SIEMENS

White Paper

EQ•PET: Achieving NEMA-referenced SUV Across Technologies

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Answers for life.

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Introduction

PET is a valuable tool for helping diagnose, stage and monitor cancer, as well as enabling clinicians to quantify active disease and measure response to therapy. Accurate quantification aids clinicians in benchmarking disease and identifying effective therapies earlier in the treatment cycle, thus improving the efficiency and efficacy of patient care.

The Standardized Uptake Value (SUV) is the most widely-used metric for quantifying radiotracer uptake in tumors, providing normalization for differences in patient size, body composition and injected dose; however, differences in scanner hardware and reconstruction protocol can introduce clinically significant variation in PET quantification that are not addressed by SUV alone[1].

EQ•PET is a new reference-based quantification technology within *syngo*®.via that provides clinicians with harmonized SUVs across patient scans, even if acquired on different scanners or reconstructed with different protocols[2].

EQ•PET achieves this without requiring the clinical site to modify their reconstruction protocol or reconstruct additional datasets. With EQ•PET, the clinician reads from the original patient image, reconstructed with their preferred protocol to maximize image quality and detectability. SUV is harmonized using an EQ•PET parameter selected to align contrast recovery between scanners and reconstructions (Figure 1), relative to a reference such as the EANM specification[3].

This white paper presents three clinical use cases for SUV harmonization along with an approach for determining the EQ•PET parameter for the scanner model and reconstruction protocol. The clinical use cases presented are:

- **Cross-scanner response assessment** for patients imaged with different PET/CT systems;
- **Multi-center clinical trials** that require strict alignment of acquisition protocol and quantitative performance of scanners;
- **Inter-site SUV thresholds** to facilitate the exchange and adoption of SUV-based protocols between clinical sites

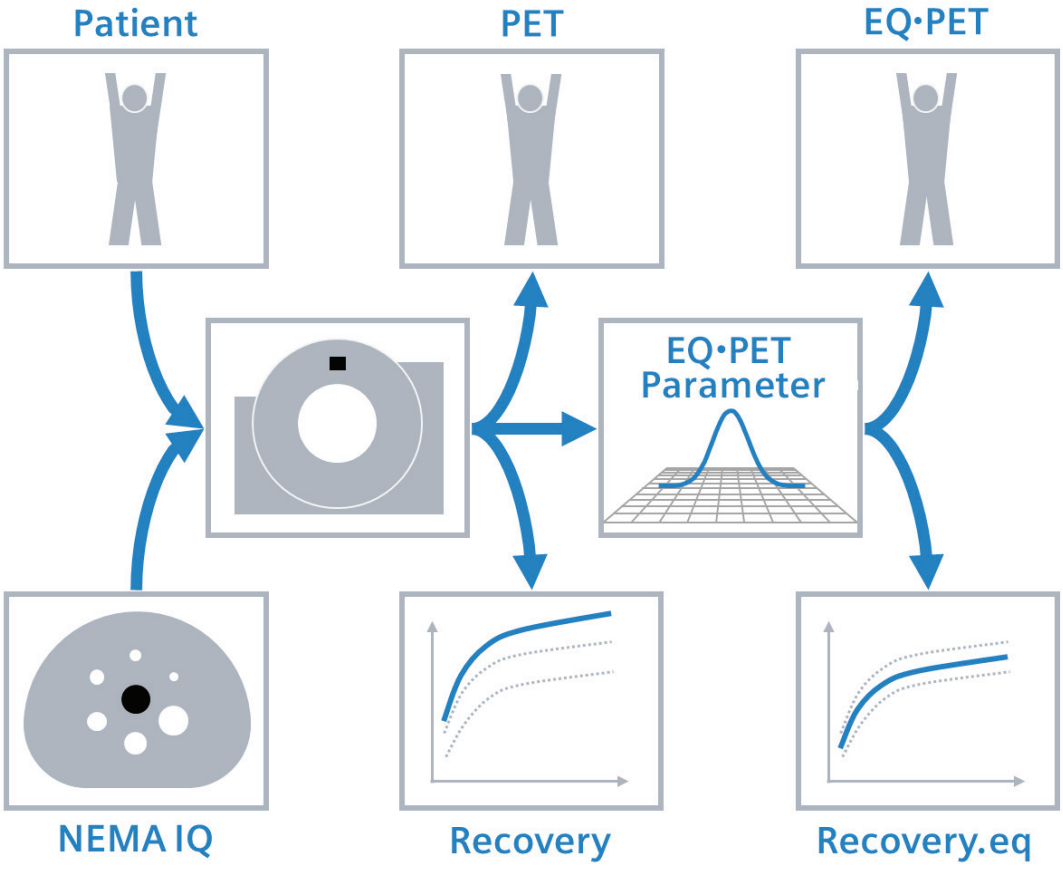

Figure 1. *EQ•PET harmonizes SUVs across different scanners and reconstructions by applying a phantom-derived reference-based EQ•PET parameter optimized to align contrast recovery coefficients.*

Case Study 1 – Cross-Scanner Response Assessment

Challenge: *Assess treatment response in patients quantitatively, even if imaged on different PET/CT systems.*

PET/CT imaging is used clinically to assess a cancer patient's response to treatment. While dramatic disease progression or treatment response can often be reliably determined from a qualitative review of the images, more subtle changes require quantitative assessment[4]. Furthermore, quantitative assessment enables objective evaluation of change, with standardized response criteria such as PERCIST[4], improving inter-reader agreement.

