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THE USEFULNESS OF T2 RELAXOMETRY IN DIFFERENTIATING INFECTIVE FROM NEOPLASTIC RIM ENHANCING BRAIN LESIONS: EARLY EXPERIENCE

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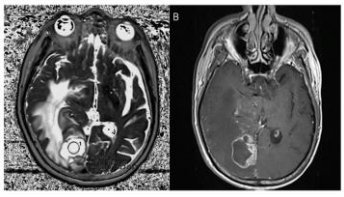
Graphical abstract



Abstract

Characterizing a rim enhancing brain lesion remains a challenge and conventional MRI sequences may not be adequate. The aim of our study was to determine whether or not rim enhancing brain lesions of infective origin could be differentiated from neoplasm using MR T2 relaxometry. T2 relaxation times were measured in the central core of 29 rim-enhancing lesions from 23 patients. (10 female, 13 male, age range 12-73 years old). The mean T2 relaxation time of infective lesions was 194.6ms (range 89.5- 498.7ms; SD 144.8) and that of tumour was 893.7 ms (range 147.8-1540.0 ms; SD 431.5). Our early experience showed that T2 relaxometry is a potential quantitative MR technique that can differentiate infective from neoplastic rim enhancing brain lesions.

Keywords: Rim enhancing brain lesions; magnetic resonance imaging; T2 relaxometry

Abstrak

Mencirikan lesi otak yang mempunyai 'rim enhancement' merupakan suatu cabaran dan penggunaan turutan MRI konvensional masa kini masih tidak memadai. Tujuan kajian kami adalah untuk menentukan sama ada lesi otak yang mempunyai 'rim enhancement' disebabkan oleh infeksi boleh dibezakan dari ketumbuhan dengan menggunakan MR T2 relaxometri. Pengukuran masa releksasi T2 telah dibuat pada 29 teras pusat lesi otak yang mempunyai 'rim enhancement' daripada 23 pesakit (10 perempuan, 13 lelaki, lingkungan umur berusia 12-73 tahun). Purata masa releksasi T2 untuk infeksi adalah 194.6 ms (julat 89.5- 498.7ms ; SD 144.8) dan untuk tumor adalah 893.7 ms (julat 147.8-1540.0 ms ; SD 431.5). Kajian awal menunjukkan bahawa T2 relaxometry adalah teknik MR yang berpotensi untuk membezakan sama ada lesi otak yang mempunyai 'rim enhancement' adalah disebabkan oleh infeksi ataupun ketumbuhan.

Kata kunci: Lesi otak; pengimejan resonans magnetik; T2 relaxometri

1.0 INTRODUCTION

The differential diagnosis of a rim enhancing brain lesion is very wide and includes primary or metastatic neoplasm, abscess, resolving haematoma, tumefactive demyelination and radiation necrosis. Of these, most of the encountered rim enhancing brain lesion belongs to either infective or neoplastic group. Characterizing a rim enhancing brain lesion purely by non-invasive imaging techniques remains a challenge. In addition, the clinical findings are often non-specific leading to a diagnostic dilemma.

Magnetic resonance (MR) imaging is well accepted to be superior than computed tomography when it comes to characterize a rim enhancing brain lesion. Even so, the usage of conventional MR imaging may still not be adequate [1]. Several additional MR techniques, such as diffusion weighted imaging, MR perfusion, MR spectroscopy and susceptibility weighted imaging are utilized in differentiating infective from neoplastic lesions [2,3]. Diffusion weighted imaging in particular is high in both sensitivity and specificity to differentiate pyogenic abscess from neoplastic lesions [4]. In diffusion weighted imaging, brain abscesses demonstrate diffusion restriction whereas the cystic or necrotic neoplasms do not show evidence of diffusion restriction [5]. However, this relationship is not always straightforward and has some pitfalls [6].

T2 relaxometry is a type of MR imaging technique that provides quantitative measurement of different pathology in the form of relaxation time of their contents. To the best of our knowledge, there was only a single published study, which used T2 relaxometry in characterizing a rim enhancing brain lesion. However, the study was specific on tuberculomas versus neurocysticercal cysts and it was concluded that T2 relaxometry was a reliable mean to differentiate between the two groups [7]. The present study on the other hand was to evaluate whether or not T2 relaxometry can differentiate infective from neoplastic rim enhancing brain lesions. Based on the different underlying pathophysiology and characteristic compositions between the two groups, we hypothesized that it was possible.

