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Research article

Value of diffusion tensor imaging in differentiating malignant from benign parotid gland tumors

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ABSTRACT

Purpose: To evaluate whether diffusion tensor imaging (DTI) can be used to differentiate malignant parotid gland tumors from the benign ones.

Materials and methods: The study population comprised 59 parotid gland tumors (24 Warthin's tumors, 19 pleomorphic adenomas, seven other benign tumors, and nine malignant tumors). Single-shot echo-planar DTI was performed with motion-probing gradients along 30 noncollinear directions (b = 1000 s/mm^2) at 3.0 T. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values for benign and malignant tumors were compared using the Mann–Whitney *U* test. Receiver-operating characteristic (ROC) curve analysis was performed to assess the ability of the ADC and FA values to differentiate malignant tumors from the benign ones.

Results: ADC values showed no significant difference between malignant ($0.93 \pm 0.21 \times 10^{-3}$ mm^2/s) and benign tumors ($1.19 \pm 0.50 \times 10^{-3}$ mm^2/s) ($p = 0.225$). FA values of malignant tumors were significantly higher than those of benign tumors (0.26 ± 0.06 *vs.* 0.17 ± 0.05, $p < 0.001$). The area under the ROC curve of FA was significantly greater than that under the curve of ADC (0.884 *vs.* 0.628, $p = 0.010$).

Conclusions: DTI, particularly FA, can help differentiate malignant parotid gland tumors from the benign ones.

1. Introduction

There are several histological subtypes of salivary gland neoplasms [1]; this makes it challenging to establish their definitive diagnosis on radiological imaging. In particular, it is important to preoperatively differentiate between benign and malignant salivary gland tumors because this information influences the surgical planning. Local excision or superficial parotidectomy is performed for benign tumors, whereas total parotidectomy with or without facial nerve removal is performed for malignant tumors [2,3].

For diagnosing salivary gland tumors, several researchers have reported the usefulness of magnetic resonance (MR) imaging-based techniques, particularly dynamic contrast-enhanced MR imaging and diffusion-weighted imaging (DWI) [4–6]. However, dynamic contrast-enhanced MR imaging requires contrast injection; thus, it cannot be performed in patients with renal dysfunction or history of adverse reaction previously reported [7,8]. DWI provides additional quantitative information related to random microscopic motion of water molecules in tissues. Apparent diffusion coefficient (ADC) measurement has been reported to be useful for differentiation of benign and malignant lesions in various organs. In several organs, such as breast, liver, and uterus, ADC value has been reported to discriminate well between benign and malignant lesions. In the thyroid and pancreas, ADC values were not significantly different between benign and malignant lesions [9]. In salivary gland tumors, there are several reports on ADC value for differentiating between benign and malignant tumors [5,10]. However, the efficacy of ADC value for differentiating between benign and malignant tumors is constrained by a considerable overlap between different types of tumors, and especially for differentiating Warthin's tumor from malignant parotid gland tumors [6,11].

Diffusion tensor imaging (DTI) as an advanced MR technique provides quantitative information regarding the magnitude and directionality of water diffusion in three-dimensional space [12,13]. DTI can provide both ADC and fractional anisotropy (FA), which is a quantitative index of tissue anisotropy [14,15]. DTI has been extensively used to assess the microstructural architecture of normal and diseased brain tissues [16,17]. It has also been used to assess myocardium infarction [18], and kidney [19] and liver diseases [20,21]. Recent reports have

Abbreviations: DTI, diffusion tensor imaging; FA, fractional anisotropy; MD, mean diffusivity; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; ROC, receiver operating characteristic; ROI, regions of interest; ICC, intraclass correlation coefficient

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Table 1
Patient's characteristics.

	total (n = 53)	Benign tumors (n = 44)	Pleomorphic adenomas (n = 19)	Warthin tumors (n = 18)	Other benign tumors (n = 7)	Malignant tumors (n = 9)	p
Age (yr)	58 ± 15 (21–87)	57 ± 13 (21–79)	54 ± 15 (21–79)	61 ± 7 (48–77)	57 ± 14 (33–74)	64 ± 22 (26–87)	0.169[a]
Gender (M:F)	28:25	25:19	7:12	16:2	2:5	3:6	0.278[b]

Note: Data are presented as mean ± SD; data in parentheses are presented as range.
[a] Compared between benign and malignant tumors using the Mann–Whitney *U* test.
[b] Compared between benign and malignant tumors using Fisher's exact test.

suggested the ability of FA value to differentiate between benign and malignant lesions of the prostate [22,23], breast [24], and uterus [25]. To the best of our knowledge, only one report [26] showed the usefulness of DTI for diagnosing parotid gland tumors. The purpose of this study was to evaluate whether DTI can be used to differentiate malignant parotid gland tumors from the benign ones.

2. Materials and methods

2.1. Patients

Institutional ethics review board approval was obtained; the requirement for informed consent of patients was waived for this retrospective study because we routinely examined DTI for parotid gland MR examinations in the clinical setting.