Quantitative response assessment is typically performed using SUV, which normalizes for differences in dose injected and patient weight to facilitate inter-scan comparison. Despite this normalization, differences in scanner model and reconstruction can still have a clinically significant impact on SUV[1].

EQ•PET quantification, in combination with a standardized imaging protocol, allows a physician to assess treatment response in patients quantitatively, even if the patient's scans were acquired on different systems or reconstructed differently.

Clinical Example

The following lung cancer patient (Figure 2) received 2 cycles of chemotherapy, including granulocyte stimulating factors, prior to radiotherapy. The first PET/CT scan was performed prior to radiotherapy with the second 8 weeks later.

The pre-RT scan was reconstructed using Iterative (OSEM) with 4 iterations, 8 subsets and a 5 mm FWHM Gaussian post filter. The post-RT scan was reconstructed using HD•PET (PSF) with 3 iterations, 21 subsets and no post filter (Figure 2).

Using the EORTC criteria[5], the change in SUV_{max} between the two scans (3.74 to 7.17; +92%) indicates disease progression (Table 1). However, due to the difference in reconstruction, a confident assessment cannot be made. In fact, in an additional reconstruction of the post-RT scan with the pre-RT protocol, the SUV_{max} measured for the lesion is 4.13 (+10%), indicating stable disease according to the EORTC criteria.

Using the appropriate EQ•PET parameter to align the HD•PET reconstruction with Iterative (7.0 mm FWHM), the SUV_{max}.eq measured for the same lesion on the post-RT HD•PET scan is 4.06 (+9%). EQ•PET, therefore, enables quantitatively comparable response assessment, despite the use of a more advanced reconstruction protocol with improved image quality in the post-RT scan.

This improved comparability across reconstructions with EQ•PET is also seen with SUV_{peak} (Table 2). While the PERCIST-based response classification is not affected in this example, a difference in SUV_{peak} of +24% versus -3% has the potential to impact a clinician's assessment of treatment effect.

A prospective evaluation of the impact of applying a phantom-derived parameter to align quantification found that it allowed for a reliable pre- and post-therapy evaluation when using different generation PET systems[1].

Change in SUV_{max} (%)		Post-RT scan		
		Iterative	HD•PET	HD•PET.eq
Pre-RT scan	Iterative	+10% (SMD)	**+92% (PMD)**	+9% (SMD)
	HD•PET	**-28% (PMR)**	**+25% (PMD)**	n/a
	HD•PET.eq	+4% (SMD)	n/a	+4% (SMD)

Table 1. *Percentage change in SUV_{max} between pre- and post-RT scans for different reconstruction protocols. EORTC response classification is denoted by (PMD) progressive metabolic disease, (SMD) stable metabolic disease and (PMR) partial metabolic response.*

n/a = not applicable
EQ•PET is mitigating the impact of the reconstruction protocol which could impact patient management.

Change in SUV_{peak} (%)		Post-RT scan		
		Iterative	HD•PET	HD•PET.eq
Pre-RT scan	Iterative	-3% (SMD)	**+24% (SMD)**	+1% (SMD)
	HD•PET	**-23% (SMD)**	-2% (SMD)	n/a
	HD•PET.eq	-7% (SMD)	n/a	-3% (SMD)

Table 2. *Percentage change in SUV_{peak} between pre- and post-RT scans for different reconstruction protocols. PERCIST response classification is denoted by PMD, SMD and PMR.*

n/a = not applicable
EQ•PET is mitigating the impact of the reconstruction protocol which could impact patient management.

