Role of diffusion weighted magnetic resonance imaging in stratifying tumor aggressiveness in papillary thyroid carcinoma

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Introduction

A dramatic rise in the incidence of thyroid cancer has occurred in the last 25 years[1,2]. While the cause of this is unknown, the observation that nearly 50% of new thyroid cancers is due to papillary micro carcinoma suggests that increased detection/diagnosis of previously subclinical disease by ultrasonography-guided fine needle aspiration is a major factor[1,3]. Fortunately, for the low-risk tumors the recurrence rate is of less than 3-4% and a disease-specific survival rate of more than 99%[4]. Partial thyroid lobectomy or total thyroidectomy is routinely recommended to nearly all patients. However, the need for this radical treatment has been brought into question by two recent studies showing that even without any treatment, the vast majority of these still remain stable in size and confined to the thyroid gland when followed with active surveillance for up to 10 year[5,6]. There remains a pressing need of non-invasive ways to identify patients with aggressive tumor. Diffusion weighted magnetic resonance imaging (DW-MRI) allows for non-invasive measurement of the random motion of water molecular, which may provide unique imaging biomarkers in characterizing tumor aggressiveness. The purpose of this study was to evaluate the role of DW-MRI in stratifying tumor aggressiveness in patients with papillary thyroid carcinoma (PTC).

Methods

DW-MRI data acquisition: Our institutional review board approved this retrospective study and issued a waiver of informed consent. 12 patients (age: 28-66 years, M/F: 2/10, and tumor location (left/right/bilateral lobe): 4/6/2) were referred for DW-MRI study by physicians at our institution. All patients underwent pretreatment DW-MRI on a GE 1.5T Excite scanner with an 8-channel neurovascular phased-array coil prior to surgery. DW-MRI acquisitions were performed using a single-shot echo planar imaging (SS-EPI) spin echo sequence (TR = 4000 ms, TE = 98-104 ms, NEX = 4, and 3 orthogonal directions) with b value of 500 s/mm^2. The DW-MRI scans focused on the tumors: with 4-8 slices of thickness 5 mm, FOV of 20~24 cm, and acquisition matrix of 128 × 128.

DW-MRI data analysis: The regions of interest (ROI) on the tumor and normal tissues were placed by an experienced radiologist. The apparent diffusion coefficients (ADC) as well as normalized ADC value (nADC) were calculated. ADC value was calculated using the conventional mono-exponential model. For nADC, the ratio of ADC value of tumor tissue to the ADC value of a reference region i.e. normal thyroid tissue was calculated.

Histopathologic examination: All patients underwent surgery after the MRI. The surgical specimen was reviewed by an experienced pathologist. Tumor aggressiveness was evaluated for each surgical specimen using following histopathologic features: presence or absence of tall cell variants, necrosis, vascular and/or capsular invasion, extrathyroidal thyroid extension (ETE), and regional or distant metastases. The tumor was termed aggressive if any one of the above feature was present.

Statistical analysis: ADC and nADC values among 3 different groups (i.e. tumors with aggressive features, tumors without aggressive features, and normal thyroid tissue) were statistically analyzed to determine whether they significantly differed by using a Kruskal-Wallis test. Non-parametric Mann-Whitney U test was used to further determine which specific group pair has significant difference. P value <0.05 was considered significant.

Results

Figure 1 shows MRI and pathology images from a representative PTC patient without extrathyroidal extension (female; 34y; max. tumor diameter, 2.6 cm). Figures 1(e) and 1(f) show a classic PTC confined by the capsule at 10x (Fig. 1(e)) and 20x (Fig. 1(f)); the papillae are lined up by neoplastic cells, showing classical nuclear features, such as open and clear chromatin and the presence of colloid. Figure 2 shows MRI and pathology images from a representative PTC patient with extrathyroidal extension (female; 47y; max. tumor diameter, 2.4cm). Images from pathology analysis show a more aggressive phenotype, as demonstrated by the columnar and tall cell nature of the tumor without associated colloid (Fig. 2(e)) and of the tumor with extrathyroidal invasion in surrounding fibroadipose tissue (Fig. 2(f)), clearly showing an aggressive tumor. Tumors with aggressive features had significantly lower nADC values than that of tumor without tumor aggressive features (0.85±0.16 vs 1.15±0.13, p<0.0091)(Table 1). ADC values did not show any significance between these groups (Table1). Therefore, nADC was found to exhibit its promise as a surrogate biomarker for aggressiveness in PTC patients.

