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Clinical Diagnostic Potentials of Thyroid Ultrasonography and Scintigraphy: an Evaluation

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Abstract. This prospective study was designed to evaluate the potential contributions of high resolution ultrasonography (US) and Tc-99m scintigraphy in the routine diagnosis of thyroid disease. The diagnostic impacts of US and Tc-99m scintigraphy results in 177 patients visiting our thyroid clinic were assessed and scored according to the following criteria: when the information provided by either test supported, confirmed or changed the initial clinical diagnosis, they received scores of 2, 3 and 4 respectively, while score 1 was given when the test itself was useless for the differential diagnosis. US identified focal lesions that both palpation and scintigraphy had failed to detect in 14 (12.1%) of 116 patients with diffuse thyroid diseases, suggesting the necessity of routine US examinations in such patients. US scored higher than scintigraphy in the diagnosis of Hashimoto's thyroiditis, adenoma, adenocarcinoma and adenomatous goiter, and vice versa in the diagnosis of hyperthyroid and euthyroid Graves' diseases. Thus, the advantages of US over scintigraphy for morphological evaluation were confirmed. US was particularly useful for the differential diagnosis of adenomatous goiter from Hashimoto's thyroiditis or a single nodular disease. In contrast, scintigraphy gave functional images, being especially helpful for the differential diagnosis of thyrotoxicosis.

Key words: Thyroid disease, High resolution ultrasonography, Tc-99m scintigraphy.

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RESEARCH in radiology is usually conducted on the basis of pathological diagnosis. Most of the radiological studies on thyroid disease have thus focused on the relationship between the radiological appearance and histological findings rather than on the relationship between the radiological appearance and clinical features. Most patients in a typical thyroid clinic are not provided with definite pathological diagnoses, because they, especially those with diffuse thyroid disease, are diagnosed and observed only on the basis of clinical presentation and refined laboratory analyses. In most hospitals including ours, histological examination is performed only when a malignant tumor is suspected. This prospective study was designed to evaluate the relative potential contributions of the routine use of US and scintigraphy in a typical thyroid clinic.

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Methods

In our clinic, patient history taking, physical examination, Tc-99m thyroid scintigraphy, and US can be completed in the course of a half day. The subjects in this study included 150 consecutive patients (23 males, 127 females) on whom both scintigraphy and US were performed between November 1987 and May 1988, and an additional 27 patients (4 with euthyroid Graves' disease, 7 with simple goiter, 3 with subacute thyroiditis, 6

with adenocarcinoma and 7 with adenomatous goiter) who were similarly examined between June and December 1988. US was performed with an electronic linear array real-time scanner and 7.5 MHz transducer (YOKOGAWA RT 2600 and 2800) and either direct contact scanning or a water-bath technique. For scintigraphy, a single anterior image was routinely taken with a Gamma-view F camera (HITACHI) 30 min after intravenous injection of 148 MBq Tc-99m pertechnetate. Oblique images, which are known to be useful in detecting multiple nodules [1], were not taken as a routine scan in our clinic because of time limitations. The normal range of uptake values was 0.4–3.0% [2]. Triiodothyronine (T_3) suppression tests were performed in all patients suspected of having euthyroid Graves' disease. Results were judged positive when Tc-99m thyroid uptake after a 7-day administration of T_3 (75 μg) was less than half the preadministration values and less than 1.0% [2].

Initial clinical diagnoses were made by three (K.K., K.E., J. K.) of the authors, each of whom had had over 10 years' experience in thyroid work, on the basis of history, physical examination including palpation, and laboratory data such as serum thyroxine (T_4), T_3, free T_4, free T_3, TSH concentrations, and titers of antibodies to thyroglobulin (Tg) and microsomes (M). The diagnosis of each disease was based on the following findings: Hashimoto's thyroiditis: diffuse goiter, euthyroidism or hypothyroidism and positive anti-Tg and/or anti-M antibody titers; Graves' disease: diffuse goiter and thyrotoxicosis; euthyroid Graves' disease: euthyroidism and Graves' ophthalmopathy; simple goiter: diffuse goiter, euthyroidism and negative anti-Tg and anti-M titers; subacute thyroiditis: thyrotoxicosis, painful enlargement of the thyroid and/or fever; adenoma: presence of a solitary nodule; adenocarcinoma: presence or bulky tumor fixed to the adjacent structures and/or regional lymphnode swelling; adenomatous goiter: multinodular enlargement of both lobes.

