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Ultrasound-guided thyroid nodule fine-needle biopsies — comparison of sample adequacy with different sampling techniques, different needle sizes, and with/without onsite cytological analysis

Biopsje cienkoigłowe guzków tarczycy pod kontrolą USG — porównanie wydajności próbki za pomocą różnych technik pobierania próbek, rozmiarów igieł, z/bez analizy cytologicznej na miejscu

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Abstract

Introduction: The aim of this study was to compare the diagnostic adequacy of thyroid samples obtained by aspiration or capillary biopsy techniques, with 22 or 27 gauge needles, and with or without onsite cytological analysis (OCA).

Material and methods: Four hundred patients with thyroid nodules underwent ultrasound (US)-guided fine-needle biopsies. Patients were divided into eight groups according to needle size (22 *vs.* 27 gauge), biopsy technique (aspiration *vs.* capillary), and whether or not OCA was performed. Sample adequacy rates were calculated for each group and subgroups and compared using chi-square tests.

Results: When all nodes were evaluated (n = 400), the adequacy rate was significantly greater with the capillary than with the aspiration technique (97% vs. 91.5%, p = 0.032) and when OCA was than was not performed (97% vs. 91.5%, p = 0.032). When only solid nodules were evaluated (n = 205) the adequacy rate was also significantly greater with the capillary than with the aspiration technique (98.9% vs. 89.7%, p = 0.008) and when OCA was than was not performed (97.9% vs. 89.6%, p = 0.014). In contrast, the adequacy rate was similar for 22 and 27 gauge needles (94.2% vs. 93.1%, p = 0.733).

Conclusions: Optimal results were obtained with the capillary technique and OCA. The capillary technique and OCA should be the preferred approach in thyroid nodule biopsy, optimising adequacy rates and patient comfort. **(Endokrynol Pol 2015; 66 (4): 295–300)**

Key words: *thyroid nodule; biopsy technique; needle size*

Streszczenie

Wstęp: Celem niniejszego badania było porównanie diagnostycznej wydajności próbek guzków tarczycy otrzymanych metodą biopsji aspiracyjnej lub kapilarnej, wykonanej za pomocą igieł nr 22 lub nr 27 z lub bez analizy cytologicznej przeprowadzonej na miejscu.

Materiały i metody: Czterystu pacjentów z guzkami tarczycy poddano biopsji cienkoigłowej pod kontrolą USG. Pacjentów podzielono na osiem grup, według wielkości zastosowanych igieł (nr 22 *vs.* nr 27), techniki biopsji (aspiracyjnej kontra kapilarnej), a także przeprowadzonej lub nie analizy cytologicznej na miejscu. Wskaźniki wydajności próbek obliczono dla każdej grupy i podgrupy oraz porównano je za pomocą testu chi-kwadrat.

Wyniki: W grupie wszystkich ocenianych guzków (n = 400), wskaźnik wydajności był znacznie wyższy w grupie badanej techniką kapilarną niż w grupie badanej metodą aspiracyjną (97% *vs.* 91,5%, p = 0,032). Wskaźnik wydajności był również wyższy, gdy przeprowadzono analizę cytologiczną na miejscu niż gdy jej nie przeprowadzono (97% *vs.* 91,5%, p = 0,032). Wśród guzków litych (n = 205), wskaźnik wydajności również osiągnął wyższą wartość w grupie badanej techniką kapilarną względem grupy badanej techniką aspiracyjną (98,9% *vs.* 89,7%, p = 0,008), oraz gdy przeprowadzono analizę cytologiczną na miejscu (97,9% *vs.* 89,6%, p = 0,014). Inaczej niż dla powyższych wyników, wskaźnik wydajności był podobny dla igieł nr 22 i nr 27 (94,2% *vs.* 93,1%, p = 0,733).

