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Lymph node metastasis in head and neck squamous carcinoma: Efficacy of intravoxel incoherent motion magnetic resonance imaging for the differential diagnosis

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ABSTRACT

Purpose: To evaluate the value of pure molecular diffusion(D), perfusion-related diffusion (D^*), perfusion fraction (f) and apparent diffusion coefficient (ADC) based on intravoxel incoherent motion (IVIM) theory for differential diagnosis of metastatic lymph nodes (LNs) in head and neck squamous cell carcinoma(HNSCC).
Materials and methods: 29 patients with HNSCC and 20 patients with lymph node hyperplasia (LNH) were enrolled in this retrospective study, underwent magnetic resonance (MR) examination. IVIM Diffusion-weighted imaging (IVIM-DWI) was performed with 13 b values. D, D^*, f and ADC values were compared between two groups. The diagnostic value of ADC, D, D^* and $D{\cdot}D^*$ value were evaluated by Receiver operating characteristic (ROC) curve. Two radiologists measured D, D^*, f and ADC values independently.
Results: 33 malignant LNs in HNSCC group and 22 benign LNs in LNH group (minimum diameter, ≥5 mm) were successfully examined, ADC($P < 0.05$), D ($P < 0.01$) and f ($P < 0.01$) were significantly lower in malignant LNs than that in benign LNs, whereas D^* was significantly higher ($P < 0.01$). The area under the ROC curve (AUC) for $D{\cdot}D^*$ was 0.983 and was larger than that for D^* (0.952), D (0.78) and ADC (0.67).
Conclusion: Our results indicate that IVIM DWI is feasible in the diagnosis of LN metastasis. D was significantly decreased in malignant LNs reflected increased nuclear-to-cytoplasmic ratio tissue, and D^* was significantly increased reflected increased blood vessel generation and parenchymal perfusion in malignant LNs.

1. Introduction

Squamous cell carcinoma (SCC) accounts for 5% of all malignant tumors over the world [1]. It is the most common malignancy in the head and neck region. A multitude of metastatic LNs is often associated with a poor prognosis [2]. In some cases, the presence of LNs metastasis can be found before a significant clinical sign of primary head and neck tumors was observed. The detection of cervical node metastasis often helps for the preoperative determination of the necessary extent of neck dissection in patients with HNSCC. For differentiating benign LNs from metastatic LNs, node biopsy is definitive, but this method is invasive and dependent on experienced operator. In noninvasive imaging methods, computed tomography (CT) and MRI have been used for the detection. However, these image methods can differentiate malignant LNs from benign LNs accounting to the imaging features (the maximum diameter was ≥10 mm, the minimum diameter was ≥6 mm, central necrosis, indistinct nodal margins) with nonspecific diagnostic value [3].

Diffusion-weighted imaging (DWI) produces contrast due to differences in water diffusivity in distinct tissues. However, some studies have examined that diffusion estimation can be substantially confounded by perfusion based on the incoherent motion of blood in sufficiently random microvascular network at the macroscopic level. Increased perfusion and vascularisation of metastatic cervical LNs in HNSCC compared to benign LNs have been reported [4–6].

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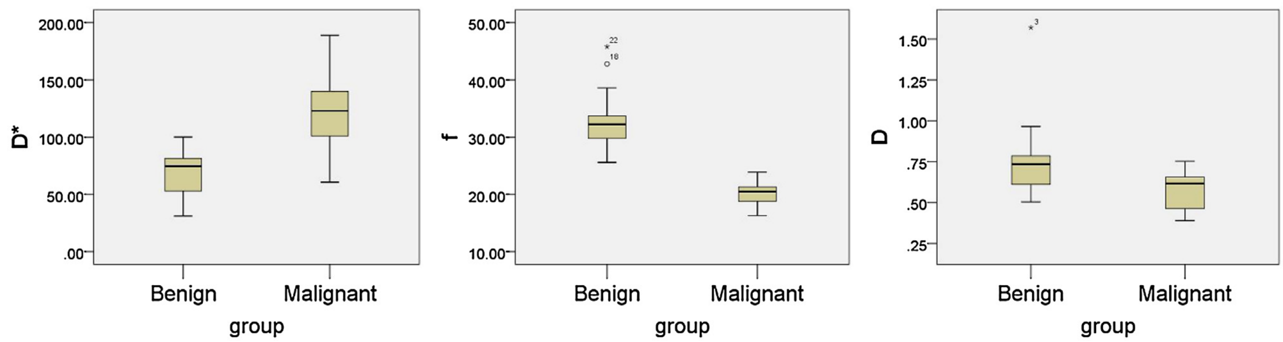

Fig. 1. Box plots of **a** D^*, **b** f, and **c** D comparing patients with malignant LNs and patients with benign LNs. The top and bottom of the boxes indicate the first and third quartiles, respectively. The length of box represents the interquartile range, within which 50% of the values were located. The solid line within each box is the median. The error bars show the minimum and maximum values (range), with outliers indicated as dots.

