The role of diffusion weighted magnetic resonance imaging in oncologic settings

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Abstract: There is growing interest in the applications of diffusion-weighted-imaging (DWI) in oncologic area for last ten years. DWI has important advantages as do not require contrast medium, very quick technique and it provides qualitative and quantitative information that can be helpful for tumor assessment. In this article, we present oncologic applications of DWI in the parts of the body. DWI has been applied to the evaluation of central nervous system (CNS) pathologies. Some technologic advances lead to using of DWI in the extracranial sites such as abdomen and pelvis. As well as tumor detection and characterization, DWI has been widely used for predicting and monitoring response to therapy. One of the most prominent contributions of DWI is differentiation of between malignant and benign tumoral process. Apparent-diffusion-coefficient (ADC) value is quantitative parameter of DWI which reflects diffusion movements of water molecules in various tissues. Most of the studies suggested that malignant tumors had lower ADC values than benign ones. DWI may be a routine sequence in oncologic settings and it provides much useful information about tumoral tissue. We think it can be added to conventional magnetic resonance imaging (MRI) sequences.

Keywords: Diffusion-weighted MRI; oncology; magnetic resonance imaging (MRI)


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Introduction

Diffusion-weighted-imaging (DWI) provides microscopic information from water protons which is not possible using conventional magnetic resonance imaging (MRI). DWI measures the random (Brownian) extra, intra and transcellular motion of water molecules (1). Apparent-diffusion-coefficient (ADC) is a quantitative parameter calculated from DWI combines the effects of capillary perfusion and water diffusion (2). ADC value is calculated for each pixel of the image and is displayed as a parametric map. By drawing regions of interests on these maps, the ADCs of different tissues can be derived (3).

In biologic tissues, the DWI signal is derived from the motion of water molecules in the extracellular space, intracellular space and intravascular space (2). Tumors have increased vascularity. So, significant proportions of signal on DWI originated from intravascular space (4).

The degree of restriction to water diffusion is correlated with tissue cellularity and integrity of cell membranes (5). Generally, malignant tumors have enlarged nuclei and show hypercellularity. These histopathologic characteristics reduce the extracellular matrix and the diffusion space of water protons in the extracellular areas, with a resultant decrease in the ADC value (6,7).

As well as tumor detection and characterization, DWI has been widely used for predicting and monitoring response to therapy. Many researchers have reported that DWI has potential for evaluating tumor response during treatment. Increase of ADC value was accepted as response to therapy in many animal studies (8). Also, results of many clinical studies show that increase in the ADC value suggest a better treatment outcome in clinical studies (9,10).

DWI has been applied to the evaluation of central nervous system (CNS) pathologies especially in stroke, for
last two decades. Applications of DWI had been limited to CNS due to effects of respiration, cardiac movement, peristalsis and blood flow may effect on image quality in these parts of the body (11). Some technologic advances as echo-planar imaging, parallel imaging, and multichannel coils led to using of DWI in the extracranial sites such as abdomen and pelvis (3).

There is growing interest in the applications of DWI in oncologic area for last ten years. DWI has important advantages which require no contrast medium and long imaging time. Also it provides qualitative and quantitative information that can be helpful for tumor assessment. In this article, we present oncologic applications of DWI in the parts of the body.

**Diffusion-weighted imaging in the CNS**

Meningiomas are the most common extraaxial brain tumors. Meningiomas show characteristic findings on conventional MRI; thus, their differentiation from intraaxial tumors is easy. Hakyemez et al. (12) evaluated the contribution of DWI to differentiation of atypical/malignant and typical meningiomas. They demonstrated that atypical/malignant meningiomas had lower ADC values than typical meningiomas (Figure 1).

Conventional MRI cannot reliably distinguish epidermoid tumors from arachnoid cysts; since both lesions are very hyperintense relative to brain parenchyma on T2-weighted images and hypointense on T1-weighted images. With the combination of T2 and diffusion effect, epidermoid tumors are more hyperintense compared with cerebrospinal fluid (CSF) and brain tissue on DWI. Arachnoid cysts are fluid filled, demonstrate very high ADCs, and appear similar to CSF on DWI (13).