Wnioski: Wyniki optymalne uzyskano techniką kapilarną oraz wykonując analizę cytologiczną na miejscu. Technika kapilarna oraz analiza cytologiczna na miejscu powinny stanowić preferowane podejście w biopsji guzków tarczycy, optymalizując wskaźnik wydajności oraz samopoczucie pacjenta. **(Endokrynol Pol 2015; 66 (4): 295–300)**

Słowa kluczowe: *guzek tarczycy; technika biopsji; rozmiar igły*

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Introduction

Thyroid nodules are among the most common endocrine disorders and are present in 10–70% of adults [1]. Fine-needle aspiration biopsy (FNAB), a minimally invasive and safe procedure usually performed on an outpatient basis, is considered the first-line test in the diagnosis of thyroid nodules as well as in distinguishing benign from malignant thyroid nodules [2, 3]. Ultrasonography (US)-guided FNAB was recently shown to have a sensitivity of 76–98% and a specificity of 71–100% in detecting thyroid cancers [4]. The specimens obtained were cytopathologically classified as benign, lesion (atypia) of undetermined significance, follicular neoplasm, suspicious, malignant, or nondiagnostic [5]. The major limitation of US-guided thyroid FNAB is non-diagnostic aspiration due to specimen inadequacy, which has been reported to occur at rates ranging from 1% to 25% [6–8]. Thyroid nodules can be biopsied by fine-needle aspiration technique (AT) or fine-needle capillary technique (CT). However, there is controversy about whether either technique is superior to the other [9–13]. The size of the needle used for biopsy also affects the accuracy of diagnosis. Although 20–27 gauge (G) needles are usually used for biopsy, few studies to date have compared the adequacy of samples obtained with different sized needles [10, 14–17]. Moreover, on-site evaluation of biopsy samples by a cytopathologist has been reported to increase the success rate of biopsy procedures, reducing the need to repeat the biopsy and decreasing the rate of false negative results [8, 18]. By reducing the number of interventions, on-site cytopathological evaluation may also reduce the risk of patient complications [8, 19].

To the best of our knowledge, no previous study has simultaneously evaluated the effects of different needle sizes, biopsy techniques and the presence of onsite cytopathological analysis (OCA) on biopsy adequacy. This study therefore compared the adequacy of biopsy samples obtained by aspiration or capillary biopsy techniques, using 22G or 27G needles, and with/ /without OCA.

Material and methods

This study enrolled 400 consecutive patients, each with one thyroid nodule, who underwent US-guided fine-needle biopsy. Patients were divided into 8 groups of 50 patients each according to needle size (22 G *vs.* 27 G), sampling technique (aspiration *vs.* capillary), and OCA (performed *vs.* not performed) (Table 1). All biopsy procedures were performed by the same researcher, using a Hitachi EUB 8500 US system and a 10 MHz linear probe. All patients provided written informed consent, and the study protocol was approved by the Local Ethics Board.

The patient was placed in the supine position with the neck slightly extended. The dimensions, location, depth, and vascularity of each nodule were evaluated, as was its relationships with neighbouring structures such as the carotid artery. Nodule vascularity was evaluated by colour Doppler sonography and classified as type 1 (no vascularity), type 2 (peripheral vascularity alone), type 3 (peripheral and minimal central vascularity), or type 4 (prominent central vascularity) [20]. The neck was cleaned with povidone-iodine solution. Coagulation screening was routinely performed. The patients were instructed not to swallow during the needle insertion and aspiration. The biopsy needles and techniques for each patient were selected sequentially, independent of the sonographic characteristics of the nodules.

After localisation of the nodule, a biopsy specimen was acquired by the aspiration or capillary method, independent of the sonographic characteristics of the nodules. The aspiration method utilised a freehand biopsy technique. The needle was attached to a 10-mL syringe and inserted obliquely into the nodule parallel to the scanning plane. Once the needle tip was visualised inside the nodule, material was aspirated with a to-and-fro motion and smeared onto glass slides. In the capillary method, once the needle tip was visualised inside the nodule the syringe was detached and the needle advanced using a to-and-fro motion within the nodule while being rotated on its axis until blood was seen in the hub of the needle. Biopsy materials of each group of patients were air-dried. Slides of patients in Group I through IV (OCA negative groups) were sent to the pathology laboratory for cytopathological evaluation. In those groups, at least two needle passes were planned, although the number of needle passes was affected by the amount of material obtained, patient cooperation, and patient comfort. Half of the slides obtained from patients in Group V–VIII (OCA positive groups) were sent to the pathology lab, while the other half was stained with May-Grunwald Giemsa quick stain and evaluated onsite for material adequacy by an experienced cytopathologist. Adequacy was defined as six or eight groups of well-preserved follicular cells with 10 or more cells per group. Needle passes were repeated until material adequate for two glass slides was obtained, with a minimum of two needle passes. The cytopathologist evaluating the aspirates informed the researcher directly about 'acceptance' of any given slide as a diagnostic one by on-site assessment. This enabled evaluation of whether on-cite cytological assessment reduced the number of interventions. For partial cystic nodules, biopsies were taken from the solid parts. Pure