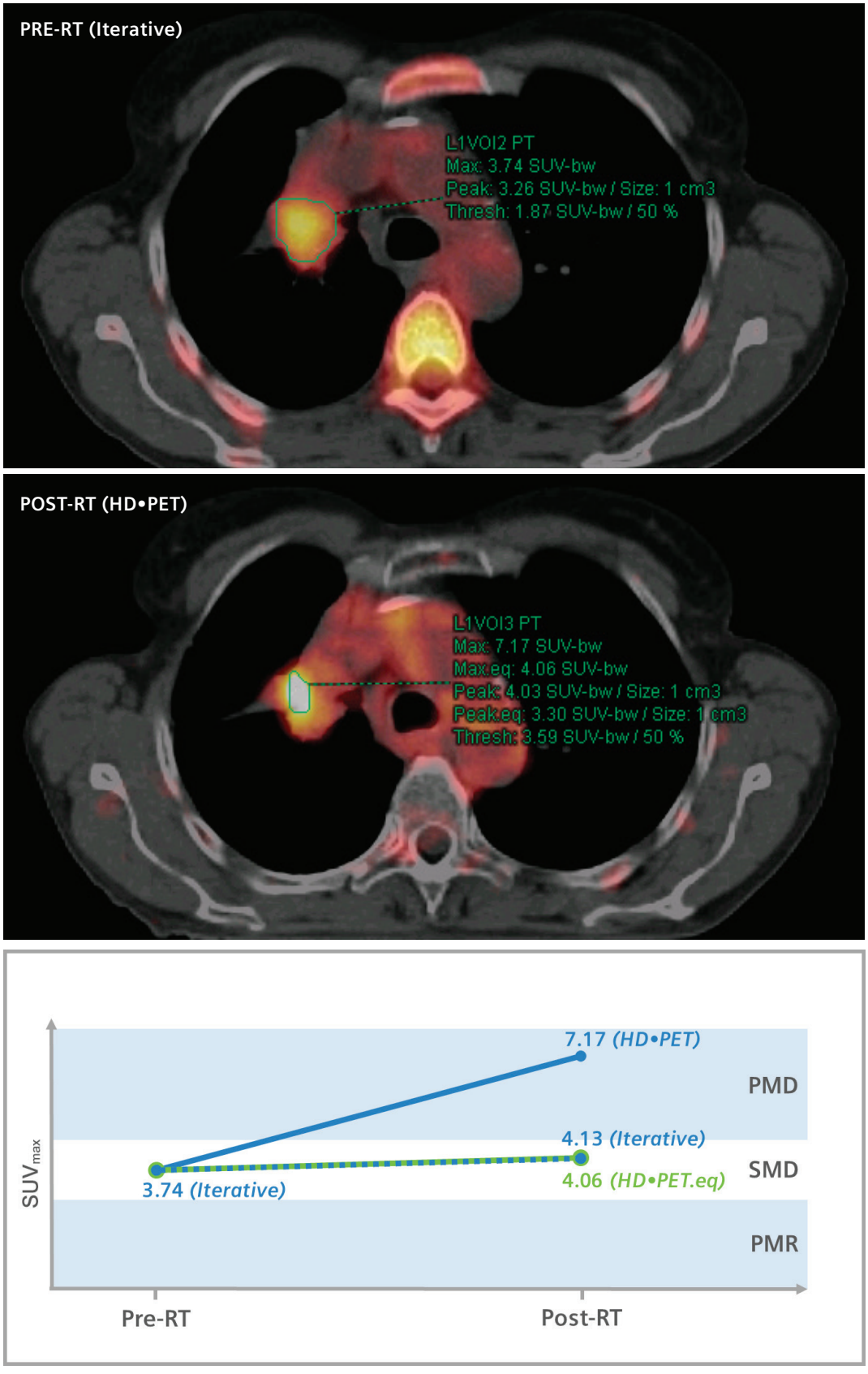

Figure 2. *Pre- and post-RT PET/CT scans for lung cancer patient. A single lesion in the right lung is identified and the quantitative assessment is dependent on the reconstruction method used. This dependency is minimized with EQ•PET.*

Data courtesy of François Baclesse Cancer Centre, Caen, France.

Case Study 2 – Multi-Center Clinical Trials

Challenge: *Participate in multi-center clinical trials, without needing to modify established reconstruction protocols.*

Multi-center clinical trials facilitate the recruitment of a larger number of subjects in a shorter time period. Medical imaging techniques, including PET/CT, are frequently used in clinical trials for patient stratification or as surrogate endpoints.

The need for quantitative comparability in clinical trial imaging typically requires a form of site accreditation prior to participation, such as that provided by the Society of Nuclear Medicine and Molecular Imaging's Clinical Trials Network (CTN) or EANM Research Limited (EARL). As part of this accreditation, each site must conform to a commonly achievable standard for quantification.

Typically, this will require the modification of a site's reconstruction protocol to conform with the trial protocol (usually leading to a loss of resolution) or, if this is undesirable, the reconstruction of an additional PET dataset for quantification.

EQ•PET, in combination with a standardized imaging protocol, allows a site to adhere to the quantitative requirements for a multi-center clinical trial without having to reduce image quality or reconstruct and manage a second dataset.

Clinical Example

To demonstrate the quantitative impact of reconstruction, a lung cancer patient scan (Figure 3) has been reconstructed with three different protocols:

- Iterative (OSEM) with 2 iterations, 24 subsets and a 5 mm FWHM Gaussian post filter
- HD•PET (PSF) with 3 iterations, 24 subsets and a 4 mm FWHM Gaussian post filter
- ultraHD•PET (PSF+TOF) with 3 iterations, 21 subsets and no post filter

In each reconstruction, the SUV_{max} was measured for a small lesion in the left lung. When compared with the basic Iterative reconstruction, both HD•PET and ultraHD•PET produce a clinically significant increase in SUV_{max}[5] (Table 3). However, by applying the EQ•PET parameters necessary to align with the EANM specification[2], this variability is reduced to within the reported test-retest variability for ^{18}F-FDG uptake in tumors[6].

	SUV_{max}	SUV_{max}.eq	EQ•PET parameter
Iterative	4.04	3.80	3.3 mm
HD•PET	**6.37 (+58%)**	3.45 (-9%)	6.5 mm
UltraHD•PET	**7.51 (+86%)**	3.21 (-16%)	7.1 mm

Table 3. *Effect of reconstruction on SUV_{max} and SUV_{max}.eq for the lung lesion shown in Figure 3. Percentage change relative to Iterative is shown in parentheses. EQ•PET parameters FWHMs required to align with the EANM specification are shown in the final column.*

EQ•PET is mitigating the impact of the reconstruction protocol which could impact patient management.