Gliomas are the most common primary neoplasms of the CNS. A number of studies showed that intraaxial tumors have higher ADC values than normal brain tissue (14-17) (Figure 2). Various investigators suggested that DWI be used in differentiation between high and low grade gliomas or between tumor types (15-17). In contrast to these results, Server et al. (18) suggested that differentiation between low
and high grade gliomas is possible using ADC measurement. Metastasis is the most common intracranial tumor in adults. The most common metastasize to the brain are lung, breast, skin, genitourinary tract (Figure 3), colon and rectum, and paranasal sinus (19). Kono et al. (20) studied 21 patients with metastasis and have found a mean ADC value of 0.78×10⁻³ mm²/s (used b 1,000 s/mm² gradient). ADC values of the metastasis were not statistically significant from glioblastomas. Duygulu et al. (21) evaluated the 76 patients with intracerebral metastasis using DWI. ADC value in metastasis showing restricted diffusion was 0.72×10⁻³ mm²/s (used b 1,000 s/mm² gradient).

DWI has also important role in the evaluation of extracranial tumors such as thyroid (22), orbit and head and neck tumors (Figure 4). We studied the diagnostic role of DWI in differentiating of malignant and benign thyroid nodules. Mean ADC values of malignant and benign nodules were 0.96×10⁻³ mm²/s and 3.06×10⁻³ mm²/s for b-100, respectively. Mean ADC values of malignant nodules were lower than benign nodules for all b values. We concluded that DWI may be helpful in differentiating malignant and benign thyroid nodules (22) (Figure 5).
Liver pathologies were studied using DWI in many literature (23-25). They concluded that ADC measurements can be used in the differential diagnosis of liver pathologies.

Liver hemangioma is the most common benign tumor of the liver. Hemangiomas are characterized by an enlargement of the extracellular space compared to normal tissue. So, hemangiomas have increased ADC values (26) (Figure 6). Moteki et al. (25) reported that mean ADC value of hemangioma (used following b values 3, 50 and 300) was $2.23 \times 10^{-3}$ mm$^2$/s. Demir et al. (27) mentioned that mean ADC value of hemangioma (used b 1,000 s/mm$^2$ gradient) was $2.46 \times 10^{-3}$ mm$^2$/s. According to our study mean ADC value of 61 hemangiomas was $1.98 \times 10^{-3}$ mm$^2$/s for $b$-600 (28).

Hepatoma (Figure 7), metastasis (Figure 8) and focal nodular hyperplasia (FNH) (Figure 9) have lower ADC values than normal parenchyma. In recent study, Miller et al. (29) evaluated the ADC values for characterization of a variety of focal liver lesions. Mean ADC values (used $b$-0 and $b$-500 s/mm$^2$ gradients) of hepatoma, metastasis and FNH were $1.53 \times 10^{-3}$ mm$^2$/s, $1.50 \times 10^{-3}$ and $1.79 \times 10^{-3}$ mm$^2$/s, respectively. They concluded that benign lesions have higher ADC values than malignant lesions. However, ADC value of benign lesion (FNH) is similar to malignant lesion.

Demir et al. (27) evaluated the diagnostic role of DWI in differentiation between benign and malignant liver lesions. Mean ADC values (used $b$-0 and $b$-500 s/mm$^2$ gradients) of hepatoma and metastases were $0.90 \times 10^{-3}$, and $0.79 \times 10^{-3}$ mm$^2$/s, respectively. They concluded that DWI...
can be useful in the differentiation of benign and malignant liver lesions.

There are many studies related to diagnostic utility of DWI in the renal tumors. Malignant tumors have lower ADC values than benign ones (Figure 10). Restricted diffusion in renal neoplasms is probably multifactorial. It is related to cell membrane integrity and tissue cellularity (30). Taouli et al. (31) characterized renal lesions using DWI. The mean ADC value (used b-0, b-400 and b-800 s/mm² gradients) of 28 renal cell carcinomas (RCC) (1.41×10⁻³ mm²/s) was significantly lower than benign lesions (2.23×10⁻³ mm²/s). Cutoff ADC value for the diagnosis of RCC was less than or equal to 1.92×10⁻³ mm²/s. They also mentioned that renal oncocytomas had significantly higher ADCs compared with solid RCC. Mean ADC value of oncocytomas reported as 1.91×10⁻³ mm²/s. They concluded that DWI can be used to characterize renal lesions especially; it can be used to differentiate solid RCC from oncocytomas.

