

MetroMRT 3rd Workshop

**“Clinical implementation of dosimetry
for molecular radiotherapy”**

**National Physical Laboratory, Teddington, UK
20-21 April 2015**

The way forward?

**Experience with a dosimetry-based PRRT trial
at Reggio Emilia**

Annibale Versari*, MD and Elisa Grassi**

***Nuclear Medicine and **Medical Physics Departments
S.Maria Nuova Hospital-IRCCS
Reggio Emilia – Italy**



versari.annibale@asmn.re.it
grassi.elisa@asmn.re.it

Disclosure Slide

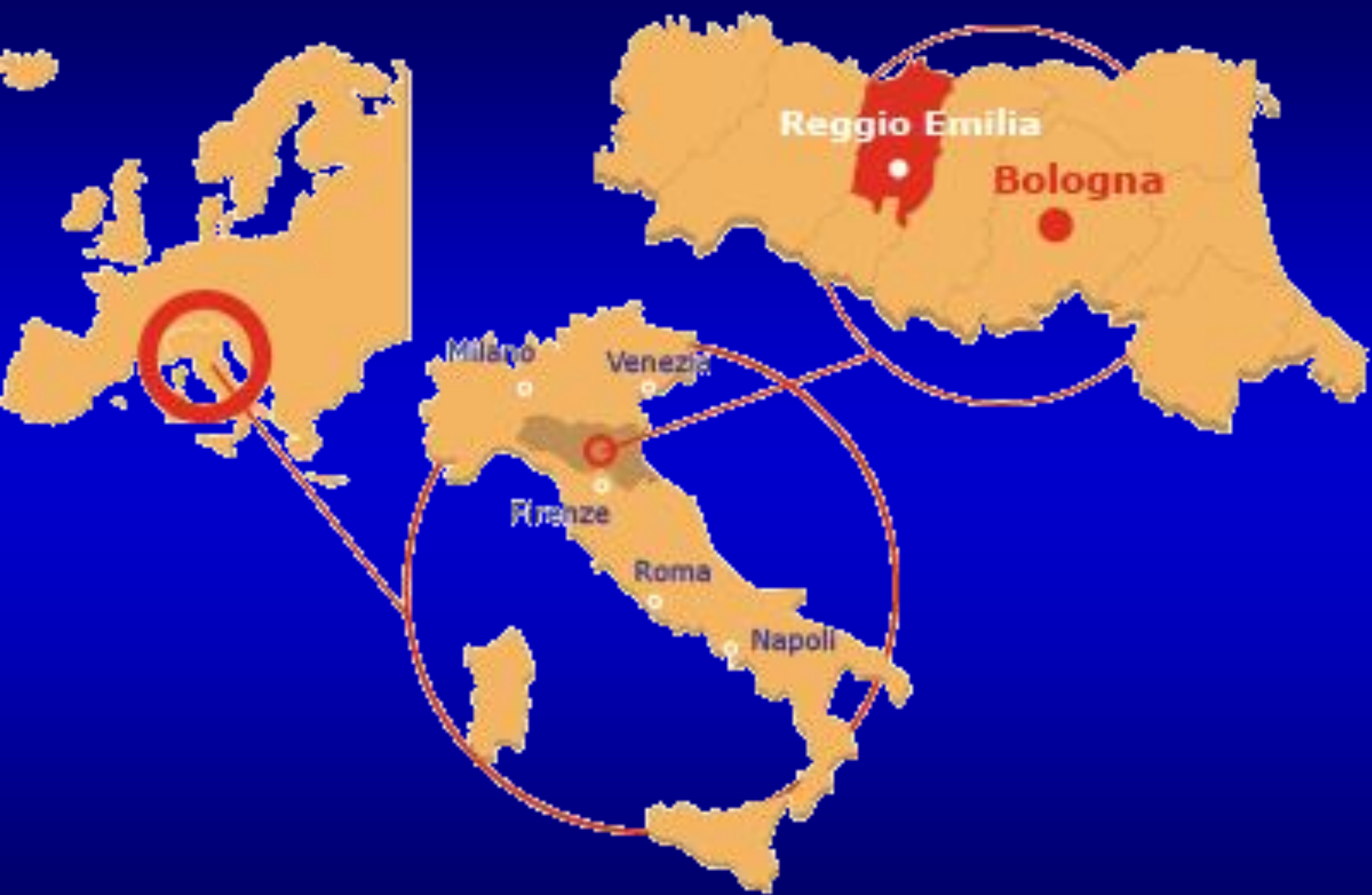
Il sottoscritto **Annibale Versari**

DICHIARA

X che, nell'esercizio delle funzioni di Relatore, **NON E'** in alcun modo portatore di interessi commerciali propri o di terzi; dichiara altresì che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le proprie funzioni al fine di trarne vantaggio;

che negli ultimi due anni HA AVUTO i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario (aziende farmaceutiche, biomedicali e di diagnostica):

- 1.....
- 2.....
- 3.....
- 4.....
- 5.....



Nuclear Medicine-PET Center



800 beds

SANTA MARIA NUOVA HOSPITAL – IRCCS

REGGIO EMILIA - ITALY



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliera di Reggio Emilia

Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia
Istituto di Ricovero e Cura a Carattere Scientifico



Nuclear Medicine Department Reggio Emilia (Italy)

ARCISPEDALE
SANTA MARIA NUOVA
AZIENDA OSPEDALIERA
REGGIO EMILIA
Regione Emilia-Romagna

Traditional Nuclear Medicine

- 1 small field gamma camera
- 1 SPECT
- 1 SPECT/CT

PET Center

- 1 Cyclotron
- 1 PET/CT
(^{18}F -FDG, ^{18}F -Choline,
 ^{68}Ga -DOTATOC)

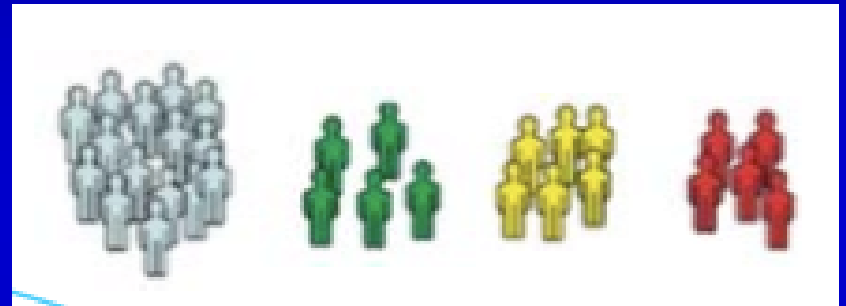
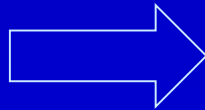
Nuclear Medicine Therapy

- 8 beds
(16 pts/week)
- ^{131}I
- ^{90}Y -DOTATOC
- ^{177}Lu -DOTATOC
- ^{90}Y -Zevalin



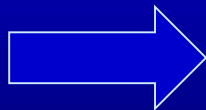
Towards

“ a personalized medicine ”



From

Same Diagnosis
Same Treatment



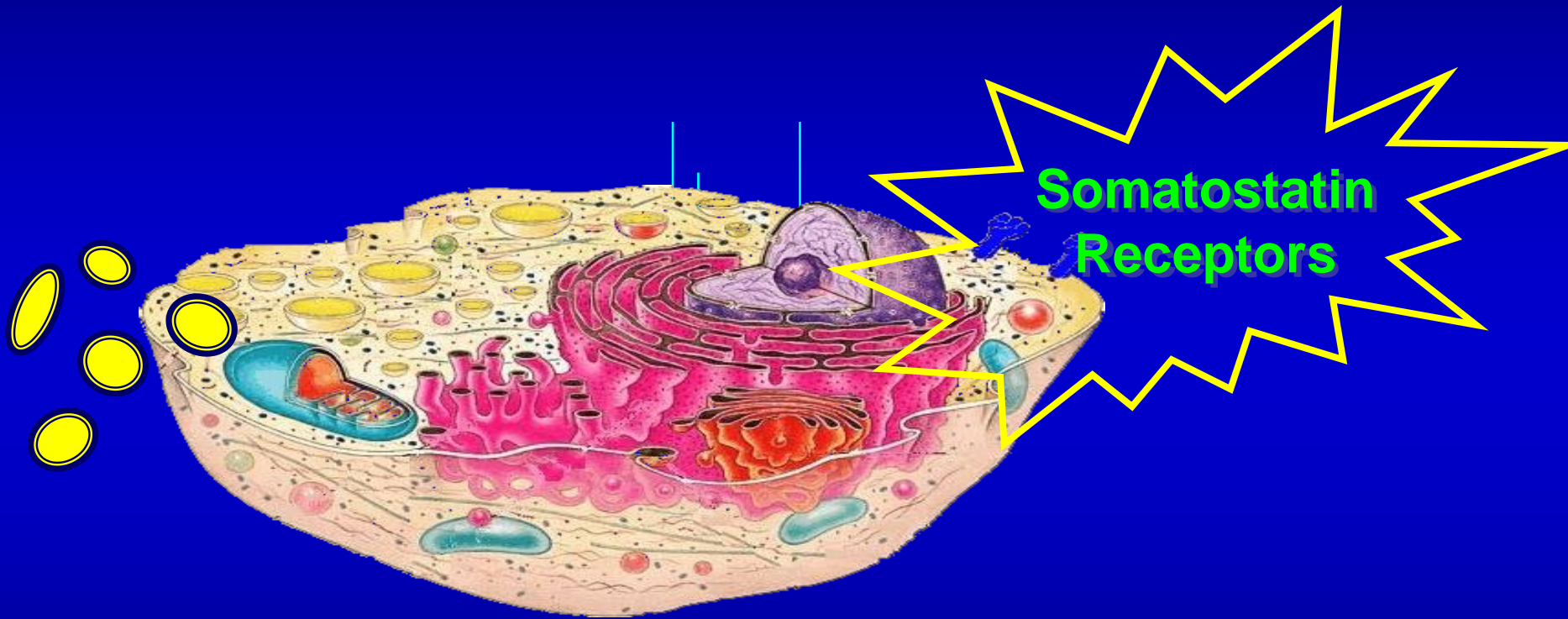
To

Molecular Diagnosis
Molecular Imaging
Individualized Treatment

PET Radiopharmaceuticals

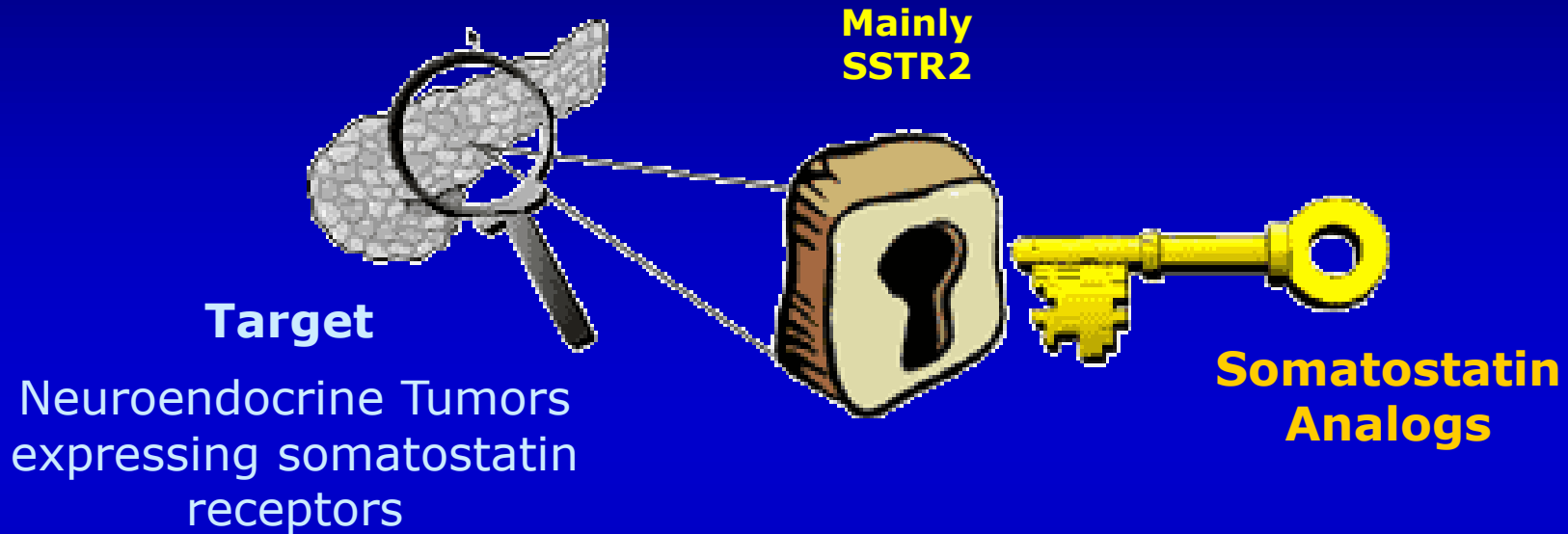
FUNCTION/METABOLISM	TRACER
Glucose metabolism	^{18}F -fluoro-deoxy-glucose (FDG)
DNA replication/cellular proliferation	^{11}C -carbon-thymidine ^{18}F -fluoro-thymidine (FLT)
Protein synthesis, amino acid transport	^{11}C -carbon-methionine (MET) ^{18}F -fluoro-ethyl-tyrosine (FET), etc
Membrane lipid synthesis	^{18}F -fluoro-acetate ^{11}C -carbon-choline ^{18}F -fluoro-choline (FCH)
Hypoxia	^{18}F -fluoro-misonidazole (FMISO) ^{64}Cu -copper-ATSM
Apoptosis	^{18}F -fluoro-annexin V
Angiogenesis	^{18}F -fluoro-galacto-RDG
Reporter genes	^{18}F -fluoro-deoxy-arabinofuranosyl nucleosides
Tumor therapy control	^{18}F -fluoro-uracil (FU)
Receptor binding (estrogen)	^{18}F -fluoro-estradiol (FES)
Receptor binding (somatostatine)	^{68}Ga -gallium-DOTATOC/DOTANOC

Neuroendocrine Tumors (NET)



NETs

Nuclear Medicine Imaging (molecular imaging)



