Why Perfusion With MRI?

- A number of neurological illnesses can be traced to abnormal blood flow
  - Ischemic Stroke
  - Cerebral Neoplasia
  - Many, many others, from Alzheimer’s to MS

- MRI is heavily used already
- It works!
Tracer Measurement over time
Dynamic DSC Perfusion Data

Seconds

MRI image removed due to copyright restrictions.
DWI / PWI mismatch vs. Final Infarct

Four MRI images removed due to copyright restrictions.
Better outcomes with earlier treatment

Meta-analysis of 6 trials, 2775 patients


Figure 3: Model estimating odds ratio for favourable outcome at 3 months in rt-PA-treated patients compared with controls by OTT

Adjusted for age, baseline glucose concentration, baseline NIHSS measurement, baseline diastolic blood pressure, previous hypertension, and interaction between age and baseline NIHSS measurement.

Diffusion and Perfusion in Stroke

- DWI is now widely used
- PWI is in increasing use
  - No approved contrast agent
  - Most use some sort of timing map (e.g., time to peak)
  - ASL continues its testing / development
- Desmoteplase or other innovations suggest MRI use may become more widespread
The so-called ‘ischemic penumbra’ -- now accepted (too widely?)

Initial core \(=\) DWI Lesion
Or maybe CT edema?

Initial PWI Lesion

Follow-up Infarct (can be variable)
MTT ≠ Tissue at Risk

N= 90; see Schaefer et al AJNR 24 (2003): 436

• DWI is core, but PWI not penumbra when PET is used.
Heiss et al Stroke 2004 35(11 Suppl 1)2671

Courtesy of Dr. Pamela Schaefer. Used with permission.
Problems (and Potential Solutions)

• Monitoring Treatment?
• Closing the gap between imaging and clinical outcome
  – Location matters!
• MTT as currently calculated may be overestimating due to delay
  – Choice of AIF? (delay, dispersion)
  – New CBF approaches: Local AIF, circular deconvolution
• Other markers besides perfusion
  – Microvascular status
  – Vasomotion
• Imaging Time: still too much time in the scanner
Monitoring Treatment with Diffusion / Perfusion MRI

- A number of clinical trials have DWI/PWI now as endpoints

- One new treatment: hyperoxia for ischemic stroke

- Evidence that treatment with 100% oxygen at room pressure widens the therapeutic window
Example: NBO attenuates DWI abnormalities
72-yr woman with right MCA stroke, treated with NBO

Baseline (13 hrs after onset)
Large DWI lesion
Larger MTT lesion
RMCA occlusion

During NBO (after 4 hrs)
DWI lesion smaller (arrows)
Stable MTT
Stable RMCA occlusion

Post-treatment (after 24 hrs)
DWI lesion growing
MTT smaller
Stable RMCA occlusion

Singhal et al MGH

Images removed due to copyright restrictions.
NBO: mostly transient effects!

Images removed due to copyright restrictions.
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Lesion Size Alone Correlates Moderately

- **RANNTAS** *(Stroke 1999 30:293-298):*

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>All infarcts (95% CI)</th>
<th>Visible infarcts only (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI (n=150)</td>
<td>0.43 (0.28-0.58)</td>
<td>0.46 (0.29-0.64)</td>
</tr>
<tr>
<td>GOS (n=170)</td>
<td>0.53 (0.40-0.65)</td>
<td>0.59 (0.47-0.71)</td>
</tr>
<tr>
<td>NIHSS (n=131)</td>
<td>0.54 (0.41-0.68)</td>
<td>0.56 (0.40-0.71)</td>
</tr>
<tr>
<td>Mortality (n=191)</td>
<td>0.31 (0.18-0.45)</td>
<td>0.32 (0.16-0.49)</td>
</tr>
</tbody>
</table>

- **ASPECTS** *(Lancet 2000 355:1670): r=0.56*
Why doesn’t imaging better predict / improve outcome?

• Specificity of techniques
  – Not all lesions are equal

• The Real Estate factor:
  – Location
  – Location
  – Location
This is in part because location matters...

