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Inspiring Minds

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 gliomas¹

Kleihues P, Cavenee WK. World Health Organization classification of tumours: pathology and genetics of tumours of the central nervous system. Lyon, France: International Agency for Research on Cancer, 2000.

- Despite aggressive treatment, outcomes are variable and prognosis often poor²

Salzman M. Glioblastoma multiforme and anaplastic astrocytoma. In: Kaye AH, Law ER Jr, eds. Brain tumors: an encyclopedic approach. 2nd ed. London, England: Churchill Livingstone, 2001.

- DWI has become a useful tool in characterization of tumours³

Bulakbasi N, Guvenc I, Onguru O, Erdogan E, Tayfun C, Ucoz T. The added value of the apparent diffusion coefficient calculation to magnetic resonance imaging in the differentiation and grading of malignant brain tumors. J Comput Assist Tomogr 28(6):735-746, 2004.

Diffusion Weighted MR Imaging

- Potential in cancer patients for **detection, diagnosis, staging, and assessment**⁴

Padhani AR, Liu G, Koh DM, et al.. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. *Neoplasia* 11(2):102-125, 2009.

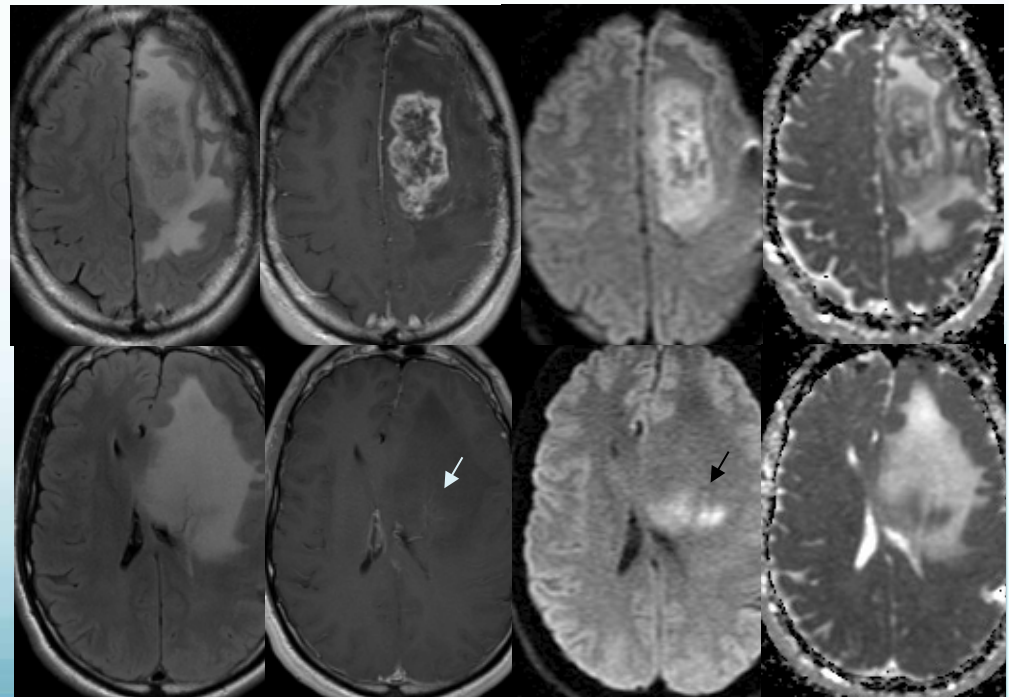
- DWI provides information derived from Brownian motion of a water proton
- High cellular density (tumours) = reduced Apparent Diffusion Coefficient (i.e. restricted diffusion)⁵

Chen J, Xia J, Zhou YC, Xia LM, Zhu WZ, Zou ML et al. Correlation between magnetic resonance diffusion weighted imaging and cell density in astrocytoma [in Chinese]. *Zhonghua Zhong Liu Za Zhi* 27:309-311, 2005.

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?

62 Y M



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 mm²/s** (compared to **888.7 mm²/s** for comparison group)

Results

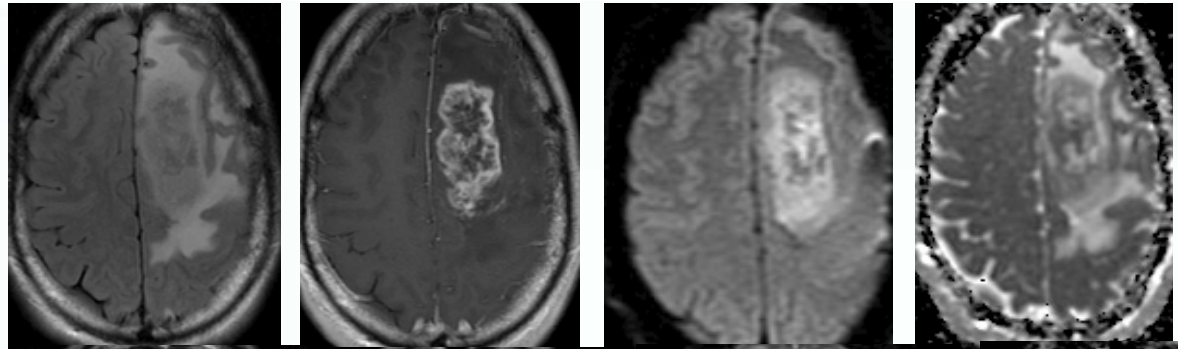
- Patients with **isolated diffusion restriction** had **longer duration of survival** from initial diagnostic imaging compared to those without isolated diffusion restriction
 - 486 ± 363.5 days vs. 291.9 ± 344.3 days ($p=0.036$)
- No significance difference between the two groups in degree of resection

