Combined Functional and Metabolic Assessment of Brain Tumors using Hybrid PET/MR Imaging


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Disclosure

Work principally supported by CAI\(^2\)R and/or performed by CAI\(^2\)R personnel

• The Center for Advanced Imaging Innovation and Research (CAI\(^2\)R, www.cai2r.net) at New York University School of Medicine is supported by NIH/NIBIB grant number P41 EB017183.
Perfusion Imaging: Glioma Grading

Grade III Glioma

Grade II Glioma
PET

FDG-PET: Radiation Necrosis

\(^{11}\text{C}\)-methionine PET: Recurrent Tumor

Hybrid PET/MR Imaging: Clinical Rationale and Applications in Brain Tumor Imaging

• Anatomical MRI to localize PET signal
  • Structural MRI helps with attenuation correction
  • PET helps to characterize the lesion
  • Reduced radiation dose compared to PET/CT

• Diagnostic MRI with PET
  • One-stop shop
  • Higher accuracy for diagnosis and follow up

• Multi-parametric MRI with dynamic PET acquisition
  • Tumor perfusion and hypoxia
Purpose

To correlate concurrently acquired rCBV with FDG uptake in brain tumor patients using hybrid PET/MR imaging

• To assess the diagnostic accuracy of each modality
  • Low versus High grade gliomas (treatment naïve group, Group A)
  • Recurrent tumor versus TIE/Treatment Induced Effects (post-treatment group, Group B)

• To evaluate if concurrently acquired functional (perfusion) and metabolic (FDG uptake) increases diagnostic accuracy of the imaging assessment

• To correlate rCBV with FDG uptake
Materials and Methods

Patients population

20 patients and 34 lesions

Group A (Treatment naive)
9 patients and 16 lesions

Group-B (Post-treatment)
11 patients with 18 lesions
Materials and Methods
PET /MR Imaging Protocol

PET/MR system (Biograph mMR; Siemens Healthcare)

Inject FDG (10 mCi of 18F fluoro-deoxyglucose)

Diagnostic MR for 60 minutes

List Mode PET for 60 minutes

Recon 30–60 minute data

Recon 40–60 minute data

Recon dynamic PET data (research)
Materials and Methods
MR-PWI Imaging Protocol

PET/MR system (Biograph mMR; Siemens Healthcare)

• Dynamic Susceptibility Contrast-enhanced T2* (DSC)
  • 0.1 mmol/kg of gadobutrol

• T2* sequence was acquired (single-shot echo planar imaging sequence; TE 30 ms; flip angle, 45 degrees, image matrix, 64x64; field of view, 24 cm; slice thickness, 4 mm).

• Perfusion parametric maps were generated using leakage correction and commercially available software (Olea Medical Inc.)
Materials and Methods

Image Analysis

- Image analysis was performed by a radiologist and a nuclear medicine physician in consensus.

- Results were recorded from the whole tumor in terms of $r\text{CBV}_{\text{mean}}$ and $r\text{CBV}_{\text{max}}$ for PWI and of $\text{SUV}_{\text{max}}$ and $\text{SUV}_{\text{mean}}$ values for PET.

- Both readers, blinded to the location of the lesions, predicted the tumor histological grade in group A and the likelihood of tumor recurrence versus TIE in the group B based solely on PWI and PET numerical data.

- Final diagnosis for each lesion was then cross-referenced to histopathology results when available (7 patients, 12 lesions) or clinical and imaging follow-up (13 patients, 22 lesions).
Materials and Methods
Statistical Analysis

• **ROC** curve analysis was conducted to assess the diagnostic utility of rCBV\textsubscript{max}, rCBV\textsubscript{mean}, SUV\textsubscript{max} and SUV\textsubscript{mean} in both groups and in the entire population

• **The Youden index** was used to identify an optimal cut-off value of each measure for classifying lesions as test positive in the sense of maximizing the average of sensitivity and specificity

• **Logistic regression** for correlated data was used to assess and compare modalities (PWI, PET) in terms of diagnostic accuracy in both groups and in the entire population

• **Pearson correlations** were used to characterize the association of rCBV\textsubscript{max} and rCBV\textsubscript{mean} with SUV\textsubscript{max} and SUV\textsubscript{mean} values.
# Results

