Data Supplement I

METHODS

Scanning protocol effective CT radiation dose:

The effective dose of CT (including localizer, attenuation correction and CT angiography) was estimated from the product of the dose length product and an organ weighting factor for the chest (0.014 mSv x mGy^{-1} x cm^{-1}).

Definition of ROIs

CT and PET images were inspected to identify any subject motion between the two scans. In the event of misalignment, the CT angiography images were manually re-aligned to the PET images using anatomical landmarks such as the vertebrae and sternum. CT images were first rebinned to a matrix size of 128 x 128 x 47 to match the reconstructed PET images. Based on image visual inspection, summed PET images at different time intervals were used to optimize image contrast between the ROIs and surrounding tissue:

- 5 to 25 min (frames 10-13) post injection for the aortic wall;
- 30 to 60 sec (frames 2-4) post injection for the lumen of the aorta;
- 45 to 90 sec (frames 3-5) post injection for the lung parenchyma;
- 30 to 50 min (frames 15-17) post injection for the bone marrow.

For all subjects five tissue ROIs were defined in: bone marrow, lung parenchyma, wall of the ascending aorta, aortic arch, and descending aorta. The lung parenchyma and vertebral body were defined on axial sections. In the thoracic aorta 3 main central axes equidistant from the arterial wall were defined in the ascending, arch and descending aorta in sagittal view (Supplemental Figure 1 Panels A-B). Images were then re-sliced into 1 mm thick short axis images perpendicular to the main central axes. The inner and outer aortic walls were manually defined on the overlaid PET/CT images and the contour was radially divided into four quadrants. In symptomatic patients the quadrants were visually adjusted to include in full the high uptake region (Supplemental Figure 1 panel H). The aortic section presenting the highest uptake was included in the subsequent analysis.

In asymptomatic patients (Supplemental Figure 1 panel E) at least 3 ROIs from each aortic region were included in further analysis. The 4 quadrants of each SA slice were grouped and the slices corresponding to the same section of the aortic arch were averaged.

ROIs were grouped in VOIs. In asymptomatic patients 3 VOIs corresponding to the descending, horizontal (arch) and ascending aortic sections were considered.

Tissue time activity curves (TACs) were generated by applying the selected ROIs to the dynamic 3DRP PET images. In addition ROIs for extracting image derived whole blood TACs were defined on 10 consecutive planes at the center of the aortic lumen.

Consistent with previous methodology for the definition of image-derived input functions from iteratively reconstructed images *(1)*, whole blood TACs (18 data points corresponding to each frame of the scanning protocol) were generated by sampling the dynamic OSEM images. Subsequently, a second-by-second whole blood curve was created by cubic spline interpolation. In order to improve the quantification of the image-derived blood curve that is affected by partial volume effects, this curve was multiplied by a factor obtained from the cross-calibration with the first four discrete blood samples. Further processing of the image-derived input function was carried out similarly to the externally sampled input function (see next section).

