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Original Article

Application value of diffusion weighted magnetic resonance imaging in head and neck cancer

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Abstract: Diffusion weighted Magnetic Resonance Imaging (DWI) is currently the only imaging technology that reflects the diffusion motion of water molecules in living tissues. At present, DWI has been widely used in the diagnosis and differential diagnosis of various malignant tumors, assessment of tumor differentiation, clinical stage and therapeutic effect evaluation, with or without metastasis and recurrence, etc. This article will review the application value of DWI and the apparent diffusion coefficient (ADC) value in head and neck cancer.

Keywords: Head and neck cancer, diffusion weighted imaging, apparent diffusion coefficient

Introduction

Diffusion weighted Magnetic Resonance Imaging (DWI) is currently the only imaging technology that reflects the diffusion motion of water molecules in living tissues. At present, DWI has been widely used in the diagnosis and differential diagnosis of various malignant tumors, assessment of tumor differentiation, clinical stage and therapeutic effect evaluation, with or without metastasis and recurrence, etc. This article will review the application value of DWI and the apparent diffusion coefficient (ADC) value in head and neck cancer.

Application of DWI and ADC value in diagnosis of primary lesion in head and neck cancer

DWI is a functional imaging technique that use special sequences which highlighted the bulk phase function caused by diffusion, while in the macroscopic imaging reflects microscopic diffusion of water molecules in living tissues. DWI with ADC values quantitatively reflect the organization diffusion properties of water molecules, the space distribution between the internal molecular of imaging materials determines the size value of ADC. The increased tissue cell density, restriction of water molecular diffusion inside and outside of cells can lead to a drop in ADC values [1]. The malignant tumors show a high signal intensity on DWI and low ADC values due to a high malignant cell density, small intercellular space and low diffusion of water molecules. Sakamoto et al measured the ADC values of 32 cases of head and neck benign lesions and 19 cases of head and neck malignant tumors, and found that the average ADC values of 32 cases of head and neck benign lesions and 19 cases of head and neck malignant tumors were $1.48\pm0.62\times10^{-3}$ mm^2/s and $1.23\pm0.45\times10^{-3}$ mm^2/s, respectively [2]. But there was no statistical significance ($P = 0.246$). Srinivasan et al measured the ADC values of 17 cases of head and neck benign lesions and 16 cases of head and neck malignant tumors, and found that the average ADC values of 17 cases of head and neck benign lesions and 16 cases of head and neck malignant tumors were $1.505\pm0.487\times10^{-3}$ mm^2/s and $1.071\pm0.293\times10^{-3}$ mm^2/s, respectively. There was statistical significance ($P = 0.004$) [3]. They also proposed that the ADC value 1.3×10^{-3} mm^2/s of 3.0 T MRI may be the best threshold to identify benign and malignant lesions of the head and neck [3].

Table 1. The differentiating diagnostic role of ADC value in the head and neck cancer in literatures

Study first author	ADC ($\times10^{-3}$)		p	Threshold ($\times10^{-3}$)	Accuracy (%)	Sensitivity (%)	Specificity (%)
	Benign lesions	Malignant tumors					
Sakamoto [2]	1.48±0.62	1.23±0.45	0.246	1.61	66	79	60
Srinivasan [3]	1.505±0.487	1.071±0.293	0.004	1.3	76	81	71
Wang [4]	1.56±0.51	1.13±0.43	0.002	1.22	86	84	91
Shang [5]	1.780±0.32	1.195±0.32	< 0.001	1.455	92.9	94.1	90.9

Wang et al measured the ADC values of 22 cases of head and neck benign solid lesions and 36 cases of head and neck malignant tumors, and found that the average ADC values of 22 cases of head and neck benign solid lesions and 36 cases of head and neck malignant tumors were $1.56\pm0.51\times10^{-3}$ mm^2/s and $1.13\pm0.43\times10^{-3}$ mm^2/s, respectively [4]. There was statistical significance (P = 0.002). They proposed that ADC values below 1.22×10^{-3} mm^2/s forecast head and neck malignant tumor, the accuracy, sensitivity and specificity were 86%, 84%, 91%, respectively. We have found that ADC values were lower for patients with laryngeal carcinoma (mean $1.195\pm0.32\pm10^{-3}$ mm^2/s) versus those with laryngeal precancerous lesions (mean $1.780\pm0.32\pm10^{-3}$ mm^2/s; P, 0.001). The optimum threshold for the ADC was 1.455 ± 10^{-3} mm^2/s, the accuracy, sensitivity and specificity were 92.9%, 94.1%, 90.9%, respectively [5] (**Table 1**). The difference of ADC values in different studies of head and neck malignant tumors is large, and lack of unified diagnostic criteria. The causes of this phenomenon are, first and foremost, the researchers in the selection of the research object, secondly, although in theory the ADC values are not affected by machinery and equipment and comparable between different machines, but in the actual work, hardware, scan sequence and b value selection are still influence the outcome of the ADC values. Generally, the higher the b value, the higher the lesion detection rate, but the image SNR is reduced at the same time. Blood perfusion can affect diffusion at low b value [6], while high b value inhibits the blood perfusion of richly vascularized tissues on the impact of diffusion [7], but b value higher than 1000 s/mm^2 will lead to poor image quality [8].

