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Residual tumour detection in post-treatment granulation tissue by using advanced diffusion models in head and neck squamous cell carcinoma patients

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ABSTRACT

Purpose: To evaluate the detectability of the residual tumour in post-treatment granulation tissue using parameters obtained with an advanced diffusion model in patients with head and neck squamous cell carcinoma (HNSCC) treated by chemoradiation therapy.
Materials and methods: We retrospectively evaluated 23 patients with HNSCC after the full course of chemoradiation therapy. The diffusion-weighted image (DWI) acquisition used single-shot spin-echo echo-planar imaging with 11 b-values (0–1000). We calculated 10 DWI parameters using a mono-exponential model, a bi-exponential model, a stretched exponential model (SEM), a diffusion kurtosis imaging (DKI) model and a statistical diffusion model (SDM) in the region of interest (ROI) placed on the post-treatment granulation tissue. The presence of residual tumour was determined by histological findings or clinical follow-up.
Results: Among the 23 patients, seven patients were revealed to have residual tumour. The univariate analysis revealed significant differences in six parameters between the patients with and without residual tumour. From the receiver operating characteristic curve analysis, the highest area under curve was detected in the center of the Gaussian distribution of diffusion coefficient (D_s) obtained by the SDM. The multivariate analysis revealed that the D_s and diffusion heterogeneity (α) obtained by the SEM were predictors for the presence of residual tumour.
Conclusion: DWI parameters obtained by advanced fitting models will be one of the diagnostic tools for the detection of residual tumour.

1. Introduction

Surgical resection, chemotherapy, radiotherapy, and their combinations are common treatments for head and neck squamous cell carcinoma (HNSCC) [1]. In particular, the use of super-selective arterial infusions of cisplatin with concomitant radiotherapy has become popular for HNSCC. because of its higher local control rate in advanced cases, especially those in the nasal or sinonasal cavity, oral cavity and pharynx SCCs [2–4].

After nonsurgical treatment, the presence or absence of residual tumour must be determined before selecting the next treatment — such as additional surgical resection and chemotherapy — or deciding the details of a follow-up strategy. Although computed tomography (CT) and magnetic resonance imaging (MRI) have been widely used to evaluate the presence of residual tumour tissue, these modalities mainly achieve a morphological evaluation only, and thus it is often difficult to distinguish whether or not post-treatment granulation tissue contains residual tumour

Abbreviations: ADC, apparent diffusion coefficient; AUC, area under curve; DDC, distributed diffusion coefficient; DKI, diffusion kurtosis imaging; DWI, diffusion-weighted image; EPI, echo-planar imaging; HNSCC, head and neck squamous cell carcinoma; IVIM, intravoxel incoherent motion; ROC, receiver operating characteristic; ROI, region of interest; SDM, statistical diffusion model; SEM, stretched exponential model.

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[5]. As another method, positron-emission tomography (PET) with 18F-fluorodeoxyglucose (FDG) is widely used for the detection of residual tumour by depicting the high glucose metabolism of residual tumour [6]. However, especially at the early time point after the treatment, post-treatment inflammatory changes (particularly in the sinonasal cavity) cause FDG uptake by their biological activity due to inflammation, which makes it difficult to distinguish post-treatment granulation and residual tumour, resulting in a failure to detect residual tumour in post-treatment granulation tissue [7]. In such post-treatment granulation tissue, the microstructure is thought to contain the post-treatment inflammatory or granulation tissue, but if a certain amount of residual tumour tissue is present, the microstructural characteristics may be different compared to those of only inflammatory granulation tissue. The details of tissue microstructure can be assessed using diffusion-weighted imaging (DWI), which reveals the micro-water diffusion; this indirectly reflects aspects of the microstructural architecture such as the cell membrane [8]. Compared to the conventional model of the apparent diffusion coefficient (ADC) obtained by mono-exponential fitting, multiple advanced models have been reported to well reflect the complicated signal decay of multiple b-value data in DWI [9–12]. Such advanced models can reflect the microstructural information in greater detail and may detect residual tumour in post-treatment granulation tissues.

We conducted the present study to evaluate the detectability of residual tumour in post-treatment granulation tissue, using parameters obtained with multiple advanced diffusion models in HNSCC patients treated with chemoradiation.