Methods

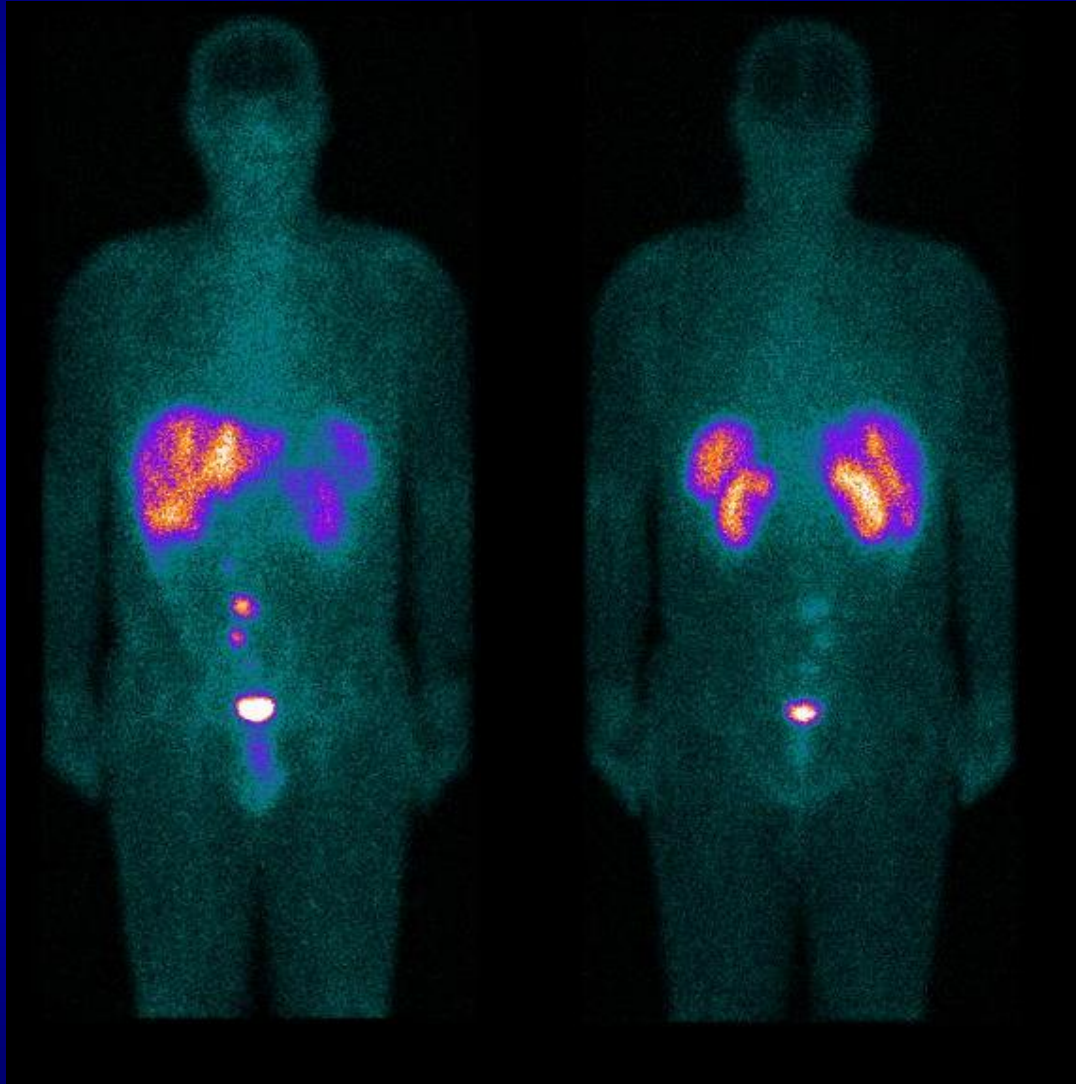
Scintigraphy, SPECT, SPECT/CT with

- ^{111}In -Octreoscan

PET/CT con

- ^{68}Ga -DOTATOC
- ^{68}Ga -DOTANOC
- ^{68}Ga -DOTATATE

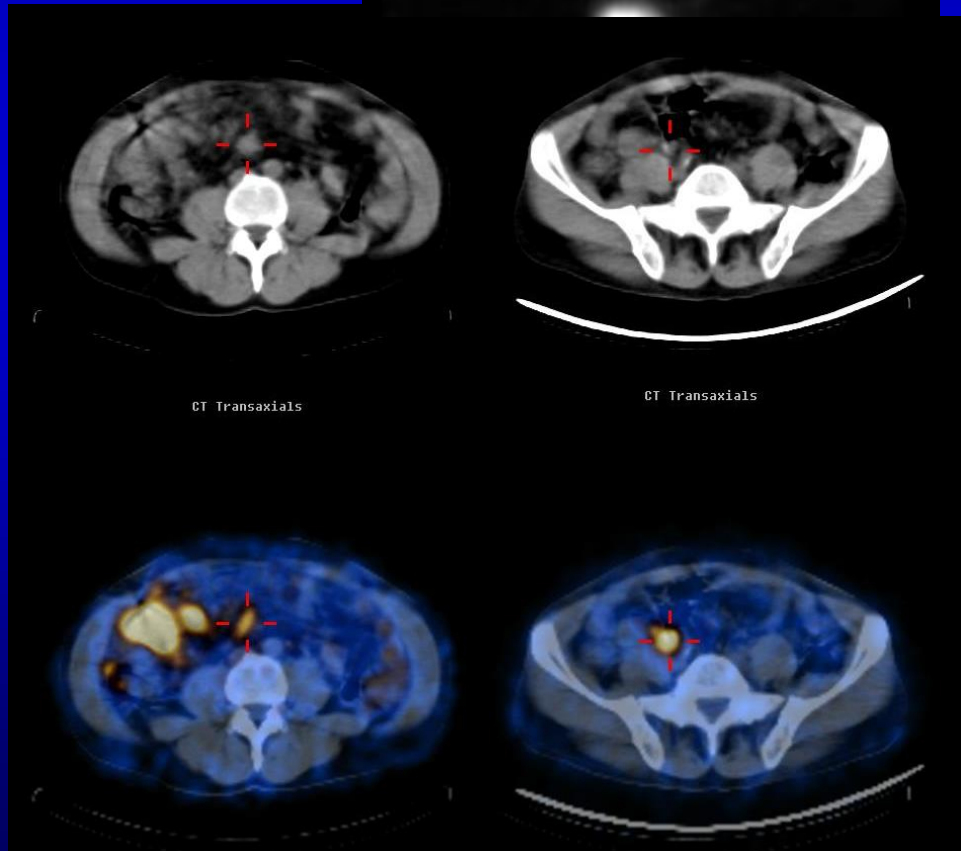
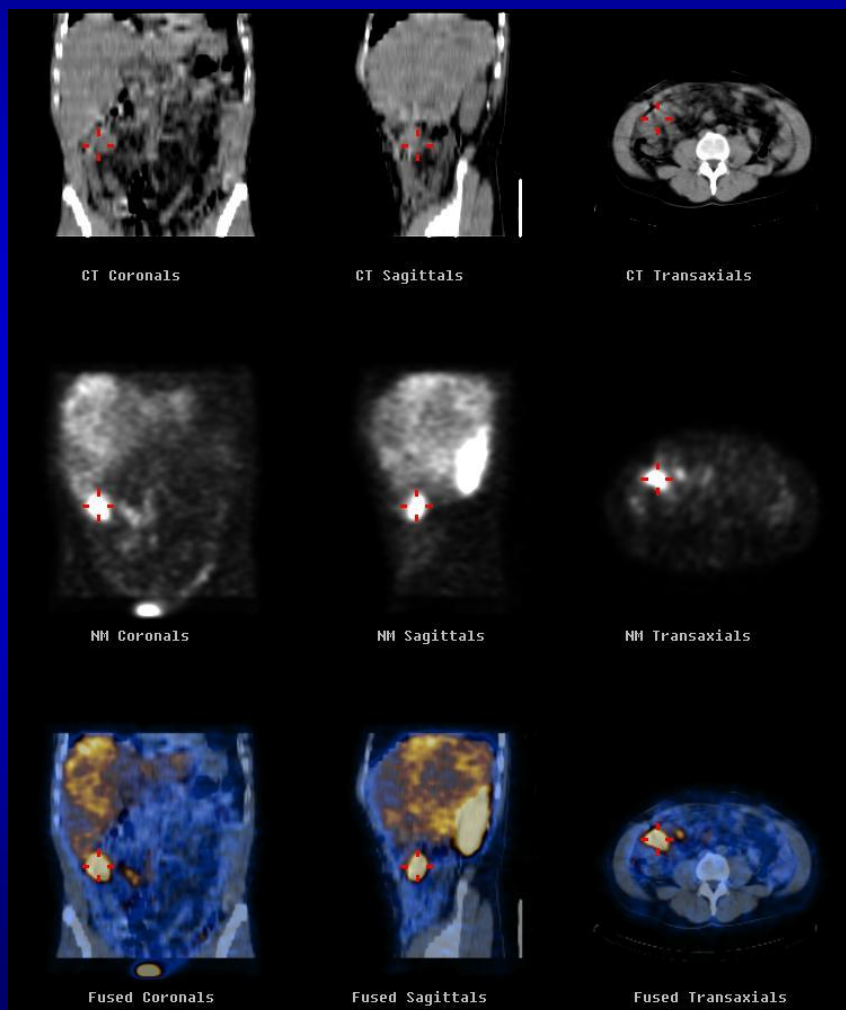
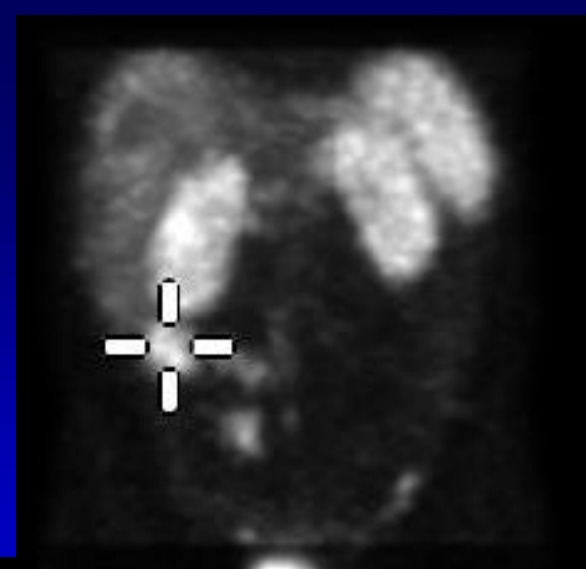
^{111}In -Octreoscan



Ileum NET

Octreoscan®: SPECT/CT

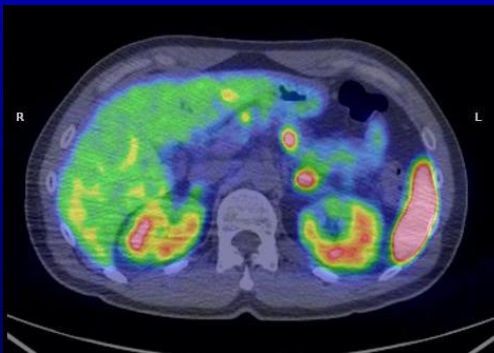
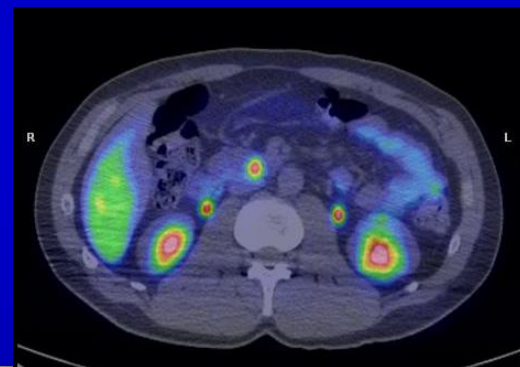
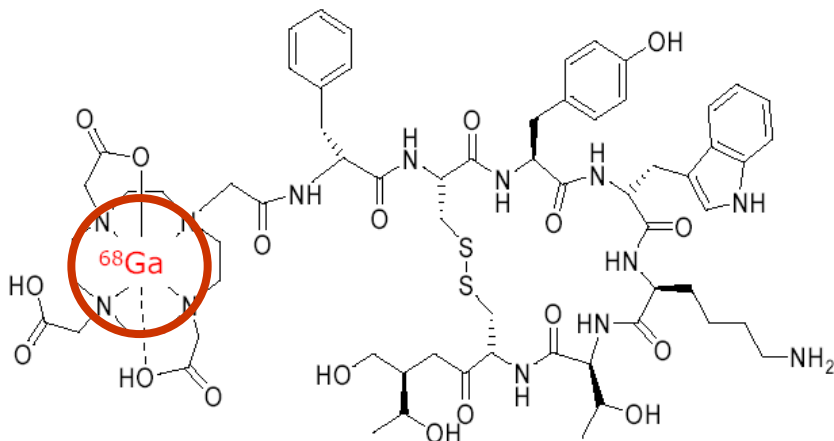
Ileum NET



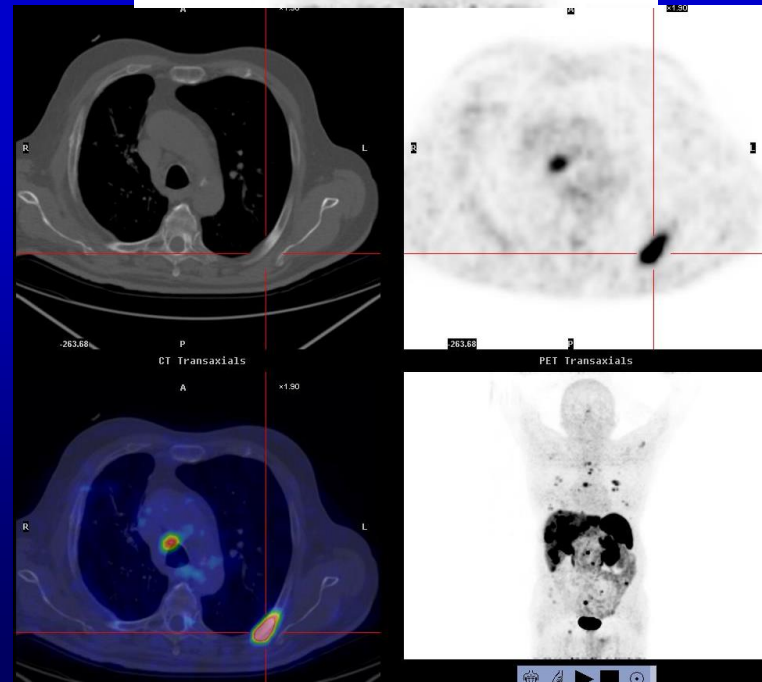
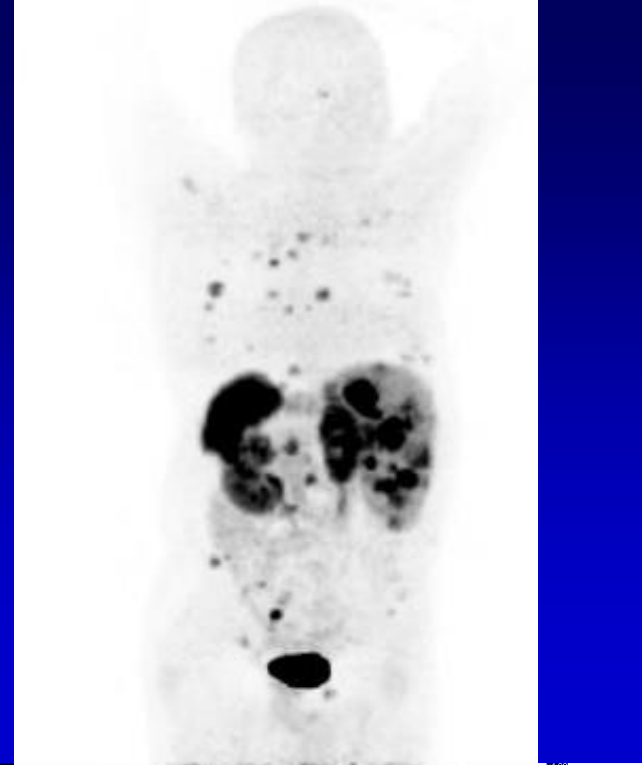
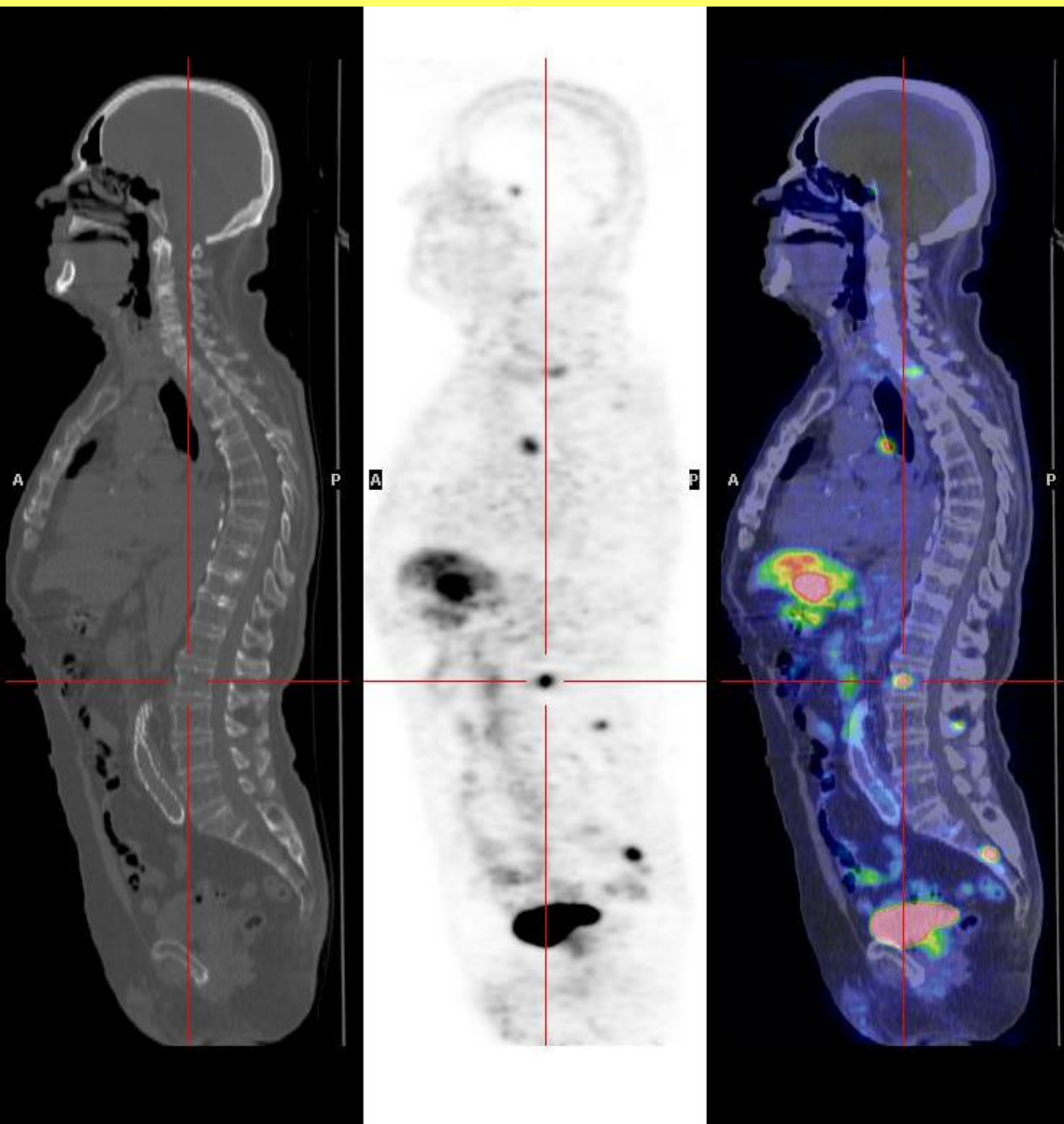
^{68}Ga DOTATOC PET/CT



Generatore $^{68}\text{Ge}/^{68}\text{Ga}$



^{68}Ga -DOTATOC PET/CT



Multiple Metastases from Bowel NET

Interdisciplinary Discussion

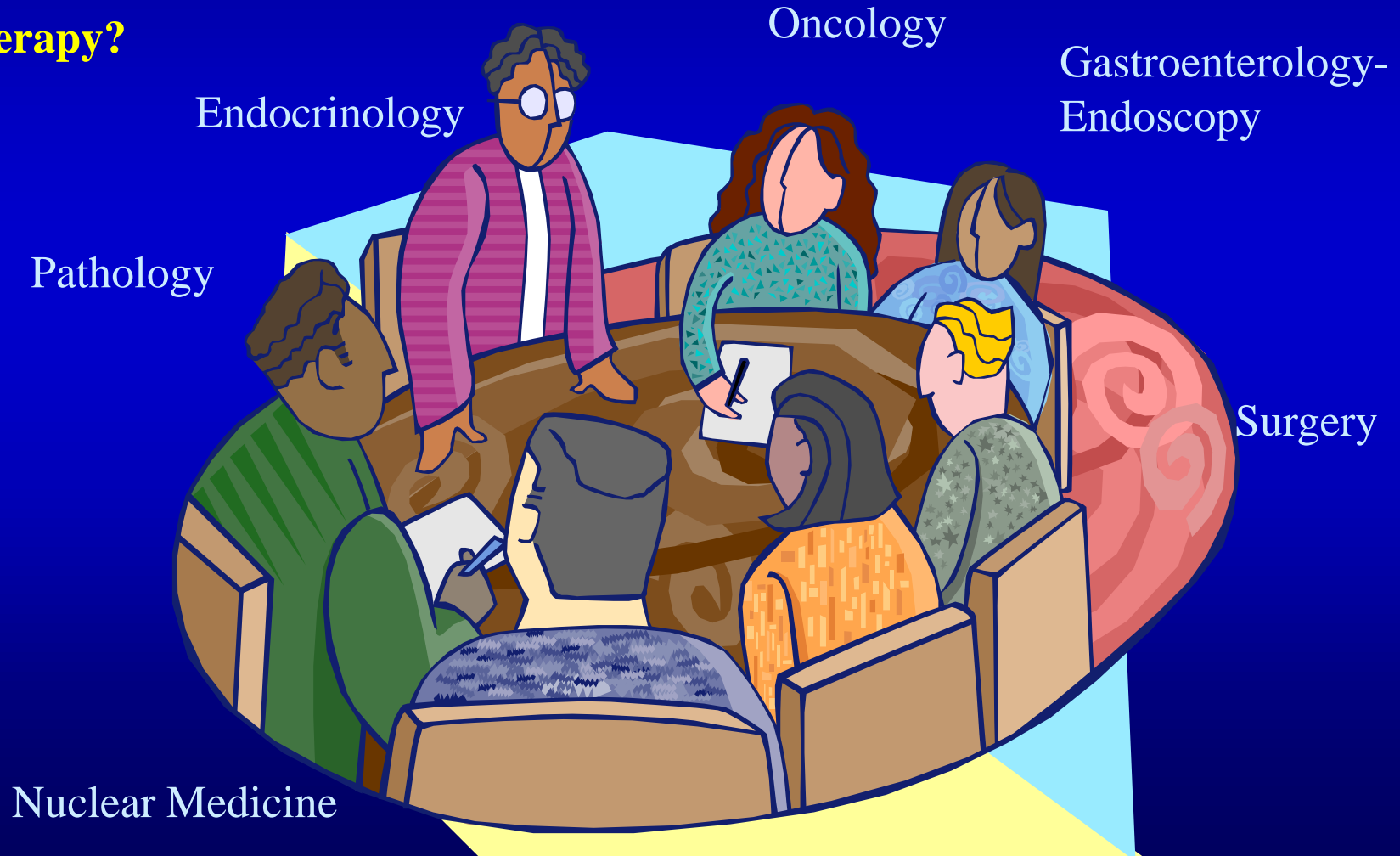
What treatment?