Blood Sampling Protocol

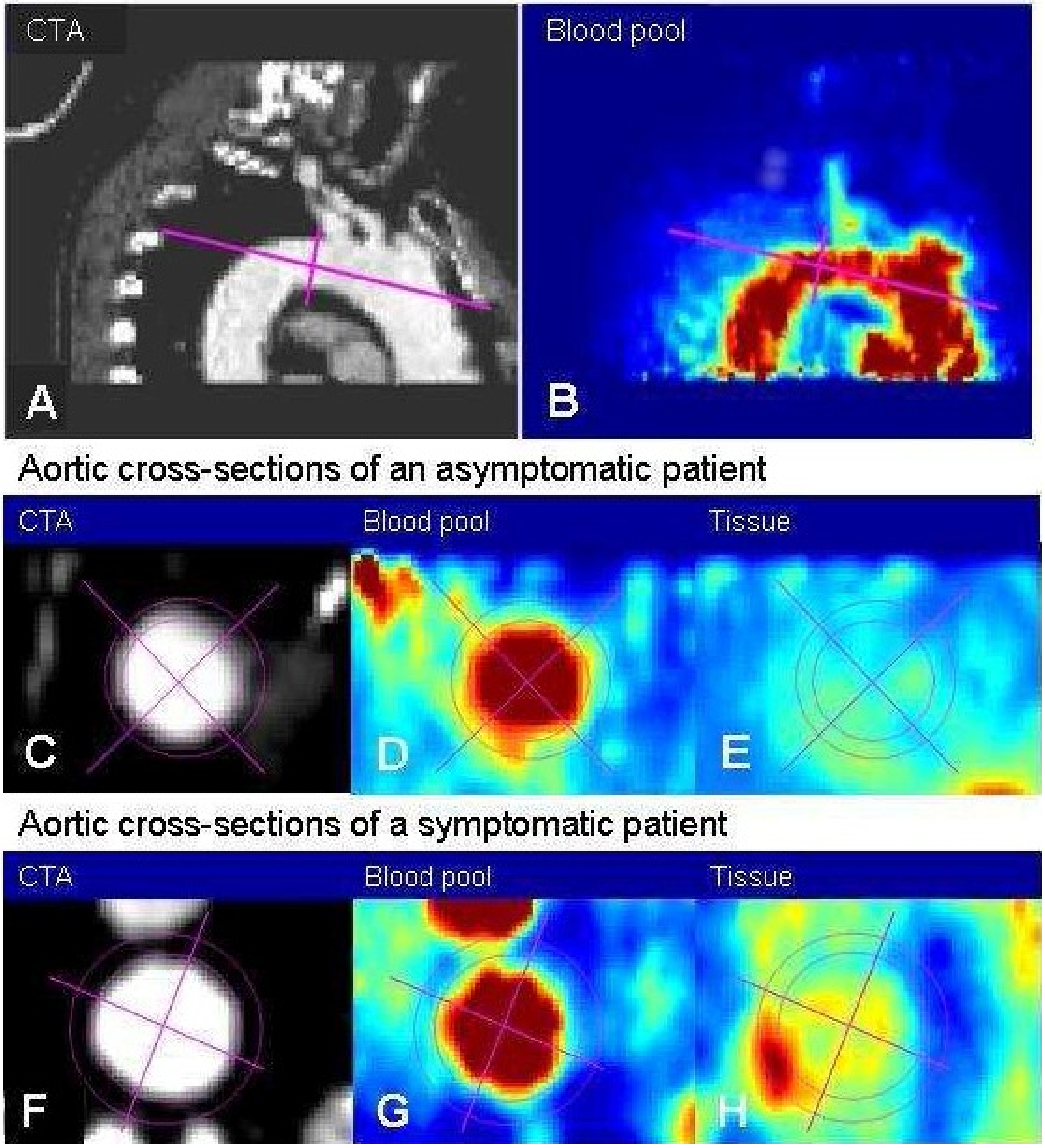
Continuous arterialized venous blood sampling was withdrawn using a peristaltic pump; the whole-blood radioactivity concentration was monitored using a BGO detection system *(2)*. Eight discrete arterialized venous blood samples were taken at 5, 10, 15, 20, 30, 40, 50, and 60 min into heparinized syringes. In addition, five plasma samples per scan (at 5, 10, 20, 40, and 60 min) were analyzed for radiolabeled metabolites using a semi-automated system with online solid-phase extraction followed by reverse-phase chromatography with online radioactivity and ultraviolet detectors and integration.

