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Advanced diffusion models in head and neck squamous cell carcinoma patients: Goodness of fit, relationships among diffusion parameters and comparison with dynamic contrast-enhanced perfusion

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A B S T R A C T

Purpose: We assessed advanced fitting models of diffusion weighted imaging (DWI) in head/neck squamous cell carcinoma (HNSCC) patients to determine the best goodness of fit and correlations among diffusion parameters. We compared these results with those of dynamic contrast-enhanced (DCE) perfusion parameters.
Materials and methods: We retrospectively evaluated 32 HNSCC patients (12 sinonasal, 20 pharynx/oral cavity). The DWI acquisition used single-shot spin-echo echo-planar imaging (EPI) with 12 b-values (0 − 2000). We calculated 14 DWI parameters using mono-exponential, bi-exponential, and tri-exponential models, stretched exponential model (SEM) and diffusion kurtosis imaging (DKI) models. We compared each model's goodness of fit using the residual sum of squares (RSS), Akaike Information Criterion (AIC) and Bayesian information criterion (BIC) value. We determined the correlation between each pair of DWI parameters and between each DWI parameter and DCE perfusion parameter.
Results: The tri-exponential fit's RSS, AIC and BIC values were significantly smaller than those for bi-exponential fit. The RSS, AIC and BIC values of the SEM fit and DKI fit were significantly smaller than mono-exponential model. Significant correlations were observed in 30 pairs (sinonasal cavity) and 31 (sinonasal cavity group) among 91 DWI parameter combinations. Significant correlations were also observed in nine pairs (both sinonasal cavity and pharynx/oral cavity group) among 64 DWI/DCE perfusion parameter pairs, in particular, high positive correlations between the tri-exponential model's intermediate diffusion fraction (f_2) and the volume of the extracellular extravascular space per unit volume of tissue (v_e) were observed in both patient groups.
Conclusion: We identified several correlations between DWI parameters by advanced fitting models and correlations between DWI and DCE parameters. These will help determine HNSCC patients' detailed tissue structures.

1. Introduction

Diffusion-weighted imaging (DWI) is a well-known noninvasive technique that is used to obtain tissue microstructural information by measuring water diffusivity in various tissues, including cancer [1]. DWI signal intensity changes in different b-values were proposed to be caused by microstructural conditions such as cell density, length of cell membrane, cell size or shape, and the ratio of intracellular to extracellular space that influences the water diffusion [2,3].

The apparent diffusion coefficient (ADC), calculated using the mono-exponential decay function of DWI signal intensity with two or more b-values, has been reported to be useful in head and neck squamous cell carcinoma (HNSCC) cases for differentiating benign and malignant tissues, and to assess therapeutic efficacy and predict treatment outcomes [4,5]. Although the biological characteristics of sinonasal and pharynx SCC are somewhat different and these two types of HNSCC also slightly differ in regard to characteristics such as causes, risk factors, frequency of lymph node and distant metastases, and treatment strategies, the utility of the ADC was reported for both types of HNSCC [4–6]. However, the water diffusion behavior in cancer tissues is complicated, and it is difficult to explain the water diffusion behavior in a completely free water diffusion model using the mono-exponential decay function. This is due to the complex structures such as the capillary network and

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cell membranes in each pixel. Such a complicated structure can cause the behavior of water diffusion to resemble non-Gaussian (restricted) diffusion rather than Gaussian diffusion calculated by mono-exponential fitting.

Advanced fitting models for DWI were recently described [7–13]. For example, a model using intravoxel incoherent motion (IVIM) was proposed; by using the bi-exponential decay function, it divides the fast and slow diffusion components, which reflects the true tissue diffusivity and capillary perfusion, respectively [7,8]. A tri-exponential fitting model was also described that divides the three different diffusion components by using a tri-exponential decay function [9,10]. This multi-component analysis by a tri-exponential model may reveal more details of the water diffusion in cancer tissue compared to a bi-exponential model. A stretched exponential model (SEM) diffusion model was described as follows: the SEM model was used to describe the heterogeneity of water diffusion in each voxel. In this model, to obtain a good fit to multiple b-value signal decay data, the two parameters of diffusion heterogeneity and diffusion coefficient are respectively calculated [11,12]. A diffusion kurtosis imaging (DKI) model also uses the diffusion distribution information. In this method, the degree of difference (= kurtosis value) from the Gaussian distribution in the water diffusion distribution is calculated by the Taylor expansion, and this kurtosis value was used for the correction of the multiple b-value signal decay curve [8,13]. These different non-Gaussian diffusion models can fit the diffusion signal decay curve more precisely, reflecting tissue characteristics such as lesions of the capillary network, the extracellular extravascular space (EES), and the cellular space more clearly and in greater detail.

The three purposes of the present study were to: (1) determine which diffusion model best fitted the multiple b-value signal decay curve, (2) assess the correlations among the multiple diffusion parameters obtained by the various fitting models, and (3) identify the correlations between the diffusion parameter derived from the multiple fitting models and the parameters derived using the dynamic contrast-enhanced (DCE) perfusion technique.

