Table 1: Time table

	N	Minimum	Maximum	Mean ± SD
Pre-FLT	20	-3 h 43 m	-37 d	-5.4 d ± 8.7 d
Immediate <5 h	18	1 h 24 m	4 h 12 m	2 h 20 ± 41 m
5 – 24 Hours	18	5 h 37 m	21 h 24 m	9 h 43 ± 5 h 42
First Week	18	1.1 d	6.0 d	4.4 d ± 1.1 d
> 1 week	19	7.4 d	155.8 d	29.3 d ± 39.8 d

m = minutes, h = hours, d = days

Results

Laboratory assays

Different laboratory values monitored for this study are plotted with respect to the time categories for each of the 20 study participants (Figures 1 and 2). Table 2 summarizes the mean and standard deviation for each parameter over time. No statistically significant change was observed in sodium, potassium, chloride, glucose, creatinine, BUN, SGOT, SGPT, Alk Phos, total bilirubin, WBC, and platelet levels ($p > 0.05$). The mean for each of these parameters remained within normal limits over time (Table 2). Albumin, RBC, and hematocrit show a statistically significant decrease over time. Bonferroni analyses demonstrated that albumin decrease results mainly from an initial decrease of 11.5% between the pre-^{18}F-FLT PET measure and the immediate post-^{18}F-FLT PET blood draw ($p < 0.001$). However, mean albumin values stayed within normal limits. For RBC and hematocrit (as well as for hemoglobin level, not plotted), significant decreases of respectively 4.7% and 4.5% occur between pre-^{18}F-FLT and immediate post-^{18}F-FLT blood drawn ($p < 0.001$), followed by decreases of respectively 8.3% and 8.4% between 5–24 hours and 1–7 days ($p < 0.001$). However, average levels for RBC remained within normal limits for the 1–7 days time point. Average values were just below normal for RBC after 1 week and for hematocrit for the first week and onwards. Because they are the only laboratory parameters to exhibit a change, raw data, mean and standard deviations (SD) for albumin, RBC, and hematocrit are also plotted for illustration (Figures 1F, 2A, 2C). The effect of surgical intervention on hemoglobin, hematocrit and RBC values was assessed by re-analyzing the data after excluding all post-surgical lab values from the original dataset. Bonferroni post-test performed on this reduced dataset still demonstrates the same significant decrease in hemoglobin, hematocrit and RBC values from pre-^{18}F-FLT to immediately post-^{18}F-FLT times but without subsequent lowering at later time points. Haptoglobin levels measured for the last 3 patients of the study did not reveal any evidence of hemolysis.

No side effects including nausea, vomiting, dizziness, or headache were reported during 18F-FLT injection or during the following 2.0–2.5 hours.

Neurological evaluations

No change was observed in the results of the neurological examinations performed on all patients before and immediately after the ^{18}F-FLT PET imaging sessions. A review of each subject's clinical record covering the 4 months following ^{18}F-FLT PET imaging revealed no interval development of new neurological complaints, signs or symptoms by the study participants. In particular, no new peripheral neuropathy was reported in any of the 20 patients.

Calculation of AUC_{12} for a 5 mCi radiotracer dose of ^{18}F-FLT

Figure 3 depicts 4 blood-derived TACs, each normalized to a standard 5 mCi ^{18}F-FLT injected dose. These decay-corrected curves illustrate the variability observed across patients in the elimination of ^{18}F-FLT from blood. They also illustrate the observation that at the conclusion of imaging the quantity of residual ^{18}F-FLT in the blood was small in all 20 patients. At 90 minutes post-^{18}F-FLT injection, the concentration of decay-corrected activity is on average 0.0454 ± 0.0272 μCi/mL. With a lowest acceptable specific activity of 0.1 Ci/μmol, this corresponds to a concentration of FLT of 0.111 ± 0.0665 ng/mL if all radioactivity is assumed to be in the form of ^{18}F-FLT (FLT has a molecular weight of 244 g). Therefore, for the purpose of this study we are not considering the main labeled metabolite of FLT, ^{18}F-FLT-glucuronide, separately from ^{18}F-FLT.

The imaging-derived AUC_{12} values range from 0.405 ng*h/mL to 1.26 ng*h/mL with a mean of 0.770 ± 0.285 ng*h/mL. The calculated blood sample-derived AUC_{12} ranged from 0.232 ng*h/mL to 1.34 ng*h/mL with a mean of 0.802 ± 0.303 ng*h/mL. No significant difference in the AUC_{12} values obtained by the 2 different methods was found (Wilcoxon signed rank test, $p = 0.66$, Figure 4).

Discussion

The purpose of this study was to evaluate the potential toxicity of ^{18}F-FLT when administered in a radiotracer dose for PET imaging. Such a study was made necessary because of previously reported toxicity in clinical trials employing therapeutic doses. In 1994, Flexner et al. published a concentration-control trial involving initially 14