Somatostatin Analogs?

Biological Pharmaceutical?

Chemotherapy?

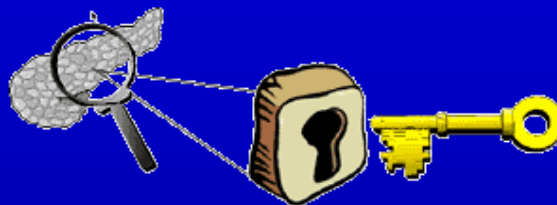
PRRT?



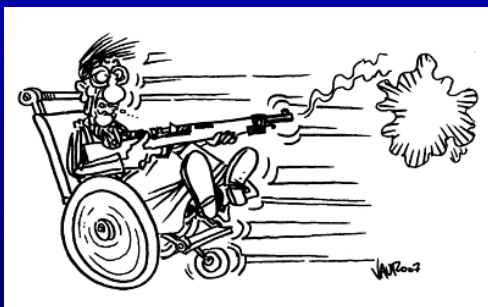
From diagnosis to treatment



Diagnosis
 ^{68}Ga



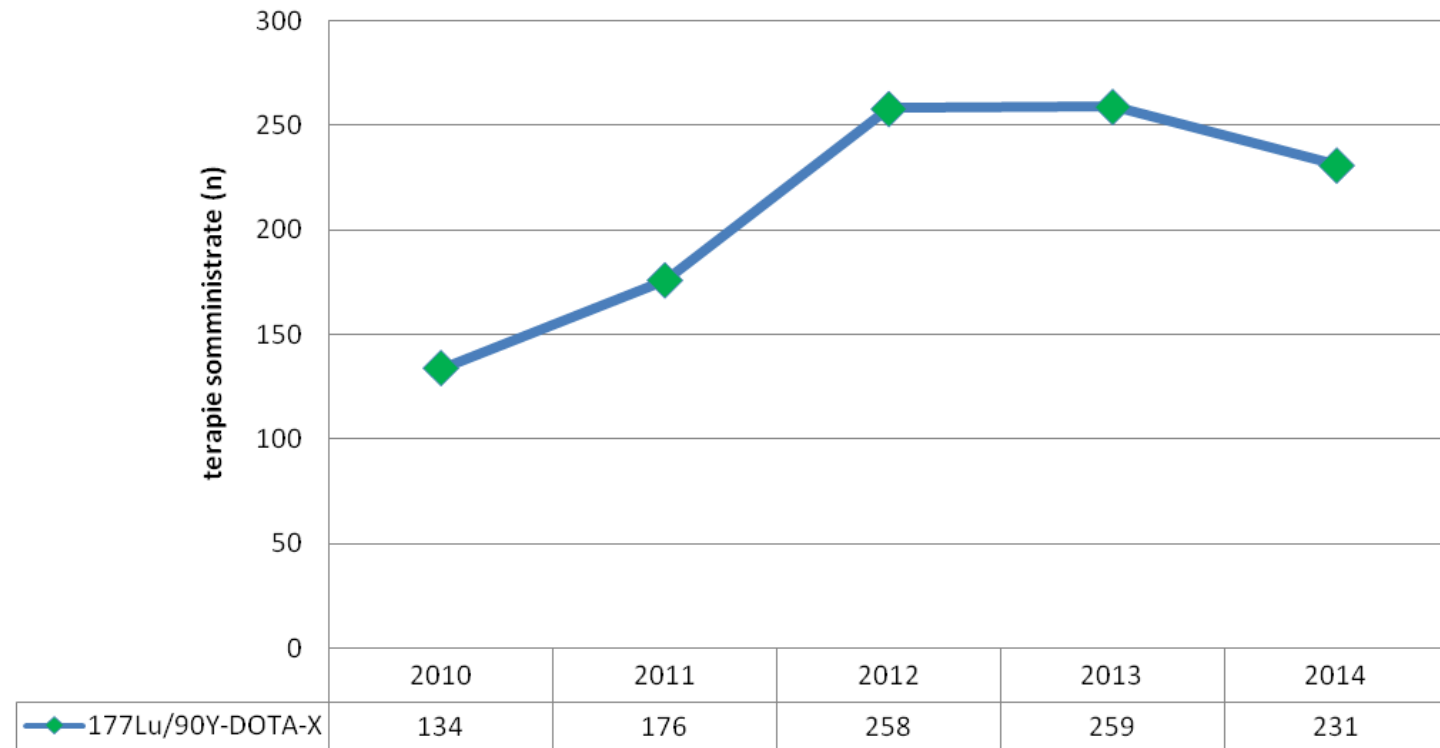
DOTA-TOC



Therapy (PRRT)
 ^{90}Y / ^{177}Lu

Peptide Receptor Radionuclide Therapy (PRRT) Reggio Emilia 2010-2014

PRRT treatments

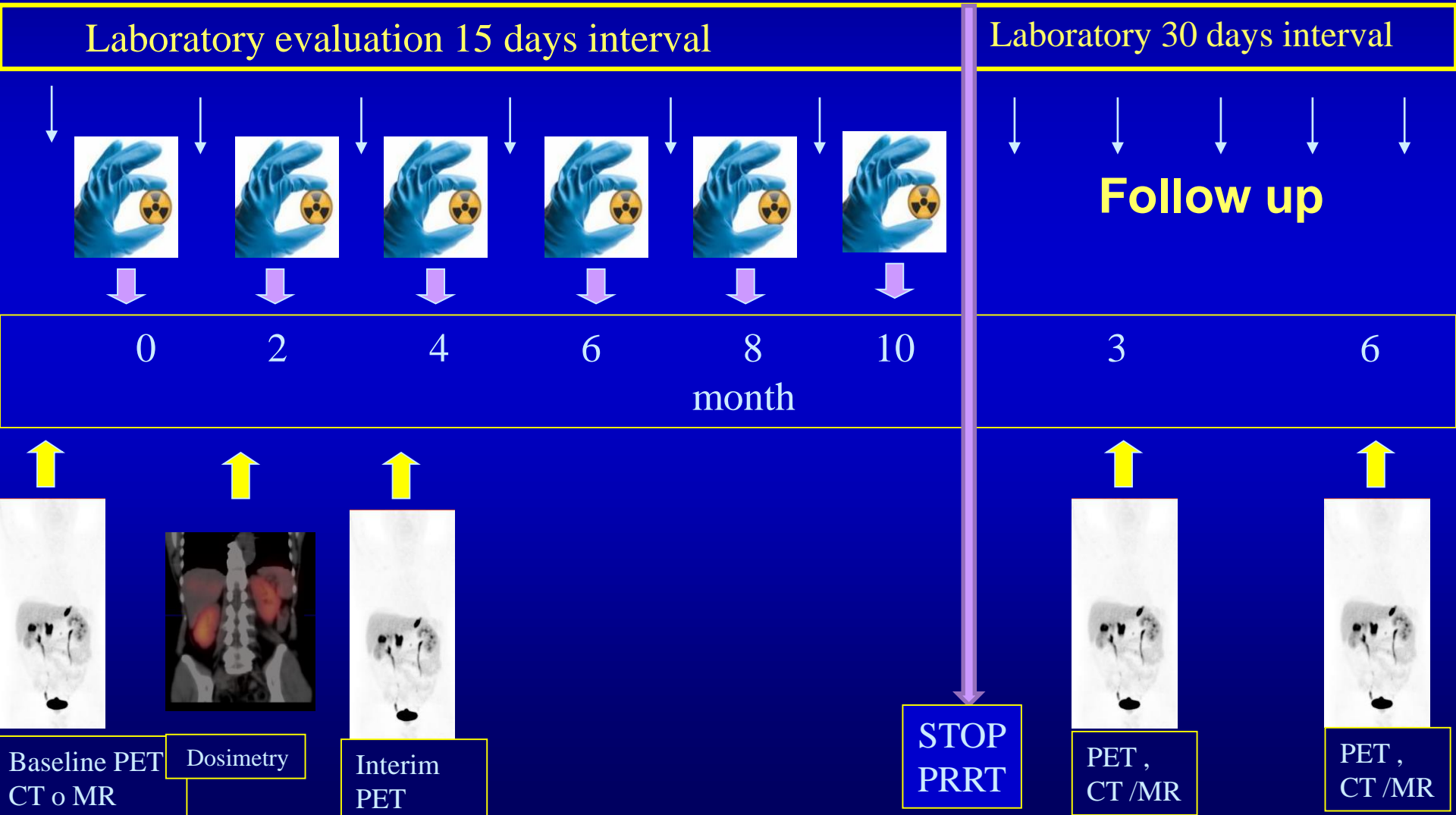


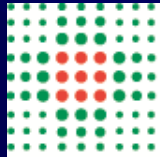
Start in 2007: 4 PRRT/month
2015: 6 PRRT/week

PRRT

DOTATER Trial - Reggio Emilia

(NETs, 100 pts, 2 years, ongoing)





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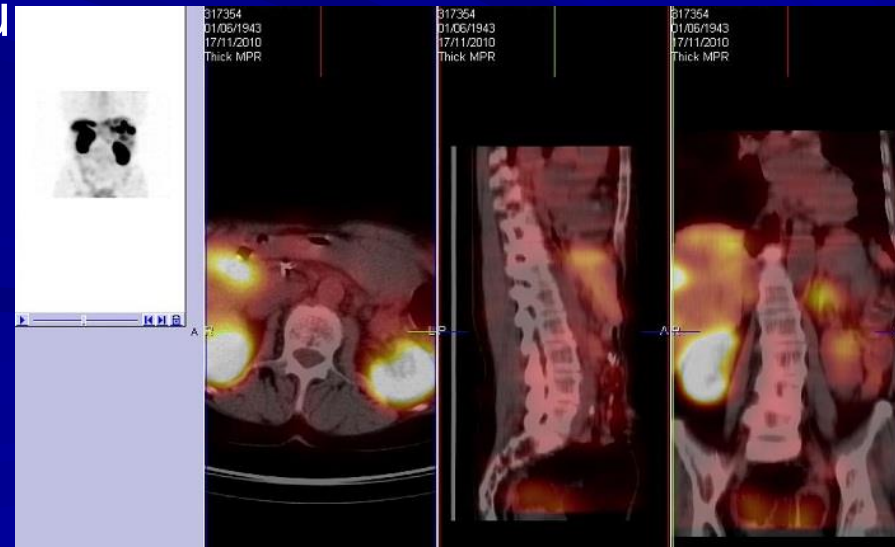
^{177}Lu 3D dosimetry for PRRT with ^{177}Lu
and ^{90}Y in DOTATER protocol: a
prospective, non-randomized,
monocenter, phase II trial

Our present workflow

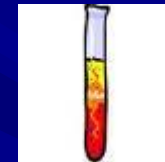
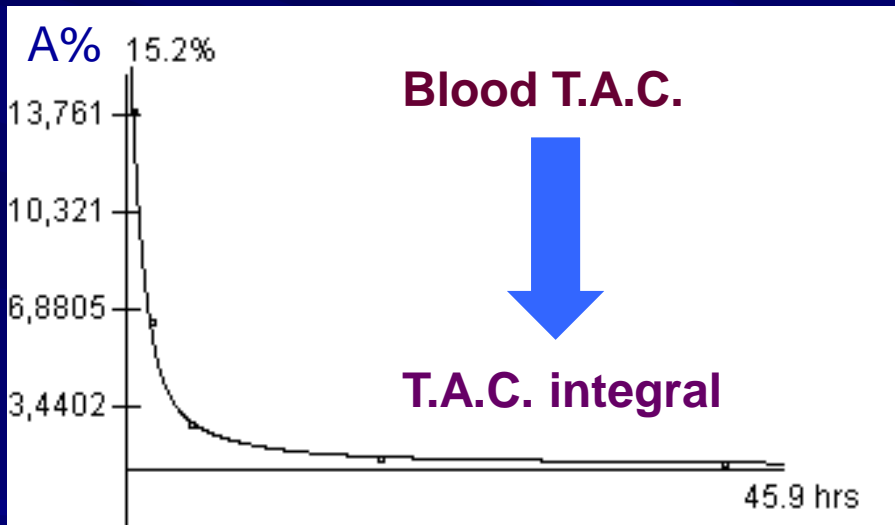
- Each patient undergoes a series of **5 SPECT-CT scans** of the **abdomen** at 1, 4, 24, 44, 72 h p.i., with the standard clinical acquisition protocol for body studies
- No particular method for assuring reproducibility of patient repositioning in imaging was adopted: patients were positioned in supine configuration with arms raised and placed on a shaped pillow.
- If any lesions aren't included in the abdomen, 3 extra **SPECT-CT scans** are acquired at 4, 40, 70h p.i. over **thorax or brain**.
- Dosimetry is performed only once.
- Tandem treatment: ^{90}Y and ^{177}Lu

SPECT/CT acquisition

1 h, 4h, 24h, 44h, 72h p.i.
optionally
4h, 40h, 70h p.i.



- Dose calculation for kidneys, liver and spleen is usually performed with a mean dose computation technique using the **OLINDA/EXM package**
- **Red Marrow toxicity** is estimated through the analysis of the activity concentration in blood (5 samples collected from 1h to 44h p.i.)



Blood samples
10', 40', 4h, 20h e 44h t.p.i.

Voxel dosimetry of organs is performed exclusively in a selection of cases...

- Mesh Representation
- Contouring
- Derive new structure
- Copy from one scan to other
- Consensus
- View all structures
- View no structures
- Structure Set 1

Window: --Manual-- Colormap: gray256

Interactive Windowing

Center: 0 Width: 300

Dose

Scan

Loop

S+ S- Ruler

Contouring

Struct: 1. rene_sx

Rename: rene_sx

Scan: 1. CT SCAN

Category: ORGAN

As copy of current

As new on scan 1. CT SC...

New Structure: Create

Mode: Draw

Copy +Z Copy -Z

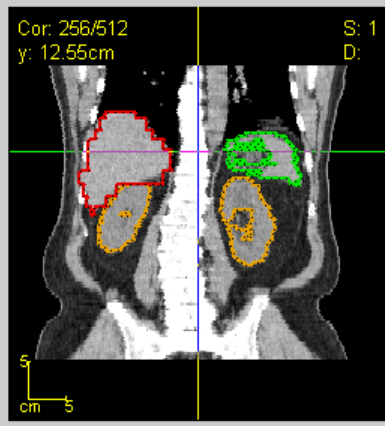
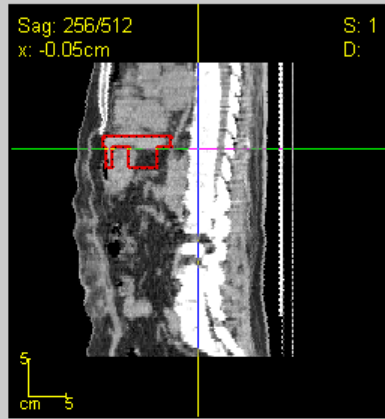
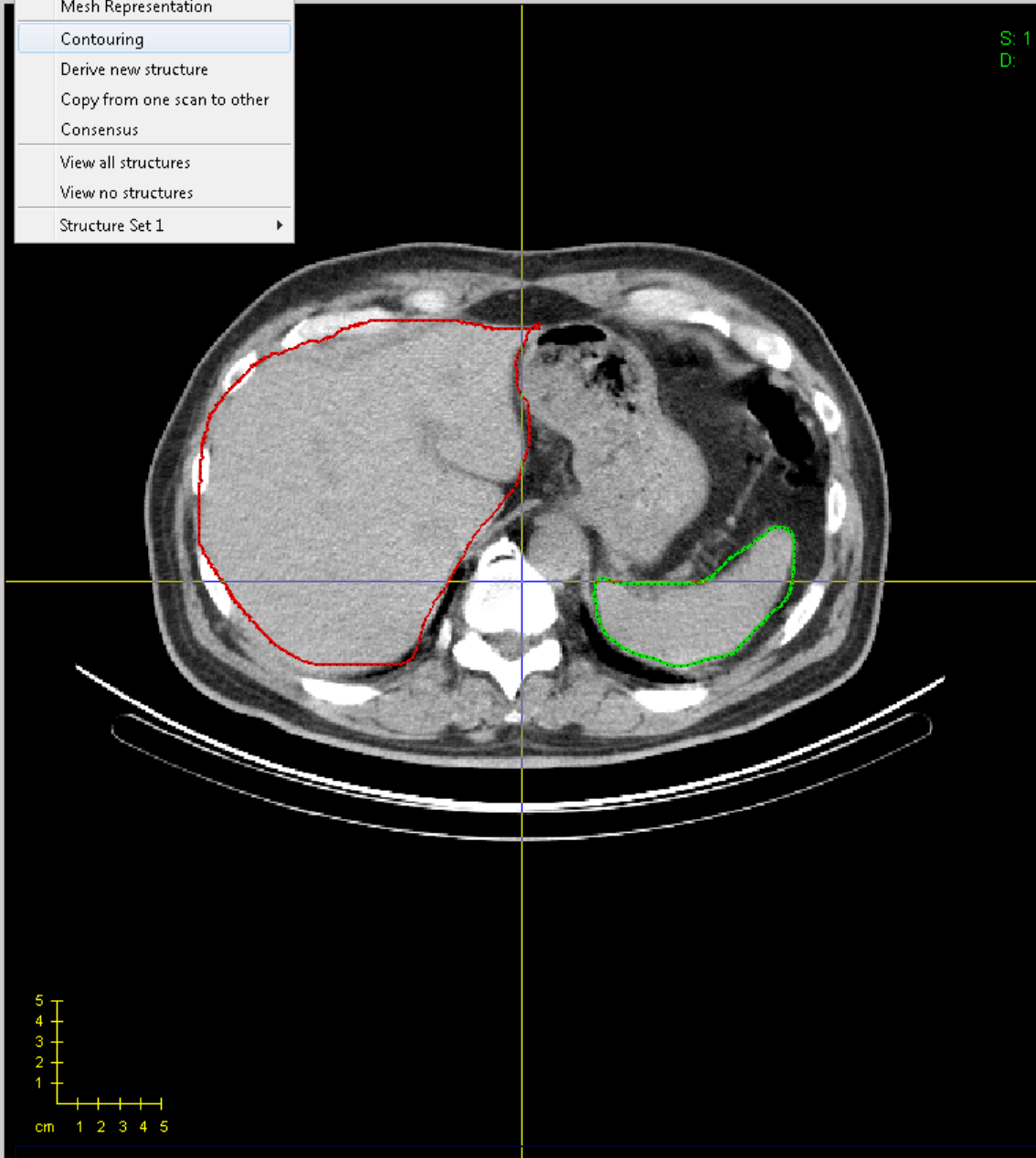
Delete Selected Segment

Move to: 1. rene_sx

Overlay Scan: 1 AbdRo... Options

Save Cancel

Command: help



- Legend**
- rene_sx
 - spleen
 - liver

VoxelMed developed by Dr. Valentina Ferri, ASMN-IRCCS Reggio Emilia

Grassi E, Fioroni F, Ferri V, et al. Phys Med 2015 Feb;31(1):72-9.

