

Dosimetry with ^{177}Lu -DOTATATE in clinical routine

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Start of the story ...



« First treatment with ^{177}Lu -DOTATATE :
I really want to know, at least, the absorbed dose to the
kidneys .
No stress, it is planned for next month. Thanks ! »



¹⁷⁷Lu-DOTATATE

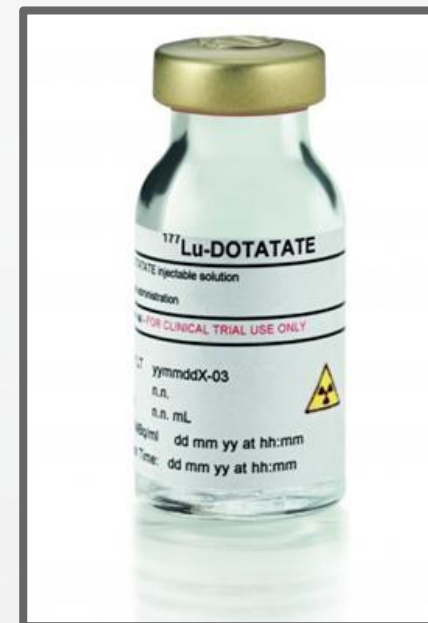
T=6,647 jours

Traitement des tumeurs neuroendocrines gastro-entéro-pancréatiques bien différenciées de l'intestin moyen à l'état métastatique ou inopérable

Surexpression de récepteurs à la somatostatine

Type d'émission	Energie (keV)	Probabilité d'émission (%)
Particules β^- Thérapie	498,30	79,30
Rayonnements γ - Principaux pics	208,37 112,95	10,40 6,20

Imagerie post traitement et imagerie pour la dosimétrie



Absorbed dose determination

Mean absorbed dose (Gy)

to an organ of interest

$$\overline{D}_k = \sum_h \tilde{A}_h \times S_{(k \leftarrow h)}$$

Gy

MBq.h

Gy/(MBq.h)

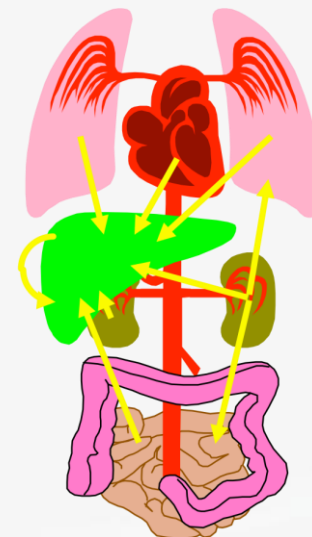
Mean absorbed dose
in target k from source h

Cumulated activity
Total number of decays
in source h

S factor
Absorbed dose in target k
per decay in source h

**BIOLOGICAL
COMPONENT**
(pharmacokinetics)

**PHYSICAL
COMPONENT**
(calculation)



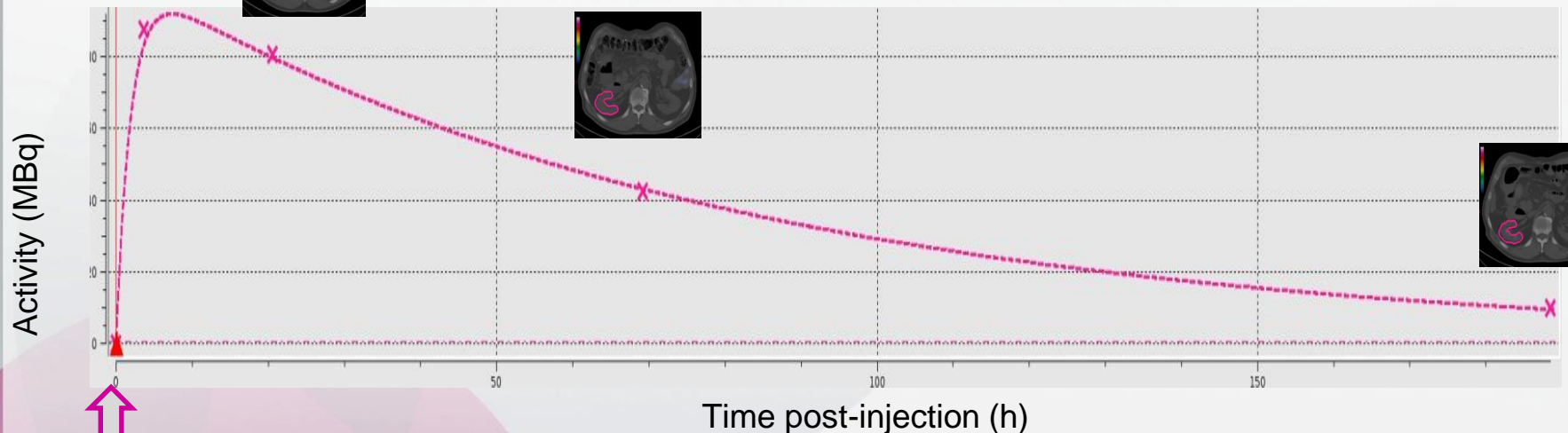
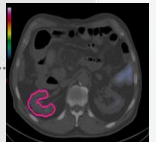
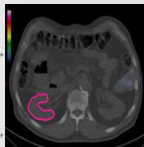
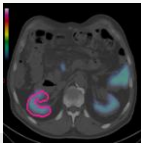
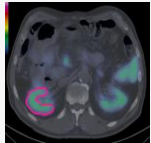
BIOLOGICAL COMPONENT

Cumulated Activity in MBq.h

*Total number of decays
in a segmented organ during
the exploration time period*

Spatial and temporal
distribution of the radiopharmaceutical

- ❖ Quantitative imaging
- ❖ Time Activity Curve fitting



Injection

PHYSICAL COMPONENT

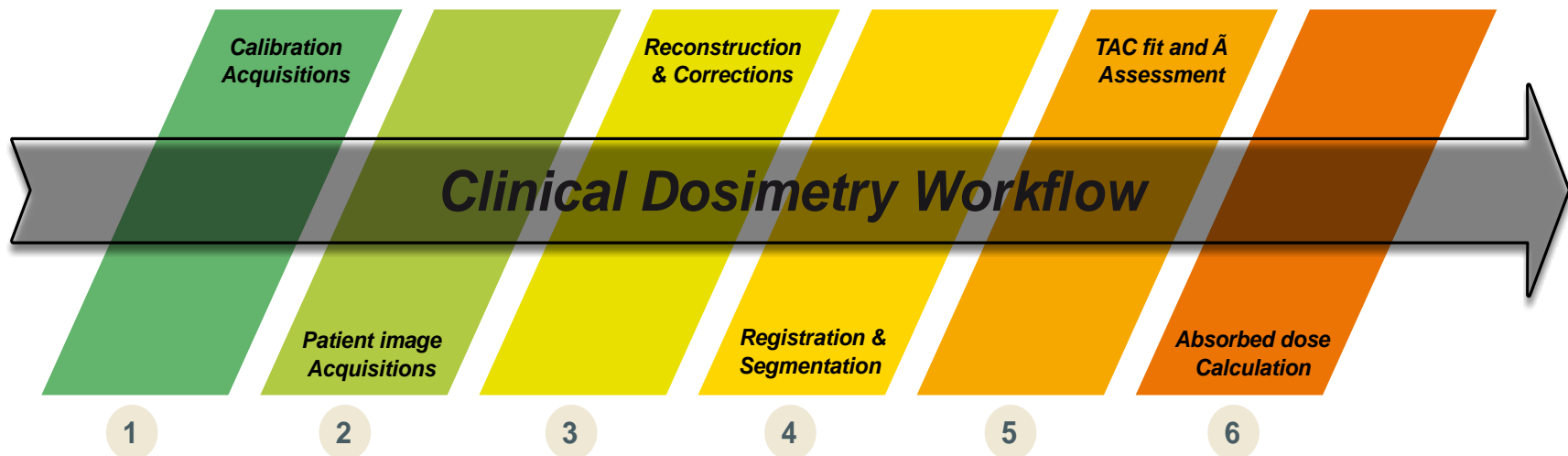
How much of the energy emitted by the radioactive source is absorbed in organs of interest ?

Depends on :

- Type and energy of radiation emitted from the radionuclide
- Shape, size and mass of the source and target organs
- Distance and type of material between the source and target organs

Determined by :

Calculation algorithms : Local deposition method (LDM), convolution of Voxel Dose Kernels (DK), full radiation transport modelling with Monte Carlo codes



- **Equipment**

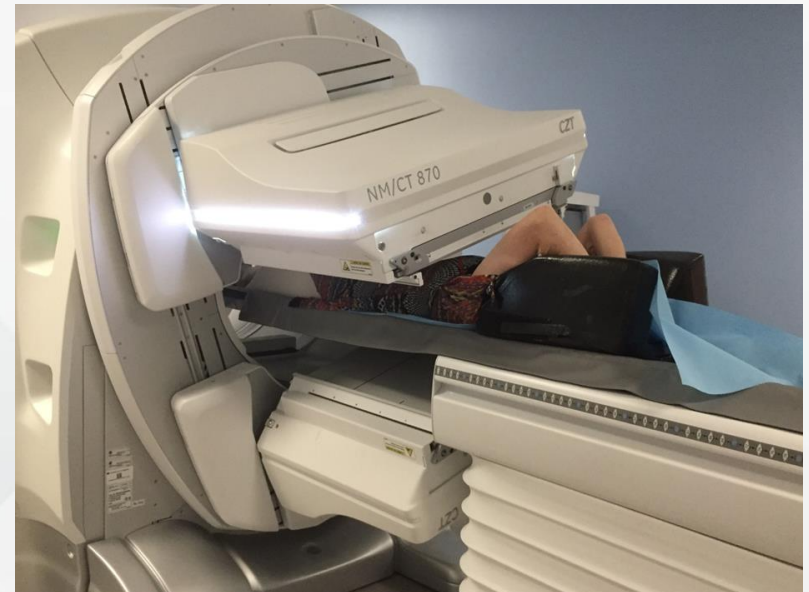
SPECT/CT Discovery NM/CT 670 (GE)

*Medium-Energy General Purpose collimator
3/8-in NaI(Tl) crystal thickness
Bright Speed 16 CT*



SPECT/CT Discovery 870 CZT (GE)

