2nd Symposium on Molecular Radiotherapy Dosimetry:
The future of theragnostics
November 13th - 15th 2025, Athens, Greece

Clinical Trials with Dosimetry

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Conflicts of Interest

- Katarina Sjögreen Gleisner has no COI
- Yuni Dewaraja is a consultant for Rayzebio (Bristol Myers Squibb), Novartis, MERIT CRO, GE Healthcare's MIM Software

Dosimetry in clinical trials

- *How* is dosimetry being incorporated in ongoing clinical trials (beyond dosimetry sub-study reporting) ?

- From Clinicaltrials.gov
  (data from the next presentation*: *N. Varmenot, J. Taprogge, G. Flux*)

- Aim: To get a feel for how dosimetry is evolving (curiousity, not systematic)
  - Therapies with ^{131}I, microspheres, ^{177}Lu and ^{161}Tb, alpha emitters

**Landscape of clinical trials in molecular radiotherapy, N. Varmenot*

Therapies with ^{131}I

- Differentiated thyroid cancer, remnant ablation: ^{123}I / ^{124}I / ^{131}I-NaI
  Recurrent medulloblastoma: ^{131}I-MAb

Among trial descriptions / outcome measures:

- Correspondence ^{124}I-predicted ADs and therapy ADs
- Dose-effect relationships (remnants, lesions, salivary glands, bone marrow)
- Proportion of patients with lesion AD $\geq$ 20 Gy (concomittant drug, ^{123}I-dosimetry)
- Patient stratification based on ^{124}I-PET:
  - to avoid remnant ablation of low-risk patients (randomized)
  - thyroid cancer: eligibility, predicted lesion ADs $\geq$ 20 Gy,
    blood AD $\leq$ 2 Gy, limited whole-body retention at 48 h

AD = Absorbed dose (Gy)

Therapy with microspheres

- ^{99m}Tc-MAA / ^{99m}Tc-HIDA / ^{90}Y, ^{166}Ho
- Hepatocellular carcinoma, metastatic colorectal cancer, renal cell carcinoma

Among trial descriptions / outcome measures:

- Correspondence ^{99m}Tc / ^{166}Ho - predicted and therapy ADs
- Dose-effect relationships (tumor, normal liver) based on predicted and therapy ADs
- Outcome individualised treatment based on predicted ADs

AD = Absorbed dose (Gy)

Therapies with ^{177}Lu and ^{161}Tb

- ^{68}Ga / ^{177}Lu, ^{161}Tb / ^{177}Lu
- SSTR-targeting, PSMA (incl. prior to prostatectomy), FAP-targeting, MAb, FAb, PDL1, angiogenesis, nanoparticles, etc, .. a broad range of indications

SSTR / PSMA, among trial descriptions / outcome measures:

- Compare ^{68}Ga prediction with therapy ADs
- Dose-effect relationship (tumors, kidneys, salivary glands)
- PSMA: AD to prostate and lymph nodes (before prostatectomy)
- SSTR ^{161}Tb / ^{177}Lu: AD ratio tumor / kidney, tumor / bone marrow (randomized)
- SSTR ^{177}Lu: Tumor AD in dosimetry-based vs standard treatment (randomized)

AD = Absorbed dose (Gy)

Therapies with alpha emitters

- ^{225}Ac, ^{111}In / ^{225}Ac, ^{68}Ga / ^{225}Ac, $^{203}Pb/^{212}Pb$
- MAb, PSMA, SSTR-targeting

- Mostly biodistribution / dosimetry sub-studies
- Maximum tolerated AD for kidneys ($^{203}Pb/^{212}Pb$)

AD = Absorbed dose (Gy)

Examples of Trials using Dosimetry in Study Design/Primary Objective

Dosimetry-guided α-PRRT and β-PRRT for GEP-NET (U-Iowa)