Table 1 shows the number of patients with various initial clinical diagnoses. No patient was diagnosed as having silent thyroiditis, because of a rather low incidence of this disorder in thyrotoxic patients and no typical signs such as subsiding thyrotoxicosis and a low T_3/T_4 ratio [3]. The US and scintigraphy images were interpreted by four

Table 1. Initial clinical diagnoses & scores determined according to the impacts of US & scintigram results in 177 patients with various thyroid diseases

Initial clinical diagnosis	Score	Number of patients classified by US	Number of patients classified by scintigram
Hashimoto's thyroiditis	1	0	0
	2	42	55
	3	8	0
	4	5	0
	total	55	55
Graves' disease	1	0	0
	2	32	4
	3	0	27
	4	0	1
	total	32	32
euthyroid Graves' disease	1	0	0
	2	11	7
	3	0	4
	4	0	0
	total	11	11
simple goiter	1	0	0
	2	18	18
	3	0	0
	4	0	0
	total	18	18
subacute thyroiditis	1	0	0
	2	1	0
	3	6	7
	4	0	0
	total	7	7
adenoma	1	0	4[a]
	2	11	21[b]
	3	7	0
	4	7	0
	total	25	25
adenocarcinoma	1	0	3[c]
	2	3	15[d]
	3	12	0
	4	3	0
	total	18	18
adenomatous goiter	1	0	0
	2	0	11
	3	6	0
	4	5	0
	total	11	11
	Total	177	177

[a], Two patients were scored 2, 1 was scored 3, and 1 was scored 4 by US. [b], Nine patients were scored 2, 6 were scored 3, and 6 were scored 4 by US. [c], Two patients were scored 2 and 1 was scored 4 by US. [d], One patient was scored 2, 12 were scored 3, and 2 were scored 4 by US.

of the authors (T. T., H.H., K.K., Y.I.), all of whom already knew the initial clinical diagnosis. The impact of US and scintigraphy results was then assessed in comparison with the initial diagnosis and scored on a scale of one to four according to the following criteria:
Score 1: The examination neither provided any information nor helped with the diagnosis.
Score 2: The findings were compatible with the initial diagnosis, but not diagnostic.
Score 3: The findings were diagnostic, or the probability of the diagnosis was substantially increased.
Score 4: The diagnosis was changed or the high possibility of another clinical diagnosis was proposed.

When incidental findings were obtained that were significant but not inconsistent with the initial diagnosis, these were scored separately as "additional findings". Typical US and scintigraphic findings which convinced us of classifying as score 3 are demonstrated in Table 2 [4–15].

Fine needle aspiration biopsy (FNAB) was performed with a 21-gauge needle, which was inserted into the palpable nodule. Negative pressure was applied by withdrawing the plunger, maintaining the position for a few seconds, releasing, and then withdrawing the needle. In some patients, large needle biopsy was performed according to the Silverman needle procedure.

Results

Among the US results for 55 patients with an initial diagnosis of Hashimoto's thyroiditis, 8 (14.5%) scored 3, and 42 (76.4%) scored 2 upon showing diffuse goiter compatible with but not typical of Hashimoto's thyroiditis [4–10]. Five patients (9.1%) scored 4, exhibiting multiple nodules on US images, and were consequently diagnosed as having adenomatous goiter (Table 3) [4, 5, 16].

When scintigraphy results were evaluated, all patients with Hashimoto's thyroiditis were scored 2, because of the wide variety of scan patterns possible, including increased, normal, decreased, and even absent trapping, as well as homogeneous and heterogeneous radionucleid distribution occasionally in the presence of hot or cold areas [17].

The US results for all 32 patients with hyperthyroid Graves' disease were scored 2 because of the lack of findings typical of Graves' disease in the published literature. Scintigraphic findings, on the

Table 2. Typical US and scintigraphic findings in score 3 in various thyroid diseases

Clinical diagnosis	US or scintigram	findings
Hashimoto's thyroiditis	US	diffuse hypoechogenicity
Graves' disease	scintigram	high uptake
euthyroid Graves' disease	scintigram	T_3-nonsuppressible uptake
subacute thyroiditis	US	ill-defined hypoechoic area(s)
	scintigram	markedly decreased uptake
adenoma	US	a well-defined and homogeneous focal lesion accompanied by a complete hypoechoic marginal zone
adenocarcinoma	US	an ill-defined hypoechoic lesion with fine calcification and marginal irregularity and/or extrathyroidal extension
adenomatous goiter	US	asymmetrically enlarged diffuse goiter with multiple nodules, cystic degeneration and coarse calcification
	scintigram	presence of hot, warm and/or cold area(s)