*Medium-Energy collimator MEHRS
130 CZT modules 39.4x39.4x7.25mm
Optima CT540*

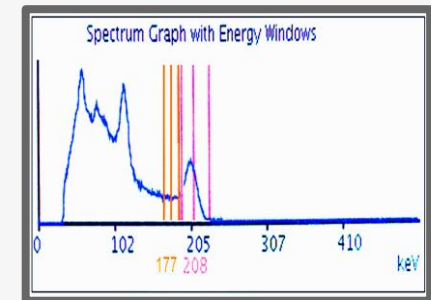
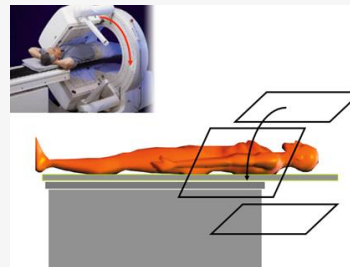


- **Correction maps creation for ^{177}Lu : energy and uniformity**
- **Acquisition imaging protocol implementation**

*L Santoro et al.
EJNMMI Res. (2018)*

(MIRD Pamphlet 26)

3D SPECT/CT imaging protocol



Collimator	Emission Window	Scatter Window	Matrix (pixel)	Number of Projections	Time per projection (s/p)	Angle projections (°)	Acquisition duration (min)	Auto-Contour
MEGP	208 keV 20%	177 keV 10%	128×128	60	45	6	22.5	Body Contour

- **Reconstruction parameters**

**Volumetrix MI
Xeleris Software (GE)**

Reconstruction method	Corrections	Number of iterations	Number of subsets
OSEM	AC + SC + RR	6	10

Calibration process

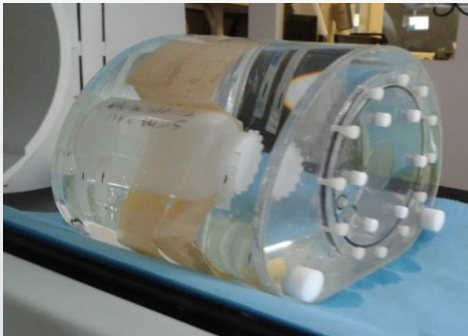
- Calibration factor (CF) => Conversion Counts → MBq

$$CF = \frac{C \text{ (number of counts)}}{A_{t_{acq}} \text{ (MBq)} \times T_{acq} \text{ (s)}}$$

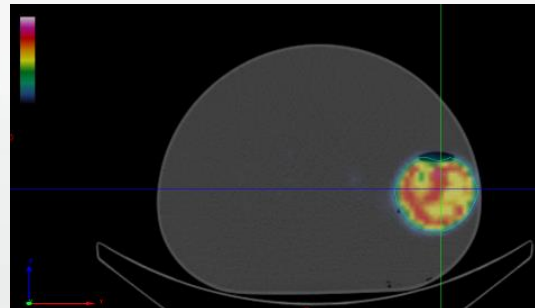
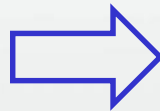
Decay activity corrected at t_{acq} Acquisition duration

A (MBq)

C (number of counts)



500 mL bottle
273 ± 15 MBq of ^{177}Lu



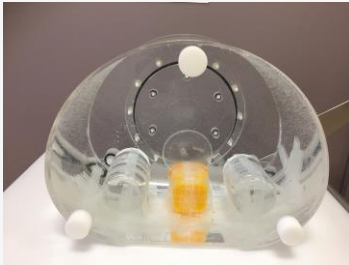
Isocontour representing a volume of 500 mL automatically segmented on the nuclear medicine image

**SPECT/CT
Imaging and
reconstruction
with clinical
protocol**

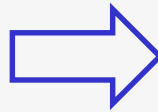
Calibration process

- Calibration factor (CF) => Conversion Counts → MBq

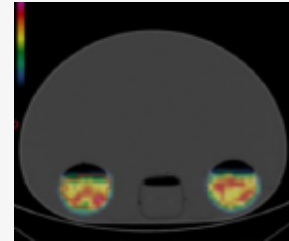
A (MBq)



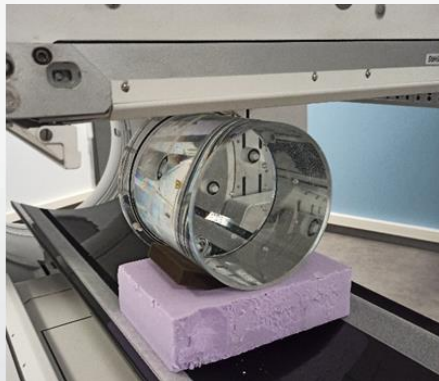
2 bottles of 250 mL filled with
200 mL of 82.2 ± 4.1 MBq of ^{177}Lu



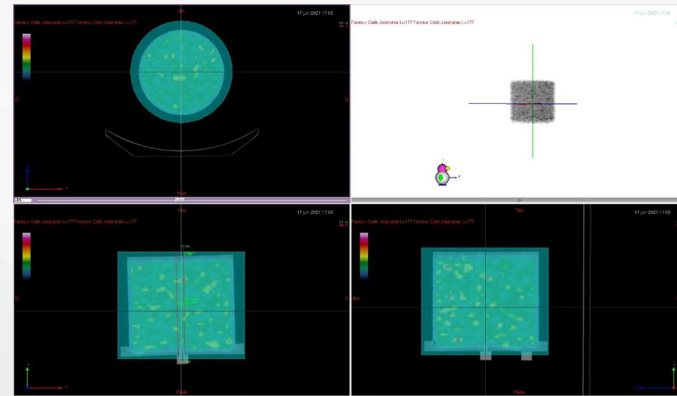
C (number of counts)



Isocontour representing a volume
of 200 mL automatically segmented
on the nuclear medicine image



Jaszczak phantom without insert
625 MBq of ^{177}Lu

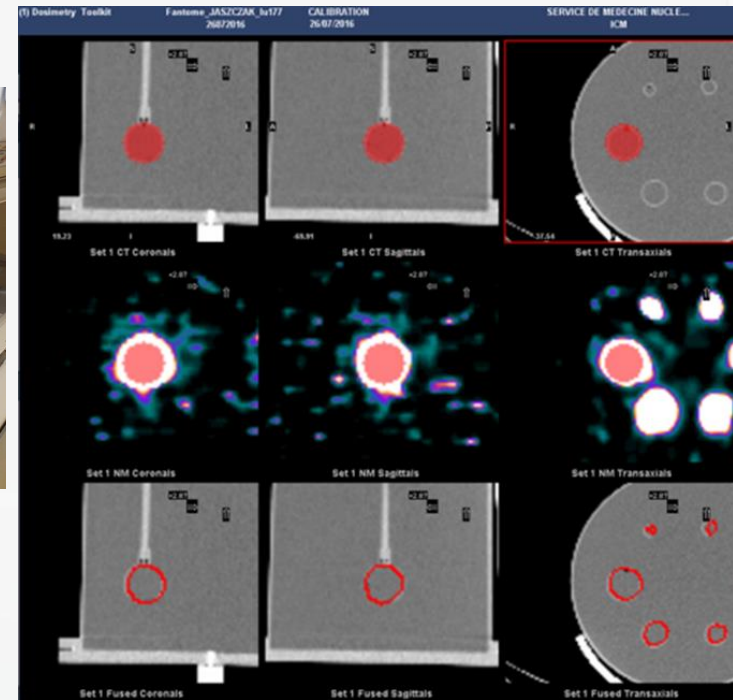
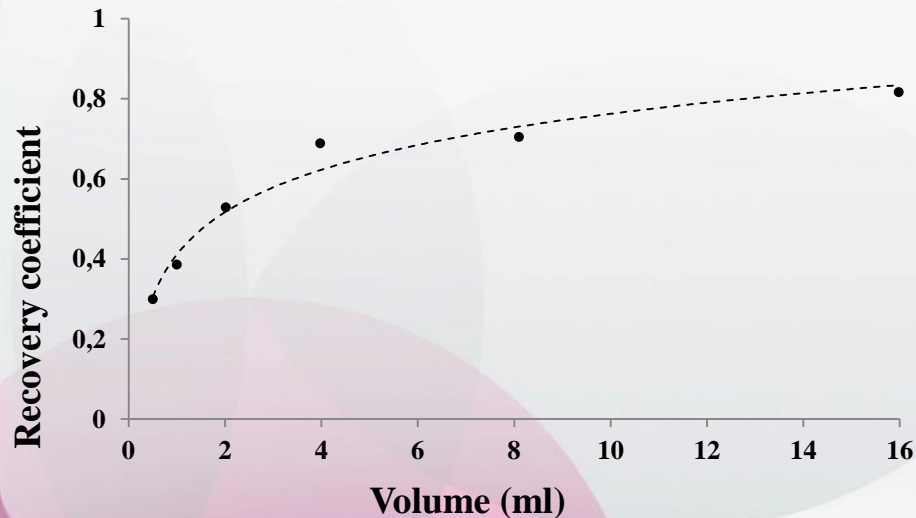
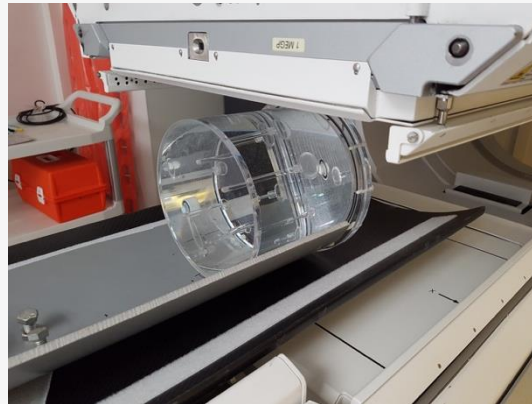


