The goal of this study was to use ADC histograms from patients with AC and OD to generate a visual RGB color map representation that shows oligo-like (red), normal-appearing white matter-like (green), and astro-like (blue) regions to easily visualize the variability within the lesion. The long-term objective is to use these images to direct tissue sampling for patients undergoing surgical resection in order to assist in biopsying the
most variable regions within the tumor to ensure the dominant tumor characteristics and determine which form of adjuvant therapy would be most appropriate.

MATERIALS AND METHODS

Study Population

A total of 53 newly diagnosed patients with grade II gliomas were included in this study. These patients were accrued between July 2002 and April 2006. Eleven patients with grade II AC (five female, six male) ranged in age from 22 to 51 years, with a median of 28 years. Nineteen patients with grade II OD (7 female, 12 male) ranged in age from 21 to 71 years, with a median of 44 years. Twenty-three patients with grade II OA (9 female, 14 male) ranged in age from 18 to 62 years, with a median of 41 years. Diagnosis was based on histologic examination using criteria defined by the World Health Organization (WHO). Patients provided informed consent as approved by the Committee on Human Research at our institution.

Conventional MRI

Patient exams were performed on a 1.5T GE Signa Echospeed scanner (GE Healthcare Technologies, Milwaukee, WI) using a standard quadrature head coil. The MRI examination included axial T1-weighted pre- and postgadolinium three-dimensional spoiled gradient echo (SPGR) images (TR = 34 msec, TE = 3 msec, slice thickness = 1.5 mm, matrix = 256 × 192, FOV = 260 × 195 mm²). After each examination the images were transferred to a SUN Ultra 10 workstation (Sun Microsystems, Mountain View, CA) for postprocessing. The FSE and postgadolinium SPGR images were aligned to the postgadolinium SPGR using software developed by Nelson et al (14).

Diffusion-Weighted Imaging

Patients were scanned with three-directional diffusion-weighted echo-planar imaging (EPI) sequences (TR = 10,000 msec, TE = 110 msec, matrix size = 256 × 256, slice thickness = 5 mm, b = 1000 s/mm²) or six-directional diffusion tensor imaging (TR = 10,000 msec, TE = 108 msec, matrix size = 256 × 256, slice thickness = 3 mm, b = 1000 s/mm²). The ADC was calculated on a pixel-by-pixel basis using software developed in-house based on published algorithms (15). The ADC map was aligned to anatomical imaging by rigidly aligning the T2-weighted (b = 0) diffusion image to the T2-weighted FSE that had been registered to the postgadolinium SPGR and applying the transformation to the ADC (16).

Data Processing

An in-house semiautomated segmentation method, described in detail elsewhere (17), was used to define the contrast enhancing lesion (CEL) on the postgadolinium T1-weighted image (in the 6/53 patients showing enhancement: 3 ODs, 1 AC, 2 OAs) and the T2 hyperintense region (T2All) on the T2-weighted FSE image. The nonenhancing region (NEL) was defined as T2All minus the CEL. The normal-appearing white matter (NAWM) mask was segmented using FAST (FMRIB’s Automated Segmentation Tool) Software from the postgadolinium T1-weighted image (18).

Derivation of Color Maps

The color maps were generated by translating the ADC gray scale intensity to an RGB matrix. The red, green, and blue components of the color maps were derived from normalized ADC (nADC) histograms. Normalization was performed in order to combine three- and six-directional data. The differences between the groups were maintained whether or not the normalization was performed. Normalized histograms were generated within the NAWM and NEL. The histogram of the nADC values within the NAWM of each of the 30 patients with OD and AC were summed together to generate the NAWM histogram (green) seen in Fig. 1. The (red) OD and (blue) AC histograms correspond to the sum of the individual NEL nADC histograms of each of the 19 ODs and 11 ACs, respectively.

The nADC maps were generated by dividing the ADC maps by the median ADC value found within the NAWM mask. Translating the nADC voxel value to the RGB matrix values was performed in three steps. First, each nADC value was mapped to the appropriate bin value. The histogram bins ranged from 0 to 4 with a bin size of 0.05. Second, the R (red), G (green), and B (blue) weighted heights were calculated at the bin value for each histogram, where R = OD(bin value)/OD(max), G = NAWM(bin value)/NAWM(max), and B = AC(bin value)/AC(max). Lastly, the first and second steps were repeated for all nADC values. Figure 1 shows the example of nADC = 1.5 for the first and second steps and the full color map for the example nADC slice shown.

Estimate of OD and AC components

An nADC cutoff value of 1.8 best separated the median nADC values for OD and AC subtype. Therefore, the percentage volume equal to or less than 1.8 and the percentage volume greater than 1.8 was calculated as the percentage oligo-like and astro-like tumor for a quick estimate of the relative amounts of OD and AC components within the tumor.

RESULTS

Color maps were generated for each of the 53 grade II glioma patients. Color maps from 18 patients, 6 patients from each subtype showing the least distortion were randomly chosen and presented in Fig. 2. The normal-appearing white and gray matter tended to have similar ADC values and therefore appear green. Black regions can be seen within the normal-appearing green tissue. These are regions with nADC values that fall below the NAWM histogram and therefore contain no colored pixels. The edge of gray matter and cerebrospinal fluid (CSF) generally appears pink due to the partial
voluming of gray matter and CSF. The CSF surrounding the brain and the CSF within the ventricles include values found within the astro-like nADC values and higher, therefore appearing blue to black. Distortion could be seen in some cases for tumors that were more anterior, close to the orbits or sinuses.

