# Healthy Tissue Uptake of <sup>68</sup>Ga-Prostate Specific Membrane Antigen (PSMA), <sup>18</sup>F-DCFPyL, <sup>18</sup>F-Fluoromethylcholine (FCH) and <sup>18</sup>F-Dihydrotestosterone (FDHT)

Bernard H.E. Jansen<sup>1,2</sup>, Gem M. Kramer<sup>1</sup>, Matthijs C.F. Cysouw<sup>1</sup>, Maqsood M. Yaqub<sup>1</sup>, Bart de Keizer<sup>3</sup>, Jules Lavalaye<sup>4</sup>, Jan Booij<sup>5</sup>, Hebert A. Vargas<sup>6</sup>, Michael J. Morris<sup>6</sup>, André N. Vis<sup>2</sup>, Reindert J.A. van Moorselaar<sup>2</sup>, Otto S. Hoekstra<sup>1</sup>, Ronald Boellaard<sup>1</sup>, Daniela E. Oprea-Lager<sup>1</sup>

 <sup>1</sup>Department of Radiology & Nuclear medicine, Amsterdam University Medical Centers (location VU University Medical Center), the Netherlands
 <sup>2</sup> Department of Urology, Amsterdam University Medical Centers (location VU University Medical Center), the Netherlands
 <sup>3</sup>Department of Radiology and Nuclear Medicine, University Medical Center Utrecht, the Netherlands
 <sup>4</sup>Department of Nuclear Medicine, St-Antonius Hospital, Nieuwegein, the Netherlands
 <sup>5</sup>Department of Radiology and Nuclear Medicine, Amsterdam University Medical Centers, (location Academic Medical Center), the Netherlands.
 <sup>6</sup>Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, United States of America

> <u>First author</u> Bernard H.E. Jansen, MD, PhD candidate De Boelelaan 1117, 1081 HV Amsterdam T: 020-4446033 E: <u>bh.jansen@vumc.nl</u>

> <u>Corresponding author</u> Daniela E. Oprea-Lager, MD, PhD De Boelelaan 1117, 1081 HV Amsterdam T: 020-4444366 E: <u>d.oprea-lager@vumc.nl</u>

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#### ABSTRACT

Positron Emission Tomography (PET) is increasingly used for prostate cancer (PCa) diagnostics. Important PCa radiotracers include <sup>68</sup>Ga-Prostate-Specific Membrane Antigen HBED-CC (<sup>68</sup>Ga-PSMA), <sup>18</sup>F-DCFPyL, <sup>18</sup>F-fluoromethylcholine (<sup>18</sup>F-FCH) and <sup>18</sup>F-dihydrotestosterone (<sup>18</sup>F-FDHT). Knowledge on the variability of tracer uptake in healthy tissues is important for accurate PET interpretation, since malignancy is suspected only if the uptake of a lesion contrasts with its background. Therefore, the aim of this study was to quantify uptake variability of PCa tracers in healthy tissues and identify stable reference regions for PET interpretation. Methods: A total of n=232 PCa PET/CT scans from multiple hospitals was analyzed, including n=87<sup>68</sup>Ga-PSMA scans; n=50<sup>18</sup>F-DCFPyL scans; n=68<sup>18</sup>F-FCH scans and n=27 <sup>18</sup>F-FDHT scans. Tracer uptake was assessed in the blood pool, lung, liver, bone marrow and muscle - using several Standardized Uptake Values (SUVmax, SUVmean, SUVpeak). Variability in uptake between patients was analyzed using the Coefficient of Variation (COV%). For all tracers, SUV reference ranges (95<sup>th</sup> percentiles) were calculated, which could be applicable as image-based Quality Control for future PET acquisitions. Results: For <sup>68</sup>Ga-PSMA, the lowest uptake variability was observed in the blood pool (COV 19.9%), which was significantly more stable than all other tissues (COV 29.8-35.2%, p=0.001-0.024). For <sup>18</sup>F-DCFPyL, lowest variability was observed in the blood pool and liver (COV 14.4% and 21.7%, p=0.001-0.003). The least variable <sup>18</sup>F-FCH uptake was observed in the liver, blood pool and bone marrow (COV 16.8-24.2%, p=0.001-0.012). For <sup>18</sup>F-FDHT, low uptake variability was observed in all tissues, except the lung (COV 14.6-23.6%, p=0.001-0.040). The different SUV-types had limited effect on variability (COVs within 3 percentage points). Conclusion: In this multicenter analysis, healthy tissues with limited uptake variability were identified, which may serve as reference regions for PCa PET interpretation. These reference regions include the blood pool for <sup>68</sup>Ga-PSMA and <sup>18</sup>F-DCFPyL, and the liver for <sup>18</sup>F-FCH and <sup>18</sup>F-FDHT. Healthy tissue SUV reference ranges are presented and applicable as image-based Quality Control.

Keywords: prostate cancer; PET interpretation; healthy tissue; PSMA

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#### INTRODUCTION

Prostate cancer (PCa) is the most common cancer in men in the Western world (*1,2*). *Positron Emission Tomography* (PET) imaging is increasingly used for PCa diagnostics, as it enables early lesion detection and molecular characterization of lesions *in vivo*. Several PET radiotracers for PCa imaging have been developed, among which <sup>68</sup>Ga-Prostate-Specific Membrane Antigen HBED-CC (<sup>68</sup>Ga-PSMA), <sup>18</sup>F-DCFPyL, <sup>18</sup>F-fluoromethylcholine (<sup>18</sup>F-FCH) and <sup>18</sup>F-dihydrotestosterone (<sup>18</sup>F-FDHT).

<sup>68</sup>Ga-PSMA, <sup>18</sup>F-DCFPyL and <sup>18</sup>F-FCH are widely used diagnostic radiotracers, offering superior lesion detection compared to conventional imaging modalities (CT, MRI, bone-scan) (*3,4*). Both <sup>68</sup>Ga-PSMA and <sup>18</sup>F-DCFPyL are ligands targeting the *Prostate-Specific Membrane Antigen*, a type 2 membrane glycoprotein significantly overexpressed by malignant prostate cells (*5*). <sup>18</sup>F-FCH enables visualisation of PCa lesions for choline is a precursor of cell membrane phospholipids and its uptake is upregulated in PCa cells (*6*). <sup>18</sup>F-FDHT is a radiolabeled analogue of dihydrotestosterone, directly binding the androgen receptor (AR). The AR is crucial for PCa growth and AR targeted therapies are mainstays in PCa treatment. <sup>18</sup>F-FDHT might enable monitoring of AR directed treatment and predict treatment response (*7*).

In clinical practice, PET-images are assessed qualitatively as well as semi-quantitatively. For qualitative evaluation, tracer uptake of suspected tumors is *visually* compared to the background (i.e. surrounding tissue or a reference region). Semi-quantitative analysis is typically performed using the *Standardized Uptake Value* (SUV), which provides a (simplified) measure of tracer accumulation in a region of interest. SUV is defined as the tissue's radioactivity concentration, normalized to the injected dose per distribution volume (body weight, lean body mass or body-surface area) (*8*). For both visual and SUV-based analysis, only the lesions with tracer uptake distinct from the background are characterized as potentially malignant. High variability of healthy tissue uptake between patients

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hampers reliable interpretation of suspected lesions, as the contrast between lesions and healthy tissues would be variable.