Data Supplement II

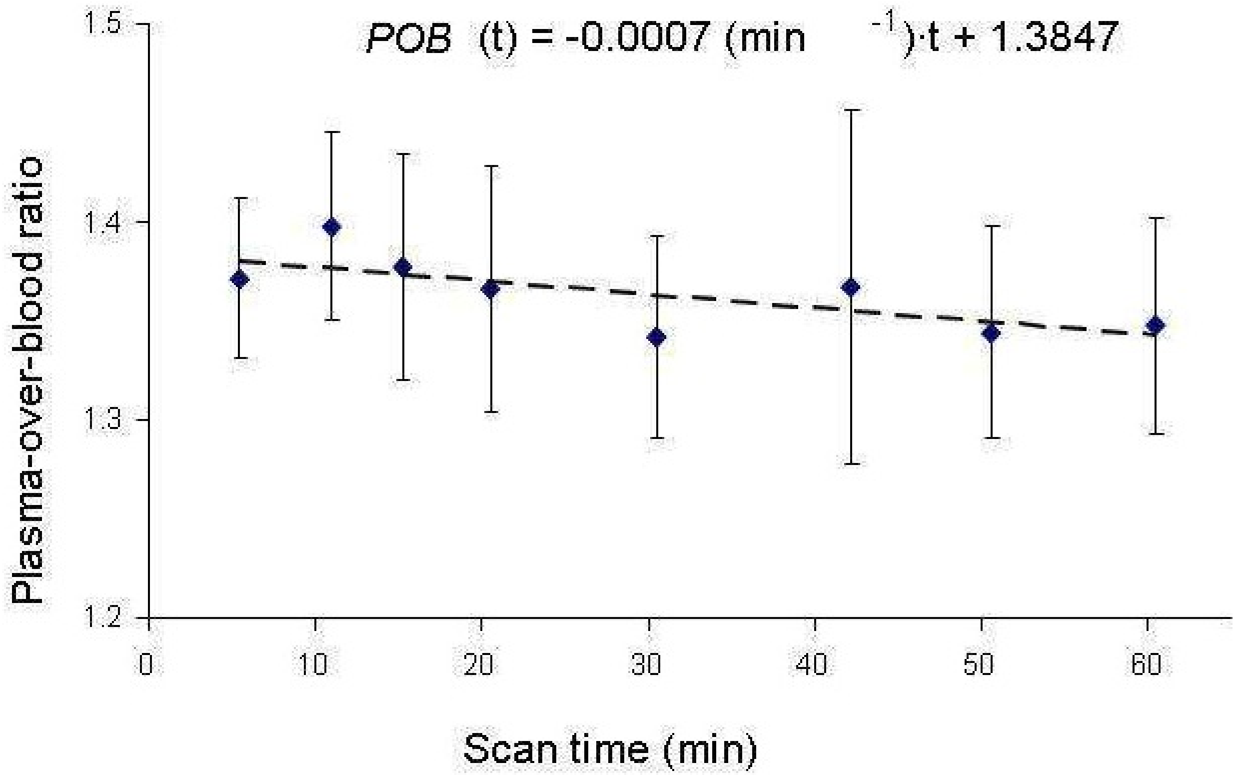
RESULTS

The mean population decline of POB(t) was 0.0007min^{-1}, (Supplemental Figure 2). The mean value in the 7 patients was 1.372 ± 0.040 at 5 min and 1.348 ± 0.055 after 60 min (Supplemental Figure 2). As described by equation $POB(t) = p_0 + p_1.t$ (1) a straight line was used to fit the data.

