ARMA Modeling for Estimation of Permeability From Perfusion MRI

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Theory and Methods

$$C_{tis}(t) = rC_a(t) \otimes FE' e^{-\frac{FE'}{V_{ees}}t} + r\alpha \quad C_a(t)$$

$$C_{tis}(n) = rC_a(n) \otimes FE' e^{-\frac{FE'T}{V_{ees}}n} + r\alpha \quad C_a(n) + e(n)$$

$$n = 0,1,\ldots, N-1$$

Model Parameters

t = time [min]

$C_a(t)$ = arterial concentration of indicator [ml/g]

$C_{tis}(t)$ = tissue concentration of indicator [ml/g]

F = Flow [ml/gr-min]

FE' = Blood-to-Brain Transfer Constant

V_{ees} = Extravascular, Extracellular Space

α = Microvascular volume fraction

r = (Hematocrit capillary/Hematocrit artery)

Application of Z Transform

$$C_{tis}(Z) = C_a(Z) \cdot \frac{FE'}{1 - e^{-\frac{FE'T}{V_{ees}}} Z^{-1}} + \alpha \quad C_a(Z) + E(Z)$$

$$C_{tis}(Z) - b_1 Z^{-1} C_{tis}(Z) = a_0 C_a(Z) - a_1 Z^{-1} C_a(Z) + \eta(Z)$$

$$b_1 = e^{-\frac{FE'T}{V_{ees}}}, \quad a_0 = FE' + \alpha, \quad and \quad a_1 = -\alpha e^{-\frac{FE'T}{V_{ees}}}$$

Resulting ARMA Model

$$H(Z) = \frac{C_{tis}(Z)}{C_a(Z)} = \frac{a_0 + a_1 Z^{-1}}{1 - b_1 Z^{-1}}$$

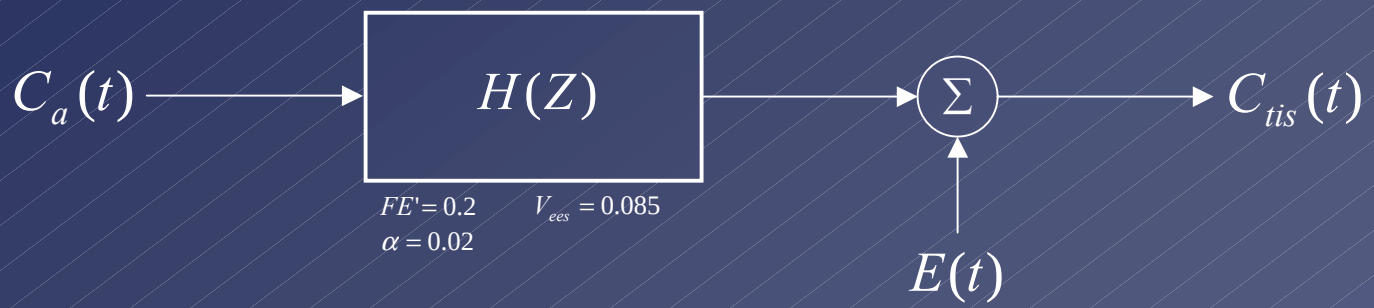
$$E = \sum_{n=0}^{N-1} \left\{ C_{tis}(n) - b_1 C_{tis}(n-1) - a_0 C_a(n) - a_1 C_a(n-1) \right\}^2$$

