

**Electronic Supplementary Material**  
**Assessing Response to Therapy Using Simultaneous PET/MRI in**  
**Preclinical Model of Pancreatic Cancer**

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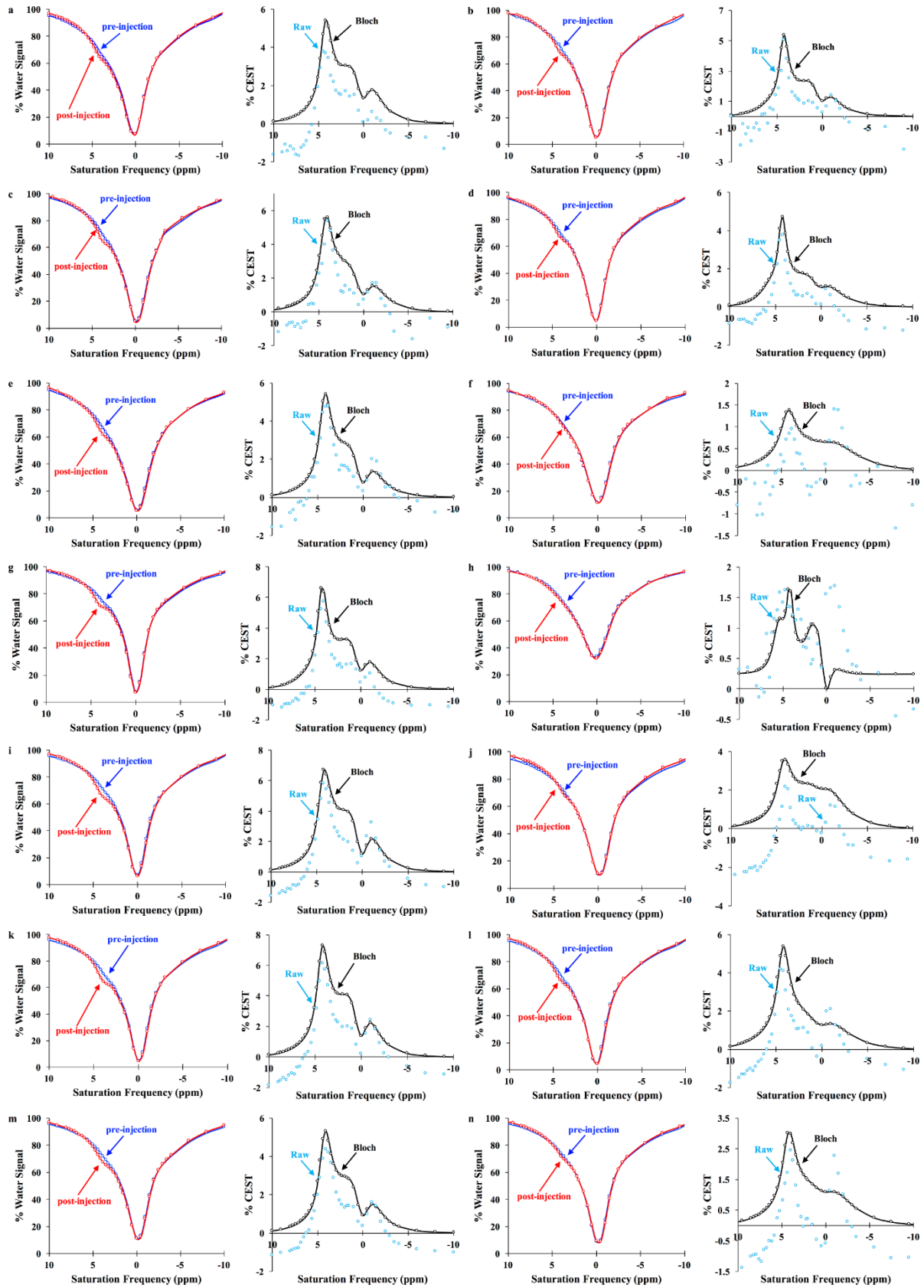