<table>
<thead>
<tr>
<th></th>
<th>$r\text{CBV}_{\text{max}}$</th>
<th>$r\text{CBV}_{\text{mean}}$</th>
<th>$\text{SUV}_{\text{max}}$</th>
<th>$\text{SUV}_{\text{mean}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criterion</strong></td>
<td>$\leq 5.01$</td>
<td>$\leq 1.74$</td>
<td>$\leq 5.6$</td>
<td>$\leq 4$</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>100%</td>
<td>100%</td>
<td>50%</td>
<td>75%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>31.0%</td>
<td>74%</td>
<td>89.5%</td>
<td>89.7%</td>
</tr>
</tbody>
</table>

*The Youden index*
## Results

<table>
<thead>
<tr>
<th></th>
<th>r(\text{CBV}_{\text{max}})</th>
<th>r(\text{CBV}_{\text{mean}})</th>
<th>(\text{SUV}_{\text{max}})</th>
<th>(\text{SUV}_{\text{mean}})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AUC</strong></td>
<td>0.65</td>
<td>0.89</td>
<td>0.63</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
<td>0.45 to 0.82</td>
<td>0.71 to 0.98</td>
<td>0.42 to 0.80</td>
<td>0.60 to 0.93</td>
</tr>
<tr>
<td><strong>P Value</strong></td>
<td>0.220</td>
<td>&lt;0.001</td>
<td>0.321</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Below are the receiver operating characteristic (ROC) curves for r\(\text{CBV}_{\text{mean}}\) and \(\text{SUV}_{\text{mean}}\):
Comparison of the effectiveness of MRI perfusion and fluorine-18 FDG PET-CT for differentiating radiation injury from viable brain tumor: a preliminary retrospective analysis with pathologic correlation in all patients

Vaios Hatzoglou\textsuperscript{a,b,*}, Gary A. Ulaner\textsuperscript{a}, Zhigang Zhang\textsuperscript{c}, Kathryn Beal\textsuperscript{d}, Andrei I. Holodny\textsuperscript{a,b}, Robert J. Young\textsuperscript{a,b}

Table 2
Sensitivity and specificity of proposed threshold values for four variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Threshold (%)</th>
<th>AUC</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_{\text{UVR}}$</td>
<td>$\geq 1.4$</td>
<td>.943</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>$r_{\text{CBV}}_{\text{max}}$</td>
<td>$\geq 1.8$</td>
<td>.771</td>
<td>100</td>
<td>71</td>
</tr>
<tr>
<td>PSR</td>
<td>$\geq 74$</td>
<td>.829</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>rPH</td>
<td>$\geq 2.2$</td>
<td>.757</td>
<td>60</td>
<td>100</td>
</tr>
</tbody>
</table>
Glioblastoma

rCBV
Mean: 3.50
Max: 5.79

FDG
Mean: 5.5
Max: 7.8
Recurrent lymphoma

rCBV
Mean: 1.87
Max: 2.07

FDG
Mean: 12.0
Max: 14.4
Radiation Necrosis (previously treated anaplastic meningioma)

rCBV
Mean: 1.74
Max: 5.1

FDG
Mean: 4.0
Max: 5.4
## Results

<table>
<thead>
<tr>
<th></th>
<th>Group A: Treatment naïve</th>
<th></th>
<th>Group B: Post-therapy</th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Accuracy</td>
<td>Lower</td>
<td>Upper</td>
<td>Accuracy</td>
<td>Lower</td>
</tr>
<tr>
<td>PWI</td>
<td>90.0% (9/10)</td>
<td>48.4%</td>
<td>98.9%</td>
<td>94.1% (16/17)</td>
<td>64.4%</td>
</tr>
<tr>
<td>PET</td>
<td>40.0% (4/10)</td>
<td>6.5%</td>
<td>86.5%</td>
<td>55.6% (10/18)</td>
<td>28.2%</td>
</tr>
<tr>
<td>P Value</td>
<td></td>
<td>0.056</td>
<td></td>
<td></td>
<td>0.033*</td>
</tr>
</tbody>
</table>

**Logistic Regression**
Clinical Study

Relative value of magnetic resonance spectroscopy, magnetic resonance perfusion, and 2-(18F) fluoro-2-deoxy-D-glucose positron emission tomography for detection of recurrence or grade increase in gliomas