Tra: 33/112
z: -134.05cm

S: 1
D:

Sag: 256/512
x: -0.05cm

S: 1
D:

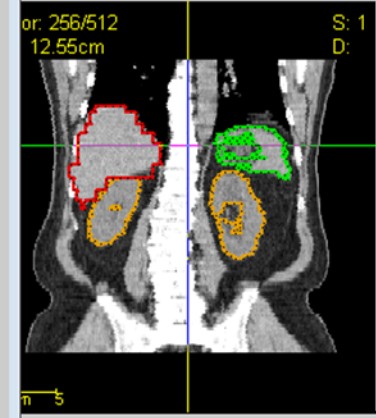
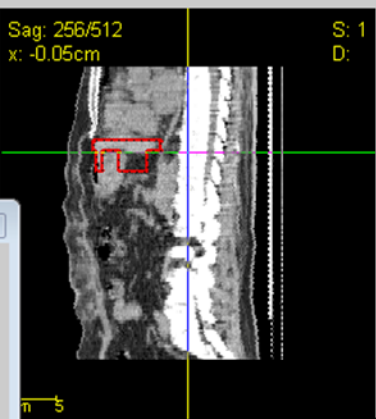
Calculate Dose Menu

Select structure

rene_sx spleen liver

Activity/dose

Dose Set	Residual	Average Dose [Gy]
	<div style="border: 1px solid gray; padding: 2px;"> Initializing... </div>	



- legend**
- rene_sx
 - spleen
 - liver

Window: --Manual-- Colormap: gray256

Center: 0 Width: 300

Ruler

Registration

No registration Rigid

Use SPECT Elastic

Use CT

Input data

Isotope: Y90 t0 [s]: 1800

A0 [GBq]: 5.55 tailend [h]: 200

Calibration factor [Bq/counts]: 26

Voxel S Values: 3_3.90_3.90

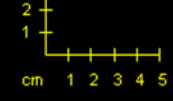
Activity/Dose analysis

Tail Eff. Tail Phys.

Tail Eff. Int. Tail Phys. Int.

Eff.

Command: voxelMed





Calculate Dose Menu

Select structure

rene_sx
 spleen
 liver

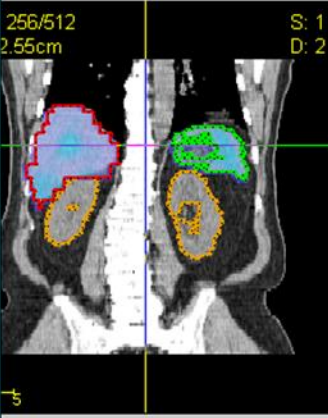
Select all

Calculate dose

Time-activity curves

Activity/dose

Dose Set	Residence time (tot.) [h]	Residence time (voxel) [h]	Average Dose [Gy]
Trapez.	1.085e+00	2.944e-05	1.734e+00
TailEff	8.565e-01	2.324e-05	3.081e+00



- end
- rene_sx
- spleen
- liver

Window: --Manual-- Colormap: gray256

Interactive Windowing

Center: 0 Width: 300

Loop

S+ S- Ruler

Registration

No registration
 Rigid
 Use SPECT
 Elastic
 Use CT

Register

Input data

Import SPECT

Isotope: Y90 t0 [s]: 1800

A0 [GBq]: 5.55 tailend [h]: 200

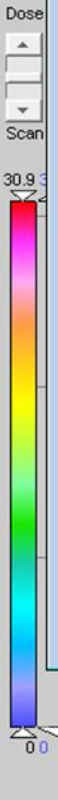
Calibration factor [Bq/counts]: 26

Voxel S Values: 3_3.90_3.90

Activity/Dose analysis

Tail Eff.
 Tail Phys.
 Tail Eff. Int.
 Tail Phys. Int.
 Eff.

Calculate dose



Command: voxelMed

Save Exit


TailEff

General overview of this trial

- Unlike the previous trials, DOTATER gives a strong importance to dosimetry in the clinical practice
- A dose limit to kidneys is set as a total BED value: 46Gy with no risk factor pts, 28Gy with risk factor pts.
- Kidney BED values for recruited pts mustn't exceed the set limit
- Red marrow dose mustn't exceed 2Gy
- Dosimetry studies must be performed at worst at the second therapy administration to have a predictive scope

Dosimetry Reporting

- The dosimetry results must be reported before the following administration of the pt.
- A physical report is included in the medical record (kidney and red marrow doses at present)

		SERVIZIO SANITARIO REGIONALE EMILIA ROMAGNA Azienda Ospedaliera di Reggio Emilia Azienda Ospedale S. Maria Nuova IRCCS in Tecnologie Avanzate e Modelli Assistenziali in Oncologia Dipartimento Tecnologie Avanzate		S.C. di Medicina Nucleare Centro PET/CT e Ciclotrone Centro di Eccellenza AIMN "Utilizzo della PET in Radioterapia" Terapia Medico Nucleare Direttore : Dott. Annibale Versari			
Cod. Cartella Data di Nascita Luogo di Nascita Codice Fiscale			Name surname Address				
Ente o Reparto di provenienza HRE-TERAPIA RADIOMETABOLICA		Letto		Radiofarmaco		Dose (MBq)	
Data Indagine 23/03/2015		Nomenclatore - 92.18.5 -		Codici di Casa - 004B - 5107 -			
WHOLE BODY LU177-DOTATOC-DOSIMETRIA							
Lo studio dosimetrico del paziente trattato con peptidi radiomarcati ha fornito le seguenti dosi agli organi a rischio per unità di attività somministrata:							
90Y ai reni (Gy/GBq): 5.40							
90Y al midollo (Gy/GBq): 0.0265							
177Lu ai reni (Gy/GBq): 0.892							
177Lu al midollo (Gy/GBq): 0.00715							
La scelta dell'attività effettiva da somministrare per ciclo di trattamento e cumulativa necessita di ulteriori valutazioni che dipendono dallo schema di frazionamento, dagli aspetti radiobiologici e dal quadro clinico.							
Reggio Emilia il 16/03/2015				Operatore		Medico Nucleare FISICO E. GRASSI	
Il presente Referto serve come dichiarazione degli isotopi Radioattivi somministrati a scopo diagnostico o terapeutico nelle quantità riportate							
Telefono 0522-296540 Fax 0522-296193			www.asmn.re.it		Pag. 1 di 1		

Stressing the tumour dose evaluation

- Correlating the therapy response to the dose of every target lesion
- Evaluating the therapy response with ^{68}Ga -PET/CT and correlating the functional data with the morphological ones (from CT and/or MRI)
- **Aim:** no tumour overtreatment
no renal toxicity / no blood toxicity
no tumour undertreatment
- **Advantages:** it may be **very useful** to calculate the tumour-to-kidney ratio

What lesions are to be selected and included in the trial?

- Up to 5 lesions must be identified as target lesionshowever, which ones are the best choice?
- Tumour-to-kidney ratios range in a wide interval
- It seems lesions from the same pt have similar ratios...however, it is a so small sample to lead us to accurate conclusions ... BUT.....

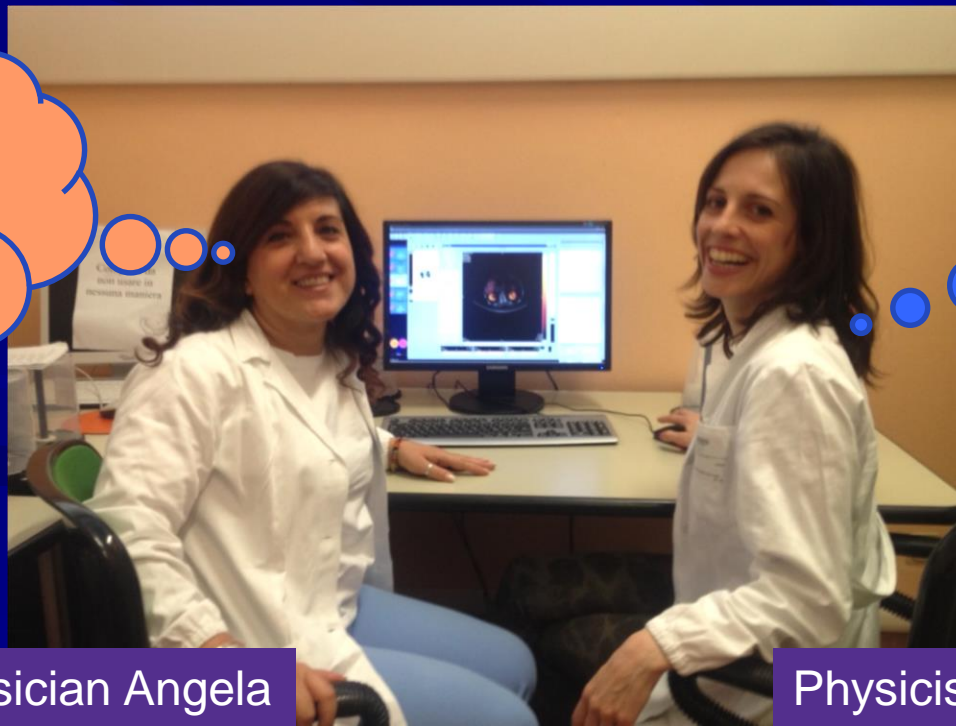
it is enough to stress the need to evaluate a variety of lesions in the same pt

	Lesion to kidney dose ratio	HI D in lesions
pt 2 – lung lesion	1,85	24,15
pt 4 – sternal bone lesion	0,38	76,60
pt 8 - liver lesion 1	4,12	23,41
pt 8 - liver lesion 2	4,88	7,67
pt 11 – liver lesion	0,22	22,73
pt 11 - abd lesion	0,18	3,00
pt 12 - liver lesion	0,26	2,75
pt 13 - liver lesion 1	1,01	130,00
pt 13 - liver lesion 2	1,34	13,05

Clinical and physical know-how converging into.....

- the right time for discussing together....
- a summarizing tool to plan the best therapy option.....
- a deeper interest in comparing OAR doses to lesion doses

these
physicists
are so odd 😞



these
physicians
are so
strange 😞

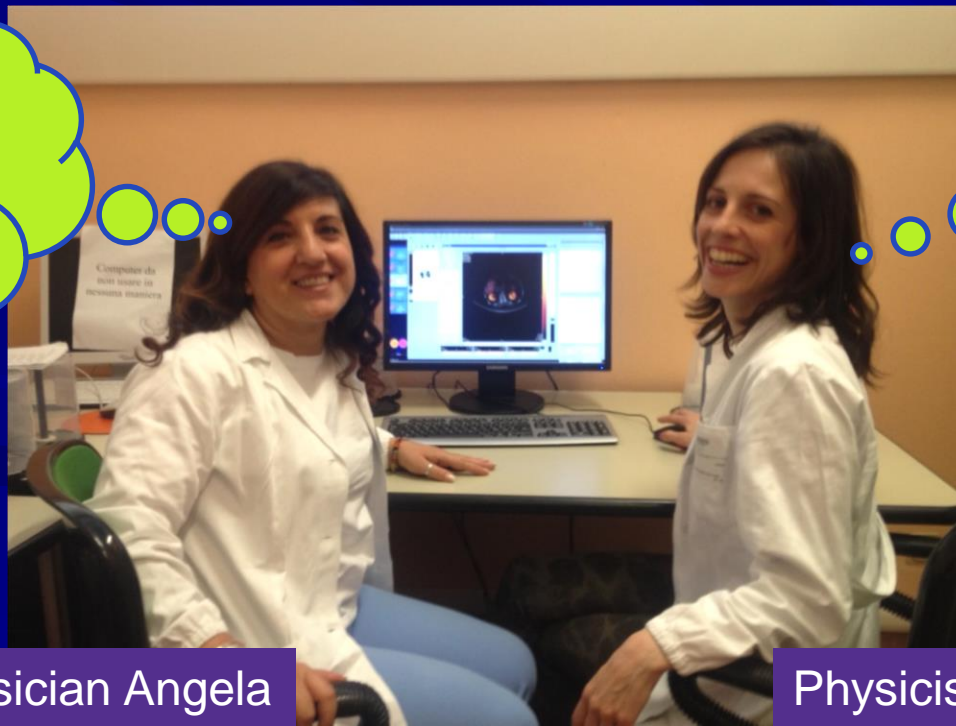
Physician Angela

Physicist Valentina

Clinical and physical know-how converging into.....

- the right time for discussing together....
- a summarizing tool to plan the best therapy option.....
- a deeper interest in comparing OAR doses to lesion doses

these
physicists
are so nice



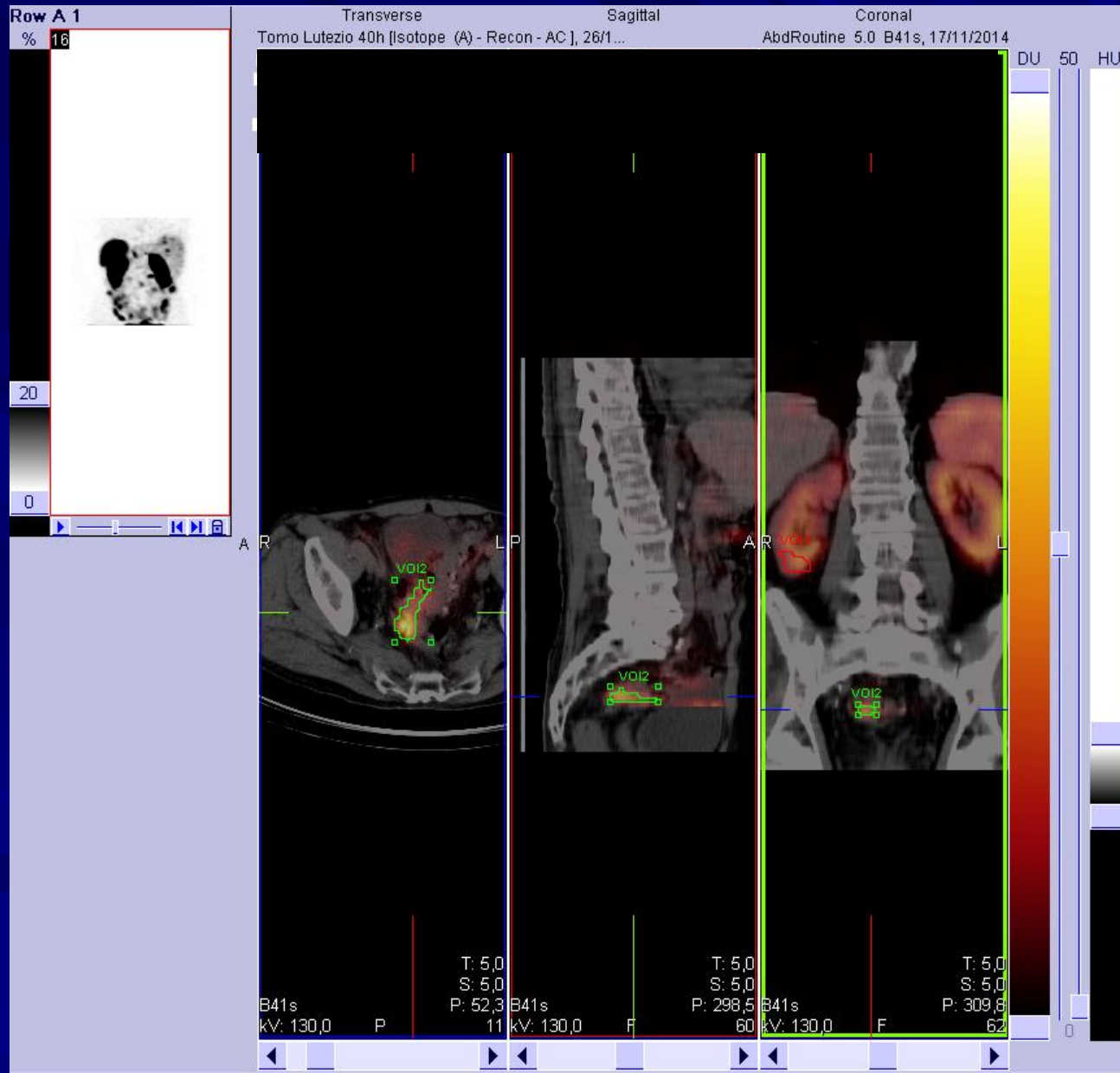
these
physicians
are so nice



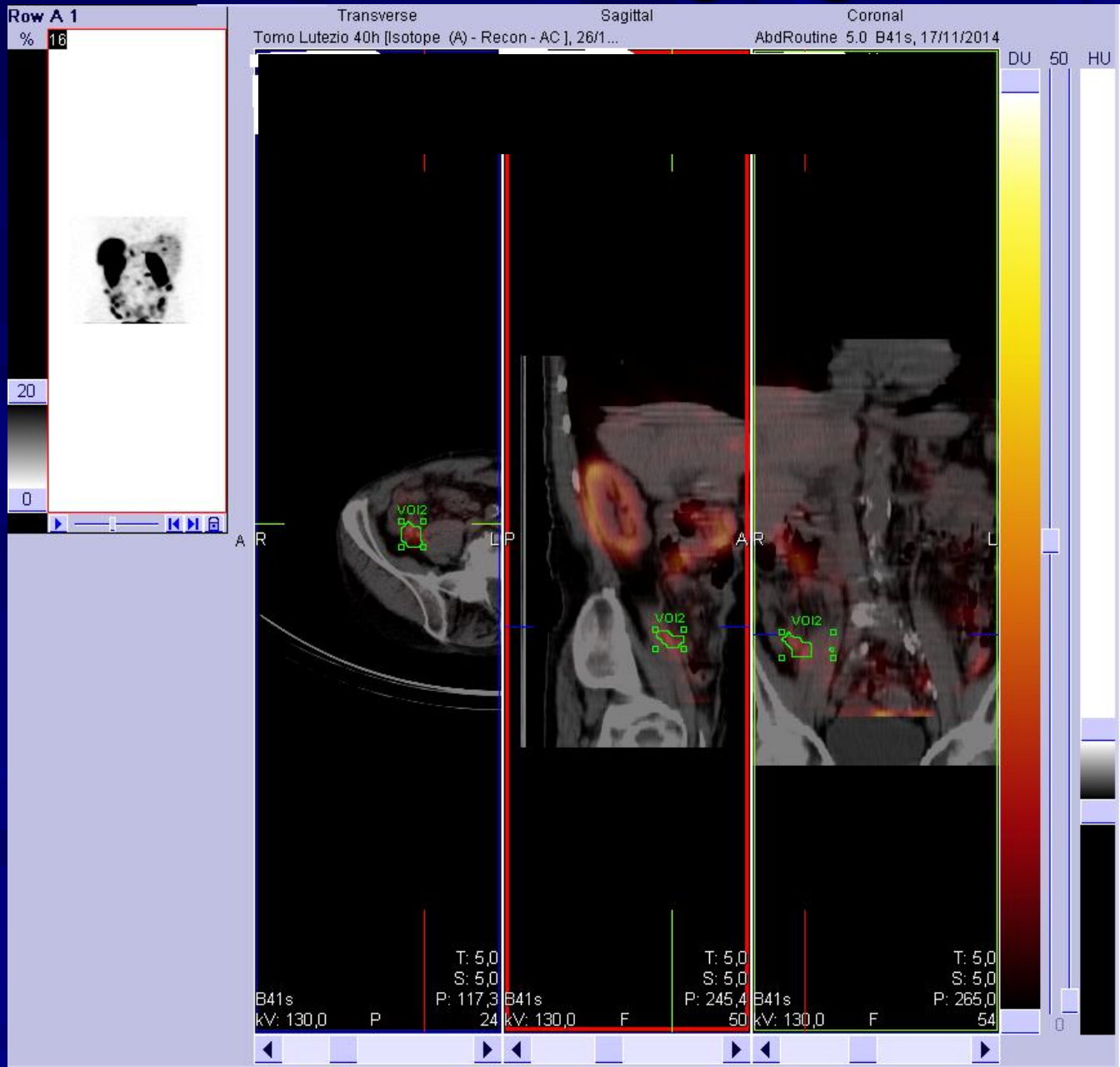
Physician Angela

Physicist Valentina

Pt 1 SPECT-CT imaging: lesion 1



Pt 1 SPECT-CT imaging: lesion 2



Pt1:

