Evaluation of Regions of Increased CBV in Gliomas using MRI without Contrast Injection

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Introduction. Treatment of cerebral gliomas remains difficult, largely due to the biological heterogeneity of tumors and lack of imaging methodologies to accurately characterize this anatomy (1,2). Neuro-oncologists rely on T1-weighted gadolinium (GAD-T1w)-MRI and FLAIR images in guiding treatment decisions, but additional imaging approaches would be useful, for example, to determine the true tumor margin postoperatively. Here, a cerebral blood volume (CBV)-weighted MRI sequence called vascular space occupancy (VASO) (3) is applied to brain tumor imaging. This approach has been shown to be effective in tumor grading when combined with Gd-DTPA imaging (4). Here we show that VASO-MRI without exogenous contrast can outline tumor regions and provide complementary information to GAD-T1w and FLAIR.

Methods. *Experiment.* GAD-T1w, FLAIR and VASO-MRI were performed on a 3.0T MRI scanner for seven subjects: two anaplastic astrocytomas (AA), two glioblastoma multiformes (GBM), one anaplastic oligodendroglioma (AO) and two presumed low grade. Written consent was obtained from all patients prior to the study. Scan parameters: *FLAIR*: 60 slices, turbo inversion recovery, TR/TE=11/0.12s, FOV=212, in-plane spatial resolution 0.83x0.83 mm^2; *GAD-T1w*: 150 slices, 3D turbo-gradient-echo, TR/TE=7.9/3.7 ms, FOV=256, in-plane spatial resolution 1x1 mm^2;*VASO*: 22 slices, TR/TE/TI=6/0.019/1.086s, FOV=220, in-plane spatial resolution 2.3x2.3 mm^2. To allow for multi-slice VASO to be performed in a time-conscious manner, two slices were acquired in each TR and the null-time of blood (TI=1.086s) was centered between the two readouts. *Analysis*. Images were motion-corrected and slices were co-registered between scans using a 12 parameter affine FLIRT routine. Cases were divided into those which showed abnormal GAD-T1w enhancement and those which did not. FAST segmentation was applied to all slices in co-registered FLAIR images to obtain an outline of total tumor + edema volume. Using this region as a mask, GAD-T1w and VASO images were segmented according to hyperintense regions in GAD-T1w (suggesting BBB breakdown) or hypointense regions in VASO (high CBV). Fig. 1 shows an example of this process for a second-recurrence GBM patient. Volume ratios (GAD-T1w:FLAIR and VASO:FLAIR) were calculated for each patient.

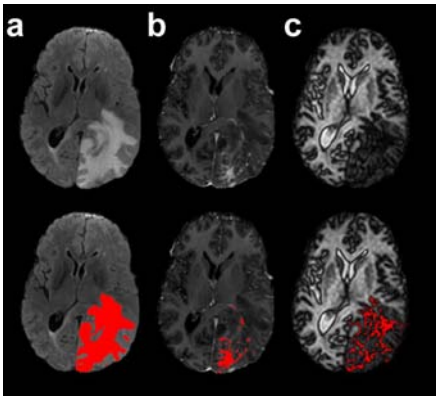

Fig. 1. Anatomical images (upper) and corresponding tumor segmentation (lower) for FLAIR (a), GAD-T1w (b), and VASO (c).

Results. Fig. 2 shows an example of FLAIR (a), GAD-T1w (b) and VASO (c,d) imaging for a first recurrence AA patient. Enhancement in GAD-T1w suggests BBB breakdown surrounding likely necrotic tissue, where vessels are no longer compliant. This is supported by the VASO image, which shows hypointensity surrounding a central region of presumed low CBV (angiogenesis). A summary of all patients is presented in Table 1, including volume ratio analysis for individual cases. Notice that VASO:FLAIR volume ratios are generally higher than GAD-T1w ratios, suggesting that VASO-MRI may provide complementary (physiological) information concerning tumor histology before abnormal enhancement is apparent in GAD-T1w (e.g. Fig. 1).

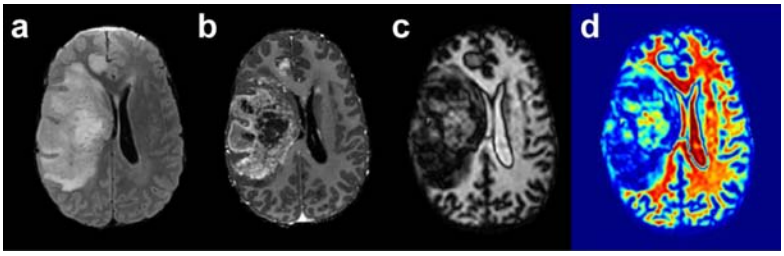

Fig. 2. FLAIR (a), GAD-T1w (b) and VASO (c) for a first recurrence AA patient. A VASO color image (d) is included as well.

Histologic Diagnosis	Disease Status	GAD-T1w : FLAIR Volume	VASO : FLAIR Volume
GBM	Second recurrence	0.14	0.21
GBM*	New diagnoss	0.13	0.19
AA*	New diagnosis	0.00	0.05
AA*	First recurrence	0.25	0.21
AO	New diagnosis	0.17	0.20
Presumed low grade	New diagnosis	0.04	0.23
Presumed low grade	New diagnosis	0.14	0.23

Table 1. Individual case analysis. *GAD-T1w enhancing tumor.

Discussion. VASO provides contrast complementary to GAD-T1w and FLAIR in glioma imaging. This important finding has many potential clinical implications. First, VASO-MRI is noninvasive, making it an easily incorporable complement to existing protocols and a potential alternative to GAD-CBV. Second, VASO contrast has previously been shown to reflect a physiological parameter, CBV (3). Therefore, novel therapeutic strategies which focus on controlling growth factors associated with vascular proliferation may incorporate VASO as a method for determining good candidates for such therapies and tracking therapy response. Finally, VASO is itself a T1w sequence, similar in principle to FLAIR. This early application of VASO to glioma imaging is promising, but more studies are needed to determine the optimal clinical application of VASO-MRI for improving the management of gliomas.

References. 1. Kaba SE,et al.Drugs.1997;53:235-244.**2.** Nitta T,et al.Cancer.1995;75:2727-2731.**3.** Lu H,et al.MRM.2003;50:263-274. **4.** Lu et al, ISMRM 2006 Abs#757; Grant support from NCRR RR015241.