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The role of diffusion weighted MR imaging for differentiation between Graves' disease and Hashimoto thyroiditis

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Abstract. – OBJECTIVE: The aim of this study was to evaluate the usefulness of diffusion-weighted magnetic resonance imaging (DWMRI) for differentation between Graves' disease and Hashimoto's thyroiditis.

PATIENTS AND METHODS: Fifty patients (27 Graves diseases and 23 Hashimoto thyroiditis) and twenty healthy volunteers were examined using T1, T2 and DWMRI. The patients were diagnosed on the basis of physical findings and the results of thyroid function tests and serological tests. Circular ROIs were positioned on the bilateral thyroid lobes and isthmus. All measurements were repeated three different b values including 100, 600 and 1000 s/mm² in all cases. ADC (Apparent diffusion coefficient) maps were calculated automatically with the MR system.

RESULTS: Mean ADC values were 2.93 × 10^{-3}, 1.97 × 10^{-3} and 1.62 × 10^{-3} mm²/s in the healthy volunteers; 3.47 × 10^{-3}, 2.25 × 10^{-3} and 1.64 × 10^{-3} mm²/s in Graves' disease; 2.53 × 10^{-3}, 1.76 × 10^{-3}, 1.28 × 10^{-3} mm²/s in Hashimoto thyroiditis for b100, b600 and b1000, respectively. The ADC values of the Graves diseases were higher than healty volunteers and Hashimoto thyroiditis. ADC values were statistically significant for differentation between Hashimoto thyroiditis and Graves' disease all b values ($p < 0.05$).

CONCLUSIONS: DWMRI is fast sequence and does not require contrast agent. Quantitative assessment of the lesion is possible using ADC map. So, DWMRI may be useful differentiation of the Hashimoto thyroiditis and Graves' disease.

Key Words:
Diffusion weighted magnetic resonance imaging, Grave disease, Hashimoto thyroiditis.

Introduction

Graves' disease (GD) and Hashimoto's thyroiditis (HT) are most common autoimmune thyroid diseases[1,2]. Autoimmune thyroid diseases (ATD) affect about 2-5 percent of population in western countries[3]. GD is caused by stimulation of TSH receptor located on the thyroid gland by an antibody and this may lead to hyperplasia and hyperfunction of the thyroid gland. On the contrary, the cause of HT is due to TSH stimulation-blocking antibodies which blocks the action of TSH hormone and subsequently atrophy to thyroid gland[4,5].

To evaluate thyroid diseases, a radionuclide scintigraphy (RS) and ultrasonography (US) is usually performed after serological examination[1,6]. Usefulness of RS has been well known[7]. But there is little information about diagnostic role of magnetic resonance imaging (MRI) and DW (Diffusion-weighted) MRI in GD and HT. DWMRI is based on the tissue- dependent signal attenuation caused by incoherent thermal motion of water molecules. An apparent diffusion coefficient (ADC) is a quantitative parameter calculated from DW images[8,9]. Sometimes, these two pathologies are existent together in thyroid gland and they can not be differentiated by clinical and laboratory findings alone. The aim of this study was to evaluate usefulness of DWMRI for differentiation between GH and HT.

Patients and Methods

Subjects and Serological Examination

Twenty nine patients with GD and 26 patients with HT, and 20 healthy subjects were included this study between March 2008 and March 2009. Written informed consents were obtained from all patients before the study. The study was approved by our local Ethics Committee.

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Four patients were excluded from the study due to motion artifacts and poor image quality especially on DWI. One patient with HT was excluded from the study due to biopsy proven malignancy. Eventually, firstly and previously diagnosed upon laboratory and clinically findings, 50 patients were included the study. 27 patients with GD (7 male and 20 female patients; mean age = 37.11 years) and 23 patients with HT (2 male and 21 female patients; mean age = 39.78 years) composed the patients group.

Serum levels of free triiodothyronine (fT3), free thyroxine (fT4), thyroid-stimulating hormone (TSH) and TSH receptor antibodies were obtained from the clinical records. The results of radioimmunoassay were performed using blood samples. The values of fT3, fT4 and TSH were compared statistically for patients with GD and HT and healthy subjects.