Results

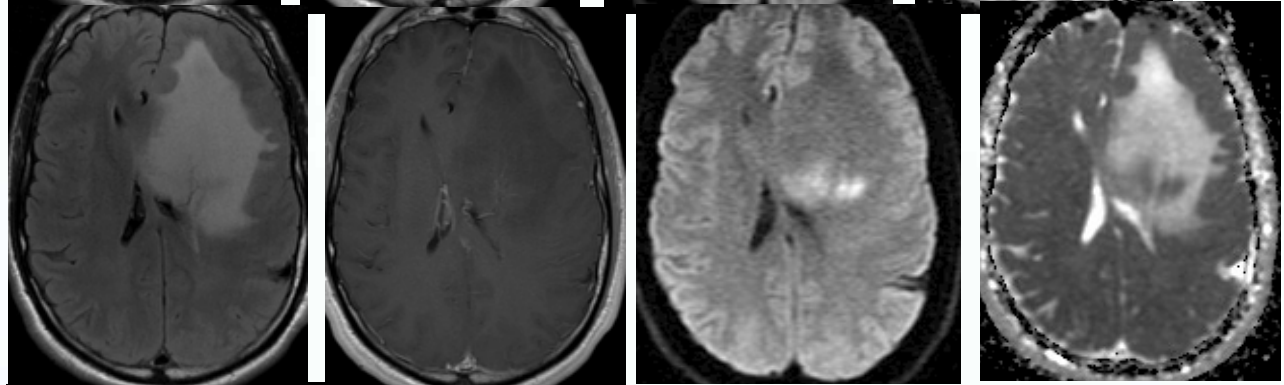
- In patients with **isolated diffusion restriction preceding** corresponding **enhancing tumour**, **survival was 474.1 ± 369.8 days** after diagnostic imaging
- In patients with **isolated diffusion restriction that did not precede** corresponding **enhancement**, **survival was 729.3 ± 404.7 days** after diagnostic imaging

Results

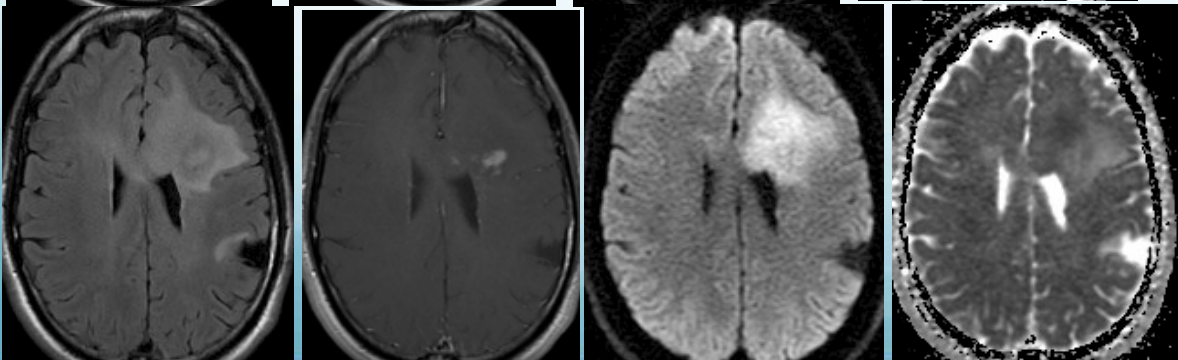
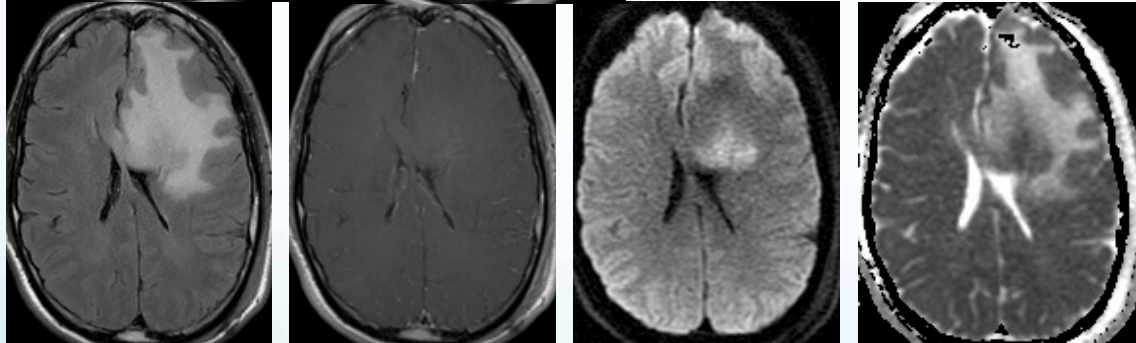
	GBM with isolated diffusion restriction (n=40)	GBM without isolated diffusion restriction (n=57)	P value
Age	59.98	62.8	0.26
Sex(M:F)	21:19	30:27	0.99
Mean ADC	721.4 ± 117.2 mm ² /s	888.7 ± 85.2 mm ² /s	<0.001
Size of the tumor (mm ³)	23048.91	29431.53	0.16
Degree of resection(1/2/3)	31.4/17.1/51.4	54.4/8.7/36.9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



62 Y M, Dec
11th,



Dec 20th



Feb 27th

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!