VOI higher than the phantom

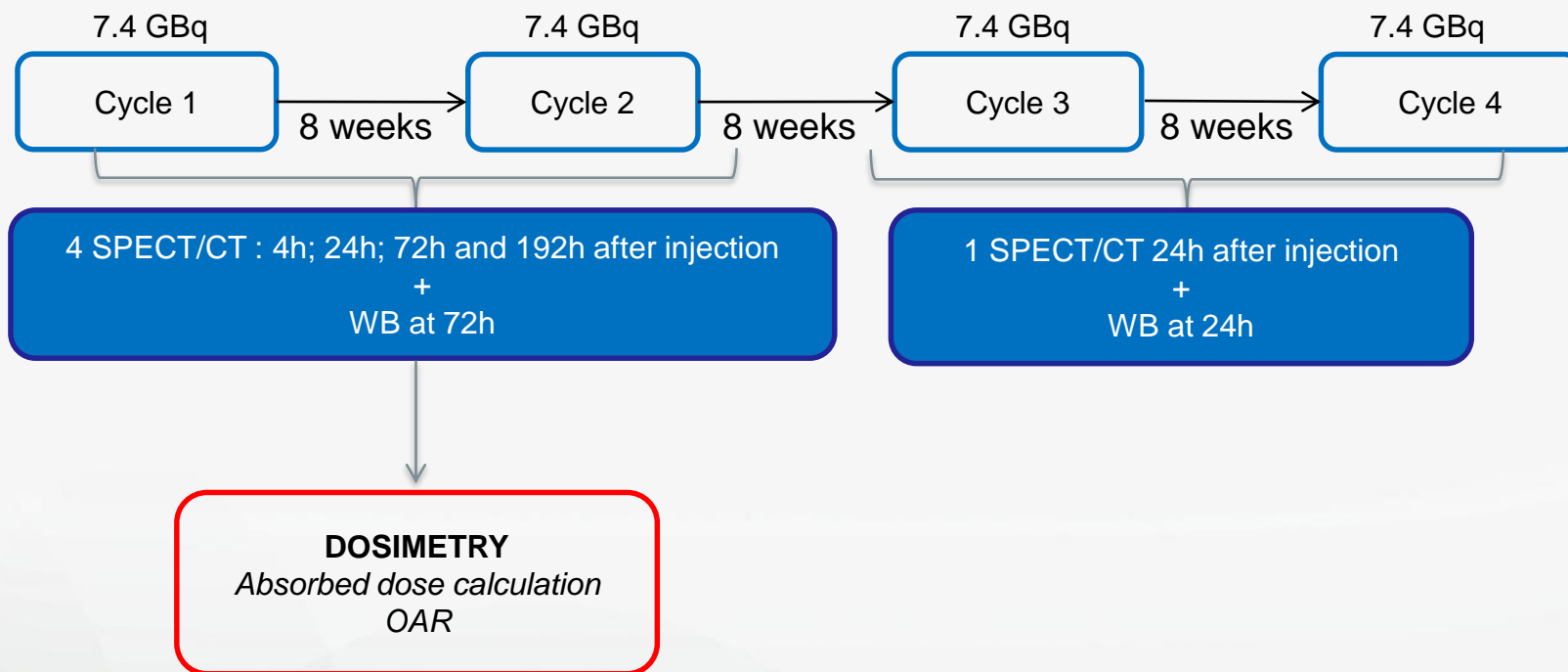
MRTDosimetry _J Tran-Gia and M Lassmann

**SPECT/CT Imaging and reconstruction
with clinical protocol**

- Recovery coefficients => Partial Volume Effect correction



$$RC_i = \frac{A_{SPECT/CT}(V_i)}{A_{(V_i) \text{ measured (dose calibrator)}}$$



D0 : SPECT/CT (4h) - CT Optimized Dose (better image quality)
 D1 : SPECT/CT (24h) - CT Low Dose
 D3 : SPECT/CT (72h) - CT Low Dose
 D8 : SPECT/CT (192h) - CT Low Dose

**Reproducible patient set up
with immobilization devices**

Reconstruction

Registration

Segmentation

Time activity
curve fitting
 \tilde{A} evaluation

Absorbed
dose
calculation

« Preparation for DTK » (GE)

DOSIMETRY TOOLKIT (GE)

TIAC
(h)

OLINDA/EXM®
V1.0
AD
(Gy)

TIAC, time integrated activity coefficient; DTK, Dosimetry Toolkit; AD, absorbed dose

OLINDA - Organ Level Internal Dose Assessment Code

Organ Doses:

File View

Organ Doses (mSv/7,40E003 MBq), Nuclide: Lu-177 (6,73E00 day), Adult M

Target Organ	Alpha	Beta	Photon	Total
Adrenals	0,00E000	0,00E000	7,89E001	7,89E001
Brain	0,00E000	0,00E000	1,68E-01	1,68E-01
Breasts	0,00E000	0,00E000	1,12E001	1,12E001
Gallbladder Wall	0,00E000	0,00E000	1,39E002	1,39E002
LLI Wall	0,00E000	0,00E000	3,18E000	3,18E000
Small Intestine	0,00E000	0,00E000	2,05E001	2,05E001
Stomach Wall	0,00E000	0,00E000	3,01E001	3,01E001
ULI Wall	0,00E000	0,00E000	3,11E001	3,11E001
Heart Wall	0,00E000	0,00E000	3,77E001	3,77E001
Kidneys	0,00E000	3,09E003	1,05E002	3,19E003
Liver	0,00E000	6,90E003	2,94E002	7,19E003
Lungs	0,00E000	0,00E000	3,33E001	3,33E001
Muscle	0,00E000	0,00E000	1,34E001	1,34E001
Ovaries	0,00E000	0,00E000	6,75E000	6,75E000
Pancreas	0,00E000	0,00E000	7,30E001	7,30E001
Red Marrow	0,00E000	6,28E000	1,54E001	2,17E001
Osteogenic Cells	0,00E000	2,92E000	1,96E001	2,25E001
Skin	0,00E000	0,00E000	6,36E000	6,36E000

Main Input Form Nuclide Input Form Models Input Form Kinetics Input Form Help Form

The previously used quantity of residence time was confusing to many users. This was only a measure of the number of disintegrations occurring in a source organ. This code works with the number of disintegrations per unit activity administered (uCi-hr/uCi or Bq-hr/Bq), either entered directly, or as calculated from formulas. This is mathematically equivalent to residence times, but is perhaps easier to understand. You may also enter data from a kinetic model, involving values of activity and half-lives, and fit them to a function.

Enter the number of disintegrations for the source organs, or use some of the special options below.

Note: for the Tot Body/Rem. Body field - enter value for Rem. Body if any other organ has been chosen.

Adrenals	0.0000
Brain	0.0000
Breasts	0.0000
GB Cont	0.0000
LLI Cont	0.0000
SI Cont	0.0000
StomCont	0.0000
ULI Cont	0.0000
HeartCon	0.0000
Hrt Wall	0.0000
Kidneys	1.47
Liver	20.97
Lungs	0.0000
Muscle	0.0000
Ovaries	0.0000
Pancreas	0.0000
Red Mar.	0.30
ContBone	0.0000
TrabBone	0.0000
Spleen	0.0000
Testes	0.0000
Thymus	0.0000
Thyroid	0.0000
UB Cont	0.0000
Uterus	0.0000
Tot Body/Rem Body	0.0000

