An Analysis of T2 Mapping on Brain Tumors

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 Abstract *Purpose* : Vasogenic edema on glioblastoma multiforme (GBM) or a metastatic brain tumor (METS) may have different T2 relaxation time values because it involves an increased water component. In this study, we assessed the diagnostic utility of T2 mapping techniques in distinguishing GBM from METS.

Materials and Methods: We studied a glioblastoma (GBM) patient and a metastatic brain tumor (METS) patient who had not undergone previous surgery or treatment. All MR imaging was carried out using a 3.0-T whole-body unit, and axial T2 maps were generated with five TEs (TE = $20, 40, 60$, 80, and 100 ms). Data were analyzed by using image processing and analysis software.

Results: The T2 map of a GBM case showed that the peritumoral area at a T2 relaxation time of 120–160 ms is prominent compared with the area at 210–240 ms. In contrast, the peritumoral area at 210–240 ms was prominent compared with the area at 120–160 ms in a METS case.

Conclusion: The distribution of T2 relaxation time in the peritumoral area shows different patterns in glioblastomas and metastatic brain tumors.

 Keywords T2 relaxation time • T2 mapping • Glioblastoma multiforme • Metastatic brain tumor

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Introduction

 Conventional radiological characteristics that are thought to favor cerebral lesions being metastatic as opposed to primary brain cancer include a peripheral location, spherical shape, ring enhancement, and multiple lesions [1]. Gliomas may, however, be multifocal (showing gross or microscopic continuity or evidence of cerebrospinal fluid spread and/or local metastases) or multicentric (no macroscopic or microscopic connection) and are therefore potentially indistinguishable on conventional imaging from metastatic disease with multiple enhancing lesions $[2]$.

 Currently, conventional MRI consists of a combination of proton density-, T1-, and T2-weighted sequences. T2 weighted imaging is sensitive to the identification of pathological change, and T2 relaxation is governed by both the total amount of water and the ratio of free to bound water, which is itself dependent on the macromolecular environment. A disturbance to this environment, such as neuronal loss or demyelination, results in an increase in free water, with a longer T2 relaxation time and greater signal intensity on a T2-weighted image. Quantitative evaluation of T2-weighted images is more sensitive and objective than visual assessment for the identification of subtle cerebral pathology. Quantitative T2 mapping has been applied to cerebral neoplasia $[3]$, neurodegenerative conditions [4], ischemia [5], head injury $[6]$, encephalitis [7], and, most frequently, multiple sclerosis (MS) [8], where increased T2 signal has been observed within lesions as well as in cerebral tissue that appeared normal on conventional MRI.

 Most of the new MRI techniques, with reported use in distinguishing glioma from metastatic disease, rely on detecting differences in the peritumoral region. In metastases, this area consists of vasogenic edema, whereas in glioma, neoplastic cells may also be present. As a result, a relative reduction in the peritumoral T2-weighted fluid-attenuated inversion recovery (FLAIR) hyperintense signal is expected in glioma, in contrast to cerebral metastases. Many exciting new developments in MR imaging techniques have been used to differen-

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tiate between a solitary metastasis and a high-grade glioma in the peritumoral region, including the use of spectroscopy, diffusion and perfusion imaging, and absolute apparent diffusion coefficient (ADC) measurements. Magnetic resonance spectroscopy alone has been shown to allow discrimination between metastases and glioblastomas $[9, 10]$. Diffusion tensor imaging has also shown promise in this distinction $[11]$, 12]. Tang et al. suggested that non-enhancing adjacent cortical signal abnormality detected by FLAIR has the potential to differentiate between solitary gliomas and metastases [13]. These studies have all involved differentiating solitary cerebral lesions. No study to date has specifically assessed the T2 relaxation time and the detection of non-enhancing adjacent cortical signal abnormality for differentiating between multicentric and/or multifocal gliomas and other cerebral tumors with multiple enhancing foci.

 The key to making the distinction between these two entities appears to lie in detecting the changes within the peritumoral area, the area beyond the enhancing margin on imaging. In metastases, this consists essentially of vasogenic edema, while in glioma, this may also contain neoplastic cells. Our hypothesis is that vasogenic edema on glioblastoma multiforme (GBM) and that on a metastatic brain tumor (METS) should show different T2 relaxation time values because it involves an increased water component. In this study, we investigated the diagnostic utility of T2 mapping in assessing non-enhancing signal intensity abnormality to distinguish GBM from METS. To the best of our knowledge, no previous similar studies have considered the implications of these findings.

Materials and Methods

Subjects

 We studied a patient with glioblastoma (GBM) and a patient with metastatic brain tumor (METS) who had not undergone any previous surgery or treatment. Diagnosis was confirmed by histological examination.

Magnetic Resonance Imaging

 All MR imaging was carried out using a 3.0-T whole-body unit (Achieva3T; Philips, Eindhoven, The Netherlands) with a SENSE-head-8 coil.

 Axial T2 maps with fat saturation were generated by using a multishot GRASE protocol with 5 TEs (TE=20, 40, 60, 80, and 100 ms). Other sequence parameters were TR = 3,705 ms (shortest); field of view (FOV), 230×183 mm; section thickness, 2 mm; section gap, 0 mm. and number of acquisitions = 1.

