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GENERAL ARTICLE

Diffusion-weighted MR Imaging and ADC map of Brain Tumors

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Key words: Apparent diffusion coefficient map, MR imaging.

Abstract

Gold-Magnetic Resonance Imaging (MRI) plays an important role in the detection of brain tumors. It is generally accepted that conventional magnetic resonance imaging (MRI) tends to underestimate the size of a tumor, which in turn can lead to a suboptimal treatment. Diffusion-weighted imaging (DWI) is an acceptable technique for studying the movements of water molecules of tissue. In diffusion-weighted imaging we may face with drastically different signals, depending on cell density and the type of tissue. Measuring the diffusion coefficient in brain tumors allows the classification of tumor types and provide a definitive diagnosis of some kinds of tumors. The main goal of any non-invasive imaging technique is to determine the location and size of the tumor and also the detection of its infiltration in brain tissue. Many attention was paid for the proper identification of reversible changes of tumor in normal brain tissue, such as edema and translocation. DWI technique has become an important part of MRI for patients suffering from brain tumors. Differential diagnosis of benign and malignant tumors of the brain are vital, and it facilitates to choose strategies for treatment of malignant tumors. Indeed DWI does not need to contrast enhancement, so it is a non-invasive method. Measuring the average of ADC map is helpful, especially when T_1 and T_2 images do not give enough diagnosis information because it provides the study of tissue definitive features. In the present article, the merits and demerits of the techniques have been discussed.

Introduction:

The main goal of any non-invasive imaging technique is to determine the location and size of a tumor and also the detection of its infiltration in brain tissue. Till date, many attention was paid for the proper identification of reversible changes of tumor in normal brain tissue, such as edema and translocation. This information is very important in reaching favorable treatment results with the least damage to the basic functional structures of the brain. Non-invasive imaging techniques are very effective in the treatment of brain tumors before surgery, for planning and at the time of surgery and also for control and evaluating of treatment response (Cha, 2006; Belden *et al.*, 2011; Bangiyev *et al.*, 2014).

Brain tumor response to treatment has been assessed using the MacDonald scale. MacDonald scale is based on a bi-dimensional measurement of tumor enhancement by MRI or CT scan (MacDonald, 1990).

Computerized tomography imaging technique may be used as the first method for diagnosing the patients with brain tumor, but MRI is the most important imaging technique in this regard. CT scan is an emergency imaging technique in diagnosing bleeding, hernia, and hydrocephalus but it is less successful in studying brain tumors and calcification (Lee & Van Tassel, 1989; Eskandary *et al.*, 2005).

MRI is one of the most valuable techniques in studying brain tumors (Tsuruda et al., 1990). At first, features of the tumor is investigated by T_1- weighted imaging of before and after injection and also the same is investigated by T2- weighted imaging. Enhancement happens in T_1- weighted images after paramagnetic injection due to a local breakdown in the blood-brain barrier.

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Given that tumor enhancement primarily reflects the breakdown of the blood-brain barrier, it may not reflect true changes in tumor growth. Such as, for patients treated with chemoradiation, 'pseudoprogression' can occur where there is an increase in tumor enhancement on MRI suggestive of tumor progression, but without increased tumor activity (Brandsma & Van den Bent, 2009).

However, tumor growth is not always associated with the breakdown in the blood-brain barrier, and as an enhancement with not happen in contrast. In this case, we can study the tumor based on the tissue type, inflammation, having increased permeability in blood vessels or other abnormal changes. In comparison with spin echo T_1-weighted imaging with contrast injection, and fast spin echo T2-weighted imaging, DWI is a very powerful technique in diagnosing of tissue abnormality and microscopic changes in different brain diseases (Okamoto *et al.*, 2000).

Basic principles of DWI:

Diffusion or spreading is a physical property which explains accidental movements of water molecules in response to heat in the microscopic scale. These movements are limited by cellular membrane of macro-molecules. 90% of protons which produce MRI signals exist in water molecules, so movements of water molecules could have significant role in MRI.