Parameter Estimation

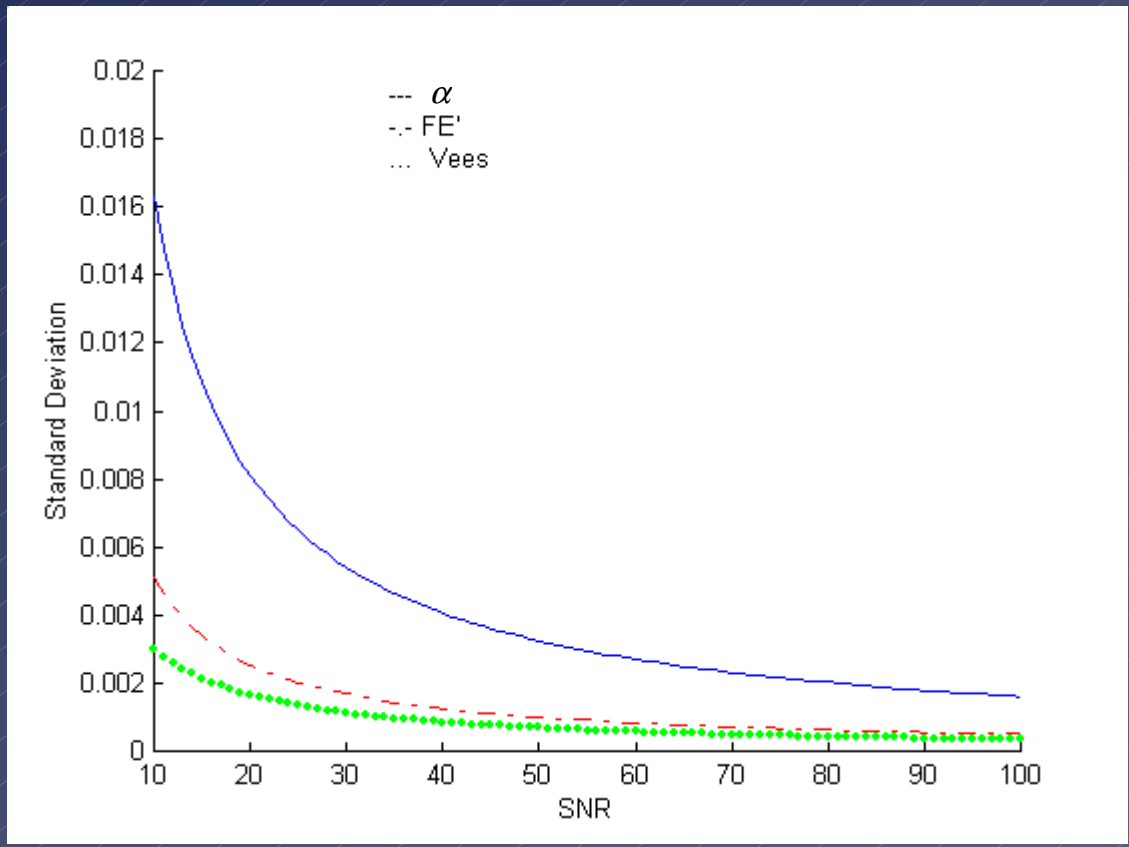
$$\frac{\partial E}{\partial b_1}=0,\quad \frac{\partial E}{\partial a_0}=0,\quad and\quad \frac{\partial E}{\partial a_1}=0$$

$$\begin{cases} b_1\sum_{n=1}^{N-1} C_{tis}{}^2(n-1)+a_0\sum_{n=1}^{N-1} C_a(n)\cdot C_{tis}(n-1)+a_1\sum_{n=1}^{N-1} C_a(n-1)\cdot C_{tis}(n-1)=\sum_{n=1}^{N-1} C_{tis}(n)\cdot C_{tis}(n-1) \\ b_1\sum_{n=1}^{N-1} C_{tis}(n-1)\cdot C_a(n)+a_0\sum_{n=1}^{N-1} C_a{}^2(n)+a_1\sum_{n=1}^{N-1} C_a(n-1)\cdot C_a(n)=\sum_{n=1}^{N-1} C_{tis}(n)\cdot C_a(n) \\ b_1\sum_{n=1}^{N-1} C_{tis}(n-1)\cdot C_a(n-1)+a_0\sum_{n=1}^{N-1} C_a(n)\cdot C_a(n-1)+a_1\sum_{n=1}^{N-1} C_a{}^2(n-1)=\sum_{n=1}^{N-1} C_{tis}(n)\cdot C_a(n-1) \end{cases}$$

Simulation Study



Accuracy of estimated parameters at different noise levels



Simulation Results

- α estimation is very sensitive to noise.
- V_{ees} estimation is robust and is the least sensitive to noise.
- FE' estimation has a good accuracy in experimental noise levels (SNR = 10).

Experimental Procedures

1. Animal Model of Cerebral Tumor

Five hundred thousand U251MGn human glioma cells in 5μl were injected at a rate of 1μl/min into a location 2.5 mm anterior to the bregma, 2.0 mm to the right of the midline, and a depth of 3.0 mm into a rat brain.