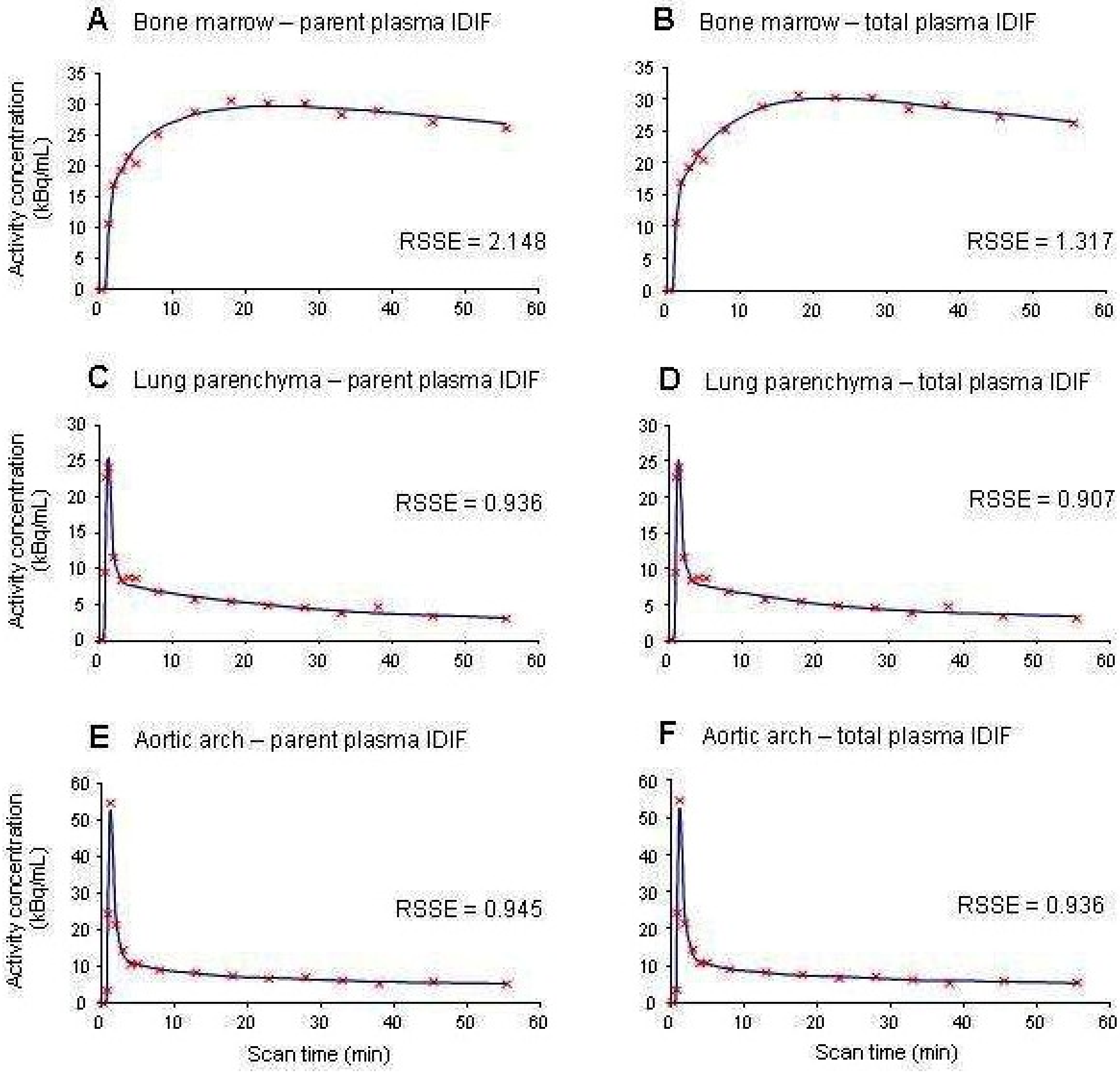
Supplemental Figure 3 depicts the TACs of three tissue ROIs fitted with the one-tissue compartment model using either the total plasma IDIF or the parent plasma IDIF in an asymptomatic patient. For each ROI, no difference can clearly be observed between the fitted model computed using either of the 2 IDIFs. This observation is confirmed by the very close values of the residual sum of squared errors of the fits.



Supplemental Figure 1: Illustration of the definition of the tissue ROIs: CT angiography (CTA) (A) and summed PET images for the visualization of the vessel lumen (i.e. at 30-70s) (B) were used as anatomical references to obtain 1mm-thick short-axis sections of the vessel (C-E). On A and B, parameters for the reslicing of the horizontal portion of the arch are shown. The contours of the vessel ROI's were then manually divided into 4 quadrants for both the asymptomatic patients (C-E) and the symptomatic patients (F-H). For the symptomatic patients, the lines encompassing the quadrants were placed so that the inflamed area of the aortic wall was included in one of the quadrants (H).



Supplemental Figure 2: Manual blood samples analysis: ratio of plasma activity concentration over whole blood activity concentration (POB) obtained from the 7 subjects .The mean values with their standard deviations are given for each of the 10 discrete arterial blood samples.



