HERMES Dosimetry Software

Current overview and future directions

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HERMES

HERMES *Medical Solutions*

Summary of Dosimetry Techniques

MIRD Anthropomorphic (Hybrid Viewer™ -Dosimetry)

- Presently standard, assumptions of homogenous organ and tumour uptake (preferably for tracer development)
- OLINDA2.0 with new phantoms soon to be released

S-Voxel / Dose-Point-Kernel

- Moves MIRD into 3 dimensions
- Less affected by registration challenges than full Monte-Carlo as only assuming one density
- Still assumes homogeneous organ and lesion dose distribution i.e. not as accurate as a Monte Carlo method

Monte-Carlo (Hybrid3Dose)

- Scientifically most accurate
- Novel for most users

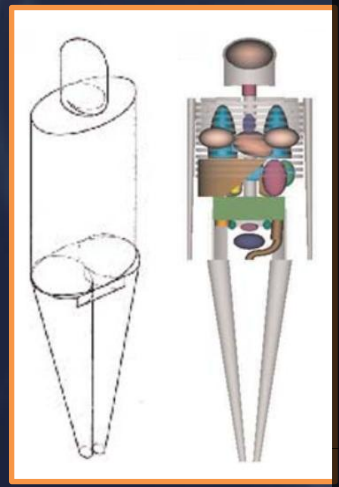
SIRT

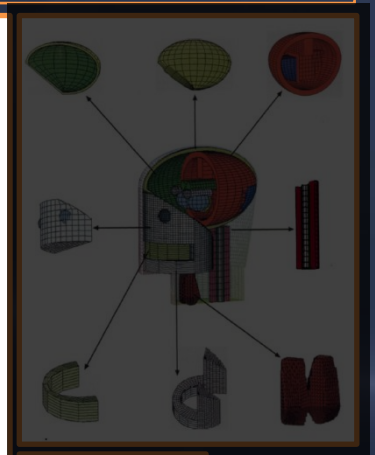
- Empirical, BSA and partition model are all standards used clinically throughout the world
- Although partition model is considered to be most accurate, it is not used much due to complexity
- ^{90}Y reconstruction needed to image

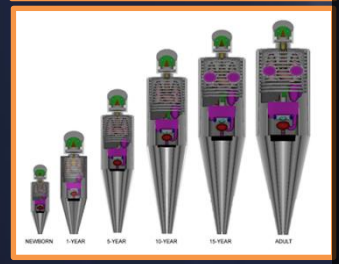
Standard methods for dosimetry

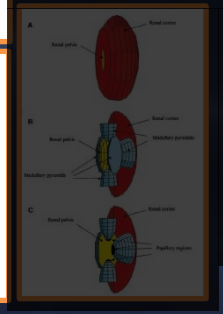
Whole Organ	Sub-organ

MIRD Anthropomorphic model



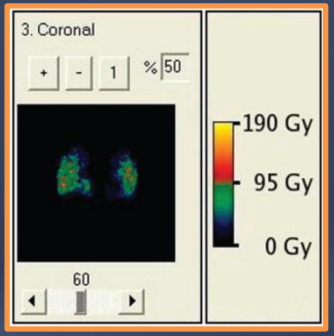






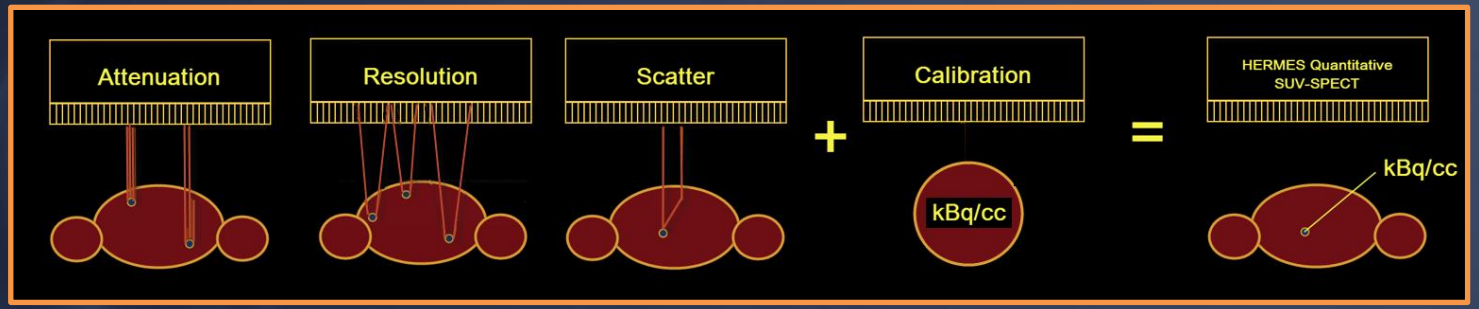
Partition

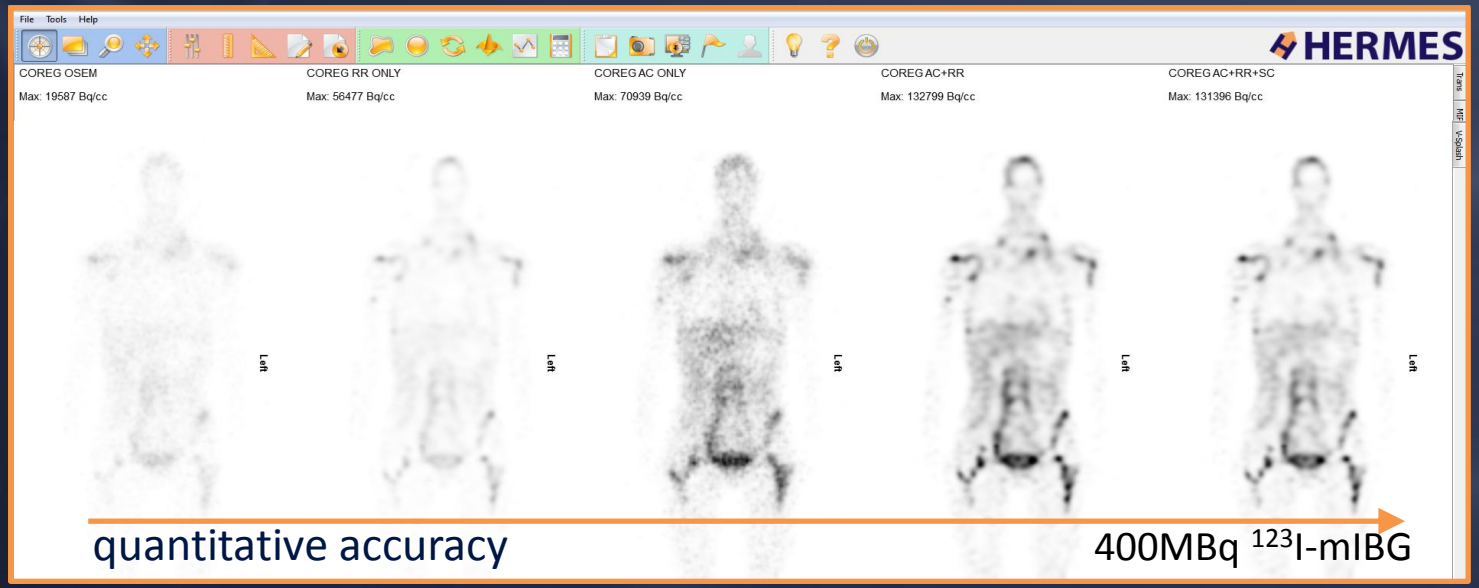
Voxel	
Dose-point-kernel (e.g. MIRD S-voxel)	Patient Specific Monte-Carlo



Non-uptake based	
Nominal (Standard activity)	Nominal (Adjusted for patient/organ/tumour size)