Pathological differentiation degree of tumors has certain correlation with the size of ADC values, ADC values can quantify the degree of diffusion of water molecules, in theory, the higher the degree of malignancy, the lower the ADC value of diseased tissue. Kato et al [9] found that the average ADC values of poorly and highly differentiated head and neck squamous cell carcinomas were $0.95\pm0.17\times10^{-3}$ mm^2/s and $1.24\pm0.23\times10^{-3}$ mm^2/s, respectively. There was a significant difference (P < 0.01). Sumi et al [10] also reported that the ADC values of moderately or highly differentiated squamous carcinomas was higher than the low differentiated squamous carcinomas, the ADC values of poorly differentiated squamous carcinomas was close to malignant lymphomas. This is because those poorly differentiation tumors have an increased number of cells, reduced extracellular space, limited diffusion motion of water molecules, and the ADC values are relatively lower, while contrary to the well differentiated tumors.

Assessed value of DWI for the efficacy of radiochemotherapy and prognosis in head and neck cancer

How to early predict the efficacy of radiation and chemotherapy in order to individualized treatment is an increasingly concerned topic to clinical workers. DWI plays an important role in assessment and prediction of tumor curative effect, the changes of ADC values before any tumor volume reduction, ADC values measured to predict tumor early response to treatment. The measurement of ADC values can predict tumor early response to treatment. Most scholars [11, 12] believe that after radiotherapy: tumor cell membrane was damaged, cell apoptosis increased, density decreased, extracellular gap widened and the diffusion motion ability of water molecules enhanced, which may result in higher ADC values. It suggests that the treatment is effective if ADC values of tumors and lymph nodes progressively increased after the treatment; if the ADC values slightly increase or

progressive decrease, showing that the tumor radiation therapy is low or no reaction; there are difference in ADC values between valid and invalid for radiotherapy of tumors, this difference will become increasingly apparent as the duration of treatment [13]. There are also other studies [14] believe that in early radioactive radiation, high viscosity and abundant inflammatory cells infiltration of necrosis tissues may led to restriction of water molecular diffusion, and ADC values will be transient decrease. Similar findings had been found in the application of DWI to evaluate the curative efficacy of neoadjuvant chemotherapy in breast cancer research [15]. Vandecaveye et al [16] found that by monitoring the ADC values of head and neck squamous cell carcinomas at 2 weeks and 4 weeks after concurrent chemoradiotherapy, the ADC values of patients with complete response compared with recurrence were significantly increased, and there was statistical significance between them. Kim et al [17] through the study of 40 patients with head and neck squamous cell carcinomas, patients with complete response and partial response before treatment, the ADC values were 1.04±0.19×10^{-3} mm^2/s and 1.35±0.30×10^{-3} mm^2/s, respectively. The ADC values of patients with complete response were significantly lower than the partial response, which was statistically significant ($P < 0.05$). They also found that the ADC values increased during the first week of chemoradiation, and the patients with complete response had a greater increase than the partial response. It indicates that the determination of ADC values before treatment and the range of the ADC values change after treatment can predict the effect of head and neck malignant tumors to radiation and chemotherapy.

