MODEL SELECTION FOR MR STUDIES OF STROKE

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Chronic Stroke

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CASE 046

53 YO male arrives in ER at 17:50 by ambulance with L-sided flaccid paralysis, slurred speech, deviation of eyes to right, perseveration. Wife found him lying on floor at 17:30. Patient spoke normally with son at 17:00.

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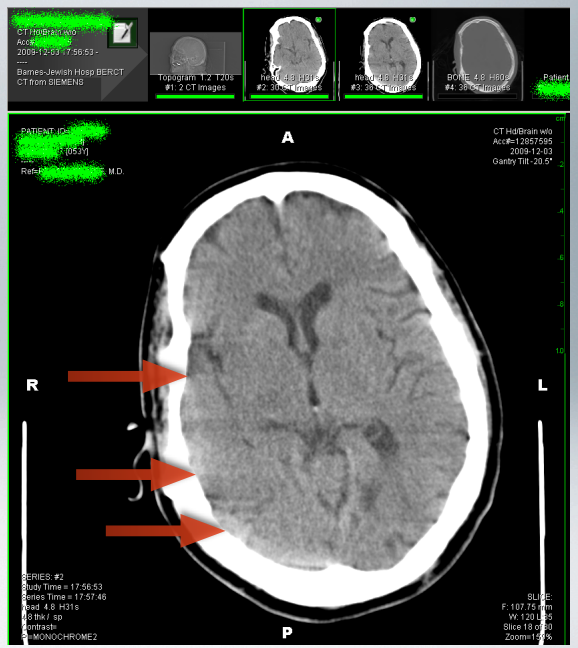

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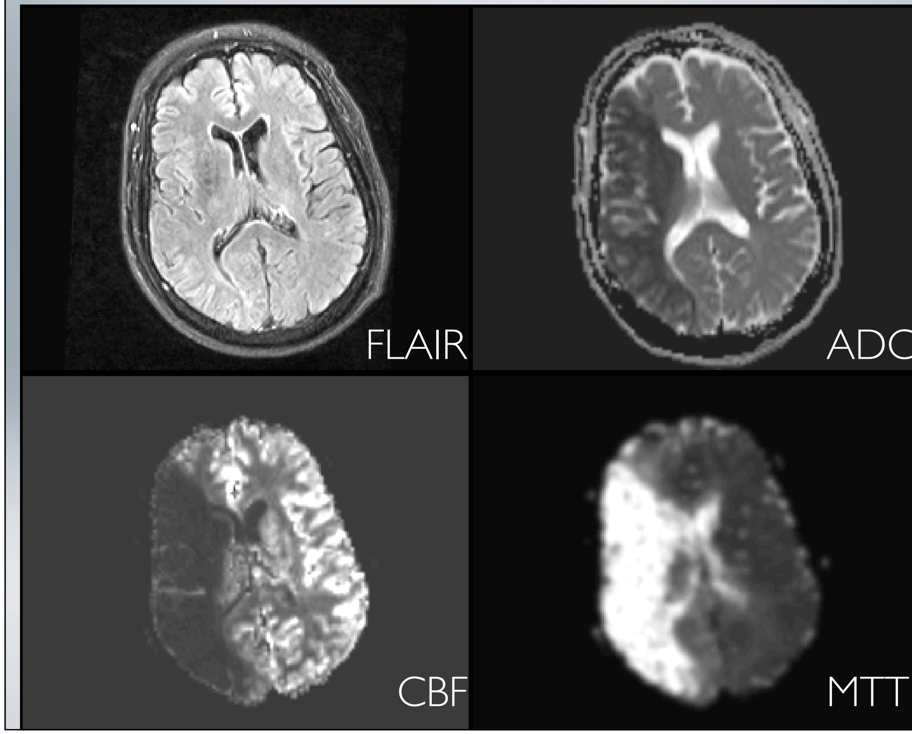
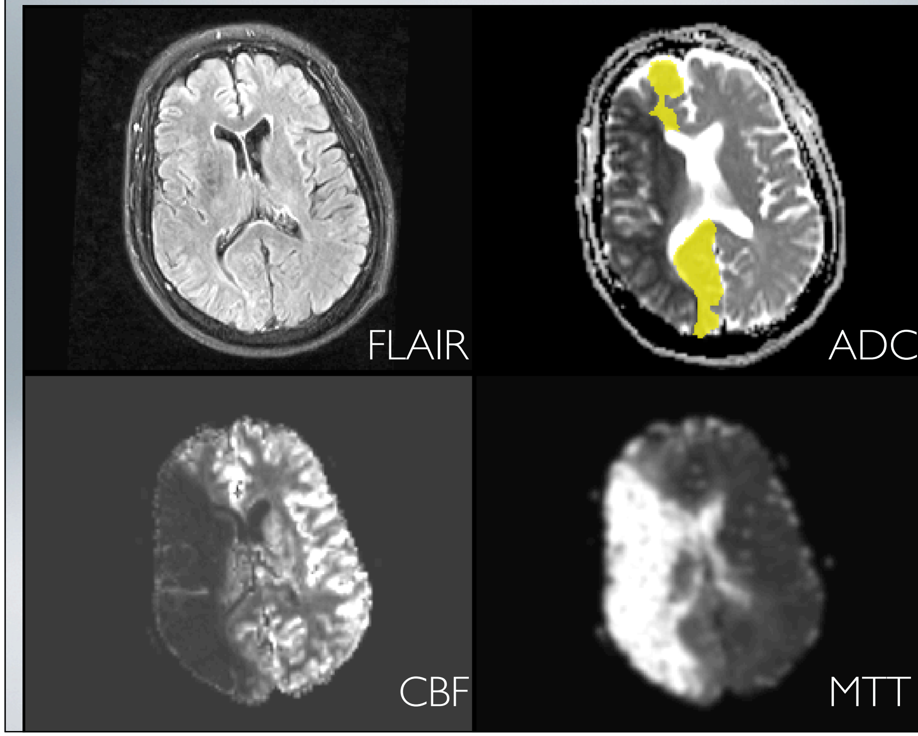
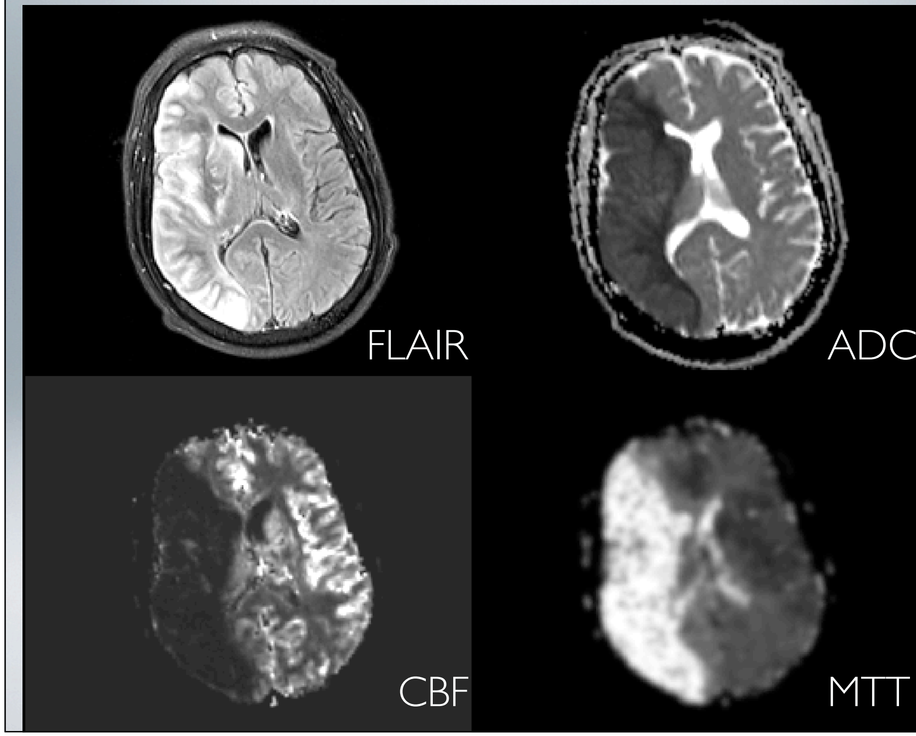
3 HRS



