**INTRODUCTION**

Multiple intracranial ring-enhancing lesions are one of the most commonly encountered neuro imaging abnormalities. Widely available imaging techniques, computed tomography and magnetic resonance imaging (MRI) are used to detect these lesions.[1,3] A wide range of etiologies may present as cerebral multiple ring-enhancing lesions. On neuroimaging, these lesions appear as hypodense or isodense mean lesions on non-contrast computed (plain) tomography studies. After contrast administration, there is a ring- or a homogeneous disk-like enhancement within the region of hypodensity. The enhancing lesions are often of variable size and are usually surrounded by a varying amount of perifocal vasogenic edema. Typically, the ring-enhancing lesions are located at the junction of the gray and white matter, but they could be located in the subcortical area, deep in the brain parenchyma or may even be superficial.[2]

Diffusion weighted MRI (DW MRI) is a relatively recent MRI technique which provides image contrast that is different from that provided by conventional MR techniques. The uninhibited motion of water molecules in biologic tissue is free diffusion. By contrast, the movement of water molecules in biologic tissues is restricted because their motion is modified and limited by interactions with cell membranes and macromolecules. The degree of restriction to water diffusion in biologic tissue is inversely correlated to the tissue cellularity and the integrity of cell membranes. Thus, DW MRI is based upon the biologic tissue is inversely correlated to the tissue cellularity and the macromolecules. The degree of restriction to water diffusion in biologic tissues is different from that provided by conventional MR techniques. Therefore, diffusion of water molecules is free diffusion. By contrast, the movement of water molecules in biologic tissues is restricted because their motion is modified and limited by interactions with cell membranes and macromolecules. The degree of restriction to water diffusion in biologic tissue is inversely correlated to the tissue cellularity and the integrity of cell membranes. Thus, DW MRI is based upon the principle of assessment of movement of water molecules (diffusion) in the pathological areas by applying magnetic gradients in various planes. Using DW MR sequences, the quantitative assessment of diffusion in the lesions can be obtained and is represented as Apparent Diffusion Coefficient (ADC) values, which can be used for comparison between various pathologies.

**BASICS OF DIFFUSION WEIGHTED IMAGING:**

The basic principle of diffusion weighted imaging is that the small random motion of the molecules results in a Gaussian distribution of phases.[4] The effect of these variations is enhanced by using a T2 weighted SE, gradient echo, or echo planar technique and applying strong gradients. The ability of these special pulse sequences to depict diffusion depends on the strength and duration of the diffusion gradients and on the direction in which they are applied. Diffusion is independent of the relaxation times and thus adds another factor to contrast.[5]

**Apparent Diffusion Coefficient (ADC):**

According to Fick's law, true diffusion is the net movement of molecules due to a concentration gradient. However, MR imaging, cannot differentiate molecular motion due to concentration gradients from molecular motion due to pressure gradients, thermal gradients or ionic interactions. Also, with MR imaging, we do not correct for the volume fraction available or the increases in distance traveled due to tortuous pathways.

Therefore, when measuring molecular motion with DW imaging, only the apparent diffusion coefficient can be calculated. Substituting ADC for $D'$, the signal intensity of a voxel on a DW image is thus expressed as

$$S1 = S0 \times \exp(-b \times \text{ADC})$$
AIMS AND OBJECTIVES: 1. To study the imaging findings and establish a differential diagnosis of various ring enhancing lesions on MRI. 2. To differentiate neoplastic and non-neoplastic ring enhancing lesions using Diffusion Weighted Imaging. 3. To differentiate primary and secondary neoplastic lesions using Diffusion Weighted Imaging. 4. To correlate imaging findings of ring enhancing lesions with histopathological findings wherever possible.

MATERIALS AND METHODS:
- The study was done in Department of Radiology and Imageology, Nizam's Institute of Medical Sciences, Hyderabad.
- The study period was from May 2014 to May 2016.
- 40 cases referred to the radiology department for MRI brain with clinical diagnosis/suspicion of cerebral ring enhancing lesions, irrespective of age and sex, were studied during this period.
- Informed and written consent was taken from all the subjects participating in the study.