Treat.1 Treat.2 Tr 3 Tr 4

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	
Pt name		Y - GBq						Attività tot
	Attività già somministrata	1,81	0,00	0,00	0,00	0,00	0,00	1,81
	Attività prospettica	1,81	1,11	0,00	0,00	0,00	0,00	2,92

Real Adm. activity
Scheduled activity

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	VII tratt.	
		Lu - GBq							Attività tot
	Attività già somministrata	3,66	0,00	0,00	0,00	0,00	0,00	0,00	3,66
	Attività prospettica	3,66	3,70	3,70	0,00	0,00	0,00	0,00	11,06

Real Adm. acti
Scheduled acti

Kidney BED

	RENI (valori in Gy)					RED MARROW (valori in Gy)	
	BED Y	BED Lu	BED tot reale	BED tot prospettica	BED tot consentita	Dose Y	Dose Lu
Attività già somministrata	11	3	15	---	28	0,048	0,024
Attività prospettica	18	11	---	28	28	0,078	0,072

RMdose
Real Adm. activity
Scheduled activity

LESIONI (valori in Gy)											
lesione 1				lesione 2				lesione 3			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
39,43	14,10	---	---	44	15	---	---	8	3	---	---
---	---	63,58	42,59	---	---	70,33	46,80	---	---	13,48	9,45

lesione 4				lesione 5			
Dose reale Y	Dose reale Lu	Dose propsettica Y	Dose propsettica Lu	Dose reale Y	Dose reale Lu	Dose propsettica Y	Dose propsettica Lu
0	0	---	---	0	0	---	---
---	---	0,00	0,00	---	---	0,00	0,00

lesione	volume (ml)
ABD-peritoneo pararettale dx	13
ABD - peritoneo sottoneatico dx	17
TOR retrosplenica	4,00
0,00	0,00
0,00	0,00



Interdisciplinary Discussion

What PRRT strategy?

How many cycles?

90Y or 177Lu?

What total dose?

Nuclear Medicine
Physician

Physicist

Endocrinologist/
Oncologist



Physics properties (LET)

	β^- (Mev)	γ (Kev)	T1/2 (days)
^{177}Lu	0.49	110-210	6.7
^{90}Y	2.27		2.7

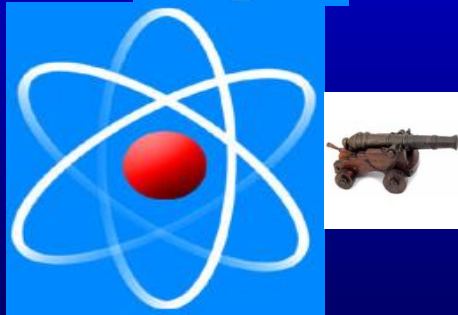
mean range in body tissue

^{177}Lu



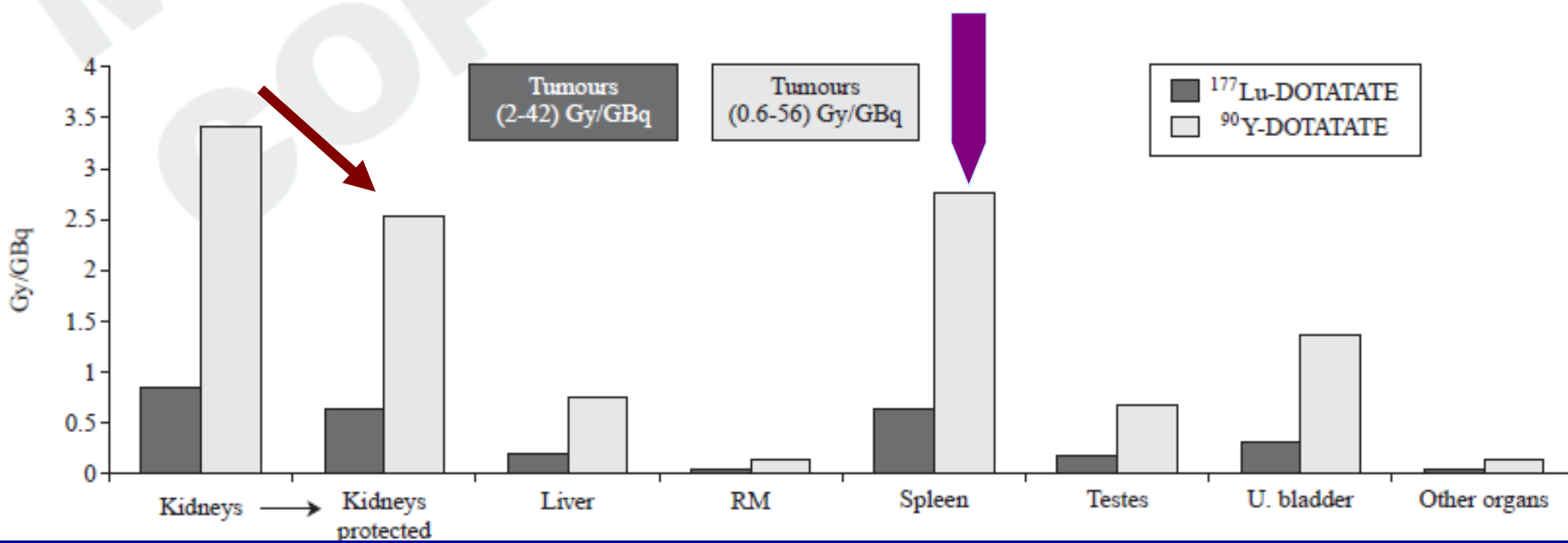
0.5-2mm

^{90}Y



3-11 mm

Organs and tumour doses estimates for ^{90}Y / ^{177}Lu -DOTATATE



Estimates of tumour and OAR doses per unit activity in patient undergoing PRRT trial

Dose response of pancreatic neuroendocrine tumors treated with peptide receptor radionuclide therapy using ^{177}Lu -DOTATATE

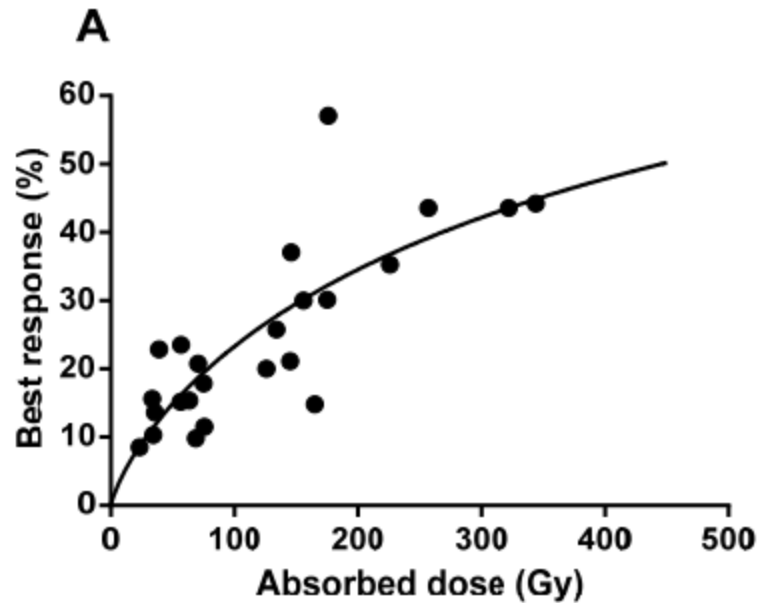
....

The largest tumor reduction was 57% after a total absorbed dose of 170 Gy.

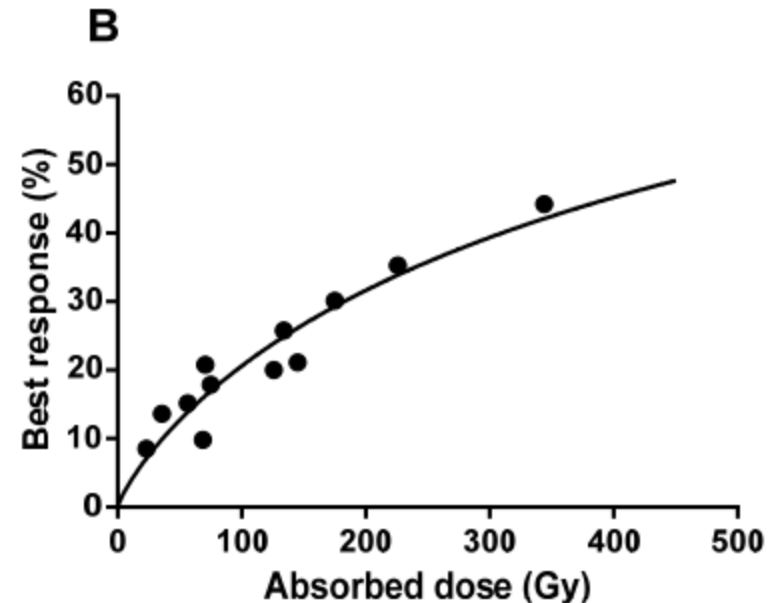
Conclusion

The results imply a **significant correlation between absorbed dose and tumor reduction**

Dose response of pancreatic neuroendocrine tumors treated with peptide receptor radionuclide therapy using ^{177}Lu -DOTATATE



Tumor <4 cm



Tumor >4 cm

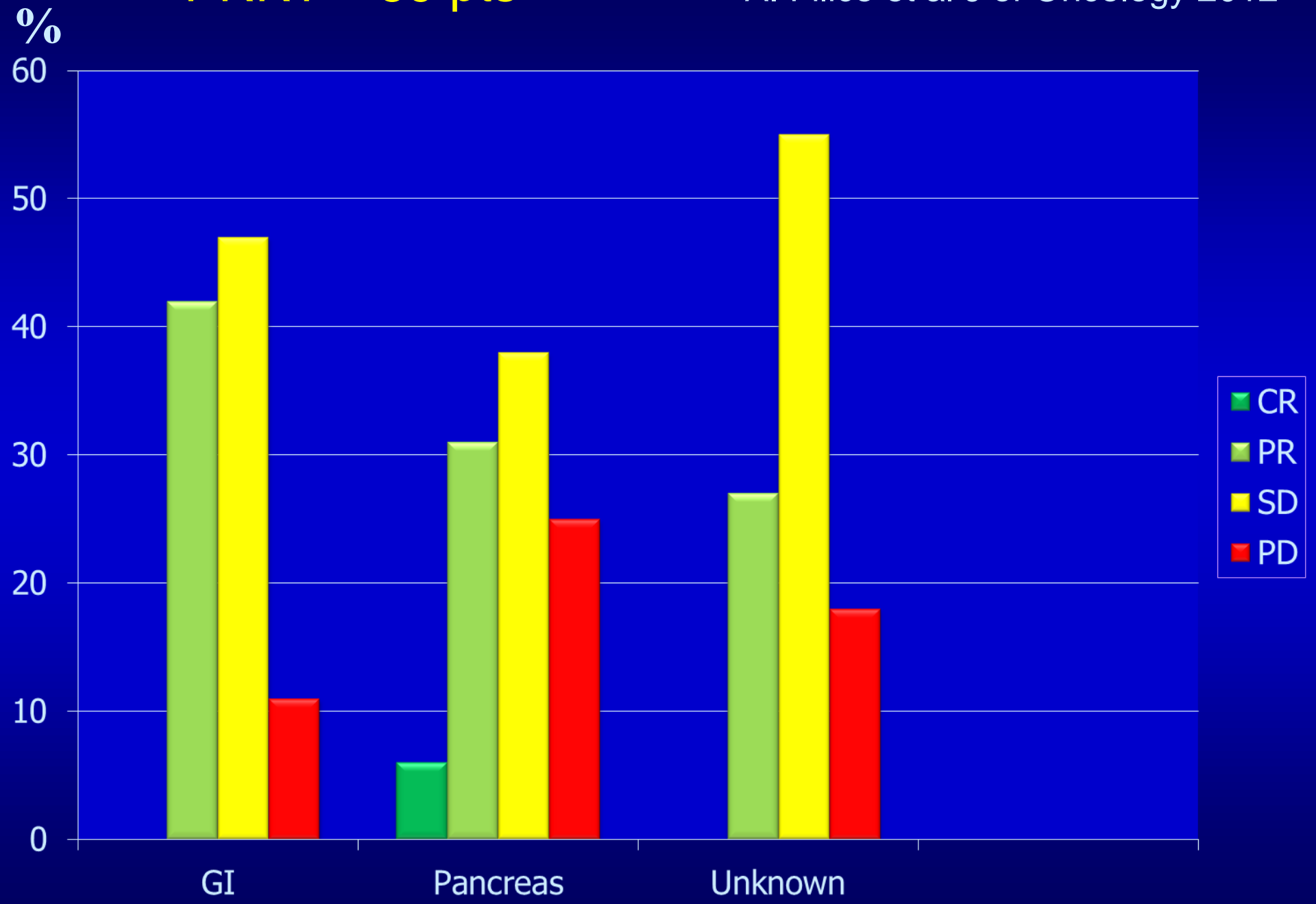
PRRT strategy

According to

- Tumor histology and primary site
- Clinical situation
- Lesion size
- Other treatments available

