^{18}F-FPRGD2 radiosynthesis

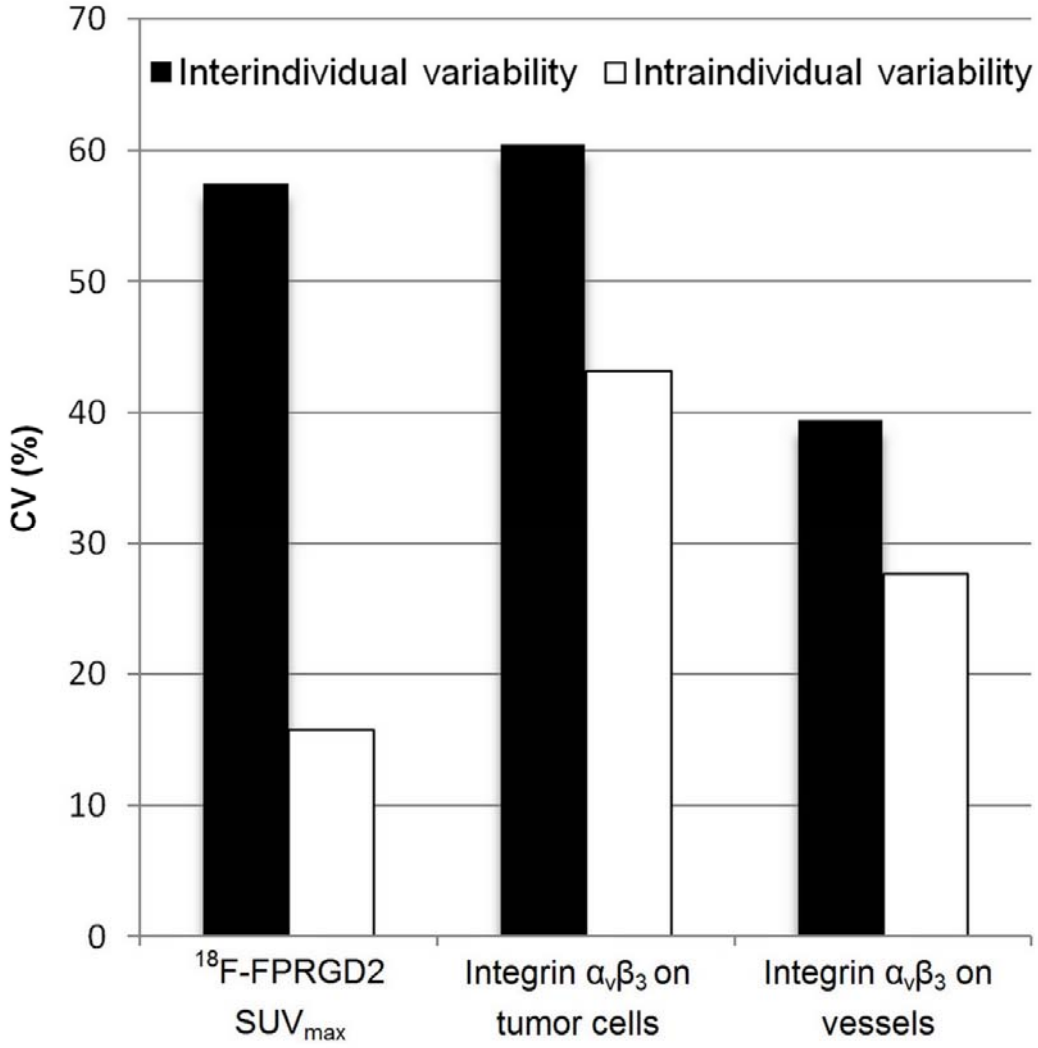
^{18}F-FPRGD2 was produced following a published method in compliance with cGMP regulations. The radiosynthesis of N-succinimidyl 4-^{18}F-fluorobenzoate (^{18}F-SFB) was automatically performed on a commercial synthesis module (GE Healthcare FASTlab) with a radiochemical yield (decay-corrected) of 32% and a radiochemical purity of more than 96%. The coupling reaction between ^{18}F-SFB and the FPRGD2 was performed using a second disposable cassette clamped onto the FASTlab. The crude product was purified on an HPLC system; the fraction containing the pure ^{18}F-FPRGD2 was collected on the FASTlab, diluted with saline, and then concentrated on a C18 cartridge. The cartridge was eluted with ethanol and saline, and the eluted solution was sterilized through a 0.22-μm filter. The mean activity of the purified ^{18}F-FPRGD2 obtained was in the range of 3,750 MBq in 130 min with an overall radiochemical yield (from the ^{18}F-fluoride) of 13% (decay-corrected), radiochemical purity of 98%, and specific activity of 140 ± 40 TBq/mmol.