2. MRI Procedures

- Rat with 18-day-old tumor
- 0.8 - 1.5% Halothane anesthesia
- 7 Tesla Animal System
- Sequence: TOMROP, TE = 4 ms
- FOV = 32 mm, Matrix Size: 128x64
- Slice thickness = 2 mm
- Imaging time per data set: 84 s

Clinical Significance

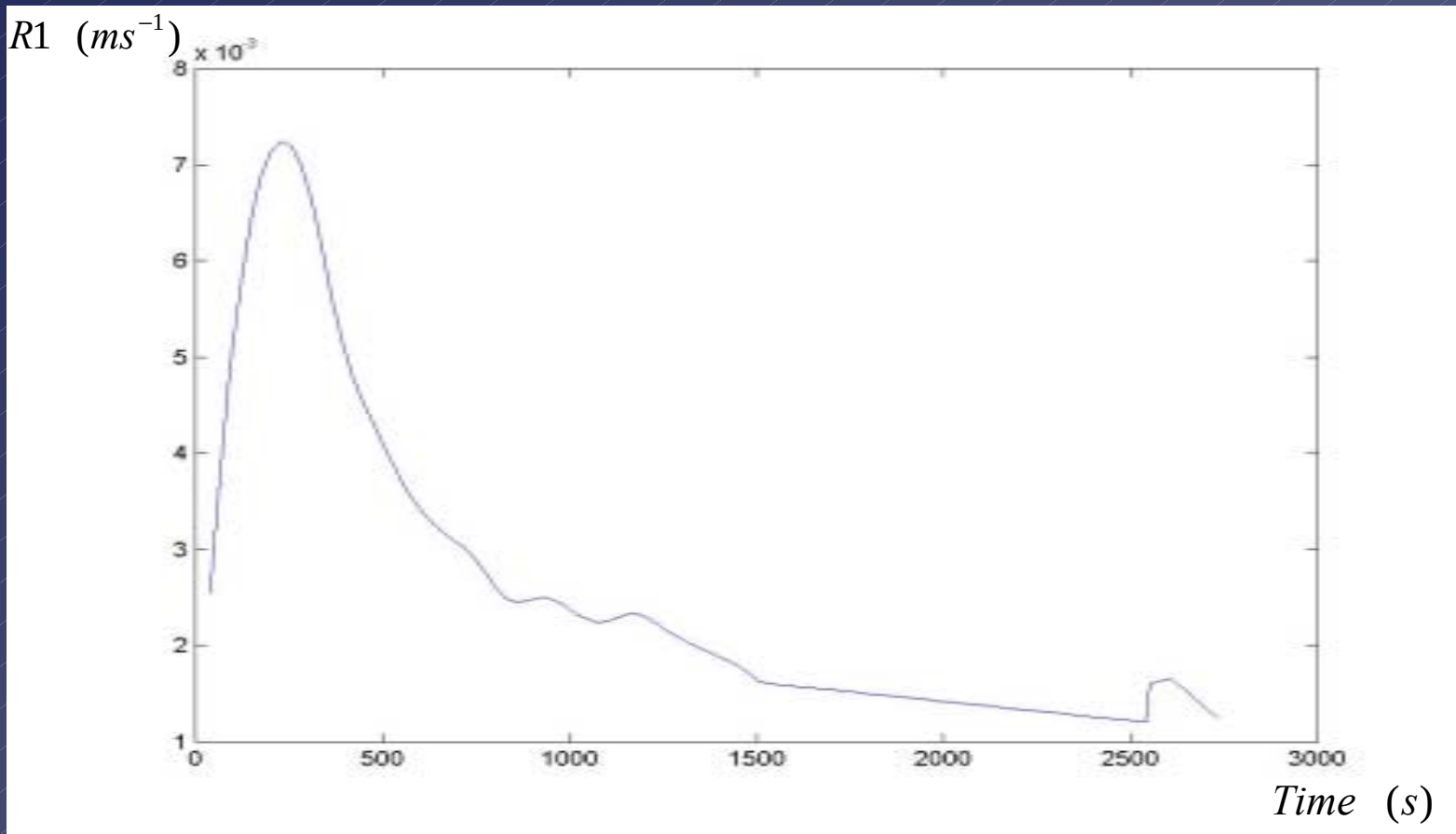
- Tumor microvascular beds are much leakier than normal brain microvasculature.
- Normal vasculature becomes leaky when converted by tumor-induced angiogenesis.
- Increased permeability identifies tumor tissue.
- Anti-angiogenic therapies can be evaluated by quantitative assessments of permeability.

