Observational Study

Medicine®

OPEN

The role of histogram analysis of grayscale sonograms to differentiate thyroid nodules identified by ^{18}F-FDG PET-CT

Ko Woon Park, MD[a], Jung Hee Shin, MD, PhD[a,*], Soo Yeon Hahn, MD, PhD[a], Jae-Hun Kim, PhD[a], Yaeji Lim, PhD[b], Joon Young Choi, MD, PhD[c]

Abstract

The role of histogram based on ultrasound (US) images for thyroid nodules found in fluorine-18 fluorodeoxyglucose (18F-FDG) Positron Emission Tomography/Computed Tomography (PET-CT) is unknown. We aimed to assess whether histogram analysis using gray scale US could differentiate thyroid nodules detected by PET-CT.

In this study, 71 thyroid nodules ≥1 cm were identified in 71 patients by conducting 18F-FDG PET-CT, from January 2010 to June 2013. Subsequently, either grayscale US-guided fine needle aspirations or core needle biopsies were performed on each patient. Each grayscale US feature was categorized according to the Korean Thyroid Imaging Reporting and Data System (K-TIRADS). Histogram parameters (skewness, kurtosis, intensity, uniformity, and entropy) were extracted from the grayscale US images followed by statistical analysis using the Chi-Squared or Mann–Whitney *U* tests.

The 71 nodules comprised 30 (42.3%) benign nodules, 30 (42.3%) primary thyroid malignancies, and 11 (15.4%) metastatic lesions. Tumor size, US findings, and histogram parameters were significantly different between the benign and malignant thyroid nodules ($P = .011$, $P = .000$, and $P < .02$, respectively). A comparison showed that parallel orientation and an absence of calcifications were found more frequently in metastatic thyroid nodules than in primary thyroid malignancies ($P = .04$, $P < .000$, respectively). However, histogram parameters and K-TIRADS were not significantly different between primary thyroid malignancies and metastatic lesions.

There is a limit to replacing cytopathological confirmation with texture analysis for the differentiation of thyroid nodules detected by PET-CT. Therefore, cytopathological confirmation of nodules appearing malignant on US images cannot be avoided for an ultimate diagnosis of metastasis.

Abbreviations: 18F-FDG = Fluorine-18 fluorodeoxyglucose, K-TIRADS = Korean Thyroid Imaging Reporting and Data System, PET-CT = Positron Emission Tomography/Computed Tomography, PTCs = papillary thyroid carcinomas, ROI = region of interest, US-FNA = US-guided fine needle aspiration.

Keywords: histogram, metastasis, PET, thyroid nodule, ultrasonography

1. Introduction

Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) is a whole-body imaging technology that is useful for diagnosing metastatic disease in patients with various types of malignancies. The extensive use of ^{18}F-FDG PET/CT leads to an increasing number of discovered thyroid incidentalomas.[1] "Thyroid incidentaloma" with focal or diffuse ^{18}F-FDG uptake in the thyroid gland is a relatively common finding in clinical practice. Whereas diffuse uptake has been widely ascribed to benign conditions such as thyroiditis or Graves disease,[2] focal ^{18}F-FDG uptake in the thyroid gland occurs in 1% to 2% of patients scanned for nonthyroidal causes and is reported to be associated with malignancy in 14% to 81% of those cases.[3–7]

The accuracy of thyroid imaging has improved with the introduction of high-resolution ultrasound (US). Moreover, updated risk stratification systems, including the Korean Thyroid Imaging Reporting and Data System (K-TIRADS), have supported consistent US descriptors and diagnosis of thyroid nodules.[8] However, the interpretation of US findings is still subjective, and diagnoses may vary based on the radiologists level of experience. To overcome the limitations of US, texture analysis

Editor: Ismaheel Lawal.

The authors report no conflicts of interest.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, [b] Department of Applied Statistics, Chung-Ang University, 221, Heukseok-dong, Dongjak-gu, [c] Department of Nuclear Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of.

[*] Correspondence: Jung Hee Shin, Department of Radiology and Center for Imaging Science, Thyroid Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81, Irwon-ro, Gangnam-gu, Seoul 06351, Korea, Republic of (e-mail: jhshin11@skku.edu).