Table I. *Description and sample adequacy of the study groups*
Tabela I. *Opis i wydajność próbek grup poddanych badaniu*

Group	n	Needle size	Sampling technique	OCA	Sample adequacy*
I	50	22 G	Aspiration	No	44 (88.0%)
II	50	27 G	Aspiration	No	44 (88 .0%)
III	50	22 G	Capillary	No	47 (94.0%)
IV	50	27 G	Capillary	No	48 (96.0%)
V	50	22 G	Aspiration	Yes	48 (96.0%)
VI	50	27 G	Aspiration	Yes	47 (94.0%)
VII	50	22 G	Capillary	Yes	50 (100.0%)
VIII	50	27 G	Capillary	Yes	49 (98.0%)
Overall	400				377 (94.3%)

G — gauge; OCA — on-site cytological analysis; Chi-square test, p = 0.054

cysts were aspirated and emptied; their contents were centrifuged and the pellet was examined for the presence of thyroid cells.

All slides were stained with haematoxylin and eosin for final cytopathological evaluation. All cytology specimens were finally interpreted by the same cytopathologist and were classified as benign, lesion (atypia) of undetermined significance, follicular neoplasm, suspicious, malignant, or nondiagnostic.

Statistical analysis

Categorical variables (sample adequacy, haematoma existence) were compared in sampling methodology sub-groups by using chi-square or Fisher's exact tests whereas continuous variable (needle pass number) was compared in needle size sub-groups with Mann-Whitney U test. Effects of sampling methods to estimate having adequate sample were assessed by univariate evaluation and mutually adjusted logistic regression models. Type 1 error was set to 0.05.

Results

The study population consisted of 400 patients (85.8% female, mean age: 48.1 years; min-max: 17-80 years) with thyroid nodule and who underwent US-guided fine-needle biopsy.

Nodule and biopsy characteristics

Of the 400 nodules, 205 (51.2%) were solid, 185 (46.3%) were partially cystic, and 10 (2.5%) were predominantly or purely cystic.

Nodule diameters ranged from 5 to 46 mm (mean: 16.1 mm) while 23% were larger than 20 mm, 58.5% between 10 and 20 mm, and 18.5% smaller than 10 mm. Study groups (definitions given in Table I) were similar in terms of nodule size (p = 0.227).

OCA sub-groups (used *vs.* not used) and needle size subgroups (22G *vs.* 27G) were similar in terms of nodule sonographic characteristics (p values = 0.679 and 0.438, respectively). However dominantly or pure cystic nodule percentage was higher in the capillary technique subgroup than in the aspiration one (56.0% *vs.* 41.5%, p = 0.008).

None of the patients had a history of thyroid surgery or radioactive iodine therapy. Chronic thyroiditis was reported in 7.3% of the patients, and all patients were euthyroid at the time of thyroid biopsy.

Using OCA significantly reduced the number of needle passes compared to not using it (median pass number 2 *vs.* 3 respectively, p < 0.001).

In terms of complications, 2.5% of patients in whom a 22G needle had been used and 0.0% of patients in whom a 27G needle had been used developed haematoma, respectively. Needle size sub-groups were statistically similar in terms of haematoma incidence (p = 0.061).

Sample adequacy

Adequacy rates of the study groups varied from 88.0% to 100.0%, and no statistically significant difference between groups was found (P = 0.054) (Table I).

Nodule size sub groups (< 10 mm, 10–20 mm, and > 20 mm) were similar in terms of sample adequacy rate (90.5%, 95.7%, and 93.5%, respectively; p = 0.232). The nodular vascularity pattern degree did not affect the sample adequacy rate in either capillary or aspiration technique subgroups (p value = 0.714 and 0.238, respectively).

