Quantitative assessment of gliomas grade: comparison the minimum ADC value of DWI at $b=3000\text{s/mm}^2$ and that of DWI at $b=1000\text{s/mm}^2$

Poster No.: C-2380  
Congress: ECR 2014  
Type: Scientific Exhibit  
Authors: L. Zhu; Shanghai/CN  
Keywords: CNS, MR-Diffusion/Perfusion, Technology assessment  
DOI: 10.1594/ecr2014/C-2380

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Aims and objectives

Gliomas account for almost 80% of primary malignant brain tumors, and they result in more years of life lost than do any other tumors(1). Accurate preoperative grading of tumors is extremely important, because different grades have different biological behavior and prognosis, influencing the choice of therapeutic approach.

The Ki-67 labeling index#LI# is an immunohistochemical examination for the evaluation of tumor proliferation(2), showing a good correlation between histological alignancy, neuronal differentiation and seeding potential. High tumor cellularity has been associated with increased proliferative activity, as assessed by the Ki-67 index(2).

Diffusion is defined as the process of random molecular thermal motion occurring at a microscopic scale. DWI has been studied in clinical situations, including detection of chemic stroke, differential diagnosis as well as assessment of tumor grades(3-10). Several investigators found an inverse correlation between the apparent diffusion coefficient (ADC) and tumor cellularity(3,8,11,12). Some authors reported that the minimum ADC values were negatively correlated with Ki-67 LI and related to tumor prognosis(13,14). It has been reported that images obtained with higher b values were better than those acquired with the standard b value (b=1000 s/mm$^2$) for predicting the glioma grade, for the diagnosis of acute stroke, and for lesion-to-normal contrasting in neurodegenerative diseases(15-17).

The purpose of this study was to retrospectively determine whether minADC$_{3000}$ is more useful for tumor grading by comparing minADC values calculated at b=3000 s/mm$^2$ and b=1000 s/mm$^2$. 
Methods and materials

Patients

The ethics committee of Huashan Hospital, Fudan University, China, approved this retrospective study and did not require patient informed consent, because DWI scans are routinely performed in clinical practice at our institute. Between 2008 and 2011, 81 patients (51 males, 30 females; mean age, 44.4 years), including 31 low grade gliomas (LGG)(G1:3#G2:28) and 50 high grade gliomas (HGG)(G3:21#G4:29) were included in this study.

Magnetic Resonance Imaging and Data Analysis

All MR studies were performed with a 1.5-T MR imaging system (Signa EXCITE HD; GE Healthcare, Milwaukee, WI, USA) using a conventional quadrature head coil. Unenhanced and contrast-enhanced transverse and sagittal T1-weighted imaging, unenhanced transverse T2-weighted imaging, fluid-attenuated inversion recovery (FLAIR) imaging and DW images were obtained during the same imaging session without repositioning each patient's head.

DWI was performed by using fat-suppressed spin-echo echo-planar imaging. The effective gradient was 33 mT/m, the slew rate 120 mT/m/ms. The parameters were: TR/TE 4800/68.6 ms (b=1000) and TR/TE 4800/92.2 ms (b=3000); NEX, 2; FOV, 24×24 cm; matrix size, 128×128; section thickness, 6 mm; section gap, 2 mm).

ADC maps (0s/mm$^2$ and 1000s/mm$^2$ for ADC map b=1000, and 0s/mm$^2$ and 3000s/mm$^2$ for ADC map b=3000) were calculated from isotropic DWI by using Functool software on a SUN GE AW 4.3 workstation on a pixel-by-pixel basis. Several continuous round or round-like shaped regions of interest (area, approximately 30mm$^2$) were manually and carefully placed on each slice of ADC maps of tumors, avoiding the cystic, necrotic, hemorrhagic or calcific areas based on the conventional MR images. About ten to twenty regions of interest (ROI) were placed in each case, and the lowest ADC value was selected as a minimum ADC (minADC) value of the tumor. Two senior neuroradiologists blinded to the pathologic diagnosis compared the ADC maps and other MR images by means of consensus.