MRI Techniques and Image Interpretation

MRI was performed using a 1.5 T whole-body superconducting MR scanner (General Electric, Signa excite high-speed scanner, Milwaukee, WI, USA). All sequences were obtained in axial plans. Following sequences were obtained from thyroid tissue: Fast spin- echo (FSE) T1-weighted sequence [TR (time to repetiation)/TE (time to echo): 532/15 msec]. FSE T2-weighted sequence (TR/TE: 4100/102 msec). The field of view (FOV) was 24 × 24 cm, slice thickness: 4 mm, number of excitations (NEX): 2, intersection gap: none, matrix: 28 × 128.

DWI was performed using single-shot spin echo echo planar imaging sequences with diffusion gradient *b* values of 100, 600 and 1000 s/mm^2. The following DWI parameters were used; TR/TE: 8000/minimum, FOV: 24 × 24 cm, slice thickness: 4 mm, NEX: 2, intersection gap: none, matrix: 128 × 128.

T1 and T2 weighted images were used to evaluation of signal characteristics of thyroid tissue. T1 and T2 weighted images and DWIs were obtained at same levels of thyroid tissue. T1 and T2 weighted images also used to cope with low signal to noise ratio of DWI images with especially high *b* values. The DWI was transferred to a workstation (Advantage Windows, software version 2.0, GE medical systems). Circle region of interests (ROIs) were placed to thyroid tissue with groups of patients and healthy subjects. ROIs were placed superior and inferior portions of right lobe, left lobe and isthmus of the thyroid for each groups. All measurements were repeated for following gradient values of *b*-100, *b*-600 and *b*-1000. ADC maps were calculated automatically by the MRI systems and ADC values are expressed in square millimeters per second.

Statistical Analysis

Statistical calculations were performed on a PC using Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, IL, USA). An analysis of variance (ANOVA) test and Tukey test as used posthoc test were compared the results of serological tests and ADC measurements of normal and pathologic groups. A p value less than 0.05 was accepted as statistically significant. Receiver operator characteristic (ROC) curves were obtained for a cutoff value for differentiating between HT and GD.

Results

fT3, fT4 and TSH values of each group are illustrated in Table I. Mean fT3 value of GDs was higher than groups of the normal subjects and HTs. There were significantly differences for fT3 values among each group. However, there was not any statistically significant difference between mean fT4 values of each group. Mean TSH value of HTs was higher than other groups. We did not find differences among mean ADC values and fT3 and fT4 levels.

Mean ADC measurements of GD, HT and normal subjects for all *b* gradient values are illustrated in Table II. Mean ADC values of GD were

Table I. Mean fT3, fT4 and TSH values of groups.

Thyroid Hormones	fT3 (pg/ml)	fT4 (pg/ml)	TSH (µIU/ml)
Hashimoto's thyroiditis	3.36 ± 0.18	1.72 ± 0.48	6.49 ± 1.51
Graves' Disease	5.68 ± 0.76	2.30 ± 0.32	0.24 ± 0.09
Healthy Subjects	2.9 ± 0.19	1.61 ± 0.28	1.84 ± 0.20

Table II. Mean ADC values ($\times 10^{-3}$ mm^2/s) at b values of 100, 600, and 1000 s/mm^2 for groups.

Mean ADC values	Normal subjects	Hashimoto's diseases	Graves' diseases
b-100	2.93 ± 0.37*	2.53 ± 0.47*,#	3,47 ± 0.26*,#
b-600	1.97 ± 0.44	1.76 ± 0.52#	2.00 ± 0.43#
b-1000	1.62 ± 0.35	1.28 ± 0.29#	1.64 ± 0.43#

higher than HT (Figure 1). There were significantly differences between ADC values of GD and HT for all *b* values ($p < 0.05$). Mean ADC values of GD for *b*-100, *b*-600 and *b*-1000 were 3.47 × 10^{-3} mm^2/s, 2.0 × 10^{-3} mm^2/s and 1.64 × 10^{-3} mm^2/s, respectively. Mean ADC values of HT for *b*-100, *b*-600 and *b*-1000 were 2.53 × 10^{-3} mm^2/s, 1.76 × 10^{-3} mm^2/s and 1.28 × 10^{-3} mm^2/s, respectively. There was statistically significance among mean ADC values of all groups for *b*-100 (Figure 2). However these values were not significant for *b*-600 and *b*-1000. Also, mean ADC values of HT were lower than GD and normal subjects for all *b* values.

No statistically significant differences were obtained between ADC values of right lobe, left lobe and isthmus for all *b* values at the patient with GD, HT and normal subjects.