Therefore, the aim of this study was to define the interpatient variability of <sup>68</sup>Ga-PSMA, <sup>18</sup>F-DCFPyL, <sup>18</sup>F-FCH, and <sup>18</sup>F-FDHT uptake in healthy tissues and identify stable reference regions for PET interpretation. This knowledge is especially relevant, given the recent initiatives to standardize PET interpretation by using uptake in healthy tissues as thresholds to characterize malignancy (e.g. the PET Response Criteria in Solid Tumor (PERCIST) (*9*) and the *Prostate Cancer Molecular Imaging Standardized Evaluation* (PROMISE) for PSMA PET (*10*)).

Additionally, this study will provide reference ranges for healthy tissue SUV (population SUV ranges). These may be used as image-based Quality Control (QC) for future PET acquisitions, as a SUV outside this range points to image-acquisition imperfections.

#### **METHODS**

#### Design

This is a centralized analysis of multicenter data, evaluating <sup>68</sup>Ga-PSMA, <sup>18</sup>F-DCFPyL, <sup>18</sup>F-FCH and <sup>18</sup>F-FDHT PET/CT-scans. Participating centers included the Amsterdam University Medical Centers (Academic Medical Center and VU University Medical Center, the Netherlands), Memorial Sloan Kettering Cancer Center (MSKCC, New York, USA), University Medical Center Utrecht (the Netherlands), and Sint Antonius Hospital (Nieuwegein, the Netherlands).

The study has been approved by the institutional review board of the Amsterdam Medical Centers and the need for written informed consent was waived (review number 2017.075).

#### **PET-images**

For <sup>68</sup>Ga-PMSA and <sup>18</sup>F-FCH, all centers were asked to send up to 35 of their most recent, consecutively performed clinical PET examinations. As <sup>18</sup>F-DCFPyL scans were only available in a single center, 50 consecutive scans from this center were obtained to ensure an adequate sample size. No patient inclusion criteria were deployed; PET examinations for any stage of PCa were eligible. <sup>18</sup>F-FDHT scans are not routinely performed in clinical practice yet. Therefore, scans from a previous prospective research cohort were analyzed (*11*).

Only static, whole-body images were used (mid-thighs to skull vertex). All scans were corrected for decay, scatter, and random coincidences. Photon attenuation was performed using low-dose CT (120-140 kV, 30-80mA). Imaging was performed with standard Time-of-Flight PET/CT scanners from Philips Healthcare<sup>®</sup>, the Netherlands/USA (Ingenuity; Gemini TOF); Siemens Healthineers<sup>®</sup>, Germany (Biograph 40); and General Electric<sup>®</sup>, USA (Discovery 710). All centers, except for the MSKCC, used European Association of Nuclear Medicine Research Ltd (EARL) accredited scanners, ensuring harmonized quantification. Standard, vendor-provided image-reconstructions were used, that were calibrated to meet the EARL recommendations (*12*). An overview of the applied reconstruction parameters is presented in Supplemental Table 1.

#### **Data Collection:**

All PET-images were gathered in the Amsterdam UMC and analyzed using in-house developed software (*ACCURATE-tool (13)*). Because automated (DICOM-derived) acquisition information is error-prone, clinical documentation was retrieved and used for analysis (e.g. patient's length, weight; total injected dose and calibration time; injection time; starting time of PET-scan) (*8*).

Tracer uptake was measured in the blood pool (ascending aorta); lung (apically and basally); liver; bone marrow (thoracic vertebra and lumbar vertebra); and muscle (m. erector spinae). Measurements were performed using fixed sized *volumes of interest* (VOIs), shaped according to previous recommendations (*11*), see Table 1. Blood pool activity concentrations are known to be quite low and hence might be more subject to image noise. Therefore, three different VOIs were analyzed to find the optimal measurements and avoid VOI-dependent variability in SUV.

For all VOIs, SUVmax (maximum SUV value within the VOI), SUVmean (mean SUV within the VOI) and SUVpeak (mean SUV within a 12mm diameter sphere positioned within the VOI to yield the highest value) were generated. All SUVs (SUVmax/mean/peak) were normalized to *body weight, lean body mass* and *body-surface area*. See Supplemental Text 1 for the applied equations (*8*).

#### **Data Management and Statistical Analysis**

All data were congregated per tracer and checked for inaccuracies (e.g. unrealistic patient weight, erroneous scan times). For quality control, scan acquisition efficiency rates were calculated (total image-detected activity / injected dose at start scan). Acquisitions with aberrant efficiency rates were reviewed

for inaccuracies in clinical data or technical errors. Extreme SUVs of individual patients (*z-value* >3) were identified. VOI misplacements were corrected, persisting outliers were not included for further analysis. To further ensure image-quality and comparability, we assessed the institutional *intra-VOI* Coefficients of Variation (COV%) in the liver, akin the EARL harmonization procedure (SD / mean of the pixel values within the VOI) (*14*).

For all SUVs the averages and 95<sup>th</sup> percentiles (mean ±1.96\*SD) were calculated, which provides the reference ranges for image-based QC. Normality was assessed visually using histogram analyses and Q-Q plots. Variability in SUV was analyzed using COV% and differences were analyzed using Levene's Ftest with Holms-Bonferroni corrected post-hoc analysis.

Statistical analyses were performed with IBM SPSS 22.0.

#### RESULTS

#### **Patient and Scan Results**

In total, PET images of *n*=252 PCa patients were available for evaluation. *N*=20 scans were excluded due to acquisition imperfections (e.g. PET-CT mismatch / excessive patient movement; imageartefacts; missing scan information). The final analysis included *n*=87 <sup>68</sup>Ga-PSMA scans (3 centers); *n*=50 <sup>18</sup>F-DCFPyL scan (1 center); *n*=68 <sup>18</sup>F-FCH scan (2 centers); and *n*=27 scan <sup>18</sup>F-FDHT scans (2 centers). Overall, patients were scanned at low PSA levels (<10 ng/ml), with the exception of the patients in the <sup>18</sup>F-FDHT research cohort (median PSA 28.5ng/ml). The use of Androgen Deprivation Therapy (ADT) at the time of the scan was more prevalent in the <sup>18</sup>F-FCH and <sup>18</sup>F-FDHT group (49% and 100% respectively) than in the PSMA cohorts (<sup>68</sup>Ga-PSMA 33%; <sup>18</sup>F-DCFPyL 7%). Patients' characteristics and scan data are presented in Table 2.

The average scanner efficiency rate for <sup>68</sup>Ga-PSMA was 75% (95% CI 59-91%; COV 10.7%); <sup>18</sup>F-DCFPyL 74% (95% CI 58-95%; COV 11.2%); <sup>18</sup>F-FCH 88% (95% CI 69-108%; COV 9.9%); <sup>18</sup>F-FDHT 83% (95% CI 73-93%; COV 6.2%). All intra-VOI COV% (liver) remained under the 15% threshold (*12*) (COV% range 6.1-13.3%).