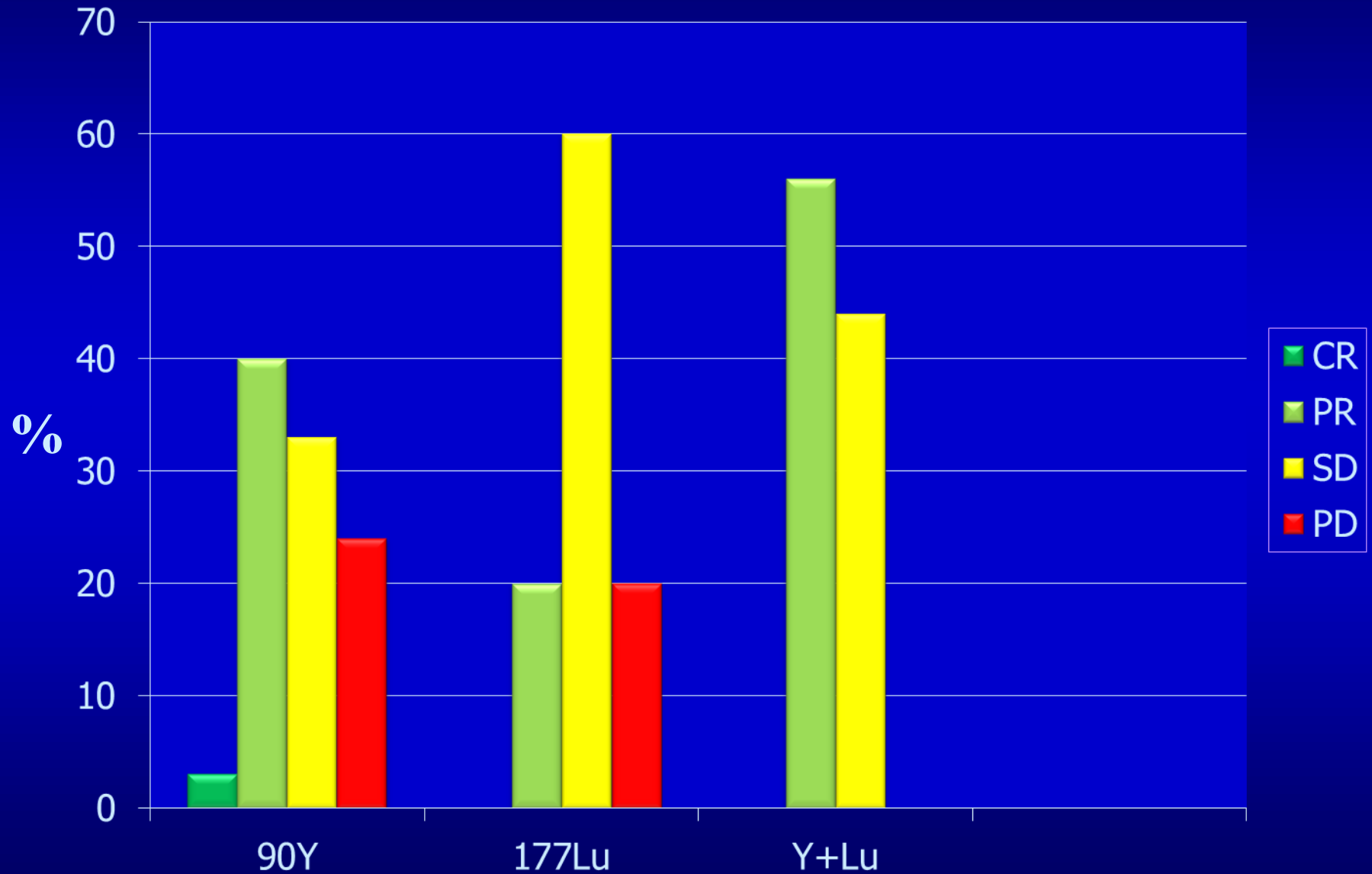
PRRT 59 pts

A. Filice et al J of Oncology 2012



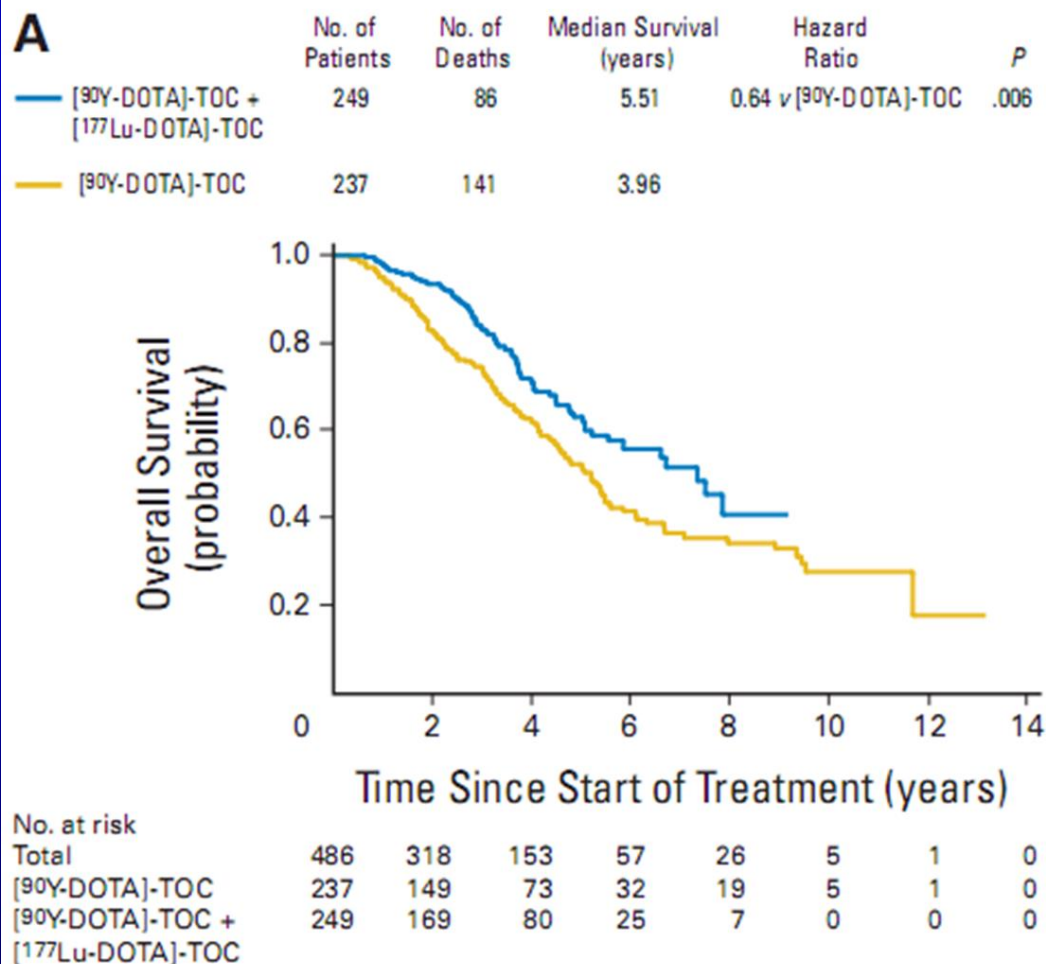
PRRT 59 pts

A. Filice et al J of Oncology 2012

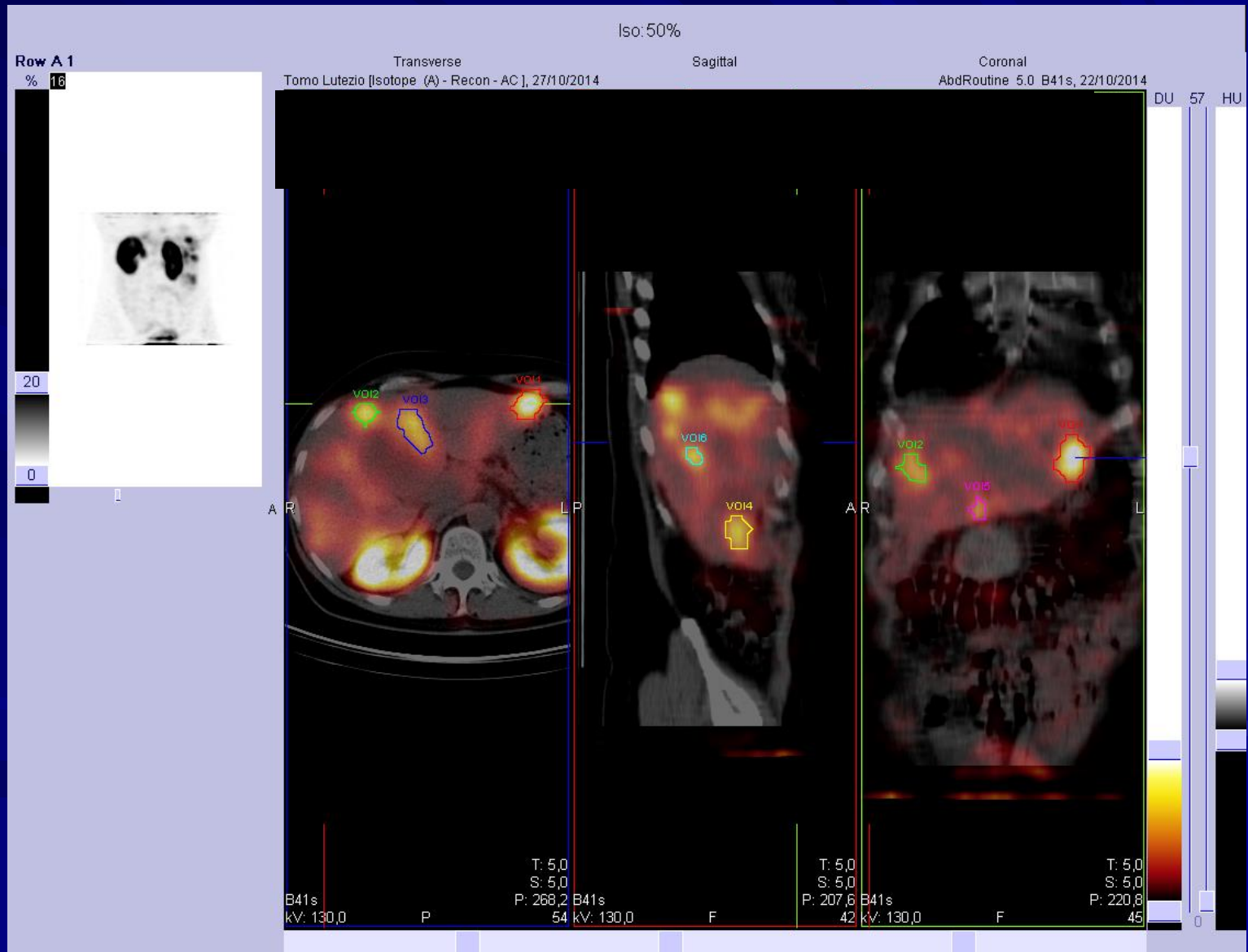


Cohort Study of Somatostatin-Based Radiopeptide Therapy With [⁹⁰Y-DOTA]-TOC Versus [⁹⁰Y-DOTA]-TOC Plus [¹⁷⁷Lu-DOTA]-TOC in Neuroendocrine Cancers

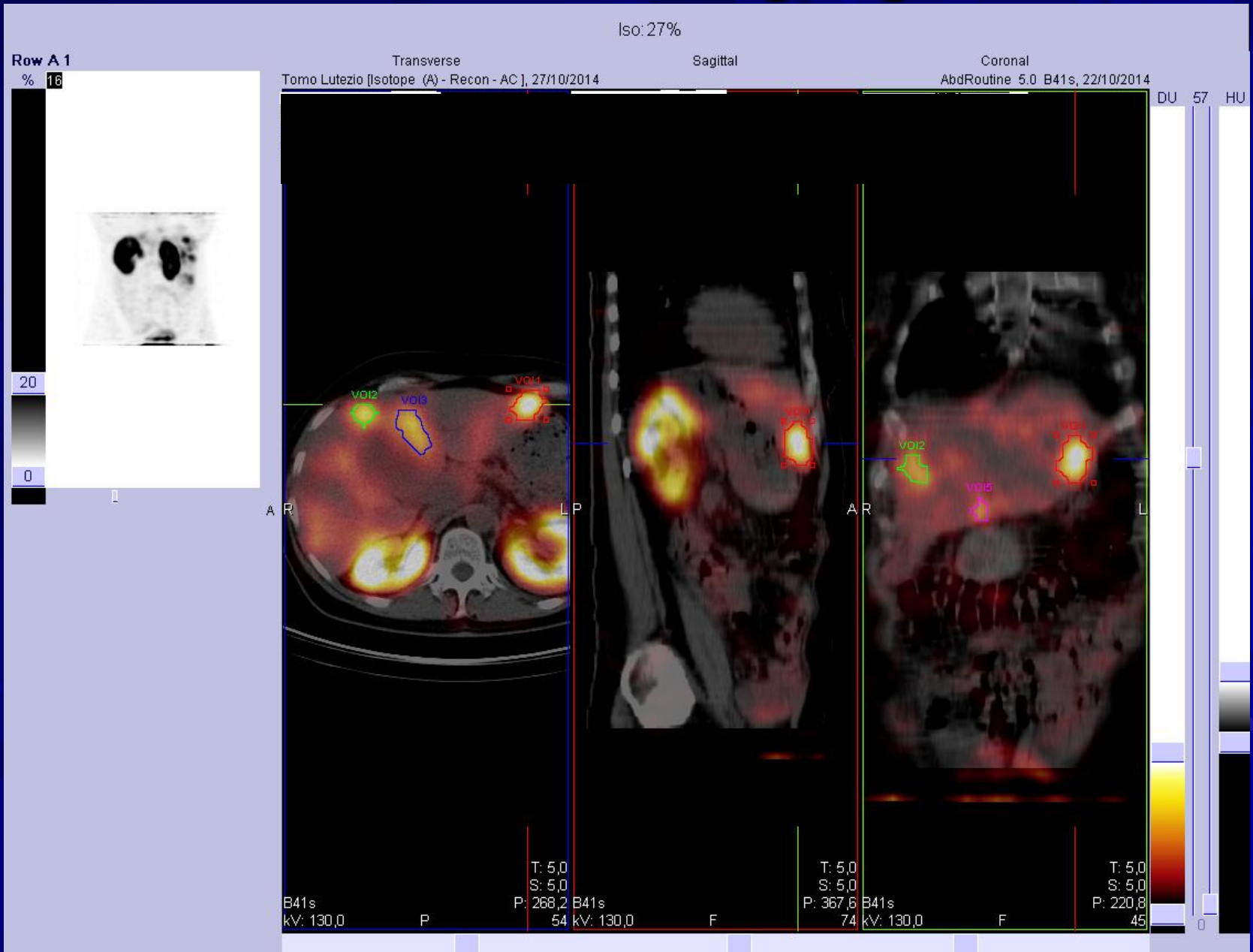
Linda Villard, Anna Romer, Nicolas Marincek, Philippe Brunner, Michael T. Koller, Christian Schindler, Quinn K.T. Ng, Helmut R. Mücke, Jan Müller-Brand, Christoph Rochlitz, Matthias Briel, and Martin A. Walter



Pt 2 SPECT-CT imaging: lesion 1



Pt 2 SPECT-CT imaging: lesion 2



Pt2:

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	
		Y - GBq						Attività tot
	Attività già somministrata	0,00	0,00	0,00	0,00	0,00	0,00	0,00
	Attività prospettica	1,85	1,85	1,85	0,00	0,00	0,00	5,55

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	VII tratt.	
		Lu - GBq							Attività tot
	Attività già somministrata	5,51	0,00	0,00	0,00	0,00	0,00	0,00	5,51
	Attività prospettica	5,51	5,55	5,55	0,00	0,00	0,00	0,00	16,61

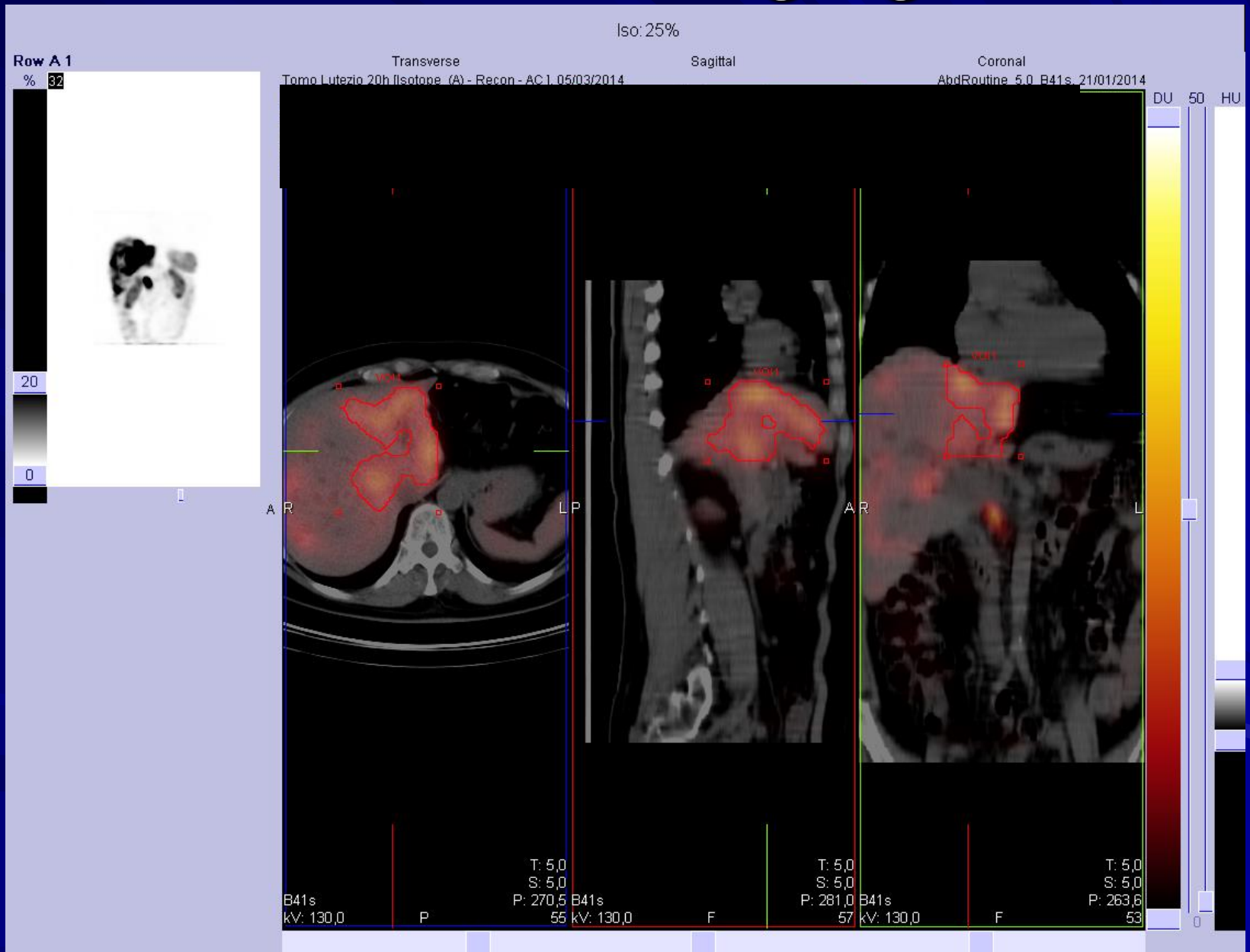
	RENI (valori in Gy)					RED MARROW (valori in Gy)	
	BED Y	BED Lu	BED tot reale	BED tot prospettica	BED tot consentita	Dose Y	Dose Lu
Attività già somministrata	0	4	4	---	46	0,000	0,032
Attività prospettica	29	13	---	42	46	0,134	0,095

LESIONI (valori in Gy)											
lesione 1				lesione 2				lesione 3			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
0,00	9,27	---	---	0	8	---	---	0	9	---	---
---	---	52,24	27,94	---	---	45,32	24,22	---	---	50,32	26,93

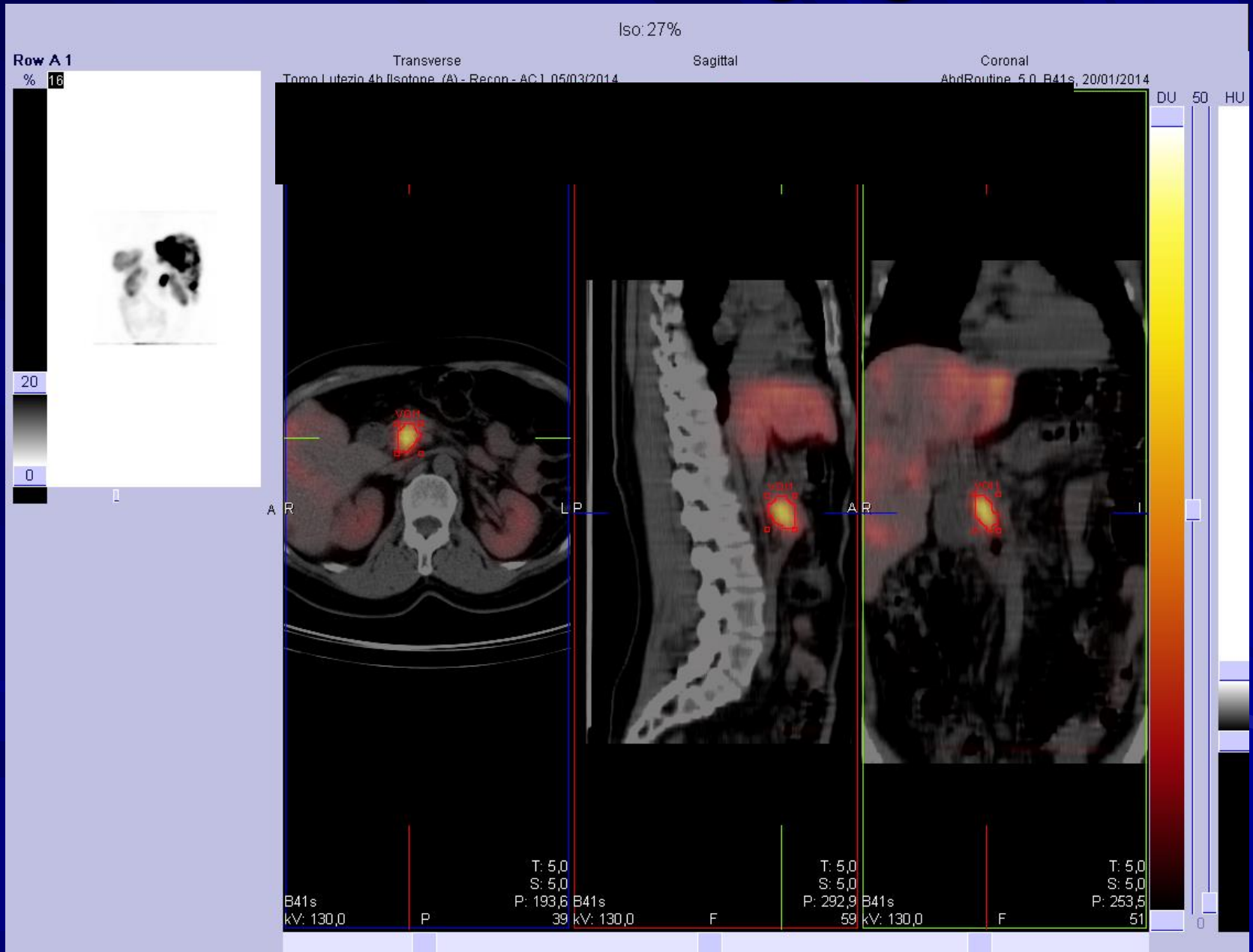
lesione 4				lesione 5			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
0	7	---	---	0	9	---	---
---	---	39,87	21,18	---	---	48,57	26,05

lesione	volume (ml)
ABD - VI seg. Epatico	9
ABD -Fegato lobo sx	9
ABD-VI seg epatico	8,30
ABD - VII seg. Epatico-accanto ciambella	9,70
ABD - IV segmento epatico	8,20

