Diffusion Restriction Precedes Contrast Enhancement in Glioblastoma Multiforme

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Conflict of Interest

- None to declare

- The study was supported by Radiology Research Foundation summer student grant, Dalhousie University, Halifax, Canada.
Background

- Astrocytic tumours, including GBM, account for more than 70% of all gliomas\textsuperscript{1}


- Despite aggressive treatment, outcomes are variable and prognosis often poor\textsuperscript{2}


- DWI has become a useful tool in characterization of tumours\textsuperscript{3}

Diffusion Weighted MR Imaging

- Potential in cancer patients for detection, diagnosis, staging, and assessment\(^4\)


- DWI provides information derived from Brownian motion of a water proton

- High cellular density (tumours) = reduced Apparent Diffusion Coefficient (i.e. restricted diffusion)\(^5\)

Background

- Isolated foci of low ADC lesions that precede concordant MR contrast enhancement in GBM

- Could early detection of increased cellularity provide earlier indications of:
  - Progression?
  - Recurrence?
  - Overall survival?

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Purpose

- Frequency of isolated diffusion restriction preceding the appearance of corresponding MR enhancement

- Restriction diffusion can predict the development of new enhancing mass lesions

- Relationship between isolated diffusion restriction and overall survival
Patient Selection

- Retrospective study- January 2007 to January 2010
- 102 patients with confirmed GBM

- MRI inclusion criteria:
  - 1) DWI;
  - 2) ADC maps;
  - 3) Axial Post gadolinium T1W images;
  - 4) Axial Fluid-attenuating inversion recovery (FLAIR) images
Image Acquisition

- 1.5 T magnet (Singa, GE Healthcare)

- DWI- single-shot echo-planar imaging:
  - 8000 ms TR;
  - 73.6 ms TE;
  - 260-mm FOV;
  - 160x192 matrix size;
  - 5-mm section thickness with 1.5 mm intersection gap;
  - 1000 and 0 mm²/s b-values obtained in 3 orthogonal directions
Materials and Methods

In the tumour

- Minimum Apparent Diffusion Coefficient (Min ADC)
- Mean ADC
- Normalized ADC (nADC)
  - comparing areas of low ADC lesion regions to normal regions of contralateral NAWM

Corresponding enhancement

Follow up- survival
Image Analysis and Interpretation

- Restricted diffusion was identified where hyper-intensity of DWI corresponded with hypo-intensity in the same site on ADC map

- Did areas of restricted diffusion appear w/o corresponding post-gad enhancement?

- On follow-up, did these areas eventually develop concordant tumour enhancement?
Results

97/102 (95.1%) - restricted diffusion detected during treatment

41/97 (42.3%) - low ADC lesion without corresponding enhancement

- 10 of 41 (24.4%) developed corresponding enhancement during follow up
- 10/41 (24.4%) had no corresponding enhancement during follow up
- 10/41 (24.4%) were lost to follow up
- 11/41 (26.8%) lacked appropriate follow up (after resection, lack of imaging)
Results

- Concordant enhancement appeared during follow up on average 145 days after appearance of low ADC lesion

- In one case, restricted diffusion preceded corresponding enhancement by 359 days

- Isolated low ADC lesions had an average ADC of 721.4 mm$^2$/s (compared to 888.7 mm$^2$/s for comparison group)
Results

- Patients with **isolated diffusion restriction** had **longer duration of survival** from initial diagnostic imaging compared to those without isolated diffusion restriction
  - $486 \pm 363.5$ days vs. $291.9 \pm 344.3$ days ($p=0.036$)

- No significance difference between the two groups in degree of resection
Results

- In patients with isolated diffusion restriction preceding corresponding enhancing tumour, survival was $474.1 \pm 369.8$ days after diagnostic imaging.

- In patients with isolated diffusion restriction that did not precede corresponding enhancement, survival was $729.3 \pm 404.7$ days after diagnostic imaging.
## Results

<table>
<thead>
<tr>
<th></th>
<th>GBM with isolated diffusion restriction (n=40)</th>
<th>GBM without isolated diffusion restriction (n=57)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.98</td>
<td>62.8</td>
<td>0.26</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>21:19</td>
<td>30:27</td>
<td>0.99</td>
</tr>
<tr>
<td>Mean ADC</td>
<td>721.4 ± 117.2 mm²/s</td>
<td>888.7 ± 85.2 mm²/s</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Size of the tumor (mm³)</td>
<td>23048.91</td>
<td>29431.53</td>
<td>0.16</td>
</tr>
<tr>
<td>Degree of resection (1/2/3)</td>
<td>31.4/17.1/51.4</td>
<td>54.4/8.7/36.9</td>
<td>0.12</td>
</tr>
<tr>
<td>Survival</td>
<td>486 ± 363.5 days</td>
<td>291.9 ± 344.3 days</td>
<td>0.036</td>
</tr>
<tr>
<td>Karnofsky at Diagnosis</td>
<td>75.05</td>
<td>74.64</td>
<td>0.48</td>
</tr>
</tbody>
</table>
Discussion

- Areas of **restricted diffusion** should be included in the **treatment planning** of GBM for both surgery or radiotherapy.

- **Could isolated diffusion restriction** serve as a new imaging marker to **predict survival** of patients with GBM?

- Inclusion of these may potentially result in more predictive outcome in these patients.

- Future: Is isolated diffusion restriction associated with any of the known molecular prognostic markers?
Conclusion

- Appearance of isolated regions of restricted diffusion lacking corresponding post-gad enhancement was relatively common, occurring in approximately 40% of GBM patients
- Appearance of isolated diffusion restriction associated with longer overall survival
- Isolated low-ADC lesions preceded the development of enhancing tumour in approximately 1/5th of GBM patients who initially presented with non-concordant restricted diffusion lesions
- Further examination in a prospective study of this phenomena is needed

Thank you!