#### **Healthy Tissue Tracer Uptake Variability**

<sup>68</sup>Ga-PSMA: Healthy tissue SUV and variability are presented in table 3A. Tracer uptake in the blood pool showed the lowest uptake variability between patients and was significantly more stable than the uptake in other tissues (difference in COV%, p=0.001-0.024). Only minor differences in variability were observed using different normalizations factors (average COVs were within 1.0 percentage point [pp] of each other, see Supplemental Table 2). Similarly, the differences in variability between SUVmax/mean/peak were small (COVs within 2.0pp, Supplemental Table 2). Therefore, only SUVmax and SUVmean normalized to body-weight are presented, as these SUVs are clinically most frequently used.

An illustration of the heterogeneity in <sup>68</sup>Ga-PSMA uptake in the liver is presented in Fig. 1, showing patients with tracer uptake 1.2 SD above and below the population average.

<sup>18</sup>*F*-*DCFPyL:* Tracer uptake in the blood pool showed the lowest variability and was significantly more stable than the uptake in other tissues (difference in COV%, *p*=0.001-0.003), except for the uptake in the liver (*p*=0.078), see Table 3B. Similar to <sup>68</sup>Ga-PSMA, different normalizations factors and SUV types had limited effect on variability (average COV within 2.0pp and 1.0pp respectively) (Supplemental Table 2).

<sup>18</sup>*F-FCH:* Liver uptake showed significantly less variability than the uptake in lung and muscle tissue (p=0.001-0.012), but not compared to the blood pool or bone marrow (p>0.17), see Table 3C. The COV% of different SUV normalization factors and SUV types were within 1.0pp and 2.0pp respectively (Supplemental Table 2).

<sup>18</sup>*F-FDHT:* Tracer uptake in the liver was least variable, though only significantly different to the uptake in the lung (p=0.001-0.040), see table 3D. Variability (COV%) between different SUV normalization factors and SUV type was within 3.0pp and 2.0pp respectively.

Table 4 provides a summary per tracer of the tissues with least variable tracer uptake, which might serve as reference region for interpatient analysis.

#### **Blood Pool VOIs**

The different blood pool measurements had limited influence on variability (average COV within 3.0pp, see Supplemental Table 2). We choose the 3x3 VOI for uptake variability analysis, as it slightly

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outperformed the 2x2 VOI in terms of stability, and is more practical compared to the multi-slide 2x2 VOI.

#### Differences in Variability between Institutes and PET/CT System Vendors

To assess differences in SUV variability between the different institutes and PET/CT system vendors, we calculated the institutional and scanner averages for the suggested reference regions (see Fig. 2). Upper and lower thresholds for inter-institutional recovery coefficients were computed, in analogy to the EARL procedure guidelines (total sample average as base) (*15*). All institutional SUV averages were within the given limits. No significant differences were observed in variability between the institutes or vendors (Fig. 2).

#### Influence of ADT on Tracer Uptake Variability

ADT has been shown to affect the expression of PSMA (*16-18*). Hence, we separately analyzed healthy tissue uptake for patients using ADT and those not using ADT. For <sup>68</sup>Ga-PSMA, blood pool uptake was higher for ADT users than in non-ADT users (SUVmax 1.46 versus 1.27 respectively, *p*=0.002), yet the variability was equal (COV 19.4% and 18.8%, *p*=0.84), see Fig. 3. For <sup>18</sup>F-FCH, SUVmax of the liver was 11.4 in the ADT group versus 10.4 in de non-ADT group (*p*=0.03), without differences in variability (COV 16.9% versus COV 15.9%, *p*=0.52). The <sup>18</sup>F-DCFPyL and <sup>18</sup>F-FHDT cohorts did not include a meaningful number of respectively ADT and non-ADT users to allow similar analyses (Table 2).

#### DISCUSSION

Knowledge on variability of tracer uptake in healthy tissues is crucial for clinical PET interpretation. In this multicenter analysis, *n*=232 PCa PET scans were evaluated and uptake variability of <sup>68</sup>Ga-PSMA, <sup>18</sup>F-DCFPyL, <sup>18</sup>F-FCH, and <sup>18</sup>F-FDHT was assessed in healthy tissues. For all tracers, tissues with stable tracer uptake were identified and suggested as reference regions (Table 4). As a secondary outcome, SUV reference ranges are presented for image-based QC. Any SUV outside these ranges should prompt careful evaluation of the image quality of the PET examinations. We additionally observed stable scan acquisition efficiencies (COV 6.6-11.2%), which could therefore also be used for image-based QC.

Visual assessment of PET images is hampered by interpatient variability, but also by interobserver variability, as evaluation of lesions is done at the discretion of the individual reader. To standardize PET reading, uptake values of healthy tissues are proposed as thresholds to characterize measurable lesions and determine therapeutic response (e.g. <sup>18</sup>F-FDG uptake in the liver in the PERCIST criteria (*9*); uptake in the liver, blood pool and mediastinum in the Deauville score for malignant lymphoma (*19*)). Clearly, the validity of these thresholds depended on the uptake variability of the reference region between patients.

In our study, the blood pool was identified as reliable reference region for both <sup>68</sup>Ga-PSMA and <sup>18</sup>F-DCFPyL. However, stable uptake in the liver was only observed for <sup>18</sup>F-DCFPyL. These findings are important, since both the blood pool and liver are proposed reference regions in the recent PROMISE protocol for PSMA PET interpretation (*10*). Our analysis supports the use of blood pool uptake, but causes concern regarding the use of liver uptake for <sup>68</sup>Ga-PSMA PET interpretation. Furthermore, the PROMISE protocol suggests to use the spleen as a reference region for tracers with a liver-dominant excretion (i.e. <sup>18</sup>F-PSMA-1007). We argue for a careful validation of this reference region for <sup>18</sup>F-PSMA-1007 first, given the observed variability of PSMA tracer uptake in many organs.

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To the best of our knowledge, no prior studies have been performed that explicitly analyzed healthy tissue uptake variability of <sup>68</sup>Ga-PSMA, <sup>18</sup>F-FCH, or <sup>18</sup>F-FDHT. For <sup>68</sup>Ga-PSMA, prior biodistribution studies (including some statistical measures of spread) are available and reveal higher SUVs in the blood pool and liver than were observed in the present study (*19-21*). The comparison of results in difficult, however, as the previous evaluations included only single-center data and the reported SUVs vary widely (e.g. blood pool SUVmax 1.8–4.3) (*19-21*). Furthermore, no inter-institutional scanner calibration (e.g. EARL harmonization) is reported and the applied VOI shapes are variable and vaguely described. These limitations and varying results strengthen the need for a centralized analysis of multicenter, cross-calibrated data, as was performed in this study.

It remains unclear what causes the interpatient variability in <sup>68</sup>Ga-PSMA uptake in the liver. It has been demonstrated that the liver expresses a PSMA-like protein, which might bind <sup>68</sup>Ga-PSMA (22). Alternatively, <sup>68</sup>Ga-PSMA has some hepatobiliary excretion and its uptake might therefore be subject to metabolic differences between patients (21,23).