MR imaging database and clinical records of the department of radiology were retrospectively reviewed. Ninety one consecutive patients who underwent preoperative parotid gland MR imaging (including DTI), between September 2007 and October 2011, were identified. Among these, patients who did not undergo surgical resection were excluded from this analysis (n = 31). Seven patients (three lymphoepithelial cysts, one retention cyst, one Warthin's tumor, one adenoid cystic carcinoma, and one abscess) in which the lesions showed cystic masses without a solid part were also excluded owing to the difficulty to evaluate the solid component. Finally, 53 patients (28 men and 25 women; mean age: 58 years; range, 21–87 years) with a total of 59 parotid gland tumors were included in this study (Table 1). For all tumors, the final diagnoses were confirmed on histopathological evaluation of surgically resected specimens. The median interval between the preoperative MR examination and surgical resection was 78 days (range, 3–532days). Out of the 59 parotid gland tumors, 50 were benign (19 pleomorphic adenomas, 24 Warthin's tumors, 5 basal cell adenomas, one schwannoma, and one myoepithelioma) and 9 were malignant (3 mucoepidermoid carcinomas, 2 salivary duct carcinomas, one acinic cell carcinoma, one mucosa-associated lymphoid tissue lymphoma, one epithelial-myoepithelial carcinoma, and one squamous cell carcinoma). Four patients had multiple Warthin's tumors (two patients had two tumors each; and two had three tumors each).

2.2. MR imaging technique

All MR examinations were performed using a 3-T system (MAGNETOM Trio, Siemens Medical Solutions, Erlangen, Germany) with a standard phased-array head and neck coil. For each patient, DTI was performed in the transverse plane using a single-shot echo-planar imaging sequence with the spectral presaturation attenuated inversion recovery fat suppression technique. The following parameters were used: repetition time 8900 ms; echo time 85 ms; field of view, 220 mm; matrix, 90 × 90; generalized autocalibrating partial parallel acquisition factor, 2; number of excitations, 1; section thickness, 3 mm; section gap, 0 mm. The diffusion gradients were applied in 30 directions, which was the same method as the previous reports about DTI for several body parts [27–29], with two b values of 0 and 1000 s/mm^2 which was the same method as the previous reports [23,27]. The duration of the DTI protocol was 5 min 3 s. The clinical MR imaging study also included precontrast T1-weighted spin-echo (repetition time: 630 ms, echo time: 14 ms, field of view: 230 mm, matrix: 384 × 320, slice thickness: 5 mm, gap: 1 mm, number of excitations: 2, flip angle: 180, echo train length: 3), T2-weighted turbo spin-echo (repetition time: 4000 ms, echo time: 80 ms, field of view: 230 mm, matrix: 384 × 320, slice thickness: 5 mm, gap: 1 mm, number of excitations: 2, flip angle: 180, echo train length: 11), and postcontrast-enhanced fat-suppressed T1-weighted spin-echo images (repetition time: 620 ms, echo time: 13 ms, field of view: 230 mm, matrix: 384 × 320, slice thickness: 5 mm, gap: 1 mm, number of excitations: 2, flip angle: 180, echo train length: 3).

2.3. Imaging analysis

All MR images were transferred and diffusion data processed using commercial software (Syngo MR, Siemens Healthcare). The application of principal component analysis yielded for each pixel the three eigenvectors that define the principal diffusion directions in three orthogonal axes, which coincide with the diffusion frame of the tissue, and their corresponding three eigenvalues, arranged from high to low values, that quantify the principal diffusion coefficients [30]. Average diffusivity, defined as ADC, was calculated as the mean of the three eigenvalues. Two radiologists (Y.F. and H.H. with 23 and 7 years, respectively, of experience in radiology), who were blinded to the final pathological results, measured independently the mean ADC and FA values. With reference to T1- and T2-weighted images, the two radiologists manually drew an ovoid region of interest (ROI) as large as possible on high b value images. Mean ROI size and range were 162.3 mm^2 and 20–502 mm^2, respectively for 1st radiologist and 151.7 mm^2 and 20–572 mm^2, respectively for 2nd radiologist. There was no significant difference in the ROI size between the two readers ($p = 0.338$). Care was taken to avoid vessels and cystic parts within the tumors with reference to postcontrast-enhanced fat-suppressed T1-weighted images. The size, shape, and location of the ROIs were kept constant for ADC and FA maps in each patient, by applying a copy-and-paste function of the software. ADC and FA in each parotid tumor were measured.

2.4. Statistical analysis

Intraclass correlation coefficient (ICC) was calculated to assess inter-observer agreement of the ADC and FA values ($\kappa = 0.00$–0.20, poor correlation; $\kappa = 0.21$–0.40, fair correlation; $\kappa = 0.41$–0.60, moderate correlation; $\kappa = 0.61$–0.80, good correlation; $\kappa = 0.81$–1.00, excellent correlation) [31].

ADC and FA values for benign and malignant tumors were compared using the Mann–Whitney *U* test. Associated *p* values < 0.05 were considered indicative of a statistically significant between-group difference. For subsequent statistical analyses, benign tumors were categorized according to tumor subtype: pleomorphic adenomas (n = 19), Warthin's tumors (n = 24), and other benign tumors (n = 7). The ADC and FA values were compared between malignant tumors and each benign tumor subtype using the Kruskal-Wallis test, followed by the Mann–Whitney *U* test. Values of $p < 0.05$ and $p < 0.017$ (Bonferroni