Pt 3 SPECT-CT imaging: lesion 1



Pt 3 SPECT-CT imaging: lesion 2



Pt3:

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	
		Y - GBq						Attività tot
	Attività già somministrata	2,52	0,00	0,00	0,00	0,00	0,00	2,52
	Attività prospettica	2,52	0,00	0,00	0,00	0,00	0,00	2,52

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	VII tratt.	
		Lu - GBq							Attività tot
	Attività già somministrata	5,74	5,66	2,63	0,00	0,00	0,00	0,00	14,02
	Attività prospettica	5,74	5,66	2,63	0,00	0,00	0,00	0,00	14,02

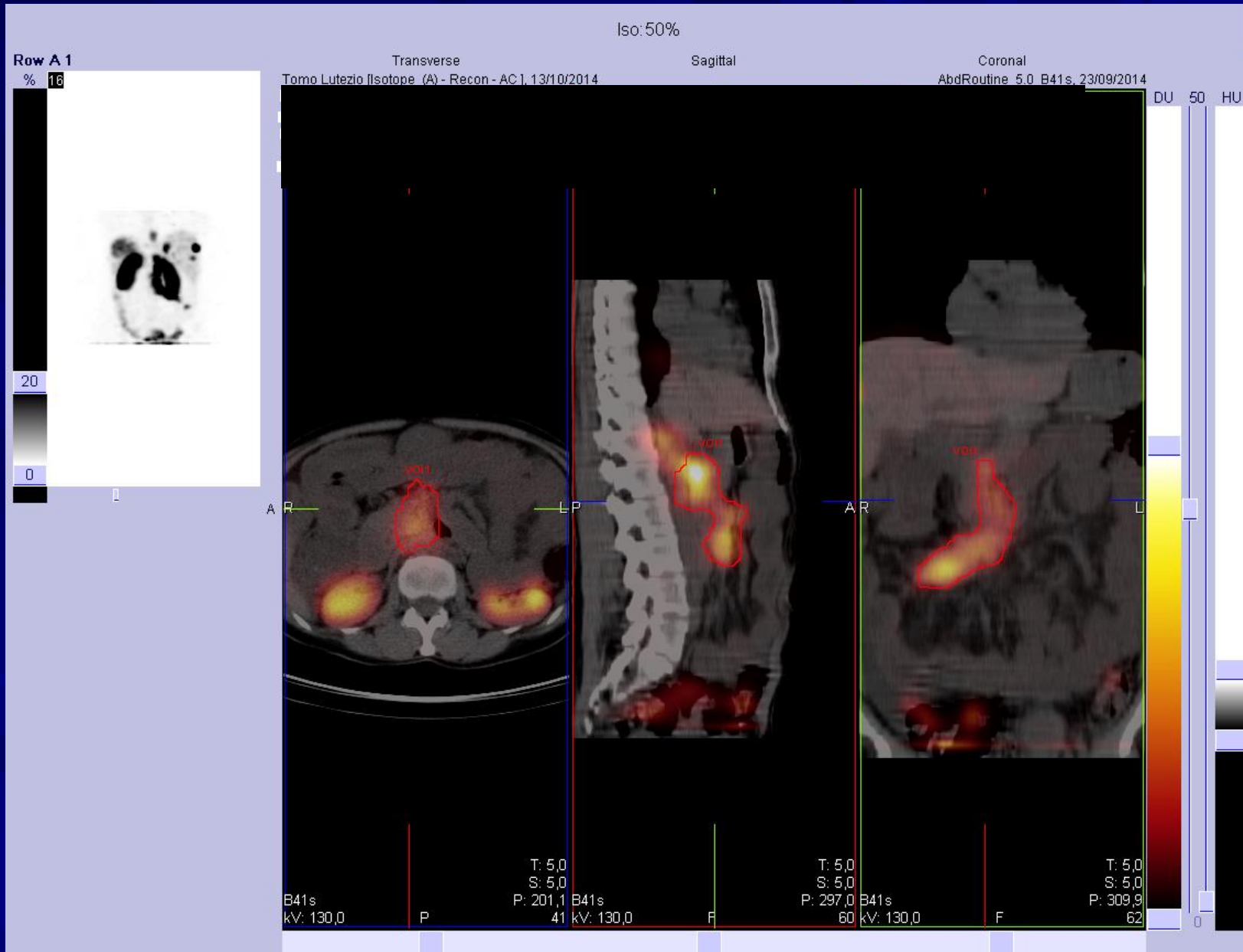
	RENI (valori in Gy)					RED MARROW (valori in Gy)	
	BED Y	BED Lu	BED tot reale	BED tot prospettica	BED tot consentita	Dose Y	Dose Lu
Attività già somministrata	16	14	30	---	28	0,068	0,120
Attività prospettica	16	14	---	30	28	0,068	0,120

LESIONI (valori in Gy)											
lesione 1				lesione 2				lesione 3			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
222,92	225,77	---	---	96	90	---	---	0	0	---	---
---	---	222,92	225,77	---	---	95,99	90,31	---	---	0,00	0,00

lesione 4				lesione 5			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
0	0	---	---	0	0	---	---
---	---	0,00	0,00	---	---	0,00	0,00

lesione	volume (ml)
addome centrale	6
ABD lesione epatica	225
0,00	0,00
0,00	0,00
0,00	0,00

Pt 4 SPECT-CT imaging: lesion 1



Pt4:

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	
		Y - GBq						Attività tot
	Attività già somministrata	1,04	1,04	0,00	0,00	0,00	0,00	2,07
	Attività prospettica	1,04	1,04	1,10	0,00	0,00	0,00	3,17

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	VII tratt.	
		Lu - GBq							Attività tot
	Attività già somministrata	5,92	0,00	0,00	0,00	0,00	0,00	0,00	5,92
	Attività prospettica	5,92	5,55	5,55	0,00	0,00	0,00	0,00	17,02

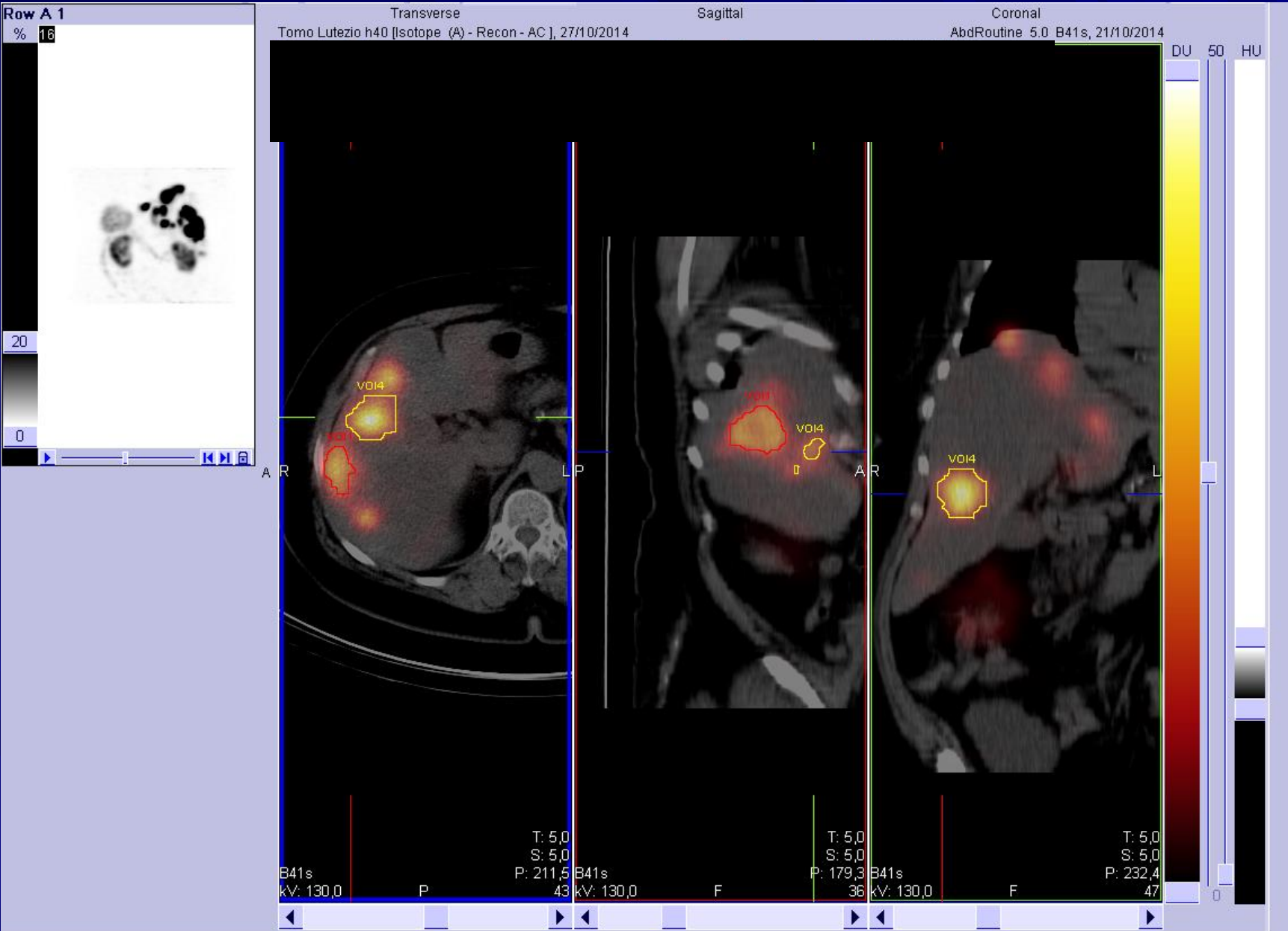
	RENI (valori in Gy)					RED MARROW (valori in Gy)	
	BED Y	BED Lu	BED tot reale	BED tot prospettica	BED tot consentita	Dose Y	Dose Lu
Attività già somministrata	11	5	16	---	46	0,048	0,033
Attività prospettica	17	15	---	31	46	0,073	0,094

LESIONI (valori in Gy)											
lesione 1				lesione 2				lesione 3			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
21,51	10,36	---	---	0	0	---	---	0	0	---	---
---	---	32,93	29,79	---	---	0,00	0,00	---	---	0,00	0,00

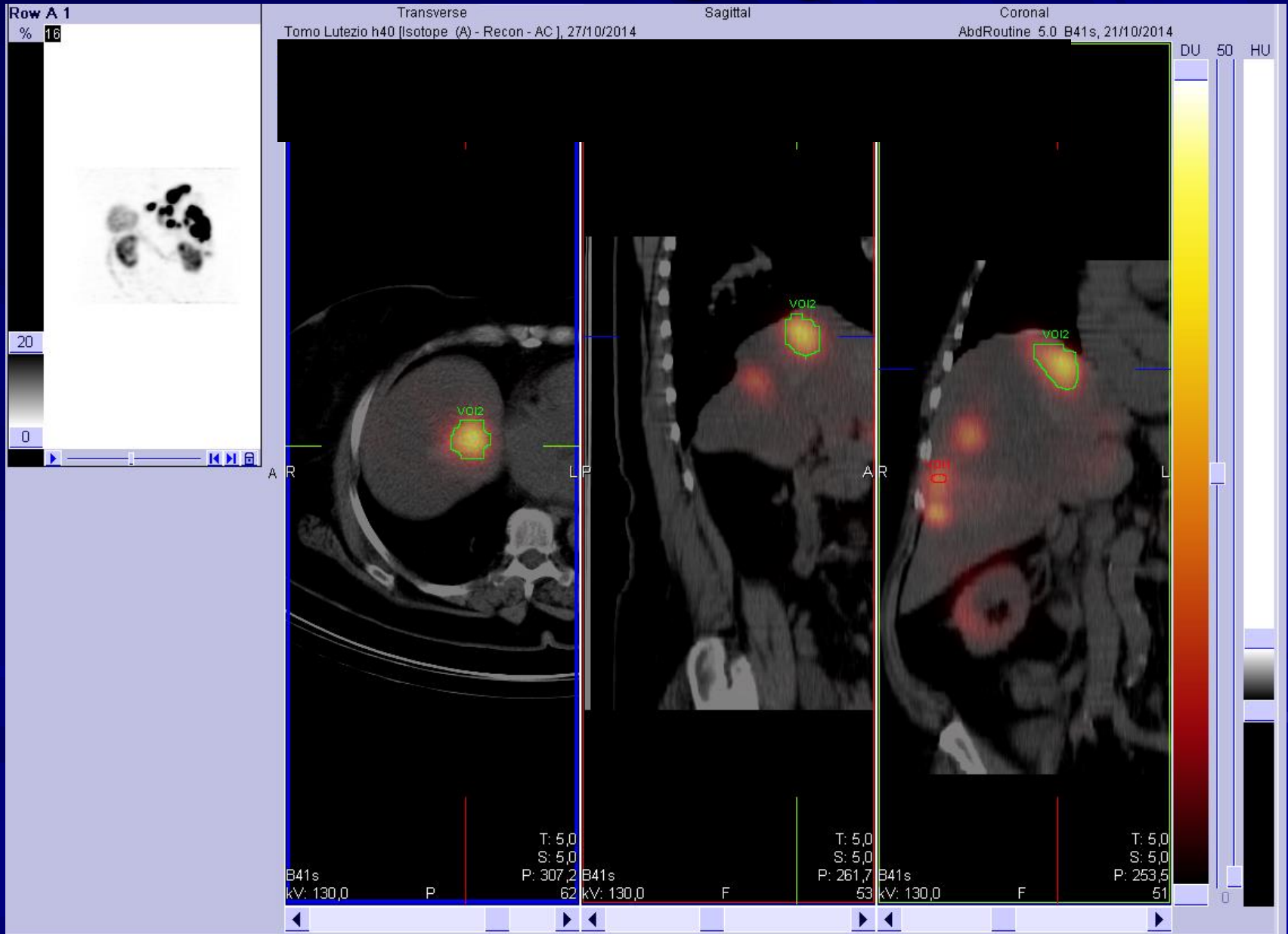
lesione 4				lesione 5			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
0	0	---	---	0	0	---	---
---	---	0,00	0,00	---	---	0,00	0,00

lesione	volume (ml)
ABD colata massiva	97
0	0
0,00	0,00
0,00	0,00
0,00	0,00

Pt 5 SPECT-CT imaging: liver lesions



Pt 5 SPECT-CT imaging: liver lesions



Pt5:

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	
		Y - GBq						Attività tot
	Attività già somministrata	1,11	1,85	0,00	0,00	0,00	0,00	2,96
	Attività prospettica	1,11	1,85	1,85	0,00	0,00	0,00	4,81

		I tratt.	II tratt.	III tratt.	IV tratt.	V tratt.	VI tratt.	VII tratt.	
		Lu - GBq							Attività tot
	Attività già somministrata	5,25	0,00	0,00	0,00	0,00	0,00	0,00	5,25
	Attività prospettica	5,25	5,55	5,55	0,00	0,00	0,00	0,00	16,35

	RENI (valori in Gy)					RED MARROW (valori in Gy)	
	BED Y	BED Lu	BED tot reale	BED tot prospetti ca	BED tot consentita	Dose Y	Dose Lu
Attività già somministrata	7	2	9	---	28	0,041	0,019
Attività prospettica	12	6	---	18	28	0,067	0,061

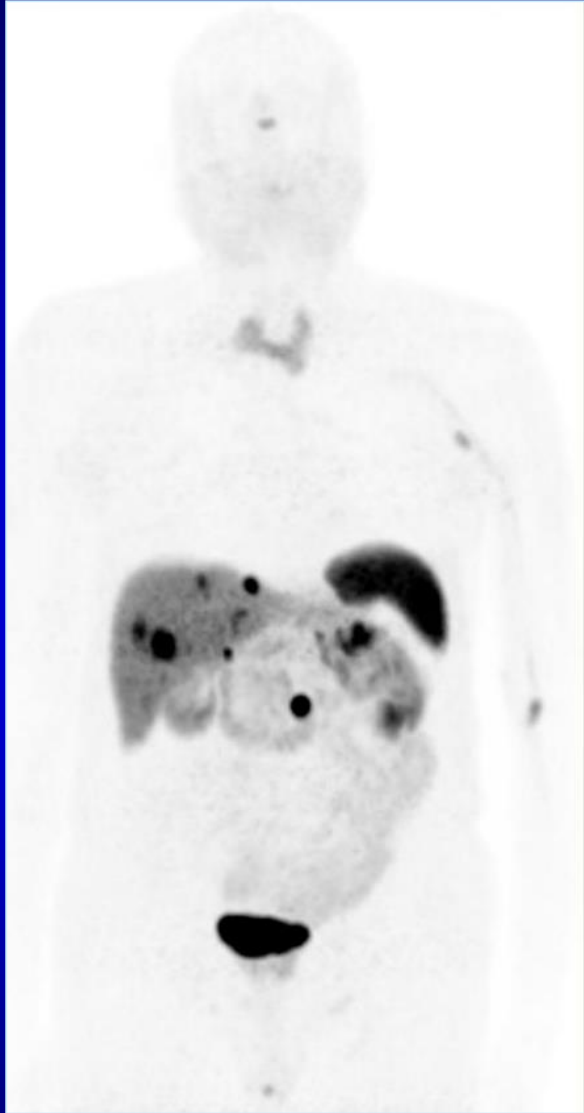
LESIONI (valori in Gy)											
lesione 1				lesione 2				lesione 3			
Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu	Dose reale Y	Dose reale Lu	Dose prospettica Y	Dose prospettica Lu
67,19	20,49	---	---	50	15	---	---	53	16	---	---
---	---	109,19	63,78	---	---	81,77	48,24	---	---	85,62	50,86

lesione 4				lesione 5			
Dose reale Y	Dose reale Lu	Dose propsettica Y	Dose propsettica Lu	Dose reale Y	Dose reale Lu	Dose propsettica Y	Dose propsettica Lu
25	8	---	---	0	0	---	---
---	---	40,40	24,53	---	---	0,00	0,00