Our results on <sup>18</sup>F-DCFPyL are in line with the report by Li et al. (*24*), demonstrating stable uptake in the liver. Furthermore, Li et al. showed that a 3 cm spherical VOI performed equally to whole-organ assessment and that lean-body mass is not superior to body weight for SUV normalization – all in agreement with our findings. In addition to Li et al., we observed high stability of uptake in the blood pool. Moreover, our results are based on PET acquisitions made at 120 minutes post injection, which currently seems the optimal time interval (*25,26*), whereas Li et al. included PET images acquired at 60 min post-injection.

Recently, PSMA tracers have attracted much attention for PCa diagnostics, as they offer superior diagnostic accuracy (*27,28*). However, <sup>18</sup>F-FCH PET/CT is still recommended by current clinical guidelines (*29*) and is used in many clinics and ongoing trials (*30,31*). Additionally, <sup>18</sup>F-FCH is used for indications

besides PCa (*32*). Our results may aid scan interpretation for any indication, although external validity might be hampered by our inherently male population. For <sup>18</sup>F-FDHT, relatively limited variability was observed. Although promising, these results should be interpreted cautiously. Only a limited number of scans was analyzed, which were all performed within a stringent research protocol. 'Real-life' clinical results might be more volatile.

To identify reliable and practical uptake measurements, different VOIs were evaluated within individual organs. For the lung, most stable results were obtained in the apex, although the results were still inferior to other tissues. The variability of basal lung measurements is likely caused by breathing artefacts and the proximity of the liver (high uptake). No differences in variability were observed in bone marrow uptake between thoracic and lumbar vertebrae, even though occult bone metastases are most frequent in the lower spine (*33*). In this study, we preferred fixed sized VOIs over whole-organ assessment, since such VOIs are clinically more practical and the assessed tissues were expected to be largely homogenous.

Our study has several limitations. Even if PET acquisitions are made in accordance to the EARL harmonization protocol, residual differences in SUV can occur (15). In our study, small dissimilarities between institutes were present (Fig. 2), yet the variability of SUV within each center was equal. By performing a multicenter evaluation, we intended to produce outcomes that may be generalized and foster standardization of PCa PET analysis, allowing meaningful exchange of results. Further, only interpatient variability was assessed. Day-to-day uptake variability *within* patients (intra-patient variability) was not evaluated. Intra-patient variability hampers longitudinal disease evaluation and assessment of treatment response, as changes in tumor uptake relative to the background would be volatile. Moreover, oncologic treatment could affect healthy tissues uptake, making intra-patient

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interpretation even more complex. To evaluate interpatient variability, robust test-retest analyses of healthy tissue uptake are desired; results for <sup>18</sup>F-DCFPyL are expected shortly.

#### CONCLUSIONS

In this multicenter analysis, healthy tissue uptake of <sup>68</sup>Ga-PSMA, <sup>18</sup>F-DCFPyL, <sup>18</sup>F-FCH and <sup>18</sup>F-FDHT was evaluated. Healthy tissues with limited uptake variability were identified, which may serve as reference regions for image interpretation. Reliable reference regions include the blood pool for <sup>68</sup>Ga-PSMA and <sup>18</sup>F-DCFPyL, and the liver for <sup>18</sup>F-FCH and <sup>18</sup>F-FDHT.

Additionally, SUV reference ranges and scan acquisition efficiency rates are provided for each tracer to be used for image-based QC.

#### DISCLOSURES

R. Boellaard reports to have a scientific collaboration with Philips Healthcare. M. Morris reports to be a consultant for Astellas, Bayer, Endocyte, Advanced Accelerator Applications, Blue Earth Diagnostics, Tokai and to have institutional research contracts with Bayer, Sanofi, Endocyte, Progenics, Corcept, and Roche. The other authors have no disclosures or potential conflicts of interest to this manuscript. No funding was received for conducting this research.

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**FIGURE 1.** Heterogeneity of <sup>68</sup>Ga-PSMA uptake in the liver.

(A) Patient with liver uptake 1.2SD above the population average (SUVmean 6.82; SUVmax 8.96). (B) Patient with liver uptake 1.2SD below average (SUVmean 2.78; SUVmax 3.62). Images with identical SUV-scaling.



**FIGURE 2.** Analysis of the uptake variability in the suggested reference regions per institute and PET/CT system vendor. Averages and SD. (A) <sup>68</sup>Ga-PSMA, blood pool (B) <sup>18</sup>F-FCH, liver (C) <sup>18</sup>F-FDHT, liver



**FIGURE 3.** Analysis of uptake variability, stratified by ADT use. Averages and SD. (A) <sup>68</sup>Ga-PSMA uptake in the blood pool: difference ADT to no ADT, P = 0.002; difference in variability, P = 0.84. Uptake in the liver: difference ADT to no ADT, P = 0.47; difference in variability, P = 0.99.

(B) <sup>18</sup>F-FCH uptake in the blood pool: difference ADT to no ADT, P = 0.29; difference in variability, P = 0.29. Uptake in the liver: difference ADT to no ADT, P = 0.03; difference in variability, P = 0.52.



# TABLE 1: VOI characteristics

VOI name	Volume specifications	Volume cm <sup>3 a</sup>
Aorta 2x2	2 voxels squared, 1 slice	(0.26 - 0.40)
Aorta 3x3	3 voxels squared, 1 slice	(0.58 - 0.88)
Aorta 5 slides 2x2	2 voxels squared, in 5 consecutive slices	(1.28 - 1.96)
Lung-apically	3 cm diameter sphere, right lung	(14.04 - 14.07)
Lung-basally	3 cm diameter sphere, right lung	(14.04 - 14.07)
Liver	3 cm diameter sphere, right upper quadrant	(14.04 - 14.07)
Thoracic vertebra	2 cm diameter sphere, bone marrow	(4.13 - 4.17)
Lumbar vertebra	2 cm diameter sphere, bone marrow	(4.13 - 4.17)
Muscle	2 cm diameter sphere, m. erector spinae	(4.13 - 4.17)

<sup>*a*</sup> Volume metrics vary due to inter-scanner differences (mostly for voxel based measures).

<b>TABLE 2:</b> Patient demographics and scan	characteristics.	Median	values and	d inter-qu	artile
ranges					

	<sup>68</sup> Ga-PSMA	<sup>18</sup> F-DCFPyL	<sup>18</sup> F-FCH	<sup>18</sup> F-FDHT
Patient characteristics				
Number of patients	87	50	68	27
Age (years)	70 (65-75)	71 (66-76)	70 (65-74)	67 (64-69)
Recent PSA (ng/ml)	4.7 (1.0-16.0)	7.2 (2.8-17.6)	9.1 (3.7-39.3)	28.5 (5.6-112.8)
Gleason score	7	7	7	8
Androgen deprivation treatment	33%	8%	48%	100%
Scan characteristics				
Originating hospitals	AMC; UMCU; St.Antonius	VUmc	VUmc; UMCU	VUmc; MSKCC
Inclusion years	2016, 2017	2017, 2018	2013-2017	2015, 2016
Administered dosage (MBq)	139.6	311.2	280.2	240.3
	(120.2-156.5)	(301.6-318.8)	(194.0-355.5)	(229.9-311.6)
Uptake time (minutes)	65	120	39	45
	(57-74)	(117-123)	(32-45)	(45-47)

### **TABLE 3:** Healthy tissue uptake of PCa PET tracers

Average SUV and 95% population reference ranges, in order of uptake variability (COV, based on SUVmax). See Supplemental Table 2 for complete results.

