Comparison of MRI Contrast Enhancement by Motexafin Gadolinium and Omniscan in Glioblastoma Multiforme

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Purpose: To study the brain tumor MRI contrast enhancing properties of the radiation sensitizer, Motexafin Gadolinium (MGd), and to compare the topographic pattern and relative brain tumor enhancement by MGd with that produced by conventional contrast agent.

Materials & Methods: Eleven post-surgical glioblastoma multiforme (GBM) patients who participated in a Phase I clinical trial of involving MGd administration for radiation sensitization underwent MRI with a conventional contrast agent (Omniscan (gadodiamide)) within 2 weeks of having an MGd-enhanced MRI study. Electronic T1-weighted image data from the MGd and conventional contrast agent MRI studies were collected for these patients. MGd and Omniscan enhanced volume images were registered to a common space so that the patterns of labeling could be directly compared. Among the eleven patients, seven had residual tumor with sufficient enhancement for study. Regions of signal enhancement were outlined on each slice where enhancement was present by three expert readers who were blinded to the contrast agent and patient. Outlines were drawn around the volume that would be hypothetically used for radiation therapy planning. In other words, necrotic core regions that did not enhance were included if they were surrounded by a "ring" of enhancement. This produced 3-dimensional images of contrast enhancing volumes for each type of contrast agent (MGd and Omniscan) in a common space. The percentage of overlap between the two volumes of contrast enhancement, the volume enhanced by MGd but not by Omniscan and the volume enhanced by Ominscan but not MGd were determined for each of the seven cases. Intensities of the enhancement produced by the two agents were compared using a normal white matter area as a reference signal. MedX imaging processing software was used for image processing, including image segmentation, logistical calculation, and statistics. Paired t-test was performed with StatView software. Figure 1 shows an image enhancement comparison for one of the seven patients.

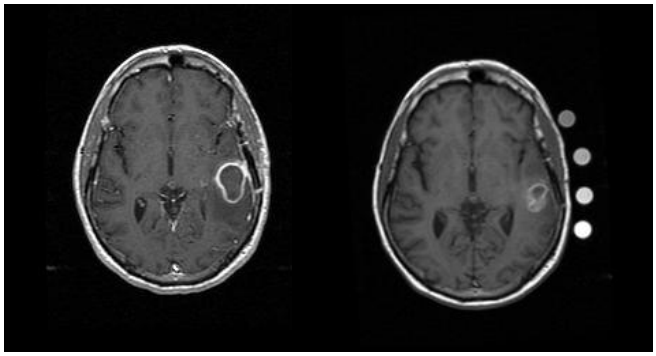

Figure 1. A representative image-enhancement-comparison for a patient
Left: Omniscan, 03/02/2001. Right: MGd, 03/02/2001
Note: The four dots on the right image are reference tubes used to estimate MGd concentration in tumor

Results: The volume of Omniscan enhancement was significantly larger than the volume of MGd enhancement ($p < 0.0001$ paired t-test, 21 comparisons). Omniscan enhancement volumes were on average 1.70 times larger than those of MGd (range 0.82 – 4.4). The two contrast enhancing volumes showed a high degree of overlap. On average 89.3% (range 77.9% – 98.3%) of the MGd enhancing volume also enhanced with Omniscan. The volume that solely enhanced with MGd was significantly smaller ($p < 0.0001$ paired t-test, 21 comparisons) than the volume that enhanced solely with Omniscan. MGd produced a significantly smaller ($p = 0.0048$, paired t-test, 21 comparisons) signal enhancement relative to the white matter reference than did Omniscan. The average ratio of Omniscan to MGd signal enhancement referenced to white matter was 1.20 (range 0.73 – 1.82) (Table). On visual observation, MGd appeared to label both active and necrotic tumor areas while the Omniscan tended to label only the outer tumor ring.

Conclusions: In GBMs, the MGd enhancement is weaker and smaller in volume compared with that of Omniscan. The weaker MGd enhancement may result from the tendency of GBMs to be relatively necrotic tumors combined with the fact that MGd localizes on or inside tumor cells rather than in the extracellular space as Omniscan does. The enhancement volumes produced by the two contrast agents have considerable volume overlap. The absence of substantial MGd enhancement outside of the Omniscan enhancement suggests there is not detectable MGd labeling in areas that do not enhance with Omniscan but that may contain infiltrating tumor cells.

patients	$S_{(Omniscan)}/S_{(MGd)}$
#1	1.235
#2	1.144
#3	1.144
#4	1.193
#5	0.724
#6	1.225
#7	1.75
Mean	1.202

Table 1. Signal intensity comparison