INCLUSION CRITERIA:
- All patients referred to MRI with clinically suspected neurological symptoms of infection/neoplasm.
- Cases of all age groups irrespective of sex will be included in the study.

EXCLUSION CRITERIA:
- Patients having general contraindications of MRI like history of claustrophobia and history of metallic implants insertion, cardiac pacemakers and metallic foreign body in situ.
- Unstable patients on life support mechanisms.

METHODOLOGY:
The patients with clinical suspicion of ring enhancing lesion and referred from clinical departments for MRI brain study having ring enhancing lesions in the brain were included in the study. The study was done in Department of Radiology and Imageology, Nizam's Institute of Medical Sciences, Hyderabad from May 2014 to May 2016 after institute ethics committee approval.

Technique:
The study was conducted using 1.5 Tesla MRI machine (Signa LX, GE) Diffusion weighted MR sequence was performed at two 'b' values, b = 0 s/mm2 and b = 1000 s/mm2 to obtain axial index DW images. Then, by using a software application (FuncTool in GE Signa LX), Apparent Diffusion Coefficient (ADC) maps were obtained for each subject and for each lesion (if multiple lesions found in the same subject). The ADC values (measured in mm2/s) at the core (center) of the lesion, periphery / enhancing rim of the lesion were recorded. In lesions that were too small or more linear on MR morphology or each subject and for each lesion (if multiple lesions found in the same subject). The ADC values (measured in mm2/s) at the core (center) of the lesion, periphery / enhancing rim of the lesion were recorded. In lesions that were too small or more linear on MR morphology or each subject and for each lesion (if multiple lesions found in the same subject). The ADC values (measured in mm2/s) at the core (center) of the lesion, periphery / enhancing rim of the lesion were recorded. In lesions that were too small or more linear on MR morphology or each subject and for each lesion (if multiple lesions found in the same subject).

Confirmation of the etiology of infection was considered according to the data obtained by cerebro-spinal fluid (CSF) analysis and other relevant laboratory investigations performed, clinical response to the treatment, in the form of symptomatic improvement / deterioration or looking for treatment response on follow up MRI scan in the form of reduced / increased perilesional edema or change in the number of lesions or lesion size.

Confirmation of primary brain neoplasms was done by surgical excision and histopathological diagnosis of the neoplasm.

Statistical Analysis:
Descriptive and analytical statistical analysis was carried out using the data obtained on Microsoft Excel software.

Continuous / quantitative data were stated as Mean ± SD (Standard Deviation) and range while results on categorical / qualitative data were presented in numbers (%).

2-tailed Student independent t-test was used and P values calculated to assess the difference in the mean ADC values obtained in the study. Significance was assessed at 5 % level of significance i.e. if P values were < 0.05, the findings or the difference in the findings was considered significant. Various diagrams and charts were used to represent obtained data.

OBSERVATIONS AND RESULTS:
The study population consists of 40 patients with intracranial ring enhancing lesions. The demographic profile of the study is as follows:

Etiological distribution of patients:
Out of 40 patients, 28 patients had (70%) non neoplastic lesions and 12 had (30%) neoplastic lesions. Hence, in our study, non neoplastic ring enhancing lesions were more common than neoplastic lesions. Among the non neoplastic lesions, tuberculosis (64.2%) was the most common followed by NCC, toxoplasmosis and bacterial infection. Among the neoplastic lesions, metastasis (58.3%) was more common than primary neoplasm. So, the most common ring enhancing lesion encountered in our study was tuberculosis (40 %) with the least common being bacterial CNS infection (5 %). Total 5 patients were with HIV positive status; 1 of them had toxoplasmosis, infection, 3 had tuberculosis infection and 1 patient had bacterial CNS infection in the form of abscess.

Table 1: The following table showing all the patients MR Diffusion & ADC findings.