С

#### Α

<sup>68</sup> Ga-PSMA	SUVmax	SUVmean	COV
Blood pool	1.33	1.08	
	(0.81-1.85)	(0.64-1.52)	19.9%
Lung apically	1.05	0.56	
	(0.44-1.66)	(0.2-0.91)	29.8%*
Muscle	0.94	0.50	
	(0.37-1.51)	(0.14-0.86)	30.8%*
Liver	6.41	4.78	
	(2.41 - 10.4)	(1.61 - 7.96)	31.8%*
Th. Vertebra	1.25	0.69	
	(0.44-2.05)	(0.25-1.13)	33.0%*
Lum. Vertebra	1.24	0.67	
	(0.39-2.09)	(0.16-1.17)	35.0%*
Lung basally	1.36	0.73	
	(0.42-2.3)	(0.27-1.19)	35.2%*

## В

<sup>18</sup> F-DCFPyL	SUVmax	SUVmean	COV
Blood pool	1.12	1.01	
	(0.81-1.44)	(0.74-1.27)	14.4%
Liver	6.84	5.92	
	(3.93-9.75)	(3.31-8.53)	21.7%
Th. Vertebra	1.06	0.75	
	(0.49-1.62)	(0.33-1.16)	27.2%*
Lung apically	0.64	0.44	
	(0.28-1)	(0.19-0.68)	28.5%*
Lung basally	0.78	0.50	
	(0.31-1.25)	(0.25-0.76)	31.0%*
Lum. Vertebra	1.07	0.77	
	(0.39-1.75)	(0.28-1.26)	32.3%*
Muscle	0.79	0.55	
	(0.26-1.33)	(0.14-0.97)	34.5%*

\* Significantly different from the least variable tissue

<sup>18</sup> F-FCH	SUVmax	SUVmean	COV
Liver	10.84	9.17	
	(7.27-14.42)	(6.11-12.23)	16.8%
Th. Vertebra	3.68	2.78	
	(2.22-5.13)	(1.64-3.93)	20.2%
Blood pool	0.75	0.63	
	(0.42-1.08)	(0.34-0.91)	22.5%
Lum. Vertebra	3.13	2.33	
	(1.65-4.62)	(1.13-3.53)	24.2%
Lung apically	1.03	0.64	
	(0.46-1.6)	(0.23-1.05)	28.2%*
Muscle	1.72	1.25	
	(0.66-2.78)	(0.33-2.16)	31.4%*
Lung basally	1.48	0.95	
	(0.56-2.4)	(0.4-1.5)	31.6%*

# D

<sup>18</sup> F-FDHT	SUVmax	SUVmean	COV
Liver	5.12	4.10	
	(3.65-7.08)	(2.83-6.06)	14.6%
Blood pool	5.24	4.71	
	(3.06-7.2)	(2.45-6.67)	21.2%
Th. Vertebra	1.95	1.36	
	(1.12-3.91)	(0.86-3.32)	21.6%
Muscle	1.14	0.76	
	(0.62-3.1)	(0.47-2.72)	23.1%
Lum. Vertebra	2.18	1.60	
	(1.17-4.14)	(0.89-3.56)	23.6%
Lung basally	1.61	1.00	
	(0.71-3.57)	(0.51-2.96)	28.6%*
Lung apically	1.36	0.90	
	(0.31-3.32)	(0.26-2.86)	39.3%*

	Reference region	VOI	Alternative reference
<sup>68</sup> Ga-PSMA	Blood pool	3x3 voxel, 1 slide	
<sup>18</sup> F-DCFPyL	Blood pool	3x3 voxel, 1 slide	Liver
<sup>18</sup> F-FCH	Liver	3 cm sphere	Blood pool; bone marrow
<sup>18</sup> F-FDHT	Liver	3 cm sphere	Blood pool; bone marrow; muscle

# **TABLE 4.** Summary table – Suggested healthy tissues for interpatient analysis

### SUPPLEMENTAL TEXT 1: Applied equations

Standarized Uptake Values were calculated as follows\*:

$$SUV = \frac{ACvoi(kBq/ml)}{total tracer activitiy (MBq) / Body Weight (kg)} a^{a}$$

<sup>*a*</sup> AC, activity concentration; VOI, Volume-Of-Interest

<sup>b</sup> Body Weight (*BW*) can be replaced by Lean Body Mass (LBM) or Body-Surface Area (BSA), for which the following formulas were used:

\* Boellaard R, Oyen WJ, Hoekstra CJ, et al. The Netherlands protocol for standardisation and quantification of FDG whole body PET studies in multi-centre trials. *Eur J Nucl Med Mol Imaging.* 2008;35:2320-2333.

SUPPLEMENTAL TABLE 1: Overview of the applied reconstruction parameters.

Center	PET/CT system	Tracer	Matrix Size	Reconstruction Algorithm	Time-of- Flight	Point-Spread- Functions	Filter	Voxel size (mm)	EARL calibrated
VUmc	Philips, Ingenuity / Gemini TF	<sup>18</sup> F-FCH / <sup>18</sup> F-DCFPyL	144x144	BLOB-OS-TF (3 iterations, 33 subsets)	yes	no	none	4x4x4	yes
UMCU	Siemens, Biograph40	<sup>18</sup> F-FCH / <sup>68</sup> Ga-PSMA	200x200	PSF-TOF (4 iterations, 21 subsets)	yes	yes	Gaussian 7.50 mm	4.07x4.07 x3.00	yes
MSKCC	General Electric, Discovery 710	<sup>18</sup> F-FDHT	128x128	VPFXS (2 iterations, 24 subsets)	yes	yes	n/a	5.47x5.47 x3.27	no
AMC	Philips, Gemini TF	<sup>18</sup> F-FCH / <sup>68</sup> Ga-PSMA	144x144	BLOB-OS-TF (3 iterations, 33 subsets)	yes	no	none	4x4x4	yes
St-Anton	Philips, Gemini TF	<sup>68</sup> Ga-PSMA	144x144	BLOB-OS-TF (3 iterations, 33 subsets)	yes	no	none	4x4x4	yes

