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Original contribution

Oral carcinoma: Clinical evaluation using diffusion kurtosis imaging and its correlation with histopathologic findings☆

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ABSTRACT

Purpose: In this study, we aimed to determine the usefulness of diffusion kurtosis imaging (DKI) as a noninvasive method for evaluation of the histologic grade and lymph node metastasis in patients with oral carcinoma.

Materials and methods: Twenty-seven patients with oral carcinoma were examined with a 3-T MR system and 16-channel coil. DKI data were obtained by a single-shot echo-planar imaging sequence with repetition time, 10,000 ms; echo time, 94 ms; field of view, 250 × 204.25 ms; matrix, 120 × 98; section thickness, 4 mm; four b values of 0, 500, 1000, and 2000 s/mm^2; and motion-probing gradients in three orthogonal directions. Diffusivity (D) and kurtosis (K) were calculated using the equation: $S = S_0 \cdot \exp(-b \cdot D + b^2 \cdot D^2 \cdot K/6)$. Conventional apparent diffusion coefficient (ADC) was also calculated. The MR images were compared with the histopathologic findings.

Results: Relative to the histologic grades (Grades 1, 2, and 3) of the 27 oral carcinomas, D values showed a significant inverse correlation ($r = -0.885$; $P < 0.001$) and K values showed a significant positive correlation ($r = 0.869$; $P < 0.001$), whereas ADC values showed no significant correlation ($r = -0.311$; $P = 0.115$). When comparing between metastatic and non-metastatic lymph nodes, significant differences in the D values ($P < 0.001$) and K values ($P < 0.001$), but not the ADC values ($P = 0.110$) became apparent.

Conclusions: In patients with oral carcinoma, DKI seems to be clinically useful for the evaluation of histologic grades and lymph node metastasis.

1. Introduction

Oral carcinoma is one of the most common and fatal malignant neoplasms worldwide [1–3]. The prognosis of patients with oral carcinoma strictly depends on the histologic grade, as well as on the presence and extent of lymph node metastasis; therefore, accurate preoperative assessment of these prognostic factors has a definitive impact on the selection of the optimal therapy for oral carcinoma [2,3]. Preoperative staging of oral carcinoma is currently performed on the basis of computed tomography (CT), ultrasound (US), and magnetic resonance (MR) imaging; however, the histologic grade and lymph node metastasis cannot be reliably assessed by these methods. CT has poor soft tissue contrast and indeterminate size criteria [4,5]. US carries several inherent problems, including high operator dependency, artifactual interface echoes, and a limited sonographic range [6,7]. MR imaging is an alternative to CT and US, but conventional MR imaging remains incapable of evaluating the histologic grade and lymph node metastasis in oral carcinoma [8,9].

Previous reports have shown that the findings of non-Gaussian diffusion kurtosis imaging (DKI) were associated with this histologic grade

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Table 1
D, K, and ADC values in the different histologic grades of oral carcinomas.

Histologic grades	D values ($\times 10^{-3}$ mm^2/s)	K values (a.u.)	ADC values ($\times 10^{-3}$ mm^2/s)
Grade 1 (n = 13)	2.062 ± 0.231*	0.735 ± 0.061*	0.808 ± 0.064
Grade 2 (n = 11)	1.609 ± 0.133	0.858 ± 0.055	0.751 ± 0.057
Grade 3 (n = 3)	1.397 ± 0.053	1.027 ± 0.103	0.774 ± 0.134

Note: Grade 1 = Well-differentiated, Grade 2 = Moderately differentiated, Grade 3 = Poorly differentiated. a.u. = arbitrary units. * = Significantly different for the different histologic grades of the oral carcinomas ($P < 0.001$).

of gliomas, prostate cancer, and breast cancer [10–14]. Furthermore, Yamada et al. [15,16] have recently demonstrated that non-Gaussian q-space imaging (QSI) was useful for ex vivo evaluation of the histologic grade and lymph node metastasis in esophageal and gastric carcinomas. To the best of our knowledge, however, there have been no reports on the use of non-Gaussian DKI to evaluate patients with oral carcinoma in terms of the histologic grade and lymph node metastasis.

The purposes of this study were to prospectively examine patients with oral carcinoma and to assess the usefulness of DKI as a noninvasive method of evaluating the histologic grade of oral carcinomas and detecting the presence of lymph node metastasis.

2. Materials and methods

2.1. Study population

Our institutional review board provided official approval for this study, and all patients provided written informed consent prior to participating in this study. We studied 27 consecutive patients with histologically confirmed oral squamous cell carcinoma and who underwent oral and maxillofacial surgery at our department. Fifteen men and 12 women with a mean age of 63.6 ± 12.4 years (range, 43–82 years) participated in our study. The location of the oral carcinomas was the tongue in 16 patients (59.3%), upper gingiva in 5 patients (18.5%), lower gingiva in 5 patients (18.5%), and floor of the mouth in 1 patient (3.7%). All patients underwent MR imaging, including DKI, for preoperative evaluation.

2.2. Imaging technique

A 3-T MR imaging unit (Magnetom Spectra; Siemens, Erlangen, Germany), which was equipped with actively shielded gradients with a maximum strength of 33 mT/m, was used to perform all MR imaging scans using a 16-channel head and neck coil.