DWI and ADC value evaluate recurrence of head and neck cancer

Hypophaeyngeal cancer patients have a higher recurrence rate, how to early evaluate recurrence after treatment is an important link of clinical research. Accurately assess the recurrence of tumor can effectively avoid unnecessary surgery and improve the survival rate [18]. Conventional imaging examinations for early evaluation of tumor recurrence is poorer, even if FDG PET/CT because of the high sensitivity of inflammation that results in higher false positive thus affecting the correct evaluation of early tumor recurrence [19, 20]. Abdel Razek et al [21] through the study of 30 patients with head and neck malignant tumors, the average ADC value of patients with residual or recurrence was 1.17±0.33×10^{-3} mm^2/s, significantly lower than the change of the average ADC value 2.07±0.25×10^{-3} mm^2/s after treatment, there was statistical significance ($P < 0.001$). The critical point of ADC value was 1.30×10^{-3} mm^2/s, as the distinction between residual or recurrence and change after treatment, the accuracy, sensitivity, specificity, positive predictive value and negative predictive value were 87%, 84%, 90%, 94%, 76%, respectively. Tshering et al [22] through the study of 46 cases of laryngeal and hypopharyngeal cancer, the sensitivity and specificity of DWI combined conventional MRI to found cancer were 94% and 100%, respectively. The average ADC value of head and neck malignant tumor with residual or recurrence was 1.20±0.49×10^{-3} mm^2/s, significantly lower than the change of the average ADC value 1.82±0.41×10^{-3} mm^2/s after treatment, there was statistical significance ($P < 0.0002$). ROC analysis to provide the best threshold value was 1.30×10^{-3} mm^2/s, its diagnostic sensitivity, specificity and accuracy were 67%, 86% and 78% respectively. Vandecaveye et al [23] found that DWI can accurately distinguish change after radiotherapy or chemotherapy in head and neck malignant tumor and the tumor residual or recurrence, when b value was 0, the sensitivity, specificity and accuracy were 66.2%, 60.8%, 62.4%, respectively; when b value was 1000, the sensitivity, specificity and accuracy were 71.6%, 71.3%, 71.4%, respectively; compared with CT, TSE-MRI and PET, DWI had a lower false positive. King et al [24] found that in the process of concurrent chemoradiotherapy, ADC values of some lesions in the treatment of early rising, late fall, or in the treatment of early fall, late rising, no matter what type of pathology, the decline of ADC values in the process of concurrent chemoradiotherapy strongly suggested local recurrence, decreased ADC values closely associated with local recurrence ($P = 0.00001$).

Application of DWI and ADC value in evaluation of cervical lymph nodes

Hypopharyngeal cancer is a highly malignant tumor and has a higher rate of cervical lymph node metastasis, about 50-60% with cervical

lymph node metastasis at the visit, about 60% of the transferred sites along the internal jugular vein and upper-middle cervical lymph nodes, followed by retropharyngeal lymph nodes and posterior cervical lymph nodes. Accurate assessment of metastatic cervical lymph nodes before the treatment helps to judge the stage of hypopharyngeal cancer, which helps to make accurate treatment plan and estimate the prognosis accurately. Current clinical usually use conventional CT, MRI and US to assess cervical lymph nodes, also with the help of PET/CT to evaluate cervical lymph nodes. Ashraf et al [25] used 1.0 cm in diameter as the identification standard, the negative predictive value and positive predictive value of CT scanning were 84% and 50% respectively, while 0.5 cm as the identification standard, the negative predictive value was 90%, but the positive predictive value was only 44%. Schoder et al [26] found that the sensitivity and specificity of 18F-FDG PET/CT in the early detection of regional lymph nodes were 87%-90% and 80%-93% respectively, better than a single conventional MRI. But because of its high price, large radiation, long time-consuming and other shortcomings that lead to certain restrictions in clinical application. DWI can be a good assessment of cervical lymph nodes by noninvasive and nonradiative visualization and quantitative analysis of ADC values. Holzapfel et al [27] found the average ADC values of metastatic cervical lymph nodes and benign cervical lymph nodes were $0.78\pm0.09\times10^{-3}$ mm^2/s and $1.24\pm0.16\times10^{-3}$ mm^2/s respectively, in 1.02×10^{-3} mm^2/s ADC threshold standard to identify the head and neck benign and malignant lymph nodes, the sensitivity and accuracy can reach 100.0% and 94.3% respectively. Vandecaveye et al [28] found the ADC value of the head and neck squamous carcinoma metastasis lymph nodes was $0.85\pm0.27\times10^{-3}$ mm^2/s, significantly lower than the benign lymph nodes ADC value $1.19\pm0.22\times10^{-3}$ mm^2/s, the difference was statistically significant ($P < 0.0001$), using 0.94×10^{-3} mm^2/s as the best threshold, to identify the head and neck metastatic lymph nodes and benign lymph nodes, the sensitivity, specificity and accuracy were 84%, 94% and 91% respectively. However, Sumi et al [29] found the ADC value of the head and neck metastasis lymph nodes was $1.167\pm0.447\times10^{-3}$ mm^2/s, significantly higher than the benign lymph nodes ADC value $0.652\pm0.101\times10^{-3}$ mm^2/s, the difference was statistically significant ($P < 0.001$), this may be related to the different selected b value and more necrosis in metastatic lymph nodes which result in higher ADC values.