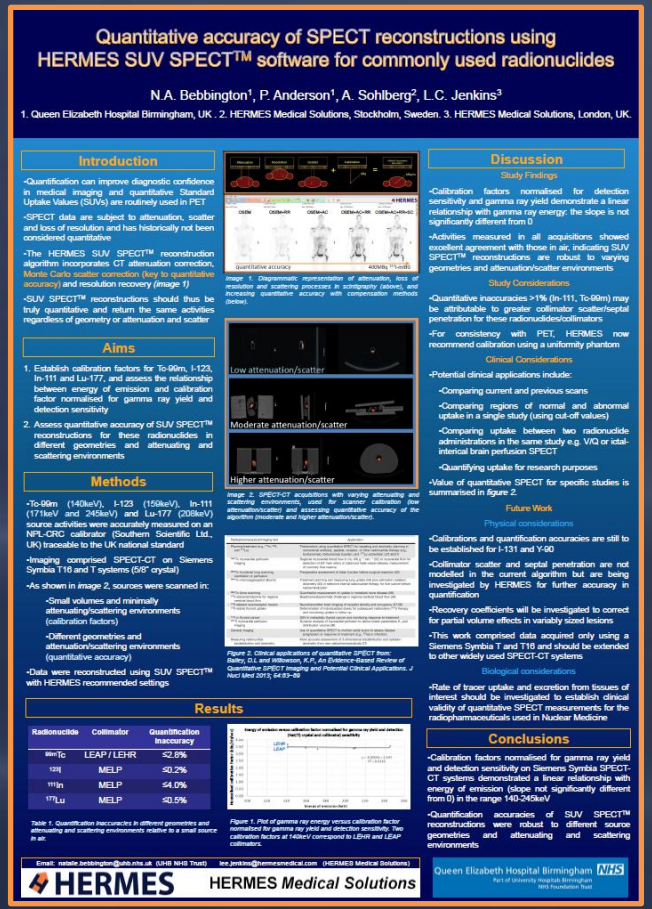
HybridRecon™ corrections





HybridRecon™ Accuracy

Quantitative accuracy	
^{99m}Tc	≤ 2.8%
^{123}I	≤ 0.2%
^{111}In	≤ 4.0%
^{177}Lu	≤ 0.5%



Quantitative accuracy of SPECT reconstructions using HERMES SUV SPECT™ software for commonly used radionuclides

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Introduction

•Quantification can improve diagnostic confidence in medical imaging and quantitative Standard Uptake Values (SUVs) are routinely used in PET

•SPECT data are subject to attenuation, scatter and loss of resolution and has historically not been considered quantitative

•The HERMES SUV SPECT™ reconstruction algorithm incorporates CT attenuation correction, Monte Carlo scatter correction (key to quantitative accuracy) and resolution recovery *(image 1)*

•SUV SPECT™ reconstructions should thus be truly quantitative and return the same activities regardless of geometry or attenuation and scatter

Aims

1. Establish calibration factors for Tc-99m, I-123, In-111 and Lu-177, and assess the relationship between energy of emission and calibration factor normalised for gamma ray yield and detection sensitivity
2. Assess quantitative accuracy of SUV SPECT™ reconstructions for these radionuclides in different geometries and attenuating and scattering environments

Methods

•Tc-99m (140keV), I-123 (159keV), In-111 (171keV and 245keV) and Lu-177 (208keV) source activities were accurately measured on an NPL-CRC calibrator (Southern Scientific Ltd., UK) traceable to the UK national standard

•Imaging comprised SPECT-CT on Siemens Symbia T16 and T systems (5/8" crystal)

•As shown in *image 2*, sources were scanned in:

- Small volumes and minimally attenuating/scattering environments (calibration factors)
- Different geometries and attenuation/scattering environments (quantitative accuracy)

•Data were reconstructed using SUV SPECT™ with HERMES recommended settings

Image 1. Diagrammatic representation of attenuation, loss of resolution and scattering processes in scintigraphy (above), and increasing quantitative accuracy with compensation methods (below).

Image 2. SPECT-CT acquisitions with varying attenuating and scattering environments, used for scanner calibration (low attenuation/scatter) and assessing quantitative accuracy of the algorithm (moderate and higher attenuation/scatter).

Figure 2. Clinical applications of quantitative SPECT from: Bailey, D.L and Willowson, K.P., An Evidence-Based Review of Quantitative SPECT Imaging and Potential Clinical Applications. J Nucl Med 2013; 54:83-89

Results

Radionuclide	Collimator	Quantification Inaccuracy
^{99m}Tc	LEAP / LEHR	≤2.8%
^{123}I	MELP	≤0.2%
^{111}In	MELP	≤4.0%
^{177}Lu	MELP	≤0.5%

Table 1. Quantification inaccuracies in different geometries and attenuating and scattering environments relative to a small source in air.

Figure 1. Plot of gamma ray energy versus calibration factor normalised for gamma ray yield and detection sensitivity. Two calibration factors at 140keV correspond to LEHR and LEAP collimators.

Discussion

Study Findings

•Calibration factors normalised for detection sensitivity and gamma ray yield demonstrate a linear relationship with gamma ray energy: the slope is not significantly different from 0

•Activities measured in all acquisitions showed excellent agreement with those in air, indicating SUV SPECT™ reconstructions are robust to varying geometries and attenuation/scatter environments

Study Considerations

•Quantitative inaccuracies >1% (In-111, Tc-99m) may be attributable to greater collimator scatter/septal penetration for these radionuclides/collimators

•For consistency with PET, HERMES now recommend calibration using a uniformity phantom

Clinical Considerations

•Potential clinical applications include:

- •Comparing current and previous scans
- •Comparing regions of normal and abnormal uptake in a single study (using cut-off values)
- •Comparing uptake between two radionuclide administrations in the same study e.g. V/Q or ictal-interical brain perfusion SPECT
- •Quantifying uptake for research purposes

•Value of quantitative SPECT for specific studies is summarised in *figure 2.*

Future Work

Physical considerations

•Calibrations and quantification accuracies are still to be established for I-131 and Y-90

•Collimator scatter and septal penetration are not modelled in the current algorithm but are being investigated by HERMES for further accuracy in quantification

•Recovery coefficients will be investigated to correct for partial volume effects in variably sized lesions

•This work comprised data acquired only using a Siemens Symbia T and T16 and should be extended to other widely used SPECT-CT systems

Biological considerations

•Rate of tracer uptake and excretion from tissues of interest should be investigated to establish clinical validity of quantitative SPECT measurements for the radiopharmaceuticals used in Nuclear Medicine

Conclusions

•Calibration factors normalised for gamma ray yield and detection sensitivity on Siemens Symbia SPECT-CT systems demonstrated a linear relationship with energy of emission (slope not significantly different from 0) in the range 140-245keV

•Quantification accuracies of SUV SPECT™ reconstructions were robust to different source geometries and attenuating and scattering environments

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Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

Introduction

SPECT Recon

MIRD Phantom

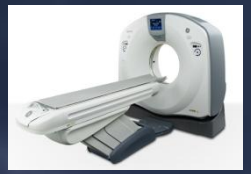
Voxel Based

SIRT Microspheres

SUV-SPECT® For Standardisation and Common Guidelines

SPECT-CT

SPECT



CT

Centre 1

SPECT-CT

Centre 2

SPECT-CT

SPECT-CT

Centre 3

SPECT

CT

Centre 4

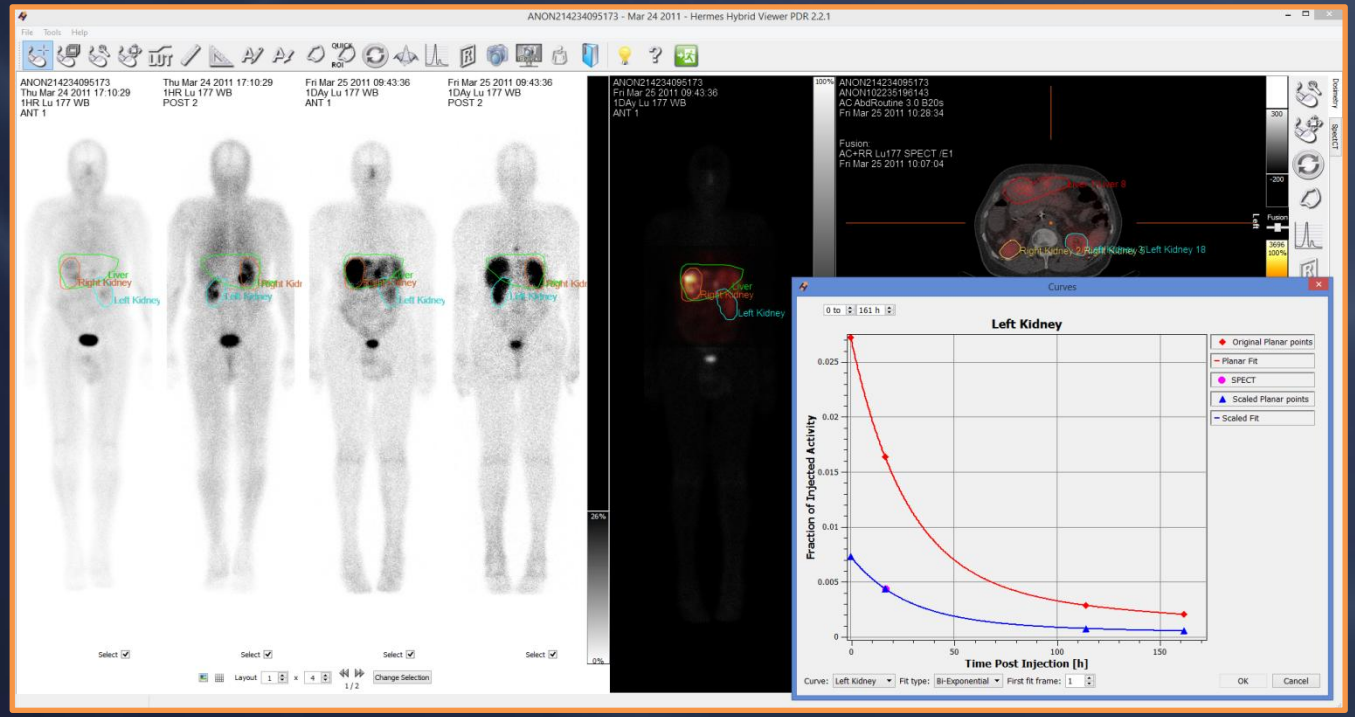
HERMES SUV-SPECT™ Quantitative Reconstruction