Surgery and Pathologic Evaluation

All patients underwent surgery in 3 to 7 days after MR imaging, removing the maximum amount of tumors, with minimum neurologic, physical, and systemic damage. The pathologic diagnosis was determined according to the World Health Organization criteria (2007), by two neuropathologists. After a generalized survey, fields with the highest number of Ki-67-labeled cells were elected, and the percentage of positively cells was determined by counting more than 1000 tumor nuclei at ×400 magnification.
Statistical Analysis

Statistical analyses were performed by using SPSS 13.0. Mann-Whitney $U$ test, one-way ANOVA, Dunnett's T3, correlation analysis and receiver operating characteristic analysis were used for statistical evaluation. All $P$ values of less than 0.05 were considered to indicate a statistically significant difference.
Results

The mean value of minADC\textsubscript{1000} for LGGs was higher than that of G3 (P<0.001), and than that of G4. But there was no significant difference between the mean value of minADC\textsubscript{1000} of G3 and that of G4 (P=0.069). The mean value of minADC\textsubscript{3000} for LGGs was higher than that of G3 (P<0.001) and than that of G4 (P<0.001). There was significant difference between the mean value of minADC\textsubscript{3000} of G3 and that of G4 (P<0.001) (Table 1; Fig.1,2,3).

There were significant negative correlation between minADC\textsubscript{1000} and different tumor grades (r##0.699#P<0.001), between minADC\textsubscript{3000} and different tumor grades (r##0.827#P<0.001). There was significant positive correlation between Ki-67 LI and different tumor grades (r#0.843#P<0.001). There were negative correlation between minADC\textsubscript{1000} and Ki-67 LI (r##0.555#P<0.001), and between minADC\textsubscript{3000} and Ki-67 LI (r##0.646#P<0.001).

Results of ROC analysis of DWIs at b=1000 s/mm\textsuperscript{2} and b=3000 s/mm\textsuperscript{2} are shown in table 2.

Table 1: Comparison of mean minADC between b=1000 s/mm\textsuperscript{2} and b=3000 s/mm\textsuperscript{2} DWI in gliomas

<table>
<thead>
<tr>
<th></th>
<th>minADC\textsubscript{1000}\texttimes10\textsuperscript{-3} mm\textsuperscript{2}/s</th>
<th>minADC\textsubscript{3000}\texttimes10\textsuperscript{-3} mm\textsuperscript{2}/s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>average range</td>
<td>average range</td>
</tr>
<tr>
<td>LGG</td>
<td>1.279±0.270 0.78#1.85</td>
<td>0.940±0.175 0.567#1.29</td>
</tr>
<tr>
<td>G1#G2#n#31#</td>
<td>0.849±0.185 0.516#1.27</td>
<td>0.535±0.119 0.337#0.821</td>
</tr>
<tr>
<td>HGG</td>
<td>0.92±0.201 0.597#1.27</td>
<td>0.609±0.116 0.438#0.821</td>
</tr>
<tr>
<td>G3#G4 #n#50#</td>
<td>0.797±0.156 0.516#1.09</td>
<td>0.482±0.091 0.337#0.652</td>
</tr>
</tbody>
</table>

Table 2: Results of ROC analysis of DWIs at b=1000 s/mm\textsuperscript{2} and b=3000 s/mm\textsuperscript{2}

<table>
<thead>
<tr>
<th></th>
<th>b</th>
<th>AUG</th>
<th>Cutoff #×10\textsuperscript{-3} mm/s</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV#%</th>
<th>NPV#%</th>
</tr>
</thead>
</table>


<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>LGG vs HGG</td>
<td>b#1000</td>
<td>0.904</td>
<td>1.125</td>
<td>77.4</td>
<td>92</td>
<td>86.8</td>
</tr>
<tr>
<td></td>
<td>b#3000</td>
<td>0.974</td>
<td>0.709</td>
<td>93.5</td>
<td>92</td>
<td>97.9</td>
</tr>
<tr>
<td>LGG vs G3</td>
<td>b#1000</td>
<td>0.853</td>
<td>1.125</td>
<td>77.4</td>
<td>81</td>
<td>70.8</td>
</tr>
<tr>
<td></td>
<td>b#3000</td>
<td>0.952</td>
<td>0.822</td>
<td>83.9</td>
<td>100</td>
<td>80.8</td>
</tr>
<tr>
<td>LGG vs G4</td>
<td>b#1000</td>
<td>0.942</td>
<td>1.115</td>
<td>77.4</td>
<td>100</td>
<td>78.4</td>
</tr>
<tr>
<td></td>
<td>b#3000</td>
<td>0.989</td>
<td>0.685</td>
<td>93.5</td>
<td>100</td>
<td>96.7</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>b#1000</td>
<td>0.686</td>
<td>0.836</td>
<td>71.4</td>
<td>62.1</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>b#3000</td>
<td>0.782</td>
<td>0.493</td>
<td>90.5</td>
<td>55.2</td>
<td>88.9</td>
</tr>
</tbody>
</table>

AUG: area under the ROC Curve; PPV: positive predictive value; NPV: negative predictive value
**Fig. 1:** Fig.1. Astrocytoma (Grade II) in a 37-year-old man. (A) Axial contrast-enhanced T1-weighted image shows tumor without enhancement in the right frontal lobe. (B) Axial DWI at b=1000s/mm² shows tumor iso-hyperintensity. (C) Axial ADC map at b=1000s/mm². (D) Axial DWI at b=3000s/mm² shows tumor hypointensity. (E) Axial ADC map at b=3000 s/mm². (F) Photomicrograph of Ki-67 LI.