Conclusion

DWI and ADC values can provide microscopic anatomical information, and has a certain application value in diagnosis of primary lesion in head and neck cancer, assessment for the efficacy of radiochemotherapy and prognosis in head and neck squamous cell carcinoma, evaluation of recurrence in head and neck cancer and evaluation of cervical lymph nodes.

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Disclosure of conflict of interest

None.

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References

[1] Jia H, Ma X, Zhao Y, Zhao J, Liu R, Chen Z, Chen J, Huang J, Li Y, Zhang J, Wang F. Meta-analysis of diffusion-weighted magnetic resonance imaging in identification of colorectal cancer. Int J Clin Exp Med 2015; 8: 17333-17342.

[2] Sakamoto J, Yoshino N, Okochi K, Imaizumi A, Tetsumura A, Kurohara K, Kurabayashi T. Tissue characterization of head and neck lesions using diffusion-weighted MR imaging with SPLICE. Eur J Radiol 2009; 69: 260-268.

[3] Srinivasan A, Dvorak R, Perni K, Rohrer S, Mukherji SK. Differentiation of benign and malignant pathology in the head and neck using 3T apparent diffusion coefficient values: early experience. AJNR Am J Neuroradiol 2008; 29: 40-44.

[4] Wang J, Takashima S, Takayama F, Kawakami S, Saito A, Matsushita T, Momose M, Ishiyama T. Head and neck lesions: characterization

with diffusion-weighted echo-planar MR imaging. Radiology 2001; 220: 621-630.
[5] Shang DS, Ruan LX, Zhou SH, Bao YY, Cheng KJ, Wang QY. Differentiating Laryngeal Carcinomas from Precursor Lesions by Diffusion-Weighted Magnetic Resonance Imaging at 3.0 T: A Preliminary Study. PLoS One 2013; 8: e68622.
[6] Orsi G, Aradi M, Nagy SA, Perlaki G, Trauninger A, Bogner P, Janszky J, Illés Z, Dóczi T, Pfund Z, Schwarcz A. Differentiating white matter lesions in multiple sclerosis and migraine using monoexponential and biexponential diffusion measurements. J Magn Reson Imaging 2015; 41: 676-683.
[7] Cereda CW, Christensen S, Campbell BC, Mishra NK, Mlynash M, Levi C, Straka M, Wintermark M, Bammer R, Albers GW, Parsons MW, Lansberg MG. A benchmarking tool to evaluate computer tomography perfusion infarct core predictions against a DWI standard. J Cereb Blood Flow Metab 2015; [Epubahead of print].
[8] Colagrande S, Carbone SF, Carusi LM, Cova M, Villari N. Magnetic resonance diffusion-weighted imaging: extraneurological applications. Radiol Med 2006; 111: 392-419.
[9] Kato H, Kanematsu M, Tanaka O, Mizuta K, Aoki M, Shibata T, Yamashita T, Hirose Y, Hoshi H. Head and neck squamous cell carcinoma: usefulness of diffusion-weighted MR imaging in the prediction of a neoadjuvant therapeutic effect. Eur Radiol 2009; 19: 103-109.
[10] Sumi M, Sakihama N, Sumi T, Morikawa M, Uetani M, Kabasawa H, Shigeno K, Hayashi K, Takahashi H, Nakamura T. Discrimination of metastatic cervical lymph nodes with diffusion-weighted MR imaging in patients with head and neck cancer. AJNR Am J Neuroradiol 2003; 24: 1627-1634.
[11] Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009; 45: 228-247.
[12] Thoeny HC, Ross BD. Predicting and monitoring cancer treatment response with diffusion-weighted MRI. J Magn Reson Imaging 2010; 32: 2-16.
[13] Chen J, Sheng J, Xing W, Aoun H, Chen M, Bi HL, Tian JM, Dai YM. Monitoring early response of lymph node metastases to radiotherapy in animal models: diffusion-weighted imaging vs. morphological MR imaging. Acta Radiol 2011; 52: 989-994.
[14] Hamstra DA, Lee KC, Moffat BA, Chenevert TL, Rehemtulla A, Ross BD. Diffusion magnetic resonance imaging: an imaging treatment response biomarker to chemoradiotherapy in a mouse model of squamous cell cancer of the head and neck. Transl Oncol 2008; 1: 187-194.
[15] Bufi E, Belli P, Costantini M, Cipriani A, Di Matteo M, Bonatesta A, Franceschini G, Terribile D, Mulé A, Nardone L, Bonomo L. Role of the Apparent Diffusion Coefficient in the Prediction of Response to Neoadjuvant Chemotherapy in Patients With Locally Advanced Breast Cancer. Clin Breast Cancer 2015; 15: 370-380.
[16] Vandecaveye V, Dirix P, De Keyzer F, de Beeck KO, Vander Poorten V, Roebben I, Nuyts S, Hermans R. Predictive value of diffusion-weighted magnetic resonance imaging during chemoradiotherapy for head and neck squamous cell carcinoma. Eur Radiol 2010; 20: 1703-1714.
[17] Kim S, Loevner L, Quon H, Sherman E, Weinstein G, Kilger A, Poptani H. Diffusion-weighted magnetic resonance imaging for predicting and detecting early response to chemoradiation therapy of squamous cell carcinomas of the head and neck. Clin Cancer Res 2009; 15: 986-994.
[18] Putten L, Bree R, Doornaert PA, Buter J, Eerenstein SE, Rietveld DH, Kuik DJ, Leemans CR. Salvage surgery in post-chemoradiation laryngeal and hypopharyngeal carcinoma: outcome and review. Acta Otorhinolaryngol Ital 2015; 35: 162-172.
[19] Ng SH, Lin CY, Chan SC, Lin YC, Yen TC, Liao CT, Chang JT, Ko SF, Wang HM, Chang CJ, Wang JJ. Clinical utility of multimodality imaging with dynamic contrast-enhanced MRI, diffusion-weighted MRI, and 18F-FDG PET/CT for the prediction of neck control in oropharyngeal or hypopharyngeal squamous cell carcinoma treated with chemoradiation. PLoS One 2014; 9: e115933.
[20] Oh JS, Kang BC, Roh JL, Kim JS, Cho KJ, Lee SW, Kim SB, Choi SH, Nam SY, Kim SY. Intratumor Textural Heterogeneity on Pretreatment (18)F-FDG PET Images Predicts Response and Survival After Chemoradiotherapy for Hypopharyngeal Cancer. Ann Surg Oncol 2015; 22: 2746-2754.
[21] Abdel Razek AA, Kandeel AY, Soliman N, Soliman N, El-shenshawy HM, Kamel Y, Nada N, Denewar A. Role of diffusion weighted echo-planar MR imaging in differentiation of residual or recurrent head and neck tumors and posttreatment changes. AJNR Am J Neuroradiol 2007; 28: 1146-1152.
[22] Tshering Vogel DW, Zbaeren P, Geretschlaeger A, Vermathen P, De Keyzer F, Thoeny HC. Diffusion-weighted MR imaging including biex-

