



HÔPITAL UNIVERSITAIRE
DE BRUXELLES
ACADEMISCH ZIEKENHUIS
BRUSSEL



Personalized dosimetry for simulation and treatment in SIRT with ^{166}Ho -PLLA - A single-center pilot feasibility study to bright the way

Benoît Collette ¹, Ana-Maria Bucalau ², Nicola Trotta ¹, Gontran Verset ², Martina Pezzullo ³, Illario Tancredi ³, Fadi Tannouri ³, Rodrigo Moreno-Reyes ¹

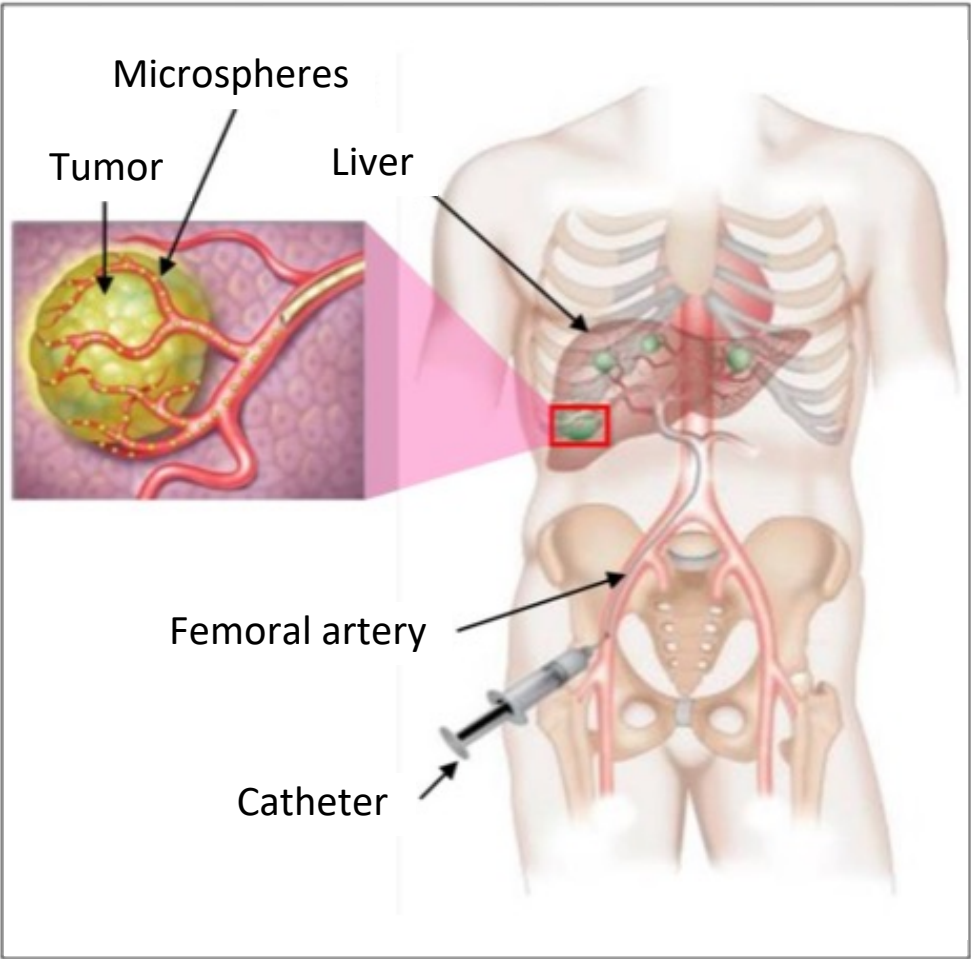
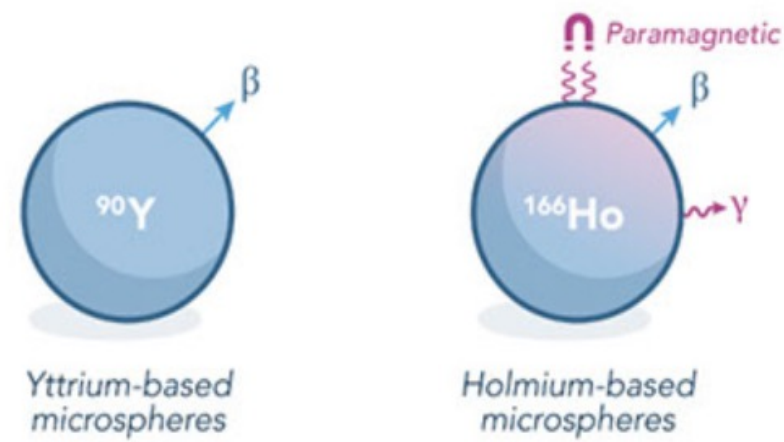
¹ Department of Nuclear Medicine, HUB Hôpital Erasme - ULB, ² Department of Gastroenterology, HUB Hôpital Erasme - ULB, ³ Department of Radiology, HUB Hôpital Erasme - ULB



Introduction

- How it works

	QuiremSpheres®	
Isotope	Holmium-166	Y -90
Beta-radiation (E _{max})	1.77 MeV (48.7%) 1.86 MeV (50.0%)	2.28 MeV
Gamma-radiation	81 keV (6.7%)	-
Visible on MRI	Yes	No
Half-life	26.8 hours	64.1 hours
Material	poly(L-lactic acid)	resin (r) or glass (g)
Diameter	15-60 µm	20-60 µm (r) 20-30 µm (g)
Density	1.4 g/cm ³	1.6 g/cm ³ (r) 3.3 g/cm ³ (g)



M. Smits et *al.*, 2010 : n particles ~ 33 x 10⁶ (¹⁶⁶Ho-PLLA), 50 x 10⁶ (⁹⁰Y-resin) and 4 x 10⁶ (⁹⁰Y-glass)



State of the art

- Reproducibility
 - M. Smits *et al.*, 2019

^{99m}Tc -MAA procedure had to be repeated because of extra-hepatic activity, only the most recent ^{99m}Tc -MAA data were used for analysis. No vessels were coil-embolized after the final ^{99m}Tc -MAA procedures. On the day of treatment, patients underwent a second treatment-planning procedure in the morning. During this procedure, the injection position(s) from the first treatment planning procedure was mimicked and patients received a scout dose of 250 MBq of ^{166}Ho -microspheres (approximately 3 million microspheres). At the end of the procedure, the catheter and microcatheter were removed.