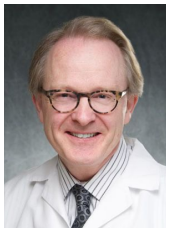
EFOMP


S. Graves

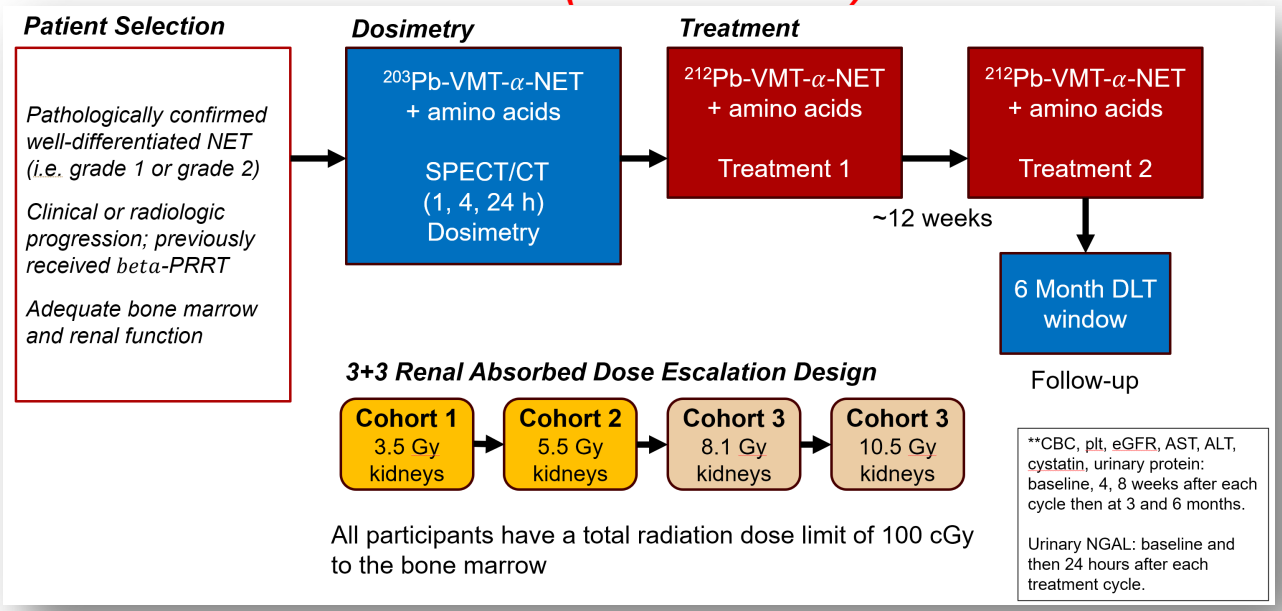

Y. Menda


M. Schultz

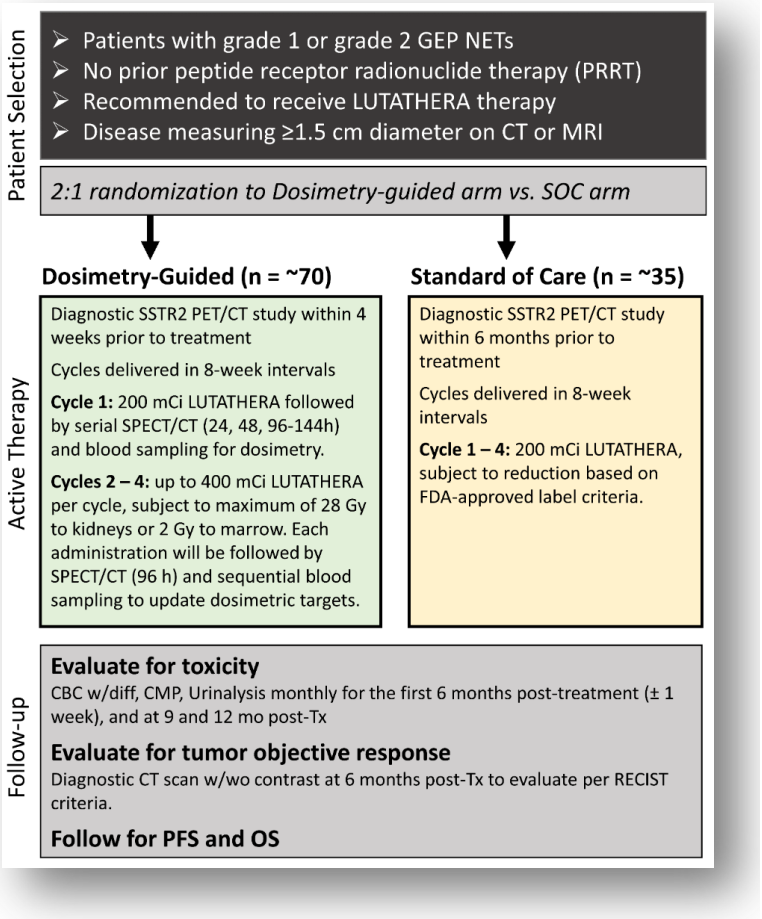

D. Bushnell


J. Dillon

[^{212}Pb] Pb-VMT-a-NET: Phase I renal absorbed dose escalation (NCT06148636)



[^{177}Lu] Lu-DOTATATE: Phase II randomized (SOC vs. dosimetry) (NCT06395402)



Courtesy of Stephen Graves, PhD University of Iowa

Randomized, controlled, single-blind pilot study of personalized vs. fixed-activity PSMA-RLT (PRODIGY-2)

CHU de Québec Université Laval

60 mCRPC post-ARPI patients:
30 pre-taxanes
30 post-taxane

- PSMA+ lesions
- no FDG+/PSMA- lesions
- stratified according to FDG+ burden

Randomization 1:1

Personalized ^{177}Lu-PSMA-617 (n=30):
6 cycles personalized activity q 6 wk.(max 22.2 GBq)
- 1st cycle: (0.07 x BSA x eGFR) GBq
- Cycles 2-6: 6 Gy / (prior cycle Gy/GBq)

C1 C2 C3 C4 C5 C6 EOT

^{177}Lu-QSPECT dosimetry (extended in ~15 patients)

24+48h 48h 48h 48h 48h 48h

C1 C2 C3 C4 C5 C6 EOT

Fixed-activity ^{177}Lu-PSMA-617 (n=30):
6 cycles x 7.4 GBq q 6 wk.
(cumulative prescribed activity of 44.4 GBq)

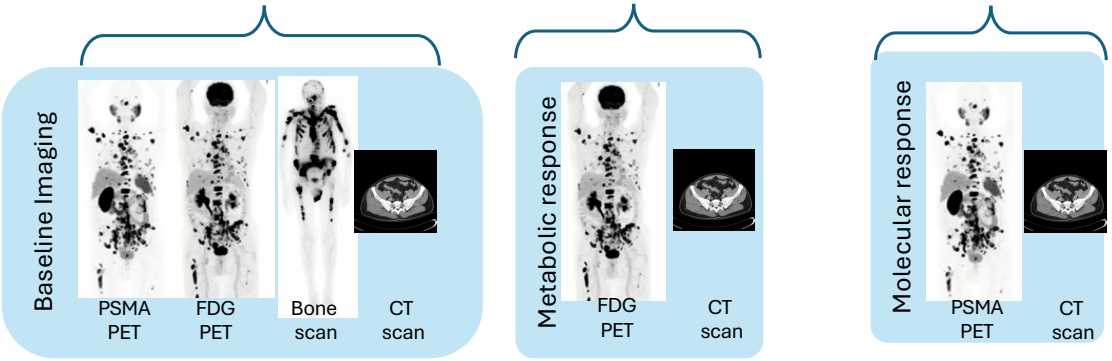
Week 1 7 13 19 25 31 37

Min 1-year follow-up from 1st cycle

PSA every 3 weeks until EOT, then every 6 weeks until progression

1ary endpoints:
- Cumulative injected activity
- Rate of Grade 3 hematological toxicity/DLT

2ary endpoints:
- PSA response
- PSA-PFS
- ORR
- rPFS
- OS
- HR-QOL
- Metabolic response at 12 wk. on FDG-PET
- Best PSMA response on QSPECT and PET

