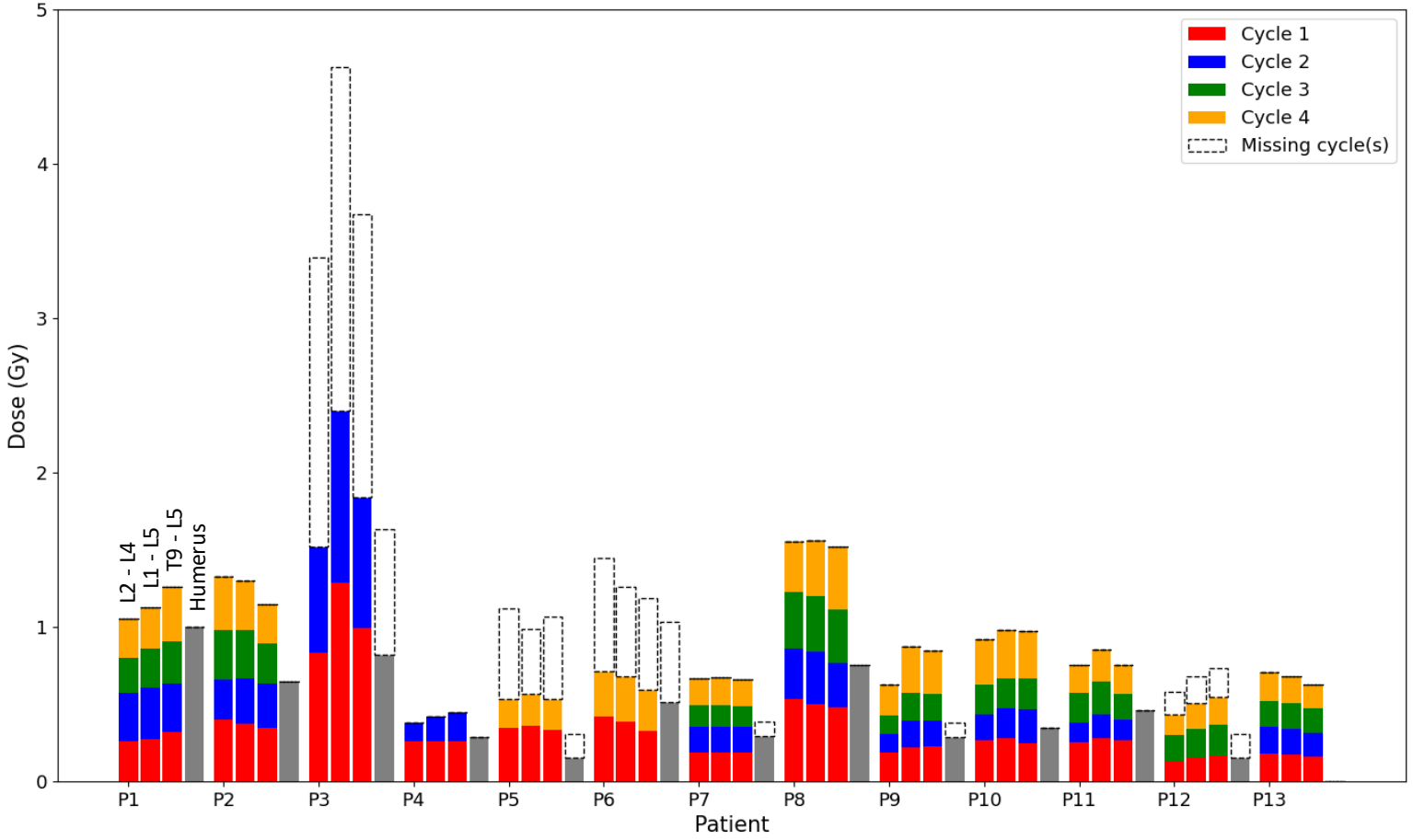
- **M3 method vs Reference method (acquisition at 7D)**

	Left kidney	Right kidney	Liver	Spleen	L2 - L4	L1 - L5	T9 - L5
Mean ± Std	5.3 ± 19.7 %	1.5 ± 11.3 %	6.8 ± 30.4 %	6.0 ± 29.6 %	0.2 ± 4.2 %	0.1 ± 4.1 %	0.1 ± 4.0 %

Dosimetric results (1)



Dosimetric results (2)



Conclusion

- A clinically applicable dosimetric workflow that adapts to the number of available SPECT/CT acquisitions has been implemented for organs at risk.
- This workflow allows to take into account the patient's physiology (one uptake phase and two elimination phases) as well as the cross-dose contribution (tumors).
- Several dosimetric methods have been evaluated.
- The dosimetric uncertainties depend on the number of SPECT/CT acquisitions and therefore on the dosimetric method used.
- This workflow may be applied in ^{177}Lu-PSMA therapy
- To be published in EJNMMI Physics (revised)