European Journal of Nuclear Medicine and Molecular Imaging
<https://doi.org/10.1007/s00259-019-04460-y>

ORIGINAL ARTICLE



The superior predictive value of ^{166}Ho -scout compared with ^{99m}Tc -macroaggregated albumin prior to ^{166}Ho -microspheres radioembolization in patients with liver metastases

Maarten L. J. Smits¹ • Mathijs G. Dassen¹ • Jip F. Prince¹ • Arthur J. A. T. Braat¹ • Casper Beijst¹ • Rutger C. G. Bruijnen¹ • Hugo W. A. M. de Jong¹ • Marnix G. E. H. Lam¹

Received: 6 May 2019 / Accepted: 23 July 2019
© The Author(s) 2019

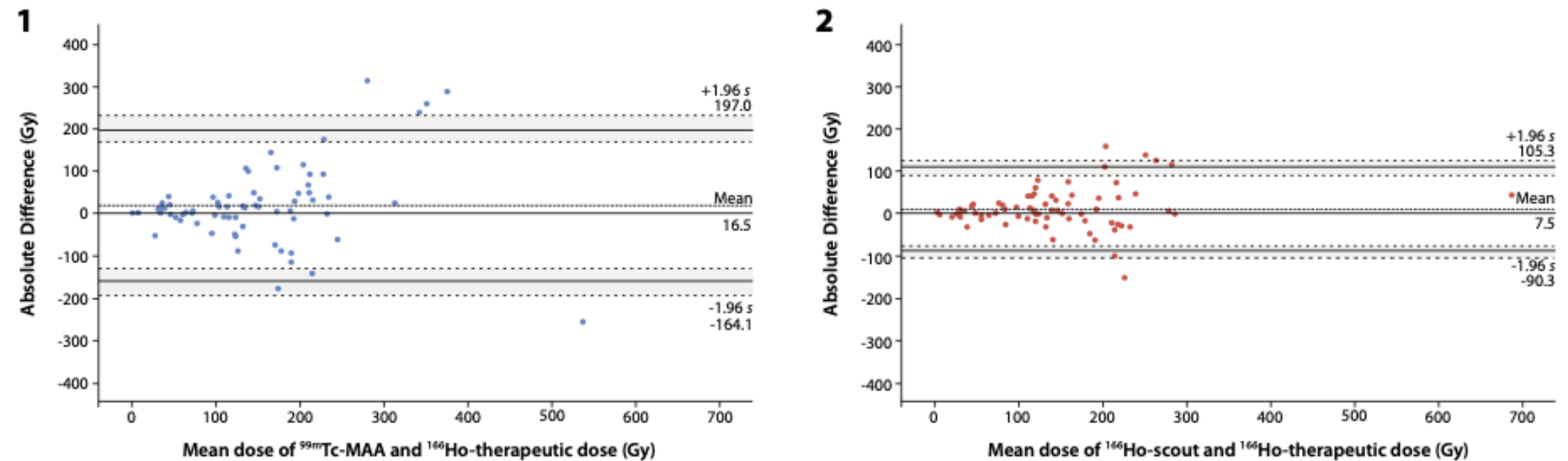


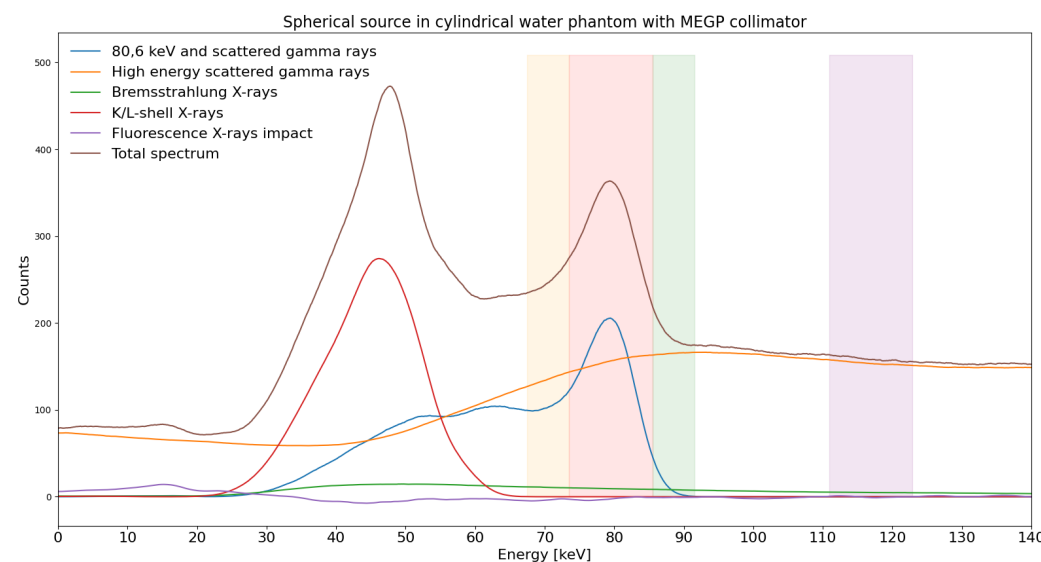
Fig. 5 Bland-Altman plots for lesion analyses. (1) Difference between ^{99m}Tc -MAA and ^{166}Ho -therapeutic dose activity in each lesion is plotted against mean activity in each lesion. (2) Difference between ^{166}Ho -scout and ^{166}Ho -therapeutic dose activity in each lesion is plotted against mean

activity in each lesion. The 95% limits of agreement (LoA) are indicated and surrounded by two dotted lines indicating the standard error of the 95% LoA



Aim

- EANM 2022 : « *Ho 166 - a Way to Bright the Future* », R. Sciuto
 - Courtesy of R. Sciuto
 - Reproducibility
 - Quantitative imaging
 - SPECT scatter correction