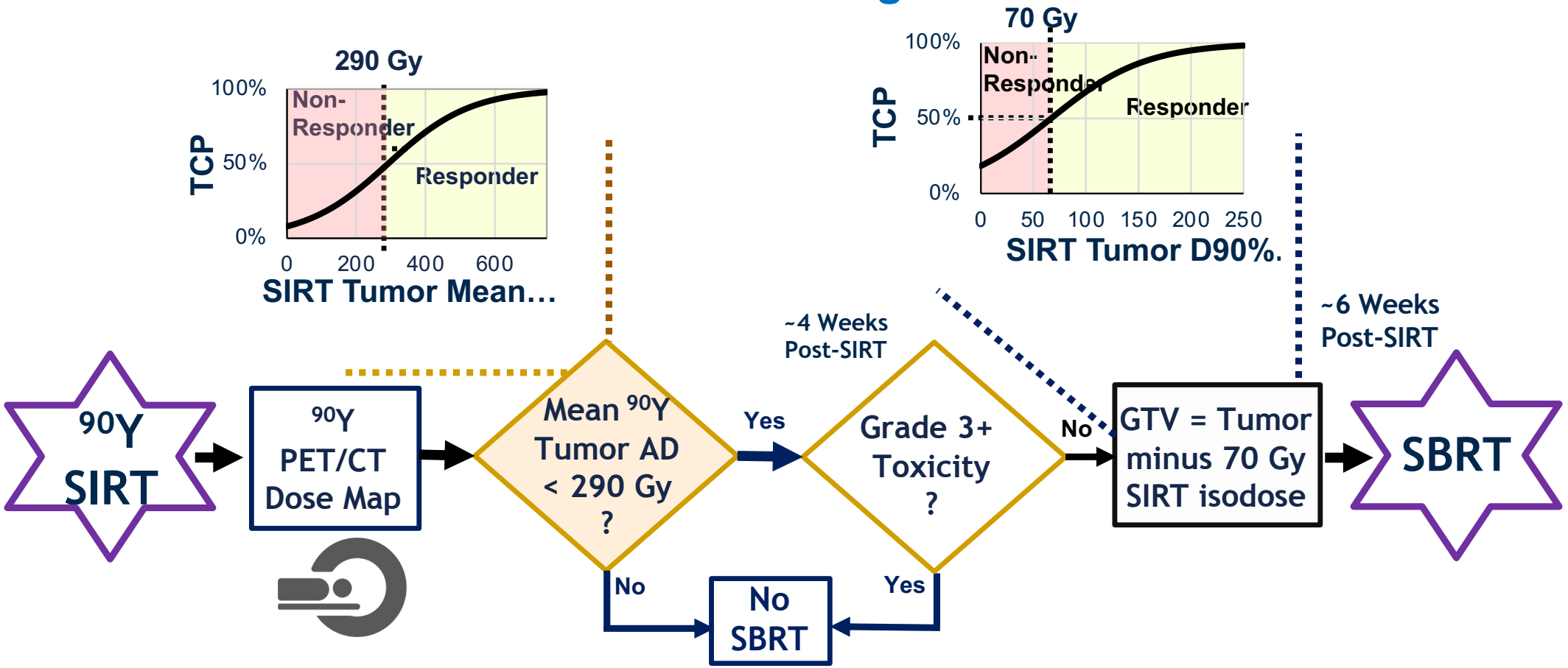


< 45 days from randomization @12 wk. @36 wk.

Courtesy of Jean-Mathieu Beauregard , MD

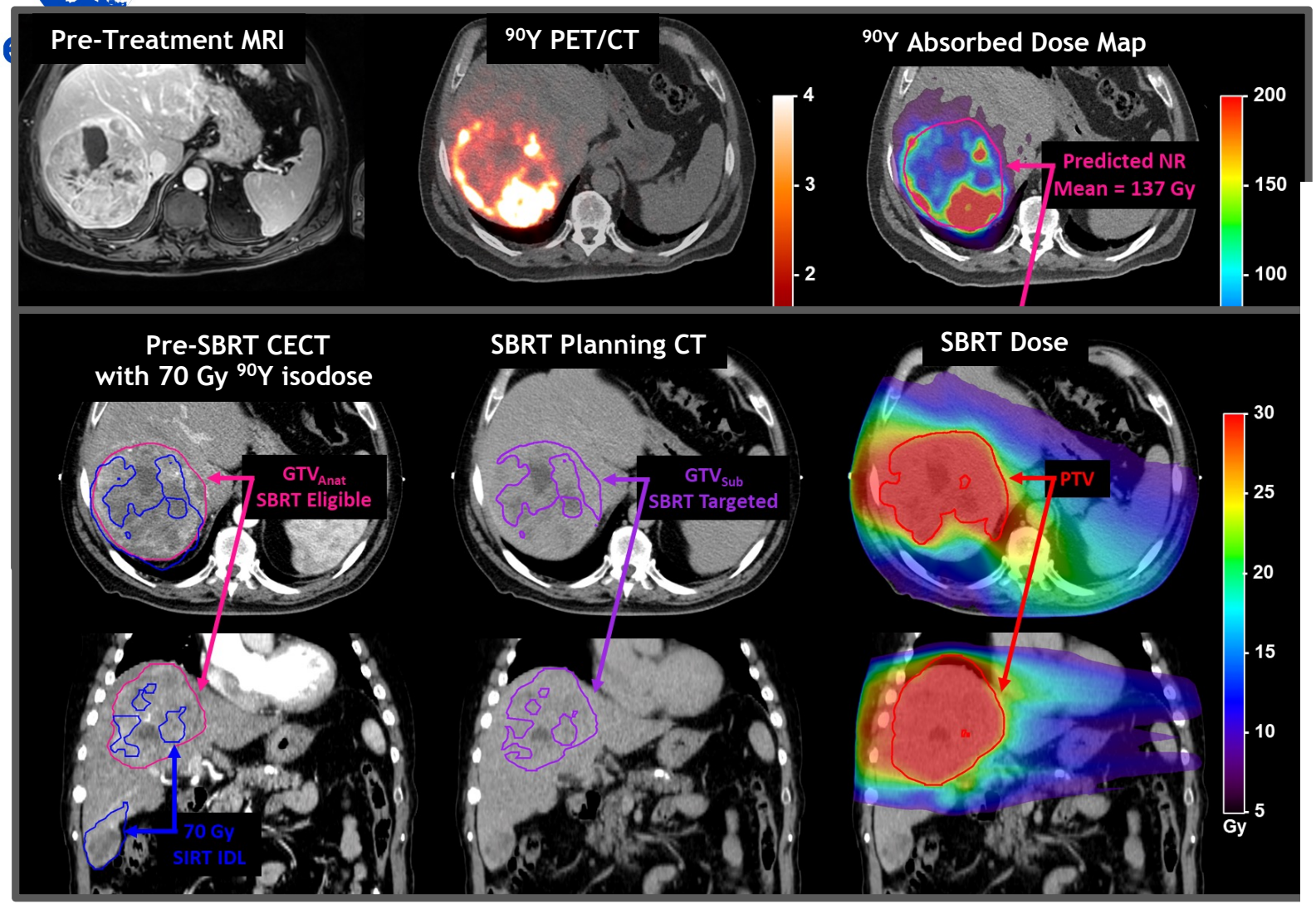
Université Laval

Novel use of Voxel Dosimetry: ^{90}Y SIRT+ Stereotactic Body Radiation Therapy Trial at Univ Michigan