Experimental Results

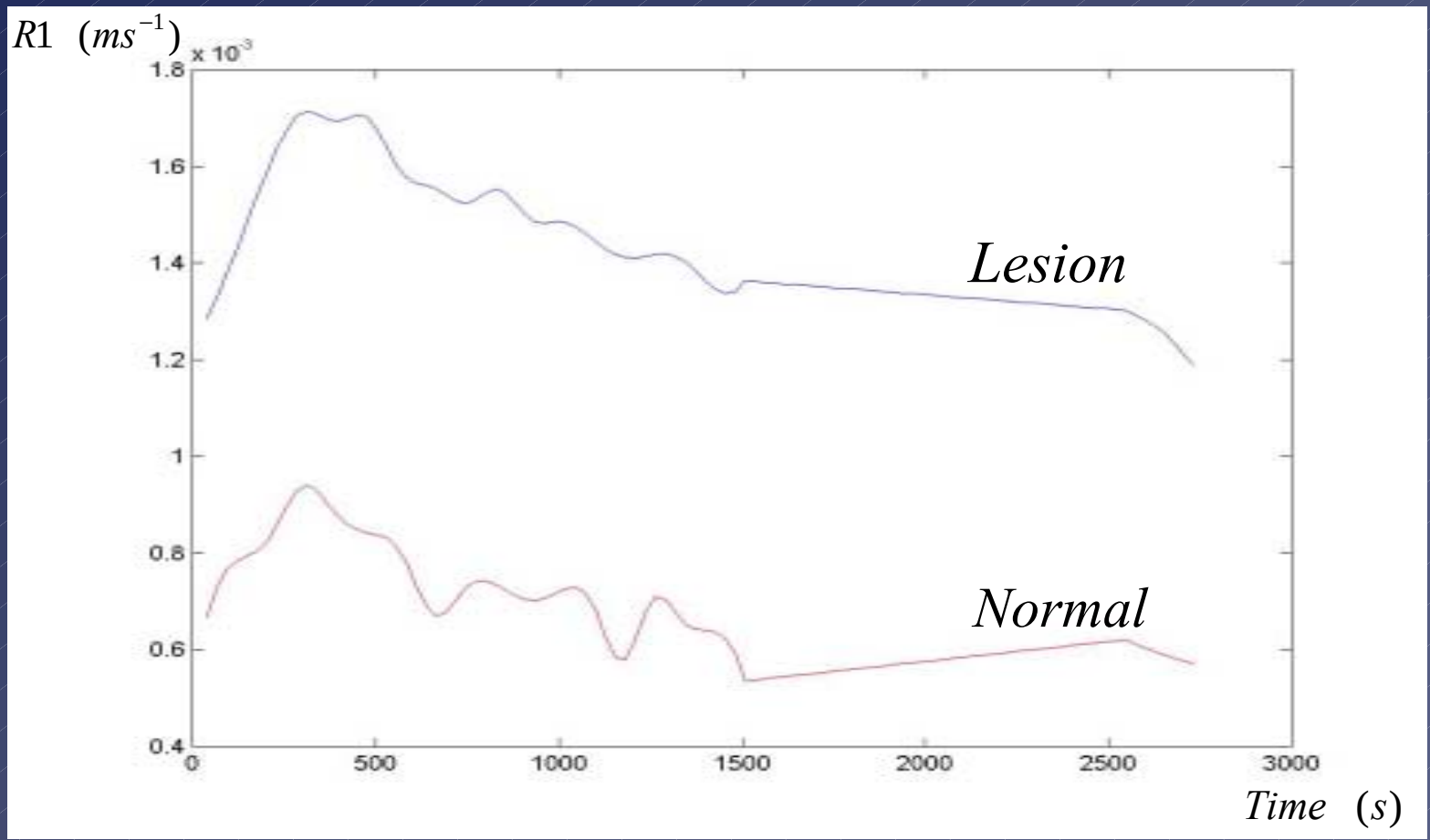
- $C_{tis}(t)$: Values of R1 maps
- $C_a(t)$: R1 values on the sagittal sinus