Ho 166 – a Way to Bright the Future

R. Sciuto

SIRT – An Example of
Successful Clinical Dosimetry

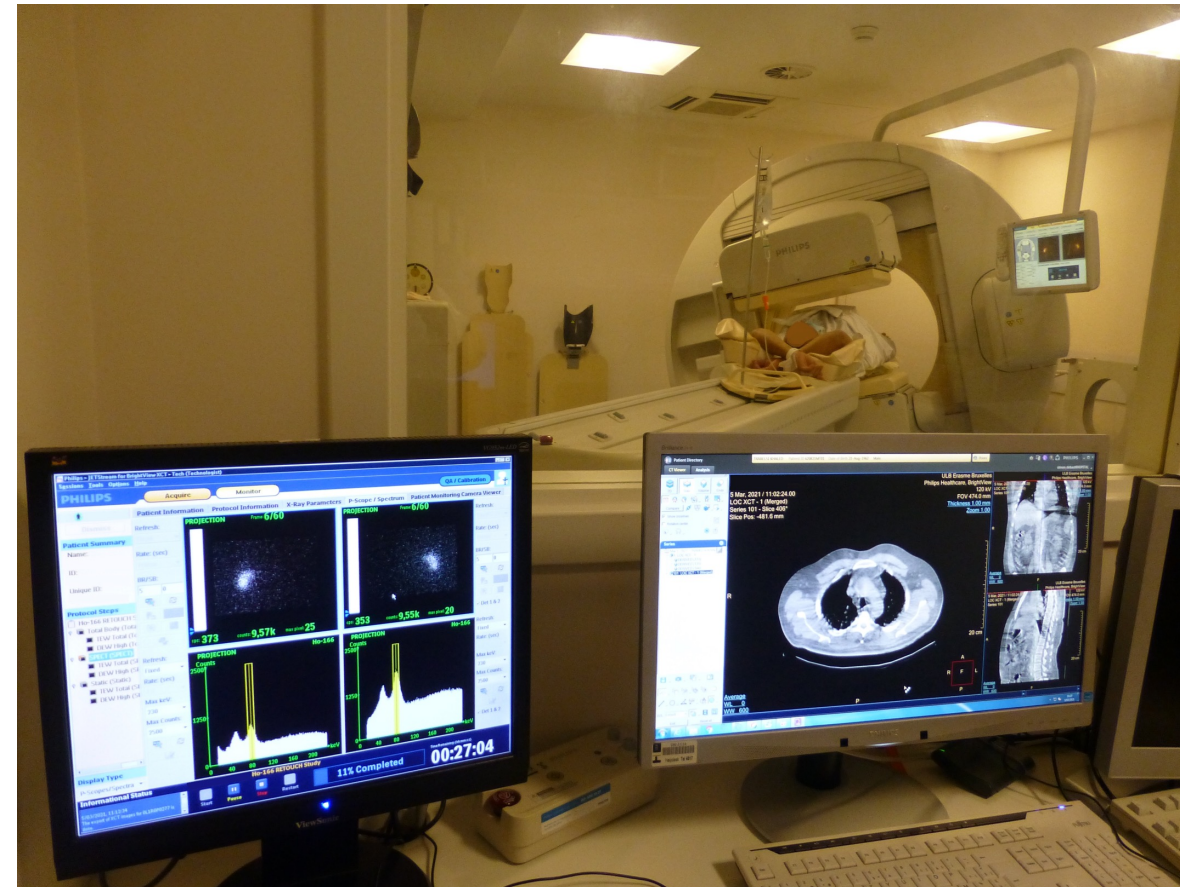
CONCLUSIONS

Given that:

- ➔ **Accurate imaging detection** of spheres distribution in target /non target tissue **is critical** for a quantitative assessment of the dose deposition
- ➔ **Voxel based dosimetry** is **mandatory** to evaluate heterogeneous radioactive microspheres intrahepatic distribution
 - **¹⁶⁶Ho** allows an accurate quantitative imaging by SPECT /CT, due to low abundance of primary gamma radiation, and MRI due to its paramagnetic property
 - **¹⁶⁶Ho Scout** dose reproduces more accurately post-treatment ¹⁶⁶Ho spheres biodistribution allowing for a fairly accurate predictive dosimetry using the certified Ho-platform

Materials and methods

- Feasibility study with (multi-)compartmental pre- and post-treatment dosimetry
 - 21 simulations using ^{166}Ho -PLLA scout and 21 treatments using ^{166}Ho -PLLA (1 week later)



Recommendations

- EANM 2022 : « *Ho 166 - a Way to Bright the Future* », R. Sciuto
 - Courtesy of R. Sciuto
- Quirem[®] guidelines
 - Thresholds for HCC
 - Efficacy : $D_T > 150$ Gy
 - Safety : $D_{NTL} < 50$ Gy
- High targeting ?
 - 150 Gy min in 90 % V_T
- High safety ?
 - 50 Gy max in 90 % V_{NTL}

Ho 166 – a Way to Bright the Future

R. Sciuto

SIRT – An Example of Successful Clinical Dosimetry

What is the STATE OF THE ART ?

European Journal of Nuclear Medicine and Molecular Imaging (2022) 37:1682–1699 1691

Table 4 Absorbed dose recommendations for ¹⁶⁶Ho microspheres and the respective level of evidence (LOE)

Clinical scenario	One-compartment		Multi-compartment		LOE
	Perfused volume dose	LOE	Whole normal liver dose	Tumour dose	
HCC					
Segmentectomy	60	3	Not applicable	Not applicable	4
Lobectomy	60	3	< 60	> 150*	3–4
Unilobar	60	3	< 60	> 150*	3–4
Bilobar	60	3	< 40*** [96]	> 150* [96]	3–4
ICC					
Segmentectomy	60	3	Not applicable	Not applicable	3
Lobectomy	60	3	< 60	> 90** [97]	3
Unilobar	60	3	< 60	> 90** [97]	3
Bilobar	60	3	< 40***	> 90** [97]	3
mCRC					
Segmentectomy	60	3	Not applicable	Not applicable	3
Lobectomy	60	3	< 60	> 90** [97]	3
Unilobar	60	3	< 60	> 90** [97]	3
Bilobar	60	3	< 40***	> 90** [97]	3

LOE, level of evidence
 *Based on median tumour absorbed dose for stable disease in a mixed population
 **Based on 100% sensitivity for response
 ***Up to 60 Gy in patients with more favourable liver function

the first steps towards multicompartiment models have been made and **threshold doses were suggested** for CRC and other tumors (non HCC)

but **prospective more robust studies** are ongoing to better define dose -relationship in various tumors and disease setting

First Evidence for a Dose-Response Relationship in Patients Treated with ¹⁶⁶Ho Radioembolization: A Prospective Study

