Grading, therapy monitoring, and predicting outcome of glioma using perfusion MR imaging

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I. Gliomas
- Most common primary brain tumor
- Grade I-IV: WHO classification (revised in 2000) based on histologic features
- Grade I: Biologically indolent, “benign” brain tumors (ex. Pilocytic astrocytoma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma)
- Grade II-IV: Fibrillary astrocytomas most common, followed by oligodendrogliomas and oligoastocytomas (a.k.a. mixed gliomas)
- Grade IV Glioblastoma Multiforme (GBM): Most common gliomas, most aggressive biologically, highly vascular and necrotic

II. Standard Imaging: MR imaging with Gd-DTPA (perfusion, diffusion, proton spectroscopy as optional imaging)

标准治疗
- Grade III & IV Gliomas: Surgical resection followed by external beam radiation therapy (50-60 Gy for 6 weeks) and chemotherapy (temozolamide most widely used)
- Grade II Gliomas: Surgical resection initially & radiation therapy and/or chemotherapy at recurrence or progression

Prognosis (Average survival in months)
- Grade IV: 12-18 months
- Grade III: 3-5 years
- Grade II: 10-15 years

II. Types of Perfusion MR Imaging
- Endogenous contrast agent: Arterial Spin Labeling (ASL)
  - No exogenous contrast agent
  - Absolute cerebral blood flow
- Exogenous contrast agent (Gd-DTPA)
  - T2 or T2* dynamic susceptibility-weighted contrast-enhanced (DSC) “perfusion” MR imaging:
    - Relative cerebral blood volume (rCBV), blood flow, and transit time
  - T1-weighted dynamic contrast-enhanced (DCE): “Permeability” MR imaging”
    - Extracellular extravascular space, blood flow, cerebral blood volume (CBV), permeability surface product (Ktrans)

III. Fundamentals of DSC Perfusion MR imaging
- Rapid repeated imaging of multi-slice sections of the brain before, during, and after bolus injection of Gd-DTPA
- Compartmentalization of intravascular Gd-DTPA before it reaches interstitial space
- T2* signal loss due to Gd-DTPA, the susceptibility contrast, is translated into T2* relaxivity contrast, ΔR2*
- Fitting of ΔR2* signal intensity time curve allow measurement of area under the curve, which is proportional to cerebral blood volume (CBV)
- Steps involved in CBV calculation from DSC MR imaging data is illustrated in Figure 1.
• In case of blood-brain barrier breakdown as in some malignant gliomas or metastasis, signal recovery to baseline does not occur due to Gd-DTPA leakage, hence CBV calculation can be erroneous.
• Alternate variables such as peak height (PH) or percent signal recovery (PSR) can be derived from $\Delta R^*$ curve as shown in Figure 2.

**Figure 1. CBV Data Analysis**

a. Obtain curves of T2* signal intensity against time (Figure 1a).

b. Estimate mean pre-contrast signal intensity ($S_0$) from ten data points acquired before arrival of the bolus. Exclude the first 3-4 images during which the steady-state MR signal is established.

c. Calculate $\Delta R^*$ and apply baseline subtraction to the $\Delta R^*$ curve (Figure 1b & 1c).

d. Calculate the area under the fitted curve (Figure 1d).

**Figure 2. $\Delta R^*$ curve analysis in two different patients with brain tumor.** Top-Malignant glioma; bottom-dural based metastasis. Peak height (A) is the maximum signal change during first-pass of Gd-DTPA; Percent signal recovery (PSR) is percentage of signal recovery to the baseline at the end of bolus and is represented by $B/A \times 100\%$. Metastasis has decreased PSR due to leaky capillaries.

*(Figure courtesy of Janine M. Lupo)*
IV. Glioma Grading based on DSC Perfusion MR imaging
- rCBV most commonly used; higher the tumor grade, greater the rCBV
- Exception: Oligodendroglioma—low and high grade tumors both tend to have increased vascularity on histology; rCBV cannot reliably differentiate between the two
- rCBV based gliomas grading should be limited to fibrillary astrocytomas

V. Glioma Grading based on Permeability MR imaging
- $K^{\text{trans}}$ most commonly used but CBV has been used
- Strong independent relationships between both $K^{\text{trans}}$ & CBV and histologic grade in gliomas
- $K^{\text{trans}}$ has higher discriminative power in distinguishing between grade II (low-grade) and grade III+IV (high-grade) than between grade III and grade IV

VI. Therapy monitoring based on Perfusion MR imaging
- Serial tumor rCBV measurements during therapy can predict early response to therapy
- Interval increase tumor rCBV tend to represent treatment failure

Table 1. Summary of various types of perfusion MR imaging

<table>
<thead>
<tr>
<th></th>
<th>Gd-DTPA</th>
<th>Perfusion MR Variables</th>
<th>Strengths</th>
<th>Weaknesses</th>
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<tbody>
<tr>
<td>ASL</td>
<td>No</td>
<td>CBF</td>
<td>No IV contrast</td>
<td>Long imaging time; no CBV; 3T or higher; motion</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Absolute measures</td>
<td></td>
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<tr>
<td>T1-DCE</td>
<td>Yes</td>
<td>fPV $K^{\text{trans}}$</td>
<td>Higher spatial resolution</td>
<td>Longer scan time</td>
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<tr>
<td></td>
<td></td>
<td>EES Initial slope</td>
<td>No susceptibility artifact</td>
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<tr>
<td></td>
<td></td>
<td>Time to peak</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Area under curve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2-DSC</td>
<td>Yes</td>
<td>rCBV rCBF MTT</td>
<td>Less distortion</td>
<td>Multiple dose of Gd-DTPA</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Fast; multislice</td>
<td></td>
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<tr>
<td>T2*-DSC</td>
<td>Yes</td>
<td>rCBV rCBF MTT</td>
<td>Fast; multislice</td>
<td>Geometric distortion</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Single dose Gd-DTPA</td>
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<tr>
<td></td>
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<td>High SNR</td>
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ASL: Arterial Spin Labeling  
DCE: Dynamic contrast-enhanced Permeability MR imaging  
DSC: Dynamic susceptibility-weighted contrast-enhanced Perfusion MR imaging  
CBF: Cerebral Blood Flow  
fPV: Fractional Plasma Volume  
$K^{\text{trans}}$: Volume transfer coefficient  
EES: Extravascular Extracellular Space
References

Glioma and angiogenesis


Plate, K. H.

Dynamic susceptibility-weighted contrast-enhanced MR imaging


Dynamic contrast-enhanced T1-weighted permeability imaging