Image Interpretation

 Data were analyzed sequentially by one author (Kanji Nakai) using image processing and analysis software (Image J, version 1.45n, available at [http://imagej.nih.gov/ij/index.html;](http://imagej.nih.gov/ij/index.html) MRI Analysis Calculator plugin, available at [http://imagej.nih.gov/](http://imagej.nih.gov/ij/plugins/mri-analysis.html) [ij/plugins/mri-analysis.html\)](http://imagej.nih.gov/ij/plugins/mri-analysis.html). T2 maps were calculated on a pixel-by-pixel basis in the transverse plane. The ROI was obtained by the primary author (K.Nakai) by manually tracing the outline of the peritumoral area where T2/FLAIR was hyperintense. The tumoral area, where the borderline was obvious with contrast enhancement and compatible with the tumor margin seen by a T2/FLAIR image, was excluded from the ROI. Addition to the ROI of the whole slices including perifocal edema on the T2 map generated a histogram of T2 distribution for each case. As patients can have different edema volumes, the histogram was normalized according to each ROI.

Results

 Normalized percentage of pixels of T2 relaxation time showed a marked peak at around 80 ms in both tumors. In the GBM case, it decreased with prolongation of the T2 relaxation time, whereas in the METS case, it decreased to around 160 ms and then increased to a second small peak at 190 ms, indicating that the profile of normalized pixels had a bimodal distribu-tion (Fig. [1](#page-2-0)). The T2 map of the GBM case showed that the peritumoral area at T2 relaxation time of 120–160 ms is prominent compared with the area at 210–240 ms (Fig. 2). In contrast, the peritumoral area at 210–240 ms was prominent compared with the area at 120–160 ms in the METS case (Fig. [3](#page-3-0)). The ratio of $160-230$ ms at T2 relaxation time of the GBM case was higher than that of the METS case (Table 1).

Conclusion

 In our study, the T2 mapping technique showed that there was a significant difference in the distribution of T2 relaxation time in the peritumoral area between the GBM group and the METS group.

 The key to differentiating between the two neoplasm types appears to lie in the peritumoral area. In a glioblastoma, the

Fig. 2 A 70-year-old man with surgically confirmed glioblastoma multiforme. (a) Axial fluid attenuated inversion recovery (FLAIR) image shows a hyperintense mass surrounded by a moderate degree of edema.

(**b**) Axial post-contrast T1-weighted image shows enhancement of the solid part. (c) , (d) T2 maps show a larger area at $120-160$ ms (c) than at $210-240$ ms (d)

peritumoral region may be infiltrated by malignant cells in addition to vasogenic edema $[14]$, whereas in a metastatic deposit, the surrounding peritumoral area comprises predominantly vasogenic edema. By appearance alone, these peritumoral changes cannot generally be used to differentiate glioma from metastatic disease; however, vasogenic edema involves an increased water component. Using diffusion tensor imaging (DTI), Lu et al. demonstrated that there are clear differences in the diffusion characteristics of the vasogenic edema surrounding brain tumors compared with those of normal-appearing white matter [12].

 Tang et al., who examined solitary enhancing cerebral lesions using FLAIR to detect non-enhancing adjacent cortical signal abnormality, reported a sensitivity of 44 % in dis-

tinguishing glioma $[13]$, whereas Stuckey et al. reported that this sign was present in all multicentric/multifocal glioma patients presenting with more than one cerebral enhancing lesion $[15]$. Thus, it appears that non-enhancing adjacent cortical FLAIR signal abnormality is more common in multicentric/multifocal disease; however, this is not entirely unexpected as, by definition, these patients have more than one enhancing lesion to evaluate for the presence of this sign. In a larger series, 100 % sensitivity would presumably not be maintained. In contrast, the positive predictive values in the studies by Stuckey et al. and Tang et al. were 67 and 84 % respectively $[13, 15]$. The presence of this sign is not necessarily as good a predictor of multicentric/multifocal glioma when multiple enhancing lesions are present as it is for **Fig. 3** A 59-year-old man with surgically confirmed metastatic renal cell carcinoma. (a) Axial FLAIR image shows a low intense mass surrounded by edema. (b) , (c) T2 maps show a smaller area at 120–160 ms (**b**) than at 210–240 ms (**c**)

 Table 1 Ratios of 160–230 ms at T2 relaxation time in glioblastoma multiforme (GBM) and metastatic brain tumor (METS) cases

 One slice means counts of the slice shown in Figs. [2](#page-2-0) and 3 , and all slices mean the sum of counts of all slices including the hyperintensive peritumoral area in the same cases. The ratio of the GBM case is higher than that of the METS case

glioma when a solitary lesion is present. The difference is presumably due to the assumption made by the treating doctors that multicentric/multifocal cerebral lesions (in the context of proven malignancy at other sites) reflect metastatic disease, lessening the perceived clinical need for a histological diagnosis.

 In conclusion, the distribution of T2 relaxation time in the peritumoral area shows different patterns in glioblastoma and metastatic brain tumors. T2 mapping may be useful for differentiating glioblastoma from metastasis in patients.

Conflict of Interest We declare that we have no conflict of interest.

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