Polan et al. Advances in Radiation Oncology, 2025, Volume 10, Issue 7, 101743

^{90}Y SIRT+SBRT Clinical Trial at U Mich: Patient Example

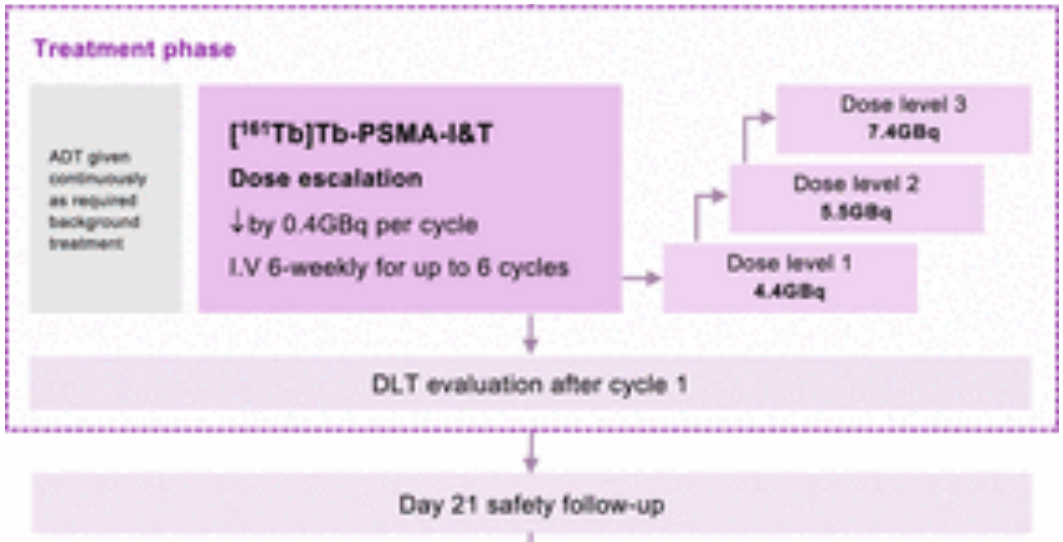


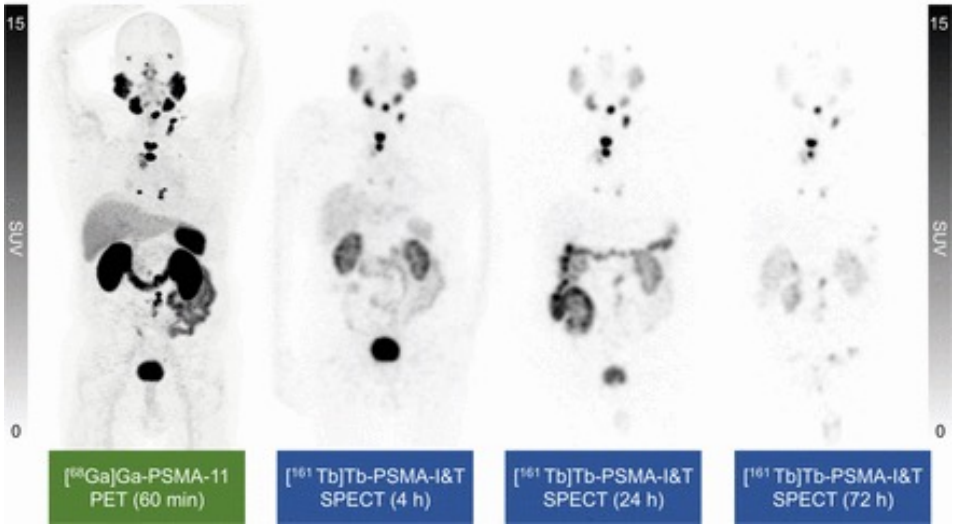
- Standard ^{90}Y SIRT
- ^{90}Y PET-Dosimetry
- Lesions with mean <
- Non-uniform SIRT AD due to blood supply?, necrosis?
- Select lesion sub-volume:voxels <70 Gy
- Standard SBRT (6 Gy x 5 Fx) to sub-volume
- Patient would not have met the mean liver absorbed dose toxicity constraints for SBRT alone

Examples of Trials Reporting Dosimetry – ‘Novel’ Radionuclides

Trial reporting dosimetry for RPT with ^{161}Tb (Auger + Conversion Electrons + Beta)

- **VIOLET Trial: First-in-human results of terbium-161 [^{161}Tb]Tb-PSMA-I&T in mCRPC (Peter MacCallum Cancer Centre, Australia**





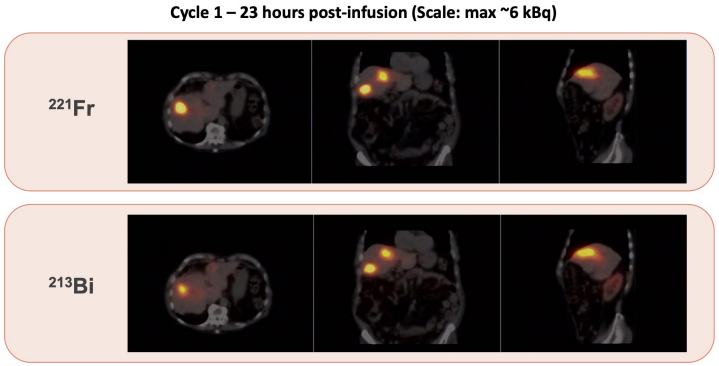
	Gy/GBq
Parotid	0.15 (0.07)
Kidney	0.36 (0.11)