How to cite this article: Park KW, Shin JH, Hahn SY, Kim JH, Lim Y, Choi JY. The role of histogram analysis of grayscale sonograms to differentiate thyroid nodules identified by ^{18}F-FDG PET-CT. Medicine 2020;99:48(e23252).

Received: 15 April 2020 / Received in final form: 3 September 2020 / Accepted: 21 October 2020

http://dx.doi.org/10.1097/MD.0000000000023252

may be performed to quantify spatial variation in gray levels within a specific region of interest (ROI) not visible to the human eye.[9–11]

Few studies have attempted to distinguish primary and metastatic cancer based on histogram analysis of US images of thyroid incidentalomas. However, we expect that this adjunctive, noninvasive method will increasingly enable differentiation of metastatic lesions from primary thyroidal malignancies in thyroid nodules with US image features commonly recognized as malignant in cancer patients with uptake of PET. Notably, this process may be avoided in patients who need to undergo aspiration or biopsy for cytopathologic confirmation. With regarding the perspectives on objective and quantitative approach, texture analysis can helpful if a sufficiently high degree of accuracy comparable to that of gray-scale US can be obtained in differentiating benign, primary thyroid malignancies, and metastatic thyroid nodules. The purpose of this study was to evaluate whether histogram analysis using gray scale sonogram can differentiate benign lesions, primary thyroid malignancies, and non-thyroidal metastatic lesions in thyroid nodules detected by ^{18}F-FDG PET-CT.

2. Methods

2.1. Patient selection

We obtained approval from the institutional review board at our medical center for this retrospective study. All patients provided written informed consent prior to undergoing US-guided fine needle aspiration (US-FNA) or core needle biopsy. In the present study, we retrospectively reviewed patients who had performed thyroid US for further evaluation of focal uptake in ^{18}F-FDG PET-CT at our hospital between January 2010 and June 2013. We assessed 363 nodules detected using ^{18}F-FDG PET-CT, in 351 consecutive patients. The exclusion criteria were as follows:

1. nodule size of <1 cm (n = 251, ROI drawings for small nodules were less accurate[12]), and
2. lack of precise correlation between pathology and US features in patients with multiple nodules (n = 29).

All patients underwent thyroid US after ^{18}F-FDG PET-CT. US-guided FNA or core needle biopsy was performed on all nodules. Finally, 71 nodules in 71 patients (mean age, 54 years: range 37–81 years) were included (Fig. 1).

2.2. Imaging methods and data collection

In our study, a focal thyroid uptake was defined as an area of focally-increased ^{18}F-FDG uptake on a PET image, or as a visible focal lesion in less than 1 lobe on a CT image. Diffuse uptake was defined as ^{18}F-FDG uptake across the entire thyroid gland.[3,13]

B-mode US was performed using an iU22 system (Vision 2010; Philips, Seattle, WA, USA) with a commercially available 7 to 12-MHz linear-array transducer. All scans were obtained by 1 of 7 radiologists with 2 to 12 years of experience in performing and interpreting thyroid US. Transverse and longitudinal images were obtained for each nodule, and some nodules were also subjected to color Doppler US.

Two radiologists with 6 to 12 years of experience in thyroid imaging reviewed the US images independently. The sonographic findings of the thyroid nodules were evaluated in terms of the following features:[8] size, shape (irregular or round-to-ovoid), margin (ill-defined, spiculated/microlobulated, or smooth), orientation (non-parallel or parallel), internal content (solid, predominantly solid or cystic, or cystic), echogenicity (marked hypoechogenicity, mild hypoechogenicity, isoechogenicity, or hyperechogenicity), calcifications(none, microcalcification, macrocalcification, or rim calcification), vascularity on color Doppler image (none, perinodular vascularity, mild intranodular vascularity [vascularity less than 50%], or marked intranodular vascularity [vascularity more than 50%]). Each gray-scale US finding was retrospectively reviewed and categorized according to the K-TIRADS. If 2 readers had a different interpretation of the US features, consensus was achieved by reviewing the images again. The patient clinical information (age, sex, and pathologic findings) was collected from the database. Pathological diagnosis was based on the pathological reports and all pathological slides were interpreted by 1 of 7 pathologists.

