Supporting Information

Monitoring the tumor response to antivascular therapy using non-contrast intravoxel incoherent motion diffusion-weighted MRI

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Running title: IVIM MRI of tumor response to anti-vascular therapies

Correlation of IVIM parameters with DCE MRI in tumor rim and tumor core

S1. Segmentation method

In the current study, we used a simple manual segmentation method to draw two regions to represent the tumor rim and tumor core. As illustrated in Figure S1, we first measured the K^{trans} map from Gd-based DCE MRI. Then we drew the tumor rim according to hyper-intense regions in the K^{trans} map. Tumor core was drawn in the center of the tumor based on the T2w image, which is independent of K^{trans} map.

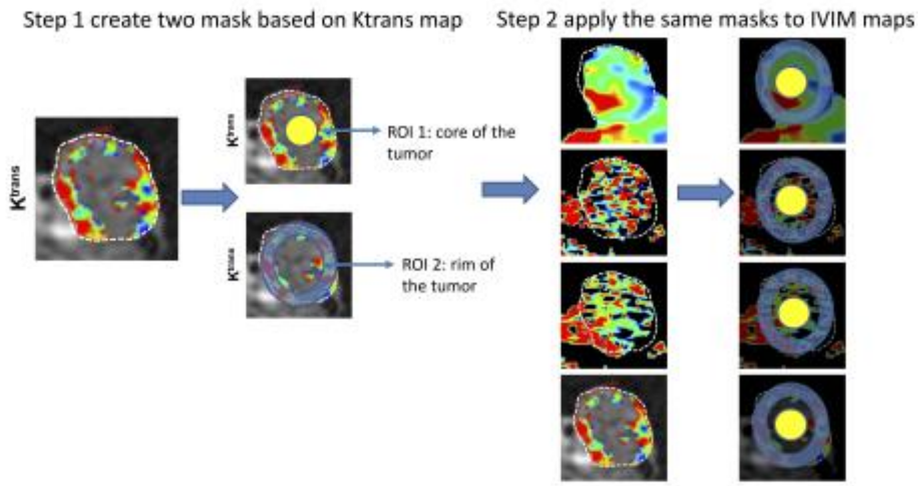

Figure S1. Illustration of manual segmentation method used in the study.

S2. The longitudinal changes in the diffusion parameters in different parts of the tumor

As shown in the Figure S2, the true diffusion coefficient D in the tumor rim remained constant in the course of the study. In contrast, the tumor core showed much higher diffusion coefficients and much stronger changes in both treatment groups than those in the tumor core. The changes in the whole tumor are likely due to the changes in the tumor core.

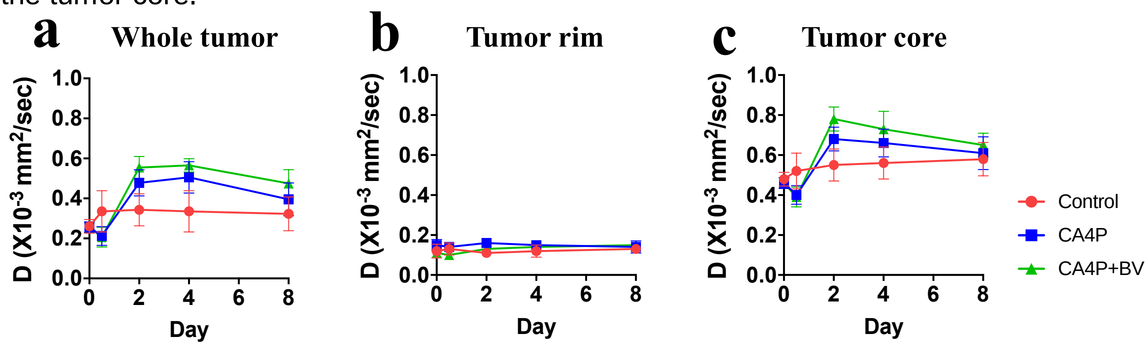

Figure S2. The longitudinal changes of the true diffusion coefficient D in **a)** whole tumor, **b)** Tumor rim, and **c)** tumor core.