- SPECT quantification is consistent between:
  - Patients
  - Equipment (SPECT-CT and SPECT with external CT)
  - Centres

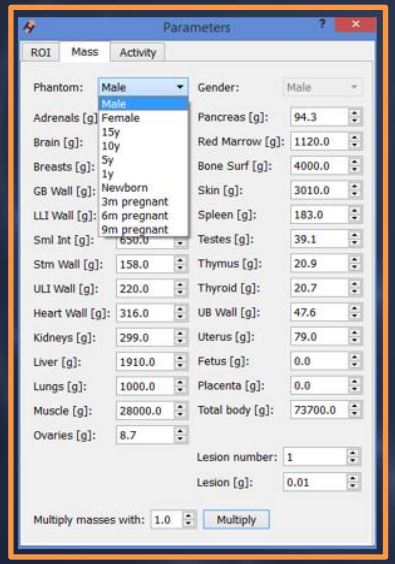
Hybrid Viewer™ Dosimetry [MIRD Calculation]

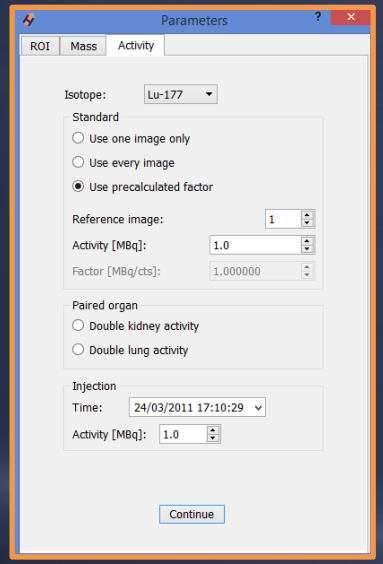
Can be used with the following combinations of data

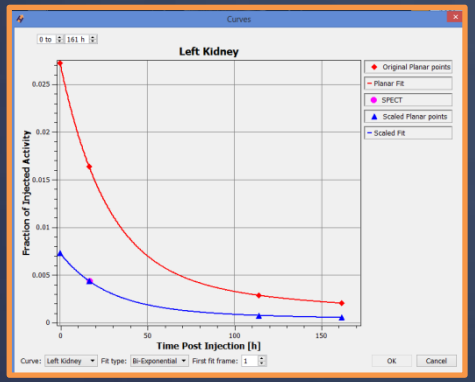
- Multiple Planar
- Multiple Planar + one SPECT-CT
- Multiple SPECT-CT or PET-CT



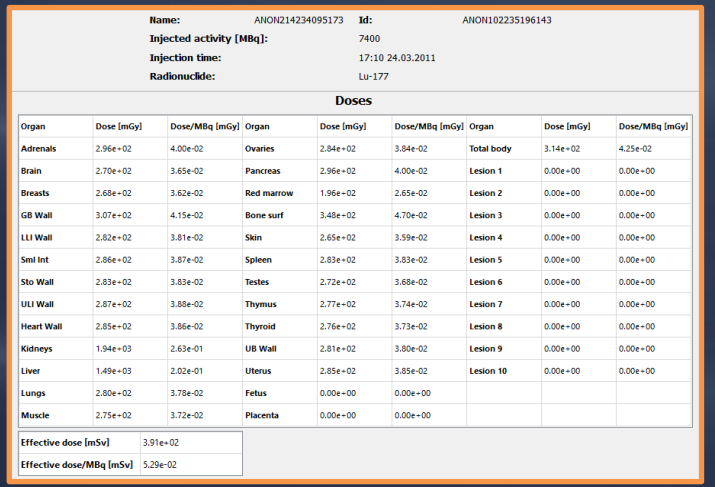
Hybrid Viewer™-Dosimetry using RADAR/MIRD







- Can change anthropomorphic phantom used and/or organ mass
- Choice of standard or pre-calculated factor (e.g. SPECT calibration factor)
- Mono/Bi-exponential fit
- Report page showing organ/lesion absorbed dose



Name: ANON214234095173 **Id:** ANON102235196143
Injected activity [MBq]: 7400
Injection time: 17:10 24.03.2011
Radionuclide: Lu-177