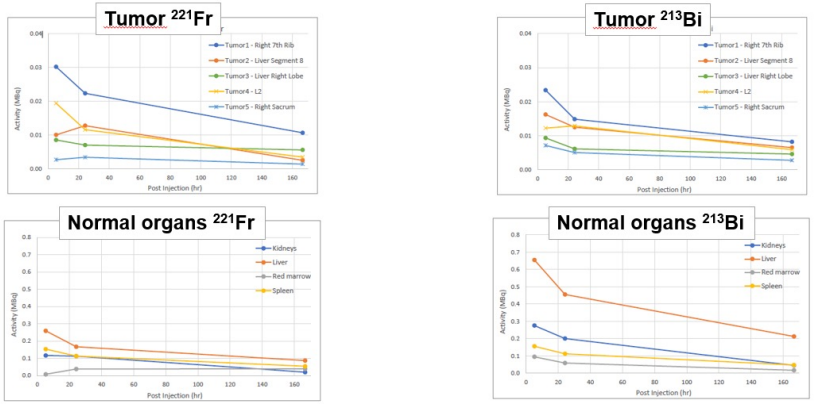
Buteau et al. JNM July 2024, DOI: https://doi.org/10.2967/jnumed.124.267650

Buteau et al. Lancet Oncol. 2025 Aug;26(8):1009-1017.

ACTION 1: ^{225}Ac-DOTATATE for GEP-NETs (RayzeBio)

- Global, randomized, Phase 1b/3 trial comparing RYZ101 to standard-of-care in patients with GEP-NETs that have progressed following ^{177}Lu-labelled PRRT
- Dosimetry sub study to determine feasibility by imaging ^{225}Ac daughters





In general, there was comparable activity of ^{221}Fr and ^{213}Bi in the tumor; however, in the kidneys and liver there was slightly greater ^{213}Bi activity than ^{221}Fr

	AD (RBE=5) across 4 cycles Mean (Gy)
Tumors	71 to 112
Kidneys	21.2
Liver	18.5
Red Marrow	1.2
Spleen	36.0

Recommended RYZ101 dose for Phase 3 is 10.2 MBq × 4 cycles

Sgouros et al, Journal of Nuclear Medicine June 2023, 64 (supplement 1) P129;

Clinical Trial using ^{211}At PSMA-5 in Prostate Cancer (U Osaka, Japan)

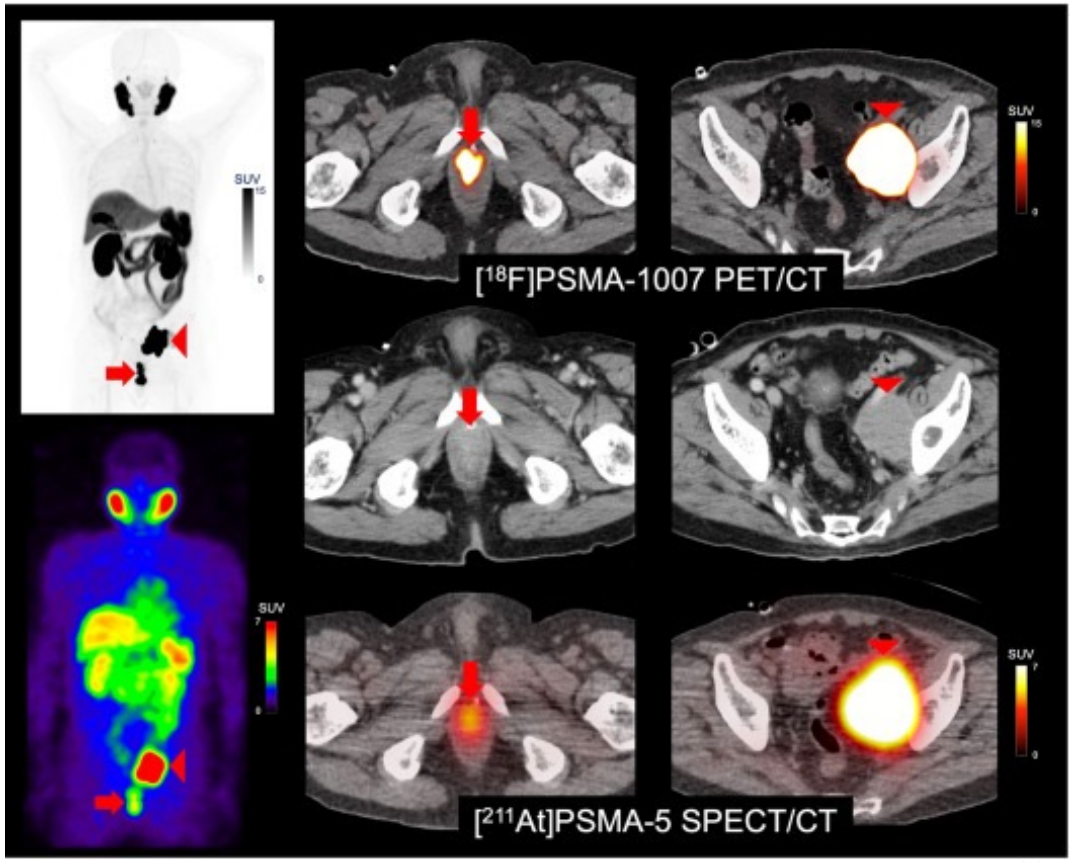
European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-024-07017-w

IMAGE OF THE MONTH

First-in-human SPECT/CT imaging of [^{211}At]PSMA-5: targeted alpha therapy in a patient with refractory prostate cancer

Tadashi Watabe[1,2] · Koji Hatano[3] · Sadahiro Naka[4] · Hidetaka Sasaki[5] · Takashi Kamiya[5] · Yoshifumi Shirakami[2] · Atsushi Toyoshima[2] · Jens Cardinale[6] · Frederik L. Giesel[2,6] · Kayako Isohashi[1] · Norio Nonomura[3] · Noriyuki Tomiyama[1,2]