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§Department of Radiation Oncology, Hospital Universitario La Fe, Valencia, Spain

Table 2
Positive predictive value and negative predictive value of different imaging modalities to predict the presence of high grade glioma

<table>
<thead>
<tr>
<th></th>
<th>MRS (%)</th>
<th>FDG-PET (%)</th>
<th>MRP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV</td>
<td>91.6</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>NPV</td>
<td>100</td>
<td>61.1</td>
<td>100</td>
</tr>
<tr>
<td>PPV (a)</td>
<td>100</td>
<td>66.6</td>
<td>100</td>
</tr>
<tr>
<td>NPV (a)</td>
<td>100</td>
<td>60</td>
<td>100</td>
</tr>
</tbody>
</table>

FDG-PET = 2-(18F) fluoro-2-deoxy-D-glucose positron emission tomography, MRP = MR perfusion, MRS = MR spectroscopy, NPV = negative predictive value, NPV(a), PPV(a) = negative predictive value and positive predictive value in the cases studied to differentiate viable tumour from radiation necrosis, PPV = positive predictive value.
# Results

## Pearson correlations

<table>
<thead>
<tr>
<th>Group</th>
<th>Parameter</th>
<th>$r_{CBV_{\text{max}}}$</th>
<th>Correlation</th>
<th>P Value</th>
<th>$r_{CBV_{\text{mean}}}$</th>
<th>Correlation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SUV</td>
<td></td>
<td>0.22</td>
<td>0.403</td>
<td>0.09</td>
<td>0.754</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>SUV</td>
<td></td>
<td>0.02</td>
<td>0.942</td>
<td>0.44</td>
<td>0.069</td>
<td></td>
</tr>
<tr>
<td>All Patients</td>
<td>SUV</td>
<td></td>
<td>0.13</td>
<td>0.482</td>
<td>0.31</td>
<td>0.076</td>
<td></td>
</tr>
</tbody>
</table>

![Graph of rCBV max vs Max FDG uptake early](image1)

![Graph of rCBV mean vs Max FDG uptake delay](image2)
Comparison of Spatial Congruence

rCBV
Mean: 2.43
Max: 5.0

Grade III Oligodendroglioma

FDG
Mean: 5.3
Max: 10.1
Comparison of ¹⁸F-FET PET and Perfusion-Weighted MR Imaging: A PET/MR Imaging Hybrid Study in Patients with Brain Tumors

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Key Words: PET/MR imaging; glioma; O-2-[¹⁸F]-fluoroethyl-L-tyrosine; PWI; rCBV; histogram

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TABLE 1
Mean Results for Glioma and Meningioma Patients

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>TBR</th>
<th>Tumor volume (cm³)</th>
<th>Spatial congruence (%)</th>
<th>Distance rCBV max. to ¹⁸F-FET max. (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>¹⁸F-FET</td>
<td>rCBV</td>
<td>rCBF</td>
<td>MTT</td>
</tr>
<tr>
<td>Glioma</td>
<td>2.28</td>
<td>1.62</td>
<td>0.92</td>
<td>1.08</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>0.99</td>
<td>1.13</td>
<td>0.44</td>
<td>0.31</td>
</tr>
<tr>
<td>Meningioma</td>
<td>2.37</td>
<td>5.33</td>
<td>0.67</td>
<td>0.64</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>0.32</td>
<td>2.63</td>
<td>0.30</td>
<td>0.50</td>
</tr>
</tbody>
</table>

NA = not applicable.
Limitations of the study

- Small sample size, retrospective
- Use of FDG, which has high uptake in the normal brain tissue
  - FET, $^{11}$C-Methionine and FDOPA
- Used only early uptake of FDG

Conclusions

• Hybrid MR-PET can be useful in brain tumor patients
  • capability of providing complementary information in terms of both functional/perfusion and metabolic assessment of brain lesions
  • Better co-registration of images

• PWI demonstrated better diagnostic accuracy in both differentiating high from low-grade tumors and recurrent tumor from TIE.

• Poor correlation between rCBV and FDG uptake was observed
  • Future work: pixel-by-pixel correlation to assess spatial congruence between FDG and rCBV estimates
Thanks!

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