Gd Concentration in Sagittal Sinus

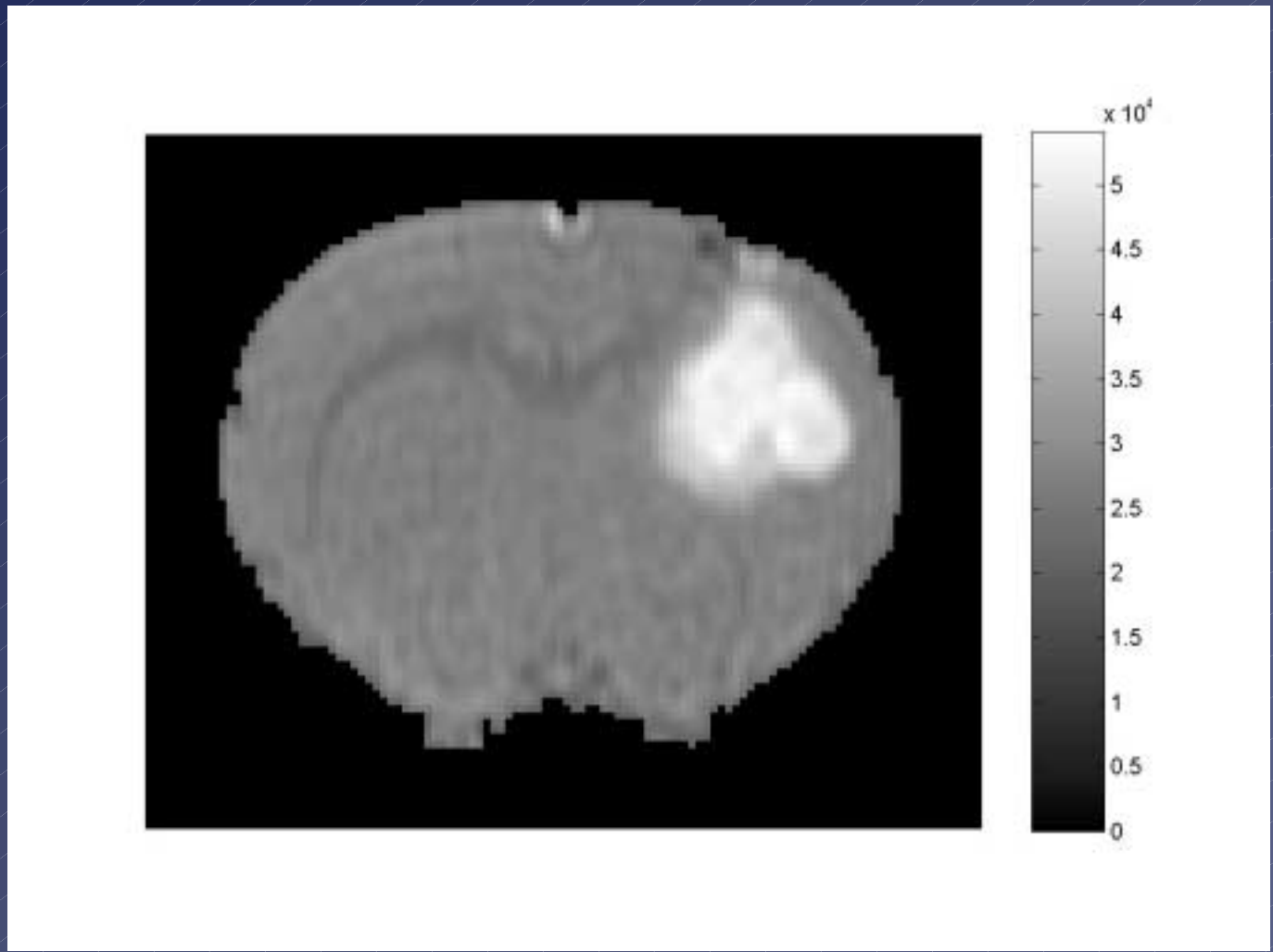
$C_a(t)$