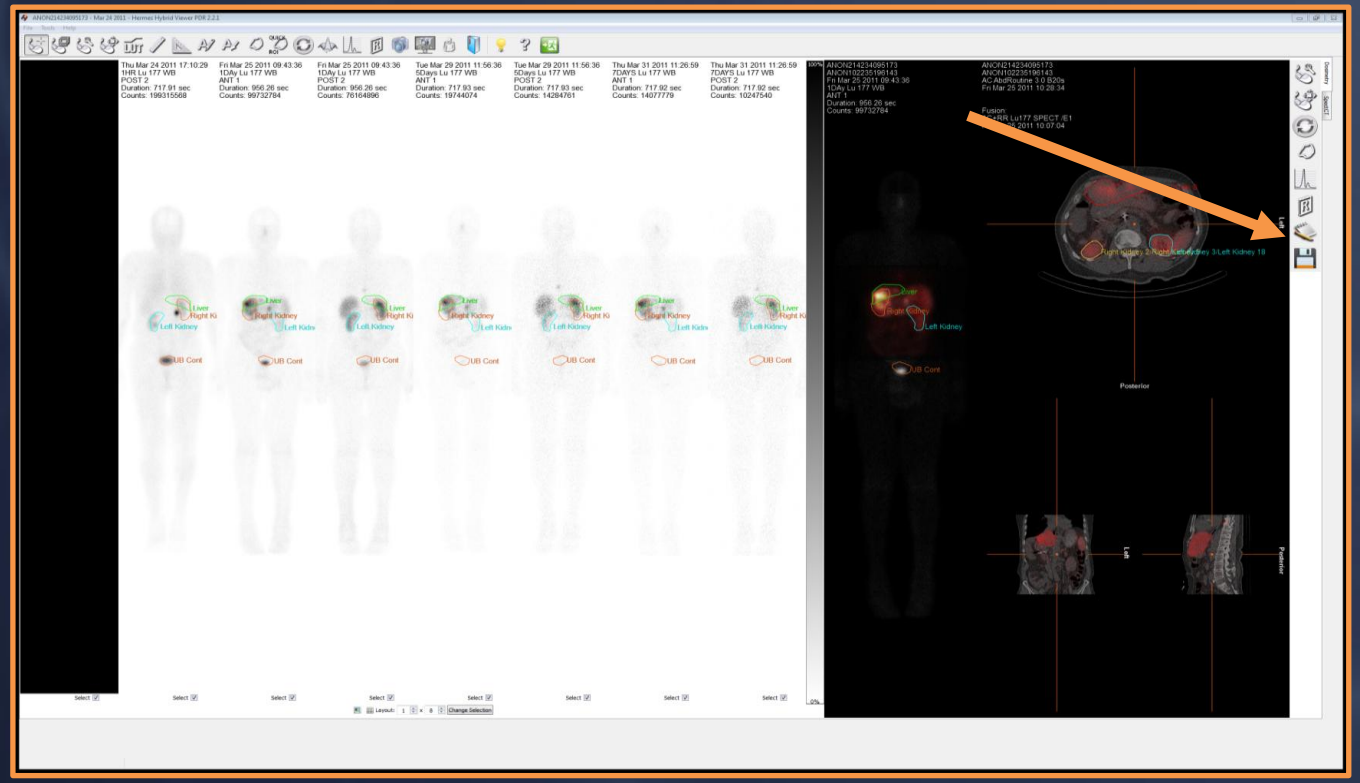
Doses

Organ	Dose [mGy]	Dose/MBq [mGy]	Organ	Dose [mGy]	Dose/MBq [mGy]	Organ	Dose [mGy]	Dose/MBq [mGy]
Adrenals	2.96e+02	4.00e-02	Ovaries	2.84e+02	3.84e-02	Total body	3.14e+02	4.25e-02
Brain	2.70e+02	3.65e-02	Pancreas	2.96e+02	4.00e-02	Lesion 1	0.00e+00	0.00e+00
Breasts	2.68e+02	3.62e-02	Red marrow	1.96e+02	2.65e-02	Lesion 2	0.00e+00	0.00e+00
GB Wall	3.07e+02	4.15e-02	Bone surf	3.48e+02	4.70e-02	Lesion 3	0.00e+00	0.00e+00
LLI Wall	2.82e+02	3.81e-02	Skin	2.65e+02	3.59e-02	Lesion 4	0.00e+00	0.00e+00
Sml Int	2.86e+02	3.87e-02	Spleen	2.83e+02	3.83e-02	Lesion 5	0.00e+00	0.00e+00
Sto Wall	2.83e+02	3.83e-02	Testes	2.72e+02	3.68e-02	Lesion 6	0.00e+00	0.00e+00
ULI Wall	2.87e+02	3.88e-02	Thymus	2.77e+02	3.74e-02	Lesion 7	0.00e+00	0.00e+00
Heart Wall	2.85e+02	3.86e-02	Thyroid	2.76e+02	3.73e-02	Lesion 8	0.00e+00	0.00e+00
Kidneys	1.94e+03	2.63e-01	UB Wall	2.81e+02	3.80e-02	Lesion 9	0.00e+00	0.00e+00
Liver	1.49e+03	2.02e-01	Uterus	2.85e+02	3.85e-02	Lesion 10	0.00e+00	0.00e+00
Lungs	2.80e+02	3.78e-02	Fetus	0.00e+00	0.00e+00			
Muscle	2.75e+02	3.72e-02	Placenta	0.00e+00	0.00e+00			

Effective dose [mSv]	3.91e+02
Effective dose/MBq [mSv]	5.29e-02

Save ROI's/VOI's and export to OLINDA

- Can save ROI's/VOI's
- Export residence time for input into OLINDA and dose calculation



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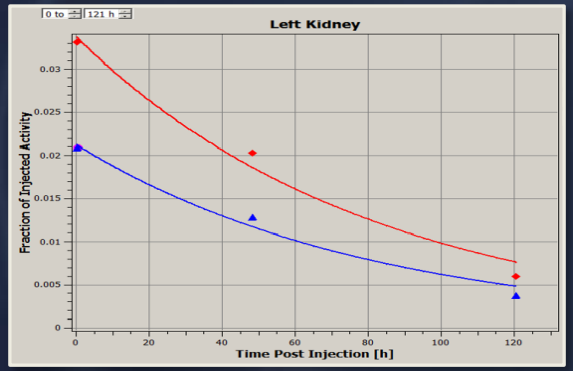
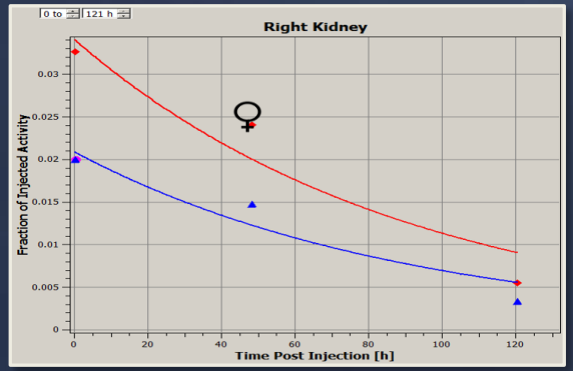
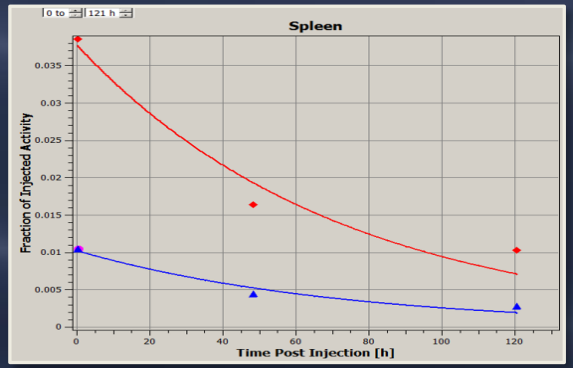
Hybrid Viewer™ Dosimetry [Results I]



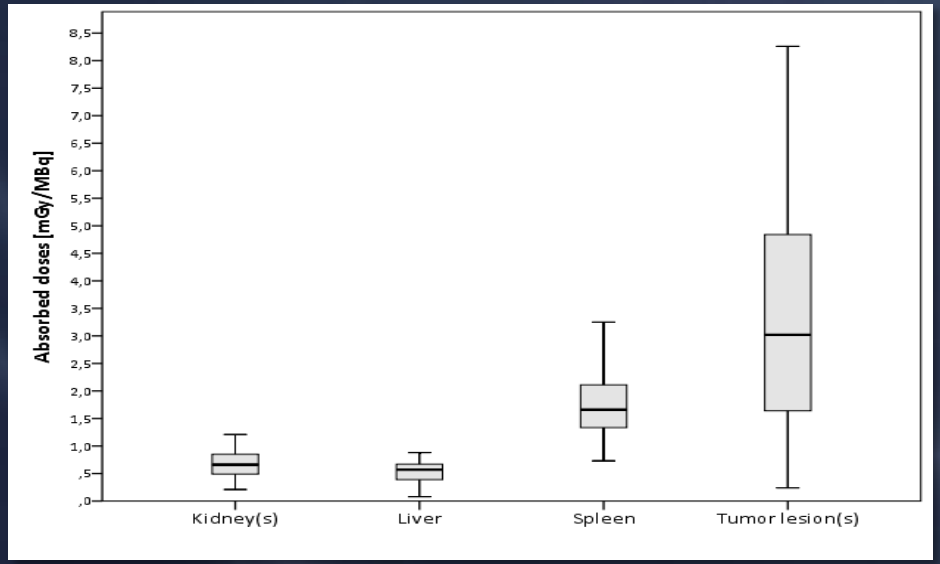




Courtesy of University of Rostock

Hybrid Viewer™ Dosimetry [Customer example]

Absorbed doses in organs and tumor lesions



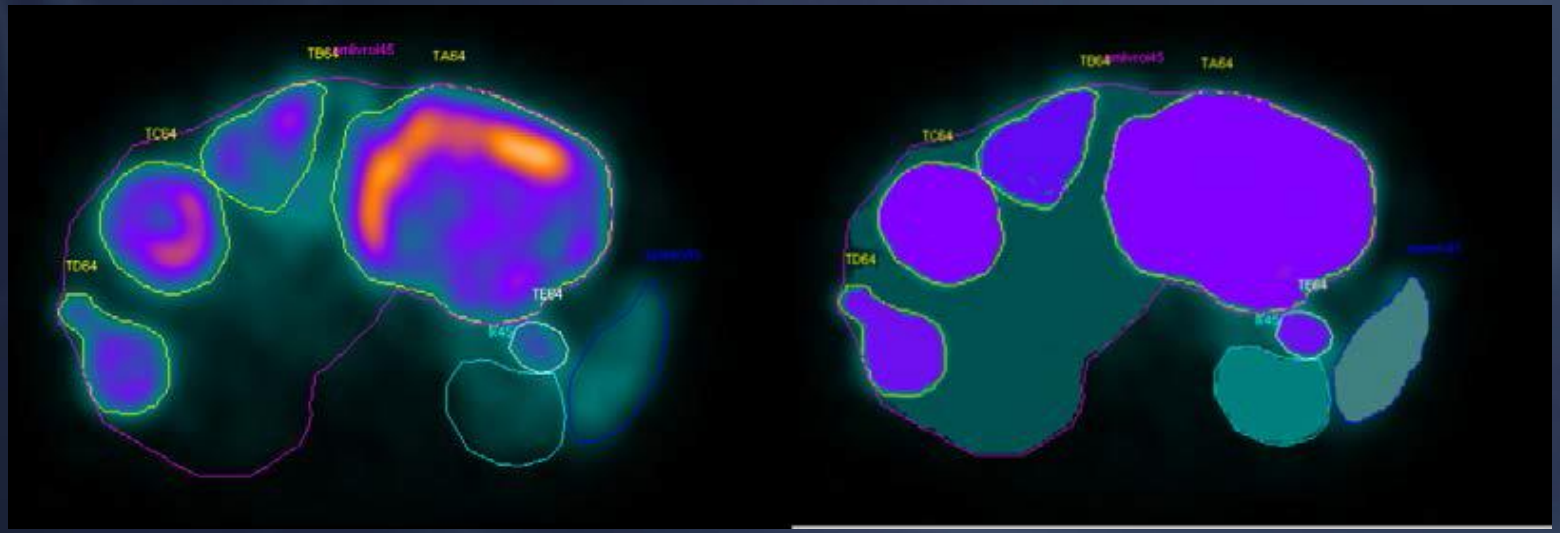
n = 30

Calculated mean values in [mGy/MBq]			
Kidney(s)	Liver	Spleen	Tumor lesions
0,69 ± 0,29	0,61 ± 0,34	1,95 ± 1,21	4,25 ± 4,98