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 23 patients with HNSCC who were treated at our hospital during the roughly 3-year period from September 2012 to February 2015. All patients fulfilled the following inclusion criteria: (1) histopathological diagnosis of SCC, (2) the patient had undergone a full course of curative treatment with 70-Gy radiation, and (3) MRI including multiple b-value DWI was performed within 1 month after the end of the full course of treatment. The characteristics of the 23 patients were as follows: 19 males and four females (mean age 59.5 yrs, range 47–73 yrs). The primary lesions involved the maxillary sinus in 20 patients and the nasal cavity in three patients. The histopathological diagnoses were SCC in all patients. The T stage was T3 in nine patients, T4a in 10, and T4b in four. The treatment regimen was a super-selective arterial infusion of cisplatin with concomitant radiotherapy for all patients. The patients' treatment details were as follows: an arterial infusion of cisplatin (100–120 mg/m^2 per week for 4 weeks) to the primary tumour's dominant blood supply, using a microcatheter, with concurrent radiotherapy of a total of 70 Gy in 35 fractions. MRI scans including multi b-value scanning were performed in all patients within 1 month after the full course of treatment. The time interval between the end of treatment and the MRI scanning was 13–21 days (15.1 ± 1.8 days).

2.2. Clinical assessment

In all patients, clinical and radiological follow-ups were performed after the treatment to determine the final diagnosis related to the presence of residual tumour at the primary site. The presence of residual tumour was determined by the histopathological confirmation of SCC by biopsy or surgical resection, the development of a mass lesion in the post-treatment granulation tissue, or the definite enlargement of granulation tissue area during the follow-up, which was ≥1 year (the minimum follow-up period was set as 1 year). The non-presence of residual tumour was determined by histopathological confirmation of the absence of SCC by surgical resection, the absence of enlargement of the suspected lesion of the residual tumour, or the absence of a new lesion in the post-treatment granulation tissue within the follow-up period.

2.3. Imaging protocols

All MR imaging was performed using a 3.0 T unit (Achieva TX; Philips Healthcare, Best, Netherlands) with a 16-channel neurovascular coil. The DWI acquisition used single-shot spin-echo echo-planar imaging (EPI) with three orthogonal motion probing gradients. Eleven b-values (0, 10, 20, 30, 50, 80, 100, 200, 400, 800 and 1000 s/mm^2) were used. The other imaging parameters were: TR, 4500 ms; TE, 64 ms; DELTA (large delta; gradient time interval), 30.1 ms; delta (small delta; gradient duration), 24.3 ms; flip angle, 90°; field of view (FOV), 230 × 230 mm; 64 × 64 matrix; slice thickness, 5 mm × 20 slices; voxel size 3.59 × 3.59 × 5.00 mm; parallel imaging acceleration factor, 2; the number of signal averages = b-value of 0–100 s/mm^2 (one average), 200–800 s/mm^2 (two averages) and 1000 s/mm^2 (three averages); scanning time, 4 min 02 s.

Conventional MR images were also obtained to evaluate the primary tumour. These images included (a) axial T1-weighted image (T1WI) with a spin-echo sequence (TR, 450 ms; TE, 10 ms; FOV, 240 × 240 mm; 512 × 512 matrix; slice thickness, 5 mm; inter-slice gap, 30%; scanning time, 2 min 12 s), and (b) axial T2-weighted image (T2WI) with a turbo spin-echo (TSE) sequence with fat suppression (TR, 4500 ms; TE, 70 ms; TSE factor, 9; FOV, 240 × 240 mm; 512 × 512 matrix; slice thickness, 5 mm; inter-slice gap, 30%; scanning time, 2 min 06 s).

2.4. Data analysis

2.4.1. ROI settings

For the region of interest (ROI) delineation, a board-certified neuroradiologist with 19 years of experience delineated each post-treatment granulation tissue with a polygonal ROI on b0 images; axial T1WI and T2WI were used as reference images (Fig. 1). By referring to the region where the primary tumour was present before the treatment, the abnormal soft tissue that was suspected to contain post-treatment granulation tissue and/or residual tumour was identified by using the T1WI and T2WI imaging findings. Such tissue was considered to present a typically slightly high or intermediate signal on T2WI with a low signal on T1WI and was different from the normal anatomical structure. The post-treatment granulation tissue did not show strong high signal intensity on T2WI that suggested inflammatory tissue (such as thickened mucosa or fluid correction) or high signal intensity on T1WI, which suggested the subacute hemorrhage or mutinous fluid, and thus such region was excluded. The ROI was then delineated so that it contained only the post-treatment granulation tissue on the b0 image with the reference information mentioned above. Mainly the T2WI image in particular was used, because the image contrast of T2WI was almost the same as the b0 image of the conventional EPI. If the granulation tissue extended into two or more slices, all slices in which the tumour was included were used for the ROI delineation. Each delineated tumour ROI was copied on each b-value image. The signal intensity in each b-value image was determined as the mean value in the delineated ROI by integrating all granulation tissue voxels from all delineated slices into the total signal intensity. The data analysis was performed using this ROI-based mean value (not a pixel-by-pixel basis) for the maintenance of a sufficient signal-to-