Get setup (stp) file

Bone Activity on Bone Surfaces

Bone Activity in Bone Volume

Voiding Bladder Model

ICRP GI Model

Fractions and Half-times

Fit data to Model

Show me some examples

Clear All Data

Modify Input Data

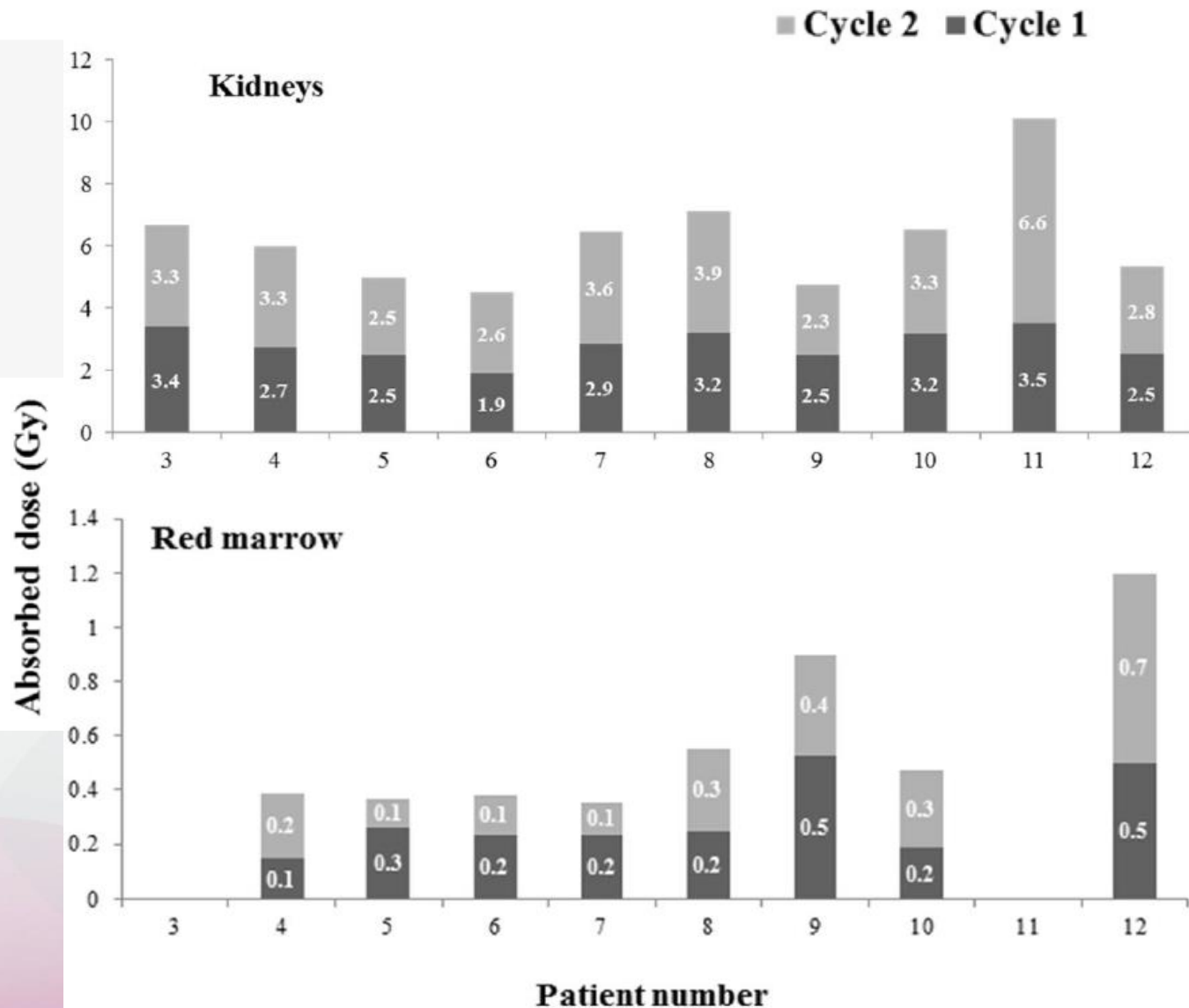
Next Phantom

Previous Phantom

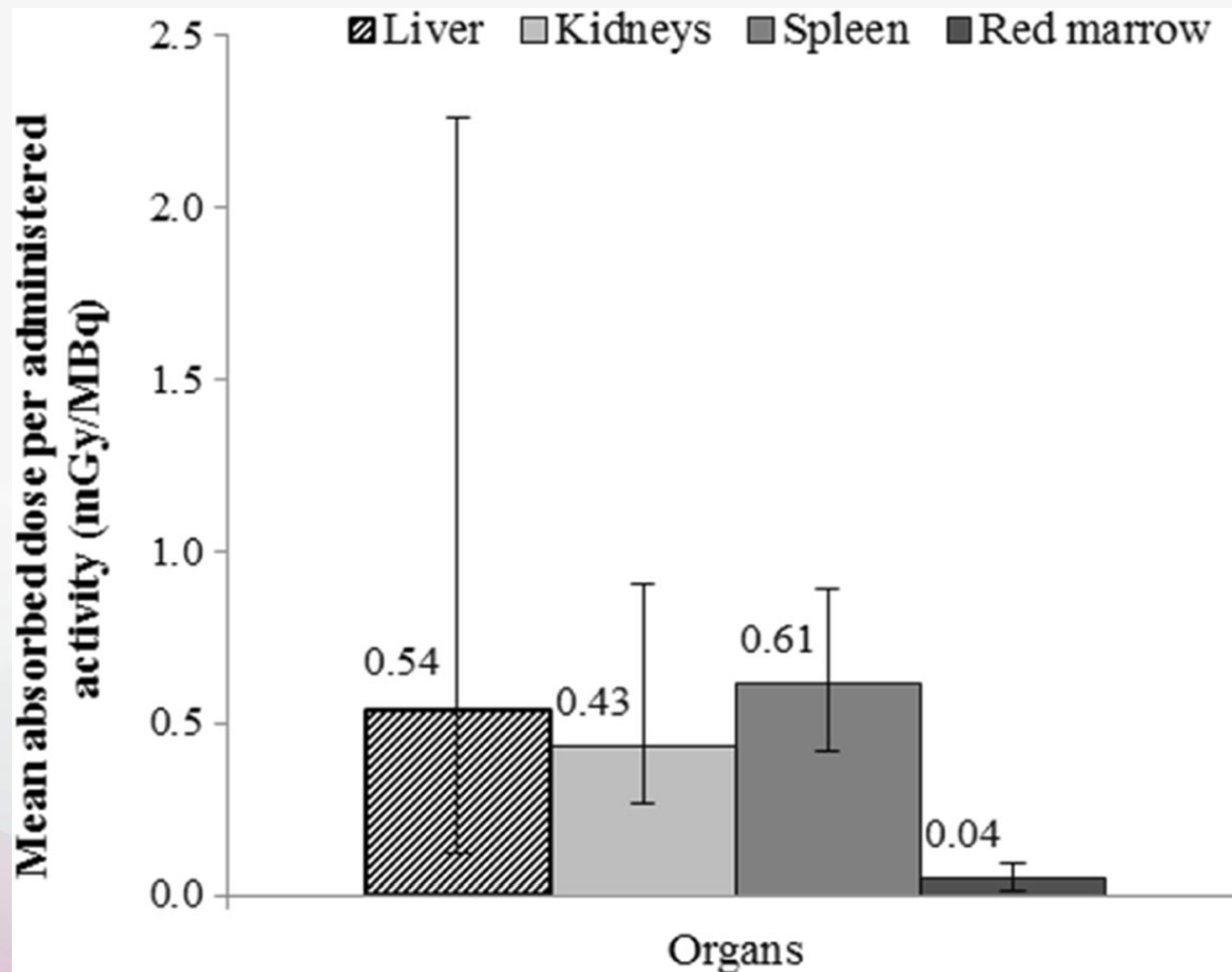
See Source Organ Contributions

Mult. Doses by (MBq): 7400

12 patients
22 dosimétries



12 patients
22 dosimétries



Reconstruction

Registration

Segmentation

**Time activity
curve fitting
 \tilde{A} evaluation**

**Absorbed
dose
calculation**

« Preparation for DTK » (GE)

DOSIMETRY TOOLKIT (GE)

TIAC
(h)

OLINDA/EXM®
V1.0

AD
(Gy)

Volumetrix MI (GE)

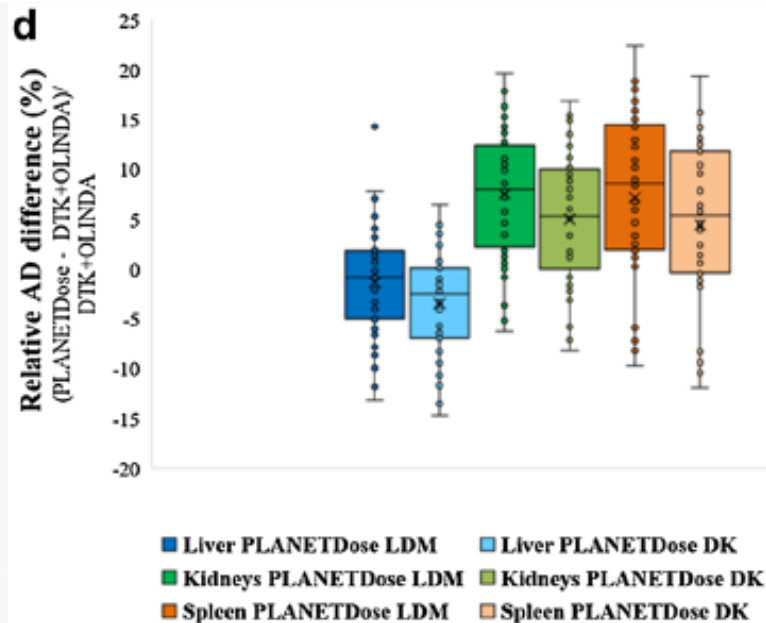
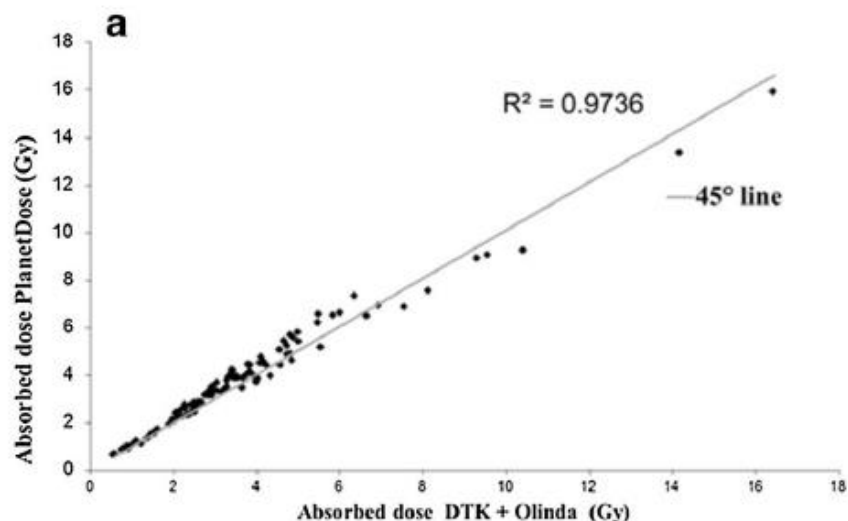
PLANET® Dose (DOSIsoft)

LDM
DK

AD
(Gy)

TIAC, time integrated activity coefficient; DTK, Dosimetry Toolkit; AD, absorbed dose; LDM, local deposition method; DK, dose kernel