The most representative image of the nodule on either the transverse or longitudinal scans, that is, the clearest visible image of the nodule without artifacts, was chosen for the texture analysis. A radiologist drew ROIs on the images along the nodule borders using the Microsoft Windows 7 Paint program (Microsoft Corporation, Redmond, WA, USA), and subsequently, a supervising radiologist reviewed the ROIs. A grayscale histogram analysis of the thyroid nodule sonograms was obtained using in-house software developed with MATLAB R2010a (The MathWorks, Natick, MA, USA). Pixel intensity values were automatically designated from 0 to 255 (0 = black; 255 = white; 256 bins) within the ROIs by the histogram analysis software. The software also automatically obtained 5 histogram parameters from the grayscale images: skewness, kurtosis, intensity, uniformity, and entropy.

Skewness is a scale based on deviation from the mean within a profile indicating the degree of asymmetry of a histogram value. Negative skewness values signify data that are deviated to the left, indicating that the left tail is longer relative to the right tail. Kurtosis is a value indicating peakedness, that is, whether the histogram distribution is concentrated into an average value. Positive kurtosis signifies a peaked distribution, and negative kurtosis indicates a flat distribution. Uniformity indicates the regularity of pixel values (a uniformity of 1 indicates a constant image). Entropy is a textural randomness feature indicating the scale of uncertainty (i.e., a measure of randomness), and is the opposite of uniformity.[14–16]

2.3. Statistical analyses

Based on pathological results, thyroid nodules were classified as benign or malignant. Malignant thyroid nodules were subdivided into primary thyroid malignancies and metastatic thyroid lesions. Categorical variables and differences in histogram parameters were compared across the 3 groups using the Chi-Squared or Mann–Whitney *U* tests. To evaluate the interobserver variability of manually drawn ROIs, 2 radiologists independently drew the ROIs in 10 randomly selected cases. We calculated the Dice coefficient, ranging from 0 (no overlap) to 1 (perfect agreement).

A P value $<.05$ was considered significant. Statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC, USA).