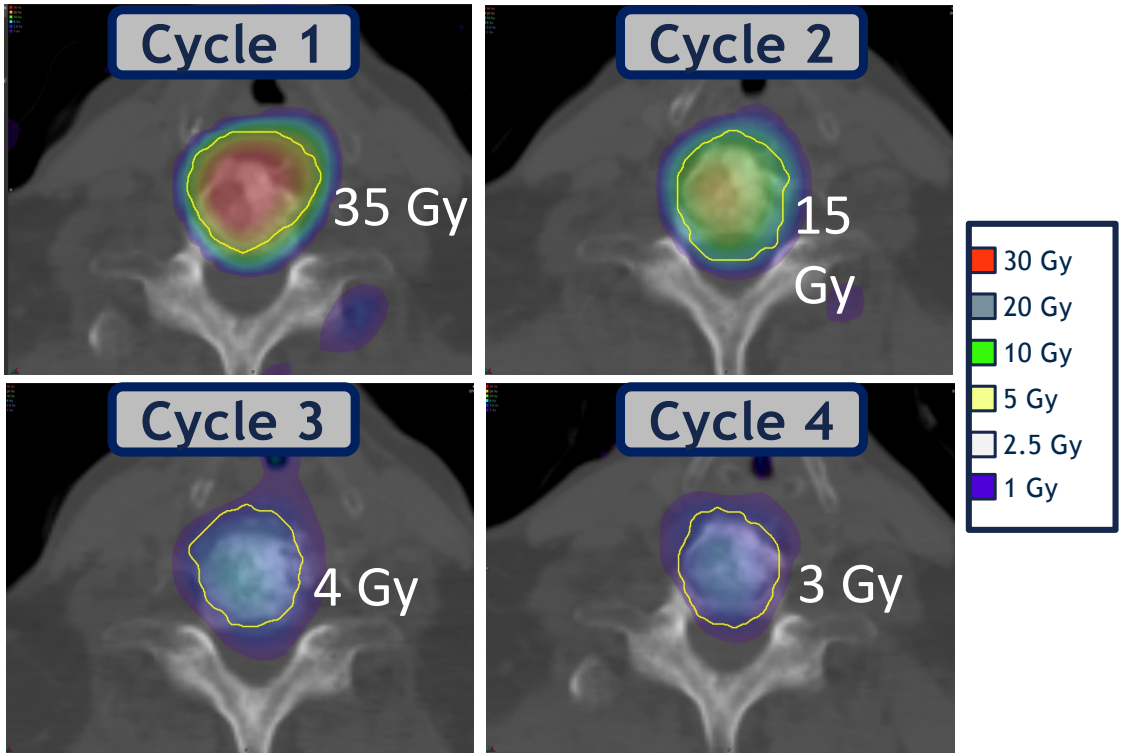
- To evaluate its tolerability, safety, pharmacokinetics, absorbed dose, and efficacy, as well as to determine the recommended dose for Phase II.
- SPECT/CT imaging (79 keV X-rays) performed 3 hours post using a VERITON-CT equipped with a full-ring CZT detector



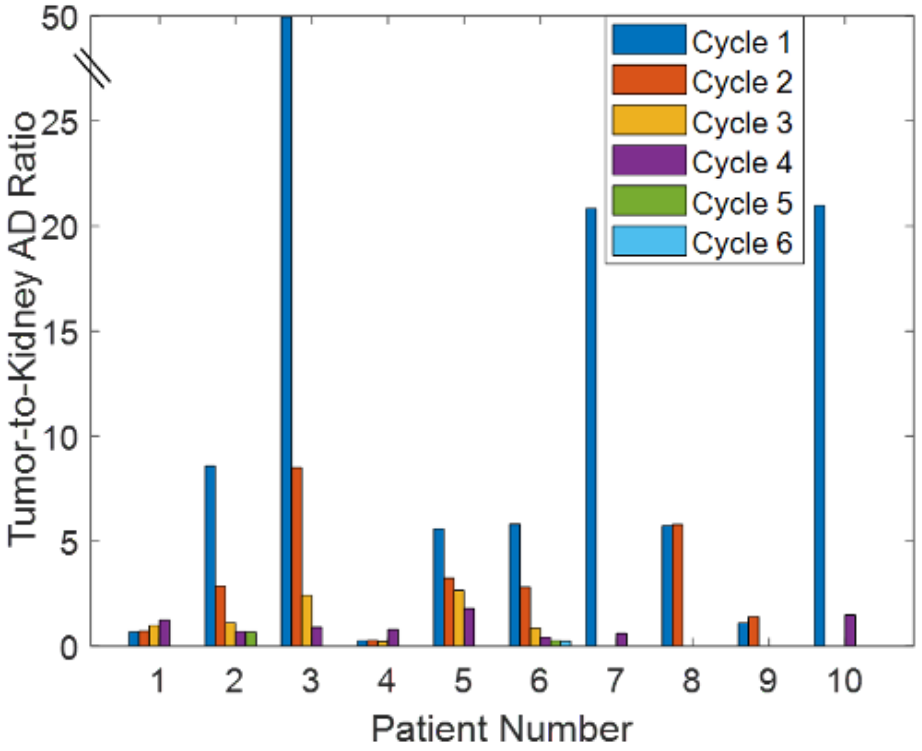
Example of RPT Trials Motivated by Dosimetry