Table 3. Twenty-three patients in which initial diagnoses were changed after US, scintigraphy and/or pathological examination

Initial clinical diagnosis	Final diagnosis	Number of patients	Score by US	Score by Scintigram
Hashimoto's thyroiditis	adenomatous goiter	5	4	2
Graves' disease	silent thyroiditis	1	2	4
adenoma	adenomatous goiter	4	4	2
adenoma	extrathyroidal cyst	1	4	1
adenocarcinoma	adenoma	1	2	1
adenocarcinoma	adenoma	3	3	2
adenocarcinoma	adenomatous goiter	3	4	1 or 2
adenomatous goiter	Hashimoto's thyroiditis	1	4	2
adenomatous goiter	adenocarcinoma	4	4	2
	Total	23		

Table 4. Number of patients with additional findings in diffuse thyroid diseases

Initial clinical diagnosis	Number of patients	Number of patients with additional findings (%)	
Hashimoto's thyroiditis	55	solid nodule	4(7.2%)
		cystic lesion	2(3.6%)
		extrathyroidal cystic lesion	2(3.6%)
		calcification	1(1.8%)
Graves' disease	32	solid nodule	1(3.1%)
euthyroid Graves' disease	11	solid nodule	1(14.3%)
simple goiter	18	cystic lesion	3(16.7%)
Total	116		14(12.1%)

other hand, were scored 3 for 27 patients (84.4%), and otherwise were scored 2. The result for one patient with typical thyrotoxicosis was scored 4 because she was diagnosed as having silent thyroiditis due to a complete lack of trapping of Tc-99m in the thyroid (Table 3) [18, 19].

The US findings for all 11 patients with euthyroid ophthalmic Graves' disease were scored 2. With regard to scintigraphic findings, 4 results (36.4%) were scored 3. The results for the remaining 7 patients (63.6%) in whom the uptake was suppressed by T_3 administration were scored 2.

There have been no reports of typical US or scintigraphic findings for simple goiter. The results for all 18 patients with simple goiter were therefore scored 2.

Among 116 cases of diffuse thyroid diseases such as Hashimoto's thyroiditis, Graves' disease, euthyroid Graves' disease and simple goiter, additional findings were obtained by US in 14 cases (12.1%) (Table 4). These focal lesions, which included 6 solid nodules, 7 cystic lesions and 1 calcification, had not been identified either by palpation or scintigraphy. FNAB was performed in all patients with a solid nodule, and the results were class I in 4 patients, II in one and III in one patient by the Papanicolaou classification.

The US and scintigraphy results of 7 and 6, respectively, out of 7 patients with subacute thyroiditis were scored 3.

In 25 patients with an initial clinical diagnosis of adenoma, US findings in 7 patients (28.0%) were scored 3, and in 7 (28.0%), scored 4. Pathological examination with US findings which scored 3 revealed follicular adenoma in 4 cases and class I by the Papanicolaou classification in 3 cases. Among the 7 patients with US results scored as 4, diagnoses were changed to adenomatous goiter because of multinodularity in 4 cases, and to an extrathyroidal cyst in 1 case (Table 3). The remaining 2 patients were suspected of having thyroid cancer but were later found to have pathologically proven benign tumors following FNAB. Nine of 11 patients who scored 2 under-

went FNAB, and all nodules were proven to be pathologically benign.

Among 18 patients diagnosed initially with adenocarcinoma, the US results for 3 (16.7%), 12 (66.6%) and 3 (16.7%) were scored 2, 3 and 4, respectively. Pathological examination revealed malignancy (papillary adenocarcinoma, follicular adenocarcinoma or class V by the Papanicolaou classification) in 9 cases, and benign tumors in 3 of 12 patients which scored 3. In 3 patients with US results which scored 4, diagnoses were changed to adenomatous goiter and were later confirmed pathologically by biopsy. In 3 patients who scored 2, pathological examination was performed, and 2 were found to have malignant lesions and 1 had a benign lesion (Table 3).

Among patients with adenoma or adenocarcinoma no scintigraphy results were scored 3, as there were no findings typical of adenoma or adenocarcinoma [20]. Results were scored 2 when a scintigraphic focal lesion was identified, but, otherwise, results were scored 1. The results for 21 patients with adenoma (84.0%, cold nodules in 16 and hot nodules in 5) and 15 patients with adenocarcinoma (83.3%) were scored 2.