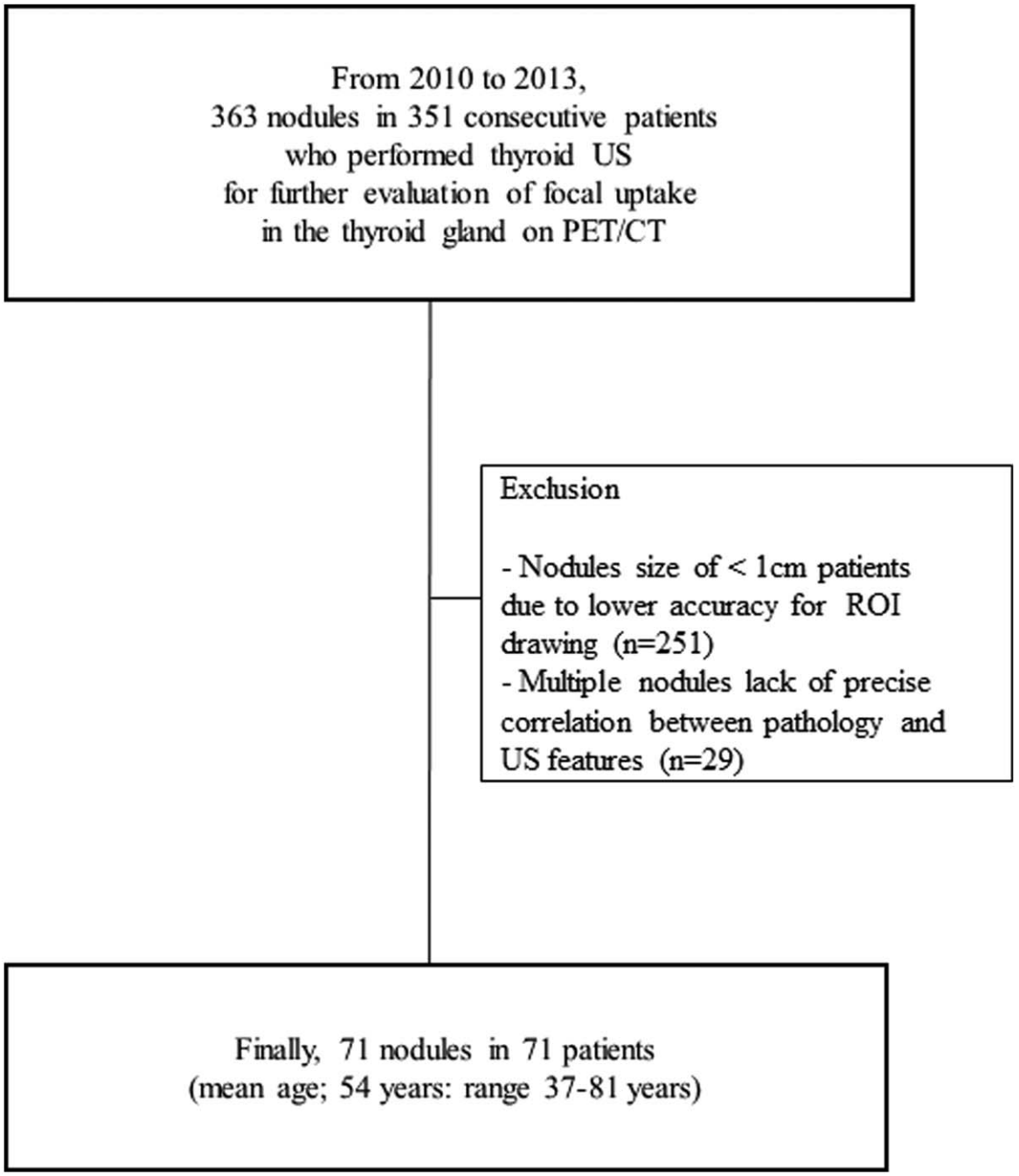

Figure 1. Flow chart of study population.

3. Results

A total of 71 patients, 35 women and 36 men, (mean age ± SD, 61 ± 11.0 years; range, 35–81 years) were included in the study. The 71 nodules included 30 (42.3%) benign lesions, 30 (42.3%) papillary thyroid carcinomas (PTCs), and 11 (15.4%) metastatic cancers from other malignancies (9 lung cancers, 1 breast cancer, and 1 multiple myeloma). Patient ages were not significantly different among the 3 groups (benign group, 60.97 ± 10.52 years; PTC group, 58.6 ± 13.26 years; and metastatic thyroid lesion group, 56 ± 10.94 years; $P = .532$). Tumor sizes were significantly different between the benign and malignant thyroid nodule groups ($P = .011$). The mean nodule size in the benign group was 20.1 ± 8.7 mm and 15.3 ± 5.3 mm in the malignant group. Tumor sizes were not significantly different between the PTC and metastatic thyroid malignancy groups (means, 14.1 ± 3.6 mm and 18.6 ± 7.8 mm, respectively; $P = .09$). The ultrasonographic characteristics of the benign vs malignant groups are shown in Tables 1, 2, and 3. All ultrasonographic findings (shape, margin, orientation, echogenicity, internal content, and calcifications), except vascularity differed between the benign and malignant groups (including PTCs and metastatic nodules) ($P < .05$ in all cases), indicating that K-TIRADS features were significantly different between the 2 groups. The ultrasonographic characteristics of the PTC vs metastatic thyroid nodule groups are shown

Table 1

Comparison of ultrasonographic features between benign and malignant thyroid nodules in patients with PET uptake.