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Diffusion restriction</th>
<th>ADC value in lesions [x 10^-5 mm^2/s]</th>
<th>Peritumoral region</th>
<th>Normal white matter</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>M</td>
<td>no</td>
<td>120</td>
<td>110</td>
<td>88</td>
<td>Tuberculomas</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>M</td>
<td>no</td>
<td>162</td>
<td>146</td>
<td>86</td>
<td>Neurocysticercosis</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>M</td>
<td>no</td>
<td>250</td>
<td>98</td>
<td>85</td>
<td>Glioblastoma multiforme</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>F</td>
<td>no</td>
<td>90.3</td>
<td>103</td>
<td>84.5</td>
<td>Tuberculosis abscess</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>M</td>
<td>no</td>
<td>125,132</td>
<td>101,107</td>
<td>83.80</td>
<td>Tuberculoma</td>
</tr>
<tr>
<td>6</td>
<td>24</td>
<td>F</td>
<td>no</td>
<td>143,135</td>
<td>152,155</td>
<td>89, 79.5</td>
<td>Toxoplasmosis abscess</td>
</tr>
<tr>
<td>7</td>
<td>25</td>
<td>M</td>
<td>no</td>
<td>155</td>
<td>120</td>
<td>78</td>
<td>Tuberculoma</td>
</tr>
<tr>
<td>8</td>
<td>32</td>
<td>F</td>
<td>no</td>
<td>130</td>
<td>115</td>
<td>78</td>
<td>Tuberculomas</td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>M</td>
<td>no</td>
<td>176</td>
<td>150</td>
<td>88</td>
<td>Neurocysticercosis</td>
</tr>
<tr>
<td>10</td>
<td>60</td>
<td>M</td>
<td>no</td>
<td>270</td>
<td>108</td>
<td>86</td>
<td>Metastasis</td>
</tr>
<tr>
<td>11</td>
<td>23</td>
<td>M</td>
<td>no</td>
<td>127, 138</td>
<td>103, 107.5</td>
<td>79.98</td>
<td>Tuberculomas</td>
</tr>
<tr>
<td>12</td>
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<td>M</td>
<td>no</td>
<td>85,95</td>
<td>105,115</td>
<td>80.85</td>
<td>Tuberculomas</td>
</tr>
<tr>
<td>13</td>
<td>65</td>
<td>F</td>
<td>no</td>
<td>230</td>
<td>119</td>
<td>88</td>
<td>Metastasis</td>
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<tr>
<td>14</td>
<td>43</td>
<td>F</td>
<td>no</td>
<td>235</td>
<td>120</td>
<td>89</td>
<td>Anaplastic astrocytoma</td>
</tr>
</tbody>
</table>
In our study, the ADC values at the core of non neoplastic lesions (123.7 +/- 5.4) x 10-5 mm2/s was significantly lower than that of neoplastic lesions (240.8 +/- 11.81) x 10 -5 mm2/s with a p value of < 0.05. ROC curve analysis showed a cut off value of 188 x 10-5 mm2/sec at the core of the lesion with 100 % sensitivity and 99.92% specificity for distinguishing neoplastic and non neoplastic lesions with neoplastic lesions showing higher ADC values than the cut off value. However, there was no significant difference in the ADC values at the periphery of the non neoplastic and neoplastic lesions.

### Comparison of ADC values of primary and secondary ring enhancing lesions

When the ADC values of primary and secondary neoplastic lesions ring enhancing lesions were compared there was no significant difference in the ADC values at the core and the periphery between the both.

However, when the peritumoral region of the neoplastic lesions were compared, the metastatic lesions (151.4 +/- 10.55) x 10-5 mm2/s showed significantly higher ADC values in the peritumoral region than the primary glial neoplasms (125.5 +/- 9.88) x 10-5 mm2/s. ROC curve analysis showed a cut off value of 136.5 x 10-5 mm2/s at the peritumoral region with 90% sensitivity and 80% specificity for distinguishing primary and secondary lesions.

### DISCUSSION

A total of 40 subjects (both outpatients and inpatients) referred to MRI with clinically suspected focal lesion in brain and those have already undergone conventional MRI sequences (plain and contrast) were subjected to diffusion weighted MR sequence on 1.5 Tesla MRI machine (Signa LX, GE) and results were analyzed.

The diffusion weighted MR findings and the ADC values in various etiologies of ring enhancing lesions were evaluated. The etiological confirmation of the diagnoses was considered according to the various laboratory investigations like blood and CSF analysis, radiological change in the number/ size of the lesions on follow up and histopathological confirmation, wherever required.