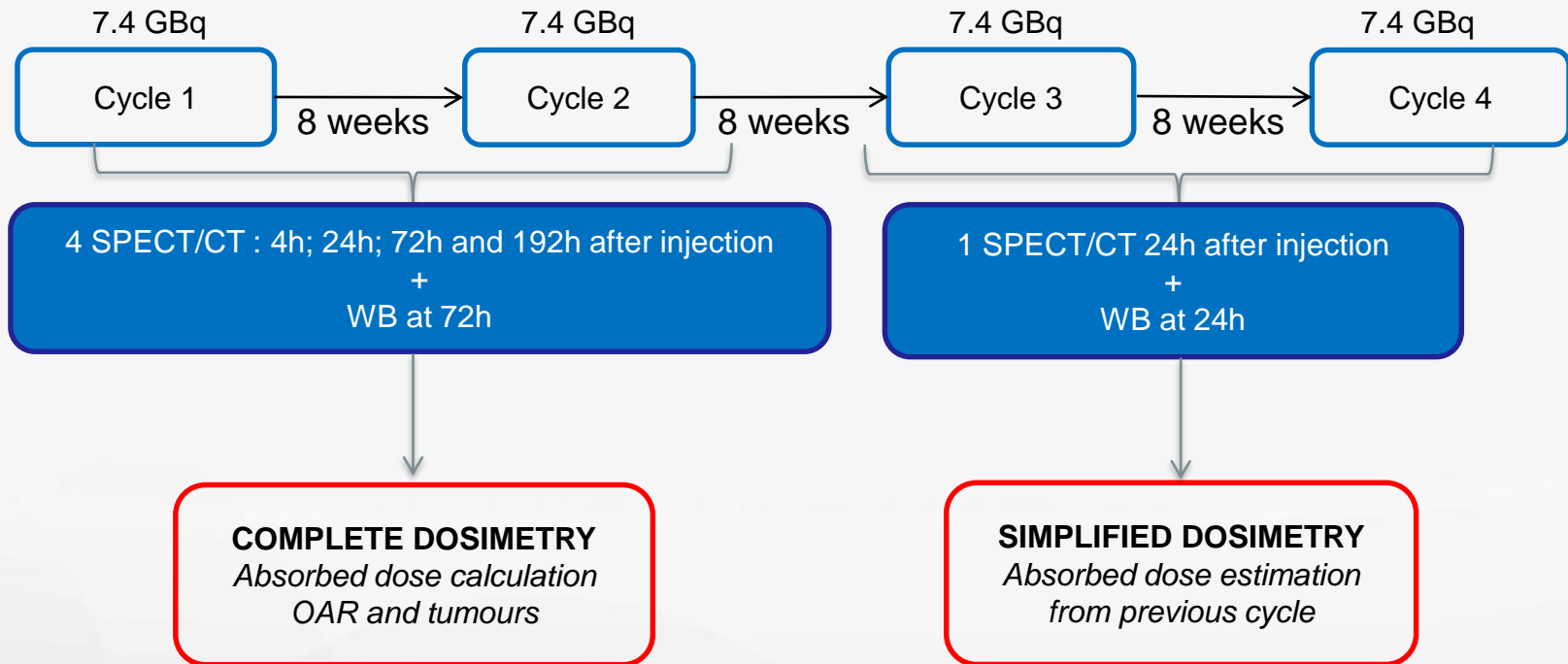
21 patients
40 dosimétries



ORGANS	Mass (g)		TIAC (h)		Absorbed dose (Gy)		
	DTK + OLINDA/EXM [®] V1.0	PLANET [®] Dose	DTK + OLINDA/EXM [®] V1.0	PLANET [®] Dose	DTK + OLINDA/EXM [®] V1.0	PLANET [®] Dose LDM	PLANET [®] Dose DK
Liver	2141.6 ± 1213.3	2191.7 ± 1205	14.9 ± 24.1	15.1 ± 24.2	3.40 ± 3.9	3.27 ± 3.7	3.21 ± 3.6
Kidneys	478.3 ± 111.4	461.5 ± 108.3	2.2 ± 0.7	2.4 ± 0.8	3.01 ± 0.9	3.23 ± 0.9	3.16 ± 0.9
Spleen	290.4 ± 181.3	281.7 ± 178.5	2.0 ± 1.5	2.0 ± 1.4	4.15 ± 1	4.45 ± 1.2	4.36 ± 1.2

Dosimetry workflow

Dosimetry imaging protocol



D0 : SPECT/CT (4h) - CT Optimized Dose (better image quality)
 D1 : SPECT/CT (24h) - CT Low Dose
 D3 : SPECT/CT (72h) - CT Low Dose
 D8 : SPECT/CT (192h) - CT Low Dose

**Reproducible patient set up
with immobilization devices**

Reconstruction

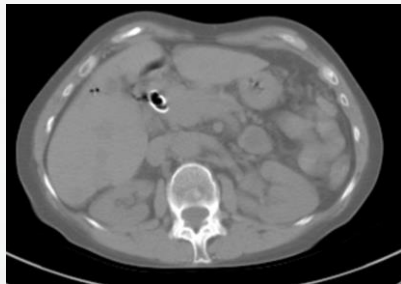
Registration

Segmentation

**Time activity
curve fitting
 \tilde{A} evaluation**

**Absorbed
dose
calculation**

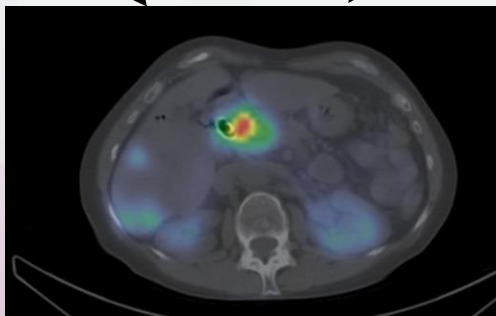
CT



NM



**Volumetrix MI
Xeleris Software (GE)**



Reconstruction method	Corrections	Number of iterations	Number of subsets
OSEM	AC + SC + RR	6	10

Reconstruction

Registration

Segmentation

Time activity
curve fitting
 \tilde{A} evaluation

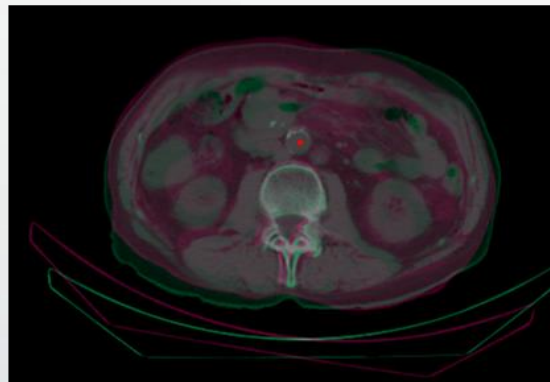
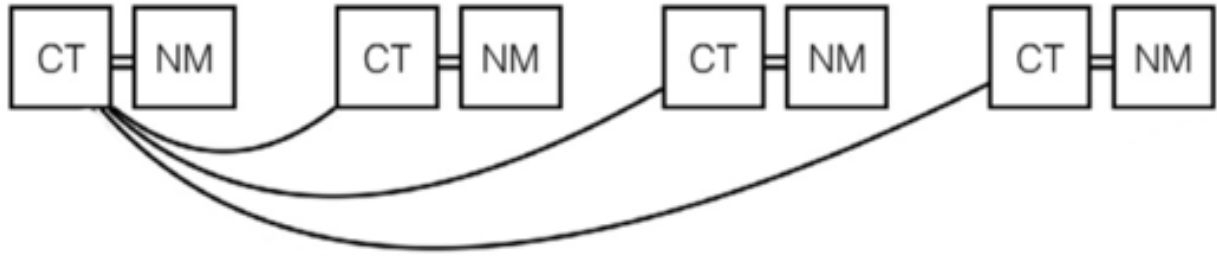
Absorbed
dose
calculation

Day 0

Day 1

Day 3

Day 8



**Rigid
Registration**
Reference = CT (4h)

PLANET® Dose
(DOSIsoft)

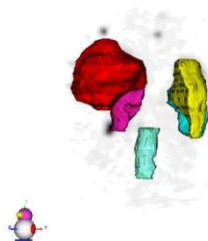
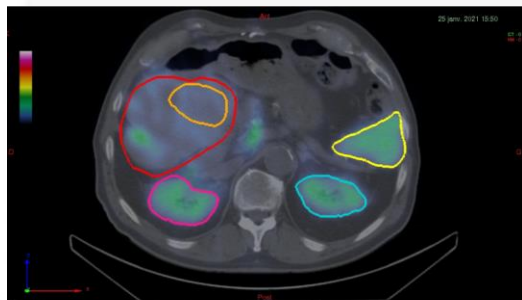
Reconstruction

Registration

Segmentation

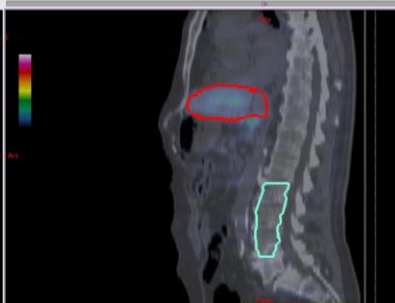
Time activity
curve fitting
 \tilde{A} evaluation

Absorbed
dose
calculation

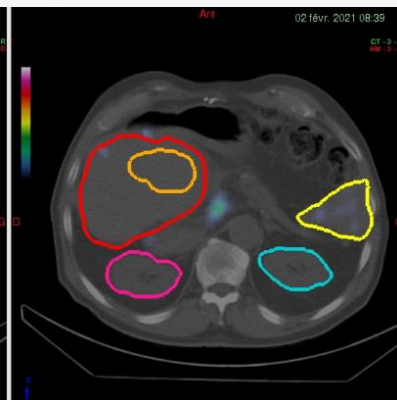
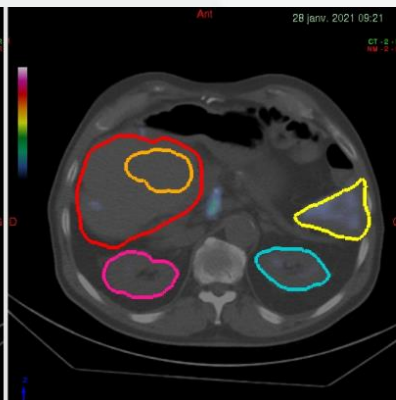
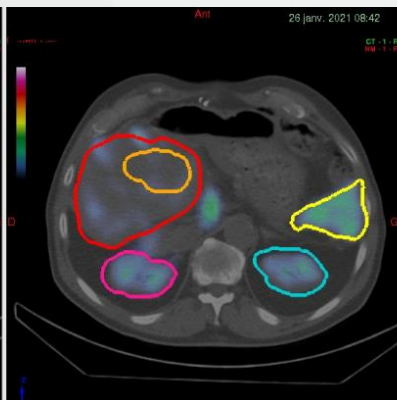
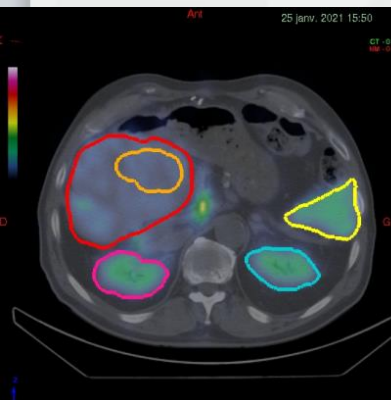


OAR segmented on the first CT (D0)

*Liver, healthy liver, right kidney, left kidney, spleen,
Bone marrow of L2,L3,L4*



OAR Copied to other time points by rigid propagation and manually corrected on each time point CT



