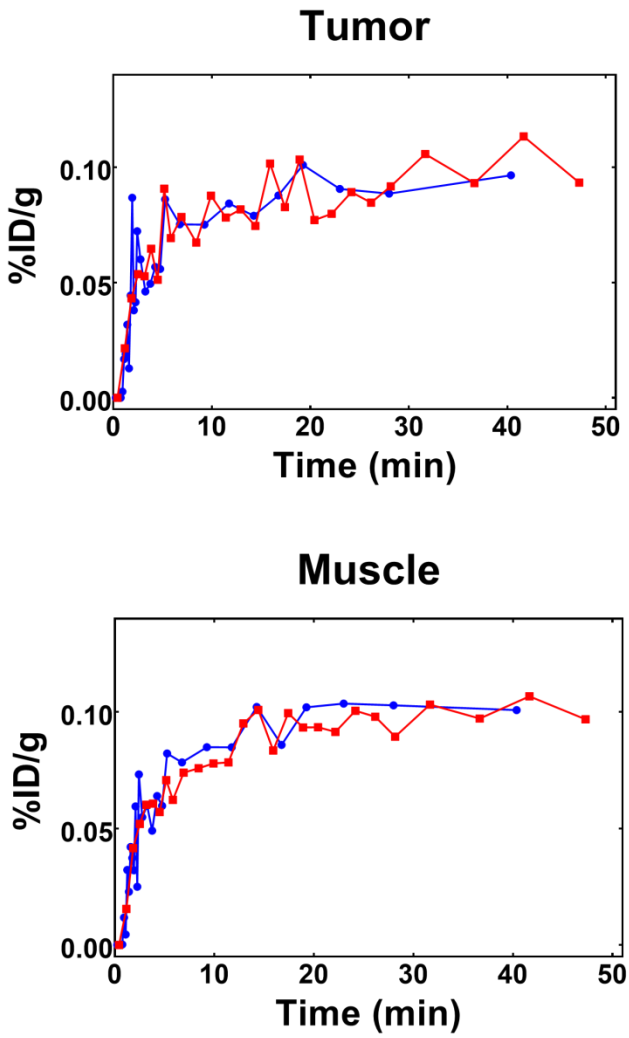
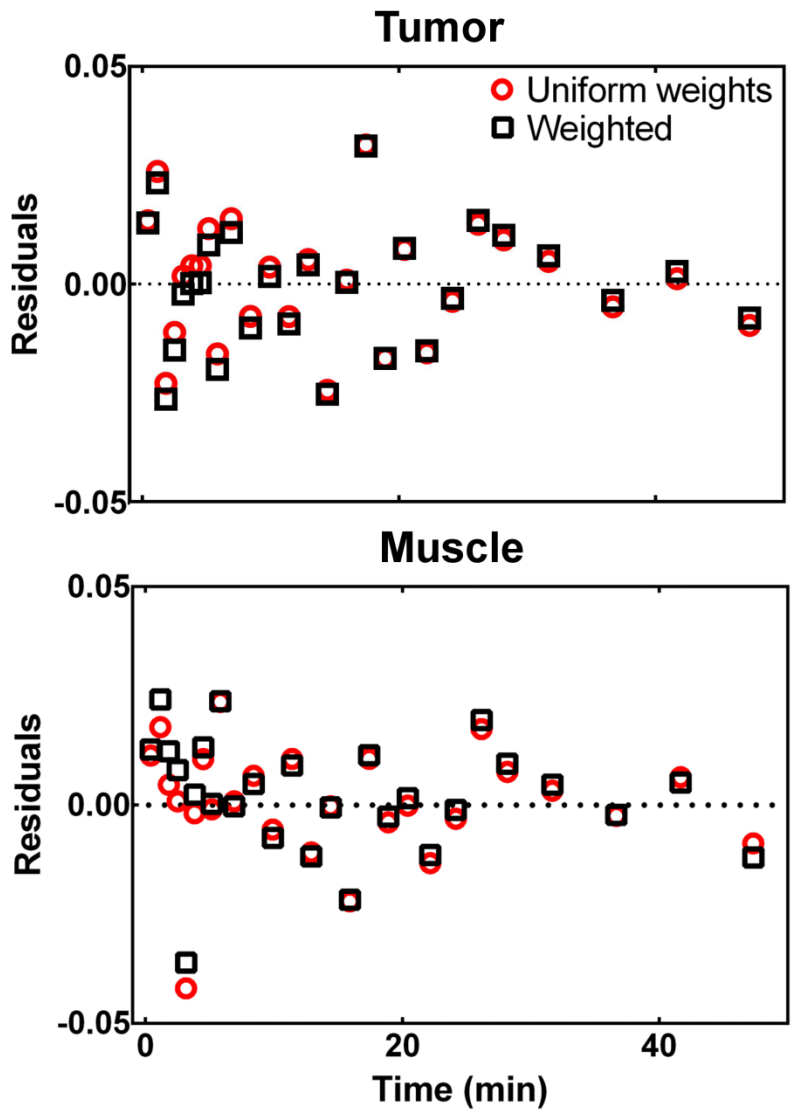
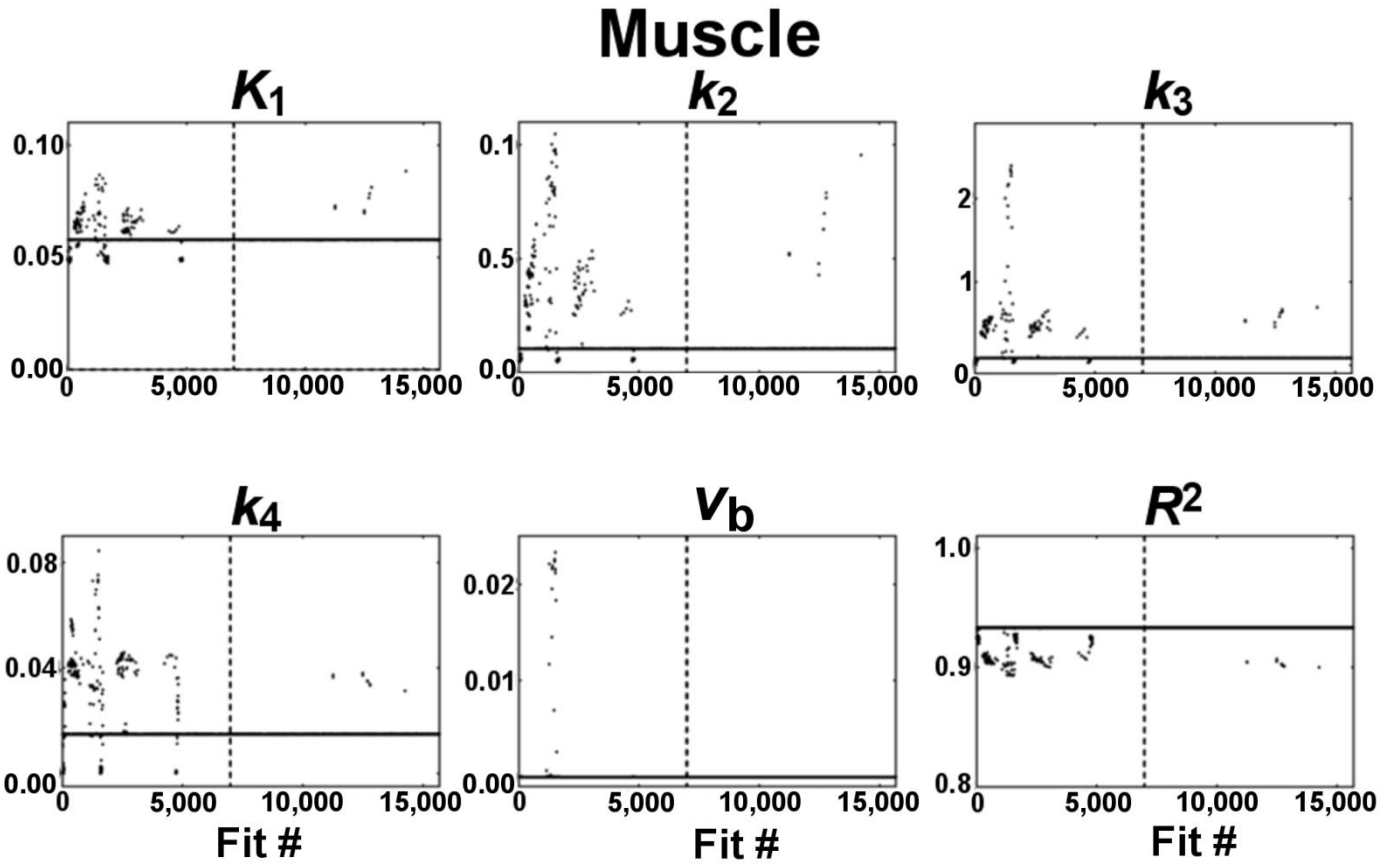


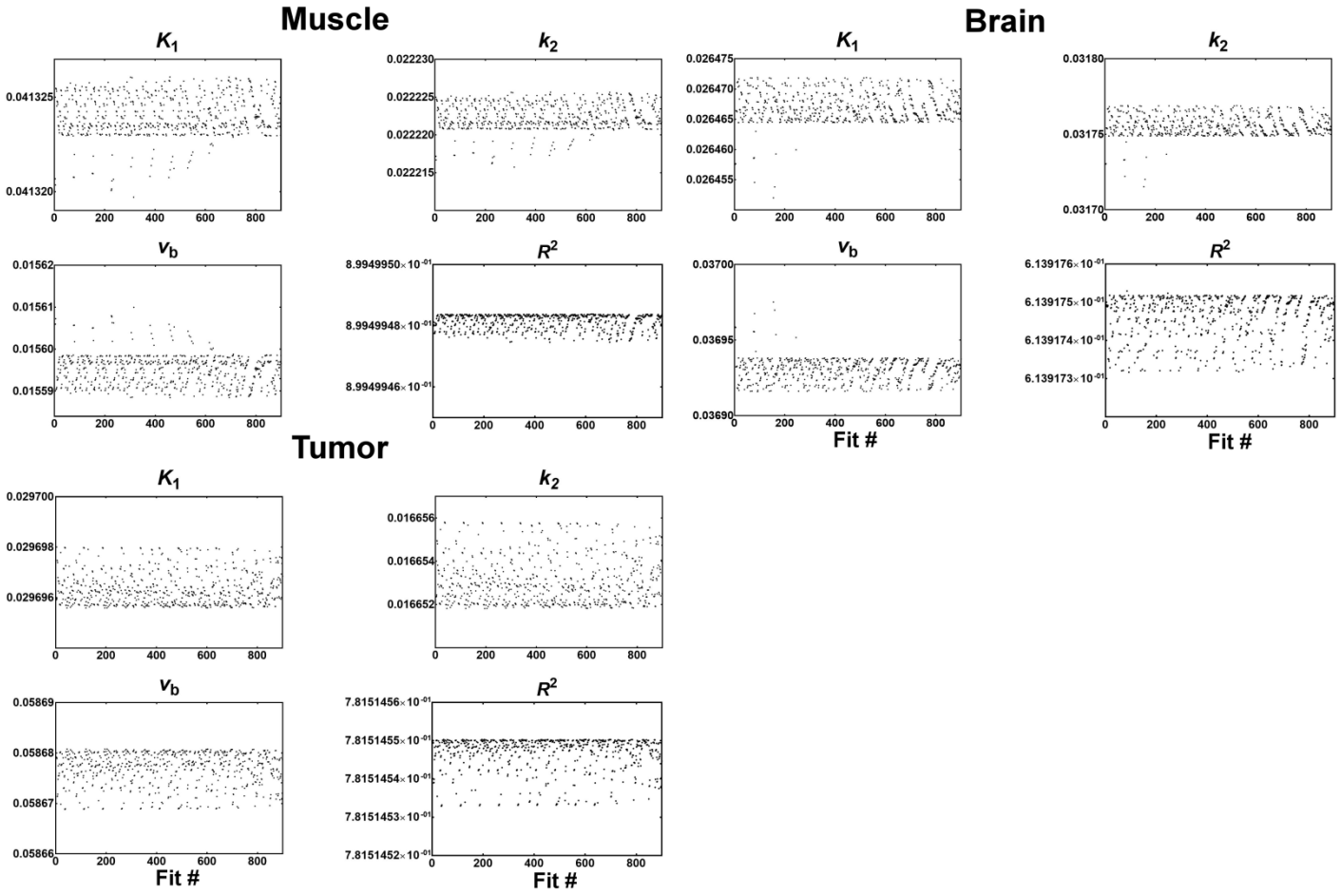
SUPPLEMENTAL FIGURE 1. Time-activity curves for representative regions with different time samplings. In red (squares): with fewer time points at the beginning (every 40 s) and more at the end (every 5 min). In blue (circles): with fine initial temporal sampling (every 5 s) and coarse sampling at the end (last point is 20 min). The shapes are very similar and the kinetic parameters for region of interest-based analysis are comparable. Longer time frames lead to lower noise, which can be helpful in identifying the initial uptake slope. However, early frames should be short enough to show this initial slope in order to obtain a precise value of K_1 from the compartment models (in the present case, a 1-minute bolus was administered after a 0.5 min background scan).