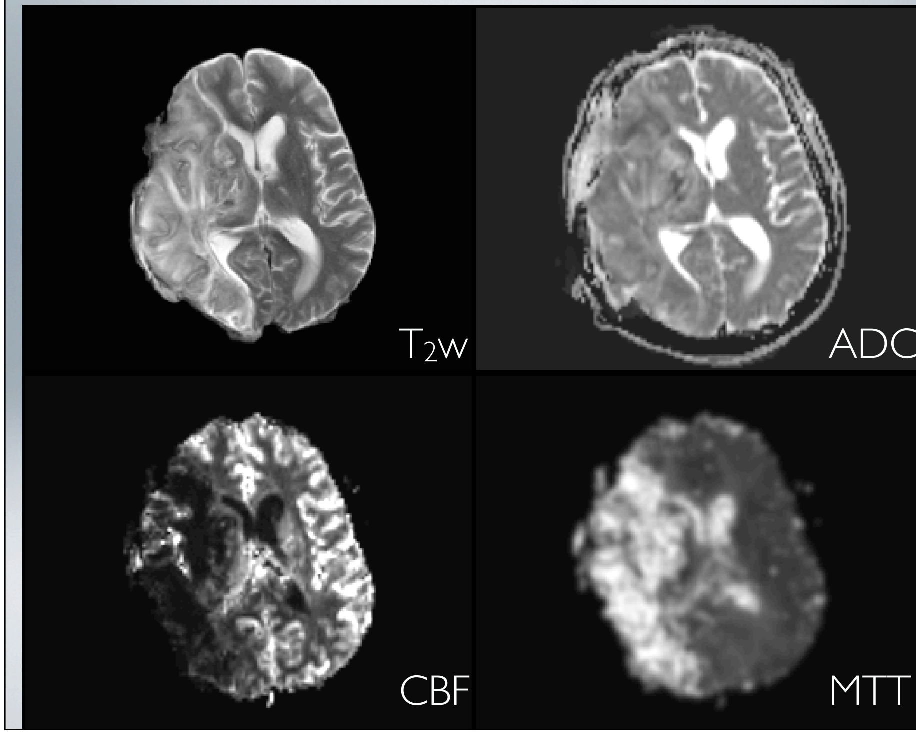
3 HRS



24 HRS



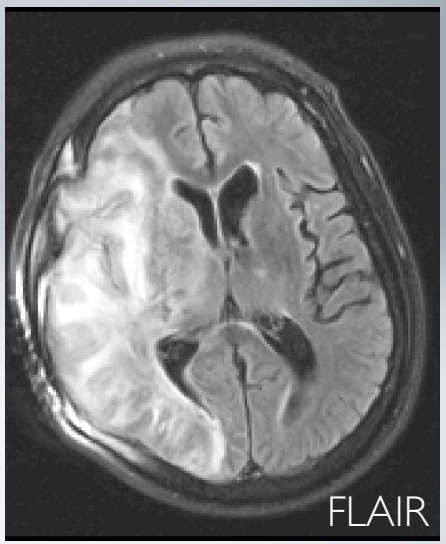
30 DAYS



DISCHARGE SUMMARY

Discharged to rehab. 28 days after admission.