Dosimetry workflow

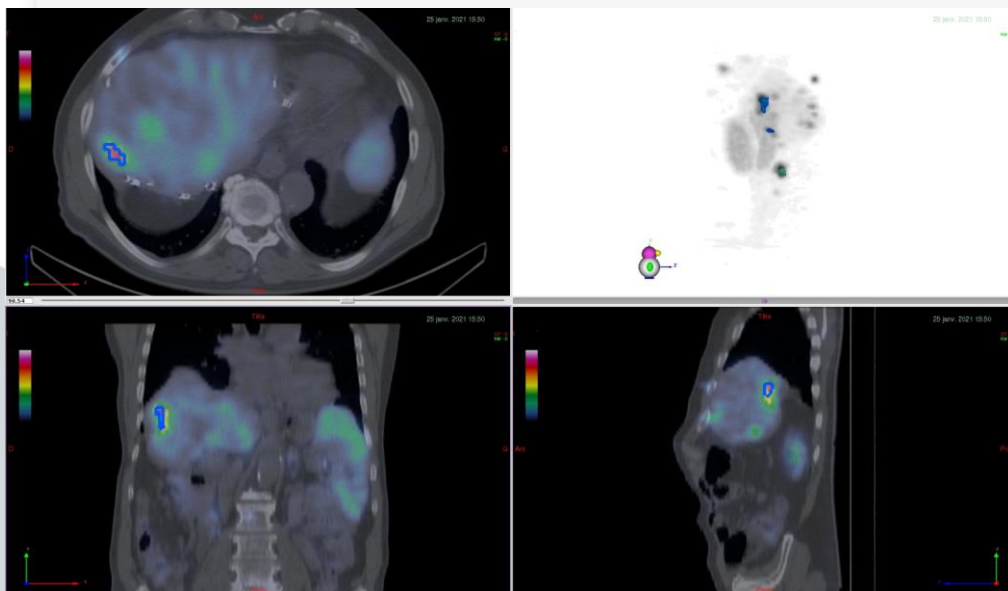
Reconstruction

Registration

Segmentation

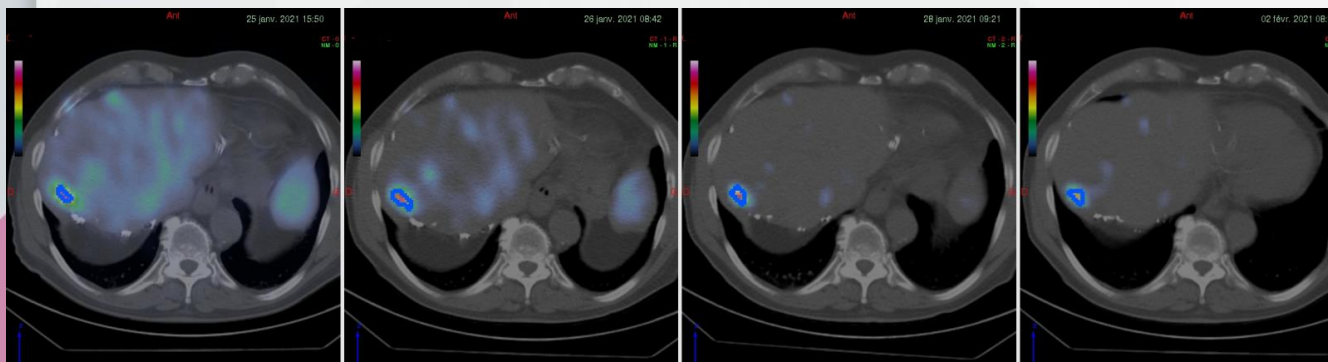
Time activity
curve fitting
 \tilde{A} evaluation

Absorbed
dose
calculation



Lesions segmented on NM images
at each time point

Isocontour representing a
volume determined from the CT
baseline (before treatment)



Reconstruction

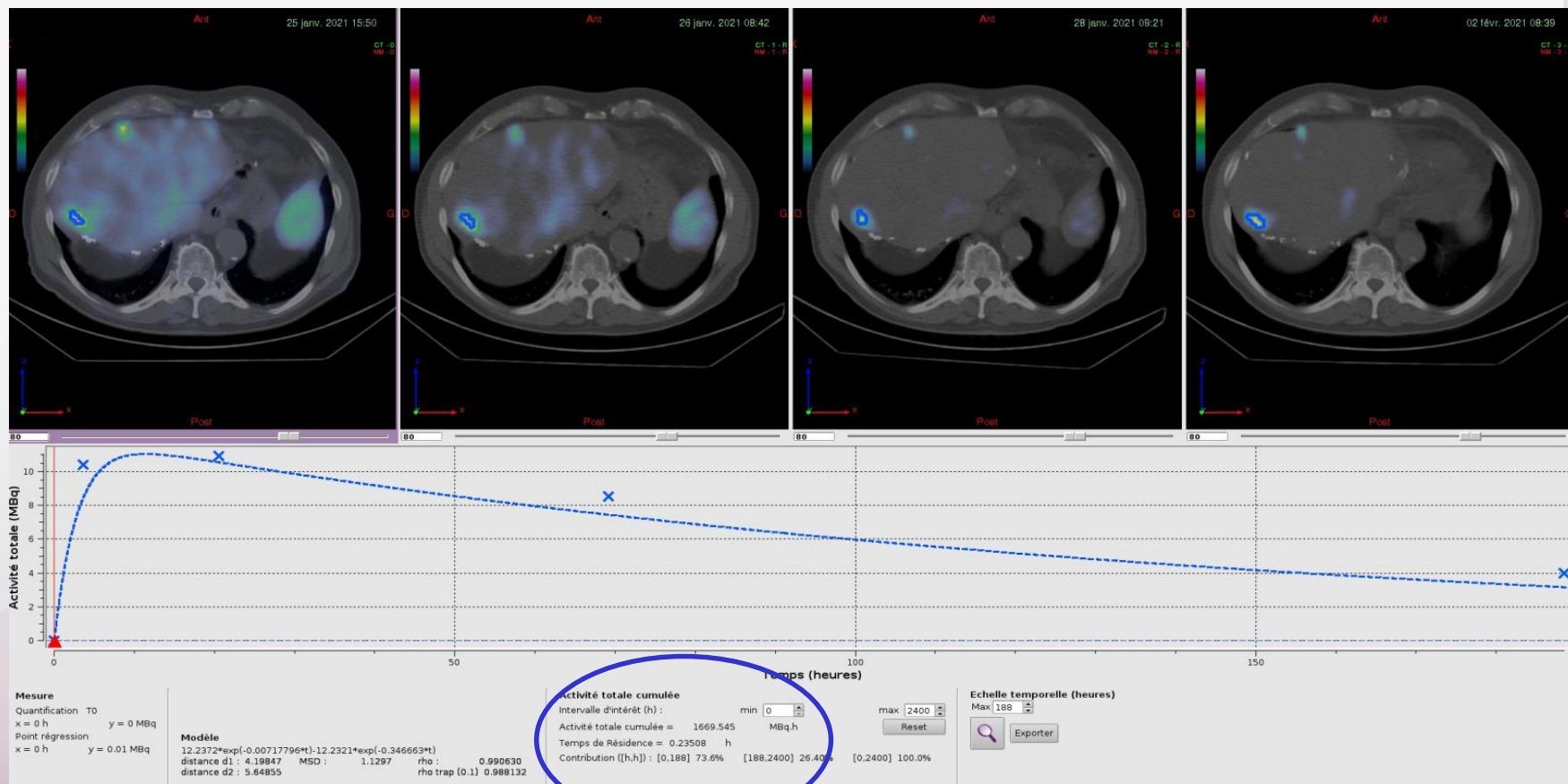
Registration

Segmentation

Time activity
curve fitting
 \tilde{A} evaluation

Absorbed
dose
calculation

- Selection of the time activity curve fitting function



Dosimetry workflow

Reconstruction

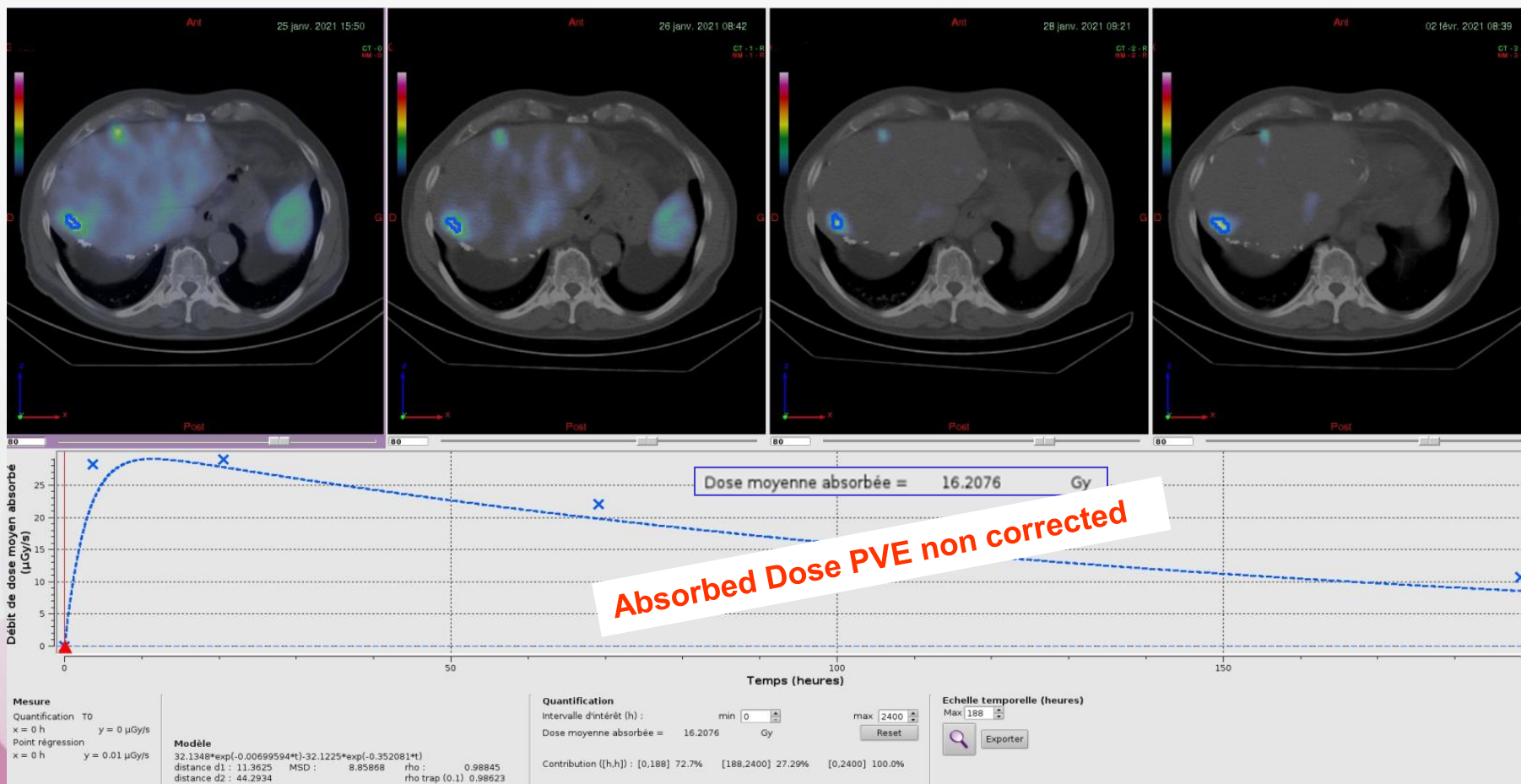
Registration

Segmentation

Time activity
curve fitting
 \tilde{A} evaluation

Absorbed
dose
calculation

- Absorbed dose calculation by **Local Deposition Method** and **density correction**