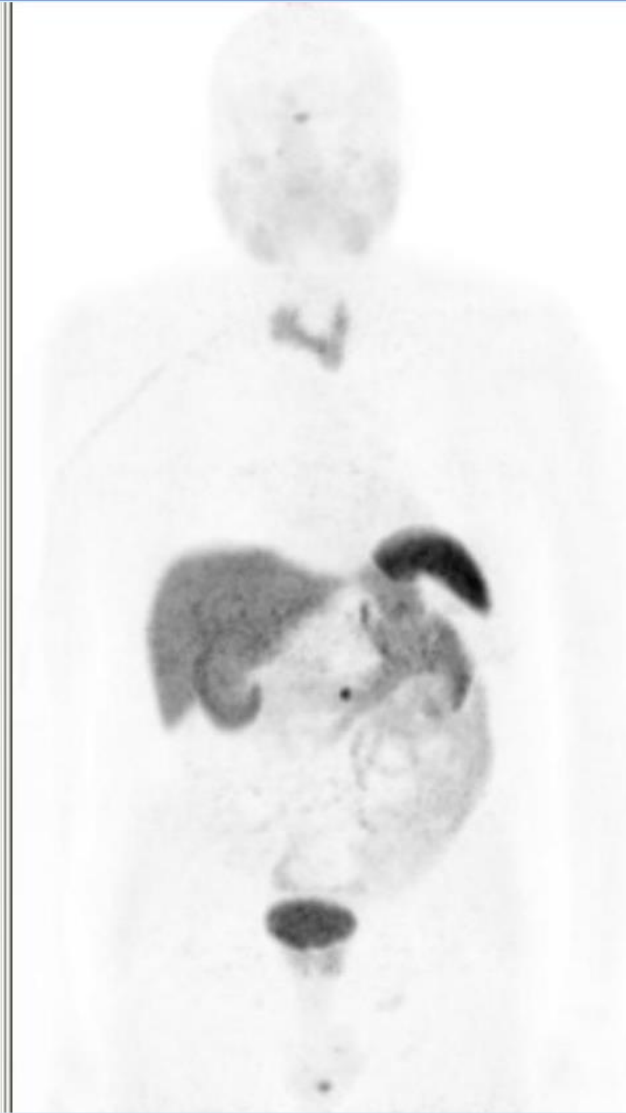
lesione	volume (ml)
ABD VI segmento epatico 1	36
ABD VI segmento epatico 2	30
ABD VI segmento epatico 3	17,80
ABD VI segmento epatico 4	9,90
0,00	0,00

^{68}Ga -DOTATATE PET/CT

Pre-therapy



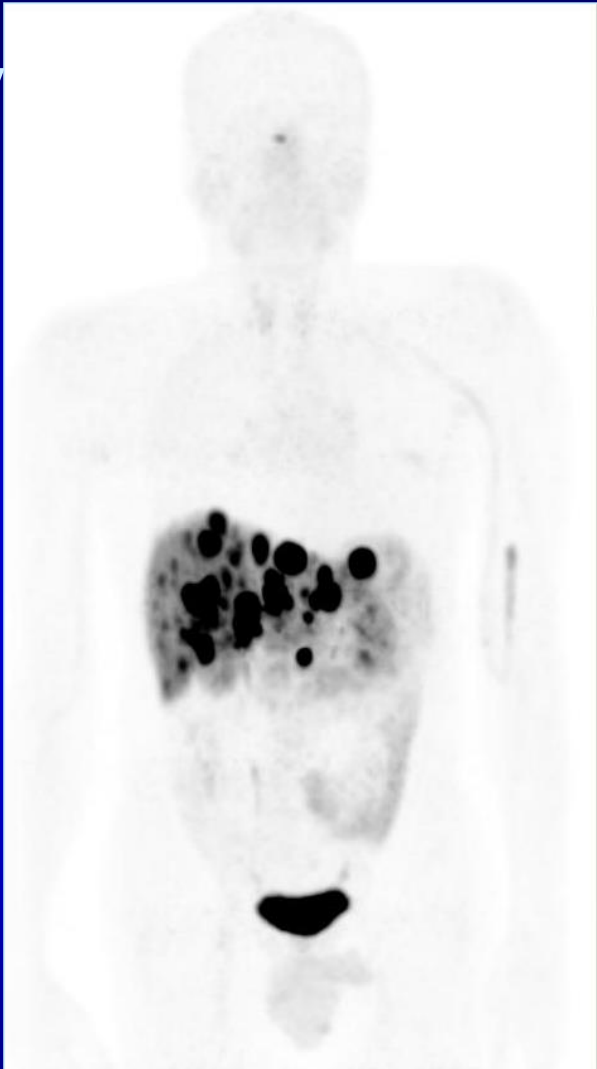
Post-therapy



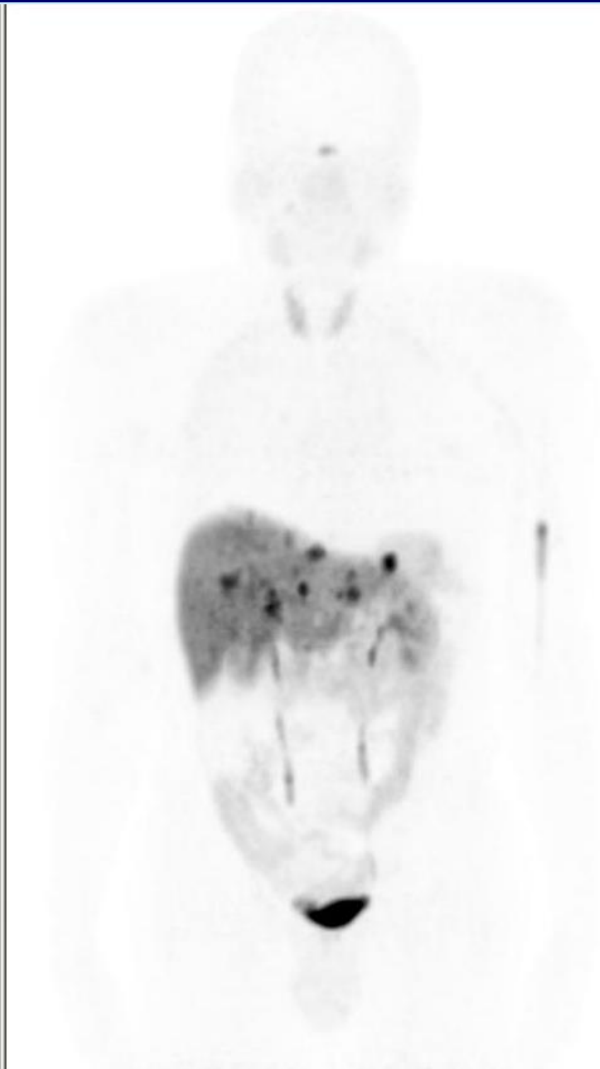
M, 73 y: Pancreas NET with liver metastases
2 cycles of ^{90}Y e 4 cycles of ^{177}Lu . Partial response

^{68}Ga -DOTATATE PET/CT

Pre-therapy

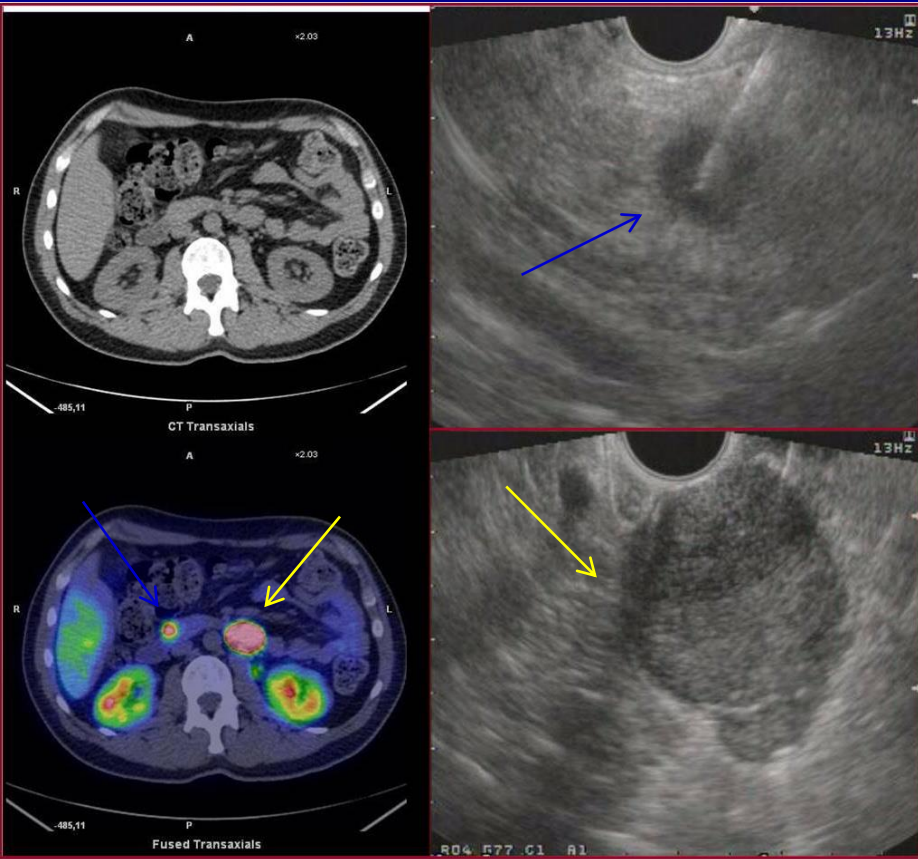


Post-therapy

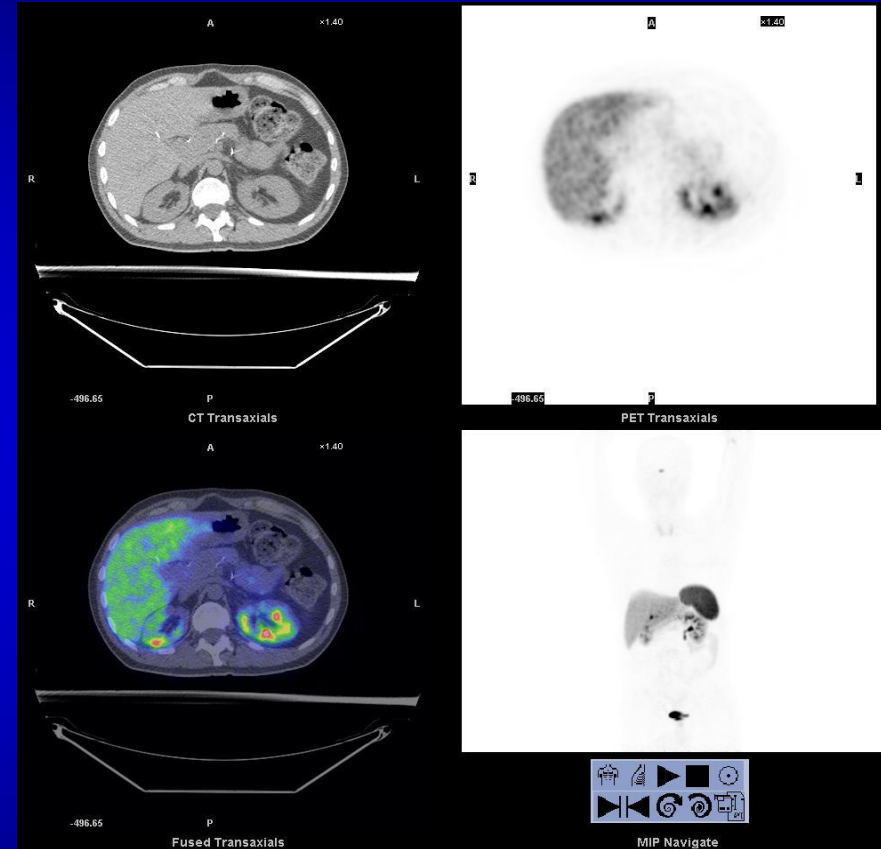


M, 56 y: Pancreas NET with liver metastases
4 cycles of ^{90}Y e 2 cycles of ^{177}Lu . Partial response

Pre-therapy



Post-therapy



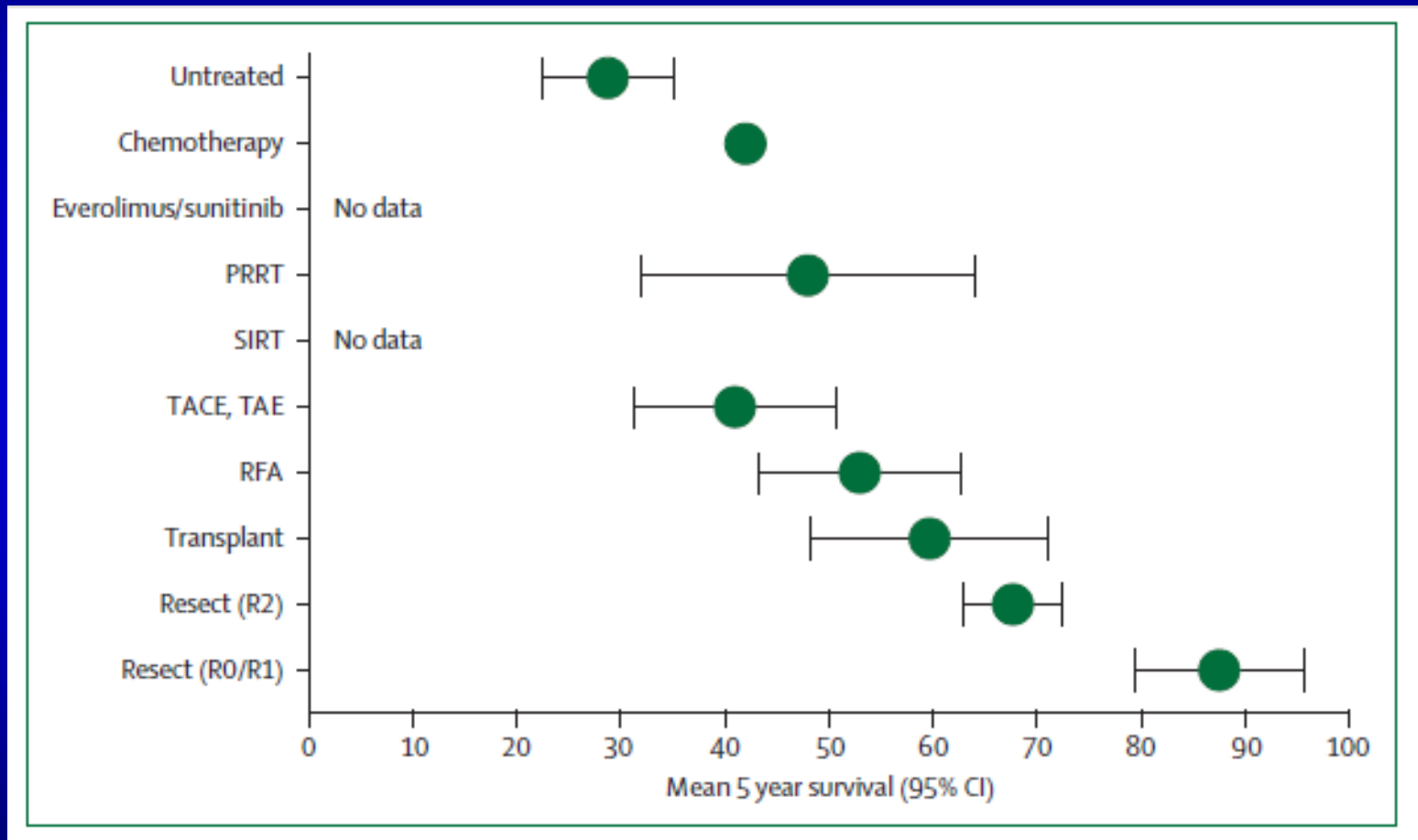
V.R.: pancreas NET with lymph node metastasis
Complete Response after 90Y-DOTATOC

Peptide Receptor Radionuclide Therapy (PRRT)

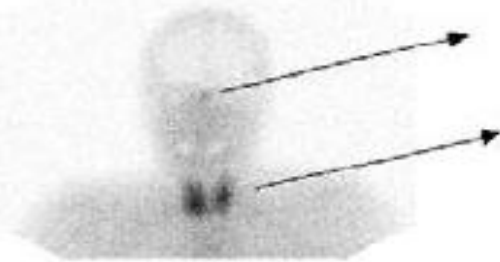
Author	Year	Radiopharmaceutical	N° Pts.	Primary NET	Response (%)				
					CR	PR	MR	SD	PD
Waldherr	2001	90Y-DOTATOC	41	GEP+lung	2	22	12	49	15
Waldherr	2002	90Y-DOTATOC	39	GEP+lung	5	18	-	65	11
Valkema	2006	90Y-DOTATOC	58	GEP	0	9	12	61	19
Kwekkeboom	2008	177Lu-DOTATATE	310	GEP	2	28	16	35	20
Bodei	2011	177Lu-DOTATATE	51	GEP+lung	2	27	26	27	18
Filice	2012	90Y/177Lu-DOTATOC	59	GEP+lung	2	40	-	40	18
Vinjamuri	2013	90Y-DOTATOC	57	GEP+lung	-	25	-	47	28

Patients with neuroendocrine liver metastases

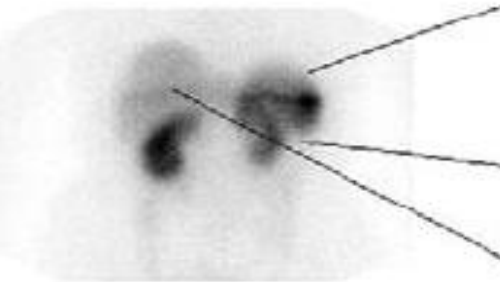
Rates of 5 year survival by treatment method



PRRT Toxicity



- No important effect on pituitary function
- No important effect on thyroid function
- Common: mild bone marrow suppression



- Common: Lymphocytopenia
- Rare: MDS, Leukemia
- Rare: Kidney impairment
- Rare: Liver toxicity

Risk factors for renal failure

Renal disease
Diabetes
Hypertension

GEP-NETs UPDATE

Radionuclide therapy in neuroendocrine tumorsWouter A van der Zwan, Lisa Bodei¹, Jan Mueller-Brand², Wouter W de Herder, Larry K Kvols³ and Dik J Kwekkeboom

Correspon

Table 3 Long-term toxicity in patients with neuroendocrine tumors, treated with different radiolabeled somatostatin analogs.

Center (reference)	Ligand	n	FU	Toxicity		
				Creatinine	MDS	Leukemia
Milan (13)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	40	19	10% Grade 1	0	0
Basel (14)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	41	15	0	0	0
Basel (15, 41)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	39	6	3% Grade 2	0	0
Multicenter (1)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	58	18	3% Grade 4	1	0
Basel (16)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	31	12	12.9% Grade 3/4 ^a	0	0
Copenhagen (3)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	53	17	0	1	0
Basel (8)	[⁹⁰ Y-DOTA ⁰ , Tyr ³]octreotide	1109	23	9.2% Grade 3/4 ^a	1	1
Rotterdam (5)	[¹⁷⁷ Lu-DOTA ⁰ , Tyr ³]octreotate	504	19	0.4% Grade 4	3	0
Milan (10)	[¹⁷⁷ Lu-DOTA ⁰ , Tyr ³]octreotate	51	29	24% Grade1	0	0

FU, follow-up; MDS, myelodysplastic syndrome. Grades pertain to World Health Organization (WHO) classification.

^aToxicity based on glomerular filtration rate.

The best technology.... The best
images.....

but ... **Don't forget!!!!!!**

Interdisciplinary Discussion





goal

... the best treatment for the patient

Thanks for your attention

Calatrava Bridge in Reggio Emilia