^{177}Lu PSMA Michigan Data: Drop in Tumor Absorbed Dose with Cycle

- Absorbed dose map showing drop in tumor AD despite fixed activity per cycle

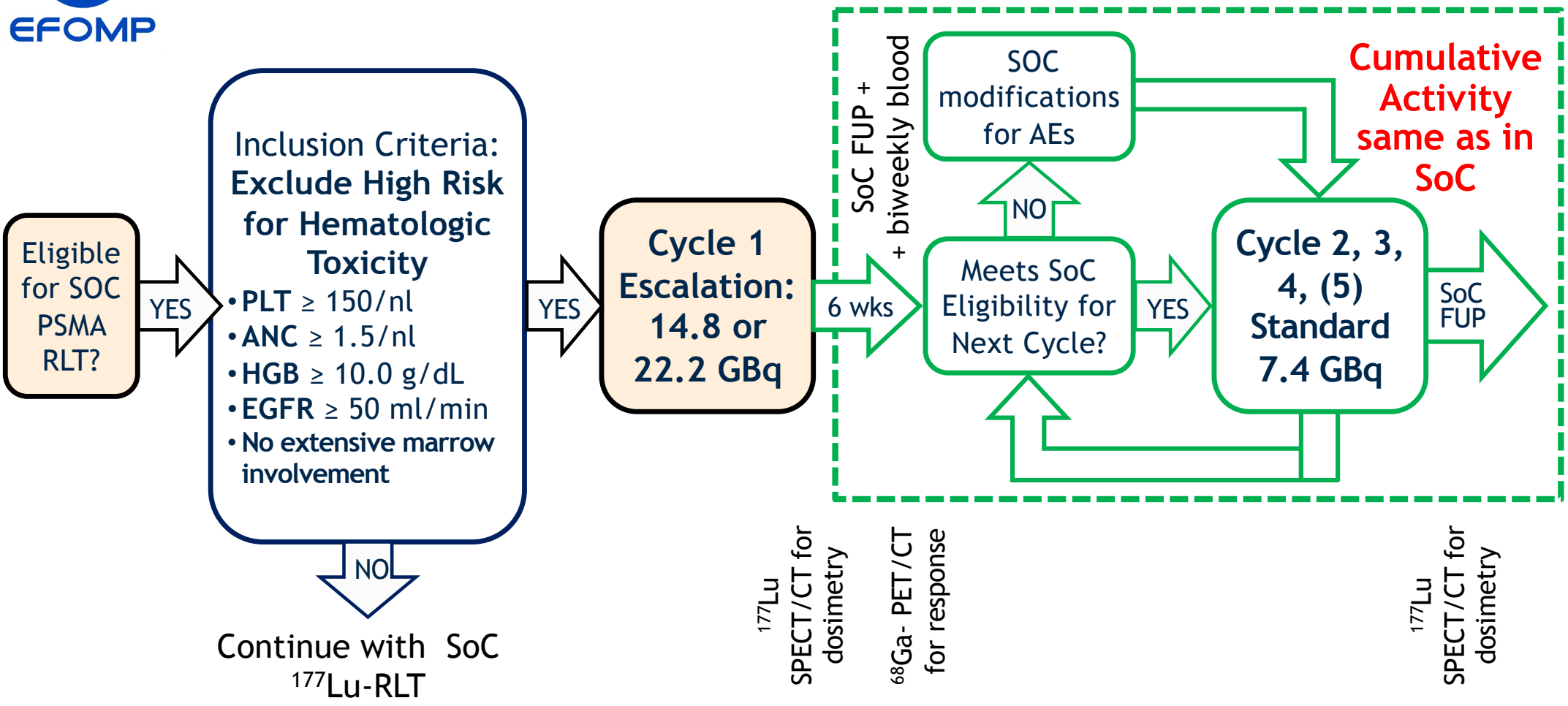


- Organ ADs remained stable across cycles
  - Drop in tumor-to-kidney AD ratio



Fitzpatrick et al. International Journal of Radiation Oncology, Biology, Physics (Red Journal)2025

Design ^{177}Lu-PSMA-617 Cycle 1 Dose Escalation Trial at Michigan

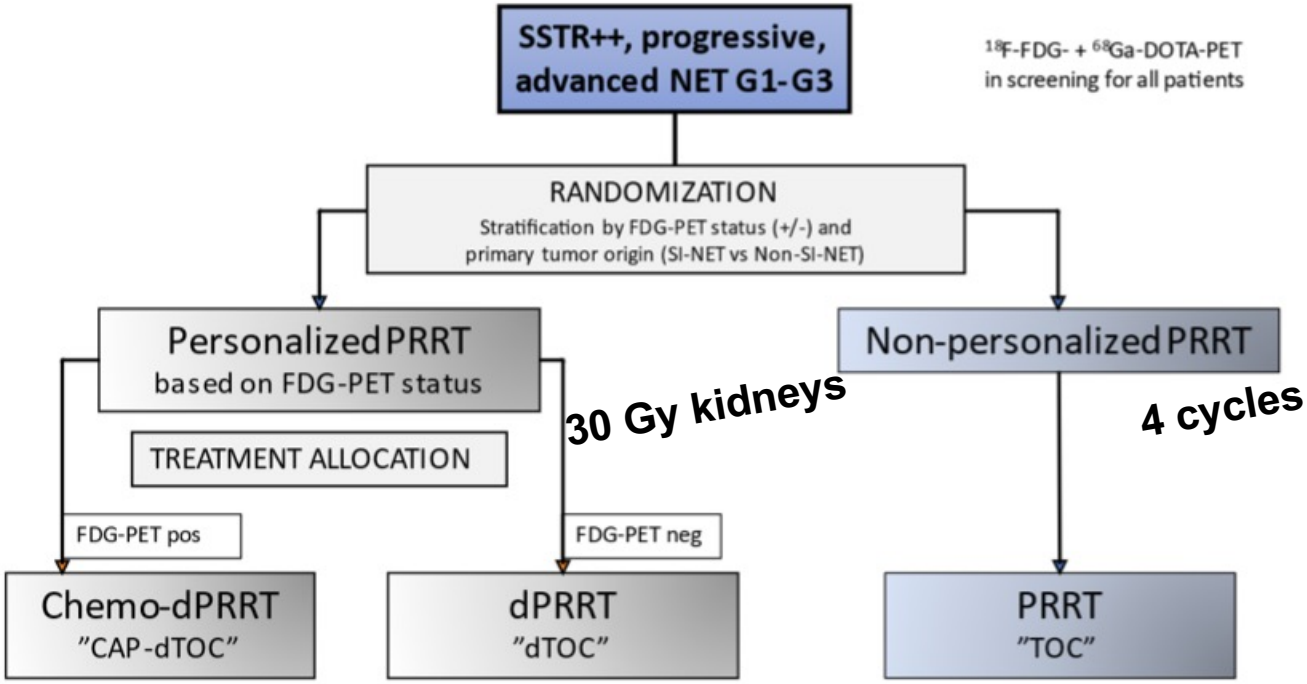


Multicenter clinical trial START-NET (Sweden)

- Randomized phase-III
- Metastatic NET
- ^{177}Lu-DOTA-TOC

- 4 hospitals:
  Lund (PI), Uppsala,
  Gothenburg, Stockholm

- Kidney dosimetry



TOC: 4 x 7.5 GBq ^{177}Lu-DOTATOC. Cycle interval 10 ± 2 weeks

dTOC: X cycles of 7.5 GBq ^{177}Lu-DOTATOC to a renal AD ≤ 30 Gy. Cycle interval 10 ± 2 weeks

CAP-dTOC: 4 x 7.5 GBq ^{177}Lu-DOTATOC + CAPECITABINE, followed by X cycles of 7.5 GBq ^{177}Lu-DOTATOC to a renal AD ≤ 30 Gy. Cycle interval 10 ± 2 weeks

Radiation protection legislations

- In Sweden, each center has its own legal responsibility for dosimetry. Especially important when treatment is dosimetry-guided.