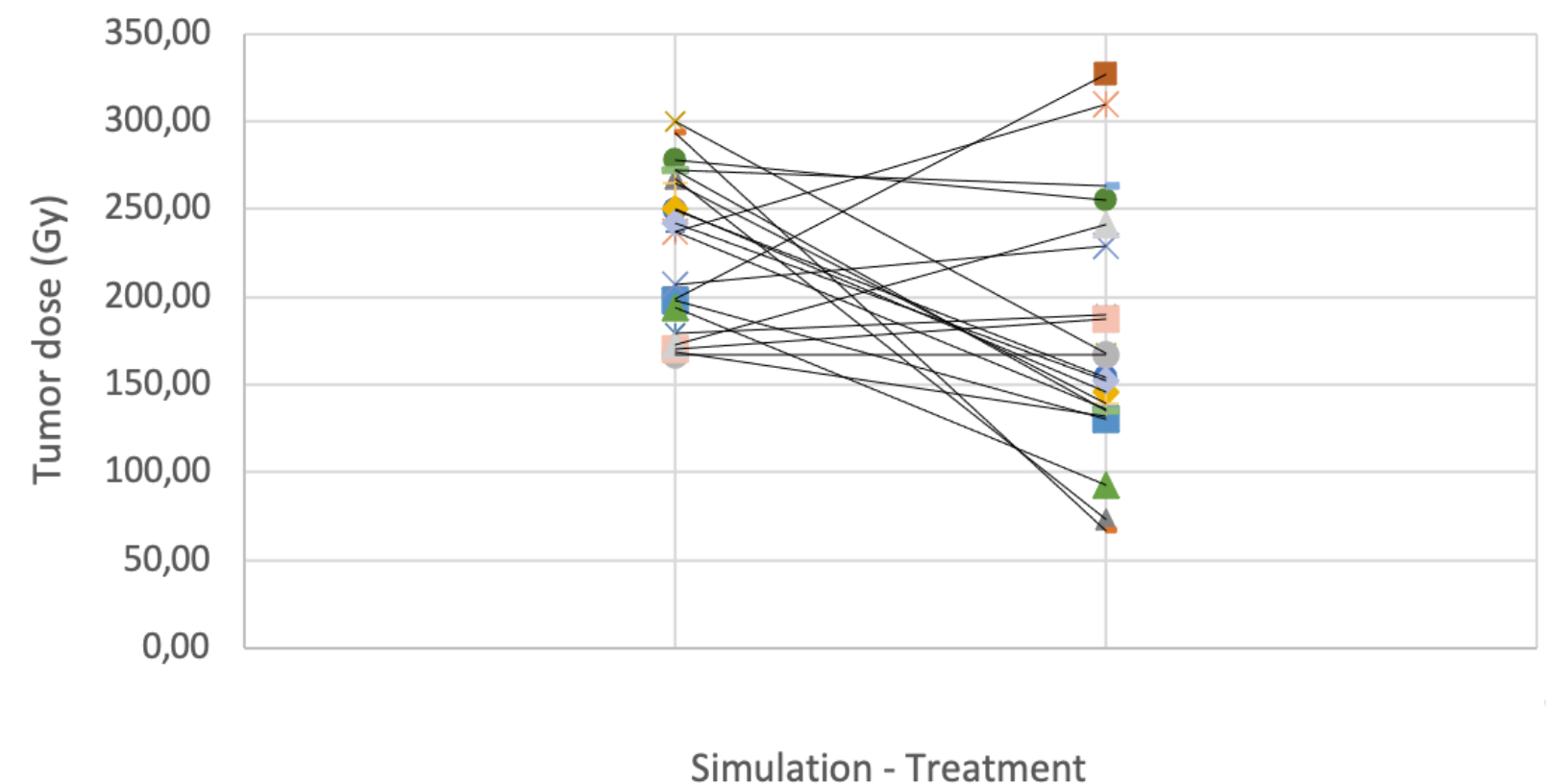
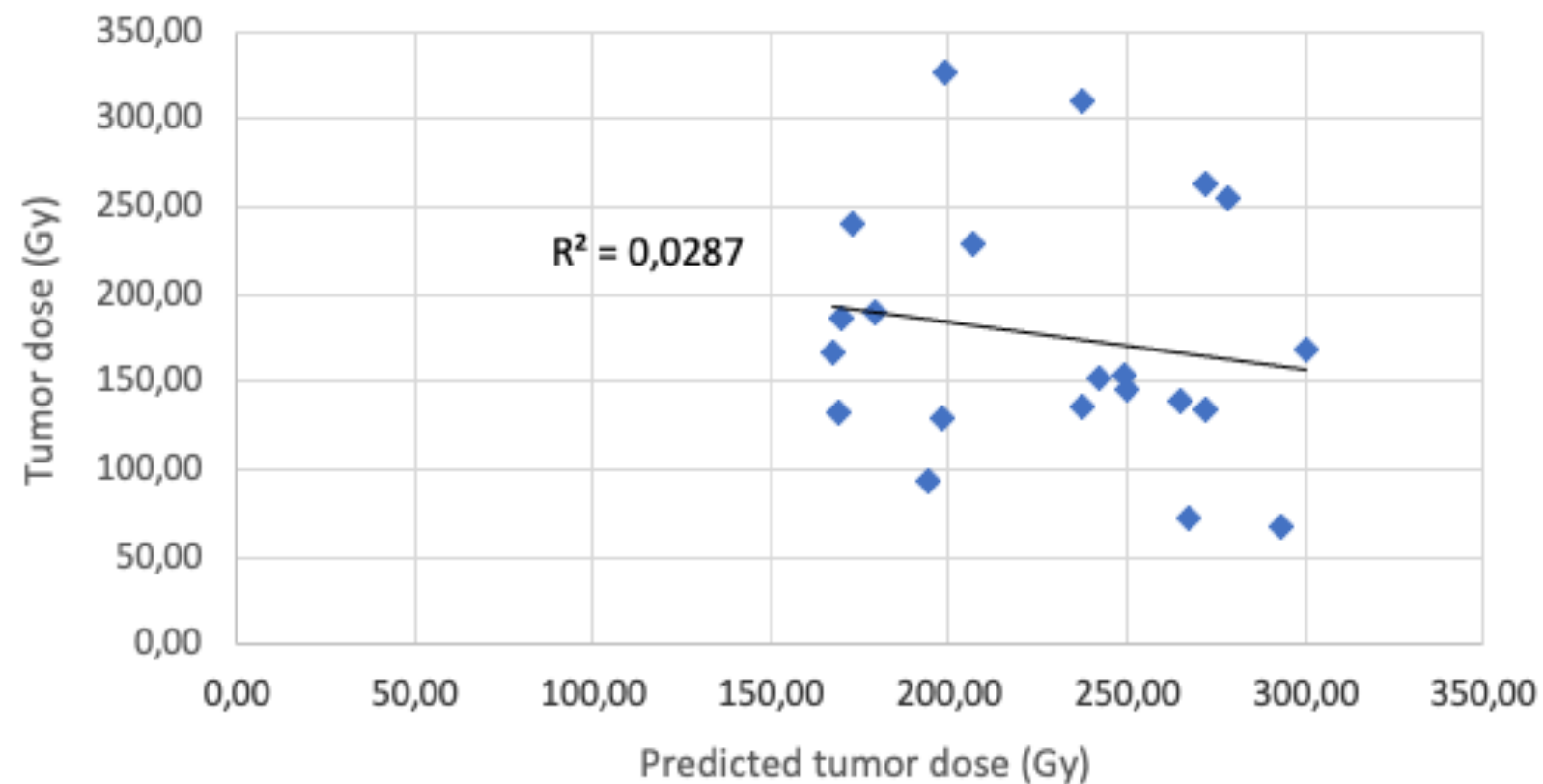
Remco Bastiaannet*, Caren van Roekel*, Maarten L.J. Smits, Sjoerd G. Elias, Wouter A.C. van Amsterdam, Dan Doan, Jip F. Prince, Rutger C.G. Bruijnen, Hugo W.A.M. de Jong, and Marnix G.E.H. Lam
 University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

Dose-Effect Relationships of ¹⁶⁶Ho Radioembolization in Colorectal Cancer

Caren van Roekel*, Remco Bastiaannet*, Maarten L.J. Smits, Rutger C. Bruijnen, Arthur J.A.T. Braat, Hugo W.A.M. de Jong, Sjoerd G. Elias, and Marnix G.E.H. Lam
 University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