In adenomatous goiter, 6 of 11 patients (54.5%) had score 3 findings. Among the results for the remaining 5 patients (45.5%) who scored 4, thyroid cancer was suspected in 4 patients and later pathologically confirmed (papillary adenocarcinoma in 2, and class IV and V in 2 by the Papanicolaou classification). Another patient had US findings typical of Hashimoto's thyroiditis (Table 3). None were scored 1 or 2. Scintigraphy results revealed uneven trapping in all 11 patients and they were scored 2.

The number of patients with various thyroid diseases diagnosed initially and finally is summarized in Table 5.

Table 5. Number of patients in thyroid diseases diagnosed initially and finally following US, scintigraphy and pathological examination

Thyroid diseases	Number of patients	
	Initial clinical diagnosis	Final diagnosis
Hashimoto's thyroiditis	55	51
Graves' disease	32	31
euthyroid Graves' disease	11	11
simple goiter	18	18
subacute thyroiditis	7	7
adenoma	25	24
adenocarcinoma	18	15
adenomatous goiter	11	18
silent thyroiditis	0	1
extrathyroidal cyst	0	1
Total	177	177

Discussion

In the present study, the results of US and scintigraphy in the diagnosis of thyroid diseases were evaluated by scoring them according to criteria based on comparisons with initial clinical diagnoses. The aim of this study is to evaluate how radiological findings seen in prior studies can contribute to routine diagnosis in a typical thyroid clinic.

Solid nodules or cystic lesions were identified by US as additional findings in a considerable number (14/116, 12.1%) of patients with diffuse thyroid diseases such as Hashimoto's thyroiditis, hyperthyroid Graves' disease, euthyroid Graves' disease, and simple goiter (Table 4). These lesions had not been identified by palpation or scintigraphy. It has been reported that nodules as small as 2–3 mm in diameter can be detected by US with a 10.0 MHz probe [5]. Sensitive detection and a high prevalence (20%) of nodules in healthy populations examined by US has recently been demonstrated [21]. US may play a more important role in detecting nodules in diffuse goiter since such nodules, especially small, soft, and posterior ones, are more easily missed by palpation or scintigraphy. Sokal estimated that thyroid carcinoma occurs about 20 times more commonly in toxic goiters and 4 times more commonly in non-toxic goiters than in normal thyroid glands [22]. Although detection of such focal lesions may not change patient management in most cases, it should definitely indicate biopsy when malignancy is suspected.

It is well known that some patients with Hashimoto's thyroiditis have a firm palpable mass in the thyroid region that can simulate adenoma, cancer, malignant lymphoma, or adenomatous nodules. In the present study, among 55 patients with initially diagnosed Hashimoto's thyroiditis, US examination revealed solid nodules in 4, and

adenomatous goiter in 5 (Tables 3 and 4). In view of the sensitive and accurate detection of focal lesion by US, we would recommend that US examination should be performed routinely in patients not only with focal lesions but also with diffuse thyroid diseases, especially Hashimoto's thyroiditis.

Scintigraphy had advantages over US for functional evaluation (Table 1). Among 32 patients with clinically diagnosed hyperthyroid Graves' disease, 27 (84.4%) had high Tc-99m thyroid uptake (score 3, diagnostic), and one was found to have silent thyroiditis because of absent Tc-99m trapping in the thyroid (Table 3). The major clinical manifestation of silent thyroiditis, thyrotoxicosis, is indistinguishable from that of Graves' disease. The mechanisms, by which thyrotoxicosis develops, however, are different. In Graves' disease, stimulation of the thyroid by TSH receptor antibodies present in the patients' sera is considered responsible for hyperthyroidism as well as the increased uptake of Tc-99m or radioactive iodine [2, 23]. In silent thyroiditis, thyrotoxicosis is caused by destruction of follicular cells followed by the release of active thyroid hormones into the circulation, which explains decreased or absent uptake of Tc-99m [18]. Among 11 patients with euthyroid Graves' disease, 4 displayed T_3 nonsuppressible Tc-99m thyroid uptake (score 3), possibly attributable to the stimulatory effects of TSH receptor antibodies detected in most patients [11, 12]. US, on the other hand, could only support the clinical diagnosis (score 2) for both hyperthyroid and euthyroid Graves' diseases.

In subacute thyroiditis, both tests were equally useful diagnostically. Decreased or absent Tc-99m trapping can be explained by the decreased activity of follicular cells due to inflammation, lymphokines produced in the thyroid subsequent to inflammation [24], or reduced levels of serum TSH following destruction-induced thyrotoxicosis. Ill-defined hypoechogenicity in the inflammed area has also been well documented [14, 15] and is considered a characteristic finding in this disorder.