Courtesy of University of Rostock

Hybrid 3Dose

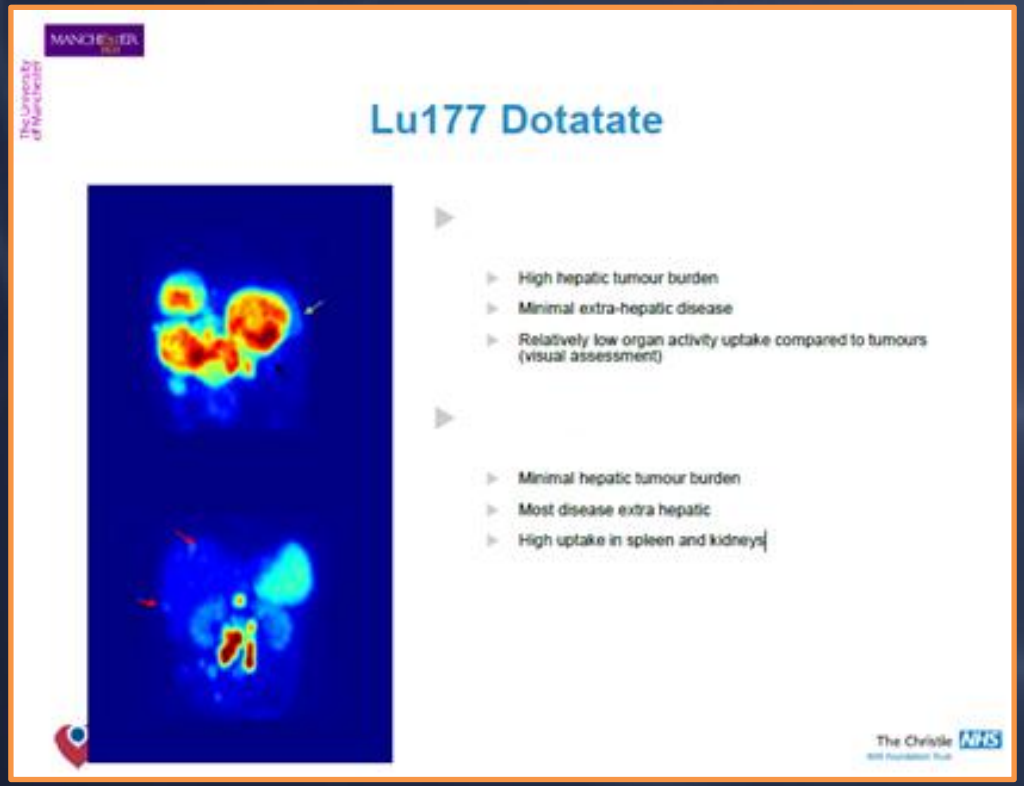
Moving from the assumption of homogenius distribution in lesions and organs to voxelbased Dose distribution



Courtesy of the Christie

Hybrid 3Dose

Moving from the assumption of homogenius distribution in lesions and organs to voxelbased Dose distribution



Courtesy of the Christie

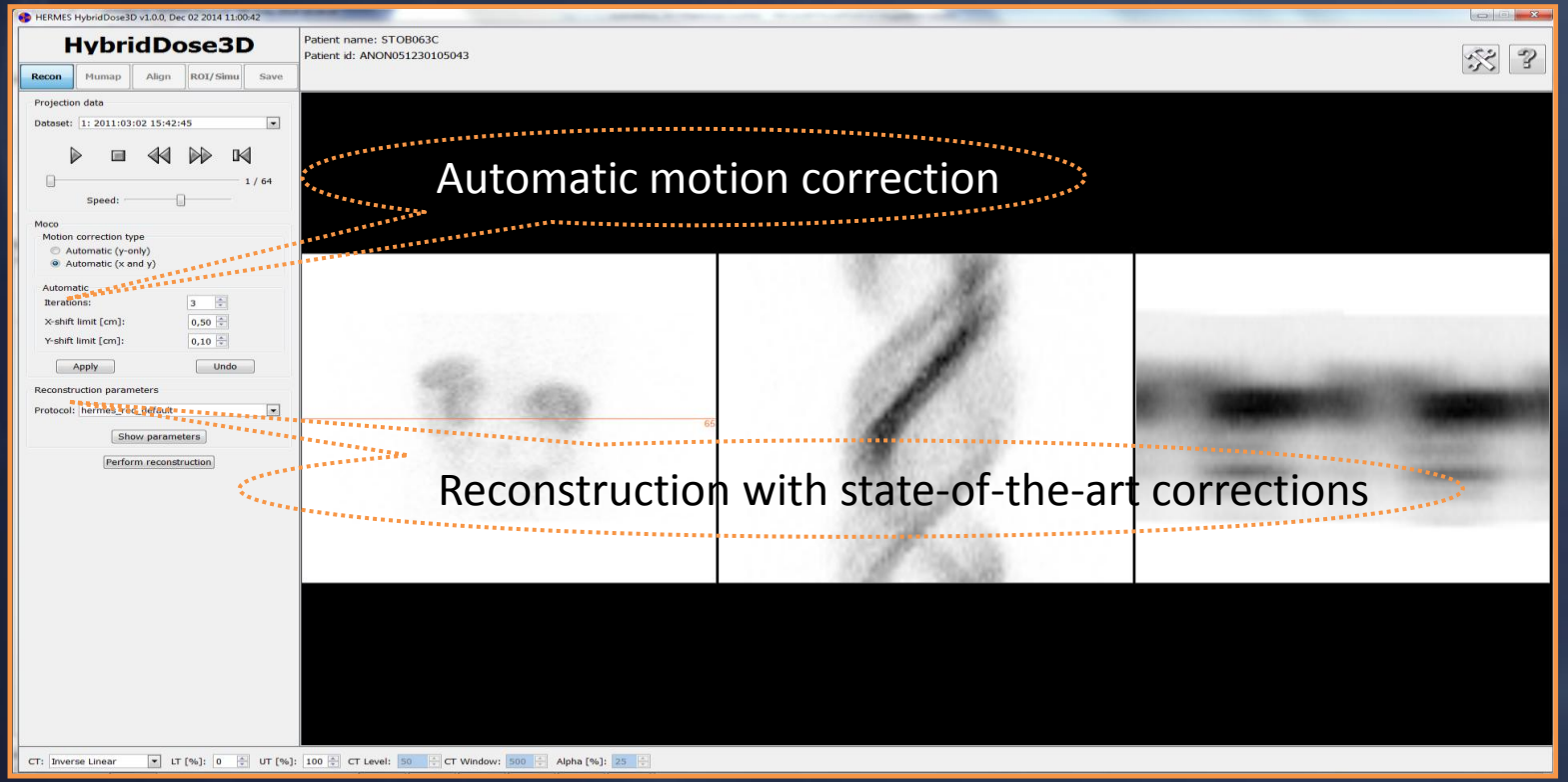
Hybrid 3Dose – Monte Carlo

- Historically 3D voxel-based dosimetry is time-consuming
- HERMES has developed Hybrid 3Dose-package, which combines the following dosimetry steps in a clinically valid time:

1. Reconstruction
2. Registration
3. Curve-fitting
4. MC-based dose calculation
5. Semiautomatic ROI drawing of organs from CT
6. Automatic lesion detection
7. Reporting