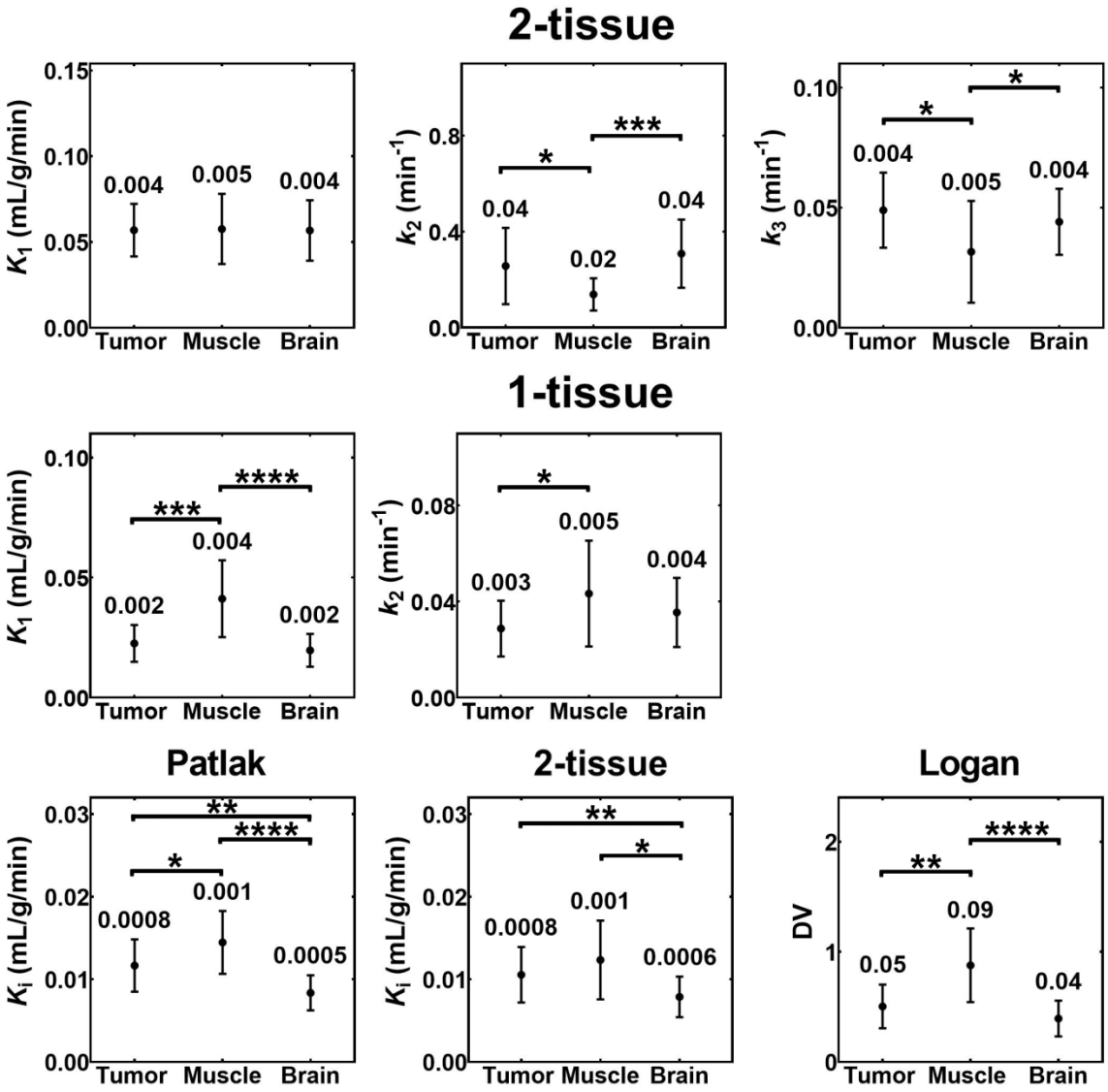
SUPPLEMENTAL FIGURE 2. Fit residuals from uniform and variable weighting for a representative animal and regions of interest. The variable weighting represented the variance of data in each frame. The differences are minimal and there is no effect on the resulting kinetic parameters. Because it is difficult to estimate weights from noisy data and because poorly estimated weights can induce errors, uniform weighting was chosen. For additional information, refer to: Thiele and Buchert, *Nuclear Medicine Communications* 2008; 29:179–188.



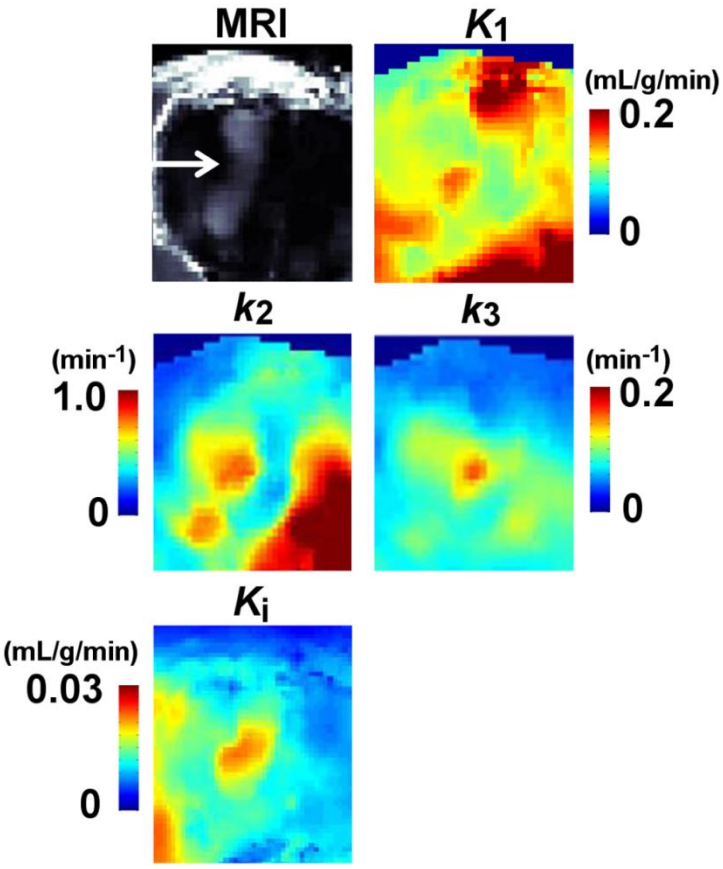
SUPPLEMENTAL FIGURE 3. Effect of the initial parameter guesses on kinetic modeling for a representative animal using the 2-tissue model. A nested loop algorithm was used