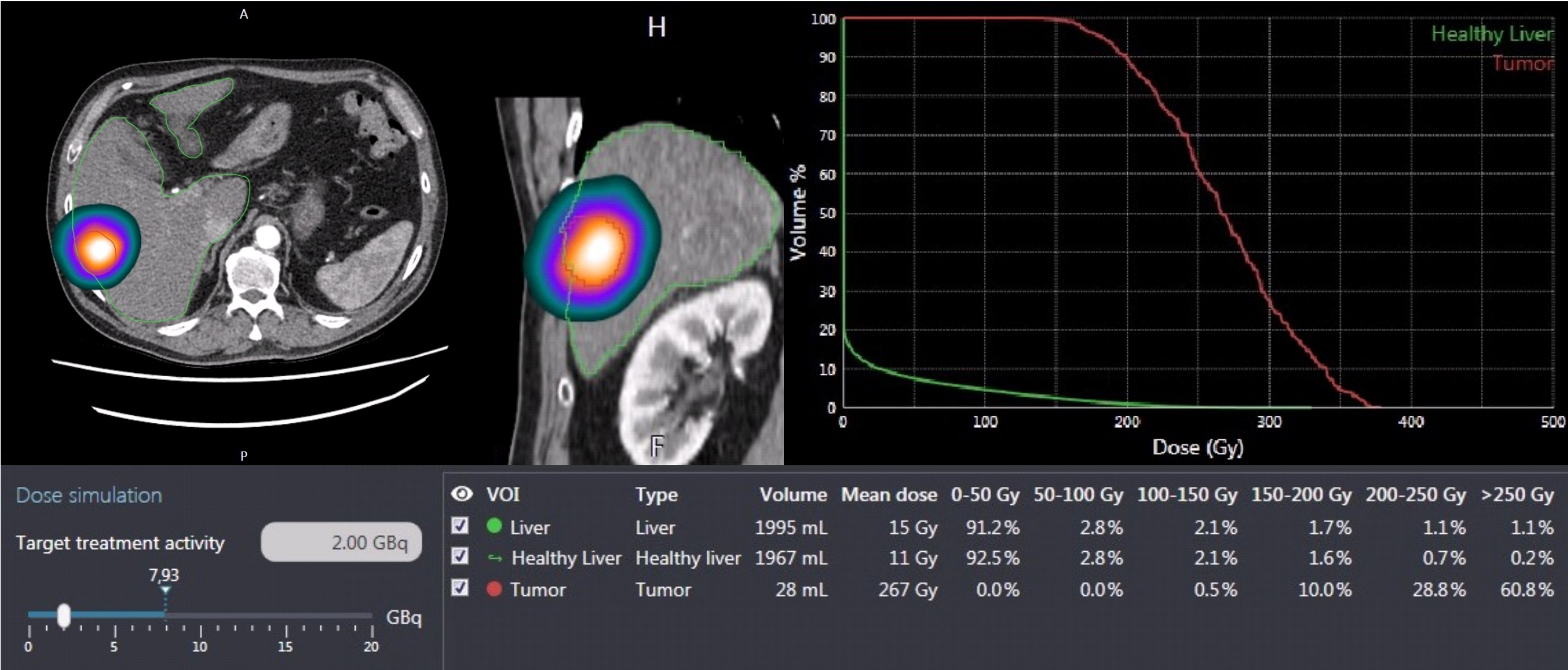
Results

- Poor reproducibility using ^{166}Ho -PLLA scout for simulation
 - Tumor dose more than 20 % lower than predicted tumor dose in 10 cases
 - Tumor dose more than 20 % higher than predicted tumor dose in 3 cases



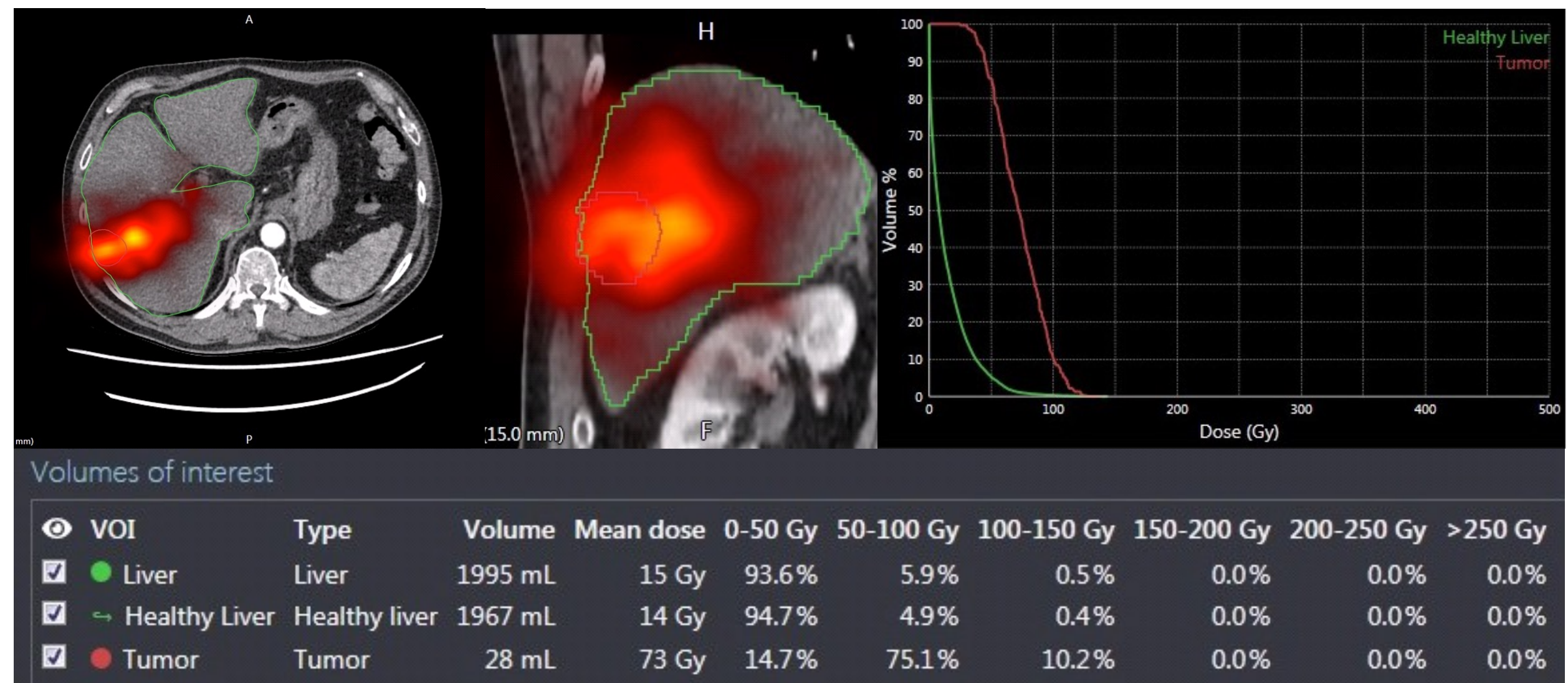
Simulation example

- Patient 3 : a 63 y.o. male with 1 HCC (28 cm³) in segment VII
 - ¹⁶⁶Ho-PLLA scout predictive dosimetry



