Schematic representation of the non-invasive absolute quantification pipeline

Supplemental Figure 1. Architecture of the established processing pipeline. (1) Dynamic AC maps are generated and aligned with the PET emission data during reconstruction with Siemens e7 tools, (2) VOI is automatically defined from TOF-MRA images, (3) motion vectors are used to align the VOIs with reconstructed PET frames along with the T1-MR images, (4) partial volume correction is performed using the PET and MRI information, (5) voxel-wise Patlak analysis is performed using dynamic PET information, and (6) spatial normalization is performed via the DARTEL algorithm either to update the normative database (controls) or to generate z-map (patients). The typical processing time of the developed processing pipeline was ~6h on a dedicated high-end PC computer (12 Core CPU, 64 GB RAM, Nvidia Titan Xp graphic card).

AIF vs **CT-IDIF**   **P12-T**   **AIF** vs **pCT-IDIF**

P04-T

P03-T
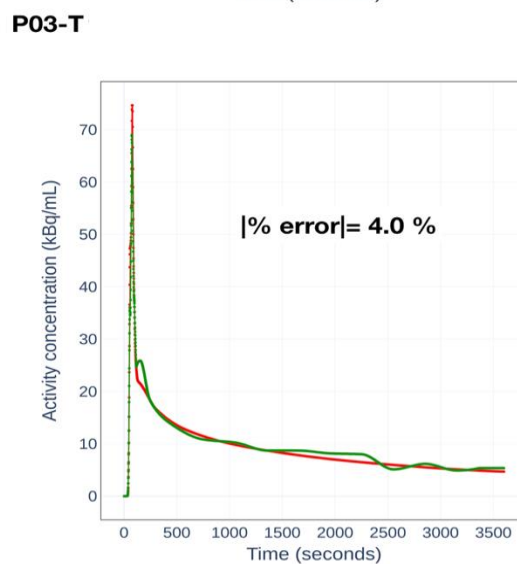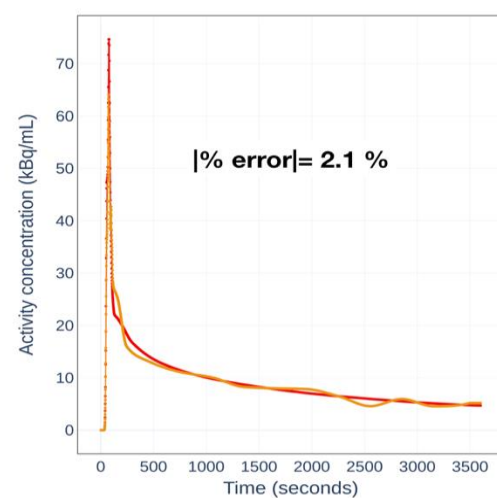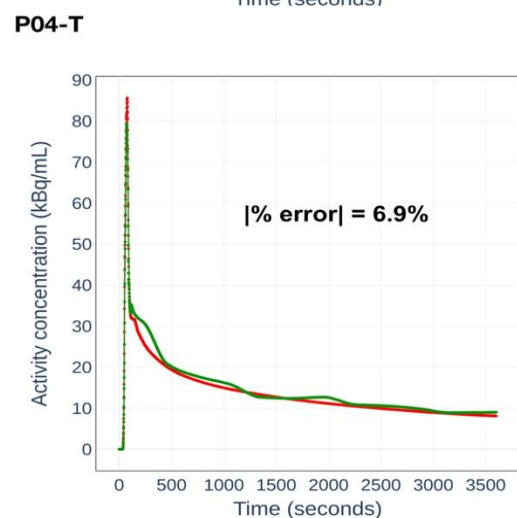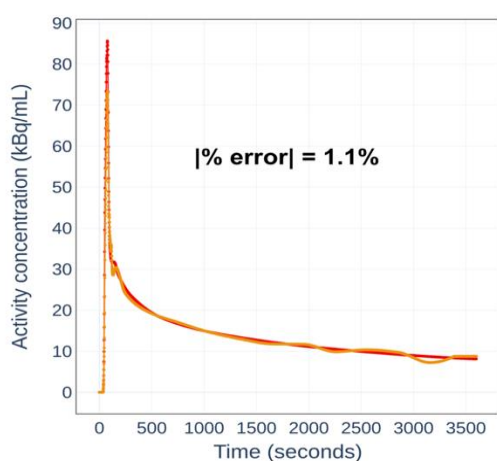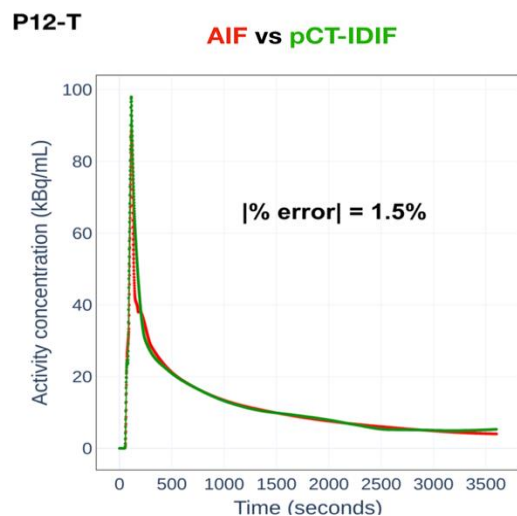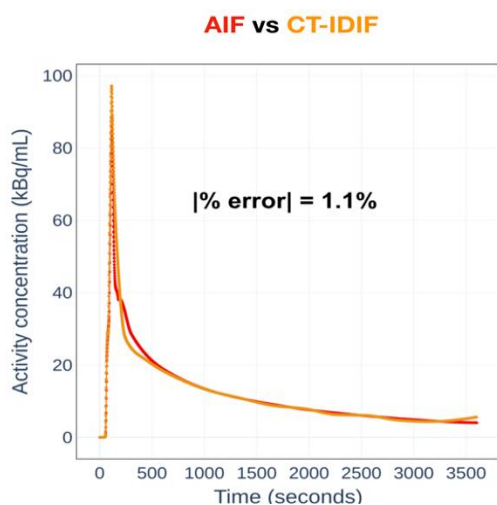
Supplemental Figure 2. Representative AIFs and IDIFs. The left row shows the comparison between the AIF (red) and the IDIF derived using CT-AC (orange), whereas the right row displays the comparison between the AIF (red) and the IDIF obtained using the pCT-AC (green). The absolute % difference with respect to the AUC is displayed for each comparison.
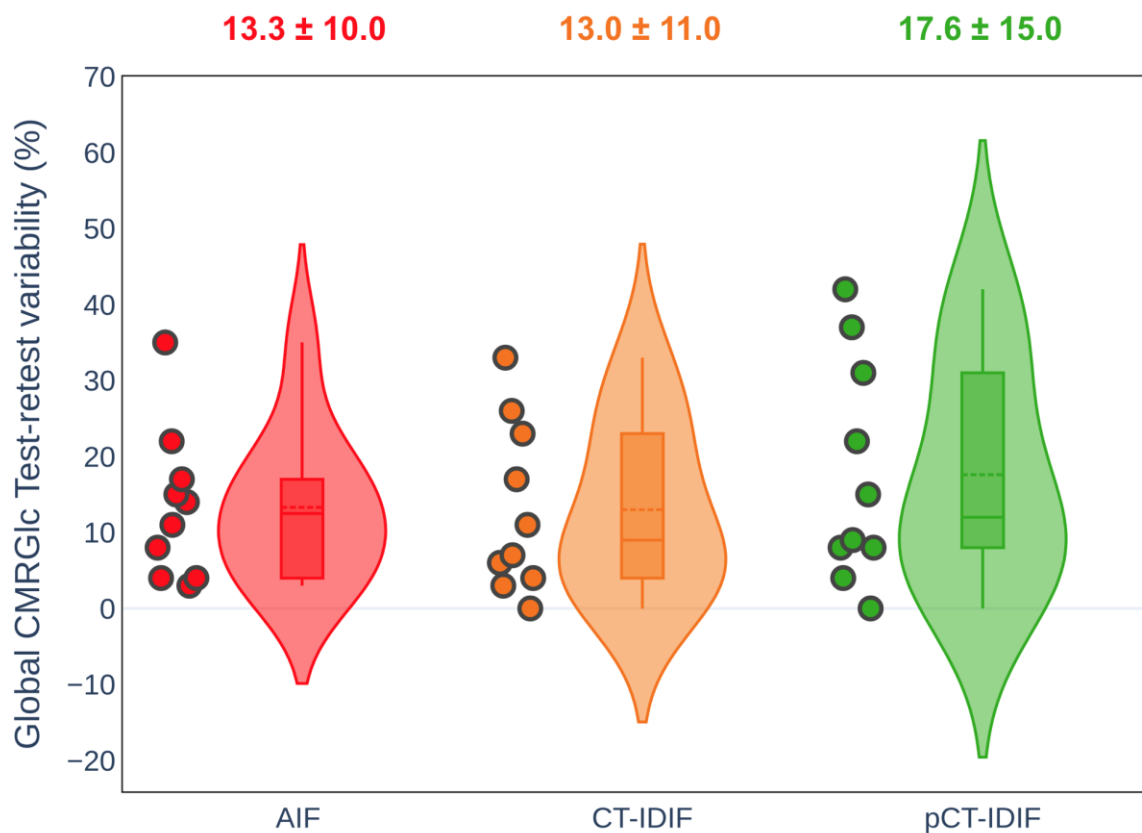
Supplemental Figure 3. Distribution of the test-retest variability of whole brain CMRGlc values derived using the AIF, CT-IDIF and