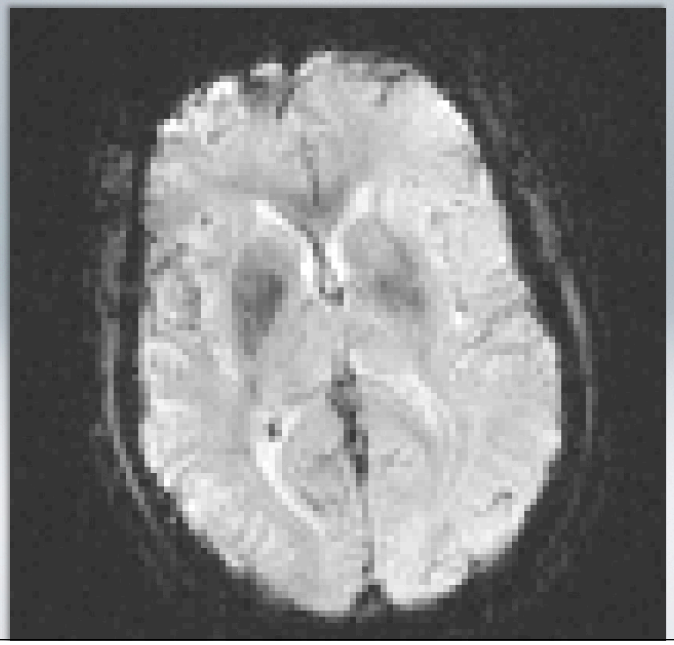
Hospital course:
massive stroke + edema.
Received tPA.
Admitted to NNICU.
Intubated.
Craniectomy x2. Coma.
DNR/DNI per family.
Gradually improved & extubated. Pneumonia.
Remaining dense hemiplegia, hemi-sensory loss,
L homonymous hemianopsia.



CLINICAL TRIALS

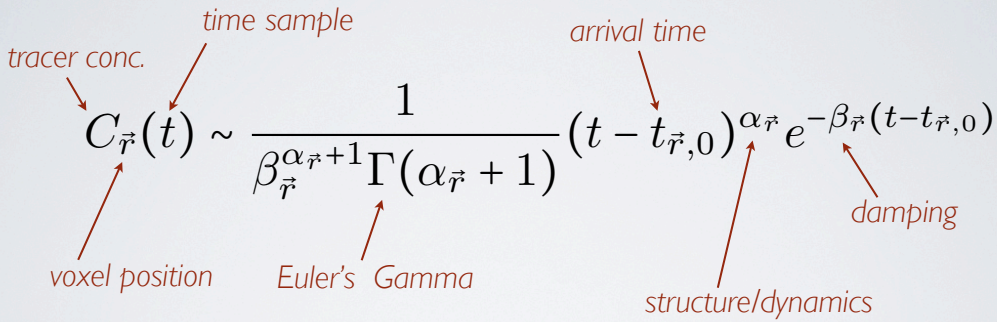
MR perfusion & penumbra estimates have no predictive value for clinical outcomes

EPI, Gd @ 5mL/s



ORGAN PERFUSION

Traditional model for circulating tracer, gamma variate:



"Good" agreement with experiments (best available)

Thompson, Circ. Res. 14:503-515 (1964).

Davenport, Nuclear Med., 24:945-948 (1983).

PERFUSION PER VOXEL

Observed tracer concentration $\boldsymbol{C}$ comprises:

unknown scaling: vascular geometry, tortuosity, variable hematocrit

time sample

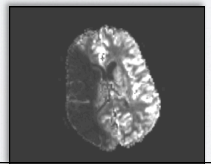
"residue function"

$$\overline{\kappa} C_{\vec{r}}(t) = F_{\vec{r}} R_{\vec{r}}(t) \otimes C_{\vec{r},a}(t)$$

voxel position

cerebral blood flow

tracer conc., arterial supply



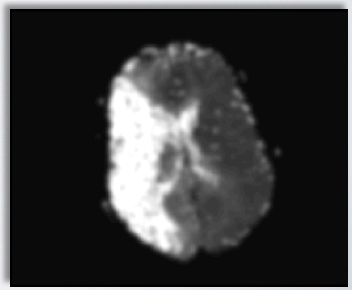
PERFUSION PER VOXEL

Other common perfusion metrics:

Cerebral blood volume (fraction):

$$V_{\vec{r}} = \int^{\infty} dt' C_{\vec{r}}(t') \Big/ \int^{\infty} dt' C_{\vec{r},a}(t')$$

Mean transit time: $T_{\vec{r}} \equiv V_{\vec{r}} / F_{\vec{r}}$, *viz.*



MR

- **Physically:** Bloch equations with fluid dynamics terms *(Torrey, Phys. Rev. 104:563-565 (1956))*
- Impractical for non-Newtonian, pulsatile flow of blood through "disordered" arterial, capillary & venous networks
- ***N.B.:*** upon oxygen-extraction in capillary beds, hemoglobin becomes paramagnetic
- **Traditionally:** assume intrinsic T_1, T_2 dynamics may be factored, leaving stationary relaxivity near the bolus passage of Gd:

$$\frac{\|M_{\vec{r}}(t)\|}{\int^{t_{\vec{r},0}} dt' M_{\vec{r}}(t')} \approx \exp\left[-\int^{t} dt' \mathscr{R}_{\vec{r}}(t')\right] = \exp\left[-\widetilde{\mathscr{R}}_{\vec{r}} \int^{t} dt' C_{\vec{r}}(t')\right]$$

QUESTIONABLE ASSUMPTIONS

- Arterial supply estimated from average of major arterial branches: $C_{\vec{r},a}(t) \Longrightarrow \overline{C_a(t)}$
- $F_{\vec{r}}$, $R_{\vec{r}}(t)$, $V_{\vec{r}}$ estimated from SVD of convolution with averaged arterial supply $\overline{C_a(t)}$ using singular value thresholds ~20%
- Tracer conc. estimated from: $\log \|M_{\vec{r}}(t)\|$
- Not needed by Bayesian inference...