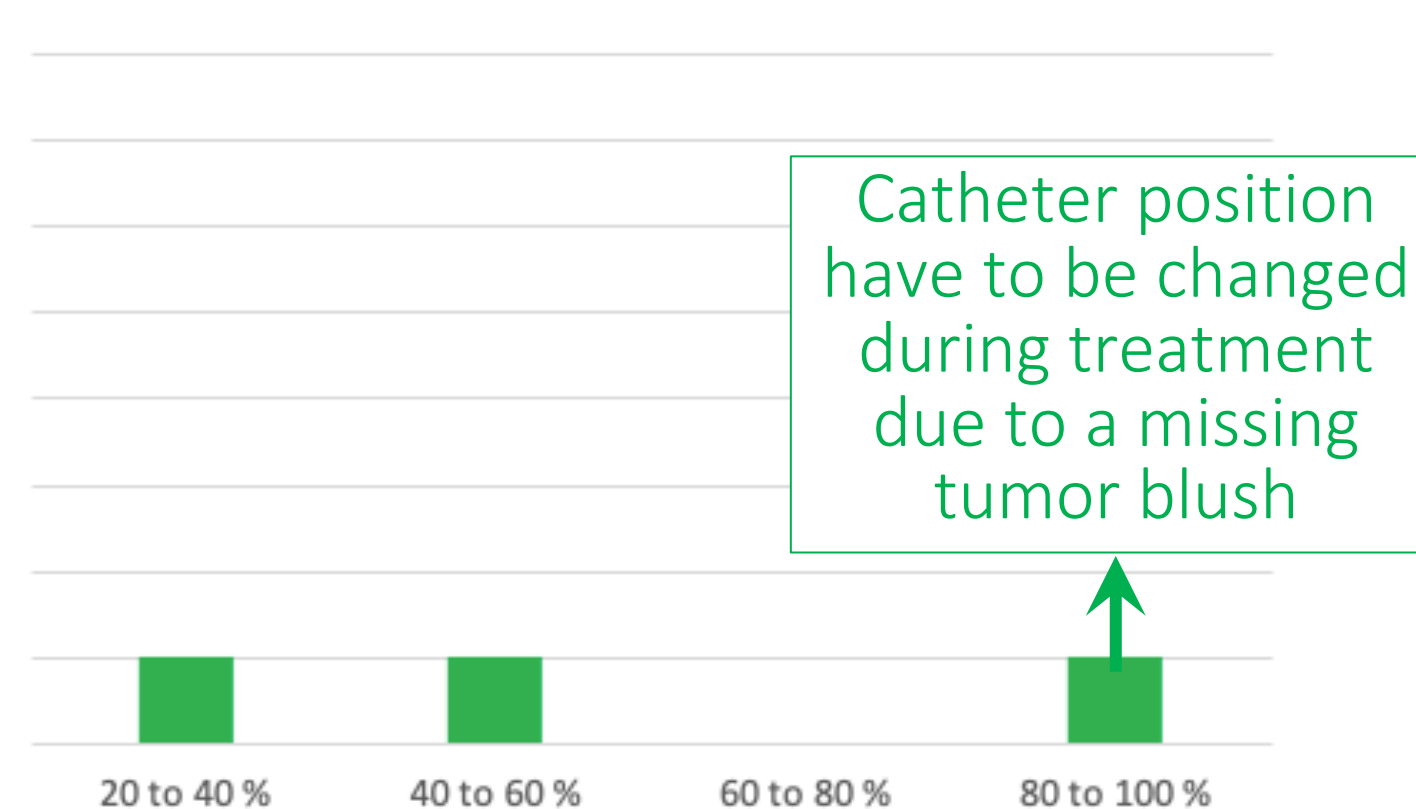
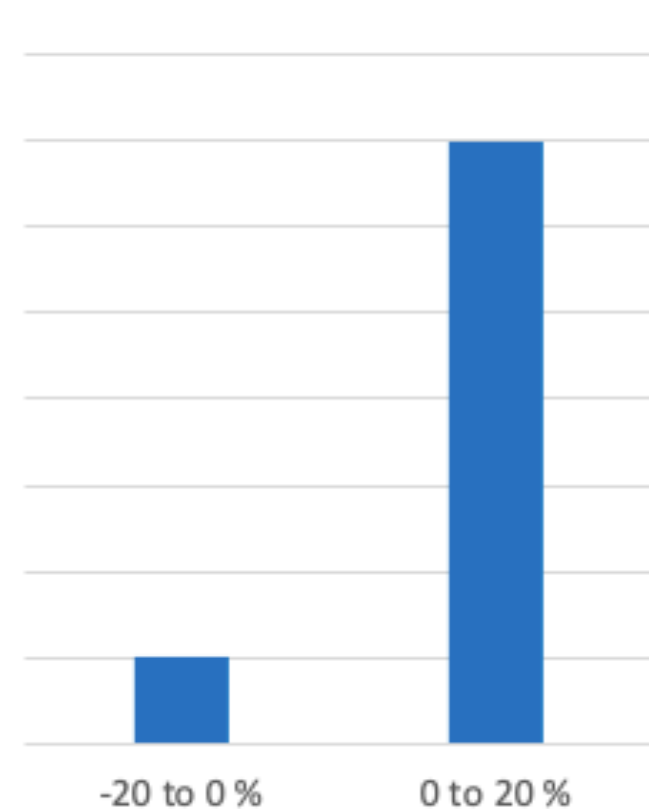
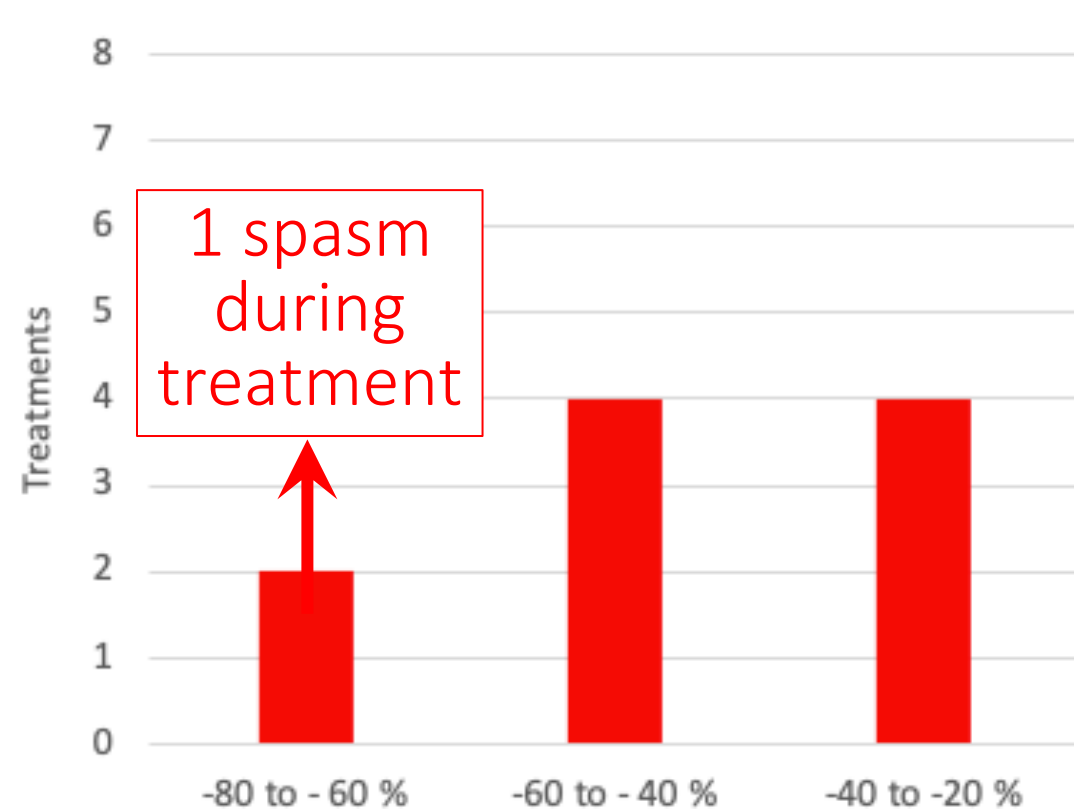
Treatment example