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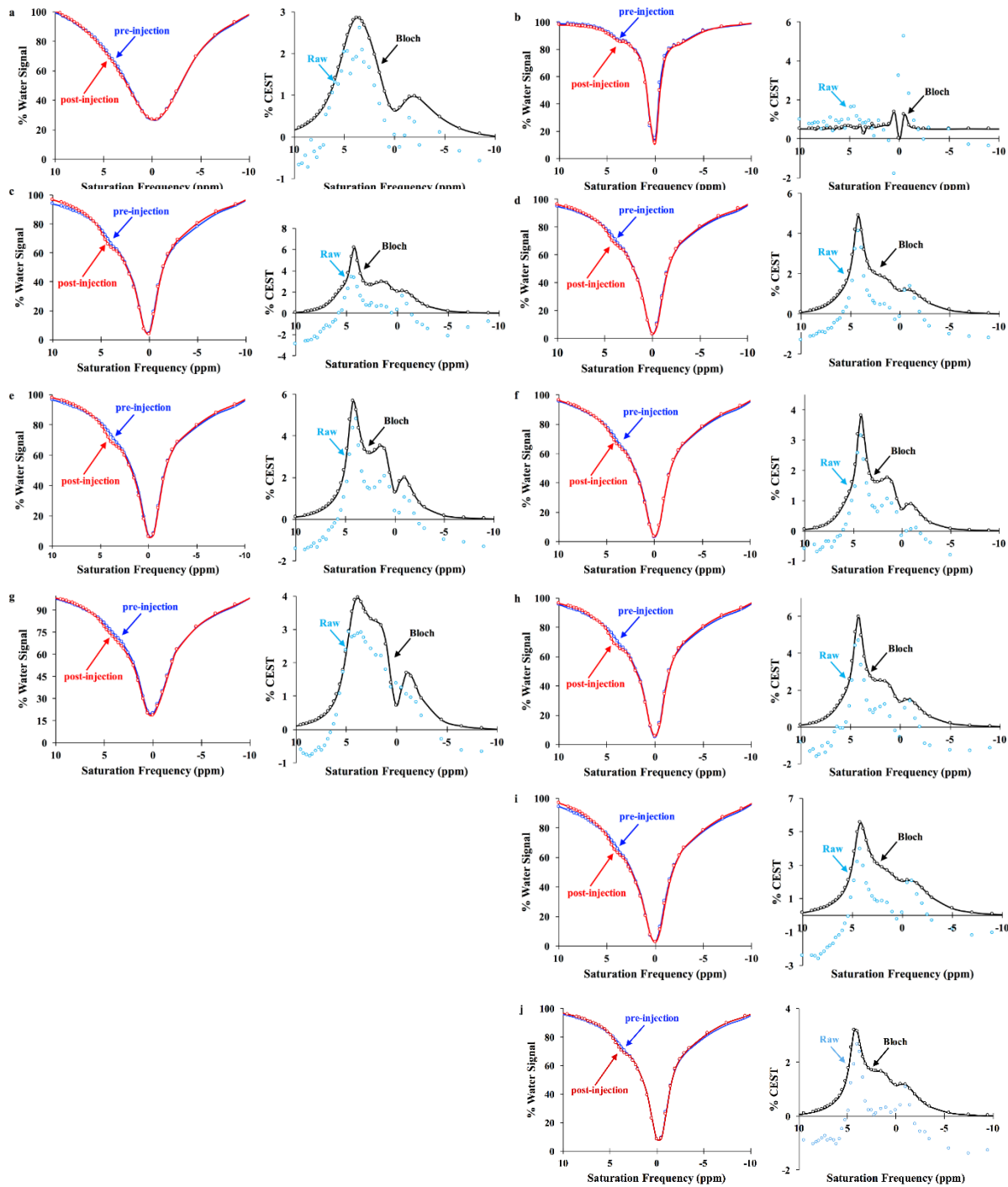
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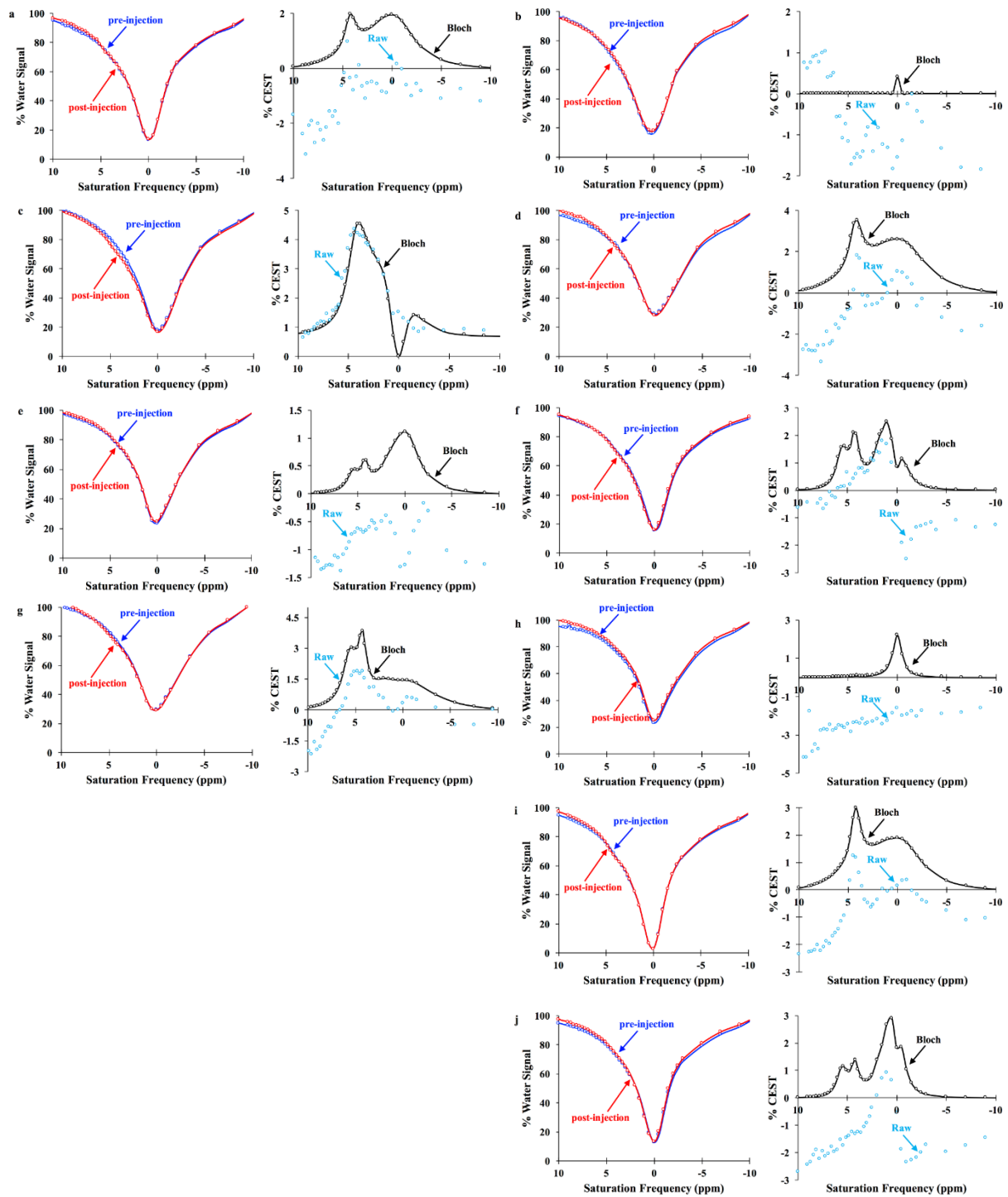
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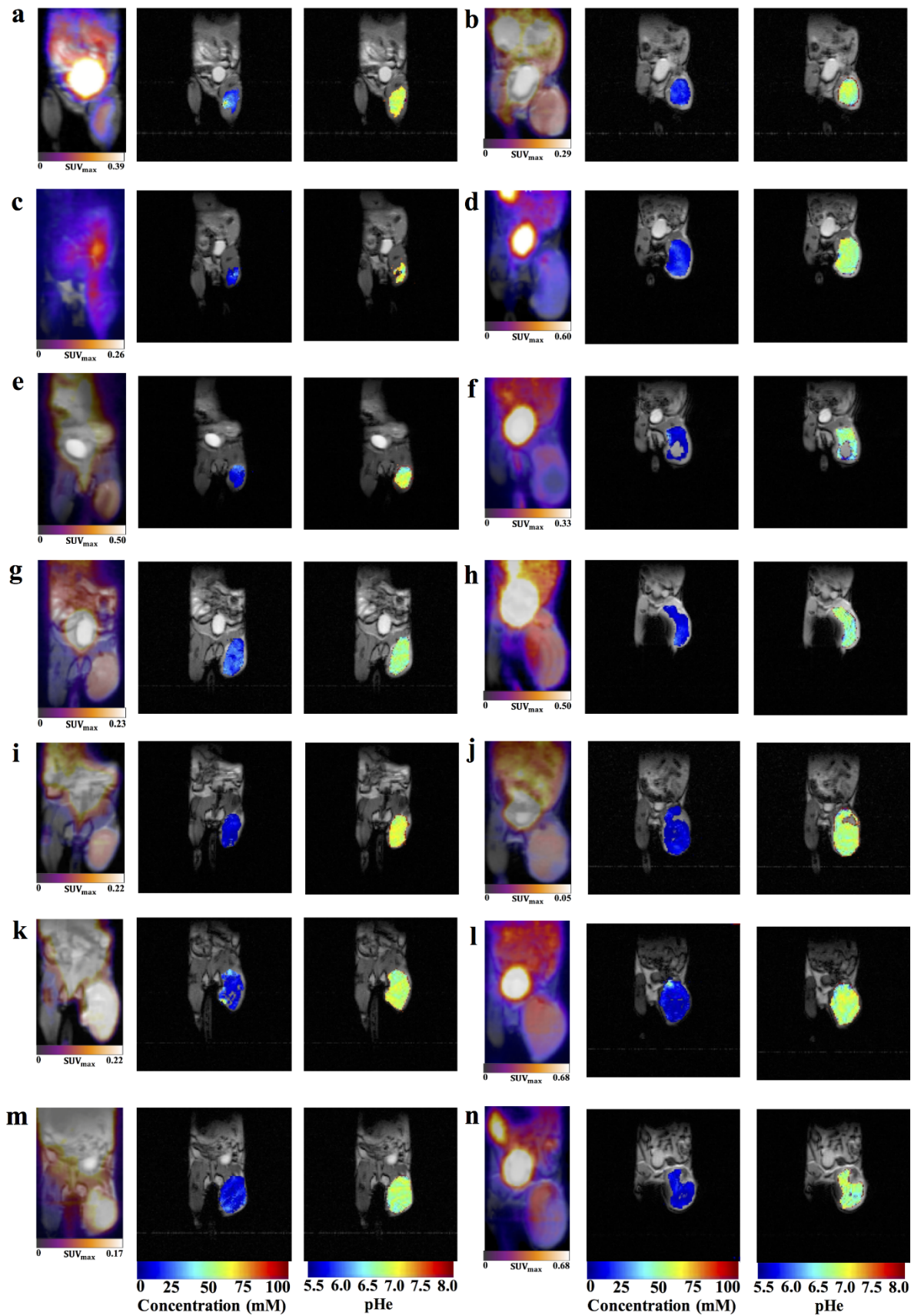
**Supplemental Figure 1. *In vivo* CEST spectra one day before treatment.** Each post-injection spectrum showed lower % water signal than the pre-injection spectrum at 4.2 and 5.6 ppm. The difference between pre-injection and post-injection CEST spectra (blue circles) were fit with the Bloch-McConnell equations modified for chemical exchange (black line). a,c,e,g,i,k,m: Spectra are shown for vehicle-treated mice. b,d,f,h,j,l,n: Spectra are shown for metformin-treated mice.