DKI data sets were obtained in the axial plane using a spin echo-based, single-shot, echo-planar imaging sequence with fat suppression by short tau inversion recovery (STIR) and the following parameters: repetition time (TR), 10,000 ms; echo time (TE), 94 ms; field of view (FOV), 250 × 204.25 mm; matrix, 120 × 98; section thickness, 4 mm without intersection gaps; voxel size, 17.37 mm^3; and number of signal averaged (NSA), 1. The diffusion gradients were applied in three orthogonal directions with a duration time (δ) of 30.4 ms, a separation time (Δ) of 42.9 ms, effective diffusion time ($\Delta_{eff} = \Delta - \delta/3$) of 32.8 ms, and four different gradient strengths (g mT/m). The resulting four b values were 0, 500, 1000, and 2000 s/mm^2. The acquisition time for the DKI was 2 min 10 s.

Although the kurtosis assessment of the diffusion tensor, or diffusion kurtosis tensor imaging (DKTI), requires diffusion images in at least 15 different directions, DKI of the body can be performed based on a directionless "trace" of the diffusion tensor, which requires acquisition of only three directions [12,13]. Thus, we performed the DKI using four b values of 0, 500, 1000, and 2000 s/mm^2 in three orthogonal directions.

The standard MR imaging protocol for oral carcinoma patients at our institution included T1-weighted turbo spin-echo (TSE) imaging (TR/TE, 650/10 ms; turbo factor, 3; NSA, 1) in the axial and coronal planes; T2-weighted TSE imaging (TR/TE, 5000/94; turbo factor, 14; NSA, 1) with fat suppression by the two-point Dixon technique in the axial plane; and T2-weighted TSE imaging (TR/TE, 5400/89 ms; turbo factor, 12; NSA, 1) with fat suppression by chemical-shift selective saturation in the coronal plane. After intravenous administration of 0.1 mmol/kg gadobutrol (Gadovist; Bayer Yakuhin, Osaka, Japan), T1-weighted TSE images (TR/TE, 640/12; turbo factor, 3; NSA, 1) with fat suppression by the two-point Dixon technique were also obtained in the axial and coronal planes. The T1-weighted, T2-weighted, and contrast-enhanced T1-weighted images were obtained with FOV of 230 × 187 mm, matrix of 384 × 312, and section thickness of 4 mm, with an intersection gap of 1 mm.

2.3. Image processing

On the basis of the DKI theory [17,18], we analyzed the signal intensity decay and calculated the DKI parameters for each voxel using the following equation:

$$S = S_0 \cdot \exp(-b \cdot D + b^2 \cdot D^2 \cdot K/6),$$

where S_0 and S represent the signal intensities at a b value of 0 s/mm^2 and at b values other than 0 s/mm^2, respectively; D stands for the diffusivity ($\times 10^{-3}$ mm^2/s); and K stands for the kurtosis [arbitrary units

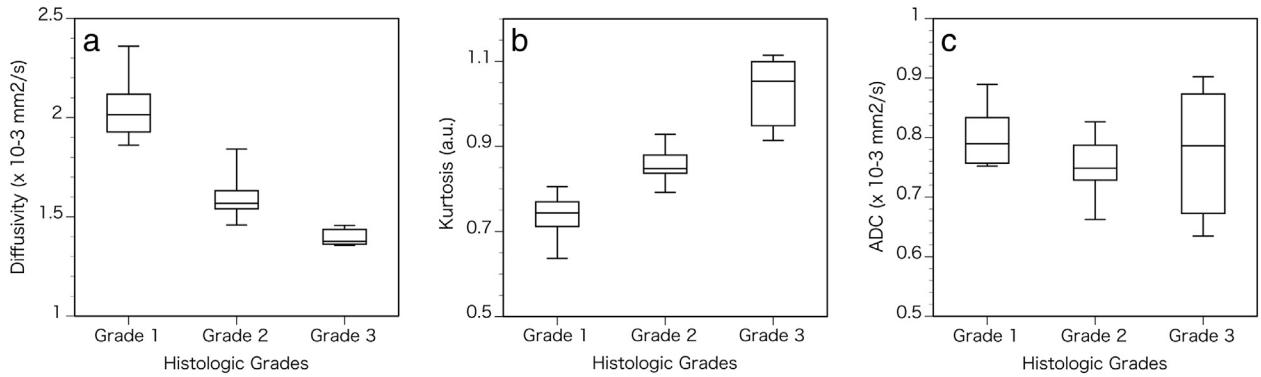

Fig. 1. Box plots of the DKI parameters in the different histologic grades of oral carcinomas.
(a) Comparison of the D values in the different histologic grades of oral carcinomas showing a significant inverse correlation (r = −0.885; $P < 0.001$).
(b) Comparison of the K values in the different histologic grades of oral carcinomas showing a significant positive correlation (r = 0.869; $P < 0.001$). (a.u. = arbitrary units.)
(c) Comparison of the ADC values in the different histologic grades of oral carcinomas showing no significant correlation (r = −0.311; $P = 0.115$).