US gave more detailed morphological information than scintigraphy. In adenoma, cancer and adenomatous goiter, US scored higher than did scintigraphy (Table 1). With regard to the differentiation of malignant from benign lesions, US appears superior to scintigraphy. The US and histological diagnoses agreed in all 7 cases of benign adenoma in the present study. However, according to Propper *et al.*, 2 of 10 lesions demonstrating the halo sign (hypoechoic marginal zone) proved to be carcinomas [25]. On the other hand, 5 of 18 patients diagnosed as having cancer by US (2/2, 3/12 and 0/4 with initial diagnoses of adenoma, cancer and adenomatous goiter, respectively) were eventually found to have only benign adenoma. Thus, the overall value of US in this instance would appear limited, and histological examination still seems required [26].

US is apparently useful in detecting multinodularity, and thus can play a major role in the diagnosis of adenomatous goiter. Among 11 patients with initially diagnosed adenomatous goiter, 6 (54.5%) showed typical US findings (score 3), 4 were suspected of having cancer, and 1 was suspected of having Hashimoto's thyroiditis. The final US diagnosis of adenomatous goiter was obtained in 9.1% (5/55), 16.0% (4/25) and 16.7% (3/18) of patients initially diagnosed as having Hashimoto's thyroiditis, adenoma, and cancer, respectively (Table 3). In accordance with this result, Solbiati *et al.* reported that approximately 20–25% of lesions thought to be solitary in radionucleid studies were found to be multinodular by US [27]. These results indicate the usefulness of US for the differential diagnosis of adenomatous goiter from Hashimoto's thyroiditis, adenoma and cancer, although the possible diagnosis of thyroid cancer superimposed on adenomatous goiter cannot be ruled out.

In summary, US seems to be more useful than scintigraphy for morphological evaluation of thyroid disease as it can detect focal lesions in diffuse goiter, even those unidentified by either scintigraphy or palpation, and it is helpful for the qualitative diagnosis of nodular lesions. For functional evaluation, on the other hand, scintigraphy is more useful, especially in the differential diagnosis of thyrotoxicosis.

The higher incidence of endemic goiter, toxic nodular goiter and Plummer's disease, and the lower incidence of Hashimoto's thyroiditis in Central Europe, an iodine deficient area, compared with non-endemic regions including Japan, have been reported [28]. Thus, there is a considerable difference between Japanese and Western populations in clinical presentations. Nevertheless, we hope the present study will give some clue to

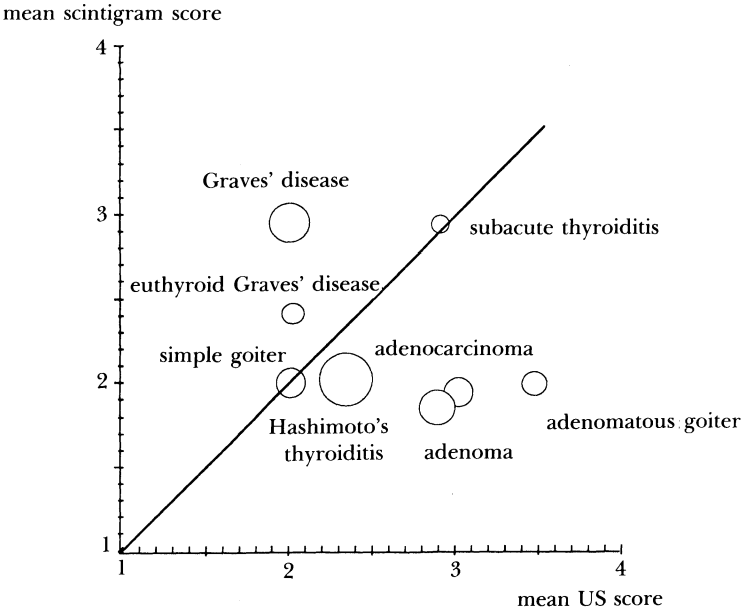

Fig. 1. The mean scores of US and scintigraphy results in thyroid diseases. —Which should be performed in each thyroid disease? The circles size is proportional to the number of patients with each thyroid disease.

thyroidologists and radiologists throughout the world as to whether US, scintigraphy, or both should be performed as screening tests in each of the clinically diagnosed thyroid diseases (Fig. 1).

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