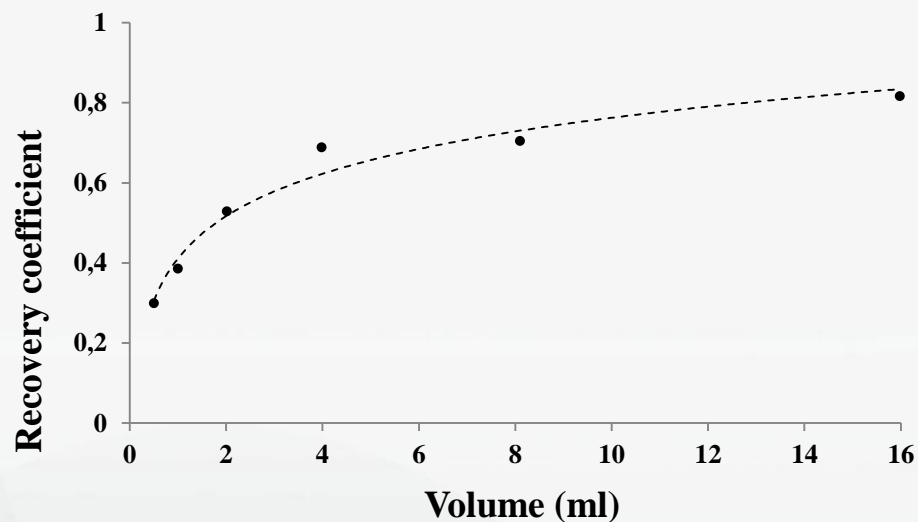
Reconstruction

Registration

Segmentation

Time activity
curve fitting
 \tilde{A} evaluation

Absorbed
dose
calculation



	VOL CT BASELINE	VOLUME (cc) MOYEN	DOSE PLANET (Gy)	CR	DOSE CORRIGEE CR (Gy)
LESION 1 : HEP SEG IV	8.5	8.62	16.2076	0.74	21.9
LESION 2 : GG COELIAQUE	2.28	2.45	14.6563	0.55	26.8
LESION 3 : GG MESENTERIQUE	4.05	4.12	24.7756	0.63	39.5



Dosimetry workflow



Fiche Dosimétrique Patient Après traitement au LUTATHERA



Fiche Dosimétrique Patient Après traitement au LUTATHERA

Nom	
Prénom	
ID Patient	
Date de naissance	XXXX/XXXX
Taille (cm)	190
Poids (Kg)	86

Traitement n° : 2
Cure n° : 1
Date de la cure : 25/01/2021

Nom	0
Prénom	0
ID Patient	0
Date de naissance	XX/XX/XXXX
Taille (cm)	190
Poids (Kg)	86

Traitement n° : 2
Cure n° : 1
Date de la cure : 25/01/2021

Traitement :		
	MBq	Heure
Activité du flacon (mesure)	7263.95	10:00
Activité résiduelle (mesure)	107.6	12:20
Activité réellement injectée au patient	7101.6	11:44

Imagerie:			
Discovery CZT 870 NUMERIQUE (GE)			
• Date et heure des examens d'imagerie :			
SPECT/CT 1:	25/01/20 à 15:24:00	J0	
SPECT/CT 2:	26/01/20 à 8:46:00	J1	
SPECT/CT 3:	27/01/20 à 9:00:00	J3	
SPECT/CT 4:	03/02/20 à 10:07:00	J8	

Données de reconstruction :	
Application utilisée (Qvala ; Vala for... ; Préparation for DTK ; ...):	Qvolumetrix MI
Nombre itérations :	6
Nombre de sous-ensemble :	10
Filtre :	Gauss 0.25

Logiciel et outils d'analyse dosimétrique:	
> PLANET Dose (Dosisoft)	

• Facteur Calibration FC = 67 (analogique) Bq/coup

• Modèle d'ajustement :	Organe:	Modèle d'ajustement :	Origine:
	Foie	Bi-exponentiel	Origine
	Foie sain	Bi-exponentiel	Origine
	Rein droit	Bi-exponentiel	Origine
	Rein gauche	Bi-exponentiel	Origine
	Rate	Bi-exponentiel	Origine
	MO de L2L3L4	Bi-exponentiel	Origine
	Lésion1	Bi-exponentiel	Origine
	Lésion2	Bi-exponentiel	Origine
	Lésion3	Bi-exponentiel	Origine

• Méthode de calcul :

Dépôt Local (LDM)

• Correction de densité :

Correction de densité

Activité réellement injectée au patient (MBq)	7101.6	11:44
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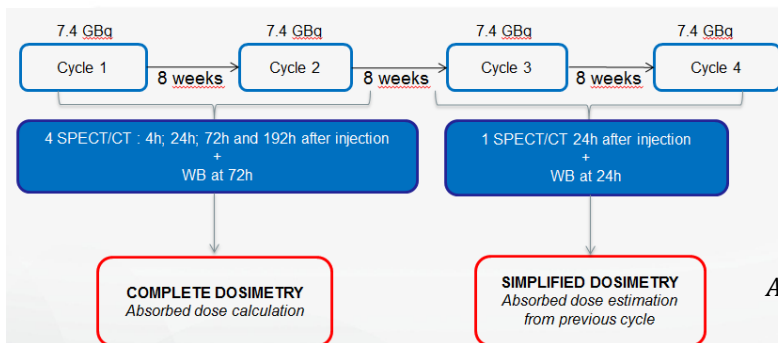
Organes sains	Dose absorbée (Gy)
Foie total	2.4
Foie sain	1.5
Rein droit	3.0
Rein gauche	2.8
Rate	5.1
Moelle osseuse hématopoïétique à partir de L2, L3 et L4	0.45

Lésions	Dose absorbée en Gy
LESION 1 : HEP SEG IV	21.9
LESION 2 : GG COELIAQUE	26.8
LESION 3 : GG MESENTERIQUE	39.5

MEDECIN NUCLEAIRE :

Dr Deshayes

PHYSICIEN : Lore Santoro



Treatment Cumulated AD =

AD cycle 1 + AD cycle 2 + AD cycle 3 + AD cycle 4

$$\text{Absorbed Dose C3/C4} = \text{AD cycle 2} \times \frac{\text{Nb counts SPECT D1 cycle 3/4}}{\text{Nb counts SPECT D1 cycle 2}} \times \frac{\text{Volume cycle 2}}{\text{Volume cycle 3/4}}$$

Ilan et al. JNM. 2015

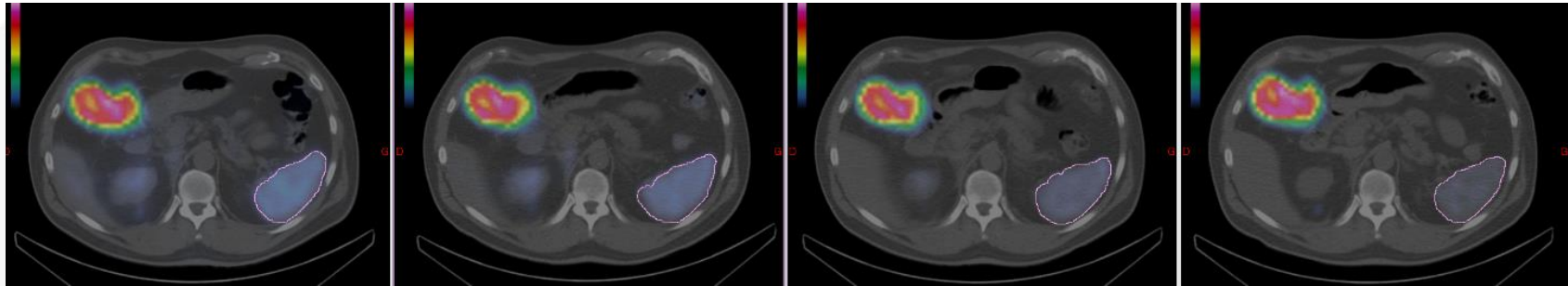
Patient Dosimetric Report after LUTATHERA treatment					
	Mean Absorbed Dose (Gy)				
	CYCLE 1	CYCLE 2	CYCLE 3	CYCLE 4	Total absorbed dose (Gy)
Liver	1.7	1.8	1.70	1.80	7.0
Healthy liver	1.3	1.4	1.30	1.60	5.6
Right kidney	2.6	2.9	2.90	2.50	10.9
Left kidney	2.7	3.0	2.60	2.60	10.9
Spleen	4.7	7.3	6.70	7.80	26.5
Bone marrow (from L2, L3 et L4)	0.20	0.25	0.30	0.28	1.03
LESION Hepatic Dome:	24.9	26.9	33.0	30.0	114.8
LESION Hepatic Segment III :	20.5	25.4	32.1	28.8	106.8
LESION Jonction Hepatic Seg V/I :	25.7	21.9	25.2	20.3	93.1

- The dosimetry analysis is requested by the physician
(low renal function, multi-focal bone involvement, retreatment...)
- Previous dosimetry results requested by the physician when re-treatment
- Since May 2016 : > 40 patients benefited from a dosimetry analysis
 - > 80 complete dosimetry analyses realized (cycle 1 and 2)
 - > 80 simplified dosimetry analyses realized (cycle 3 and 4)
- Collection and analysis of all dosimetric data (OAR and tumours) in order to establish the correlation with clinical outcome (disease control and toxicities).

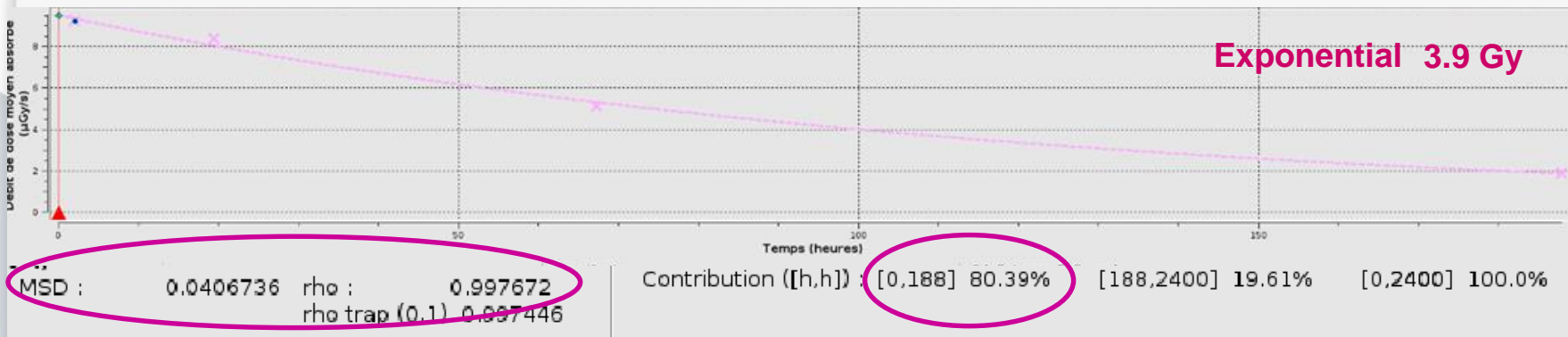
??? Remaining Question ???