**Supplemental Figure 2. *In vivo* CEST spectra one day after treatment.** Each post-injection spectrum showed lower % water signal than the pre-injection spectrum at 4.2 and 5.6 ppm. The difference between pre-injection and post-injection CEST spectra (blue circles) were fit with the Bloch-McConnell equations modified for chemical exchange (black line). a,c,e,g: Spectra are shown for vehicle-treated mice. b,d,f,h,i,j: Spectra are shown for metformin-treated mice.

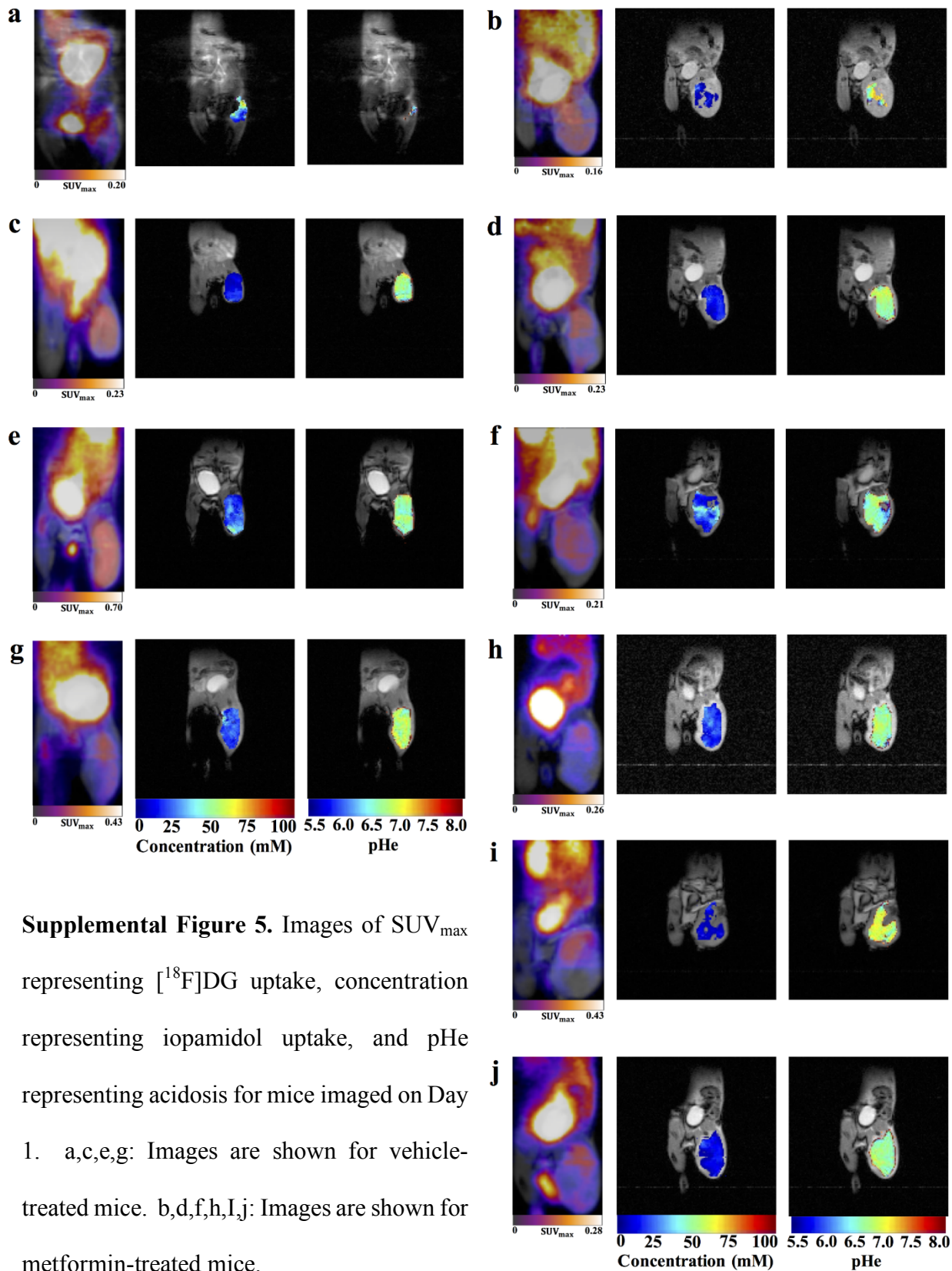


**Supplemental Figure 3. *In vivo* CEST spectra seven days after treatment.** Each post-injection spectrum showed lower % water signal than the pre-injection spectrum at 4.2 and 5.6 ppm. The difference between pre-injection and post-injection CEST spectra (blue circles) were fit with the Bloch-McConnell equations modified for chemical exchange (black line). a,c,e,g: Spectra are shown for vehicle-treated mice. b,d,f,h,i,j: Spectra are shown for metformin-treated mice.

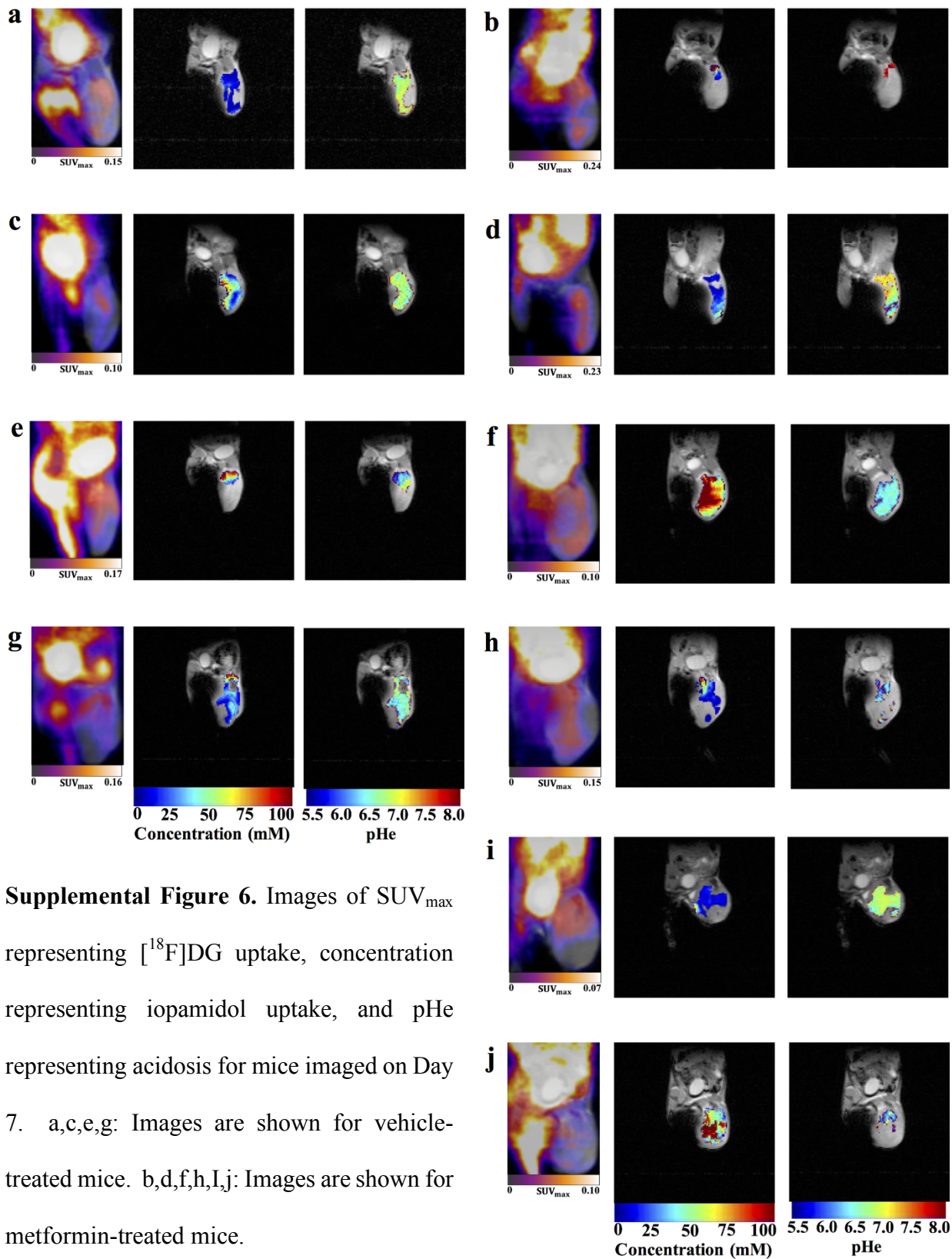




