The role of Diffusion-Weighted Magnetic Resonance Imaging in detection and characterization of Musculoskeletal Tumors

Essay

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Abstract----------

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Diffusion-weighted imaging (DWI) yields qualitative and quantitative information that reflects tissue cellularity and cell membrane integrity, which complements the morphologic information obtained by conventional MR imaging. At present, there is no role of DWI in the characterization or local staging of primary bone tumors. However, whole body DWI has a potential role in assessment of bone metastases and distant staging .DWI also has a great success in the differentiation between benign and malignant vertebral compression fractures. DWI could provide earlier identification of patients with a poor treatment response or of those with tumor recurrence**.** This is because cellular death and vascular changes in response to treatment precede changes in lesion size, Therefore, DWI could provide an opportunity to adjust individual treatment regimens more rapidly, sparing patients the unnecessary morbidity, expense, and delays in the initiation of effective treatment **.**Whole-body DW imaging is an attractive lesion detection technique because it enables “at-a-glance” assessments, where one’s attention is immediately drawn to potential abnormal regions, which helps reduce the image interpretation times of anatomic whole-body MR imaging . There are several clinical applications for DWIBS have been reported in the literature, especially for oncological imaging**.**

Key words:-Diffusion-weighted imaging (DWI), musculoskletal (MSK), magnetic resonance imaging (MRI).

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ
وَالْمُؤْمِنُونَ ۖ وَسَتُرَدُّونَ إِلَىٰ عَالِمِ الْغَيْبِ
وَالشَّهَادَةِ فَيُنَبِّئُكُمْ بِمَا كُنْتُمْ تَعْمَلُونَ ﴿١٠٥﴾

سورة التوبة الآية ١٠٥

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TA	time acquisition
TE	echo time
TR	repetition time
FOV	field of view
SE	spin-echo
EPI	echo planar imaging
ROI	region of interest
MIP	maximum intensity projection
MRI	Magnetic resonance imaging
DWI	diffusion-weighted imaging
ADC	apparent diffusion coefficient
PIDC	perfusion-insensitive diffusion coefficient
PNET	primitive neuroectodermil tumor
MSK tumors	Musculoskeletal tumors
SRBC	Small round blue cell
NSRBC	non- Small round blue cell
GCTS	giant cell tumors
99m-Tc MDP	^{99m}Tc-Methyl diphosphonate
FDG-PET	fluorine-18 fluorodeoxyglucose- positron emission tomography
G-CSF	granulocyte colony stimulating factor
DWIBS	DW whole body imaging with background body signal suppression
CEHS	chronic expanding hematomas

Introduction

MR imaging has become the diagnostic method of choice for preoperative and posttreatment staging of musculoskeletal (MSK) tumors because of the high resolution, tissue contrast, and multiplanar capability of this technique. In addition, MR imaging offers several advantages when compared with other imaging methods in the evaluation and staging of soft tissue tumors. Several studies have demonstrated morphologic parameters such as size, margin demarcation, involvement of adjacent vital structures, homogeneity in signal intensity, and measurement of relaxation time as criteria to evaluate soft tissue tumors **(Van der Woude et al., 1998).** In accordance with these criteria, malignancy can be predicted with the following parameters **(Kransdorf and Murphey, 2006)**

1 Heterogeneous signal intensity in a T1 scan
2 Tumor necrosis
3 Bone or neurovascular involvement
4 Mean diameter of more than 66 mm.

However, conventional MR imaging provides low specificity in the differential diagnosis of several MSK tumors because many of the lesions exhibit nonspecific characteristics. As a result, a correct histologic diagnosis is possible in only a quarter to one-third of cases (**Kransdorf and Murphey, 2006).**

Conventional MR imaging is unable to offer information about the extent of tumoral necrosis and the presence of viable cells, information that is crucial for the assessment of treatment response and prognosis. Therefore, advanced MR imaging techniques, such as diffusion-weighted imaging (DWI), are now used in association with conventional MR imaging with the objective of improving diagnostic accuracy and

treatment evaluation. DWI allows quantitative and qualitative analyses of tissue cellularity and cell membrane integrity and has been widely used for tumor detection and characterization and to monitor treatment response **(Koh et al., 2007).**

The tumor tissue is usually more cellular when compared with other tissues and tends to appear at high signal intensities (restricted diffusion) when DWI is used **(Koh and Collins, 2007).**

The tissue contrast obtained using DWI is different from that obtained using conventional MR imaging, which facilitates the detection of soft tissue and bone tumors, particularly bone metastasis **(Nagata et al., 2008).** In fact, previous studies have concluded that DWI is an extremely sensitive method for identifying bone metastases and is superior to both positron emission tomography (PET) and scintigraphy in terms of detection capability **(Goudarzi et al., 2010).**

The detection of bone metastasis is important for cancer staging and in the determination of treatment strategy, and some reports have demonstrated whole body DWI to be highly sensitive and efficient for this purpose. Tumors differ in cellularity characteristics, and this difference is useful in determining their histological composition. It has been reported that DWI can differentiate benign from malignant soft tissue tumors (**Costa et al., 2011)**.