- Patient 3 : a 63 y.o. male with 1 HCC (28 cm³) in segment VII
 - ¹⁶⁶Ho-PLLA post-treatment dosimetry (2 GBq)



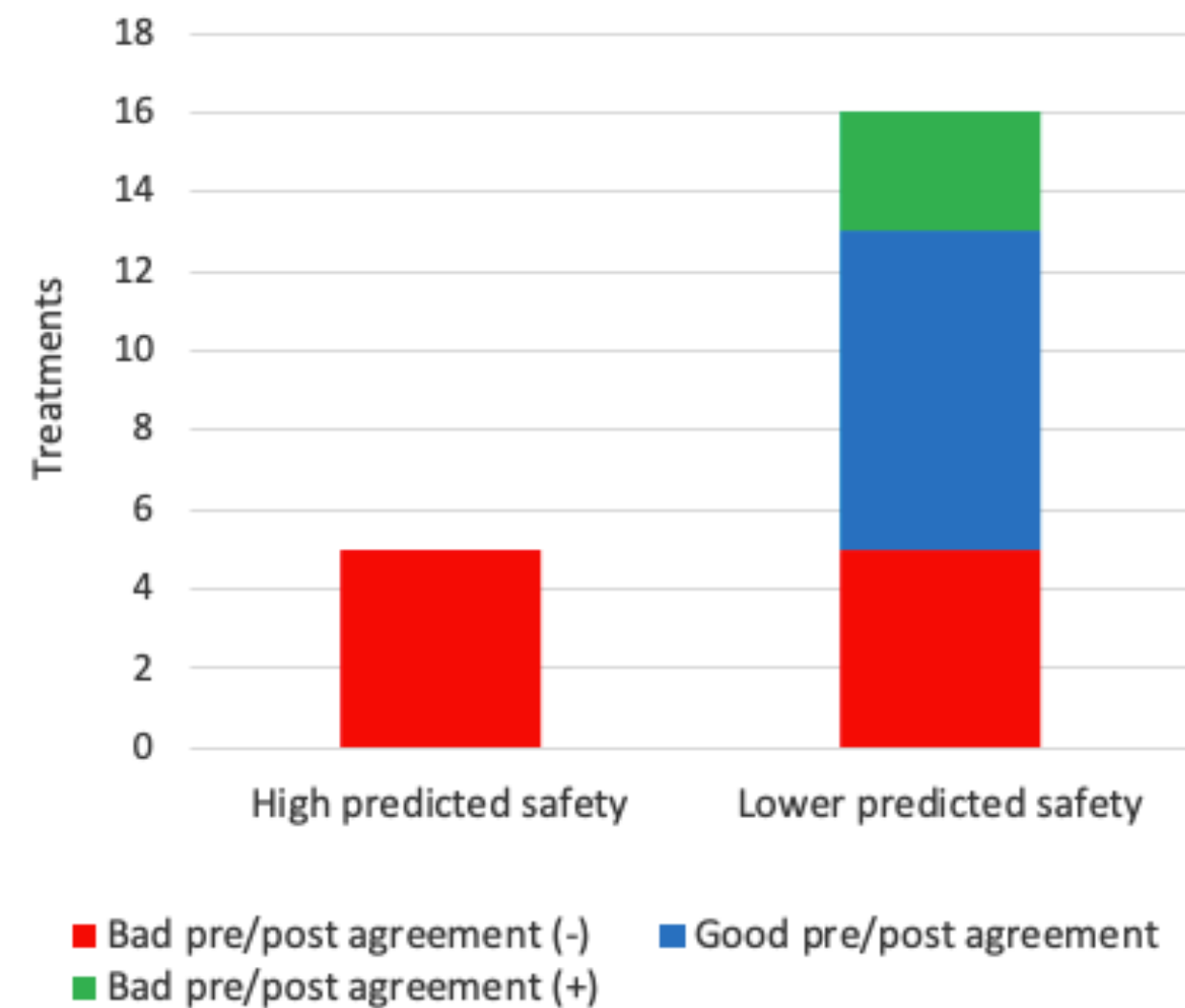
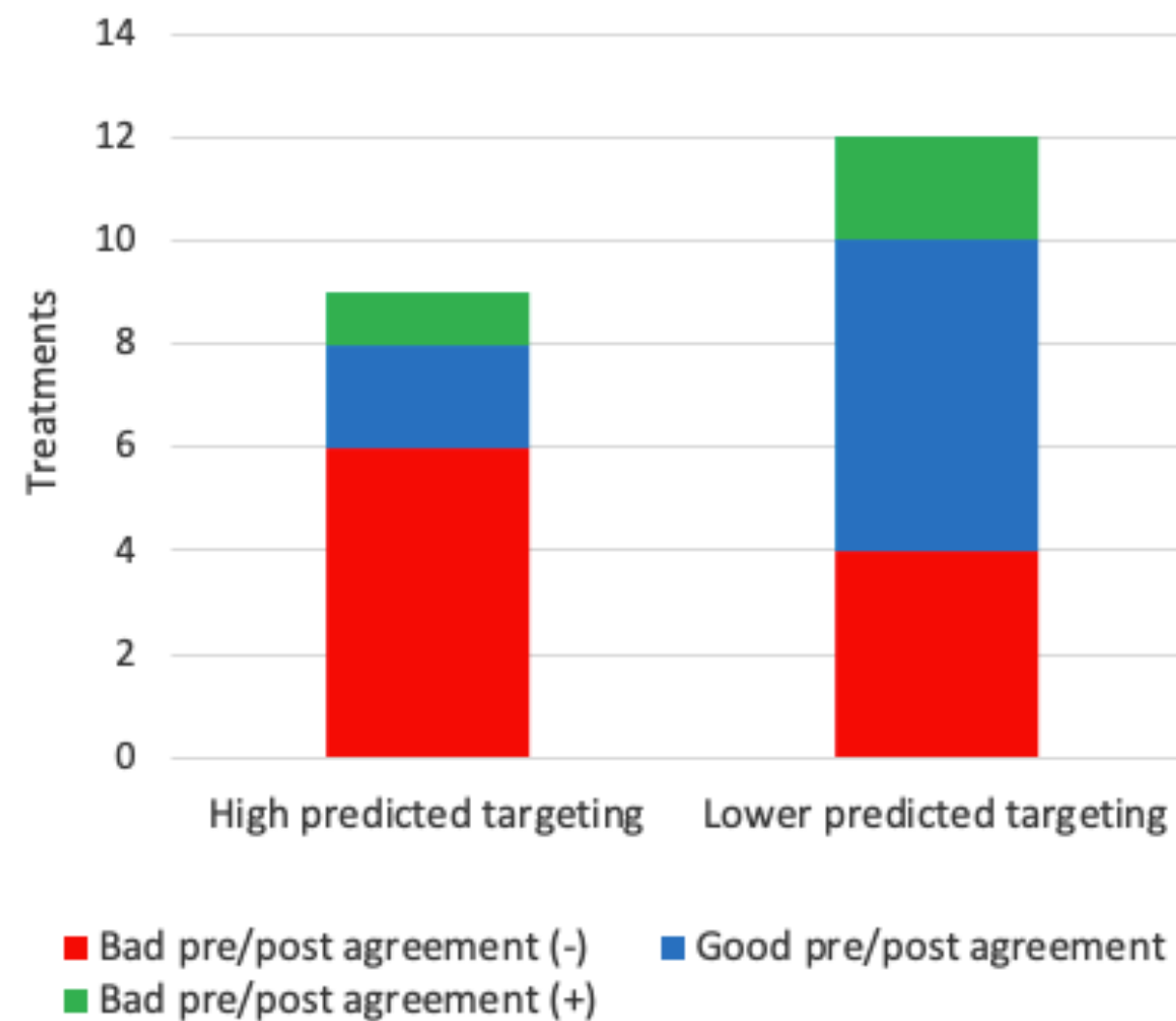
Tumor dose