**Supplemental Figure 4.** Images of  $SUV_{max}$  representing [ $^{18}F$ ]DG uptake, concentration representing iopamidol uptake, and pHe representing acidosis for mice imaged on Day -1. a,c,e,g,i,k,m: Images are shown for vehicle-treated mice. b,d,f,h,j,l,n: Images are shown for metformin-treated mice.



**Supplemental Figure 5.** Images of SUV<sub>max</sub> representing [<sup>18</sup>F]DG uptake, concentration representing iopamidol uptake, and pHe representing acidosis for mice imaged on Day 1. a,c,e,g: Images are shown for vehicle-treated mice. b,d,f,h,i,j: Images are shown for metformin-treated mice.



**Supplemental Table 1.** p-Scores for vehicle-treated (untreated) and metformin-treated (treated) mice using both a One Sample Student's t-test, and a Two-Sample Hotelling's T<sup>2</sup> Distribution test.

<b>Day -1 vs Day 1</b>	<b>Untreated</b>	<b>Treated</b>	<b>Treated vs Untreated</b>
<b>Change in pHe</b>	-0.12	0.09	0.23
<b>t-test p-value</b>	0.059	0.35	0.07
<b>Change in mean Suv<sub>max</sub></b>	0.10	-0.24	-0.25
<b>t-test p-value</b>	0.45	0.07	0.17
<b>Change in mean pHe/Suv<sub>max</sub></b>	(-0.12 , 0.10)	(0.09 , -0.24)	(0.23 , -0.26)
<b>Hotelling's T<sup>2</sup> t-test p-value</b>	0.15	0.16	<b>0.03</b>
<b>Day -1 vs Day 7</b>	<b>Untreated</b>	<b>Treated</b>	<b>Treated vs Untreated</b>
<b>Change in pHe</b>	-0.33	-0.53	-0.18
<b>t-test p-value</b>	0.10	<b>0.05</b>	0.48
<b>Change in mean Suv<sub>max</sub></b>	-0.14	-0.35	-0.12
<b>t-test p-value</b>	<b>0.02</b>	<b>0.02</b>	0.39
<b>Change in mean pHe/Suv<sub>max</sub></b>	(-0.33 , -0.14)	(-0.53 , -0.35)	(-0.184 , -0.12)
<b>Hotelling's T<sup>2</sup> t-test p-value</b>	<b>0.03</b>	<b>0.01</b>	<b>0.007</b>