Univariate analyses revealed that the capillary technique provided a better adequacy rate than aspiration technique (97.0% *vs.* 91.5%, p = 0.032) whereas using OCA was better than not using it (97.0% *vs.* 91.5%, p = 0.032). On the other hand, needle size did not have

Table II. *Adequacy rates of methodology sub-groups*
Tabela II. *Wskaźniki wydajności podgrup metodologicznych*

	Entire group (n = 400)		Solid nodules only (n = 205)	
	Adequacy rate (%)	p*	Adequacy rate (%)	p*
Biopsy technique				
Aspiration	91.5	0.032	89.7	0.008
Capillary	97.0		98.9	
Needle size				
22 gauge	94.5	0.830	94.2	0.733
27 gauge	94.0		93.1	
On-site cytological analysis				
Used	91.5	0.032	97.9	0.014
Not used	97.0		89.6	

*Fisher's exact or chi-square tests

a significant effect on sample adequacy (94.5% *vs.* 94.0%, p = 0.830) (Table II).

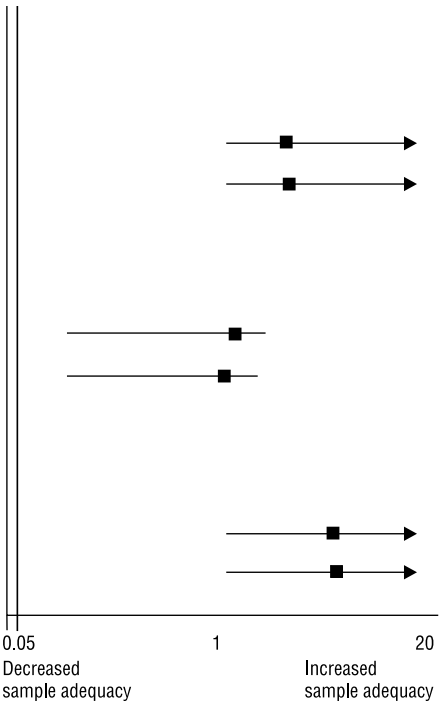
Since nodule sonographic characteristics varied significantly in biopsy technique sub-groups, univariate analysis was repeated to include solid nodules only (n = 205). Similar adequacy rates were obtained for the analysis for solid nodules, per se. The capillary technique provided better adequacy rates than aspiration technique (98.9% *vs.* 89.7%, p = 0.008) whereas using OCA was better than not using it (97.9% *vs.* 89.6%, p = 0.014). On the other hand, needle size had no significant effect on sample adequacy (93.1% *vs.* 94.2%, p = 0.733) (Table II).

Data on univariate and multivariate logistic regression analysis of parameters for sample adequacy rates in solid nodules are presented in Figure 1. Mutually adjusted multivariate logistic regression model for solid nodules (n = 205) revealed that using onsite cytological analysis and using capillary biopsy technique increases the likelihood of having an adequate sample (by 5.81 and 10.28 times, respectively). However, needle size did not significantly affect the likelihood of having an adequate sample (Fig. 1).

Discussion

Thyroid nodules can be biopsied by fine needle aspiration technique or capillary technique, but there is some controversy about whether either technique is superior to the other [9–13]. Aspiration during biopsy may lead to a number of reactive changes, such as papillary endothelial hyperplasia, haemorrhage, vascular thrombosis and proliferation, fibrosis, cystic transformation,

		OR*	95% CI*	P
Onsite cytological analysis				
Not used	Reference			
Used				
Univariate	5.62	1.21	26.01	0.027
Multivariate	5.81	1.23	27.37	0.026
Needle size				
27 gauge	Reference			
22 gauge				
Univariate	1.22	0.39	3.75	0.733
Multivariate	1.02	0.32	3.30	0.973
Biopsy technique				
Aspiration	Reference			
Capillary				
Univariate	9.94	1.27	77.99	0.029
Multivariate	10.28	1.30	81.47	0.027



*95% CI — lower and upper boundaries of 95% confidence interval of odds ratio; OR — odds ratio

Figure 1. *Odds ratios of selected parameters for sample adequacy rates in solid nodules (results of univariate and multivariate logistic regression) (n = 205)*

