MODEL SELECTION FOR MR STUDIES OF STROKE

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# ACKNOWLEDGEMENTS

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Chronic Stroke: Hongyu An, Jeffrey Baumstark, Larry Bretthorst, Timothy Carroll, Glen Foster, John Lee
MR, PET & Analysis: Lennis Lich, Mark Nolte, Joshua Shimony, Avraham Snyder, Nick Szoko, Tom Videen
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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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ADC
MTT
FLAIR
CBF
3 HRS
**Hospital course:**
massive stroke + edema.
Received tPA.
Admitted to NNICU.
Intubated.
Cranietomy x2. Coma.
DNR/DNI per family.
Gradually improved & extubated. Pneumonia.
Remaining dense hemiplegia, hemi-sensory loss, L homonymous hemianopsia.

Discharged to rehab. 28 days after admission.
MR perfusion & penumbra estimates have no predictive value for clinical outcomes
EPI, Gd @ 5mL/s
Traditional model for circulating tracer, gamma variate:

\[ C_r(t) \sim \frac{1}{\beta^\alpha r + 1 \Gamma(\alpha r + 1)} (t - t_r, 0)^{\alpha r} e^{-\beta r (t - t_r, 0)} \]

“Good” agreement with experiments (best available)


PERFUSION PER VOXEL

Observed tracer concentration $C$ comprises:

$$\tilde{\kappa} C_r(t) = F_r R_r(t) \otimes C_{r,a}(t)$$

- time sample
- "residue function"
- voxel position
- cerebral blood flow
- tracer conc., arterial supply

unknown scaling:
- vascular geometry,
- tortuosity,
- variable hematocrit
PERFUSION PER VOXEL

Other common perfusion metrics:

Cerebral blood volume (fraction):

\[ V_r = \int_0^\infty dt' C_r(t') / \int_0^\infty dt' C_{r,a}(t') \]

Mean transit time:  \( T_r \equiv V_r / F_r \), 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:

\[
\frac{\| M_r(t) \|}{\int_{t_r,0}^{t} dt' M_r(t')} \approx \exp \left[ - \int_{t_r}^{t} dt' R_r(t') \right] = \exp \left[ -\tilde{R}_r \int_{t_r}^{t} dt' C_r(t') \right]
\]
QUESTIONABLE
ASSUMPTIONS

• Arterial supply estimated from average of major arterial branches: \( C_{r,a}(t) \implies \overline{C_a(t)} \)

• \( F_r, R_r(t), V_r \) estimated from SVD of convolution with averaged arterial supply \( \overline{C_a(t)} \) using singular value thresholds \( \sim 20\% \)

• Tracer conc. estimated from: \( \log \| M_r(t) \| \)

• Not needed by Bayesian inference...
**Bayesian Analysis**

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

Residue func.: \( R_\tau(t) \approx e^{-t/T_\tau} \left[ \sum_{m=0}^\infty c_{\tau,m} \left( \frac{t}{T_\tau} \right)^m \right] \xrightarrow{\text{model sel.}} e^{-t/T_\tau} \)

Forward Problem:
\[
\frac{\|M_\tau(t)\|}{\int_{t_{\tau,0}}^{t_{\tau}} dt' M_\tau(t')} \approx \exp \left[ -\tilde{K} \int_{t_{\tau,0}}^{t} dt' \int_{t_{\tau,0}}^{t'} dt'' \ldots \right] \\
\ldots \sum_{n=0}^\infty \sum_{\text{model sel.}} F_{\tau,n} \mathcal{G}_\tau(\alpha, \beta, t_{0,n}, t'') R_\tau(t' - t'', T_\tau) \]
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

3 HRS

std_mom(F) - std_mom(CBF)

std_mom(T) - std_mom(MTT)
CASE 7377

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

Enrolled in ROI NS051631-04.
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
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
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
ACKNOWLEDGEMENTS

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