© Department of Radiology, Huashan Hospital#Fudan University
**Fig. 2:** Anaplastic oligodendroglioma (Grade III) in a 43-year-old woman. (A) Axial contrast-enhanced T1-weighted image shows tumor with slightly enhancement in the right corpus callosum. (B) Axial DWI at b=1000s/mm² shows tumor hyperintensity. (C) Axial ADC map at b=1000s/mm². (D) Axial DWI at b=3000s/mm² shows tumor hyperintensity. (E) Axial ADC map at b=3000 s/mm². (F) Photomicrograph of Ki-67 LI.

© Department of Radiology, Huashan Hospital#Fudan University
**Fig. 3:** Glioblastoma (Grade IV) in a 46-year-old man. (A) Axial contrast-enhanced T1-weighted image shows tumor with slightly enhancement in the right parietal-occipital lobe. (B) Axial DWI at b=1000s/mm² shows tumor hyperintensity. (C) Axial ADC map at b=1000s/mm². (D) Axial DWI at b=3000s/mm² shows tumor hyperintensity. (E) Axial ADC map at b=3000 s/mm². (F) Photomicrograph of Ki-67 LI.

© Department of Radiology, Huashan Hospital#Fudan University
Conclusion

DWI has been widely used for grading gliomas. The method for measuring ADC differs among reported studies(3-10). The results from various methods may be inconsistent, and a considerable overlap between ADCs in high-grade tumors and ADCs in low-grade tumors has been noted(3). Provenzale JM(18)suggested some differences in conflicting findings from different studies may be due to whether areas of necrosis are carefully excluded from the analyses of tumor ADCs. Such necrotic regions are more common in high-grade tumors and would be expected to contribute highly elevated ADCs that would raise the mean values for the tumor. Some studies have suggested that the regions of minADC values reflect the sites of highest cellularity within heterogeneous tumors, therefore, these sites may be of diagnostic value in identifying high-grade tumor components(6-10). So we use minADC value to detect difference in different grade of gliomas as the first quantitative data regarding diffusion-weighted imaging characteristics. The overlap in all minADC values of different grades decreased for all minADC measurements at b=3000s/mm$^2$ compared to b=1000s/mm$^2$.

An inverse correlation between minADC and tumor cellularity has been verified by histology in a wide variety of tumors, including high- and low-grade glioma, lymphoma, and metastases(3,8,11,12). The greater the density of structures that impede water mobility, the lower the ADC. Therefore, ADC is considered a noninvasive indicator of cellularity or cell density. The assessment of tumor proliferation rate is important to predict tumor behavior, response to therapy and prognosis. Immunohistological marker Ki-67 LI can be performed easily and routinely and may be superior to histological grade as an indicator of prognosis(19,20). High tumor cellularity has been associated with increased proliferative activity, as assessed by the Ki-67 index(2). In this study, we found the Ki-67 LI was positively correlated with tumor grading, and with significant difference in different grade. Moreover, minADC$_{3000}$ value showed more significant negative correlation with Ki-67 LI than minADC$_{1000}$ value.

Diffusion in biological tissue is most frequently quantified using a mono-exponential model. However, diffusion-weighted signal decay in the brain and in brain tumors has been shown to be multi-exponential, the bi-exponential model is probably also an oversimplification of reality(21). So the exact reason why the ADC at higher b values manifests a better correlation with tumor cellularity is not known, and it should be investigated further.

In conclusion, the minimum apparent diffusion coefficient of DWI at b= 3000s/mm$^2$ (minADC$_{3000}$) is more useful than that of DWI at b=1000s/mm$^2$ (minADC$_{1000}$) in differentiating among glioma grades.
Personal information

ZHU Li, M.D.
Department of Radiology, Shanghai Chest Hospital#Shanghai Jiaotong University, Shanghai, China;
augjuly@163.com

GENG Dao-ying, M.D.
Department of Radiology, Huashan Hospital#Fudan University, Shanghai, China
gengdy@163.com
References


15. Seo HS, Chang KH, Na DG, Kwon BJ, Lee DH. High b-value diffusion (b = 3000s/mm2) MR imaging in cerebral gliomas at 3 T: visual and quantitative comparisons with b = 1000s/mm2. AJNR Am J Neuroradiol 2008;29:458-63.