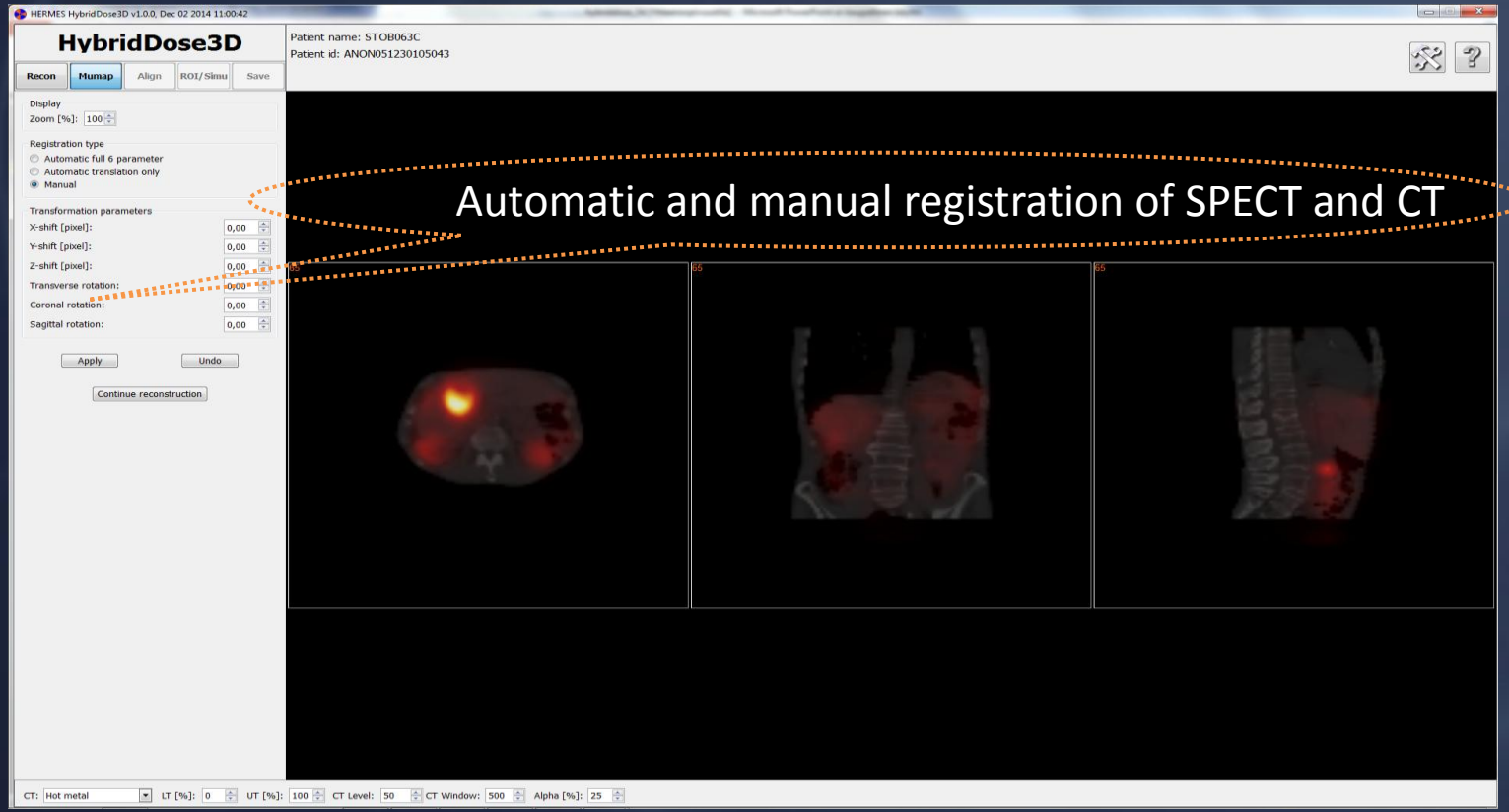
Hybrid 3Dose

Projection data quality check & reconstruction



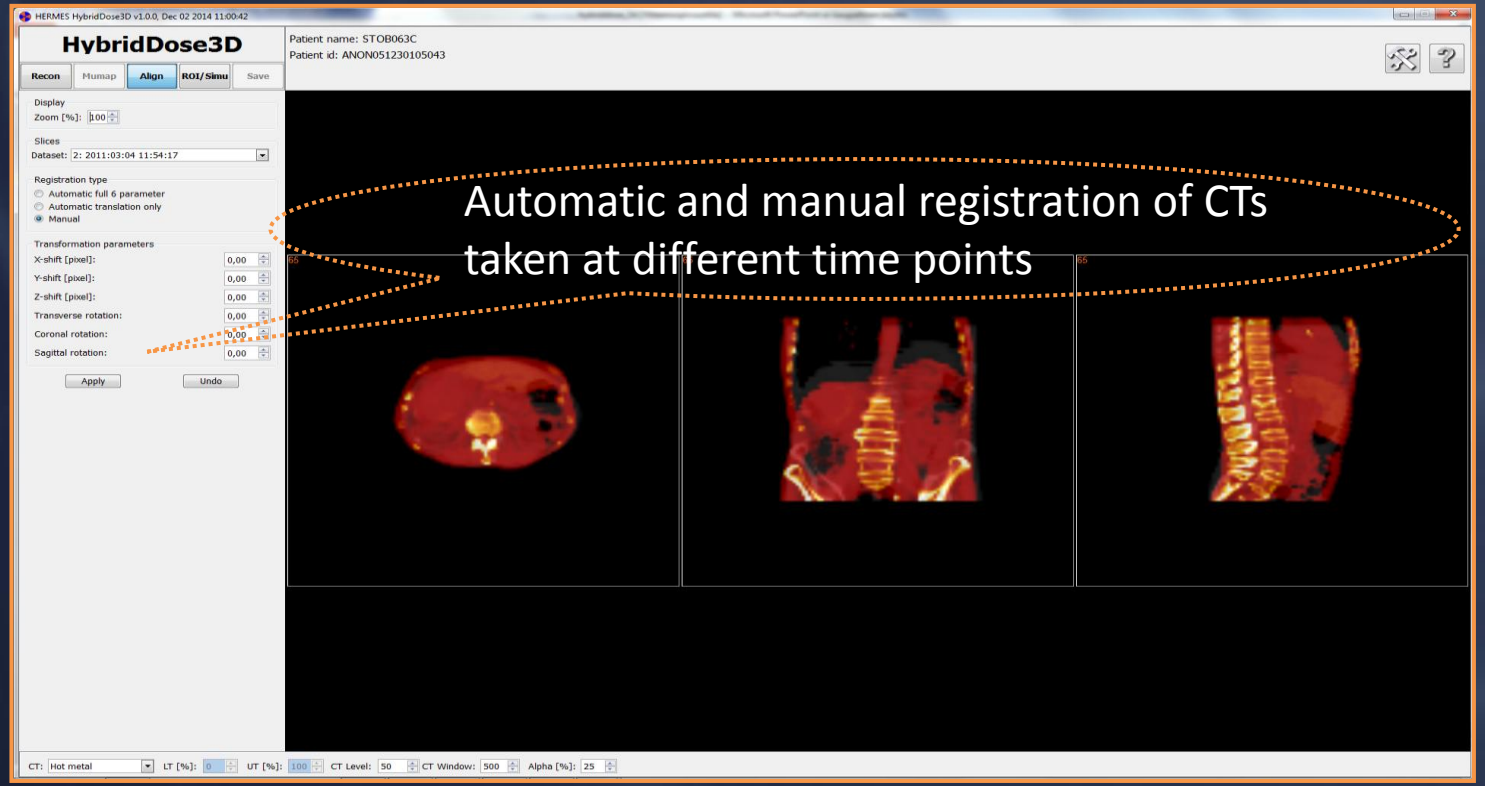
Hybrid 3Dose

Mumap-realignment



Hybrid 3Dose

Alignment of the different scans



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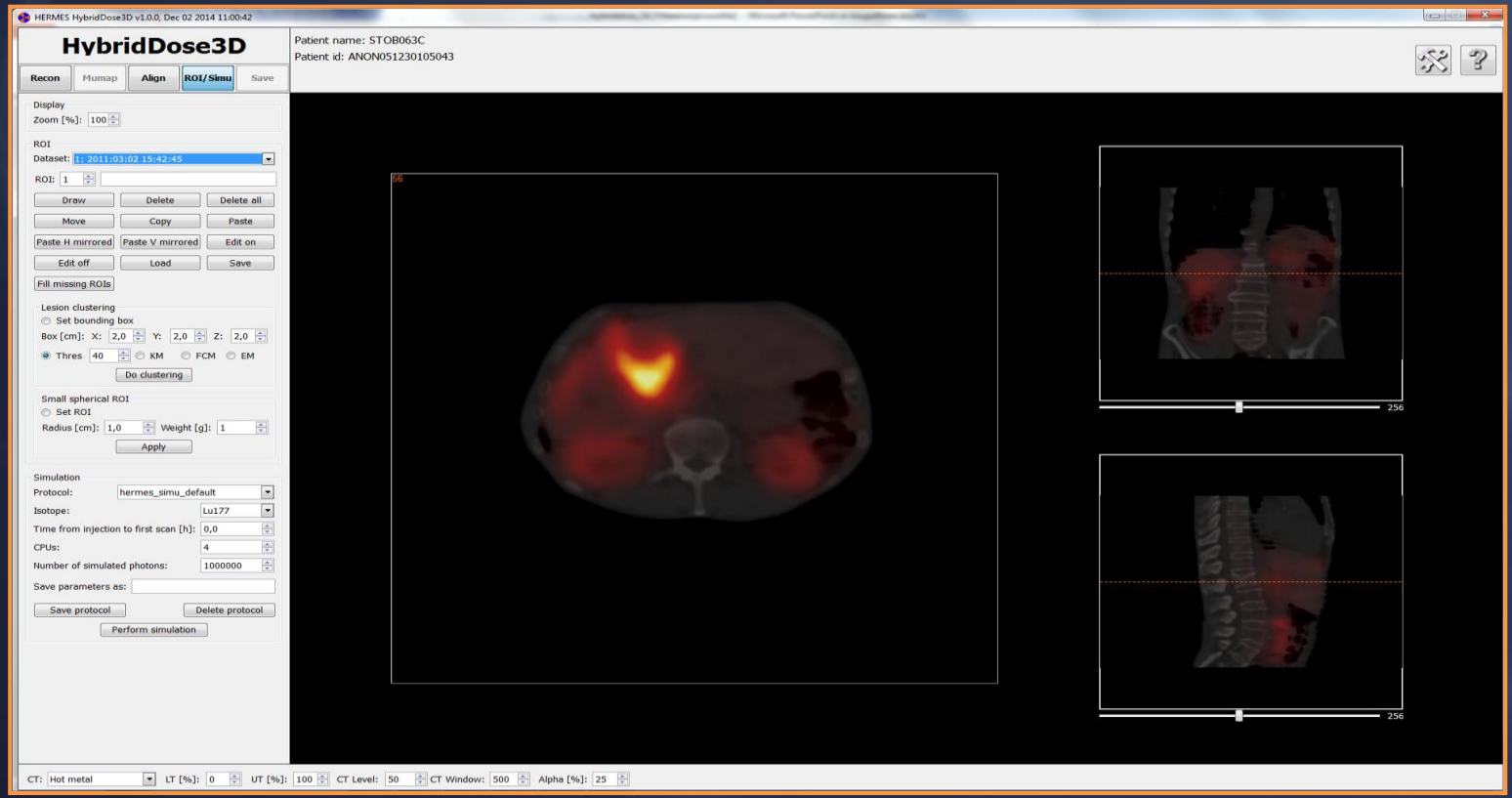
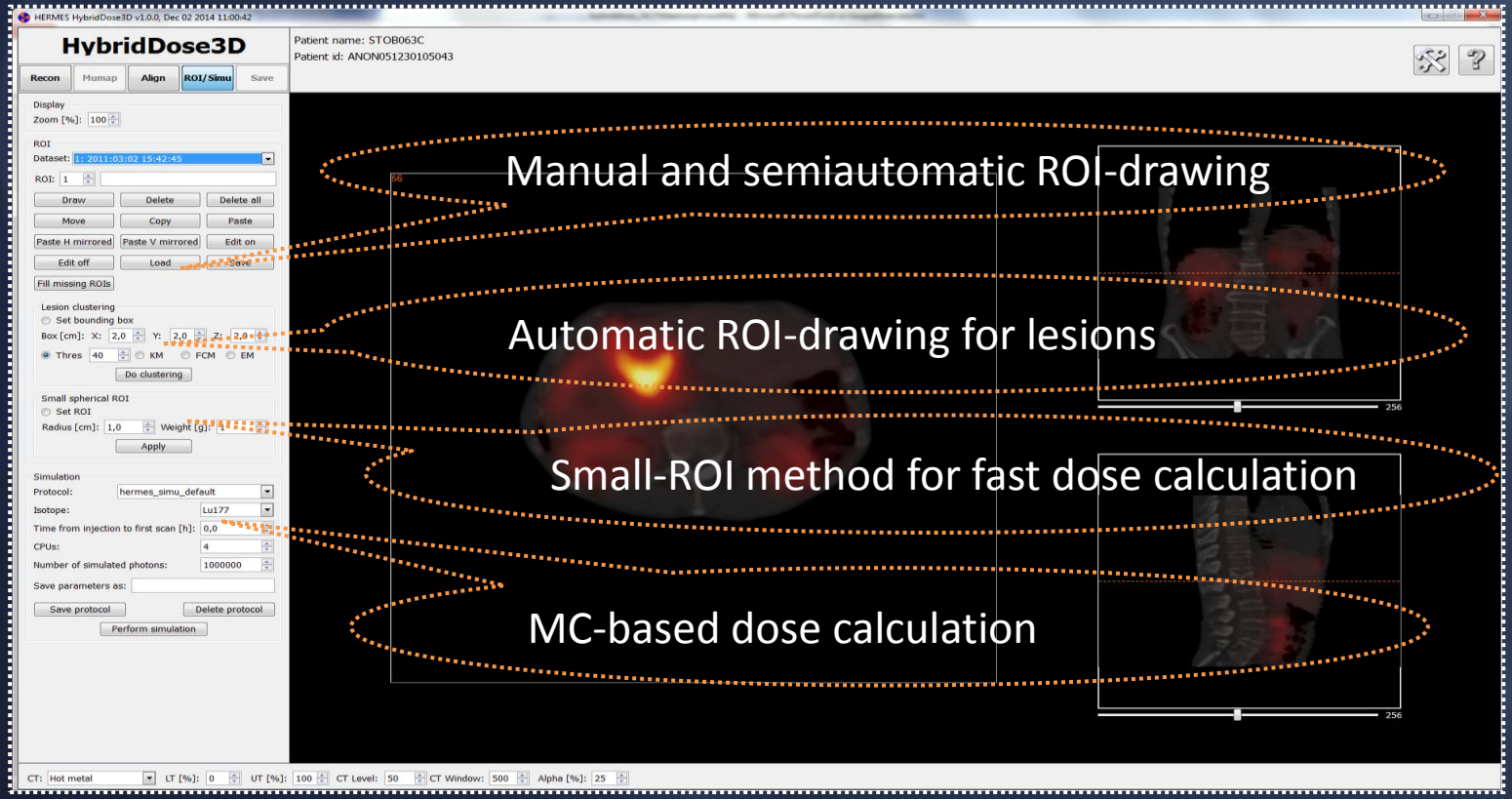
Hybrid 3Dose

ROI drawing and dose-calculation



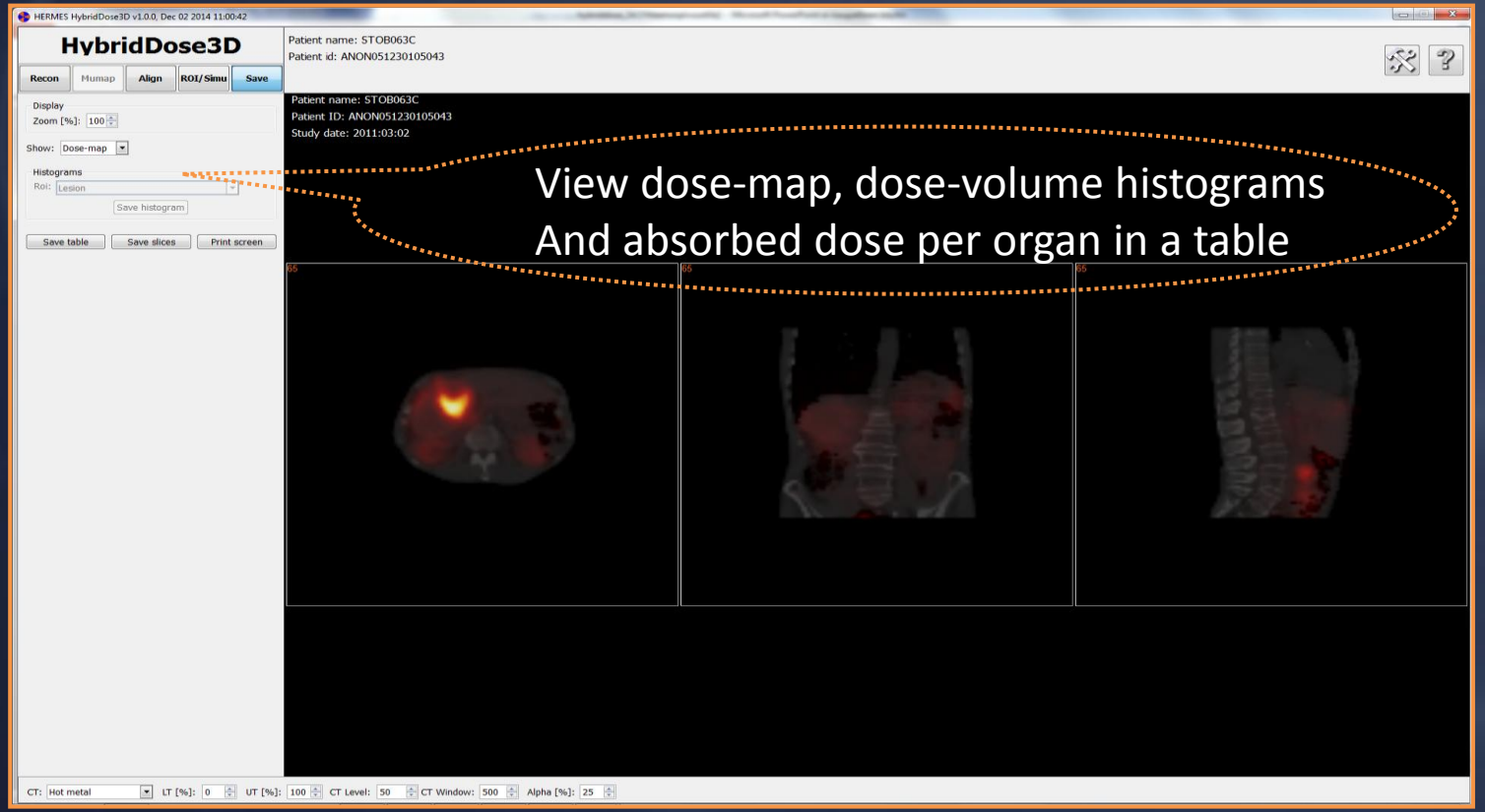
Hybrid 3Dose

ROI drawing and dose-calculation



Hybrid 3Dose

Reporting



SIRT – Dose Planning

TheraSphere®

CALCULATION OF DOSE

The recommended dose to the liver is between 80 Gy to 150 Gy (8000 rad to 15000 rad). The amount of radioactivity required to deliver the desired dose to the liver may be calculated using the following formula:

$$\text{Activity Required (GBq)} = \frac{\text{[Desired Dose (Gy)] [Liver Mass (kg)]}}{50}$$