n/a = not available

# SUPPLEMENTAL TABLE 2: Healthy Tissue Uptake of PCa PET Tracers (complete results)

[68Ga]PSMA	4								
	SUVmax (BW)	SUVmax (LBM)	SUVmax (BSA)	SUVpeak (BW)	SUVpeak (LBM)	SUVpeak (BSA)	SUVmean (BW)	SUVmean (LBM)	SUVmean (BSA)
AORTA (5 slides	2x2)								
mean	1.38	1.04	0.03	1.23	0.92	0.03	1.09	0.82	0.03
SD	0.28	0.20	0.01	0.23	0.17	0.01	0.24	0.18	0.01
COV%	20.4	19.7	19.9	19.0	18.6	19.0	22.4	22.5	22.9
95% range	(0.83-1.94)	(0.64-1.44)	(0.02-0.05)	(0.77-1.68)	(0.58-1.26)	(0.02-0.04)	(0.61-1.57)	(0.46-1.18)	(0.01-0.04)
AORTA (2x2)									
mean	1.24	0.93	0.03	1.15	0.87	0.03	1.08	0.81	0.03
SD	0.29	0.22	0.01	0.24	0.18	0.01	0.26	0.20	0.01
COV%	23.4	24.0	24.4	20.6	21.1	21.6	24.3	25.0	25.5
95% range	(0.67-1.8)	(0.49-1.37)	(0.02-0.04)	(0.69-1.62)	(0.51-1.23)	(0.02-0.04)	(0.57-1.59)	(0.41-1.21)	(0.01-0.04)
AORTA (3x3)									
mean	1.33	1.00	0.03	1.20	0.90	0.03	1.08	0.81	0.03
SD	0.27	0.21	0.01	0.22	0.17	0.01	0.23	0.18	0.01
COV%	19.9	20.7	21.1	18.7	19.2	19.7	20.9	22.0	22.5
95% range	(0.81-1.85)	(0.59-1.41)	(0.02-0.04)	(0.76-1.64)	(0.56-1.24)	(0.02-0.04)	(0.64-1.52)	(0.46-1.16)	(0.01-0.04)
LIVER									
mean	6.41	4.80	0.15	5.66	4.24	0.13	4.78	3.58	0.11
SD	2.04	1.46	0.05	1.89	1.36	0.04	1.62	1.18	0.04
COV%	31.8	30.4	30.1	33.4	32.0	31.8	33.9	32.8	32.7
95% range	(2.41-10.4)	(1.94-7.66)	(0.06-0.24)	(1.96-9.37)	(1.58-6.9)	(0.05-0.22)	(1.61-7.96)	(1.28-5.89)	(0.04-0.19)
LUNG-APICALLY									
mean	1.05	0.79	0.02	0.84	0.63	0.02	0.56	0.42	0.01
SD	0.31	0.22	0.01	0.26	0.19	0.01	0.18	0.13	0.00
COV%	29.8	28.6	28.9	30.8	30.3	30.6	32.7	32.0	32.4
95% range	(0.44-1.66)	(0.34-1.23)	(0.01-0.04)	(0.33-1.35)	(0.26-1.01)	(0.01-0.03)	(0.2-0.91)	(0.16-0.68)	(0-0.02)
LUNG-BASALLY									
mean	1.36	1.02	0.03	1.20	0.90	0.03	0.73	0.55	0.02
SD	0.48	0.35	0.01	0.45	0.33	0.01	0.23	0.17	0.01
COV%	35.2	34.0	33.1	37.1	36.1	35.4	32.1	31.5	31.0
95% range	(0.42-2.3)	(0.34-1.7)	(0.01-0.05)	(0.33-2.08)	(0.26-1.54)	(0.01-0.05)	(0.27-1.19)	(0.21-0.88)	(0.01-0.03)

LUMBAR VERTEBR	RA								
mean	1.24	0.93	0.03	0.99	0.74	0.02	0.67	0.50	0.02
SD	0.43	0.32	0.01	0.33	0.24	0.01	0.26	0.19	0.01
COV%	35.0	33.9	33.3	33.4	32.4	32.0	38.5	38.0	37.7
95% range	(0.39-2.09)	(0.31-1.55)	(0.01-0.05)	(0.34-1.63)	(0.27-1.21)	(0.01-0.04)	(0.16-1.17)	(0.13-0.87)	(0-0.03)
THORACIC VERTEE	BRA								
mean	1.25	0.93	0.03	1.02	0.76	0.02	0.69	0.52	0.02
SD	0.41	0.29	0.01	0.30	0.22	0.01	0.23	0.17	0.01
COV%	33.0	31.2	30.7	29.4	28.3	28.2	32.5	31.8	31.8
95% range	(0.44-2.05)	(0.36-1.5)	(0.01-0.05)	(0.43-1.6)	(0.34-1.19)	(0.01-0.04)	(0.25-1.13)	(0.2-0.85)	(0.01-0.03)
MUSCLE									
mean	0.94	0.71	0.02	0.76	0.57	0.02	0.50	0.38	0.01
SD	0.29	0.21	0.01	0.25	0.19	0.01	0.18	0.14	0.00
COV%	30.8	30.1	30.3	33.6	33.2	33.3	37.0	37.3	37.6
95% range	(0.37-1.51)	(0.29-1.13)	(0.01-0.04)	(0.26-1.26)	(0.2-0.94)	(0.01-0.03)	(0.14-0.86)	(0.1-0.65)	(0-0.02)

Average COV	%		
	BW	LBM	BSA
SUVmax	30.1	29.2	29.1
SUVpeak	29.9	29.2	29.2
SUVmean	32.6	32.3	32.4
total	30.8	30.2	30.3

BW, body weight; LBM, lean-body mass; BSA, body-surface area

# [18F]DCFPyL

	Vmax (BW)	/max (LBM)	Vmax (BSA)	/peak (BW)	/peak (LBM)	/peak (BSA)	/mean (BW)	mean (LBM)	'mean (BSA)
	SU	suv	su	sur	SUV	suv	SUN	SUV	SUV
AORTA (5 slides 2	2x2)								
mean	1.16	0.88	0.03	1.09	0.83	0.03	1.01	0.78	0.02
SD	0.17	0.12	0.00	0.15	0.11	0.00	0.14	0.10	0.00
COV%	14.82	13.63	13.69	14.03	12.71	12.78	14.18	13.15	13.21
95% range	(0.82-1.49)	(0.65-1.12)	(0.02-0.04)	(0.79-1.39)	(0.62-1.04)	(0.02-0.03)	(0.73-1.3)	(0.58-0.98)	(0.02-0.03)
AORTA (2x2)									
mean	1.07	0.82	0.03	1.04	0.79	0.03	1.01	0.77	0.02
SD	0.17	0.12	0.00	0.15	0.10	0.00	0.15	0.10	0.00
COV%	15.78	14.12	13.92	14.60	12.81	12.65	14.62	13.43	13.27
95% range	(0.74-1.4)	(0.59-1.04)	(0.02-0.03)	(0.74-1.34)	(0.59-0.99)	(0.02-0.03)	(0.72-1.3)	(0.57-0.97)	(0.02-0.03)
AORTA (3x3)									
mean	1.12	0.86	0.03	1.06	0.81	0.03	1.01	0.77	0.02
SD	0.16	0.11	0.00	0.15	0.10	0.00	0.14	0.10	0.00
COV%	14.38	12.44	12.15	13.76	11.82	11.71	13.51	12.39	12.25
95% range	(0.81-1.44)	(0.65-1.07)	(0.02-0.03)	(0.78-1.35)	(0.62-1)	(0.02-0.03)	(0.74-1.27)	(0.58-0.96)	(0.02-0.03)
LIVER									
mean	6.84	5.23	0.17	6.48	4.96	0.16	5.92	4.53	0.14
SD	1.48	1.12	0.03	1.43	1.09	0.03	1.33	1.02	0.03
COV%	21.7	21.3	21.0	22.1	22.0	21.8	22.5	22.5	22.2
95% range	(3.93-9.75)	(3.05-7.42)	(0.1-0.23)	(3.67-9.29)	(2.82-7.1)	(0.09-0.22)	(3.31-8.53)	(2.54-6.53)	(0.08-0.21)
LUNG-APICALLY									
mean	0.64	0.48	0.02	0.58	0.44	0.01	0.44	0.33	0.01
SD	0.18	0.12	0.00	0.17	0.11	0.00	0.13	0.08	0.00
COV%	28.5	24.6	23.9	29.4	25.6	24.9	28.5	25.1	24.6
95% range	(0.28-1)	(0.25-0.72)	(0.01-0.02)	(0.25-0.91)	(0.22-0.66)	(0.01-0.02)	(0.19-0.68)	(0.17-0.5)	(0.01-0.02)
LUNG-BASALLY									
mean	0.78	0.59	0.02	0.73	0.56	0.02	0.50	0.38	0.01
SD	0.24	0.17	0.01	0.24	0.18	0.01	0.13	0.09	0.00
COV%	31.0	29.4	29.4	33.0	31.4	31.4	26.0	23.7	23.5
95% range	(0.31-1.25)	(0.25-0.93)	(0.01-0.03)	(0.26-1.21)	(0.21-0.9)	(0.01-0.03)	(0.25-0.76)	(0.21-0.56)	(0.01-0.02)