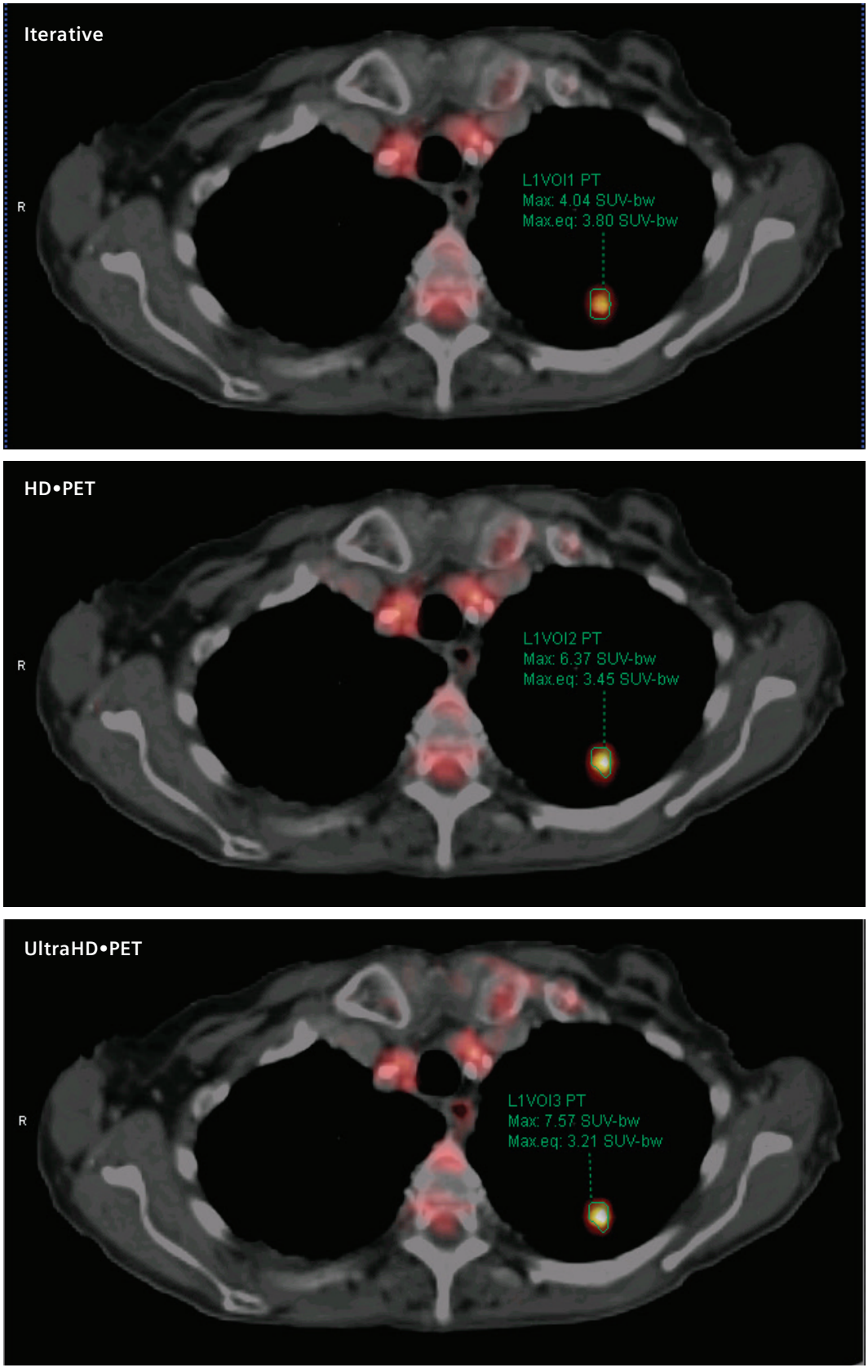

Figure 3. *Lung cancer patient reconstructed with Iterative, HD•PET, and UltraHD•PET. The SUV_{max} for a small lesion in the posterior left lung increases with the addition of advanced reconstruction techniques.*

Data courtesy of University of Tennessee Medical Center, Knoxville, TN, USA.

Case Study 3 – Inter-Site SUV Thresholds

Challenge: *Use SUV-based thresholds to guide patient management decisions, even if they were defined on an older PET/CT system.*

PET/CT is an integral part of staging many cancer types and guides subsequent patient management decisions. Initial assessment of a suspicious lesion's malignancy is commonly performed based on ^{18}F-FDG uptake, with some sites using SUV-based thresholds to categorize lesions in terms of likelihood of malignancy. Furthermore, SUV-based thresholds of change for classifying treatment response are also widely used (e.g., EORTC, PERCIST).

SUV-based thresholds determined at one site may not be applicable to patient data acquired at other sites or using other scanner models or reconstruction protocols.

EQ•PET, in combination with a standardized imaging protocol, facilitates the inter-site application of SUV-based thresholds for staging or response assessment.

Consider the clinical example in Case Study 1. Based on a 25% SUV_{max} change threshold (EORTC), there is considerable variation in response classification with the different reconstruction combinations, even when the pre- and post-RT protocols are matched. This variation is reduced with EQ•PET.