Table 1 Frequency of cases and T2 relaxation times according to the type of rim enhancing brain lesions

Lesions	Lesions	Number of lesions	T2 relaxation time [median / min – max (ms)]
Infective group (n=13)	Toxoplasmosis	6	235.1 (115.0-489.2)
	Histoplasmosis	4	109.4 (96.2 – 131.6)
	Pyogenic abscess	2	294.1 (89.5 – 498.7)
	Tuberculoma	1	93.2
Neoplastic group (n=16)	Metastasis	9	903.2 (199.2 – 1540.0)
	High-grade astrocytoma	4	895.7 (635.9 – 1350.2)
	Pilocytic astrocytoma	2	1220.4 (997.1 – 1443.6)
	Lymphoma	1	147.8

2.0 MATERIALS AND METHODS

2.1 MR Technique and Measurement

The model of MR machine that was used throughout this study was Superconducting Magnetom Verio 3.0 Tesla (Siemens, Erlangen, Germany). For scanning, the patients lied still on the gantry in supine position. A head coil was used to improve filling factor and image quality. The T2 relaxometry was performed which took an average of 5:40 minutes to complete. The T2 relaxometry that was used in this study was spin echo 16-echo with slice thickness of 5.0 mm and matrix size of 256 x 128. The time to repeat (TR) was 3000 ms and the 16 time to echo (TE) were TE 1 = 22 ms, TE 2 = 44 ms, TE 3 = 66 ms, TE 4 = 88 ms, TE 5 = 110 ms, TE6 = 132 ms, TE 7 = 154 ms, TE 8 = 176 ms, TE 9 = 198 ms, TE 10 = 220 ms, TE 11 = 242 ms, TE 12 = 264 ms, TE 13 = 286 ms, TE 14 = 308 ms, TE 15 = 330 ms and TE 16 = 352 ms. The T2 map was then generated using a special software and the mean T2 relaxation time was objectively calculated by drawing the region of interest at the centre core of the rim enhancing brain lesion (Fig 1) with careful attention was paid to avoid boundaries that could cause partial volume effect. The size of the region of interest was dependent on the size of the lesion.

2.2 Follow-up

All of the cases were followed up to ascertain the final diagnosis based on the histopathological, culture or clinical results. Any cases without any confirmation of definitive diagnosis of the brain lesions were excluded from the study.

2.3 Statistical Analysis

The measured T2 relaxation times of the rim enhancing brain lesions were tabulated according to the final diagnosis as well as the respective infective and neoplastic groups. Their T2 relaxation times were then analyzed using SPSS software version 20.Descriptive analysis was made and presented. Further analysis using Student's *t*-test and ANOVA were conducted to examine the significance of mean difference between diseases. A p-value of <0.05 was taken to be statistically significant. Receiver operating characteristic analysis was also performed to identify the best cut off point between the infective and neoplastic groups.

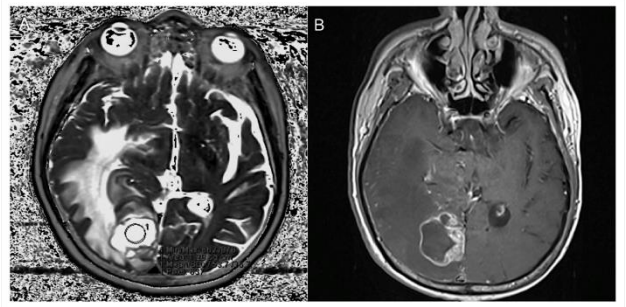


Figure 1 Axial images of (A) T2 relaxometry map with the ROI at the centre core of a lesion and the corresponding (B) T1W post gadolinium sequence. In this case the diagnosis was brain metastasis from lung carcinoma.

3.0 RESULTS AND DISCUSSION

3.1 Results

A Total of 29 lesions from 23 patients were obtained (10 female, 13 male, age range 12-73 years old). The underlying causes of rim enhancing brain lesions in this study in the order of reducing frequency were brain metastases (31.0%), toxoplasmosis (20.6%), high-grade astrocytoma (13.8%), histoplasmosis (13.8%), pyogenic abscess (6.5%), pilocytic astrocytoma (6.9%), tuberculoma (3.4%) and lymphoma (3.4%). The median values and ranges (maximum and minimum) of T2 relaxation times of the central core of the lesions according to the underlying diagnosis were summarized in Table 1. The mean of the normal contralateral white matter was calculated to be 102.4 ms.

There was a very wide range of T2 relaxation time obtained in this study. The highest T2 relaxation value was seen in brain metastasis (1540.0 ms) whereas the lowest value was demonstrated in pyogenic abscess (89.5 ms). The brain metastasis and histoplasmosis had the widest and narrowest range of T2 relaxation times respectively. This was after excluding the lymphoma and tuberculoma as they were presented as a single case each. ANOVA test analysis between the lesions revealed F-value of 5.913 and p-value of 0.001.