Adrenal masses are commonly detected on computed tomography (CT). Chemical shift MRI is useful in differentiating adenoma from nonadenoma. There is limited study related to usefulness of DWI in malignant tumors. Usually malignant tumors show bright signal on DWIs, and ADC values of malignant tumors are lower than benign tumors (Figure 11). Tsushima et al. (32) evaluated the diagnostic utility of DWI for the diagnosis of adrenal tumors. They found no difference in ADC values between adenomas and metastatic tumors. However, pheochromocytomas had higher mean ADC value.
compared with those of adenomas and metastasis.

Diagnosis of pancreatic cancer is delayed in many cases and very few patients have curative surgical treatment. Pancreatic cancer has an unfavourable overall 5-year survival of about 5% (33). Similar to other malignant tumors, it has lower ADC value compared to normal pancreatic tissue (Figure 12). ADC values of pancreatic cancer were in wide range with overlapping normal pancreatic tissue values. This may be due to histopathological components of pancreatic cancer which contain varying degrees of fibrosis, necrosis, mucin and cellular component (34). Recent studies concluded that restricted diffusion in the pancreatic cancer might be related with increased cellularity and fibrosis. In contrast to other tumors, fibrosis might be contributed to diminished ADC values as well as cellularity (34).

Prostate cancer is the most common genitourinary malignancy in men (35). There were many literature related to diagnostic utility of DWI in prostate cancer (35-38). Prostate cancer usually demonstrates low signal intensity on T2-weighted image that is well identified in the peripheral zone from the normal appearance of high signal intensity on T2-weighted image. In prostate cancer, normal tissue of the gland is replaced by adenocarcinoma. The tumor is built up of high-density malignant epithelial cells, which results a decrease in ADC values (36) (Figure 13). Kiliçkesmez et al. (35) measured the mean ADC value (used $b=0$, $b=500$ and $b=1,000$ $s/mm^2$ gradients) of prostate tissue in nine prostate cancer and 50 healthy subjects. Mean ADC value of peripheral and transitional zone of prostate were $2.07 \times 10^{-3}$ and $1.46 \times 10^{-3}$ $mm^2/s$, respectively. Mean ADC value of prostate carcinoma was $1.06 \times 10^{-3}$ $mm^2/s$. Yağci et al. (37) investigated the value of DWI for prostate cancer detection and localization. They found lower ADC value in prostate cancer than noncancerous tissue. Mean ADC values (used $b=800$ $s/mm^2$ gradient) of cancerous and noncancerous tissues were $0.94 \times 10^{-3}$ and $1.58 \times 10^{-3}$ $mm^2/s$, respectively.

Carcinoma of the urinary bladder is one of the most common malignant tumors of the urinary tract. In the literature, there are a few reports evaluating the feasibility of DWI in the diagnosis of urinary bladder cancers (Figure 14). Matsuki et al. (39) reported that the ADC value of bladder cancers was lower than ADC value of normal bladder wall. They suggested that the bladder cancers were clearly
detected using DWI. However, they did not define a cut-off value. El-Assmy et al. (40) reported high sensitivity and specificity of DWI in detection of bladder tumors depending on their site. In another study, the mean ADC values (used \( b = 0 \), \( b = 500 \) and \( b = 1,000 \) \( \text{s/mm}^2 \) gradients) of the urinary bladder wall of the control group and bladder carcinoma were \( 2.08 \times 10^{-3} \) and \( 0.94 \times 10^{-3} \) \( \text{mm}^2/\text{s} \), respectively. They concluded that ADC measurement has a potential ability to differentiate carcinomas from normal bladder wall (35).