Color maps of oligodendroglial tumor regions were generally visualized in a pink color as can be seen in the representative six patients shown in Fig. 2, while the color maps of astrocytic tumor regions were generally visualized with various shades of blue. In many cases there appears to be a thin pink rim surrounding the astrocytic tumors. These pink voxels could be attributed to the partial voluming of high nADC tumor values and normal-appearing tissue to an nADC value that is more closely visualized as pink. In the case of patients with oligoastrocytic tumor regions, generally both pink and blue regions could be seen. The color maps of patients with OA (Fig. 2) show a mixture of both blue and pink, which in many cases appear to be bleeding.

**Figure 1.** Mapping an nADC map (1) to an RGB map (2). Example of mapping an nADC value (ie, nADC = 1.5) to an RGB value set. First, find the bin value the nADC value belongs to within the 0 to 4 range (a). Next, calculate the RGB matrix based on the histogram-weighted heights (ie, R = OD(bin value)/OD(max) = 0.0744/0.0749 = 0.993, G = NAWM(bin value)/NAWM(max) = 0/0.1656 = 0, B = AC(bin value)/AC(max) = 0.0158/0.0429 = 0.368) (b). Repeat for all voxels.

**Figure 2.** Color maps of a single slice from 18 example patients, separated into groups of six patients per subtype: oligodendroglioma (OD), astrocytoma (AC), and oligoastrocytoma (OA).
into each other and blotchy. The patient presented in Fig. 1 shows primarily a pink abnormality, but with some patches of blue.

The median nADC value for each patient is plotted against the percentage of oligo-like volume as shown in Fig. 3. The percentage oligo-like volume for patients with OD, AC, and OA ranged from 66%–99%, 5%–68%, and 20%–91%, respectively, with a median value of 86.5%, 26%, and 45.5%, respectively.

**DISCUSSION**

Grade II gliomas are heterogeneous tumors that generally do not enhance on postgadolinium T1-weighted MR images. Since biopsies are generally taken from the enhancing portion of a tumor, there is currently no well-defined imaging target for surgical biopsy for these lesions. As the classification of these tumors is dependent on the extent of sampling, the ability to use imaging data to guide biopsy sampling is critical. The technique that we have proposed provides a color map of the oligo-like and astro-like regions of the tumor in order to direct tissue sampling and to assist in defining the dominant tumor characteristics. This may be important in determining which form of adjuvant therapy would be most appropriate.

In our patient population ~11% of patients showed enhancement in a very small volume relative to the nonenhancing lesion. In those patients the enhancing region is a well-defined imaging target, but for the remaining cases the color map technique may aid in defining the heterogeneous regions to sample within the tumor. Therefore, this analysis focused on using the nonenhancing lesion histograms as a basis for defining the histogram values.

This study utilized ADC histograms from the NAWM regions and from nonenhancing regions of patients with OD and AC to generate RGB color maps with oligo-like (red), NAWM-like (green), and astro-like (blue) weightings. Each gray scale voxel was visualized as a mixture of the red, green, and blue weightings. The color maps provide visualization of the biologically different regions within the whole tumor mass, which may aid in directing image-guided biopsies in order to obtain tumor tissue from representative regions of the brain. The patient presented in Fig. 1 shows primarily a pink abnormality, but with some patches of blue. The recommendation for image-guided biopsy would be to biopsy both a pink region and a blue region to ensure that this patient, who appears to have an OD, does not have a significant astrocytic component. This ensures that the biopsy is directed to regions that can possibly more accurately sample the tumor to define the dominant tumor characteristics. Even though the aim of surgery in low grades is generally radical resection, more accurate targeted biopsying may aid in more accurate assessment of subtype and by doing so may aid in determining the best course of treatment.

Plotting the median nADC value within the tumor versus the percentage oligo-like volume shows an excellent separation between the patients with OD and AC, with the patients having OA being distributed across the entire range. Examining the population of patients with AC further, it is clear from Fig. 3 that the patient with a percentage oligo-like volume of 68% appears to be an outlier and the remaining patients had a percentage oligo-like volumes ranging from 5%–38%. Tissue biopsy of this outlier appears to be too small to accurately assess histopathology and therefore the pathologist’s best estimate was AC. According to this analysis the tumor may be more consistent with an oligodendrogial or oligoastrocytic tumor.

This study focuses on the assessment of ADC values for grade II gliomas. A limitation of this study is that it does not include nonenhancing grade III gliomas. Future studies will examine the application of these color maps to nonenhancing grade III gliomas, which may include lower ADC values and therefore have a larger component of an oligo-like appearance.

Another possible limitation of this study is the analysis of both three-directional and six-directional diffusion data. A strong correlation between the ADC values from three-directional and six-directional data from the same patients has been shown in a previous study (13). The analysis from this study was performed using ADC values acquired at 1.5T. It has been shown that ADC values from 3T have smaller variances as compared to values from 1.5T, with a negligible effect on mean diffusivity (19). Therefore, analysis of 3T ADC values for ODs, ACs, and OAs may be enhanced in this type of analysis.

In conclusion, this technique generates RGB color maps with oligo-like (red), NAWM-like (green), and astro-like (blue) weightings, allowing for the visualization of the biologically different regions within the whole tumor mass. This may aid in directing image-guided biopsies in nonenhancing gliomas that have no specific enhancing lesion target in order to obtain tumor tissue.
from representative regions of the brain that can more accurately define the dominant tumor characteristics.

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