Inverse Problems

BAYESIAN ANALYSIS

Gamma-variate: $\mathscr{G}_{\vec{r}}(\alpha,\beta,t_0,t) \equiv \left[\frac{1}{\beta^{\alpha+1}\Gamma(\alpha+1)}(t-t_0)^{\alpha}e^{-\beta(t-t_0)}\right]_{\vec{r}}$

Residue func.: $R_{\vec{r}}(t) \approx e^{-t/T_{\vec{r}}}\left[\sum_{m=0} c_{\vec{r},m}\left(\frac{t}{T_{\vec{r}}}\right)^{m}\right] \overset{\text{model sel.}}{\Longrightarrow} e^{-t/T_{\vec{r}}}$

Forward Problem:

$$\frac{\|M_{\vec{r}}(t)\|}{\int^{t_{\vec{r},0}} dt' M_{\vec{r}}(t')} \approx \exp\left[-\overline{\kappa}\,\widetilde{\mathscr{R}}_{\vec{r}} \int_{t_{\vec{r},0}}^{t} dt' \int_{t_{\vec{r},0}}^{t'} dt'' \ldots \right.$$

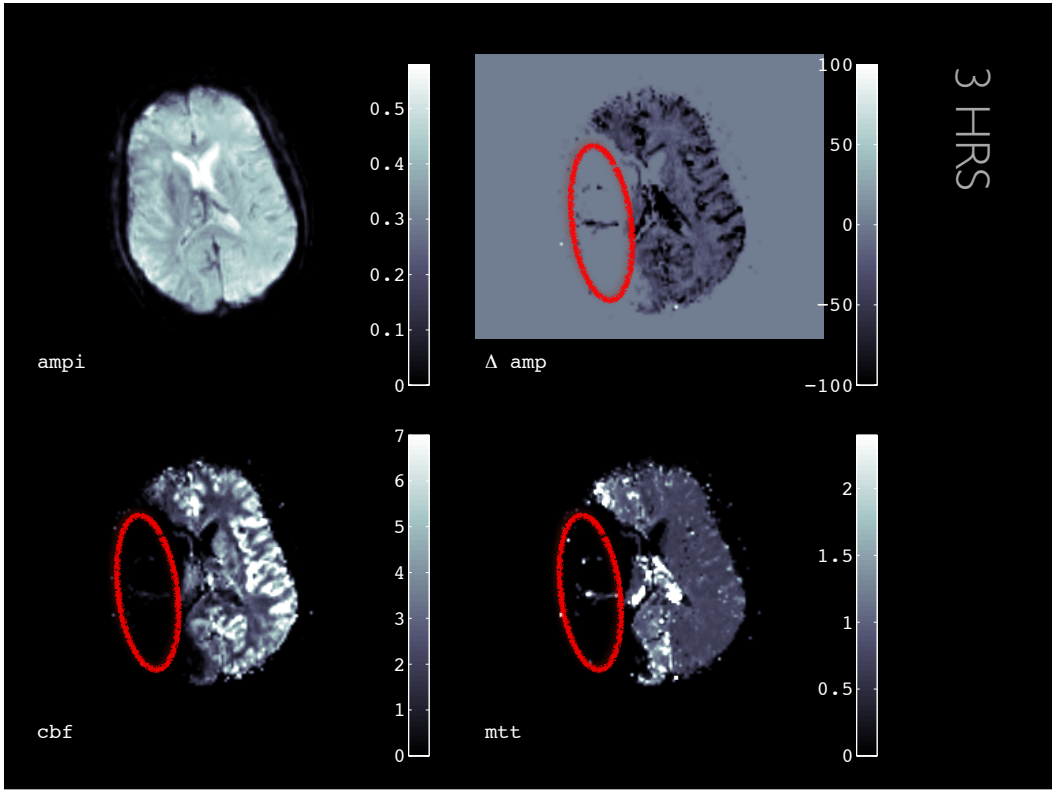
$$\left. \ldots \sum_{\substack{n=0 \\ \text{model sel.}}} F_{\vec{r},n}\,\mathscr{G}_{\vec{r}}(\alpha,\beta,t_{0,n},t'') R_{\vec{r}}(t'-t'',T_{\vec{r}})\right]$$