pCT-IDIF. The shaded areas enclosing the box plots represent the probability density distributions of the test-retest variability for each subject. Data indicates a physiological variability of glucose metabolic rate in the range of 15% – 25%.
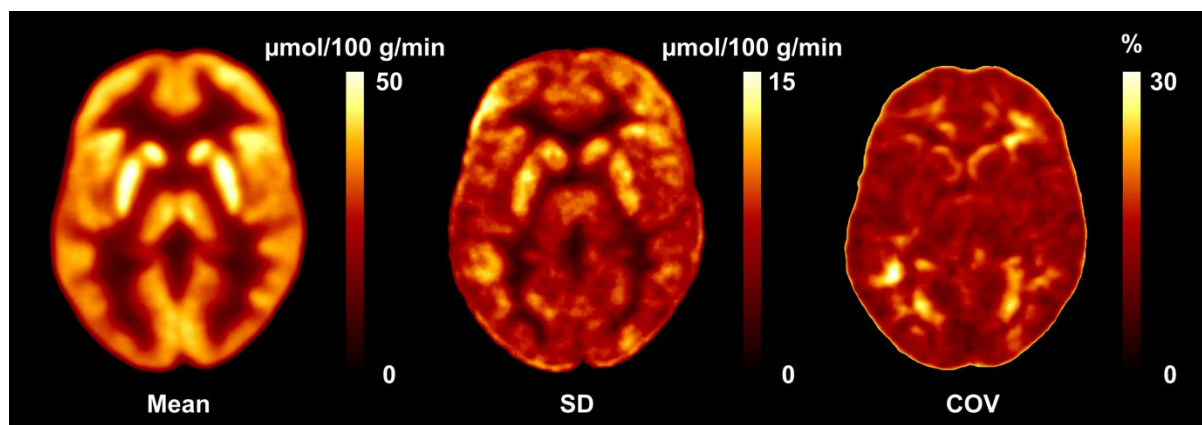
Supplemental Figure 4. Mean, SD and COV images of MRGlc derived from an adult control population. MRGlc was determined based on arterial sampled blood (AIF) and CT-AC.
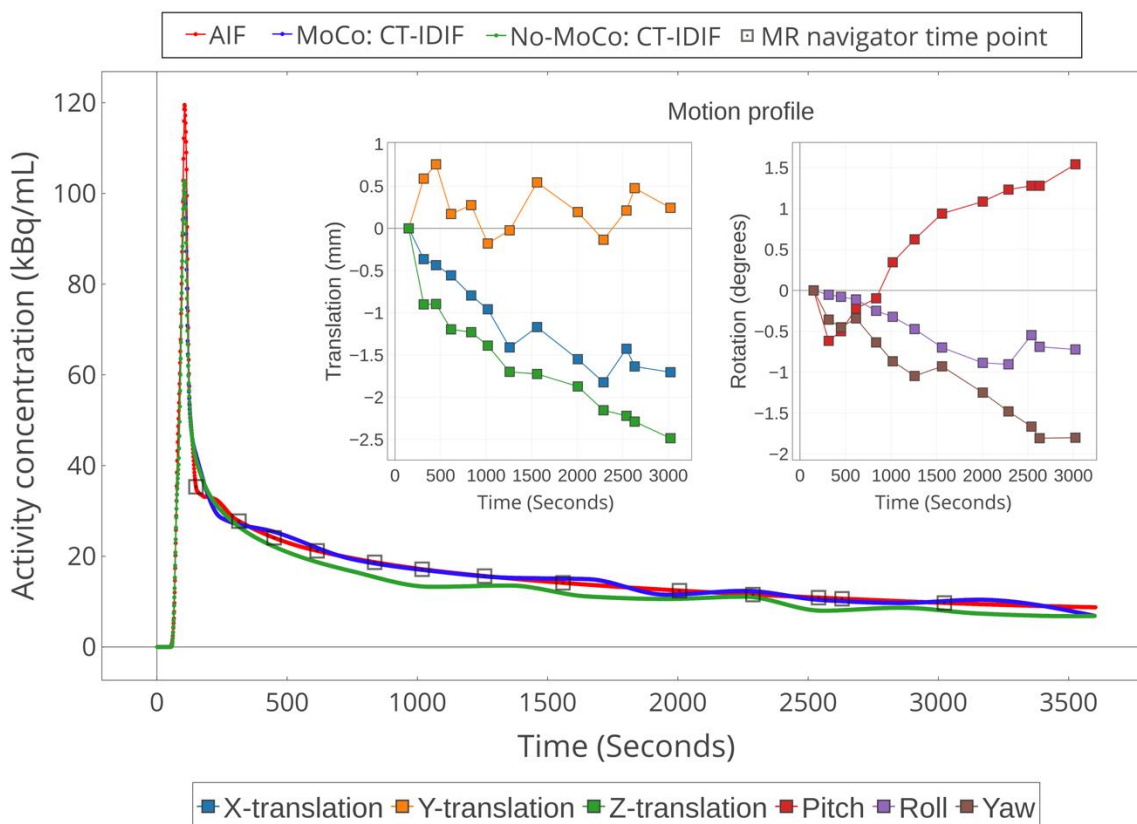
Supplemental Figure 5. Impact of subject motion on the accuracy of the IDIF. It can be

appreciated that motion compensation improves the agreement between AIF (red) and

the CT-IDIFs. The motion-corrected IDIF is displayed in blue, whereas the non-corrected

IDIF is shown in green. The inserts show motion-related translations (left) and rotations

(right) in all three axes.