In our study, total 40 patients were studied with 20 males and 20 females. The mean age and age range was 37.1 years and 15 to 75 years.

A total of 80 focal lesions in 40 patients, (30 tuberculous, 20 NCC, 19 metastasis, 5 primary glial neoplasms, 3 bacterial and 3 toxoplasma)
were identified on the MRI sequences. The non neoplastic ring enhancing lesions (70%) were more common than neoplastic lesions (30%). Among the non neoplastic lesions, tuberculosis was the most common lesion (64%).

Out of 80 focal lesions, 75 lesions were seen on DW imaging with sensitivity of 93.75%. Out of which 50 lesions (24 tuberculous, 5 NCC, 10 metastasis, 5 primary glial neoplasm, 3 toxoplasma and 3 bacterial abscess) were adequately assessed by ADC maps. Rest of the lesions could not be adequately assessed because of the small size of the lesions and the inherent poor spatial resolution of the index DW images.

**Tuberculosis (Figure 1)** –
The mean ADC values at core of the T2 hypointense lesions, T2 hyperintense lesions and tuberculous abscesses were (129.42 +/- 4.5) x 10^{-5} mm^2/s, (84.75 +/- 4.9) x 10^{-5} mm^2/s and (81.1 +/- 8.5) x 10^{-5} mm^2/s, respectively. There was no significant difference in the mean ADC values at the core of T2 hypointense lesions and abscesses, while the core ADC of T2 hyperintense lesions differed significantly from T2 hyperintense lesions and abscesses. Similar results were published in the study performed by Gupta RK et al [6].

The mean ADC at core of tubercular abscesses in our study was (81.1 +/- 8.5) x 10^{-5} mm^2/s. In study performed by Luthra G et al [7], the mean ADC value at the core was (66 +/- 23) x 10^{-5} mm^2/s. This difference in the values is due to the tubercular abscess without restriction having higher ADC value at the core and thus altering the mean. The ADC at the core of the abscess with restriction in our study was 73.3 x 10^{-5} mm^2/s, which correlates well with the values in their study.

On comparing the ADC values at core, the ADC values at core of T2 hyper intense/ hypo intense tuberculomas (129 +/- 5) x 10^{-5} mm^2/s was significantly lower than that of primary and secondary neoplastic lesions (242 +/- 8.66) x 10^{-5} mm^2/s, 239.6 +/- 10.2 x 10^{-5} mm^2/s. (p<0.05)

According to a study by S Chaterjee et al [8] observation there was overlap of mean ADC values of tuberculomas and metastasis. However, they had not compared the ADC values at the core of the lesions. But, in our study the ADC values at the core were compared and it was found that the ADC values at core of T2 hyper intense/ hypo intense tuberculomas (129 +/- 5) x 10^{-5} mm^2/s was significantly lower than that of primary and secondary neoplastic lesions (242 +/- 8.66) x 10^{-5} mm^2/s.

**NCC** – In our study, the mean ADC at the core of NCC lesions was (157.8 +/- 11.8) x 10^{-5} mm^2/s and was significantly higher (p<0.05) than the ADC values at core of T2 hypointense as well as T2 hyperintense tuberculomas. These findings correlate with a study done by Gupta RK et al [19] [6], in which the mean ADC value from the core of the NCC lesions was (166 +/- 29) x 10^{-5} mm^2/s and was significantly higher than the tuberculous granulomas.

**Toxoplasmosis (Figure 2)**:
In our study, three toxoplasmosis abscesses were studied in two HIV positive male patients. Both abscesses showed peripheral enhancement and did not show restricted diffusion, with core and periphery / wall mean ADC values of (139.33 +/- 3) x 10^{-5} mm^2/s and (155 +/- 1.6) x 10^{-5} mm^2/s.

Crispina H et al [9] studied diffusion-weighted MRI appearance of Toxoplasma abscesses. The findings correlate with those in our study in that the there was absence of diffusion restriction in the toxoplasma abscesses.

**Bacterial Abscess (Figure 3)**:
In our study, 2 out of 3 (67 %) bacterial abscesses showed restricted diffusion at the core with low mean ADC value of (67 +/- 3) x 10^{-5} mm^2/s which correlates with the study done by Luthra G et al [10], in which they obtained mean ADC of (73 +/- 18) x 10^{-5} mm^2/s at the core of restricted bacterial abscesses. The core of bacterial abscess contain inflammatory cells, bacteria, mucoid proteins, cell debris along with necrosis and hence show restricted diffusion.