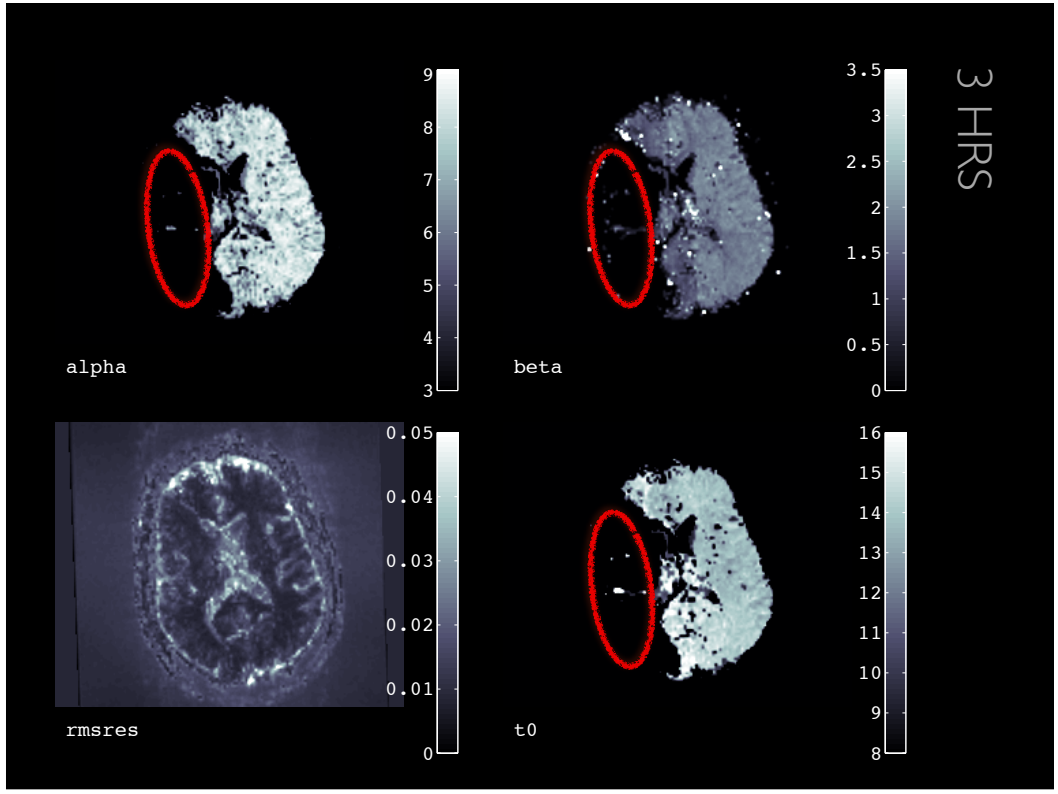
BAYESIAN ANALYSIS

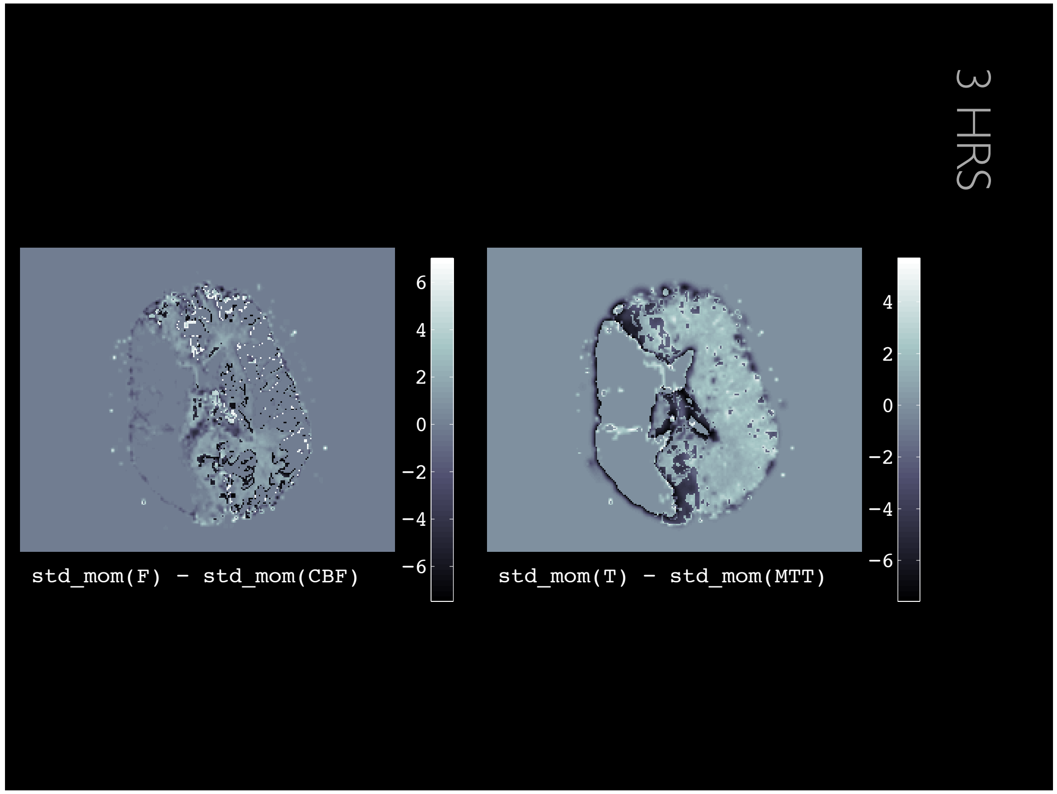
- Priors for parameters factored into independent, physiologically consistent Gaussians
- Marginalized likelihoods from Jeffreys' priors
- Joint posterior probabilities estimated with simulated annealing, Markov-chain Monte Carlo, Metropolis-Hastings sampling

Lee, et al. Magn. Res. Med. 63:1305–1314 (2010)

Shimony, et al. Bayesian Inf. & Max. Ent. Methods in Sci. & Eng. 55:805-815 (2006)


3 HRS
ampi
0.5
0.4
0.3
0.2
0.1
0
Δ amp
100
50
0
-50
-100
cbf
7
6
5
4
3
2
1
0
mtt
2
1.5
1
0.5
0


3 HRS
alpha
9
8
7
6
5
4
3
beta
3.5
3
2.5
2
1.5
1
0.5
0
rmsres
0.05
0.04
0.03
0.02
0.01
0
t0
16
15
14
13
12
11
10
9
8


3 HRS
std_mom(F) – std_mom(CBF)
6
4
2
0
−2
−4
−6
std_mom(T) – std_mom(MTT)
4
2
0
-2
-4
-6

CASE 7377

Chronic moyamoya disease in a 45 YO male with minimal symptoms.

Enrolled in RO1 NS051631-04.

2009 JAN 8

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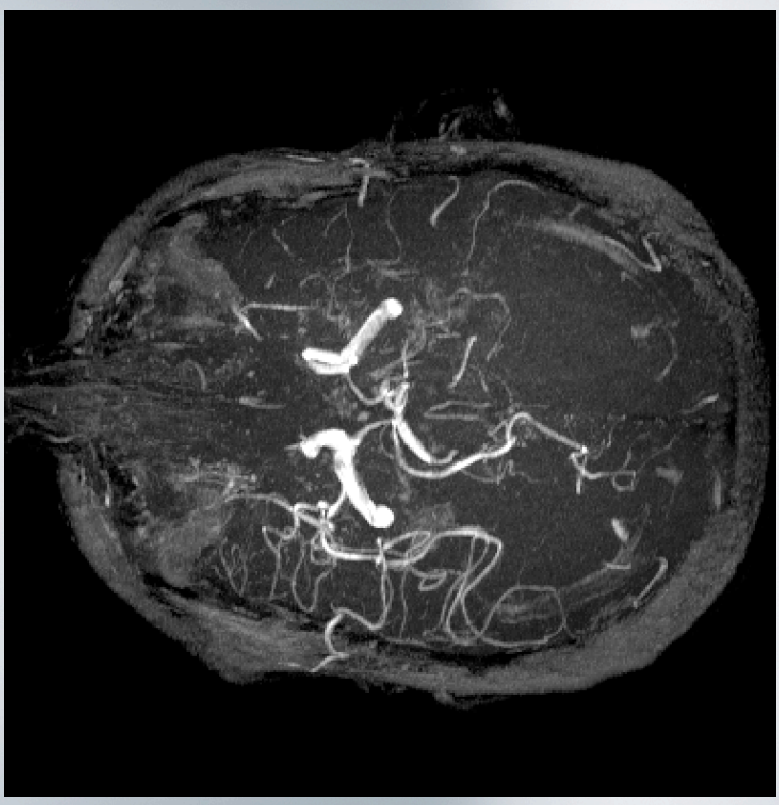