Acknowledgements

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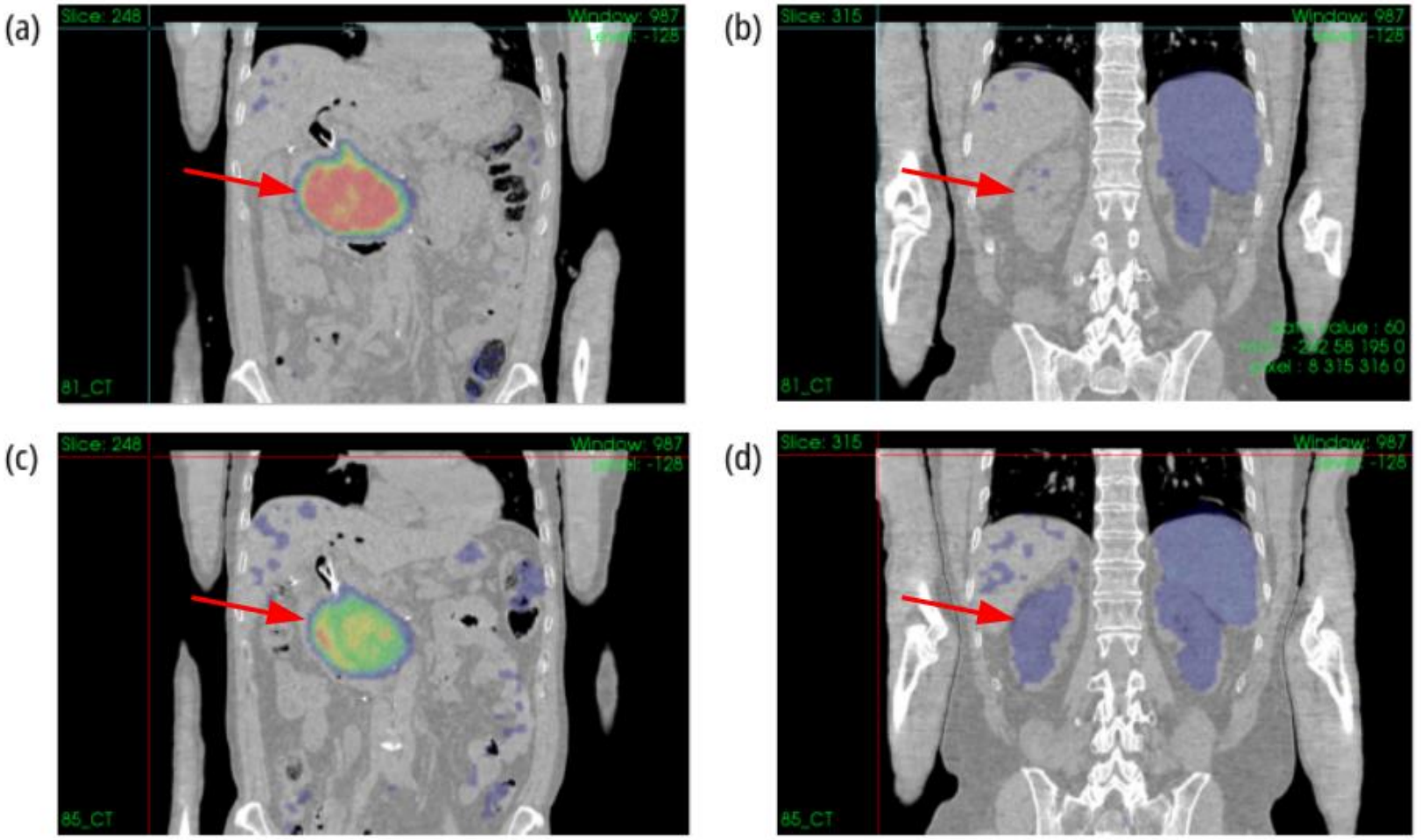
Appendix

Cross-dose contribution (1)



Cross-dose contribution (2)

	With lesion	Without lesion	Self-dose contribution	Cross-dose contribution
Left kidney	1390 mGy	1362 mGy	98 %	2 %
Right kidney	663 mGy	330 mGy	50 %	50 %
Liver	288 mGy	152 mGy	53 %	47 %
Spleen	4471 mGy	4283 mGy	96 %	4 %
L2-L4	352 mGy	15 mGy	4 %	96 %
L1-L5	361 mGy	18 mGy	5 %	95 %
T9-L5	337 mGy	24 mGy	7 %	93 %