The abscess without restriction in our study was in a HIV positive patient with causative organism isolated was staphylococcus aureus. Non restriction of the core in bacterial abscesses can occur as DWI findings differ based upon the variable concentrations of inflammatory cells and bacteria, different etiological organisms, the host immune response, a difference of the necrotic or viable inflammatory cells and the age of the abscess. In our study, the altered immune response of the HIV patient can probably be the explanation for the different diffusion characteristic (non-restriction) of the bacterial abscess.

There was significant difference in the mean ADC at the core of bacterial abscess (67 +/- 3) x 10^{-5} mm^2/s which correlates with the study done by Shigeo Ohba et al [11], Noguchi et al [12], Alam MS [13] et al, Ping Hong Lai et al [14] where significantly higher ADC values at the core of necrotic brain neoplasms were found when compared to lower ADC values at the core of brain abscess.
Primary Glial Neoplasms:

In our study, the mean ADC values at the core and the periphery of the primary glial neoplasm lesions was (242 +/- 8.66) x 10^{-5} mm^2/s and (109.6 +/- 7.5) x 10^{-5} mm^2/s, respectively. These values correlate with the ADC values (mean ± SD, 2.2 ± 0.9) x 10^{-3} mm^2/sec in the cystic/ necrotic portions, (mean ± SD, 1.1 ± 0.2) x 10^{-3} mm^2/sec in the peripheral enhancing portion of glioblastoma multiforme (Figure 4) in the study performed by Robert D. Tien et al {15}.

The mean ADC values at the core of the primary glial neoplasms were significantly higher when compared to the ADC values at the core of the non neoplastic lesions.

Metastasis (Figure 5):

The mean ADC values of the lesions at the core and periphery / wall in our study were (239.6 +/- 10.22) x 10^{-5} mm^2/s and (113.9 +/- 7.8) x 10^{-5} mm^2/s, respectively and were not significantly different from the ADC values of primary glial neoplasms.

The mean ADC values in the peritumoral region was (151.4 +/- 9.8) x 10^{-5} mm^2/s. The metastatic lesions show significantly higher ADC values than the primary glial neoplasms in the peritumoral region.

The mean ADC values in the peritumoral region of primary neoplasms was (125.5 +/- 9.8) x 10^{-5} mm^2/s. There was significant difference with p value <0.05 in the ADC values of the peritumoral region of primary glial neoplasms and the metastasis with metastasis showing higher ADC values than the primary glial neoplasms in the peritumoral region. This is due to the fact that in glioblastoma multiforme, the peritumoral region may be infiltrated with malignant cells in addition to vasogenic edema, whereas in a metastatic deposit, the peritumoral areas comprise predominantly vasogenic edema. Hence, there is restricted diffusion in the peritumoral region of glioblastoma when compared to the increased diffusion in metastasis.

A cut off of ADC value of 136.5 +/- 5.6 x 10^{-5} mm^2/s in the peritumoral region generated the best combination of 90% sensitivity and 80% specificity to differentiate the primary glial neoplasms and metastasis.

This correlated with the studies performed by Lee EJ et al [20], Chiang IC et al [21]where a cutoff value of 1.302 × 10^{-3} mm^2/s for the minimum peritumoral ADC value generated the best combination of sensitivity and specificity for distinguishing between glioblastoma and metastasis with metastasis showing higher ADC values in the peritumoral region.