Rycina 1. *Ilorazy szans wybranych parametrów dla wskaźnika wydajności próbki w guzkach litych (wyniki jednoczynnikowej i wieloczynnikowej regresji logistycznej) (n = 205)*

and infarction [18]. Trauma-related consequences may be minimised by using a fine-needle biopsy procedure without aspiration (fine-needle capillary technique). In this method, cells are detached by the cutting edge of the needle and are conducted into the lumen by capillary forces [18]. The absence of the vacuum effect of aspiration results in a significant reduction in trauma to the nodule and surrounding thyroid tissues and thus reduces blood contamination and yields higher quality material [18, 21]. The capillary technique is therefore recommended, especially for nodules found to be highly vascular on colour Doppler imaging [4, 10, 11]. However, no previous study has investigated the effects of nodular vascularity patterns on the adequacy rates of the capillary technique, and few studies have evaluated the effects of capillary technique on diagnostic adequacy. We found that inadequacy rates were significantly lower with the capillary than with the aspiration sampling technique. Moreover, adequacy rates with the capillary technique were independent of nodular vascularity. These findings suggest that the capillary technique is an easily applied method that causes less blood contamination and provides higher amounts of cytological material than the aspiration technique.

On-site evaluation of samples by a cytopathologist has been reported to increase biopsy success rates and reduce the rates of biopsy repetition and false-negative results [8, 18]. Data from a retrospective study lasting 10 years revealed that on-site cytopathological evaluation reduced inadequacy rates from 14% to 4% [22]. Another study, however, showed that adequacy rates of US-guided thyroid nodule FNAB were similar with and without immediate cytological assessment; moreover, on-site cytopathological evaluation prolonged the duration of biopsy [19]. On-site cytopathological evaluation can potentially reduce the number of needle passes, thus reducing patient discomfort and risk of complications [8, 19]. We found that inadequacy rates and the median number of needle passes were significantly lower with than without OCA. Thus, our findings seem to indicate that on-site cytopathological evaluation increases adequacy rates and patient comfort, while avoiding repeat biopsies and unnecessary interventions.

It is unclear whether the cellularity of a biopsy specimen correlates with the size of the needle [10, 14–17]. In most studies 20–27G needles are used for thyroid fine needle biopsies [10, 14, 15, 19]. If the lumen of the needle is thinner, sufficient material for diagnosis may not be obtained; whereas, if the needle is thicker, the material obtained may be contaminated with blood, making microscopic evaluation more difficult [4, 10, 14, 17]. Blood contamination is especially prevalent in hypervascular nodules [4]. We found no significant difference in adequacy rates between specimens obtained with 22G and 27G needles, and the needle size did not affect the complication rate.

Inclusion of a large cohort with 400 cases and combined evaluation of biopsy technique, needle size, and on-site cytological analysis along with nodular vascularity pattern in terms of their effects on sample adequacy rate are the major strengths of the present study. The major limitation of the present study is the lack of homogeneity between groups in terms of nodular characteristics. Nevertheless, the large sample size enables us to repeat analysis to include solid nodules, per se (n = 205), after exclusion of dominantly cystic and partially cystic nodules, which also revealed similar findings related to the effects of biopsy technique, needle size, and on-site cytological analysis on adequacy.

Conclusions

In conclusion, this study compared the adequacy of thyroid biopsy samples obtained with different sized needles (22G *vs.* 27G), different sampling techniques (aspiration *vs.* capillary), and with/without onsite cytopathological evaluation. Optimal results were obtained using the capillary sampling technique and onsite cytological evaluation. Adequacy rates and patient comfort may both be optimised by using a capillary sampling technique and onsite cytopathological evaluation.