Given the clinical example in Case Study 2, it is clear that using a fixed SUV threshold to estimate likelihood of malignancy could result in different clinical decisions being made for a same patient depending on how it was reconstructed. This dependency on reconstruction can be reduced with reference-based EQ•PET.

The results shown in the examples in this whitepaper are characteristic of a more comprehensive study[2], which demonstrated a significant reduction in reconstruction-dependent variation for both SUV_{max} and SUV_{peak}.

Conclusions

EQ•PET provides clinicians with harmonized SUVs, allowing them to:

- Quantitatively assess treatment response in patients, even if imaged on different PET/CT systems
- Participate in multi-center clinical trials, without modifying their reconstruction protocols
- Use SUV-based thresholds to inform patient management decisions, even if they were defined on an older PET/CT system

Appendix A: EQ•PET Parameter Determination

EQ•PET parameters can be selected to align PET quantification with lower recovery protocols. These include specifications published by international societies (e.g., EANM procedure guidelines), or existing PET protocols used within imaging centres.

The following illustrates one approach for selecting an appropriate harmonization parameter. This approach requires a NEMA IQ phantom acquired and reconstructed using the same protocol used for clinical PET/CT studies.

Test Protocol

In this example, we used a NEMA IQ phantom filled with an 8:1 sphere to background activity concentration ratio, acquired for 3 minutes on a Biograph mCT 64 with TrueV and reconstructed with ultraHD•PET (Table 4). The acquisition was repeated 3 times.

Property	Value
Phantom activity	5.2 kBq.ml^{-1} (background) 41.6 kBq.ml^{-1} (spheres, 8:1)
Acquisition duration	180 s (30x10^6 net trues)
Scanner model	Biograph mCT 64 with TrueV
Reconstruction method	UltraHD (PSF+TOF) 2i21s
Convolution kernel	5 mm FWHM Gaussian
Rows x columns	256x256
Pixel spacing	3.182x3.182 mm
Slice thickness	2.027 mm

Table 4. *Phantom, acquisition and reconstruction properties used in this example.*

Target Protocol

The target protocol used in this example is that specified in the EANM procedure guidelines[3] for the maximum voxel value (Table 5).

EANM Sphere diameter (mm)	Expected RC for max voxel
10	0.38
13	0.63
17	0.84
22	0.89
28	0.95
37	0.98

Table 5. *Target recovery coefficient (RC) specifications for maximum voxel value used in this example.*[3]

Recovery Coefficient Measurement

For each phantom acquisition, the recovery coefficient (R) for the maximum voxel in each sphere was computed as follows:

$$R = \frac{A_{measured}}{A_{true}},$$

where $A_{measured}$ is the maximum activity concentration (Bq.ml^{-1}) measured in an image voxel for a VOI corresponding to the sphere insert, and A_{true} is the true activity concentration (Bq.ml^{-1}) in the sphere.[3]

EQ•PET Parameter Optimization

The RCs measured for each phantom acquisition were compared to those specified in the EANM procedure guidelines (Figure 4A). The RCs were then recomputed following the application of an additional Gaussian smoothing filter (see Appendix C for details). The size of this additional filter was increased in steps of 0.1 mm FWHM until the mean absolute percentage difference between the measured RCs and those specified in the EANM guideline was minimized (Figure 4B). The filter sizes required to minimize the percentage difference for the acquisitions used in this example are shown in Table 6. Based on these acquisitions, the recommended EQ•PET parameter to align the UltraHD reconstruction protocol used in this example with the EANM guideline would be 6.8 mm FWHM.

Phantom acquisition	EQ•PET parameter FWHM (mm)
Acquisition 1	6.7
Acquisition 2	7.1
Acquisition 3	6.6
Mean	**6.8**

Table 6. *EQ•PET normalization parameters computed for the 3 phantom acquisitions used in this example.*