Comparison between ADC values of neoplastic and non neoplastic lesions at the core:

There is significant difference in the ADC values of non neoplastic lesions and neoplastic lesions. A cut off value of at 188 x 10^{-5} mm^2/s at the core of the lesion generated the best combination of 100% sensitivity and 99.92% specificity for distinguishing neoplastic and non neoplastic lesions with neoplastic lesions showing higher ADC values than the cut off value. Hence, DWI has 100% sensitivity and 99.92% specificity for distinguishing neoplastic and non neoplastic lesions. The explanation for the higher ADC values is that the necrotic portion at the core of glioblastomas contain less viscous fluid with necrotic tumor tissue and few inflammatory cells thereby resulting in free diffusion of water molecules. In contrast the core of non-neoplastic inflammatory lesions contain inflammatory cells, bacteria, mucoid proteins, cell debris along with necrosis and hence show restricted diffusion.
According to earlier studies done by Shigeo Ohba et al [22], Noguchi et al [23], Alam MS [24] et al, Ping Hong Lai et al [25] showed that diffusion weighted imaging could be used to differentiate the brain abscesses from necrotic brain neoplasms with significantly higher ADC values at the core of necrotic brain neoplasms when compared to lower ADC values at the core of brain abscess. These findings correlate with the findings in our study.

**Comparison of diffusion characteristics in the wall / periphery of the lesions**

The mean ADC values in the wall / periphery of bacterial, tubercular, NCC and toxoplasmosis abscesses, primary glial neoplasms and metastasis were (122.5 +/- 2.5) x 10-5 mm2/s, (111.5 +/- 1.5) x 10-5 mm2/s, (142.2 +/- 2.5) x 10-5 mm2/s, (153.5 +/- 1.5) x 10-5 mm2/s, (109.6 +/- 7.5) x 10-5 mm2/s and (113.9 +/- 7.8) x 10-5 mm2/s respectively.

In study performed by Shigeo Ohba et al [26] the ADC _mean values of enhanced regions were 120 +/- 0.2x 10-5 mm2/s in gliolomas, 129.3 +/- 0.4 x 10-5 mm2/s in metastasis and they were found not to differ significantly between metastatic tumors and glioblastomas. This finding correlated with the above ADC values in our study.

According to study done by Luthra G et al [27], the mean ADC values in the wall of the pyogenic, tubercular abscesses were (79 +/- 19) x 10-5 mm2/s, (83 +/- 34) x 10-5 mm2/s respectively. As compared to this study, the values in our study are significantly higher. This probably was due to the difficulty in identifying correctly the wall of the lesions in many cases due to poor inherent spatial resolution of the DW index images and resultant placement of the region of interest (ROI) in the perilesional edema or adjacent brain parenchyma while calculating the ADC values in ADC maps.

According to our study there was no significant difference in the ADC values at the periphery between the non neoplastic and neoplastic lesions or the primary and secondary neoplastic lesions.

**LIMITATIONS**

- Limited number of subjects in the study. More number of subjects could have made the statistical analysis more accurate.
- All lesions were not histo pathologically proven.
- Small lesions could not be evaluated by diffusion and ADC maps.

**CONCLUSION**

- DWI has a complimentary role in differentiating the neoplastic and non neoplastic lesions and in differentiating the etiology among the ring enhancing lesions.

**ABBREVIATIONS**

ADC – Apparent diffusion coefficient
AIDS – Acquired immunodeficiency syndrome
CNS – Central nervous system
CSF – Cerebrospinal fluid
CT – Computed tomography
DW – Diffusion weighted
DWI – Diffusion weighted imaging
EP – Echoplanar
EPI – Echoplanar imaging
FLAIR – Fluid attenuated inversion recovery
FSE – Fast spin echo
HV – Human immunodeficiency virus
Max – Maximum
Min – Minimum
mm – Millimeters
MR – Magnetic resonance
MRA – Magnetic resonance angiography
MRI – Magnetic resonance imaging
ms – Milliseconds
NCC – Neurocysticercosis
NMR – Nuclear magnetic resonance
s – Seconds
SD – Standard deviation
sec – Seconds
T1W – T1 weighted
T2W – T2 weighted
TB – Tuberculosis
TBM – Tuberculous meningitis
TE – Time to echo

**REFERENCES**


[16] Chiang IC Kuo YT, Lu CY, Yeung KW, Lin WC, Sheu FO, Liu GC, Distinction between brain abscess from necrotic brain neoplasms with significantly higher ADC diffusion weighted imaging could be used to differentiate the brain abscesses from necrotic brain neoplasms with significantly higher ADC values at the core of necrotic brain neoplasms when compared to lower ADC values at the core of brain abscess. These findings correlate with the findings in our study.