ponential fitting for the detection of recurrent or residual tumour after (chemo) radiotherapy for laryngeal and hypopharyngeal cancers. Eur Radiol 2013; 23: 562-569.

[23] Vandecaveye V, De Keyzer F, Nuyts S, Deraedt K, Dirix P, Hamaekers P, Vander Poorten V, Delaere P, Hermans R. Detection of head and neck squamous cell carcinoma with diffusion weighted MRI after (chemo) radiotherapy: correlation between radiologic and histopathologic findings. Int J Radiat Oncol Biol Phys 2007; 67: 960-971.

[24] King AD, Mo FK, Yu KH, Yeung DK, Zhou H, Bhatia KS, Tse GM, Vlantis AC, Wong JK, Ahuja AT. Squamous cell carcinoma of the head and neck: diffusion-weighted MR imaging for prediction and monitoring of treatment response. Eur Radiol 2010; 20: 2213-2220.

[25] Ashraf M, Biswas J, Jha J, Nayak S, Singh V, Majumdar S, Bhowmick A, Dam A. Clinical utility and prospective comparison of ultrasonography and computed tomography imaging in staging of neck metastases in head and neck squamous cell cancer in an Indian setup. Int J Clin Oncol 2011; 16: 686-693.

[26] Schöder H, Yeung HW. Positron emission imaging of head and neck cancer, including thyroid carcinoma. Semin Nucl Med 2004; 34: 180-197.

[27] Holzapfel K, Duetsch S, Fauser C, Eiber M, Rummeny EJ, Gaa J. Value of diffusion-weighted MR imaging in the differentiation between benign and malignant cervical lymph nodes. Eur J Radiol 2009; 72: 381-387.

[28] Vandecaveye V, De Keyzer F, Vander Poorten V, Dirix P, Verbeken E, Nuyts S, Hermans R. Head and neck squamous cell carcinoma: value of diffusion-weighted MR imaging for nodal staging. Radiology 2009; 251: 134-46.

[29] Sumi M, Van Cauteren M, Nakamura T. MR microimaging of benign and malignant nodes in the neck. AJR Am J Roentgenol 2006; 186: 749-57.