The intravoxel incoherent motion (IVIM) model [7] was developed to permit the simultaneous quantification of the signal stemming from both diffusion component (diffusion coefficient D) and vascular component (perfusion parameter f, D^*) noninvasively. This advanced imaging technique is based on DWI with an increased number of b-values. By analyzing the multiple b-value DWI data, a pronounced signal decay at low b-values can be acquired in well perfused tissue [8]. By applying an inversion recovery DWI sequence with blood suppression, previous studies have confirmed, that this non-monoexponential, pronounced signal decay at low b-values is caused by signal from the vascular component due to a combination of blood flow, blood volume and T2-signa l[9]. By using a biexponential fit on DWI data, the perfusion parameter f, D^* and the perfusion free diffusion coefficient D can be separated [9,10]. In contrast to the conventional ADC-value affected by cellularity and perfusion effects [8], the three new surrogate markers are related to tissue microstructure (D) and to the vascular component (f, D^*).

Therefore, application of IVIM analysis may be more advantageous and sensitive than conventional DWI in the evaluation of LNs metastasis of HNSCC. The purpose of our study was to characterize the perfusion parameter f, D^* and the diffusion coefficient D in metastatic LNs of HNSCC.

2. Materials and methods

2.1. Ethics statement

The study was approved by the local ethics committee

2.2. Patients

From September 2013 to December 2014, 49 consecutive patients were enrolled in this retrospective study. All the patients underwent IVIM-DWI. subsequent surgery or biopsy were performed within 2 weeks. The subjects were divided into 2 groups, group A comprised 29 patients with diagnosed HNSCC and group B comprised 20 patients with LNH. Among the A group, 20 were men and 9 were women; their age ranged from 19 to 68 years, with a mean age of 48 years. The primary cancers were of the larynx (n = 6), tongue (n = 2), nasopharynx (n = 13), nasal cavity (n = 4), oropharynx (n = 4). Among the LNH group, 12 were men and 8 were women; their age ranged from 16 to 56 years, with a mean age of 41 years. LNs with a short axis of at least 5 mm [3] were included in this study. All patients of HNSCC group underwent IVIM before chemoradiotherapy.

2.3. MRI protocol

MR imaging examinations of the LNs of HNSCC were performed using a 3.0-T whole-body system (Signa Excite HD, GE Healthcare, Milwaukee, WI) with a 40-mT/m maximum gradient capability and a standard receive-only head and neck coil. The imaging protocol included axial T1-weighted spin-echo images (repetition time (TR)/echo time (TE) 600/23 ms, 4 mm section thickness with a 1-mm intersection gap and number of excitations (NEX) equal to 2), and axial T2-weighted turbo spin-echo images with fat suppression (TR/TE 5200/137 ms; 4 mm section thickness, with 1 mm intersection gap and NEX = 2) using a 512 × 288 imaging matrix.

2.4. IVIM DW imaging sequence

The IVIM DW imaging sequence was performed after conventional MR sequence. Thirteen b values (0, 10, 20, 30, 50, 80, 100, 150, 200, 300, 400, 600 and 800 s/mm^2) were applied with a single-shot diffusion-weighted spin-echo echo-planar sequence. The lookup table of gradient directions was modified to allow multiple b value measurements in one series. Parallel imaging was used with an acceleration factor of 2. A local shim box covering the HNSCC scanning area was applied to minimize susceptibility artefacts. In total, 20 axial slices covering the HNSCC scanning area for patients respectively were obtained with a 24-cm field of view, 4 mm slice thickness, 1 mm slice gap, 3000 ms TR, 58 ms TE, 128 × 128 matrix and NEX = 2. The nominal scan time was 3 min 45s

2.5. IVIM DW MRI analysis

2.5.1. ADC value

The ADC value was calculated by fitting diffusion weighted images at b = 0 and four non-zero b values(200, 400, 500 and 600s/mm2) into Eq. (1).

$$Sb/S0 = \exp(-bADC) \quad (1)$$

2.5.2. D, D* and f value

According to IVIM, the signal intensities and b values are related as follows:

$$S_b/S_0 = (1-f)\exp(-bD) + f\exp(-bD*) \quad (2)$$

Where S_0 = signal intensity at the b value of 0; S_b = signal intensity at the b value denoted by the subscript; D = true diffusion coefficient of a water molecule; D^* = pseudo-diffusion coefficient due to microcirculation; and f = microvascular volume fraction, indicating the fraction of diffusion related to microcirculation. Because D^* is roughly one order of magnitude greater than D[8], $-b\,D^*$ would be less than -3 at a high b value (>200 s/mm^2), and the term $f$exp($-$b