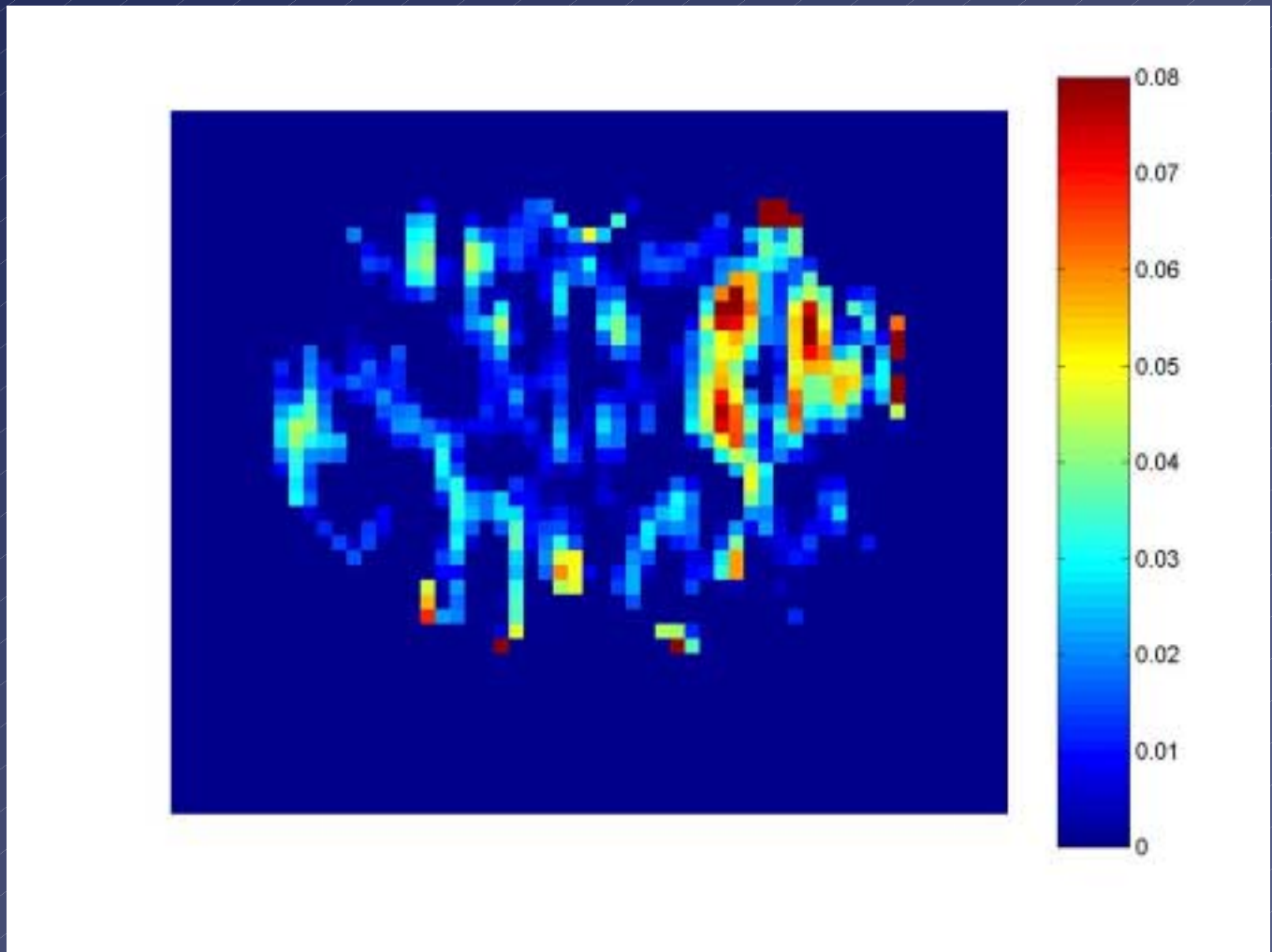
Comparison of Gd Concentration in Normal and Lesion Tissue