Total three points should be considered in the measurement of diffusion by MRI signals:

1. DWI is a non-invasive technique and does not need an injection of contrast.
2. DWI measures the movements of water molecules in diffusion gradient axis.
3. Accidental movements of water molecules (diffusion) cause a decrease in signal, while oriented membrane (stream) cause a transportation in phase in DWI, so they cannot be separated (Le Bihan, 1990; Le Bihan *et al.*, 1988).

As a whole, the relationship between a primary signal (before implementing diffusion gradients) and reversing signal after implementing diffusion gradients could be explained by this formula: $S=Soe^{-bD}$

So as a whole, image contrast of DWI is controlled by an internal (D) and an external parameter (b)(Mori & Tournier, 2013). The unit of b-value is s/mm2. D is constant in this formula and it also includes the external diffusion correlation and it is shown by mm2/s.

Diffusion-weighted and apparent diffusion coefficient:

Diffusion-weighted imaging is based on the random or Brownian motion of water molecules in relation to their thermal energy DWI which is used to assess brain tumors and while it gets some limited success as a definitive prognostic tool, its proponents suggest that in certain setting it can increase both the sensitivity and specificity of MR imaging.

One example of a specific arena in which DWI may be helpful is in distinguishing between brain abscesses and necrotic and cystic neoplasms on MRI. A differential diagnosis for benign and malignant tumors of the brain are vital, and it helps to choose strategies for treatment of malignant tumors. Tumor biopsies are classified by standards of world health organization (WHO) (Kleihues *et al.*, 1992). The WHO classified brain tumors in 4 categories: first-grade tumors are non-invasive and grade four tumors are very invasive. This classification is based on histological features such as mitosis, necrosis and permeability ratio. Several studies have described the usefulness of DWI for brain tumors (Louis *et al.*, 2007). In one study the average amount of ADC in solid benign tumors was seen much more than malignant masses (Wang *et al.*, 2003). The study included cancer, lymphoma, benign adenoma and benign cysts. Further, th study also reported that the value of ADC in lymphoma was significantly lower than malignant tumors.

Abscesses exerts a high signal on DWI with a reduced Apparent Diffusion Coefficient (ADC) within the cavity. This restricted diffusion is directly relate to the characteristic of the pus filled in the cavity, which in turn reduce water mobility, lower ADC, and a bright signal on DWI. By contrast, necrotic and cystic tumors display a low signal on DWI (similar to the CSF in the ventricles) with an increased ADC as well as isointense or hypointense DWI signal intensity in the lesion margins.

DWI is also an effective way of differentiating an arachnoid cyst from epidermoid tumors. Both lesions present similar signal intensity characteristic of cerebrospinal fluid (CSF) on T_1 and T_2 sequences (fig.-1). The ADC values of epidermoid tumors are similar to those of the brain parenchyma, whilst ADC values of arachnoid cysts are similar to those of CSF (fig.-2) (Srinivasan *et al.*, 2008; Berens *et al.*, 1990).

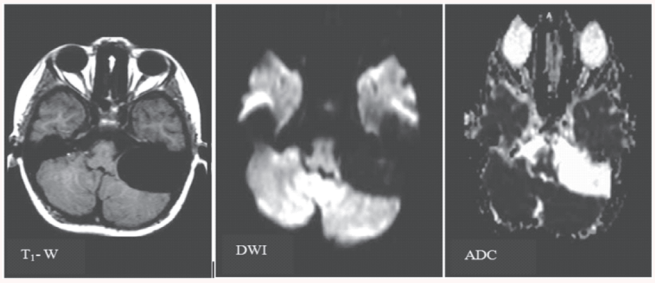

Figure-1: An expansive lesion in the left aspect of the posterior fossa, demonstrating similar signal intensity to CSF and high diffusibility. (Diagnosis: Arachnoid cyst)

An expansive lesion in the left aspect of the posterior fossa, demonstrating similar signal intensity to CSF and high signal intensity on diffusion-weighted imaging (DWI).
(Diagnosis: Epidermoid)

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In certain settings, diffusion-weighted imaging can increase both the sensitivity and specificity of MR imaging in the evaluation of brain tumors by providing information about tumor cellularity, which perhaps improve prediction of tumor grade. The mechanism in which DWI helps in the tumor grading is based on the fact that free water molecule diffusivity is restricted by cellularity increase in high-grade lesions. The reduction in extracellular space caused by tumor cellularity causes a relative reduction in the apparent diffusion coefficient (ADC) values (Jemal *et al.*, 2002; Brunberg *et al.*, 1995).