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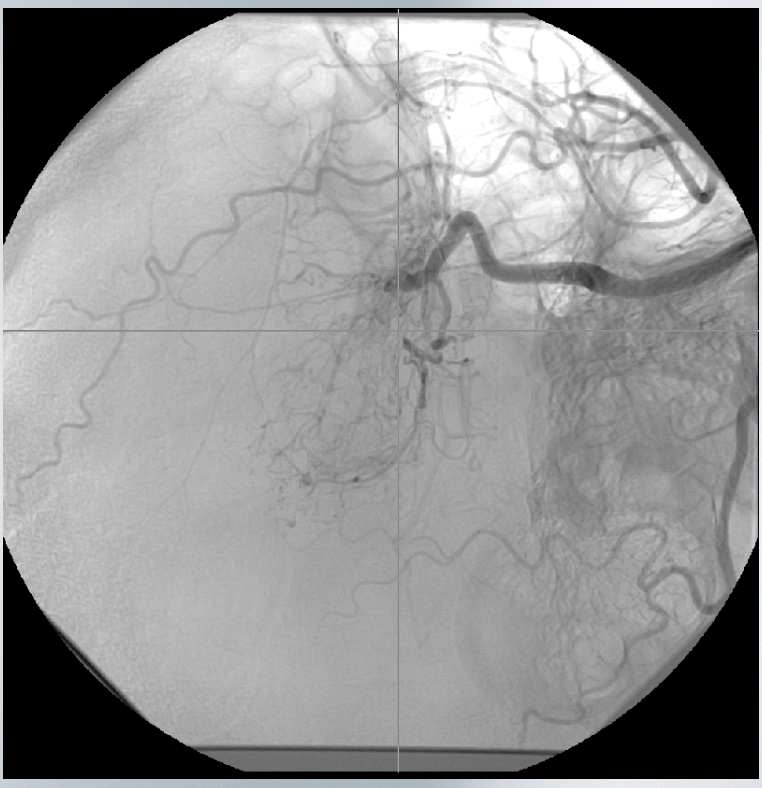
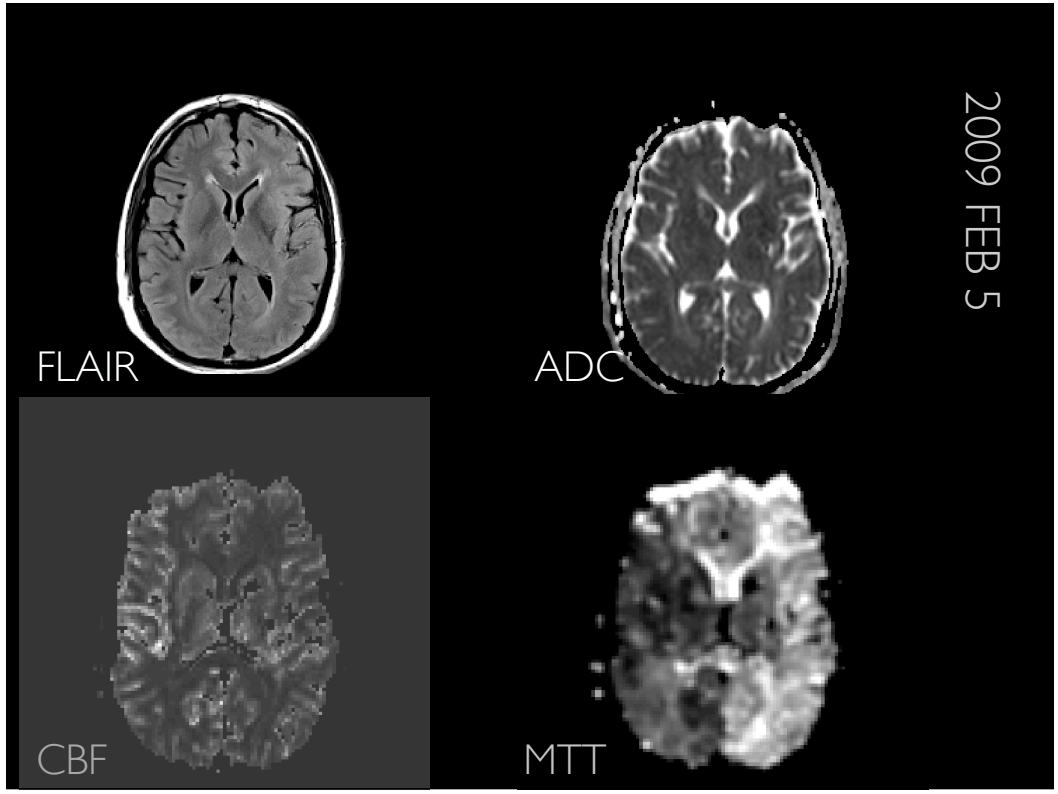