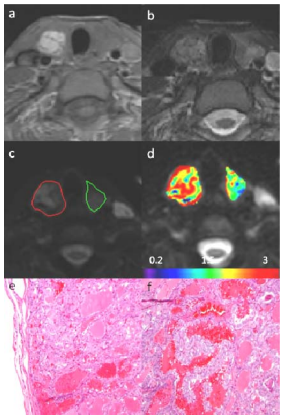

Fig.1. MRI images and histo-pathology from a representative papillary thyroid carcinoma **without** extrathyroidal extension (ETE). (a) T1 weighted MR image. (b) T2 weighted MR image. (c) diffusion weighed image (b = 0 s/mm^2). The red region of interest (ROI) is tumor tissue, and green ROI is normal thyroid tissue. (d) ADC map overlaid on diffusion weighed image (b = 0 s/mm^2). (e) Histopathology section at 10x resolution. (f) Histopathology section at image at 20x resolution.

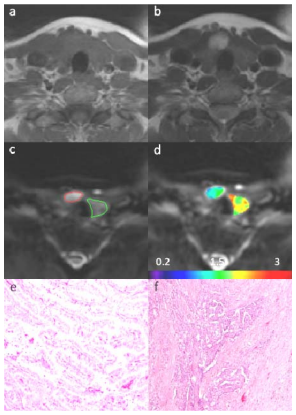

Fig.2. MRI images and histo-pathology from a representative papillary thyroid carcinoma **with** extra thyroidal extension. (a) T1 weighted MR image. (b) T2 weighted MR image. (c) diffusion weighed image (b = 0 s/mm^2). The red region of interest (ROI) is tumor tissue, and green ROI is normal thyroid tissue. (d) ADC map overlaid on diffusion weighed image (b = 0 s/mm^2). (e) Histopathology section at 10x resolution. (f) Histopathology section at image at 4x resolution.

Table 1. Statistical analysis between different thyroid tissue types

Thyroid gland	ADC (mm^2/s)	P value	nADC	P value
Normal thyroid tissue (N=12)	1.88±0.46	0.12(I) [0.18 (II), 0.16 (III), 0.15(IV)]	1	0.002(I)* [0.004 (II)*, 0.0002 (III)*, 0.0091 (IV)*]
Tumor with aggressive features defined at pathology (N=3)	1.62±0.008		0.85±0.16	
Tumor without aggressive features defined at pathology (N=9)	2.09±0.49		1.15±0.13	

Note: (I): p value among three groups i.e. normal thyroid tissue, tumor with and without aggressive features; (II): p value for normal thyroid tissue vs tumors with aggressive features; (III): p value for normal thyroid tissue vs tumors without aggressive features; (IV): p value for tumors with vs without aggressive features. *denotes significant P value

Discussion and Conclusion

In general, tumors are characterized by the increased cell attenuation and the increased amount of diffusion barriers. The motion of diffusion capacity is restricted and results in low ADC values. Our study showed that nADC outperformed ADC to distinguish tumors with and without aggressive features. Pathology features such as extra thyroidal extension, which is is associated with higher risk for local recurrence[7], can only be assessed on surgical specimens. While, DW-MRI derived biomarkers can non-invasively assess the thyroid gland and nADC exhibits potential in evaluating tumor aggressiveness in papillary thyroid carcinoma.

References and Acknowledgment

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