- *The hospital that owns license to treat, also has responsibility to ensure that the exposure is justified, and that procedures are optimised.*
  Includes responsibility for methods used for radioprotection, i.e. dosimetry.
- *Applies to all patients, including those participating in clinical trials.*

SFS 2018: 306; Health and Safety 2024: 896; Almén and Frank 2022

Achieving comparability in kidney ADs

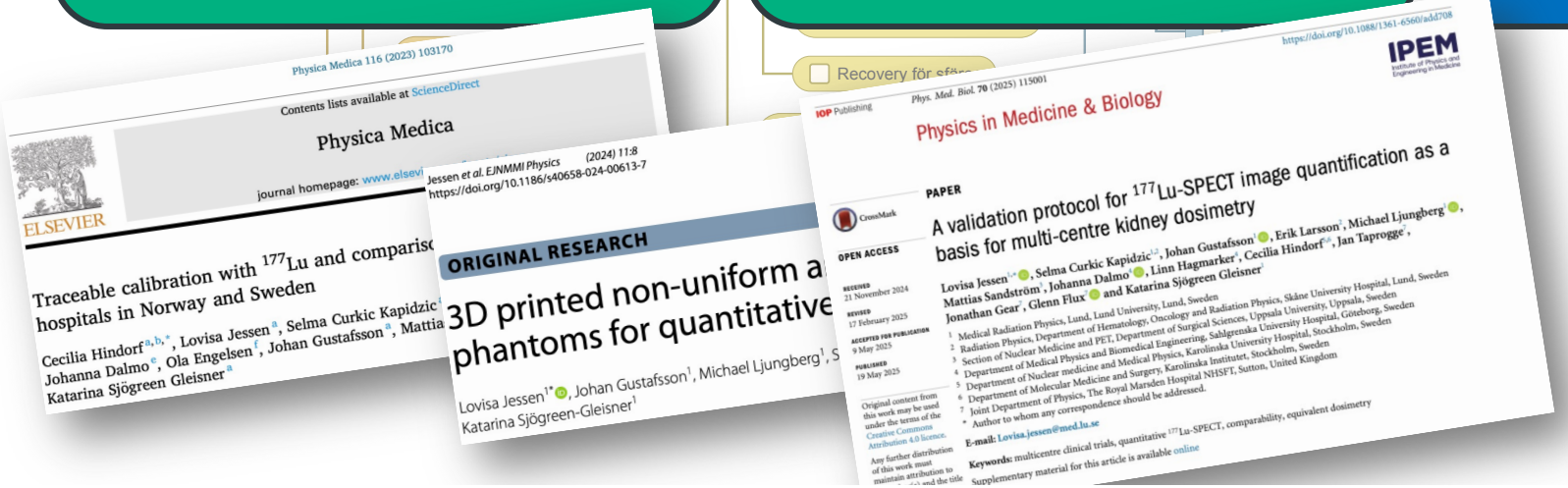
START-NET dosimetry

Aktivitetsmätare | Fantommätningar 1 | Simulerade bilder 1 | Fantommätningar 2 | Simulerade bilder 2 | Patientdosimetri

^{177}Lu radionuclide calibrators vs secondary standard

Quantitative SPECT acceptance test (kidney phantoms)

Dosimetry patient data & MC simulations



- Recovery för sfär...
- LUSEC-instruktioner + film
  - Box // START_NET_all // LUSEC //
- Var 10:e patient (patient 1, 11 osv) Cykel 1
  - Bilder till LUSEC
    - Rekonstruerad SPECT
    - CT
  - Jämförande dosimetri mellan sites

Conclusions

- Dosimetry is being incorporated as an important element in clinical trials

- Comparison of pre-therapy and therapy ADs
- Monitoring therapy ADs, AD ratios (also as trial endpoint)
- Patient stratification
- AD-effect relationships (tumor, tissues at risk)
- Treatment outcome for dosimetry-based personalisation

- Though, still mostly phase 1 cohort-average biodistribution and dosimetry (non-personalised) → maximum tolerated administered activity

We are on our way! Thank you for your attention!

Abstract	1st Author	Title
48	Nicolas Varmenot, St Herblain, France	Landscape of clinical trials in molecular radiotherapy
47	Jan Taprogge, Sutton, UK	INSPIRE – A prospective observational study of radiation dosimetry for radioiodine treatment of thyroid cancer
69	Carlo Chiesa, Milan, Italy	^{124}I PET dosimetry to optimize ^{131}I therapy of metastatic differentiated thyroid cancer: an ongoing phase II trial
5	Matteo Bagnalasta, Milan, Italy	Radioembolization of hepatocellular carcinoma with ^{90}Y glass microspheres: an earlier administration day unexpectedly improves tumour control probability
118	Meike W.M. van Wijk, Nijmegen, The Netherlands	MRI-based dosimetry for image-guided ^{166}Ho-TARE, insights in methodology and preliminary results from the EMERITUS-2 trial
76	Frida Westerbergh, Gothenburg, Sweden	Development of Terbium-161 SPECT/CT Protocols in Support of Two Early-Phase Clinical Trials: Towards Accurate Post-Therapeutic Dosimetry
114	Claudia Morsink, Nijmegen, The Netherlands	Dosimetry comparison of [^{177}Lu]Lu-rhPSMA-10.1 and [^{177}Lu]Lu-PSMA-617 in prostate cancer patients
46	Peter Frøhlich Staanum, Aarhus, Denmark	Standard vs. kidney dosimetry-based activity prescription in PRRT: Current status of the DOBATOC trial
127	Monika Kvassheim, Oslo, Norway	Tumour-to-kidney absorbed dose ratios for potential alpha-emitter DOTATATE therapies
84	Georgios Limouris, Athens, Greece	PRRT Efficacy of ^{111}In-DTPA-Octreotide Auger and Internal Conversion Electron Emission after Intra-arterial Implementation in Liver Metastasized Colorectal NETs