Grouping the lesions into infection and neoplasm gave interesting results. The mean T2 relaxation time of infective lesions was 194.6 ms (SD 144.8) and that of neoplasms was 893.7 ms (SD 431.5). The mean value of the neoplastic group was significantly greater than the infective group with t-value of 6.074 and p-value of 0.00. The 95% confidence intervals of the means for the neoplastic and infective lesions were 663.8ms to 1123.6ms and 107.1 ms to 282.1 ms respectively. The T2 relaxation times of the groups were displayed as Boxplot and Whisker diagram (Fig 2).

An overlap of T2 relaxation time was noted between the infective and neoplastic groups. The best cut off point was calculated by performing a receiver operating characteristic analysis (Fig 3). A test with perfect discrimination was taken as a curve that passed through the extreme corner (100% sensitivity, 100% specificity). Based on the receiver operating characteristic curves, the best cut off point was taken to be 493.9 ms. Values of more than 493.9ms detected neoplasm with sensitivity of 81.3% and specificity of 92.3% and values of less than 493.9ms detected infective lesion with 92.3% sensitivity and 81.2% specificity. The overlap area between the two groups was between 147.8 ms to 498.7 ms in this study.

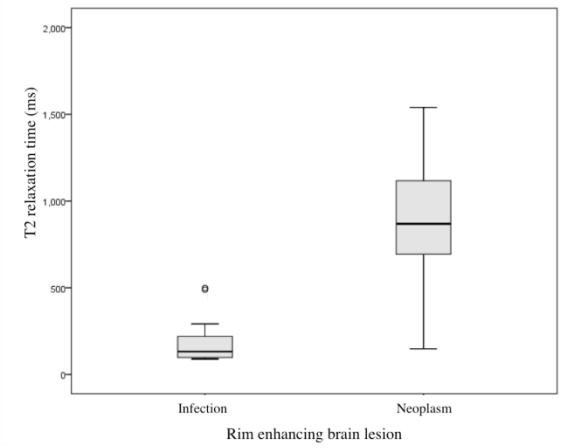


Figure 2 Boxplot and Whisker diagram of T2 relaxation time of the neoplastic versus infective groups of ring enhancing brain lesion. (Centre bars represent the medians, boxes indicate lower and upper quartiles, and range lines correspond their maximum and minimum value)

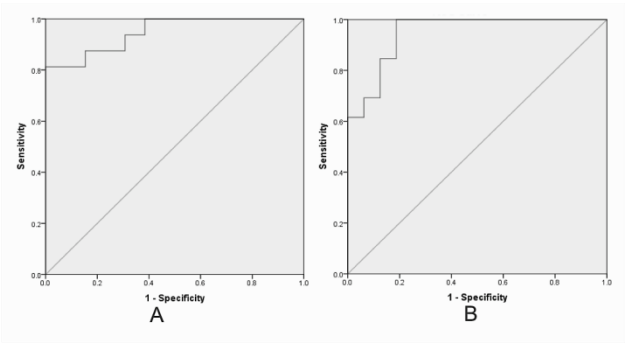


Figure 3 Diagrams of the (A) ROC curve when neoplasm was taken as the positive actual state and the (B) ROC curve when infection was taken as the positive actual state.

3.2 Discussion

Although the exact management of a rim enhancing brain lesion depends on the specific underlying diagnosis and the clinical setting of the affected patient, classifying the lesion into either infective or neoplastic groups are important to allow early empirical treatment and planning of work up. Generally, for immunocompetent patients, the leading aetiologies of rim enhancing lesions in the brain are neoplasms, both primary and metastatic, as well as pyogenic abscess [8]. In immunocompromised patient, the leading causes include primary cerebral lymphoma, toxoplasmosis and cryptococcosis [8]. Tuberculoma should be considered as the main differential diagnosis in the region where tuberculosis is an endemic. Regardless the immune status, the most frequently encountered rim-enhancing lesion in the present study was brain metastasis.