LUMBAR VERTEB	RA								
mean	1.07	0.81	0.03	0.96	0.73	0.02	0.77	0.58	0.02
SD	0.35	0.24	0.01	0.30	0.21	0.01	0.25	0.18	0.01
COV%	32.3	29.9	29.3	31.0	28.9	28.4	32.6	30.9	30.4
95% range	(0.39-1.75)	(0.34-1.29)	(0.01-0.04)	(0.38-1.54)	(0.32-1.14)	(0.01-0.04)	(0.28-1.26)	(0.23-0.94)	(0.01-0.03)
THORACIC VERTE	BRA								
mean	1.06	0.81	0.03	0.95	0.73	0.02	0.75	0.57	0.02
SD	0.29	0.19	0.01	0.23	0.16	0.01	0.21	0.15	0.00
COV%	27.2	24.0	23.1	24.7	22.4	21.8	28.4	26.5	26.0
95% range	(0.49-1.62)	(0.43-1.19)	(0.01-0.04)	(0.49-1.41)	(0.41-1.04)	(0.01-0.03)	(0.33-1.16)	(0.27-0.87)	(0.01-0.03)
MUSCLE									
mean	0.79	0.61	0.02	0.71	0.55	0.02	0.55	0.42	0.01
SD	0.27	0.21	0.01	0.26	0.20	0.01	0.21	0.16	0.01
COV%	34.5	34.2	34.4	35.9	35.8	35.9	37.8	38.1	38.4
95% range	(0.26-1.33)	(0.2-1.01)	(0.01-0.03)	(0.21-1.21)	(0.16-0.93)	(0.01-0.03)	(0.14-0.97)	(0.11-0.74)	(0-0.02)

Average COV%										
	BW	LBM	BSA							
SUVmax		27.1	25.1	24.8						
SUVpeak		27.1	25.4	25.1						
SUVmean		27.1	25.6	25.3						
total		27.1	25.4	25.1						

BW, body weight; LBM, lean-body mass; BSA, body-surface area

[18F]FCH

	ŝ	(M	SA)	() N	(W)	SA)	(M)	BM)	SA)
	ix (B	X (LB	x (B:	ak (B	IK (LE	ak (B	an (E	an (LI	an (B
	Vma	Vma	Vma	Vpe	/pea	Vpea	/me	/mea	/me
	SU	sur	SU	SU	suv	sur	suv	suv	SUN
AORTA (5 slides	2x2)								
mean	0.78	0.59	0.02	0.73	0.55	0.02	0.63	0.48	0.02
SD	0.15	0.11	0.00	0.14	0.11	0.00	0.14	0.10	0.00
COV%	19.6	19.4	20.0	19.7	19.1	19.7	22.7	21.7	22.1
95% range	(0.48-1.07)	(0.37-0.81)	(0.01-0.03)	(0.45-1.01)	(0.34-0.76)	(0.01-0.02)	(0.35-0.91)	(0.27-0.68)	(0.01-0.02)
AORTA (2x2)									
mean	0.69	0.53	0.02	0.68	0.51	0.02	0.62	0.47	0.01
SD	0.16	0.12	0.00	0.14	0.10	0.00	0.14	0.10	0.00
COV%	22.6	22.0	22.5	20.9	20.0	20.5	23.2	21.9	22.4
95% range	(0.39-1)	(0.3-0.75)	(0.01-0.02)	(0.4-0.96)	(0.31-0.71)	(0.01-0.02)	(0.34-0.9)	(0.27-0.67)	(0.01-0.02)
AORTA (3x3)									
mean	0.75	0.57	0.02	0.71	0.54	0.02	0.63	0.47	0.01
SD	0.17	0.13	0.00	0.15	0.11	0.00	0.14	0.10	0.00
COV%	22.5	22.0	22.4	20.7	19.9	20.2	23.1	22.1	22.4
95% range	(0.42-1.08)	(0.32-0.82)	(0.01-0.03)	(0.42-1)	(0.33-0.75)	(0.01-0.02)	(0.34-0.91)	(0.27-0.68)	(0.01-0.02)
LIVER									
mean	10.84	8.19	0.26	10.21	7.71	0.25	9.17	6.93	0.22
SD	1.82	1.39	0.05	1.72	1.36	0.04	1.56	1.25	0.04
COV%	16.8	17.0	17.6	16.8	17.6	18.3	17.0	18.0	18.7
95% range	(7.27-14.42)	(5.45-10.92)	(0.17-0.35)	(6.84-13.58)	(5.05-10.38)	(0.16-0.33)	(6.11-12.23)	(4.48-9.38)	(0.14-0.3)
LUNG-APICALLY									
mean	1.03	0.77	0.02	0.95	0.71	0.02	0.64	0.48	0.02
SD	0.29	0.20	0.01	0.26	0.18	0.01	0.21	0.15	0.00
COV%	28.2	26.2	26.2	27.4	25.6	25.6	32.8	30.5	30.4
95% range	(0.46-1.6)	(0.38-1.17)	(0.01-0.04)	(0.44-1.46)	(0.36-1.07)	(0.01-0.03)	(0.23-1.05)	(0.19-0.76)	(0.01-0.02)
LUNG-BASALLY									
mean	1.48	1.12	0.04	1.43	1.08	0.03	0.95	0.72	0.02
SD	0.47	0.36	0.01	0.47	0.36	0.01	0.28	0.20	0.01
COV%	31.6	32.0	32.0	33.0	33.8	33.9	29.3	28.6	28.6
95% range	(0.56-2.4)	(0.42-1.82)	(0.01-0.06)	(0.51-2.35)	(0.36-1.79)	(0.01-0.06)	(0.4-1.5)	(0.31-1.12)	(0.01-0.04)