Supplemental Figure 3: Example of the fitting of the framed data from an asymptomatic patient measured in three tissue regions (bone, lung parenchyma and aortic wall) with a reversible one-tissue compartment model using either the parent plasma IDIF (left panels A,C,E) or the total plasma IDIF (right panels B,D,F). The crosses represent the 18 measured values, whereas the solid lines correspond to the reversible one-tissue compartmental model fitted through the measured data. RSSE = residual sum of squared errors.

Supplemental Table 1

Area under the curve (AUC) in kBq/mL.min of the activity concentration (corrected for radioactive decay) in total blood.

	Total blood BSIF			Total blood IDIF			Difference between IDIF and BSIF(%)		
Time (min)	5	30	60	5	30	60	5	30	60
Patient 1	136.9	349.1	473.4	229.5	440.3	564.9	40.4	20.7	16.2
Patient 2	69.9	306	492.3	143.3	382.2	568.9	51.3	19.9	13.5
Patient 3	101.0	332.3	476.4	135.8	368.6	513.1	25.6	9.8	7.1
Patient 4	138.9	400.5	597.7	206.7	467.8	665.3	32.8	14.4	10.2
Patient 5	118.9	288.6	334.6	166.3	343.3	389.9	28.5	15.9	14.2
Patient 6	128.8	355.3	502.2	143.6	368.8	516.1	10.3	3.7	2.7
Patient 7	139.9	496.3	778.7	178.1	531.5	814.5	21.5	6.6	4.4

$$\text{Difference between IDIF and BSIF} = \frac{\text{total blood IDIF - total blood BSIF}}{\text{total blood IDIF}} \times 100$$

Supplemental Table 2

Tracer arrival delay (sec) as proposed in *(3)* of the seven patients. For all the five tissue regions considered, the tracer arrival delay was computed for the four blood sampler and image derived input functions.

		Asymptomatic				Symptomatic		
Region	Input function	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Bone marrow	Total plasma BSIF	51	70	46	64	74	9	74
	Parent plasma BSIF	51	70	46	64	74	9	74
	Total plasma IDIF	2	-5	12	10	8	1	8
	Parent plasma IDIF	2	-5	12	10	8	1	8
Lung parenchyma	Total plasma BSIF	52	81	55	57	63	10	64
	Parent plasma BSIF	52	81	55	57	63	10	64
	Total plasma IDIF	1	8	8	-1	4	1	-2
	Parent plasma IDIF	1	8	8	-1	4	1	-2
Ascending aortic wall	Total plasma BSIF	53	75	50	62	63	12	71
	Parent plasma BSIF	53	75	50	62	63	12	71
	Total plasma IDIF	-1	2	2	4	1	-2	6
	Parent plasma IDIF	-1	2	2	4	1	-2	6
Arch aortic wall	Total plasma BSIF	53	75	47	56	58	11	67
	Parent plasma BSIF	53	75	47	56	58	11	67
	Total plasma IDIF	0	4	3	3	-1	-2	1
	Parent plasma IDIF	0	4	3	3	-1	-2	1
Descending aortic wall	Total plasma BSIF	52	76	45	61	66	11	68
	Parent plasma BSIF	52	76	45	61	66	11	68
	Total plasma IDIF	-2	2	2	2	6	-1	2
	Parent plasma IDIF	-2	2	2	2	6	-1	2

Supplemental references

1. Mourik JE, Lubberink M, Schuitemaker A, et al. Image-derived input functions for PET brain studies. *European Journal of Nuclear Medicine & Molecular Imaging.* 2009;36(3):463-471.

2. Ranicar AS, Williams CW, Schnorr L, et al. The on-line monitoring of continuously withdrawn arterial blood during PET studies using a single BGO/photomultiplier assembly and non-stick tubing. *Medical Progress through Technology.* 1991;17(3-4):259-264.

3. Hinz R, Turkheimer FE. Determination of tracer arrival delay with spectral analysis. *IEEE Trans Nucl Sci.* 2006;53(1):212-219.