to test multiple initial guesses sets for three regions of interest. Here we show the effect of the guesses provided to the fitting algorithm on the resulting kinetic parameter values (K_1-v_b) and on fit quality (R^2) for the muscle. Each point represents a value obtained with one of 15680 sets of guesses. For example, x = 1 corresponds to the first set ($K_1 = 0.01$, $k_2 = 0.02$, $k_3 = 0.01$, $k_4 = 10^{-4}$, $v_b = 10^{-5}$) and x = 2 corresponds to the second set ($K_1 = 0.01$, $k_2 = 0.02$, $k_3 = 0.01$, $k_4 = 10^{-4}$, $v_b = 10^{-4}$). Note that R^2 is not a good metric to compare non-linear models, but it was deemed a good enough estimation of how a single model fits the data points. Points converging to the most common value give the impression of a bold horizontal line. More than 90% of fits returned the same kinetic parameter values (within a 1% error margin) and had high R^2. Considering the wide range of initial guesses tested, the existence of a better solution is improbable. The other ~10% of fits returned variable kinetic parameters and lower R^2. In these cases, the algorithm stopped before reaching a better solution because the variation in the sum of squares was less than the threshold (10^{-8}), which is indicative of a local minimum. The dashed vertical lines indicate the guesses selected for the remaining analyses.



SUPPLEMENTAL FIGURE 4. Effect of the initial parameter guesses on kinetic modeling for a representative animal using the 1-tissue model. Contrary to the 2-tissue model, initial guesses have very little impact on the resulting kinetic parameters (note the very narrow range on the y-axis for each parameter). The fit was deemed stable.