Cutoff ADC values differentiating Graves' disease from Hashimoto thyroiditis for *b*-100, *b*-600 and *b*-1000 were 3.27 × 10^{-3}, 1.69 × 10^{-3} and 1.43 × 10^{-3} mm^2/s, respectively. Area under the curve (AUC) and 95% confidence interval (CI) were 0.906 and 0.847-0.947; 0.729 and 0.650-0.798; 0.712 and 0.633-0.783, respectively. Sensitivity and specificity values were 77.8% and 92.7%, 85.2% and 52.2%, 69.1% and 66.7%, respectively. Positive and negative predictive values were 92.6% and 78%, 67.6% and 75%, 70.9% and 64.8%, respectively. The *b*-100 value seems to be more useful than the others due to high sensitivity and specificity values.

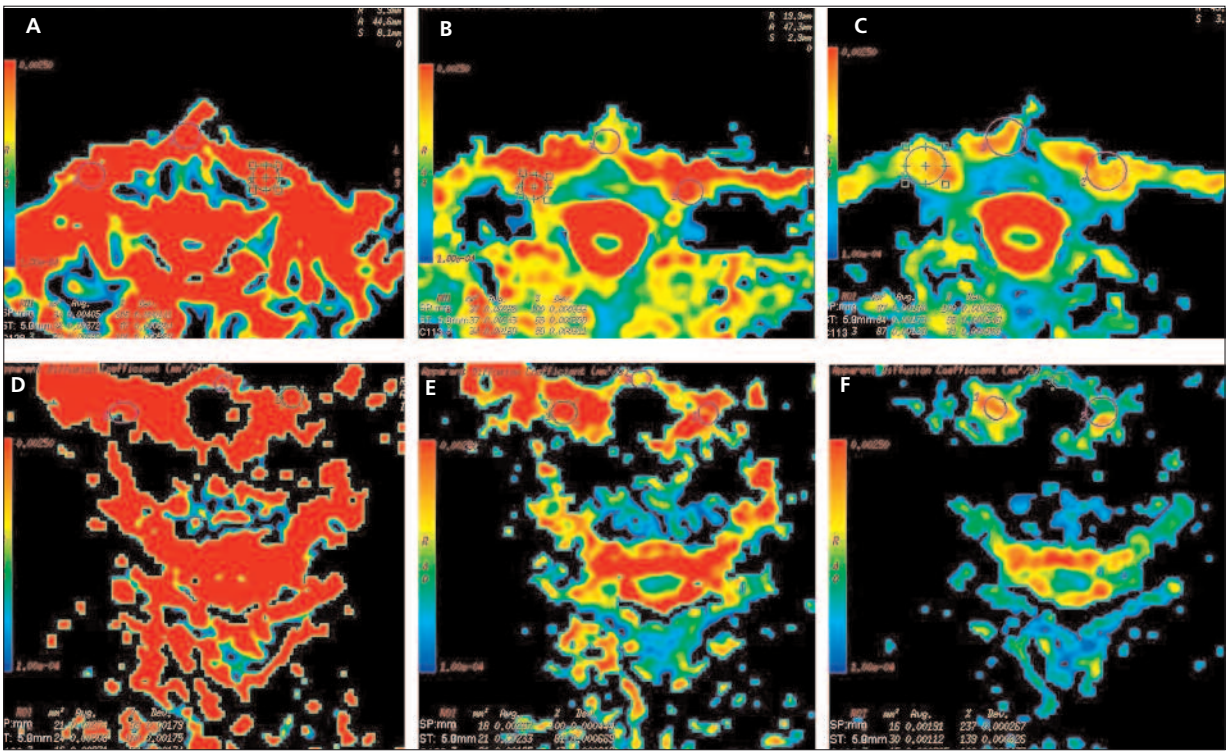

Figure 1. ***A-B,*** 12-year-old woman with Graves' disease. Color ADC maps using b-100, *b*-600 and b-1000 gradient values of the thyroid, respectively. ***D-F,*** 48-year-old woman with Hashimotos' thyroiditis. Color ADC maps (using the same *b* values) on thyroid gland, respectively. The ADC values of GD were higher than HT for all *b* values.