DWI is also widely used in evaluation of pelvic region tumors. Similar to other malignant tumors, the ADC values of uterine cancers are lower than normal tissue (Figure 15). ADC value provides useful information about the effectiveness of the therapy as well as differentiation of between malignant tumor tissue and normal tissue. Naganawa et al. (41) reported that mean ADC value (used \( b = 0 \), \( b = 300 \) and \( b = 600 \) \( \text{s/mm}^2 \) gradients) of cervical cancer was lower than of normal cervical tissue (\( 1.09 \times 10^{-3} \) \( \text{vs.} \) \( 1.79 \times 10^{-3} \) \( \text{mm}^2/\text{s} \)). In another study carried by McVeigh et al. (42) with larger group of cervical cancer, mean ADC values (used \( b = 0 \), \( b = 600 \) \( \text{s/mm}^2 \) gradients) of cervical cancer and normal tissue were reported \( 1.09 \times 10^{-3} \) \( \text{vs.} \) \( 2.09 \times 10^{-3} \) \( \text{mm}^2/\text{s} \), respectively. These studies suggested that ADC measurement has a potential ability to differentiate carcinomas from normal bladder wall. ADC values (used \( b = 500 \) \( \text{s/mm}^2 \) gradient) of pathologic bone marrow range between \( 0.7 \times 10^{-3} \) to \( 1.0 \times 10^{-3} \) \( \text{mm}^2/\text{s} \) in metastases and malignant vertebral fractures (48). Although ADC values may be indicative for benign (Figure 16) or malignant lesions, a considerable overlap between mean ADC values of benign and malignant lesions has been described in several studies (49).

**Diffusion-weighted imaging in the bone and lung tumors**

There are limited reports about diagnostic utility of DWI related to bone tumors. Many reports focused on vertebral body. Typical values of the ADC in normal bone marrow are in the range of \( 0.2 \times 10^{-3} - 0.5 \times 10^{-3} \) \( \text{mm}^2/\text{s} \). Most applications of DWI in the bone marrow are focused on the differentiation of benign osteoporotic and malignant vertebral compression fractures (45,46). According to our study mean ADC values of sacral and iliac bone marrow were \( 0.53 \times 10^{-3} \) and \( 0.56 \times 10^{-3} \) \( \text{mm}^2/\text{s} \) at \( b = 1,000 \) (47). ADC values (used \( b = 500 \) \( \text{s/mm}^2 \) gradient) of pathologic bone marrow range between \( 0.7 \times 10^{-3} \) to \( 1.0 \times 10^{-3} \) \( \text{mm}^2/\text{s} \) in metastases and malignant vertebral fractures (48). Although ADC values may be indicative for benign (Figure 16) or malignant lesions, a considerable overlap between mean ADC values of benign and malignant lesions has been described in several studies (49).

A solitary pulmonary nodule is a common condition in clinical practice. CT and PET (positron emission tomography) are common used modalities as noninvasive imaging methods. Some investigators have tried to discriminate malignancy from benign lung tumors by measuring ADC value. Mori et al. (50) examined...
the usefulness of DWI for discrimination of benign/malignant pulmonary nodules in comparison with F-fluorodeoxyglucose (PET). The receiver operating characteristics curve showed cutoff values of the ADC for benign/malignant discrimination to be $1.1 \times 10^{-3}$ mm$^2$/s. Similarity to other systems, malignant pulmonary nodules has low ADC values (Figure 17).

**In conclusion**

DWI is a useful technique that provides information about cellularity and cell membrane architecture of tumoral tissue. One of the most prominent contributions of DWI is differentiation between malignant and benign tumoral process. Despite many reports which present cut off values for differentiation between benign and malignant processes, many authors mentioned that overlapping ADC values exist in benign and malignant tumors. However, most of the studies suggested that malignant tumors had lower ADC values than benign ones. DWI is also useful to assess the response of tumors to treatment in various parts of the body. Combination of conventional MRI, DWI and ADC values provides additional information in patients with cancers. The most prominent advantages of this technique are absence of radiation, no necessity for of intravenous contrast material, very quick technique and quantitative information of tissue provided by ADC measurement. DWI may be a routine sequence in oncologic settings and it provides much useful information about tumoral tissue. We think it can be added to conventional MRI sequences.

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