Day 8 NIHSS = 11
Volume ~ 2 cm³

Day 8 NIHSS = 2
Volume ~ 2 cm³
Atlas-based approach markedly improves imaging-based predictions of outcome

\( n=46, \ p<0.01 \)

Figure by MIT OpenCourseWare.
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Global versus local AIF

Global AIF

Local AIF

$t = 16.5$ sec
$t = 21.0$ sec
$t = 25.5$ sec

Lorenz / Benner / Sorensen - Martinos MGH + HST

Estimation of CBF vs. AIFs

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MRI Measure of Vasomotion

- Shot-to-shot variability of SI in MRI time series due to noise:
  - Non-physiological (e.g., thermal, scanner)
  - Physiological (e.g., cardiac, respiratory, vasomotion)
MRI Measure of Vasomotion

- Noise quantified via standard deviation (SD) or variance maps
- No spatial distribution for non-physiological noise
  - Regional differences in SD reflect physiological noise
- CSF: cardiac, respiration
- Parenchyma: vasomotion
Methods

- Subjects: 32 acute stroke patients
- MRI (1.5 T): Acute Perfusion: <12 h, TR=1.5s, 1.7 mm resolution
  - Follow-up T2: >5 d
- CBF and CBV maps calculated from PWI
- Pre-bolus PWI (~15 images) used to calculate SD maps
SD Differences in Normal Tissue

- SD-PWI differences seen in normal tissue regions
- Normal white SD < normal gray SD (31 of 32 patients)

SD Differences in Ischemia

- No clear boundary with which to draw outlines
- Applied CBF, CBV lesion outlines to SD maps

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A Key to Speeding Up Scans?

Photos removed due to copyright restrictions.
See, for example, http://www.nmr.mgh.harvard.edu/~fhlin/reprints/abstracts/ismrm2005_96channel_array.pdf
Why Perfusion MRI In Cancer?

- Correlation of angiogenesis with tumor grade
- Perfusion measures capillary hemodynamics, which may in turn reflect angiogenesis

- Measure:
  CBV = cerebral blood volume
  CBF = cerebral blood flow
The first *in vivo* images of tumor angiogenesis

*American Journal of Roentgenology*

1939 42:891-899

Ide AG, Baker NH, Warren, SL. Vascularization of the Brown Pearce rabbit epithelioma transplant as seen in the transparent ear chamber
Tumor Perfusion MRI: Two basic types

• Dynamic Susceptibility Contrast MRI
  – Traditional PWI like in stroke
  – First pass of Gd, T2 or T2* imaging
  – CBV, CBF, plus others like MTT, permeability, etc.

• Dynamic Contrast Enhanced MRI
  – Newer
  – T1-based
  – Permeability
35 year old male with 3 years of intermittent headache and intermittent speech difficulties
Dynamic Susceptibility Contrast MRI - using Gd as T2 agent

MRI image removed due to copyright restrictions.

70% Oligodendroglioma, 30% Grade 3 astrocytoma

MRI image removed due to copyright restrictions.
High Grade Glioma

Low Grade Glioma

MRI image removed due to copyright restrictions.

26 year old female with III/IV glioma

MRI image removed due to copyright restrictions.
rCBV and $^{18}$FDG over time

Pre XRT | 6 weeks post XRT | 5 months post XRT
Another potential maker: Mean Vessel Radius

Signal change vs. Vessel Radius (µm)

GE, Sim
GE, Exp
SE, Sim
SE, Exp

SE EPI
0.2 mmol/kg
Gd-DTPA

FLASH (GE)
Iron Oxide
Gradient Echo versus Spin Echo EPI: simultaneous acquisition approach

3.0 Tesla, TR 1.5s, TE for GE: 28, TE for SE: 105
0.2 mmol/l Gd-DTPA.
GE vs SE DSC

Pilocytic astrocytoma

4.4 : 1 tumor/white on GE vs 1.75 : 1 tumor/white on SE

M Pescitides / Martinos - MGH - HST
DCE MRI

• Dynamic Contrast Enhanced MRI
• Rapid imaging during small dose of Gd
• T1 based, not T2
• Attempts to map “permeability”
• Analysis: analytic versus empiric (‘curvology’)
• Popular in assessing drug therapy
Sample DCE Time Course

Injection at about 1.5 times real speed
Images every ~5 seconds

Choroid Plexus  |  Cortex  |  Sub-cutaneous fat
Example Mapping Permeability ("K_{trans}")
Post Gd and $K_{\text{trans}}$ both show change; $K_{\text{trans}}$ will quantify.
Mechanistic Insights from MRI?

• Testing the “Vascular Normalization” hypothesis

• Blocking VEGF should result in:
  – Smaller vessels
  – Less permeability
  – Less edema
  – Decreased mass effect
  – Probably no survival benefit without combination therapy, though…

Vascular Normalization after Anti-angiogenic treatment
Winkler et al, Cancer Cell 6 no. 6 (2004): 553-563
Summary

• Perfusion MRI: Active, and still going strong
• New developments to watch out for:
  • Vasomotion
  • Therapy monitoring (stroke, tumor)
  • Location
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and many, many more...