2. Materials and methods

2.1. Patients

The protocol of this retrospective study was approved by our institutional review board, and written informed consent was waived. We evaluated the cases of 32 patients with HNSCC who were treated at our hospital during the roughly 3-year period from September 2012 to November 2015. All patients fulfilled the following inclusion criteria: (1) the patient was first diagnosed (not a recurrent case) histopathologically as having HNSCC, (2) magnetic resonance imaging (MRI)

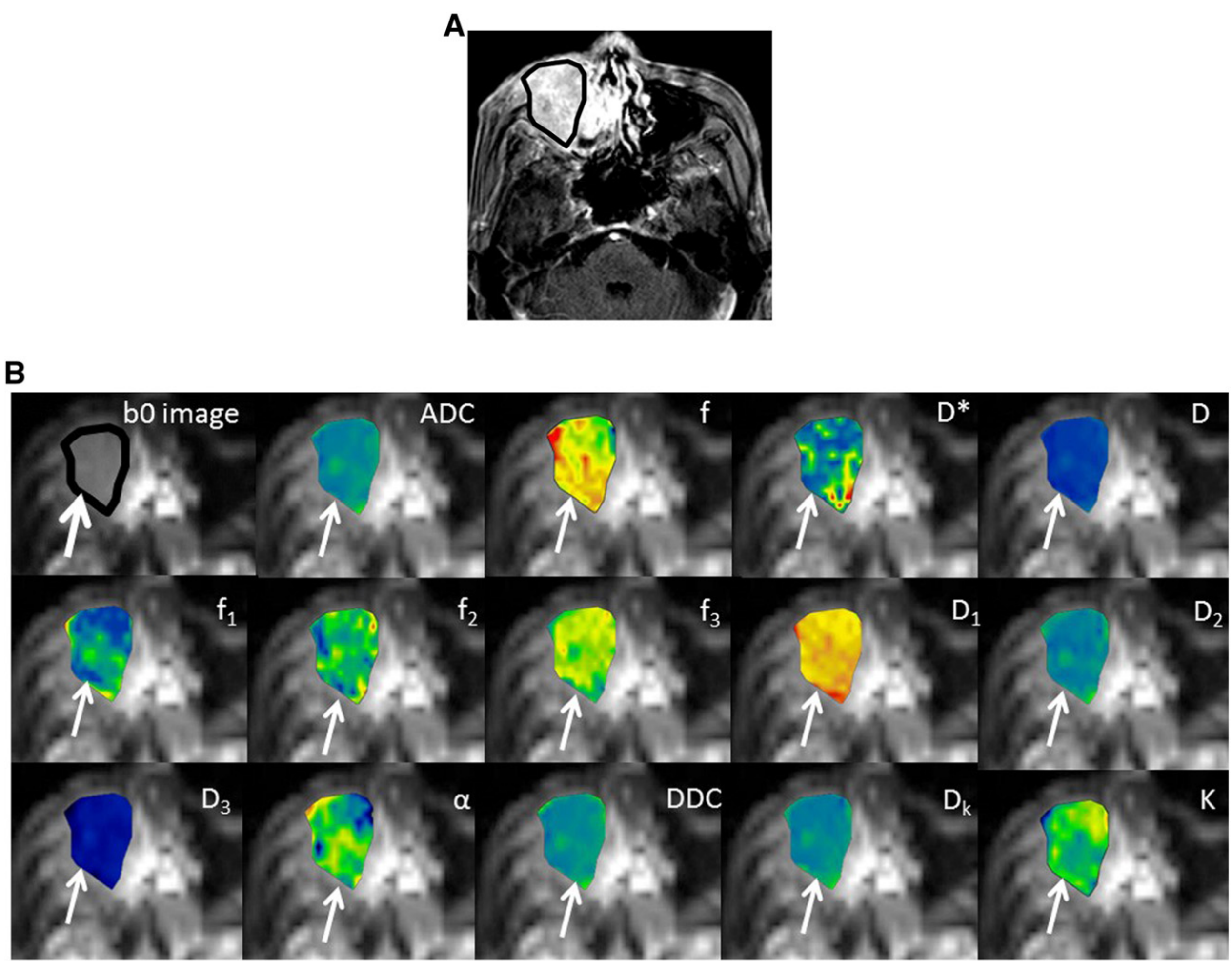

Fig. 1. ROI placement on the DWI and DCE perfusion images. A polygonal ROI was used for the delineation of the whole tumor. Necrotic areas, cystic formations and large vessels were carefully avoided. First, this ROI was placed on the last phase of DCE images (a). This ROI was then placed on the diffusion b0 image with manual adjustment based on anatomical information for the fixation of its location (b; large arrow). Finally, all diffusion parameter maps in this ROI were used for the analysis (b; small arrow).