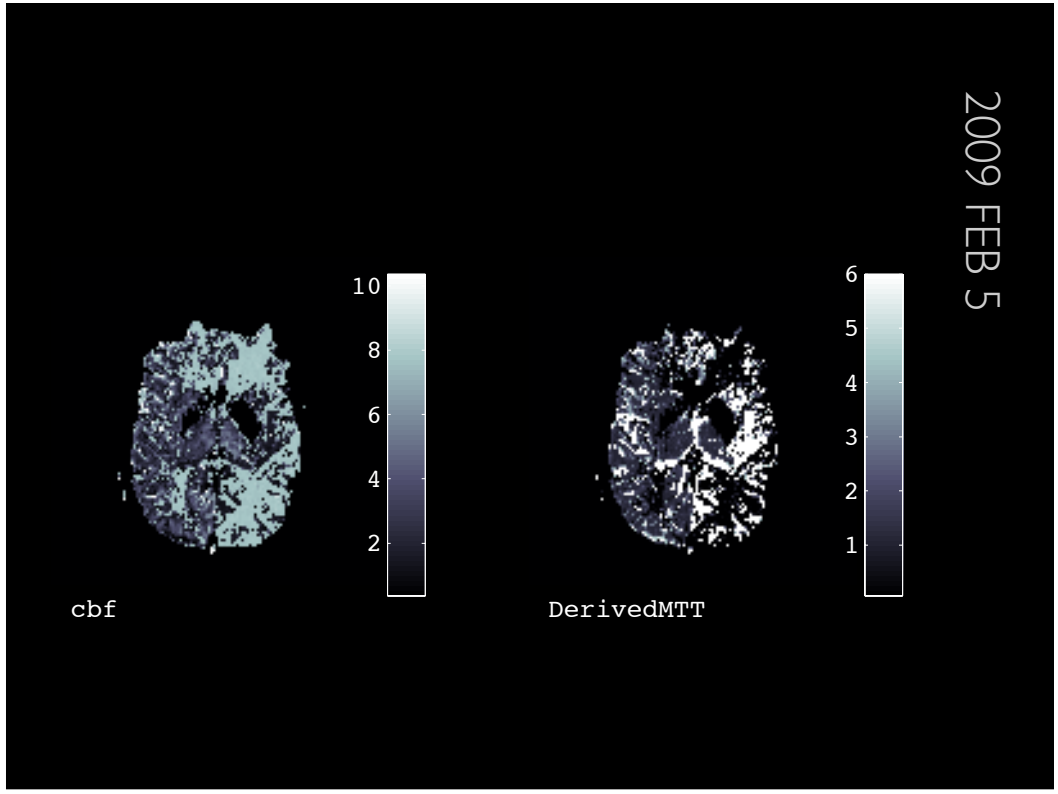
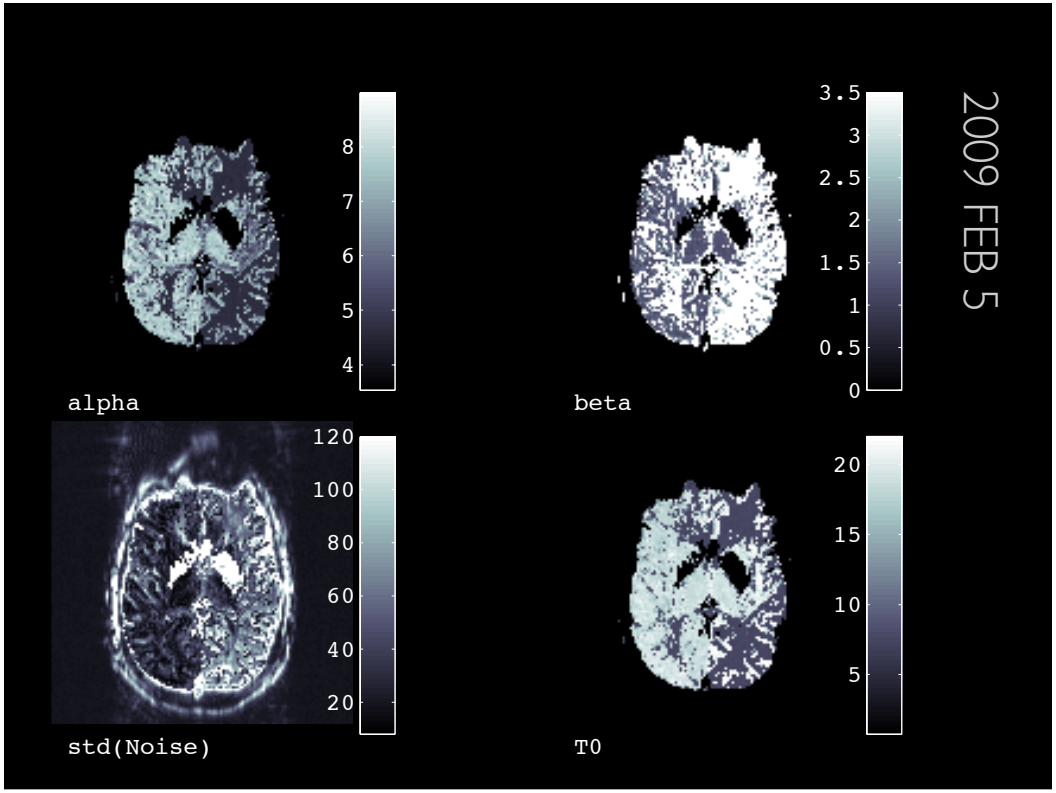
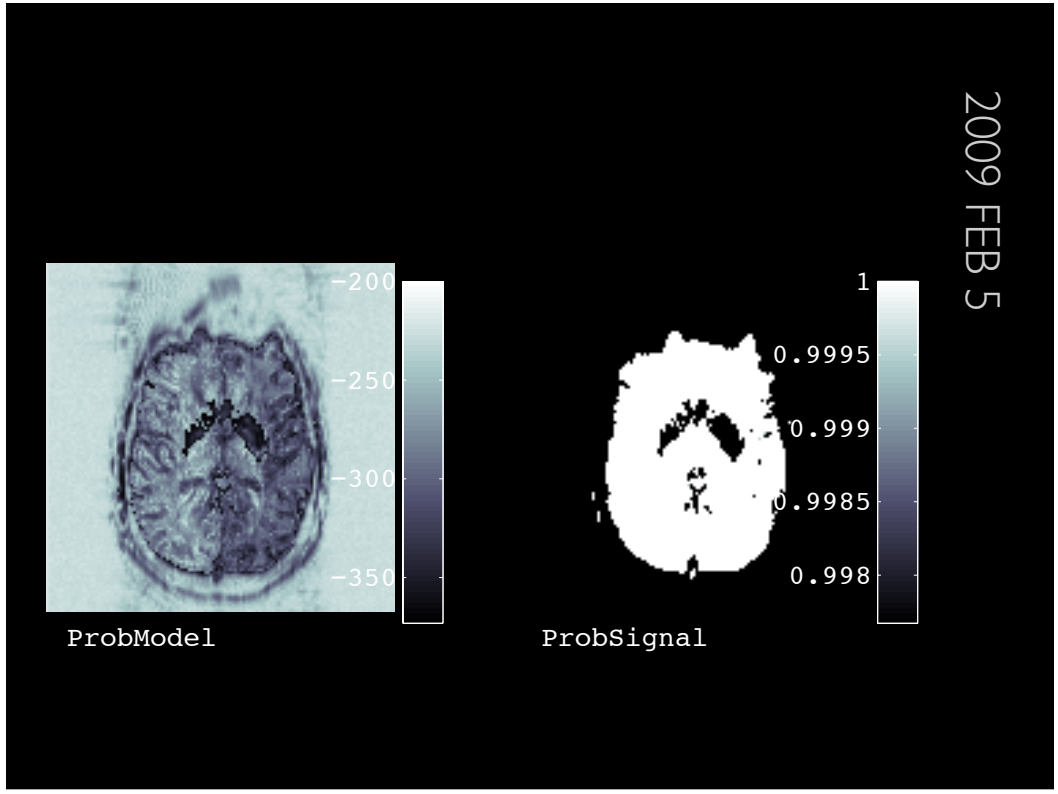