The liver volume and corresponding liver mass may be determined using CT or ultrasound scans.

For determining the actual liver dose (Gy) delivered to the liver after injection, the following formula is used:

$$\textit{Dose (Gy)} = \frac{50\ [\textit{Injected Activity (GBq)}]\ [1-F]}{\textit{Liver Mass (kg)}},$$

where F is the fraction of injected radioactivity localizing in the lungs, as measured by Tc-99m MAA scintigraphy.

The upper limit of injected activity shunted to the lungs is F x A = 0.61 GBq.

SIRT – Dose Planning

Percent Lung Shunting	Activity of SIR-Spheres†
< 10%	Deliver full amount of SIR-Spheres †
10% to 15%	Reduce amount of SIR-Spheres† by 20%
15% to 20%	Reduce amount of SIR-Spheres† by 40%
> 20 %	Do not give SIR-Spheres†

Empirical

The % Involvement by the Tumour in the Liver	Recommended Y-90 Dose*
> 50 %	3.0 GBq
25 % - 50 %	2.5 GBq
< 25 %	2.0 GBq

*When there is 10 % or more lung shunting, the patient dose should be reduced according to Table 1.

BSA

The BSA method varies yttrium-90 activity according to the size of the patient and the size of the tumour within the liver and is the most widely used method.

The BSA method uses the patient's Body Surface Area (BSA) (calculated from the patient's weight and height) and the percentage of the liver (by volume) that is replaced with tumour (calculated from the CT scan). Most patients will receive between 1.3-2.5GBq of yttrium-90 if the whole liver is to be treated.
Activity of SIR-Spheres microspheres in GBq

$$= (\text{BSA} - 0.2) + \left(\frac{\%\ tumour\ involvement}{100}\right)$$

Body Surface Area (BSA) is calculated from a weight/height chart

$$\%\ \text{tumour involvement} = \frac{\text{volume of tumour} \times 100}{\text{volume of tumour + liver}}$$

Partition Model

This method involves selecting safe radiation doses to the normal liver and lung and implanting the maximum activity that will not exceed these limits. The radiation dose to the normal liver parenchyma should not exceed 80Gy in patients with normal liver and 70Gy in patients with cirrhosis. The dose to the lung should not exceed 25Gy and preferably be less than 20Gy. The dose received by the tumour has no upper limit.

The technique requires two measurements to be made:

1. Measurement of the volume of tumour and normal liver determined from a CAT scan
2. Measurement of the proportions of technetium-99 labelled MAA activity that lodges in the tumour, normal liver and lung as determined from a gamma scan.

As the lung is largely filled with air, the CAT scan cannot be used to measure the volume of the lung parenchyma, and hence an estimation of 1000cc is made. For the purpose of calculating tissue mass, all tissue densities are all estimated at 1gm/cc.

Equation 1 is used to calculate the radiation dose received by an organ after SIR-Spheres microspheres has been delivered to that organ.

Equation 1:

$$\text{Tissue Radiation Dose (Gy)} = \frac{49670 \times \text{Total yttrium-90 activity in the organ or tissue (in GBq)}}{\text{Mass of the organ or tissue (in grams)}}$$

Therefore, to calculate the activity to be implanted, it is necessary to

1. from the liver CT scan, calculate the volumes of the normal liver and tumour
2. convert each volume to mass on the basis of 1g/cc
3. from a lung CT scan, determine the volume of the lung and convert to mass (or estimate it as 1000g)
4. from the *nuclear medicine break-through scan*, determine the activity in the lung, tumour and liver
5. determine the T/N activity ratio (calculated as activity per unit mass of organ or tissue) using *Equation 2*
6. determine the percentage shunted to the lungs using *Equation 3*.

To determine the T/N ratio, the following equation should be used.

To determine the T/N ratio, the following equation should be used.

Equation 2: $T/N = r = (A_{Tumour}/M_{Tumour})/(A_{Liver}/M_{Liver})$

Where:
T/N (r) is the tissue/normal ratio of the activity in the tumour and normal liver per unit mass of each of these compartments.
A_{Tumour} is the activity in tumour
M_{Tumour} is the mass of tumour
A_{Liver} if the activity in the normal liver
M_{Liver} is the mass of the normal liver

Equation 3: $\text{Lung Activity } (A_{Lung}) = A_{Total} \times \frac{L}{100}$

Where A_{Total} is the total activity implanted for the nuclear medicine break-through scan and L is the percentage lung shunting.

Percent lung shunting = $100 \times A_{Lung}/(A_{Lung} + A_{Liver} + A_{Tumour})$

To calculate the total activity to be implanted, use the following equations. The activity required should be calculated using the lung dose as the limiting factor, and then again using the normal liver dose as the limiting factor. The lower of the two activities calculated should be used.

To determine the activity implanted to accommodate a limiting lung dose:

Equation 4: $A_{Total} = \frac{D_{Lung} M_{Lung} 100/L}{49670}$

Where:
D_{Lung} is the dose to the lung
M_{Lung} is the mass of the lung
A_{Lung} is the activity to the lung
A_{Total} is the total activity
L = the percentage lung shunting

To determine the activity implanted to accommodate a limiting normal liver dose:

Equation 5: $A_{Total} = \frac{[D_{Liver}((T/N\ M_{Tumour}) + M_{Liver})]}{[49670\ (1\text{-}L/100)]}$

The partition model can only be used where the tumour mass is a discrete area within the liver. This is more likely patients with Primary Hepatocellular Carcinoma (HCC) where there is often a large single tumour mass. Patients with metastatic disease usually have multiple areas of metastatic spread that precludes defining the tumour and normal parenchymal compartments.

To Dicuss

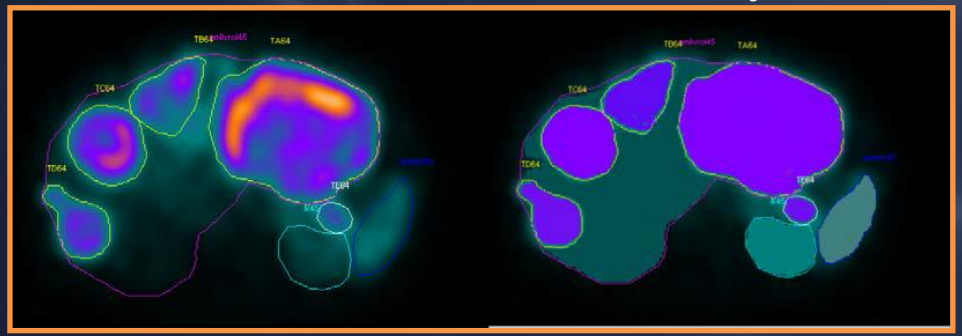
Future Direction?

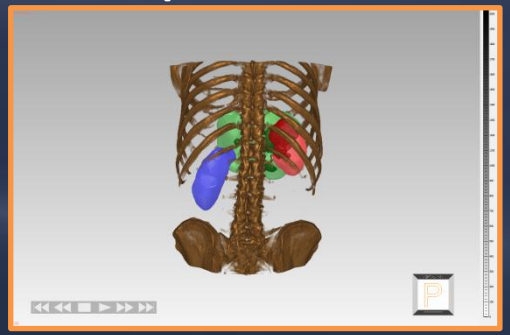
Balance the functions and accuracy to find a clinically proper method

Organ segmentation , ROI, VOI, CT, automatic, semi-automatic, certain volume positioned in each organlow dose CT, lesion involved organs

S-Voxel or Monte-Carlo or need for both?

Dose with uncertainty as final output?





Thank You!

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