Different biological tissues have different T2 relaxation time, which are also affected by many parameters including pH, temperature, water and protein [7]. Presence of more water molecules unbound to macromolecule is associated with increase of T2 relaxation, whereas high viscosity and protein content have T2 shortening effects [7]. T2 relaxometry is not new in neuroimaging and had been used as a reliable tool for the assessment of certain conditions such as temporal lobe epilepsy [9,10]. However, T2 relaxometry is not yet widely used in characterizing a rim enhancing brain lesion. To the best of our knowledge, there was only a single published study on ring enhancing brain lesion using T2 relaxometry however it was specific on tuberculomas against neurocysticercal cysts [7]

In this previous study, tuberculomas showed significantly shorter T2 relaxation times than neurocysticercal cysts, where the mean T2 relaxation time of neurocysticercal cysts was 617 ms (range 305-1365 ms) and that of tuberculomas was 161 ms (range 83-290 ms). The shortening T2 relaxation time in tuberculomas was postulated to be due to fewer tissue-free protons in the protein and lipid-rich caseous matrix [7]. The T2 relaxation times for tuberculomas from that previous study were comparable to our current findings of infective group being lower than 493.9 ms. However, the T2 relaxation times of the neurocysticercal cysts were slightly on the higher side considering that they also belonged to the infective group. However, there was not any neurocysticercal cyst in the present study to compare with. Hence, whether they behave similar to or different from the rest of the infective lesions cannot be satisfactorily concluded.

In the present study, T2 relaxation times of rim enhancing infective lesions were significantly different from both primary and metastatic neoplasm. This reflected the difference of composition of content between them. The lesions of infective process contained inflammatory cells, proteins and cell debris. The high cellularity of inflammatory cells resulted in reduction of extracellular space available for water was the most likely explanation of its relative low T2 relaxation time as compared to neoplasms.

Despite the mean difference between infective and neoplastic lesions were statistically different, slight overlap between the two groups were observed. Brain metastases had the widest range of T2 relaxation times between them. All of the brain metastases in the study were from lung carcinoma. There was no correlation between different types of tumour cells and the T2 relaxation time within the group of brain metastases. For instance, both the highest and the lowest T2 relaxation time in this group were found to be adenocarcinoma. Hence, we postulated that the wide range difference of T2 relaxation time in this group were due to different degree or stages of necrosis instead of different cellular types.

Based on the receiver operative characteristic analysis, 493.9 ms was the best cut off point to differentiate infective and neoplastic ring enhancing lesions with higher value were in favour of neoplasms and lower values pointed towards infective lesions. However this must be used with caution, as it may only be applicable to specific MR technique and machine used in the current study. T2 relaxation times slightly vary with different MR techniques or field strengths [11].

Generally, in diffusion weighted imaging, toxoplasma abscesses consistently do not exhibit restricted water diffusion in contrast to the rest of the pyogenic abscesses due to histopathological difference [12]. Be that as it may, the T2 relaxometry in the current study revealed that toxoplasma abscesses behaved similar to the rest of the infective abscesses with relatively lower T2 relaxation time. Lymphoma was one of the lesions in the neoplastic group that had a relatively low T2 relaxation time as compared to the mean value of T2 relaxation time of the neoplastic group. Unfortunately, it was the sole case of such diagnosis in our study, hence it was not adequate to deduce whether or not lymphoma behaved slightly different as compared to the rest of the neoplasm in terms of T2 relaxation time. However, it is worth to mention that lymphoma is typically regarded as a highly cellular lesion as compared to the rest of the tumour [13]. Higher cellular density with smaller extracellular space for free water results in shorter spin-

spin relaxation and T2 relaxation time of the tissue being sampled.

The present study had a few limitations. Firstly, the present study was confined to a relatively small sample size, which has weakened the power of statistical results. The diseases within both infective and neoplastic groups are heterogeneous and each disease has small number of cases for intragroup comparison. We recommend similar study of larger scale by dedicated neuroimaging centres that can potentially recruit larger number of rim enhancing brain lesions. Secondly, the sizes of the region of interest used were non-standardized. However, this method was favourable to accommodate the varying sizes of the brain lesions and reflected a more practical approach mimicking the usual real practice. Thirdly, the exact values of T2 relaxation times may not be applicable to machine of different external magnetic field strength and different T2 relaxometry protocol, limiting the use of the exact cut off point used to differentiate neoplastic from infective rim enhancing brain lesions in other machine of different settings. Lastly, whilst the sequence only added 5.40 minutes to the protocol, the post-acquisition analysis is time-consuming making routine clinical use difficult.

4.0 CONCLUSION

Our early experience shows that T2 relaxometry is a potential quantitative MR technique that can differentiate infective from neoplastic rim enhancing brain lesions. It may serve as a useful research tool as an adjunct MR technique in an attempt to diagnose a rim enhancing brain lesion. We promote similar study of a larger scale with a more homogenous disease within each group to be carried out.

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