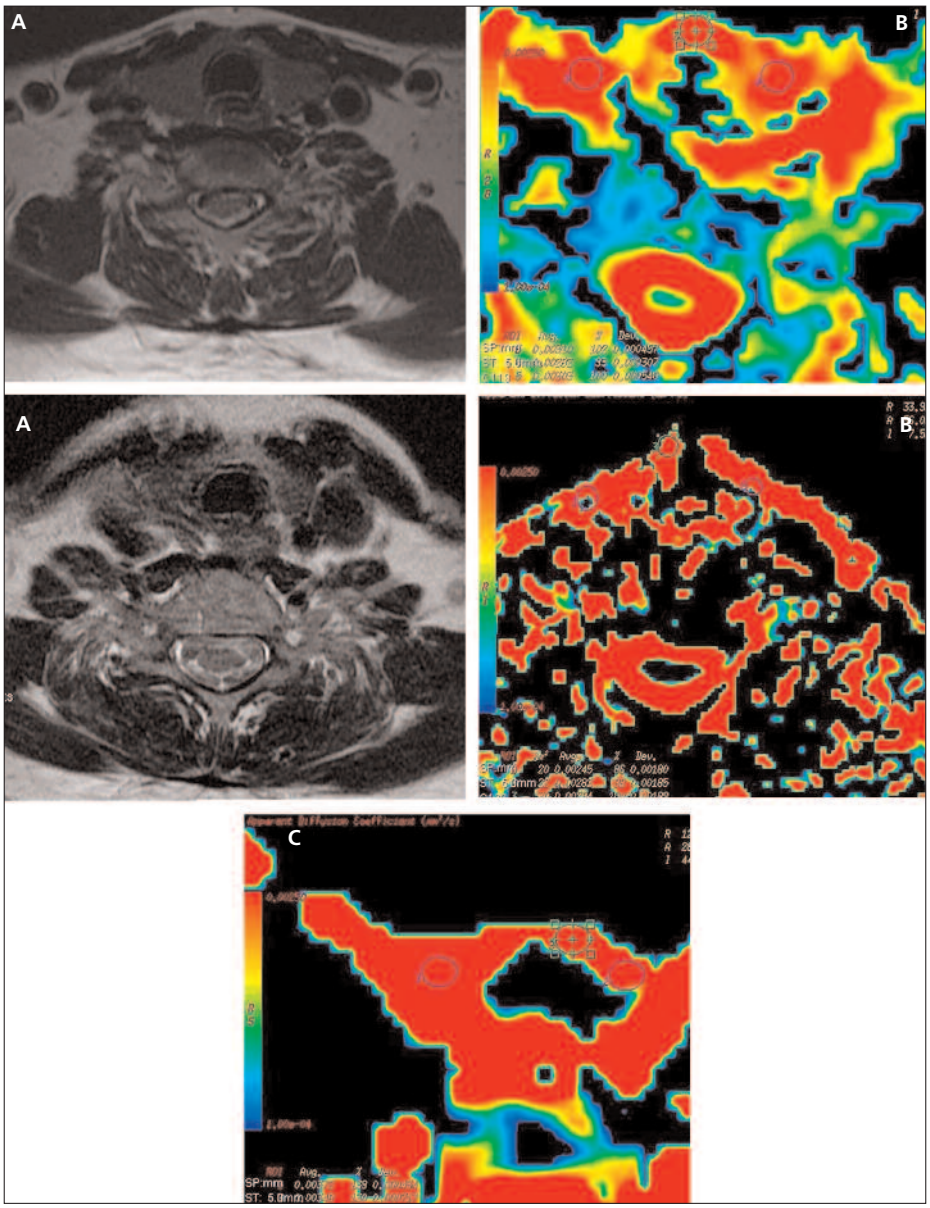

Figure 2. ***A-B,*** 47-year-old woman with Graves' disease. ***A,*** Axial T2 weighted image shows no abnormal signal intensity on thyroid gland. ***B,*** Color ADC map shows ADC values of GD using *b*-100. ***C-D,*** 57-year-old woman with Hashimotos' thyroiditis. ***C,*** Axial T2 weighted image. ***D,*** ADC values of HT using *b*-100. ***E,*** ADC values in parts of the thyroid using *b*-100. ADC value of HT was lower than GD and healthy subject.