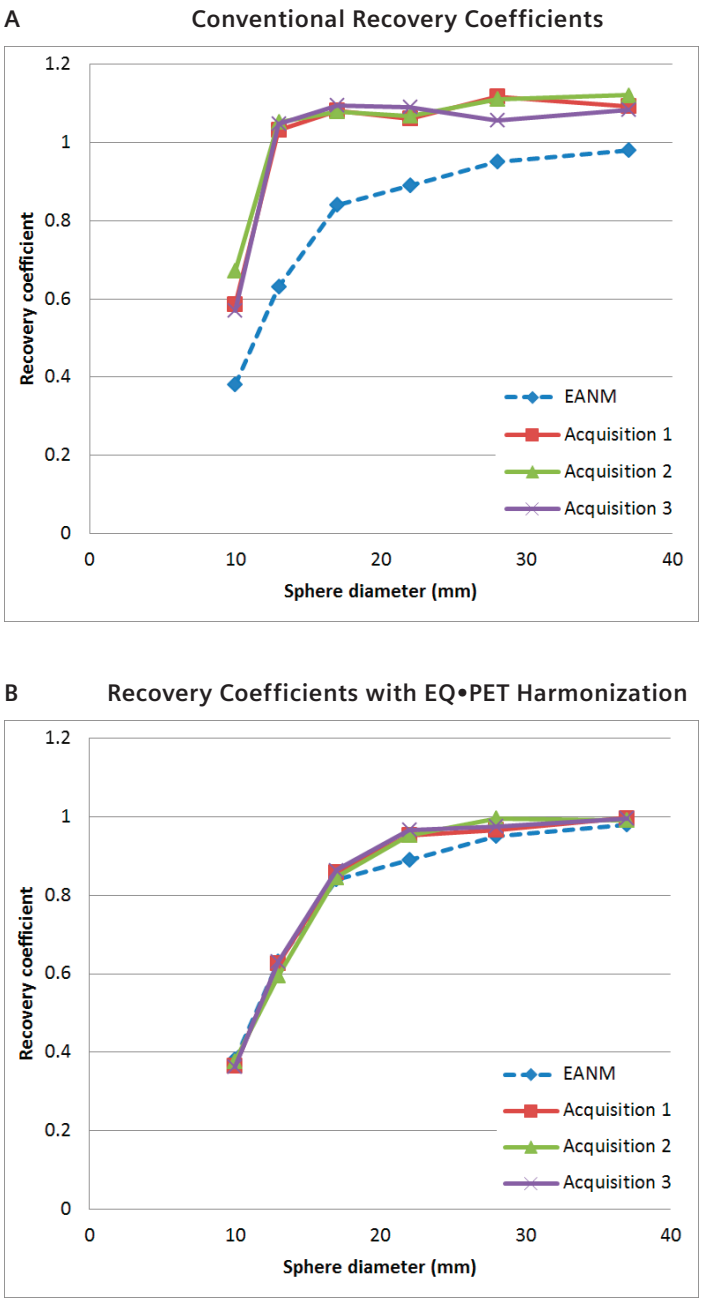

Figure 4. *(A) RCs measured for the 3 acquisitions of the NEMA phantom relative to those specified in the EANM guidelines.[3] (B) RCs measured for the same 3 acquisitions following application of the EANM-matching EQ•PET harmonization parameter.*

Appendix B: Computing EQ•PET Parameters in *syngo*.via

This section describes how *syngo*.via can be used to compute the optimal EQ parameter size for a given scanner model and reconstruction protocol.

Example Dataset

In this example, a NEMA IQ phantom was prepared and reconstructed as described in Table 7.

Property	Value
True AC in sphere	18.70 kBq.ml^{-1}
Scanner model	Biograph 6 with TrueV
Reconstruction method	HD•PET (PSF) 3i21s
Convolution kernel	All pass (0 mm)
Rows x columns	168x168
Pixel spacing	4.073x4.073 mm
Slice thickness	5.0 mm

Table 7. *Phantom preparation and reconstruction protocol used in this example.*

EQ•PET Parameter Optimization

The steps used to compute the optimal EQ parameter for the phantom dataset described above are as follows:

1. The target activity concentration for each of the phantom hot spheres (column 'EANM target AC' in Table 8) was computed by multiplying the true decay-corrected activity concentration (column 'True AC' in Table 8) by the corresponding EANM target recovery coefficient (column 'EANM target recovery' in Table 8).
2. Create a spreadsheet (e.g., in Microsoft Excel™) to compute the mean absolute percentage difference in activity concentrations for the Max.eq values with a given EQ parameter versus the target values computed in Step 1 (Table 8).
3. The NEMA IQ phantom dataset is loaded into *syngo*.via MMOncology.
4. The units are set to Bq.ml^{-1} from the units entry in the bottom right corner menu.
5. Each of the hot spheres is segmented using one of the available PET segmentation tools accessed via the top right corner menu (e.g., VOI Isocontour) (Figure 5).
6. Ensure Max.eq is displayed in the findings evaluation text. This is set in the Segmentation Properties dialogue (Figure 6) accessed by right-clicking on the chosen segmentation tool item in the top right corner menu.
7. Find the EQ parameter that minimizes the mean absolute percentage difference in activity concentrations for the Max. eq values versus the target values computed. This could be done by entering EQ parameter sizes in 0.1 mm increments until the minimum is found.
8. For the dataset used in this example, the optimal EQ parameter size was 6.5 mm with a mean absolute percentage difference of 4.43 % (Table 8).