S3. The longitudinal changes in the perfusion parameters in different parts of the tumor

We first investigated the K^{trans} measured by DCE MRI study in different parts of the tumor. As shown in the Figure S3, tumor rim showed a strong decrease on the first several days after the treatment, in a similar trend as that of the whole tumor, while the tumor core showed only negligible changes in the beginning of treatments.

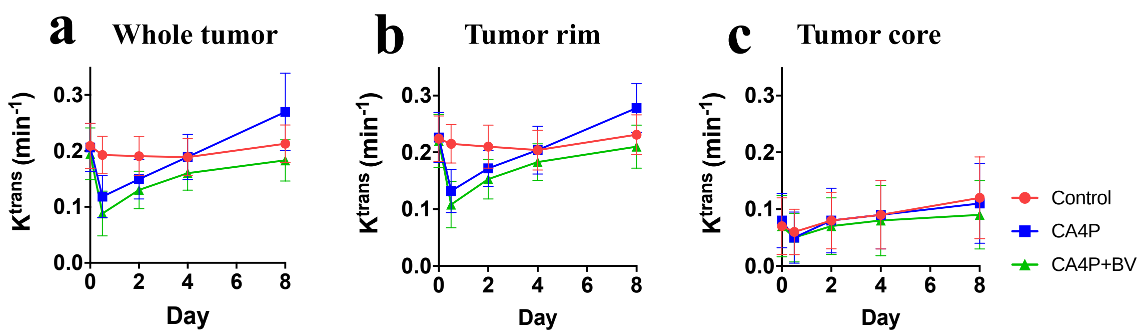

Figure S3. The longitudinal changes of K^{trans} measured in DCE MRI in **a)** whole tumor, **b)** Tumor rim, and **c)** tumor core.

Then we investigated the changes of the perfusion-related parameters in IVIM in different parts of the tumors. The results are shown in Figures S4-S6 for D*, f and fD* respectively. All these perfusion-related parameters demonstrated a much stronger changes in the tumor rim than in the tumor core. For f and D*, tumor rim showed a markedly increased correlation with K^{trans}. Interestingly, the fD* of the whole tumor showed a stronger correlation with K^{trans} than either in the tumor rim or in the tumor core.

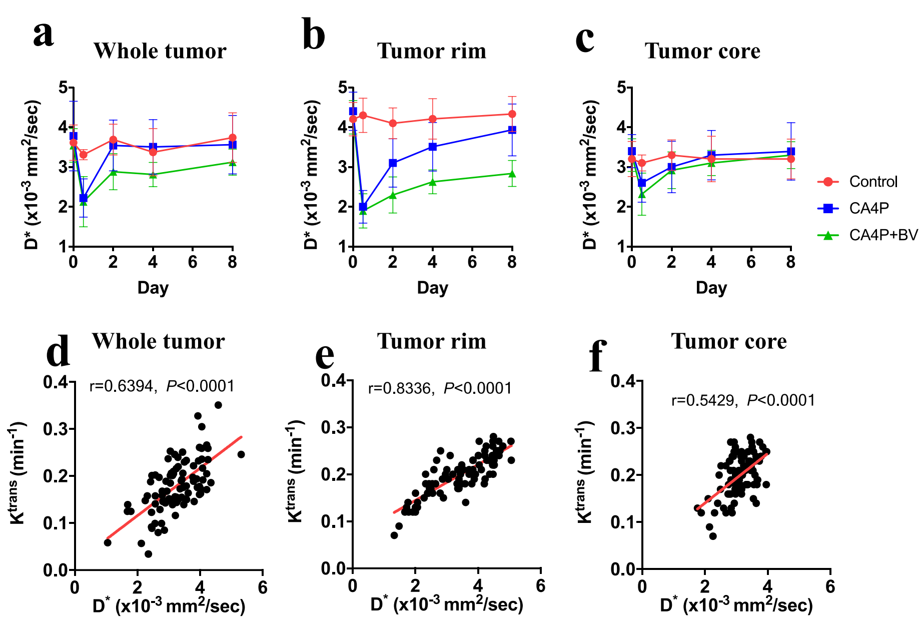

Figure S4. The longitudinal changes of pseudo-diffusion coefficient D* measured by IVIM in **a)** whole tumor, **b)** Tumor rim, and **c)** tumor core. The correlation between measured K_{trans} and D* in **d)** whole tumor, **e)** Tumor rim, and **f)** tumor core.