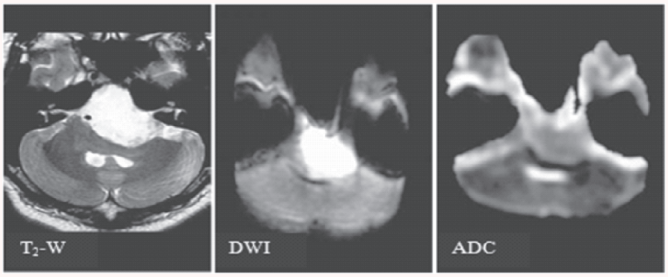

Figure-2: An expansive lesion in the left aspect of the posterior fossa, demonstrating similar signal intensity to CSF and high signal intensity on diffusion-weighted imaging (DWI). (Diagnosis: Epidermoid)

In predicting the malignancy rate, the threshold amount of ADC is 1.22 × 10-3mm2 / S with 86% accuracy, 84% sensitivity and 91% specificity. These result was reported by Maeda *et al.* (2005) as per which ADC level in lymphoma was significantly lower than malignant tumors. This study shown a significant different in ADC level between benign tumors (1.50± 0.48 $\times 10^{-3} mm^2/S$) and malignant tumors (1.07±0.29$\times 10^{-3} mm^2/S$). Some scientists believe that there is an inverse relationship between ADC and cellularity of brain tumors. There is also a limitation in spread in higher cellularity. Cellularity of tumor is an important factor in diagnosis of tumor and it can be analyzed by a specific software. A significant correlation between the ADC on the one hand and tumor cellularity and tumor grade on the other exist (Eis *et al.*, 1994; 1995; Els *et al.*, 1995; Gupta *et al.*, 1999; 2000; Sugahara *et al.*, 1999; Castillo *et al.*, 2001; Gauvain *et al.*, 2001; Nonomura *et al.*, 2001; Kono *et al.*, 2001; Guo *et al.*, 2002).

Studies also predicted the limitation of spread in high grade Gliomas (Alvarez-Linera *et al.*, 2008), brain lymphoma (Akter *et al.*, 2008) and brain abscess (Mishra *et al.* 2005). Further, ADC value is high in Vasogenic edema around tumor (fig.-3).

Pretumoral edema could be seen as an increase of signal in T_2/FLAIR hyperintense around main mass. In some of the cases, this could be vasogenic edema around the tumor, like metastasis. However, in Glioma, pretumor edema is mostly because of infiltration of tumoral cells in areas with a decrease of the signal in T_2/FLAIR sequence (Klatzo, 1967; Lu *et al.*, 2003). Perhaps most helpfully, high-grade tumors in some studies been found to have low ADC values, suggesting a correlation between ADC values and tumor cellularity. Whereas elewhere ADC values found in high and low-grade gliomas seen to be overlapped upto far extent (Law *et al.*, 2002; Barajas *et al.*, 2013).

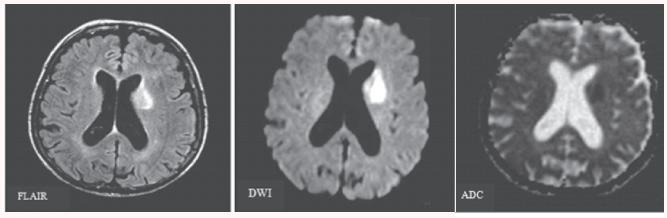

Figure-3: A 72-year-old female presented with mental and language disturbance, since 20 days. Enhancing lesion, restricted diffusion on DWI and ADC. (Diagnosis: Lymphoma).