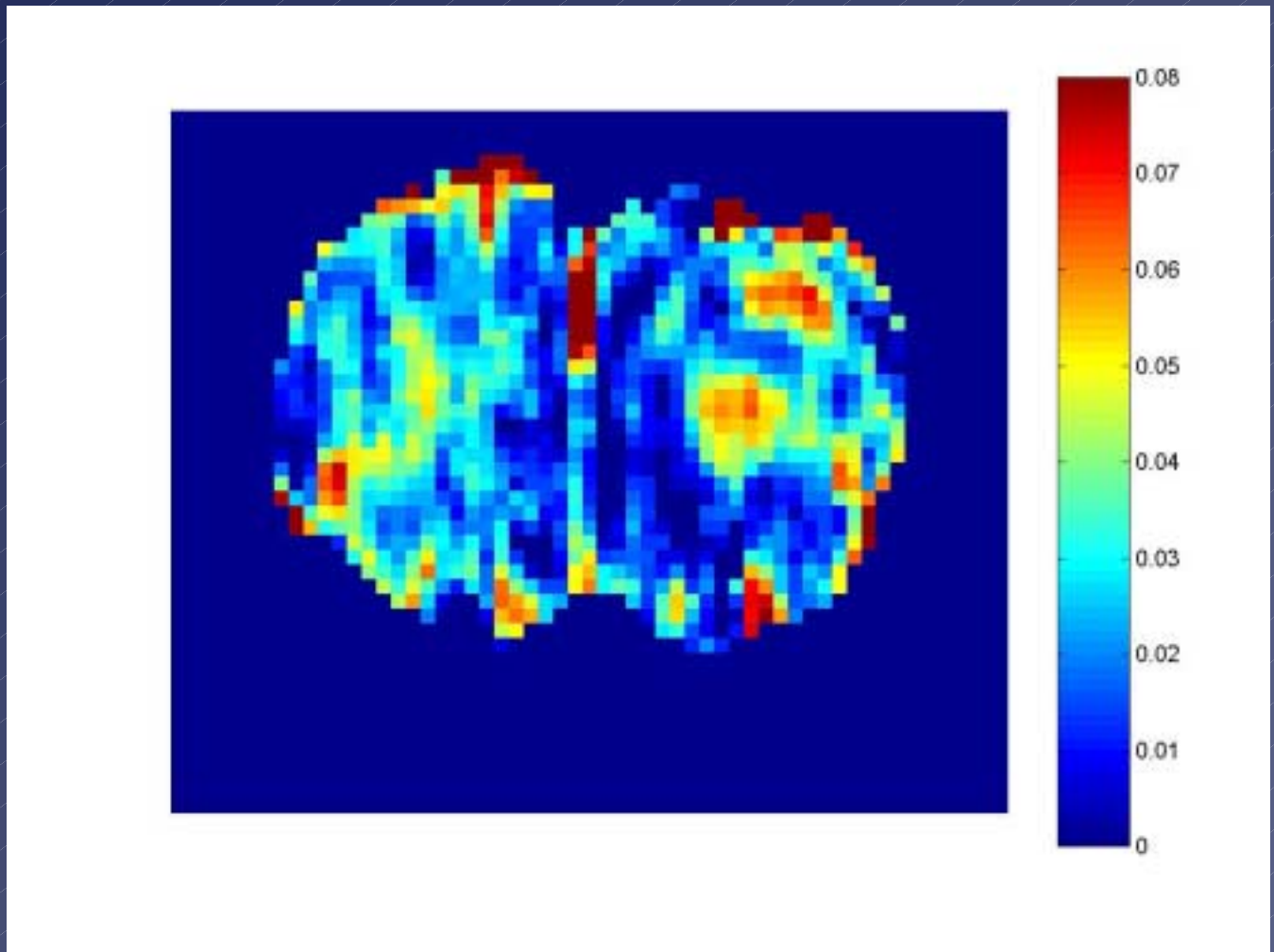
T1-weighted image of rat brain



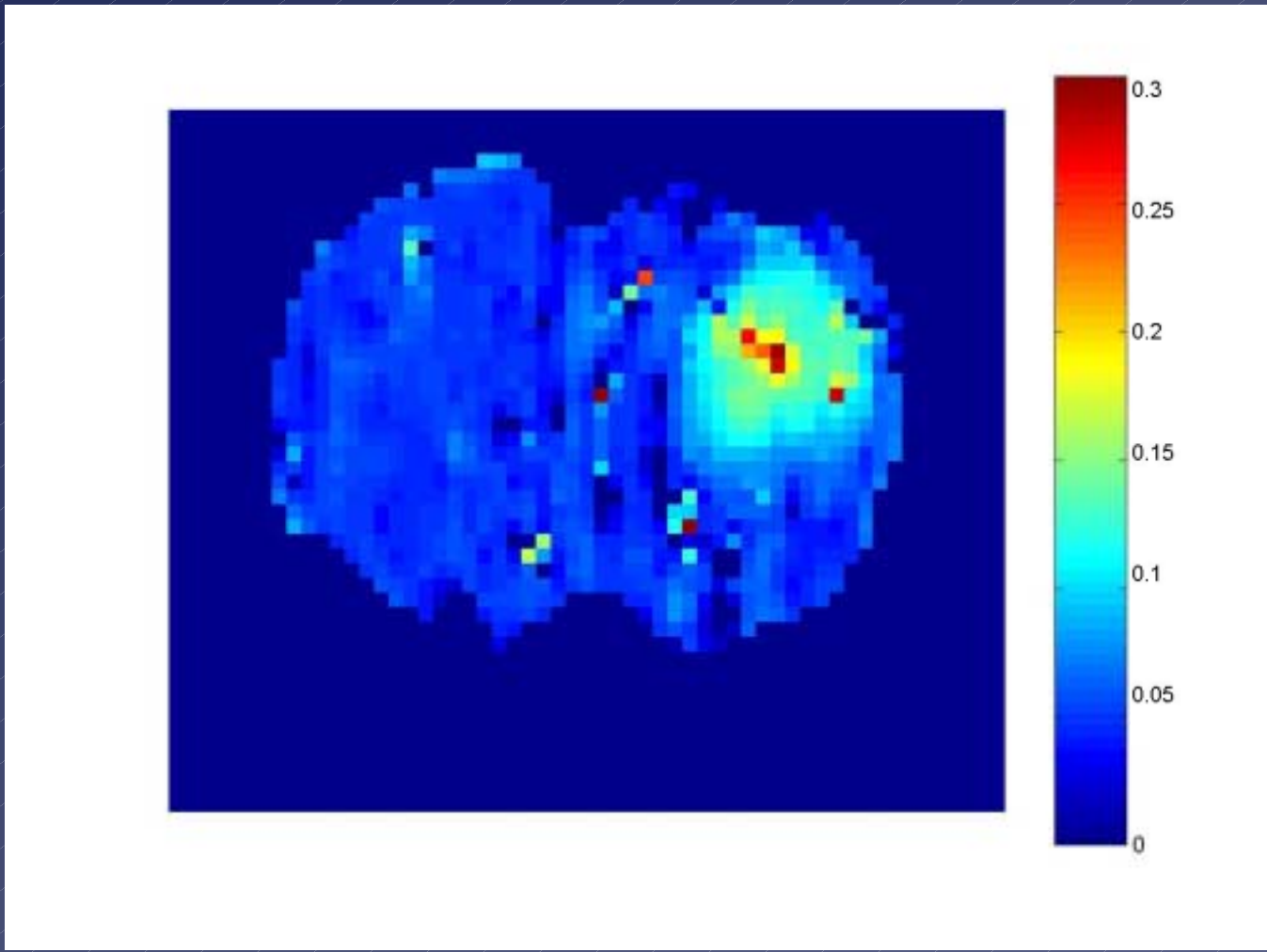
Map of α estimated by ARMA



Map of FE' estimated by ARMA



Map of V_{ees} estimated by ARMA



Conclusions

- Modeling the problem with ARMA, we can use a variety of estimation methods, e.g., LMSE (Least Mean Square Error), MAP (Maximum A Posteriori), and ML (Maximum Likelihood).

- We used LMSE method to estimate BBB parameters. Using a simulation, we showed accuracy of our method. Using rat MRI, we illustrated applicability of the method to real data.

Conclusions

- Tumors have structure reflected in maps of transfer constant, extravascular space, and vascular space.
- Maps of this structure may provide clues to effective therapies.
- Future plan: assess antiangiogenic and antivascular therapies in animal models.

THANKS