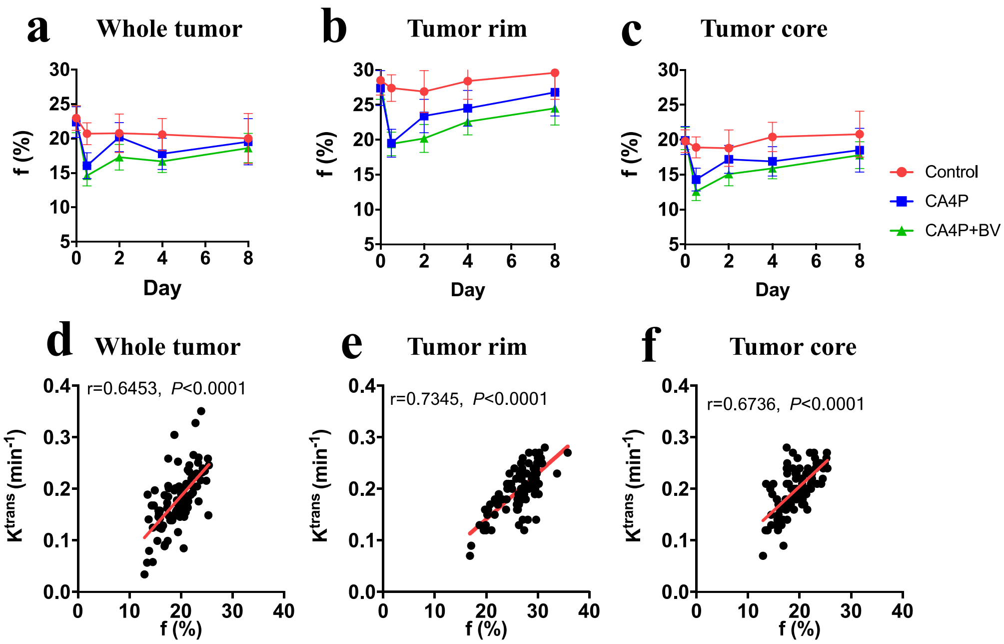

Figure S5. The longitudinal changes of perfusion fraction f measured by IVIM in **a)** whole tumor, **b)** Tumor rim, and **c)** tumor core. The correlation between measured K_{trans} and f in **d)** whole tumor, **e)** Tumor rim, and **f)** tumor core.