The malignant tumors have more cellularity than benign tumors and tend to have a more restricted diffusion **(Maeda et al., 2007).** In accordance with this finding, perfusion corrected DWI has demonstrated potential in differentiating benign from malignant soft tissue masses **(Van Rijswijk et al., 2002).** On the other hand, some investigators have reported overlapping apparent diffusion coefficient (ADC) values in benign and malignant soft tissue tumors, which consequently could not be used to differentiate them**(Einarsdo´ ttir et al., 2004).** This overlapping

is likely because of the fact that ADC values can be affected by cellularity and the extracellular matrix**.** For example, myxoid matrix is widely seen in the interstitial spaces in many soft tissue tumors, and this presence can influence the ADC values. As a result, myxoid tumors will have significantly higher ADC values than nonmyxoid tumors. It makes no difference if the tumor is benign or malignant **(Maeda et al., 2007).**

DWI can also be used to monitor tumor response to treatment, most likely because effective anticancer therapy results in changes in the tumor microenvironment, resulting in an increase in the diffusion of water molecules and a consequent increase in the ADC value **(Koh and Collins, 2007).** Furthermore, DWI has been used to provide information regarding cellular changes related to cytotoxic treatment in soft tissue sarcomas**(Schnapauff et al., 2009).** Some investigators have suggested that it could be possible to evaluate the response of osteosarcoma to chemotherapy using DWI, considering that the ADC values of viable tumor tissue and tumor necrosis differ significantly **(Oka et al., 2010)** and **(Uhl et al., 2006).** This information is a crucial prognostic factor for patients with osteosarcoma.

Aim of work:

The aim of the work to discuss the technical aspects of DWI, particularly the quantitative and qualitative interpretation of images in MSK tumors. The clinical application of DWI for tumor detection, characterization, differentiation of tumor tissue from others, and assessment of treatment response will be emphasized.

Basic principles of diffusion-weighted imaging

At human body temperature, random water molecules migrate approximately 30 um over 50 ms, but only if there are no barriers to their motion. Water movement in tissues is neither entirely free nor random, being modified by interactions with hydrophobic lipid-containing cell membranes, intracellular organelles, macromolecules and by-flows within tubular channels such as blood vessels and ducts. Thus tissue water motion is related to its microscopic structure. The thermally driven motion of water is uniquely assessed by DWI. MRI is able to measure the water diffusivity by the application of diffusion sensitising gradients (motion probing gradients) to T2-weighted spin-echo sequences usually with echoplanar readouts of the data. Signal loss on DWI is proportional to both the free motion of water molecules and the diffusion gradient strength used **(Le Bihan et al., 1992).**

The strength and duration of application of diffusion sensitizing gradients is indicated by their "b-value". Generally, a range of b-values (two or more) are used in a DW-MRI study to interrogate the water diffusion properties of tissues. In the absence of diffusion sensitizing gradients (b-value=0 s/mm^2), free water appears bright because of intrinsic T2-weighting. In images acquired with low b values (50–100 s/mm^2), vessels and cerebrospinal fluid show marked signal attenuation because water molecules will have moved over a relatively large distance during the time of application of the diffusion sensitizing gradients. Because signal intensity from blood vessels is attenuated on low b-value images, these images are often termed "black blood" images **(Khoo et al., 2011**).

With increasing b-values, signal intensity attenuates steadily in other tissues, initially disappearing in free water (e.g. urine in the bladder), then in glandular tissues (e.g. prostate, salivary glands and pancreas) and then in tissues showing highly organised cellular structure such as the liver. Because water movement is relatively impeded in highly packed tissues such as tumours, very cellular tissues appear persistently bright against a darkening background at high b-values of 500–1,000 s/ mm^2. For the same reasons, several normal but highly cellular tissues also appear bright on high b-value images, including the brain, spinal cord, spleen (variable) and normal lymphatic tissues (tonsils, adenoids, lymph nodes). **(Khoo et al., 2011**).

Technical aspects

DWI exploits the random motion of water molecules in the body, which is classically called the Brownian motion. In biologic tissues, the movement of water molecules is restricted because their motion is modified and limited by their interactions with cellular membranes and macromolecules. The DWI signal in vivo is therefore derived from the motion of water protons in extra cellular, intracellular, and intravascular spaces **(Le Bihan et al., 1988).** DWI yields qualitative and quantitative information that reflects tissue cellularity and cell membrane integrity, which complements the morphologic information obtained by conventional MR imaging **(Koh et al., 2007).** Thus, the data obtained from DWI must be interpreted using qualitative and quantitative approaches.

Qualitative analysis is achieved via visual assessment of the relative tissue signal attenuation of both the DW image and the ADC parametric map. The visual assessment of DW image enables tissue characterization based on differences in water diffusion and is performed by observing the relative attenuation of the signal intensity of images obtained at different b values. In a heterogeneous tumor, for instance, the more cystic or necrotic fraction of the tumor will show greater signal attenuation on high-b value images because water diffusion is less restricted, whereas the more cellular solid tumor areas will continue to show a relatively high signal intensity (Fig.1) (**Costa et al., 2011**). By contrast, on the ADC parametric map, visual assessment reveals a trend opposite to that of DW images: areas of restricted diffusion in highly cellular areas appear as low signal intensity areas compared with less cellular areas, which have higher signal intensity (Fig.2). (**Costa et al., 2011**)