^{18}F-FPRGD2 PET/CT

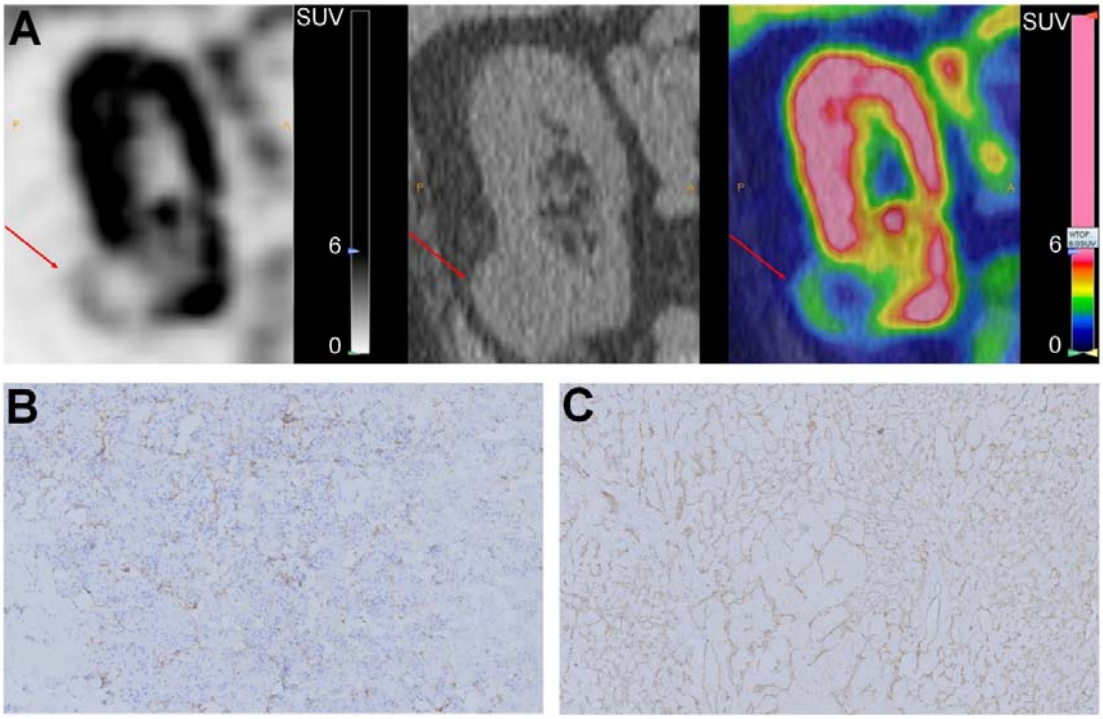
All patients fasted for 6 h before ^{18}F-FPRGD2 injection. The PET/CT images were acquired on a Gemini PET/CT system (Philips Medical Systems), TF (n = 18) or Big Bore (n = 9), and the acquisition started 60 min (median, 60 min; range, 59–86 min) after intravenous injection of a mean activity (±SD) of 309 ± 31.4 MBq of ^{18}F-FPRGD2. The mean injected mass of the active pharmaceutical ingredient was 7 ± 4.9 μg. A low-dose CT scan (5-mm slice thickness; tube voltage, 120 kV; tube current–time product, 50–80 mAs depending on the patient's weight) followed by the PET emission scan of 3 min per bed position was performed. Data were reconstructed using time of flight, including correction for decay, scatter, randoms, and attenuation (CT data were used for attenuation correction).

Statistical Analyses

The intraclass correlation coefficient was used to estimate the observers' agreement on PET/CT images. Correlations between quantitative variables were calculated after logarithmic or logit transformations to normalize the distributions. A multivariate regression was applied to estimate SUV_{max} and SUV_{mean} with respect to tissue parameters. Results were considered to be significant at the 5% level ($P < 0.05$). The generalized linear mixed model was applied to take into account multiple variables in a single patient. The coefficient of variation (CV) was calculated to estimate the variability of SUV_{max} and tissue parameter levels in biopsy samples. Calculations were done using SAS, version 9.2 (SAS Institute).



Supplemental Figure 1. Shown are the coefficients of variation of ^{18}F-FPRGD2 SUV_{max} and the expression of integrin $\alpha_v\beta_3$ on tumor cells and on vessels in renal tumors.



Supplemental Figure 2. ^{18}F-FPRGD2 PET/CT images (A) of a patient with a ccRCC and high ^{18}F-FPRGD2 tumor uptake (SUV_{max}, 3.9) at the periphery of the tumor due to high integrin $\alpha_v\beta_3$ expression in vessels only (B: brown staining of integrin $\alpha_v\beta_3$; C: brown staining of CD31).