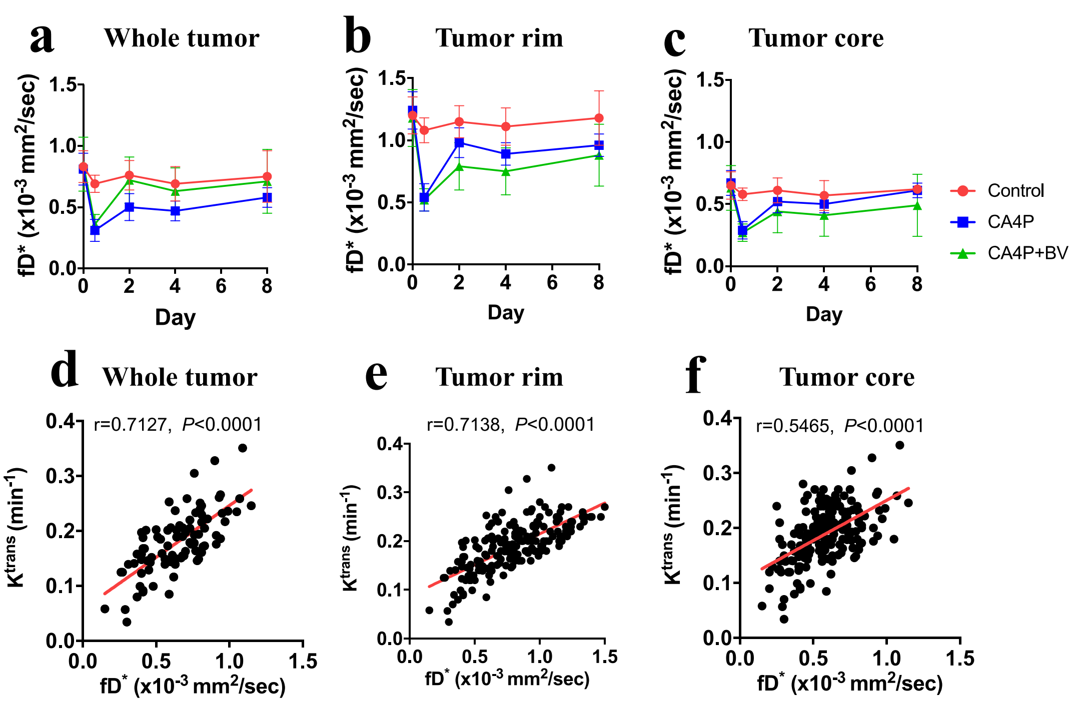

Figure S6. The longitudinal changes of fD* by IVIM in **a)** whole tumor, **b)** Tumor rim, and **c)** tumor core. The correlation between measured K_{trans} and fD* in **d)** whole tumor, **e)** Tumor rim, and **f)** tumor core.

S4. The correlation between the IVIM parameters measured on Day 2 and the tumor volume changes on day 8 in different parts of the tumor

After segmentation, the early IVIM measures can be more predictive of later tumor volume changes. We presented the new correlation studies in Figure S7. It is very clear that the correlations between IVIM parameters and tumor responses are improved remarkably, particularly for the pseudo-diffusion coefficient D*, which showed no correlation with tumor volume changes at the whole tumor scale (r = -0.03644, P = 0.9105), but a good correlation when only tumor rim was used (r = 0.8529, P = 0.0004).

It was also found that the true diffusion coefficient D in the tumor core had a stronger correlation with the changes in tumor volume at a later time point than that of the whole tumor.

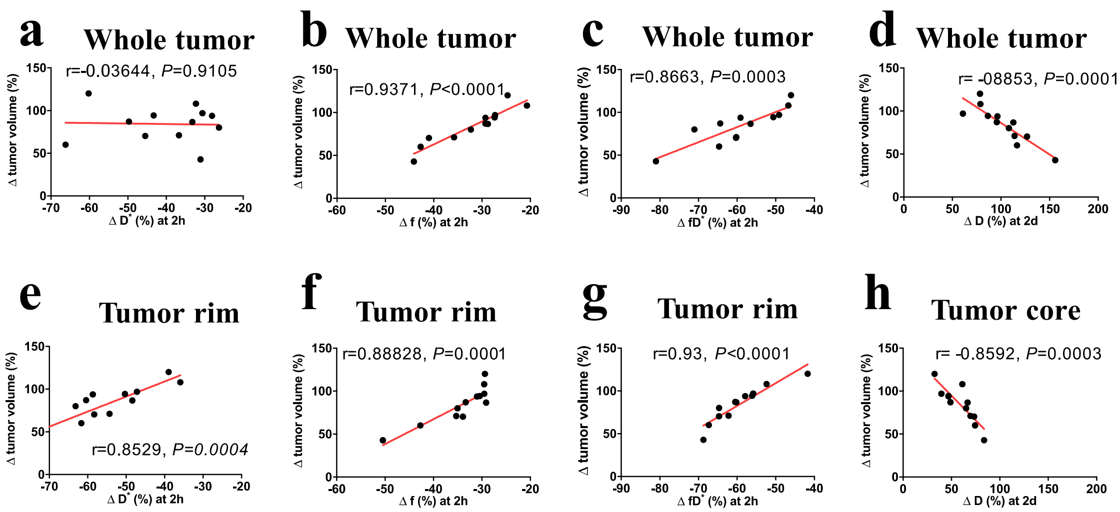

Figure S7. The comparison of the correlation between early IVIM measures (day2) and later tumor volume change (day8) in different parts of the tumor. (**a**)- (**c**) The correlation of perfusion-related parameters, D*, f and fD*, measured in IVIM in the whole tumor and (**e**)- (**g**) those in the tumor rim. (**d)** The correlation of true diffusion coefficient D measured in IVIM in the whole tumor and (**h**) that in the tumor core.