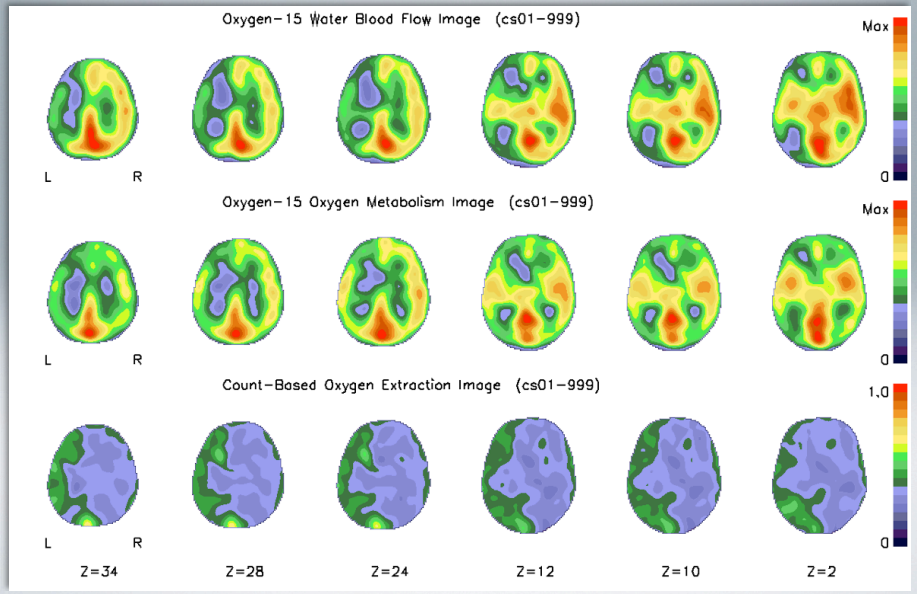

FLAIR
ADC
2009 FEB 5
CBF
MTT


2009 FEB 5
10
8
6
4
2
cbf
6
5
4
3
2
1
DerivedMTT


2009 FEB 5
alpha
8
7
6
5
4
beta
3.5
3
2.5
2
1.5
1
0.5
0
std(Noise)
120
100
80
60
40
20
T0
20
15
10
5


2009 FEB 5
-200
-250
-300
-350
ProbModel
1
0.9995
0.999
0.9985
0.998
ProbSignal

PET



2009 FEB 5

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COMPUTATION

IBM e1350 Cluster: 7x x3950 M2 SMP nodes, 16 quad core 2.4 GHz Xeon E7440 ea., **448 cores, < 17 Tflops** total

Qlogic 9240, DDR 288-port **Infiniband Switch**; 8000F GigE leaf & 8000R GigE aggregation switches

Management, Login, Gateway, General Parallel Filesystem: 9x x3650 M2 nodes, dual quad core Xeon L5520, Mellanox ConnectX 2-port, 4x DDR HCA, 4 Gb HBA ea.

DS4700 **storage controller**: 3x DS4000 EXP810 expansions

Pending: IBM iDataPlex Cluster: 168x dx360 M2 nodes, dual quad core 2.66 GHz Xeon X5550 (Nehalem-EP) ea., **1344 cores, < 57 Tflops** total

Single-model analysis, single perfusion-weighted EPI study:

~10^{17} flop, ~30 min

LARRY'S MCMC

http://bayesiananalysis.wustl.edu

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NEXT STEPS?

- Evidence (marginal likelihood, marginal density of data, prior predictive, *viz*., $Z = \int L(\theta)\pi(\theta)d\theta$)
- More informative priors: clinical information?
- Oxygen metabolism

SUMMARY

MR evaluations of stroke have been unable to predict clinical outcomes.

Bayesian inference provides new models & metrics that may improve evaluation of stroke patients

Clinical trials are underway

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