References

1. Woliński K, Szczepanek-Parulska E, Stangierski A et al. How to select nodules for fine-needle aspiration biopsy in multinodular goitre. Role of conventional ultrasonography and shear wave elastography — a preliminary study. Endokrynol Pol 2014; 65: 114–118.
2. Schoedel KE, Tublin ME, Pealer K et al. Ultrasound-Guided Biopsy of the Thyroid: A Comparison of Technique With Respect to Diagnostic Accuracy. Diagn Cytopathol 2008; 36: 787–89.
3. Rossi M, Buratto M, Bruni S et al. Role of ultrasonographic/clinical profile, cytology, and BRAF V600E mutation evaluation in thyroid nodule screening for malignancy: a prospective study. J Clin Endocrinol Metab. 2012 Jul; 97(7): 2354-61.
4. Kim MJ, Kim EK, Park SI et al. US-guided Fine-Needle Aspiration of Thyroid Nodules: Indications, Techniques, Results. RadioGraphics 2008; 28: 1869–1886.
5. Layfield LJ, Cibas ES, Gharib H et al. Thyroid aspiration cytology: current status. CA Cancer J Clin 2009; 59: 99–110.
6. Mittendorf EA, Tamarkin SW, Mchenry CR. The results of ultrasound-guided fine-needle aspiration biopsy for evaluation of nodular thyroid disease. Surgery 2002; 132: 648–654.
7. Tollin SR, Mery GM, Jelveh N. The Use of Fine-Needle Aspiration Biopsy under Ultrasound Guidance to Assess the Risk of Malignancy in Patients with a Multinodular Goiter. Thyroid 2000; 10: 235–241.
8. Redman R, Zalaznick H, Mazzaferri EL et al. The Impact of Assessing Specimen Adequacy and Number of Needle Passes for Fine-Needle Aspiration Biopsy of Thyroid Nodules. Thyroid 2006; 16: 55–60.
9. de Carvalho GA, Paz-Filho G, Cavalcanti TC, Graf H. Adequacy and diagnostic accuracy of aspiration vs. capillary fine needle thyroid biopsies. Endocr Pathol 2009; 20: 204–208.
10. Degirmenci B, Haktanir A, Albayrak R et al. Sonographically guided fine-needle biopsy of thyroid nodules: the effects of nodule characteristics, sampling technique, and needle size on the adequacy of cytological material. Clin Radiol 2007; 62: 798–803.

11. Tublin ME, Martin JA, Rollin LJ et al. Ultrasound guided fine needle aspiration versus fine needle capillary sampling biopsy of thyroid nodules. Does technique matter? J Ultrasound Med 2007; 26: 1697–1701.
12. Oertel YC. Fine-needle aspiration of the thyroid: technique and terminology. Endocrinol Metab Clin North Am 2007; 36: 737–751.
13. Zhou JQ, Zhang JW, Zhan WW et al. Comparison of fine-needle aspiration and fine-needle capillary sampling of thyroid nodules: a prospective study with emphasis on the influence of nodule size. Cancer Cytopathol 2014; 122: 266–273.
14. Titton RL, Gervais DA, Boland GW et al. Sonography and Sonographically Guided Fine-Needle Aspiration Biopsy of the Thyroid Gland: Indications and Techniques, Pearls and Pitfalls. Am J Roentgenol 2003; 181: 267–271.
15. Rausch P, Nowels K, Jeffrey RB. Ultrasonographically guided thyroid biopsy: a review with emphasis on technique. J Ultrasound Med 2001; 20: 79–85.
16. Hanbidge AE, Arenson AM, Shaw PA et al. Needle size and sample adequacy in ultrasound-guided biopsy of thyroid nodules. Can Assoc Radiol J 1995; 46: 199–201.
17. Tangpricha V, Chen BJ, Swan NC et al. Twenty-One-Gauge Needles Provide More Cellular Samples than Twenty-Five-Gauge Needles in Fine-Needle Aspiration Biopsy of the Thyroid but may not Provide Increased Diagnostic Accuracy. Thyroid 2001; 11: 973–976.
18. Ceresini G, Corcione L, Morganti S et al. Ultrasound-guided fine-needle capillary biopsy of thyroid nodules, coupled with on-site cytologic review, improves results. Thyroid 2004; 14: 385–389.
19. O'Malley ME, Weir MM, Hahn PF et al. US-guided Fine-Needle Aspiration Biopsy of Thyroid Nodules: Adequacy of Cytologic Material and Procedure Time with and without Immediate Cytologic Analysis. Radiology 2002; 222: 383–387.
20. Frates MC, Benson CB, Doubilet PM et al. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules? J Ultrasound Med 2003; 22: 127–131.
21. Zajdela A, Zillhardt P, Voillemot N. Cytological diagnosis by fine-needle sampling without aspiration Cancer 1987; 59: 1201–1205.
22. Stacul F, Bertolotto M, Zappetti R et al. The radiologist and the cytologist in diagnosing thyroid nodules: results of cooperation. Radiol Med 2007; 112: 597–602.