LUMBAR VERTEB	RA								
mean	3.13	2.36	0.07	2.69	2.03	0.06	2.33	1.76	0.06
SD	0.76	0.54	0.02	0.66	0.48	0.02	0.61	0.45	0.01
COV%	24.2	22.9	22.7	24.6	23.7	23.6	26.4	25.8	25.7
95% range	(1.65-4.62)	(1.3-3.42)	(0.04-0.11)	(1.4-3.99)	(1.09-2.97)	(0.03-0.09)	(1.13-3.53)	(0.87-2.65)	(0.03-0.08)
THORACIC VERTER	BRA								
mean	1.72	1.30	0.04	1.50	1.13	0.04	1.25	0.94	0.03
SD	0.54	0.40	0.01	0.51	0.38	0.01	0.47	0.35	0.01
COV%	31.4	30.8	30.7	34.3	33.9	33.8	37.3	37.1	37.1
95% range	(0.66-2.78)	(0.51-2.08)	(0.02-0.07)	(0.49-2.51)	(0.38-1.88)	(0.01-0.06)	(0.33-2.16)	(0.26-1.63)	(0.01-0.05)
MUSCLE									
mean	3.68	2.78	0.09	3.17	2.40	0.08	2.78	2.11	0.07
SD	0.74	0.55	0.02	0.66	0.48	0.02	0.58	0.42	0.01
COV%	20.2	19.6	19.5	21.0	20.1	20.0	20.9	20.1	20.0
95% range	(2.22-5.13)	(1.71-3.85)	(0.05-0.12)	(1.87-4.48)	(1.45-3.35)	(0.05-0.11)	(1.64-3.93)	(1.28-2.94)	(0.04-0.09)

Average COV%									
	BW	LBM	BSA						
SUVmax	25.0	24.4	24.5						
SUVpeak	25.4	25.0	25.1						
SUVmean	26.7	26.0	26.1						
total	25.7	25.1	25.2						

BW, body weight; LBM, lean-body mass; BSA, body-surface area

[18F]FDHT

	ŝ	Σ	(A)	Ñ	Σ	SA)	(M)	3M)	SA)
	x (B)	(LB	(BS	k (B	(LB	k (B;	in (B	u (FE	n (B
	(ma)	max	may	pea	oeak	peal	mea	neai	nea
	SUV	SUV	SUV	SUV	NUX I	suvi	NNI	NU	UVr
					0)	•,	0,	S	0
AORTA (5 slides 2	x2)								
mean	5.20	3.88	0.12	4.84	3.61	0.12	4.73	3.53	0.11
SD	1.06	0.73	0.02	0.95	0.67	0.02	1.02	0.72	0.02
COV%	20.4	18.8	19.4	19.5	18.5	19.2	21.6	20.3	21.0
95% range	(3.12-7.16)	(2.45-5.84)	(0.08-2.08)	(2.98-6.8)	(2.3-5.57)	(0.07-2.08)	(2.73-6.69)	(2.12-5.49)	(0.07-2.07)
AORTA (2x2)									
mean	5.10	3.80	0.12	4.87	3.62	0.12	4.86	3.62	0.12
SD	1.13	0.78	0.03	1.04	0.72	0.02	1.07	0.75	0.02
COV%	22.2	20.5	20.9	21.3	19.9	20.4	22.1	20.8	21.3
95% range	(2.88-7.32)	(2.27-5.32)	(0.07-0.17)	(2.83-6.91)	(2.21-5.04)	(0.07-0.16)	(2.75-6.96)	(2.14-5.09)	(0.07-0.16)
AORTA (3x3)									
mean	5.24	3.90	0.12	4.88	3.63	0.12	4.71	3.50	0.11
SD	1.11	0.76	0.02	1.05	0.73	0.02	1.15	0.82	0.03
COV%	21.2	19.4	19.9	21.6	20.2	20.6	24.5	23.3	23.7
95% range	(3.06-7.2)	(2.42-5.86)	(0.08-2.08)	(2.81-6.84)	(2.2-5.59)	(0.07-2.08)	(2.45-6.67)	(1.9-5.46)	(0.06-2.07)
LIVER									
mean	5.12	3.83	0.12	4.59	3.44	0.11	4.10	3.08	0.10
SD	0.75	0.62	0.02	0.64	0.56	0.02	0.65	0.58	0.02
COV%	14.6	16.1	16.2	14.0	16.3	16.7	15.9	19.0	19.6
95% range	(3.65-7.08)	(2.62-5.79)	(0.08-2.08)	(3.33-6.55)	(2.34-5.4)	(0.07-2.07)	(2.83-6.06)	(1.93-5.04)	(0.06-2.06)
LUNG-APICALLY									
mean	1.36	0.99	0.03	1.19	0.87	0.03	0.90	0.66	0.02
SD	0.53	0.32	0.01	0.44	0.27	0.01	0.33	0.20	0.01
COV%	39.3	32.3	31.4	37.4	31.0	30.3	36.5	30.5	29.9
95% range	(0.31-3.32)	(0.36-2.95)	(0.01-1.99)	(0.32-3.15)	(0.34-2.83)	(0.01-1.99)	(0.26-2.86)	(0.26-2.62)	(0.01-1.98)
LUNG-BASALLY									
mean	1.61	1.19	0.04	1.48	1.10	0.04	1.00	0.74	0.02
SD	0.46	0.29	0.01	0.44	0.28	0.01	0.25	0.16	0.01
COV%	28.6	24.2	24.0	29.4	25.8	25.6	25.3	21.1	21.1
95% range	(0.71-3.57)	(0.63-3.15)	(0.02-2)	(0.63-3.44)	(0.54-3.06)	(0.02-2)	(0.51-2.96)	(0.44-2.7)	(0.01-1.98)

LUMBAR VERTEBR	A								
mean	2.18	1.60	0.05	1.93	1.42	0.05	1.60	1.18	0.04
SD	0.52	0.30	0.01	0.44	0.28	0.01	0.36	0.23	0.01
COV%	23.6	18.6	18.0	22.7	19.5	19.3	22.6	19.4	19.3
95% range	(1.17-4.14)	(1.01-3.56)	(0.03-2.01)	(1.07-3.89)	(0.88-3.38)	(0.03-2.01)	(0.89-3.56)	(0.73-3.14)	(0.02-2)
THORACIC VERTEB	RA								
mean	1.95	1.43	0.05	1.72	1.27	0.04	1.36	1.00	0.03
SD	0.42	0.28	0.01	0.33	0.23	0.01	0.25	0.19	0.01
COV%	21.6	19.4	19.2	19.4	18.3	18.4	18.8	18.5	18.8
95% range	(1.12-3.91)	(0.89-3.39)	(0.03-2.01)	(1.06-3.68)	(0.81-3.23)	(0.03-2)	(0.86-3.32)	(0.64-2.96)	(0.02-1.99)
MUSCLE									
mean	1.14	0.84	0.03	0.96	0.71	0.02	0.76	0.57	0.02
SD	0.26	0.17	0.01	0.18	0.12	0.00	0.15	0.11	0.00
COV%	23.1	20.4	19.9	18.7	17.2	17.4	19.9	19.2	19.4
95% range	(0.62-3.1)	(0.5-2.8)	(0.02-1.99)	(0.61-2.92)	(0.47-2.67)	(0.01-1.98)	(0.47-2.72)	(0.35-2.53)	(0.01-1.98)

Average COV%										
	BW	LBM	BSA							
SUVmax	24.6	21.5	21.2							
SUVpeak	23.3	21.2	21.2							
SUVmean	23.3	21.6	21.7							
total	23.7	21.4	21.4							

BW, body weight; LBM, lean-body mass; BSA, body-surface area