SUPPLEMENTAL FIGURE 5. Kinetic parameters from different models for the cohort. The data points indicate the mean; the error bars provide the standard deviation. The standard error of the mean is indicated above each data point. Results of an unpaired *t*-test are shown (*$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$ [false discovery rate adjusted]). Generally, the paired (Figure 6) and unpaired *t*-tests agree, but the significance is lower for the unpaired *t*-test due to intersubject variability. Compared to the paired *t*-test, significance is lost between the tumor and brain for k_3 of the 2-tissue model as well as K_1 and k_2 of the 1-tissue model and DV as estimated from the Logan plot. On the other hand, significance emerges for K_i of the Patlak plot between the tumor and muscle. Because of individual differences, each animal should be its own control whenever possible. Therefore, the paired *t*-test was deemed preferable.



SUPPLEMENTAL FIGURE 6. Parameter maps for a representative animal. Kinetic modeling was performed voxel-wise for the tumor and surrounding brain region using the 2-tissue and the Patlak model. Images were denoised with a MR-guided non-local means filter prior to modeling. The magnetic resonance (using Gd-DTPA) image shows the localization of the tumor. Elevated K_1 and k_2 values correspond to areas of MRI contrast enhancement, whereas k_3 and K_i are localized towards the center of the tumor. The high K_1 and k_2 region on the bottom right may be due to spill out from the nearby internal carotid and/or be an artefact from the fitting algorithm (additional regularization terms may be necessary to account for the noise in each voxel). DV and v_b are not shown because they could not be fitted for this region.