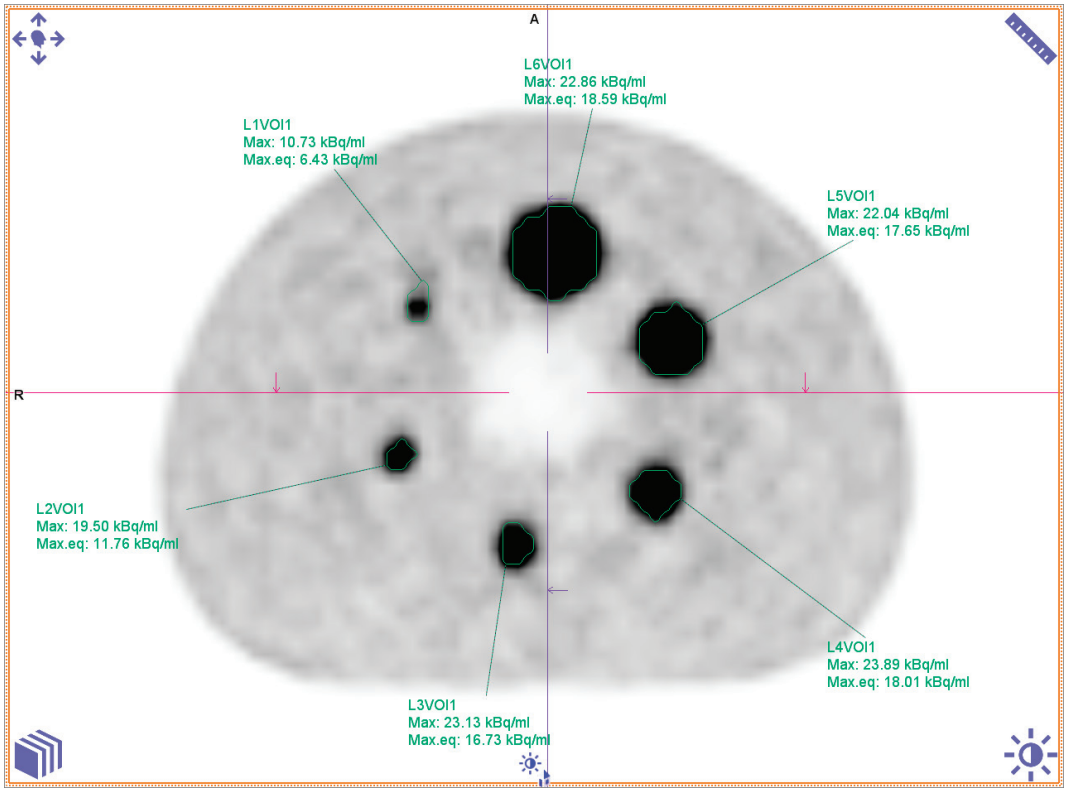

Figure 5. *Segmentation of the hot spheres in the NEMA IQ phantom with syngo.via MMOncology.*

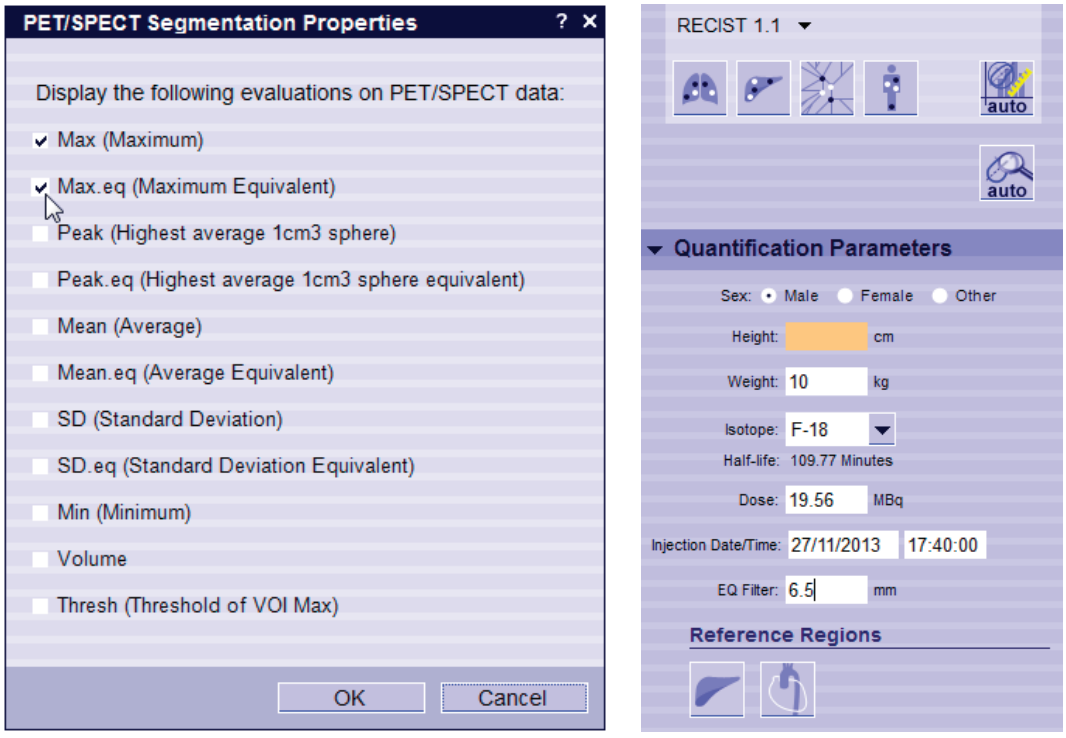

Figure 6. *Turning on display of Max.eq via the Segmentation Properties dialogue (left) and setting the EQ parameter via the Quantification Parameters blind (right).*

				EQ Parameter = 0 mm		EQ Parameter = 6.5 mm	
Sphere diameter	EANM target recovery	True AC (kBq.ml^{-1})	EANM target AC (kBq.ml^{-1})	Measured AC (kBq.ml^{-1})	% diff. vs. EANM AC	Measured AC (kBq.ml^{-1})	% diff. vs. EANM AC
10 mm	0.38	18.70	7.11	10.73	50.9 %	6.43	-9.6 %
13 mm	0.63	18.70	11.78	19.50	65.6 %	11.76	-0.2 %
17 mm	0.84	18.70	15.71	23.13	47.2 %	16.73	6.5 %
22 mm	0.89	18.70	16.64	23.89	43.6 %	18.01	8.2 %
28 mm	0.95	18.70	17.77	22.04	24.0 %	17.65	-0.7 %
37 mm	0.98	18.70	18.33	22.86	24.7 %	18.59	1.4 %
Mean absolute % difference vs. EANM target:				42.7 %		4.4 %	

Table 8. *Target and measured activity concentrations (AC) for the phantom dataset used in this example. An EQ parameter of 6.5 mm provided the best alignment (smallest mean absolute percentage diffence) with the EANM target recovery coefficients.*

Appendix C: Gaussian Smoothing Methodology

Gaussian smoothing for EQ•PET in *syngo*.via is performed using a direct convolution operation with the kernel constructed as described below.