Fitting curve

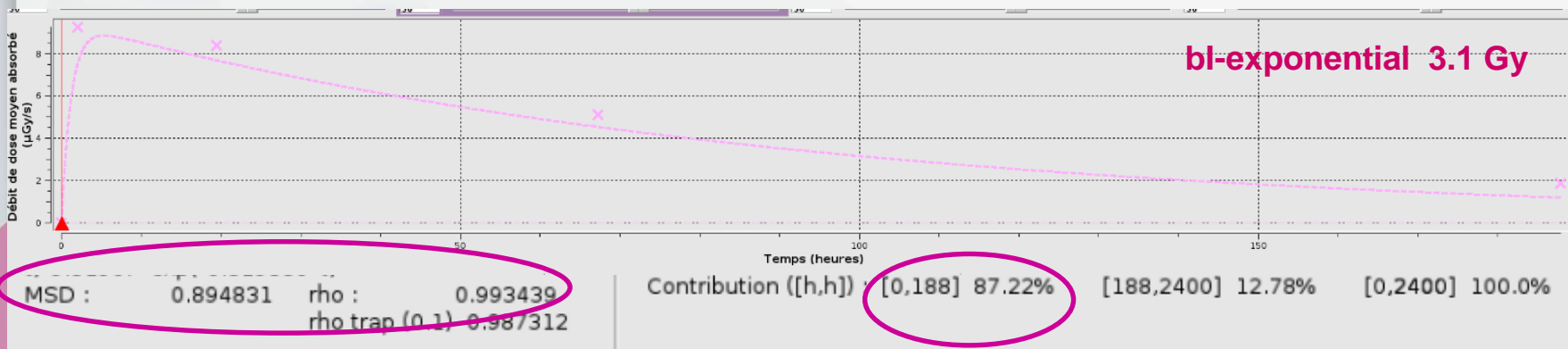
- HOW TO CHOOSE THE BEST FITTING CURVE ?



Exponential 3.9 Gy



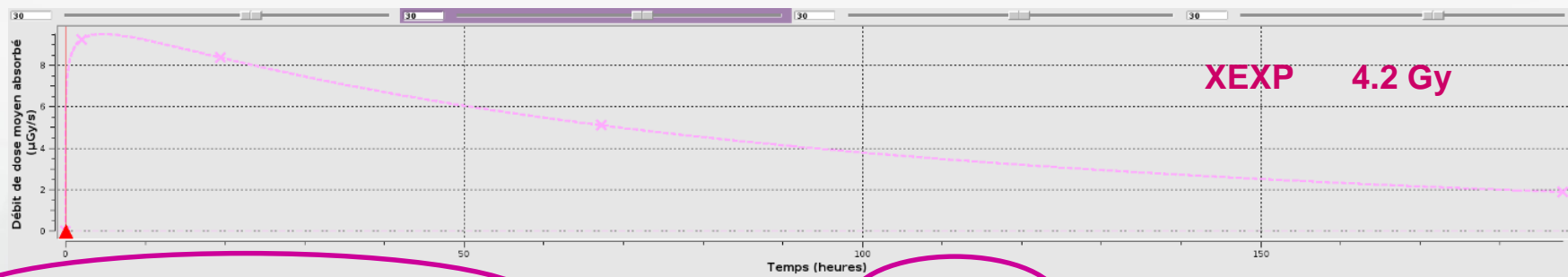
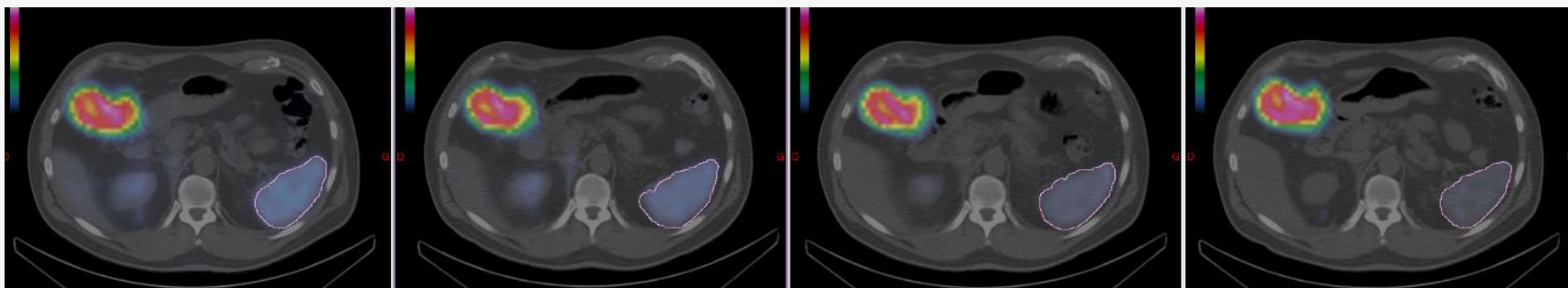
bi-exponential 3.1 Gy



??? Remaining Question ???

Fitting curve

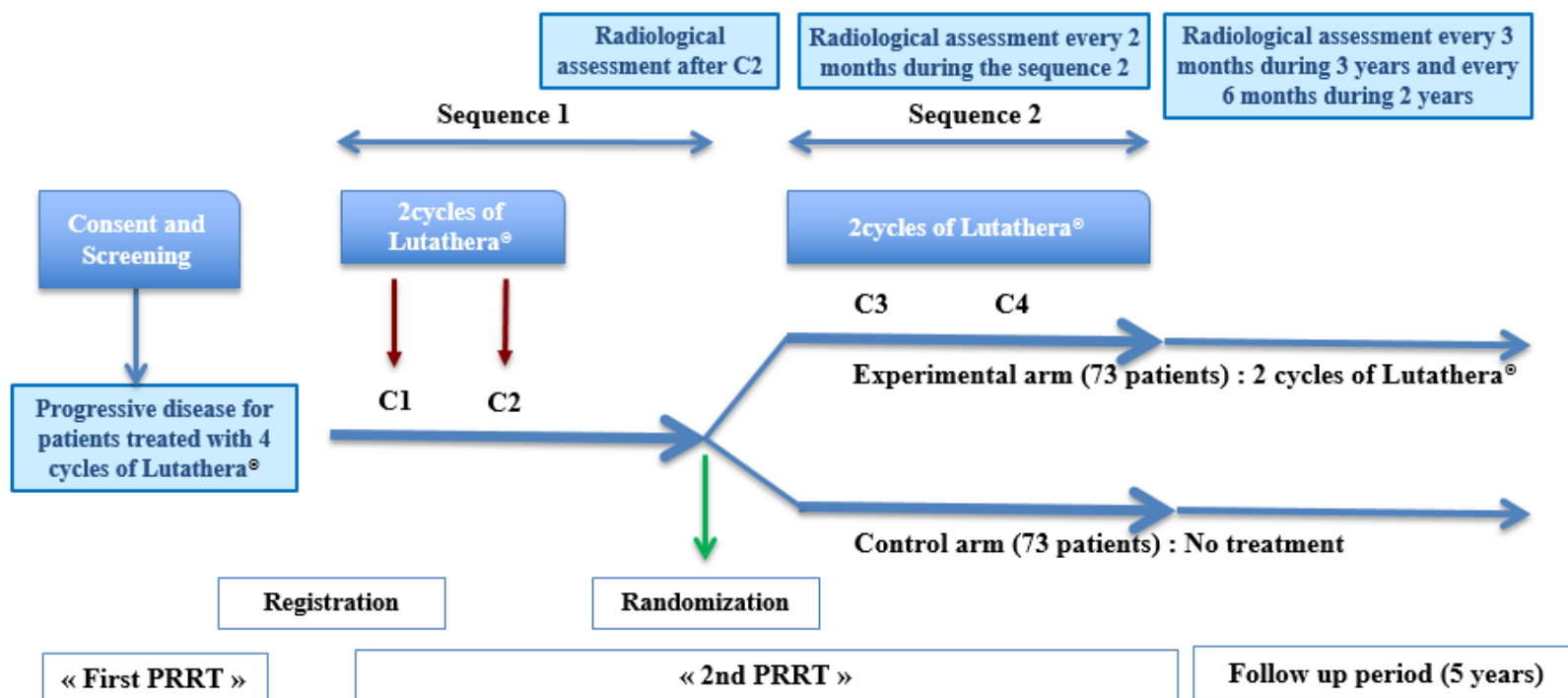
- HOW TO CHOOSE THE BEST FITTING CURVE ?



MSD : 0.0000000000 rho : 1.000
rho trap (0.1) 0.992765

Contribution ([h,h]) : [0,188] 74.09% [188,2400] 25.9% [0,2400] 100.0%

The story goes on : PHRC RELUTH



Primary objective :

To evaluate the efficacy of two additional cycles of Lutathera® (one injection every two months), compared to active surveillance during 6 months in patients already retreated with two cycles.

Ancillary Study :

This ancillary dosimetric study will collect data from various centers who already performed dosimetry for [177Lu]Lu-DOTA-TATE PRRT. It will help answering scientific questions specific to molecular radiotherapy clinical dosimetry. The exploratory objective of the ancillary study is to generate dosimetric data from patients treated with Lutathera® and establish the correlation with clinical outcome (disease control and toxicities).

Strong collaboration between physicists and physicians allows ^{177}Lu -based PRRT **dosimetry in clinical routine**

- **Technologists**
- **Radiopharmacists**
- **Physicist residents**
- **Radiations protection experts**
- **Patients**



For:

- Personalization of patient's follow-up & (re)treatment
- Better understanding of underlying mechanisms (radiobiology)

Further developments still expected :

- AI
- Less time points ?
- TAC fitting
- Standardisation
- Bone marrow dosimetry optimization



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Merci de votre attention