It is well known that the brain tumors, especially the gliomas, are heterogeneous. Usually within the same neoplasm grade, mostly high-grade, different histologic features of grades II–IV are seen. This limitation may also be explained by the fact that it is not only the tumor cellularity that is responsible for reducing the diffusibility. Lymphoma, a highly cellular tumor, has hyperintensity on DWI and reduced ADC values. While meningiomas also have a restricted diffusion, displaying low ADC values, they rarely present difficulty in diagnosis (Barboriak *et al.*, 2003; Tien *et al.*, 1994; Krabbe *et al.*, 1997).

The DWI can be helpful upto some extent in distinguishing medulloblastoma from other pediatric brain tumors, as it seems to display restricted diffusion presumably because of the densely packed tumor cells and a high nuclear-to-cytoplasm ratio (Le Bihan *et al.*, 1993). The technique of calculating the ADC coefficient for a given volume on a voxel by voxel basis for histogram analysis has been described by several authors (Pope *et al.*, 2009; 2011; Murakami *et al.*, 2007). Important differences exist among ADC analyses of these authors. Pope et al. (2009) used ADC values from regions of interest corresponding to the enhancing portion of the tumor only; they excluded regions of non-enhancing T2-weighted signal hyperintensity, which represent edema and/or infiltrative tumor (Pope *et al.*, 2009; 2011; Murkami *et al.*, 2007) included these regions of T_2 signal hyperintensity in their analysis.

Necrosis caused by therapy or tumor growth degrades cellular integrity and is thought to increase the ADC of tissue (Pope *et al.*, 2006; Mardor *et al.*, 2004). This is in contradistinction to areas of high cell density, where the ADC is low, since water molecules are more restricted in their movement within cells compared to the extracellular space (Sugahara *et al.*, 1999; Chen *et al.*, 2005). Although studies show the ability of ADC in describing brain tumors, there is a small weakness in resolution.Usually studying tumors will do after injection in spin echo weighted in T_1 sequence and also ADC would be investigated. So, the finding of DWI should always be in combination with MRI

findings for investigation of brain tumors.spin Echo T1-weighted is done after injection and the specific location would be identified and then it would be investigated in ADC map.

Influence of field strength on apparent diffusion coefficient values:

In comparison with 1.5 T systems, 3T systems with phased array coil and parallel imaging techniques help us to take high-quality images with DWI and also have a lower signal-to-noise ratio (SNR) for ADC map. But most of the previous DWI studies on brain tumors has been done with 1.5 T systems and significant differences between ADC level of white and grey matters of the brain have been reported (Guo et al., 2001). Further studies shown that the power of magnetic field in taking DWI is also very important (Chang et al., 2005).

Technical limitations:

Though initial reports suggest advantages of DWI in the evaluation of patients suffering from brain tumors, but such reports were largely single-center, uncontrolled, and preliminary findings. Therefore those results should be cautiously interpreted (Huisman *et al*., 2006). There are some limitations in taking DW images, especially in the head area. In relation to EPI, magnetic susceptibility artifact and chemical shift artifact lead to decrease of image quality (Krings *et al.*, 2001). Magnetic susceptibility artifact is because of empty spaces in the head such as paranasal sinuses and mastoids. As a result, it makes identification of ADC hard and lead to decrease in intensity of DWI signals.

Furthermore, there remain substantial technical hurdles, even though the rapidevolution of MRI systems makes ever more powerful approaches possible. Such improvements are particularly welcome given the limited signal-to-noise ratio of diffusion overall. Nevertheless, these initial data are promising(Guye *et al*., 2003).

Conclusions:

SDWI technique, a non-invasive method has become an important part of MRI for patients suffering from brain tumors. From it the measuring the average of ADC map is helpful, especially when T_1 and T_2 images do not give enough diagnosis information because it provides the study of tissues' definitive features. This technique is highly useful during treatment. However, it is not enough alone for studying brain tumors and it should be correlated with information received from Structural sequence MRI. For decreasing the scan time and other limitations in spatial resolution, we need more improvements in this regard.

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