- Pre/post relative differences distribution
 - Bad pre/post agreement (-)
 - Good pre/post agreement
 - Bad pre/post agreement (+)



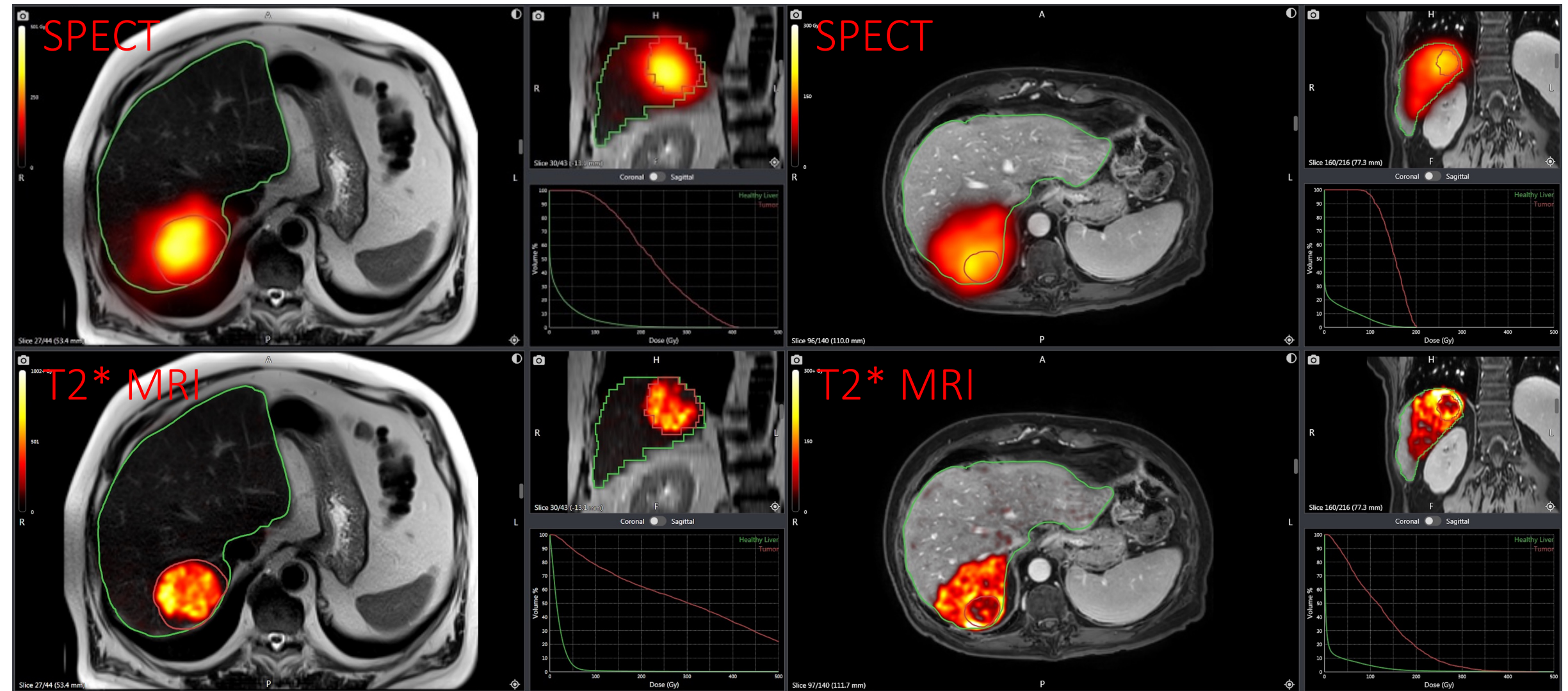
Discussion

- Too much selectivity using ^{166}Ho -PLLA scout for simulation in our study ?
 - Which link with the predicted tumor dose and the predicted NTL dose ?



T2* MRI

- 5 patients
 - Post-treatment
 - Confirmation
 - Spatial resolution
 - Way better



Conclusion and perspective

- We suspect a link between bad reproducibility and high predicted selectivity
 - When using ^{166}Ho -PLLA scout for simulation
 - Maybe due to a ^{166}Ho -PLLA scout embolic effect
 - Uncorrelated with a bad response : only 1/17 progressing disease after 1 month (mRECIST)
 - Leading to difficulties to use a predictive compartmental dosimetry and future thresholds
- We suggest to take care of the SPECT scatter correction for quantitative purposes
- Thank you for your attention !