Discussion

Graves' disease and HT are autoimmune diseases of the thyroid, and they affect prominently thyroid function. The symptoms of GD include palpitation, muscle fatigue, finger tremor and hyperthyroidism[10]. HT is characterized by easy fatigability and hypothyroidism[11]. HT is the most common cause of hypothyroidism. A subclinical disease range rate of HT is from 0.9% to 5.2% in adult females[12]. At present, in addition to a medical examination of clinical symptoms, GD and HT are diagnosed by the presence of blood serum thyroid hormones, such as fT3, fT4 and serum auto antibodies. The levels of fT4 and fT3 are increased in GD, but decreased in HT[13,14].

DWMRI characterizes tissue on the basis of differences in tissue water mobility. The motion of tissue water molecules (so-called Brownian motion) is not entirely free, because of the pres-

ence of cellular membranes and macromolecules[15]. The ADC is used as a measurement of diffusion in biologic systems because the measured diffusion coefficient may depend on factors other than Brownian water motion, such as perfusion[16]. When only high *b* values are applied, the ADC value approximates the true diffusion; low *b* values are influenced by both perfusion and diffusion[17]. Tissue changes such as edema[18], inflammation and necrosis are expected to have low cellularity and high ADC values. Contrary to this, malignant tumors have high cellularity and have low ADC values[19].

To evaluate thyroid diseases, serologic examination, US and radionuclide scintigraphy are usually performed[1,6]. Scintigraphy is a useful technique for diagnosis of thyroid gland function. However, the patients are at risk for radiation exposure with using this technique. There are little studies in medical literature related thyroid diseases using MRI and DWMRI. Razek et al[20], evaluated ADC values of thyroid nodules using different b values. They observed ADC values of malignant nodules were lower than benign ones. In another study[21], we evaluated the diagnostic role of DWMRI in differentiation between malignant and benign thyroid nodules. We concluded that DWMRI may be helpful in differentiating malignant and benign thyroid nodules.

Tezuka et al[22] evaluate the usefulness of DWI for assessing the thyroid function and confirm the clinical use of MRI for thyroid diseases. 24 patients with GD, 5 patients subacute thyroiditis and 5 patients with HT were included in this study. They used following *b* values; 0.01, 128.01 and 288.02. They found ADC values of GD were significantly higher than the other groups similar to our study. They concluded DWI may be of value for the diagnosis of thyroid diseases. Distinctively to this study, we also used high *b* values. We found there were significant differences between ADC values of the GD and HT for all *b* values. ADC values of GD were higher than ADC values of normal subjects and HT. Histopathological examinations of HT reveals, high cellularitity, increased of connective tissue and decreased amount of interstitial fluid[23]. These alterations may be contributed to decrease of ADC values. But, the GD has hyperplasia of the thyroid tissue. There are increased follicles cells and interstitial fluids[23]. Also, increased blood flow and vascularity is seen at the GD. So, increased perfusion and diffusion may be cause of high ADC values. Abdel Razek et al[24] assessed the activity and clinical course of GD with DWMRI. 51 patients with GD and 25 volunteers underwent DWMRI using *b*-factor of 0, 300 and 600. Patients with GD included untreated patients, patients under antithyroid drugs and patients in relaps. They found significant difference in the ADC value of the patients with active disease and remission. They concluded DWI can be used to assess the activity and predict the outcome of patients during and after medical treatment.

In patients with GD, after 10-15 years discontinuation of antithyroid treatment or following the subtotal thyroidectomy; about 15-20% had been reported to develop spontaneous hypothyroidism due to HT. The pathogenesis of HT in patients with GD has not been confirmed. The association between GD and HT has been controversial. At the beginning, they were accepted as two different diseases. Most authors assume that HT as part of GD since both diseases occur concurrently. Recent view considers that both diseases illustrate of the same coin[25,26].

Conclusions

DWI may be useful in differentiation between Graves' disease and Hashimoto's thyroiditis. After serologic examination, radionuclide scintigraphy may usually be preferred as diagnostic modality of GD and HT. However, it is an invasive modality for diagnosis of these diseases. The most prominent advantages of DWMRI are absence of radiation, no necessity for of intravenous contrast material, very quick technique and quantitative information of tissue provided by ADC measurement. We suggest that DWMRI may be a diagnostic modality in GD and HT especially in cases with diagnostic difficulty due to laboratory and clinical findings. Sensitivity and specificity with using low *b* value is higher than using high *b* values. We also suggest low *b* values for differentiation between GD and HT since *b*-100 value seems to be more useful than the others due to high sensitivity and specificity values.

This study was presented as an oral presentation with the number of S403A in Congress of RSNA 2010, Chicago, IL, USA.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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