Kernel Construction

The function for calculating each element's value in the Gaussian Kernel matrix can be defined as:

$$f(d_x, d_y, d_z,) = \frac{1}{N} \cdot e^{-\frac{1}{2}\left(\frac{d_x^2}{\sigma_x^2} + \frac{d_y^2}{\sigma_y^2} + \frac{d_z^2}{\sigma_z^2}\right)}$$

Where d_x, d_y and d_z are the distances (in units of number of voxels) of the center of the kernel voxel from the center of the kernel. N is the sum of all voxel values in the kernel to ensure the final values sum to 1. σ_x, σ_y and σ_z specify the sigma of the Gaussian kernel in each dimension (in units of number of voxels).

The size or extent, g, of the kernel (in units of number of voxels) is computed from the Gaussian *FWHM* (in units of number of voxels) in each dimension as follows:

$$\begin{bmatrix} g_x \\ g_y \\ g_z \end{bmatrix} = \textit{round up to the next odd number} \left(2 \cdot \begin{bmatrix} FWHM_x \\ FWHM_y \\ FWHM_z \end{bmatrix} + 1 \right)$$

The kernel extent in each dimension must be an odd number of voxels to ensure it is symmetric around the central voxel.

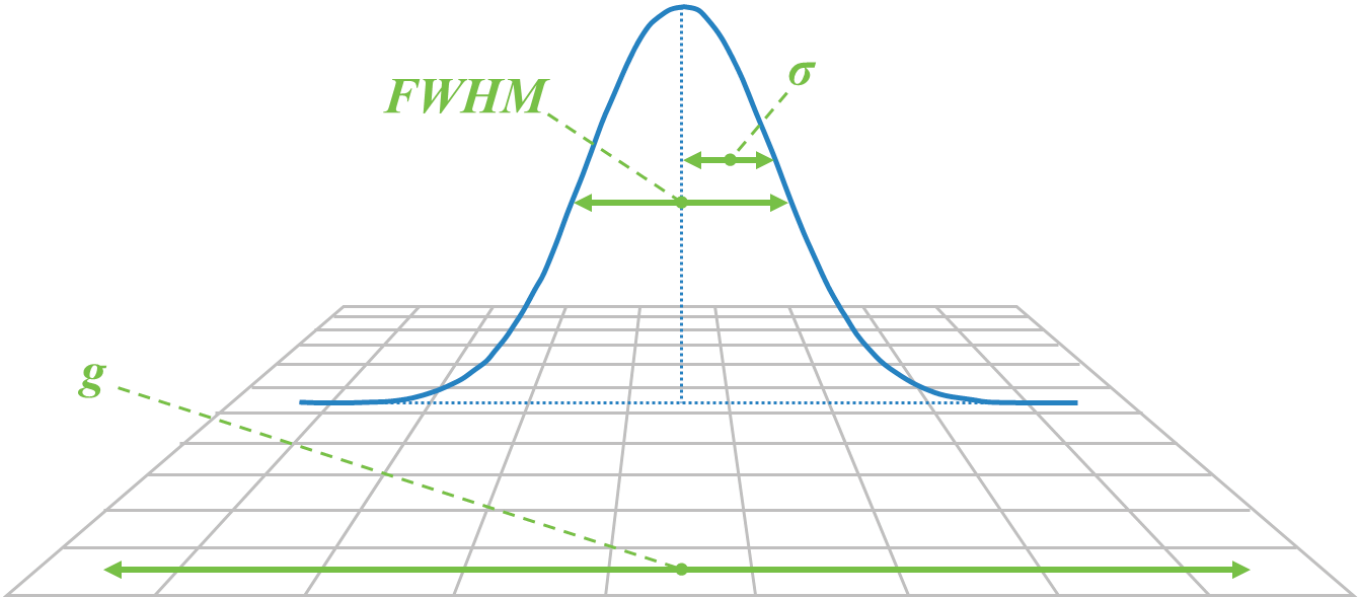

Figure 7. *Relationship between FWHM, sigma (σ) and kernel size or extent (g) for a Gaussian kernel. The intensity profile (blue) is shown for a single dimension of the kernel (grey grid). During the convolution, any image voxels outside the extent of the kernel are ignored.*

About the Author

Dr. Matthew Kelly received a B.Sc. (hons) in Applied Neuroscience from the University of Manchester in 2001, and then completed a Ph.D. in Pharmacology at the University of Cambridge in 2005. He has worked in medical imaging since 2006 at the University of Oxford and joined the Science and Technology Team of Siemens Molecular Imaging in 2007.

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