Ultrasonographic findings	Benign nodule (n = 30)	Malignant nodule (n = 41)	*P* value
Internal content			<.001*
Solid	18 (25.35)	40 (56.34)	
Predominantly solid or cystic	12 (16.9)	1 (1.41)	
Cystic	0 (0)	0 (0)	
Echogenicity			<.001*
Marked hypoechoic	3 (4.23)	22 (30.99)	
Mild hypoechoic	8 (11.27)	15 (21.23)	
Isoechoic	19 (26.76)	4 (5.63)	
Hyperechoic	0 (0)	0 (0)	
Margin			<.001*
Spiculated/microlobulated	2 (2.82)	26 (36.62)	
Ill-defined	5 (7.04)	12 (16.9)	
Smooth	23 (32.39)	3 (4.23)	
Orientation			<.001*
Non-parallel	0 (0)	20 (28.17)	
Parallel	30 (42.25)	21 (29.58)	
Shape			<.001*
Irregular	6 (8.45)	37 (52.11)	
Round-to-ovoid	24 (33.8)	4 (5.63)	
Calcification			.01*
None	25 (35.21)	21 (29.58)	
Microcalcification	1 (1.41)	13 (18.31)	
Macrocalcification	2 (2.82)	2 (2.82)	
Rim calcification	2 (2.82)	5 (7.04)	
K-TIRADS			
3 (Low suspicion)	20 (28.17)	2 (2.82)	<.001*
4 (Intermediate suspicion)	7 (9.86)	6 (8.45)	
5 (High suspicion)	3 (4.23)	33 (46.48)	

The numbers in the parentheses are percentages (%).
* *P*-value <.05 was considered statistically significant.
n = number of nodules, K-TRADS = Korean Thyroid Imaging Reporting and Data System.

Table 2

Comparison of ultrasonographic features between papillary thyroid carcinomas (PTCs) and metastatic thyroid nodules in patients with PET uptake.

Ultrasonographic findings	PTC (n = 30)	Metastatic thyroid nodule (n = 11)	*P* value
Internal content			1
Solid	29 (70.73)	11 (26.83)	
Predominantly solid or cystic	1 (2.44)	0 (0)	
Cystic	0 (0)	0 (0)	
Echogenicity			.73
Marked hypoechoic	15 (36.59)	7 (17.07)	
Mild hypoechoic	12 (29.27)	3 (7.32)	
Isoechoic	3 (7.32)	0 (0)	
Hyperechoic	0 (0)	0 (0)	
Margin			.27
Spiculated/microlobulated	20 (48.78)	6 (14.63)	
Ill-defined	7 (17.07)	5 (12.2)	
Smooth	3 (7.32)	0 (0)	
Orientation			.04*
Non-parallel	18 (43.9)	2 (4.88)	
Parallel	12 (29.27)	9 (21.95)	
Shape			.61
Irregular	28 (68.29)	9 (21.95)	
Round-to-ovoid	2 (4.88)	2 (4.88)	
Calcification			<.001*
None	10 (24.39)	11 (26.83)	
Microcalcification	13 (31.71)	0 (0)	
Macrocalcification	5 (12.2)	0 (0)	
Rim calcification	10 (24.39)	0 (0)	
K-TIRADS			
3 (Low suspicion)	1 (2.44)	1 (2.44)	.67
4 (Intermediate suspicion)	4 (9.76)	2 (4.88)	
5 (High suspicion)	25 (60.98)	8 (19.51)	

The numbers in the parentheses are percentages (%).
* *P* value <.05 was considered statistically significant.
n = number of nodules, K-TRADS = Korean Thyroid Imaging Reporting and Data System.

in Table 2. Parallel orientation ($P = .04$) and absence of calcifications ($P < .000$) were found in the metastatic thyroid nodule group more frequently than in the PTC group (Fig. 3).

The histogram parameters are shown in Tables 3 and 4. Of the 5 histogram parameters, skewness (benign group, 0.4 ± 0.49; malignant group, 0.63 ± 0.43; $P = .046$) and intensity (benign group, 28.27 ± 16.78, malignant group, 17.93 ± 14.3; $P = .013$) were significantly different between the benign and malignant thyroid nodules (Fig. 2). However, the histogram parameters and K-TIRADS features were not significantly different between the primary thyroid malignancy and metastatic thyroid lesion groups (Fig. 3).

4. Discussion

Grayscale US has been widely applied as a sensitive diagnostic tool to differentiate benign and malignant thyroid nodules. The diagnostic performance of grayscale US varies based on operator experience and skill, and better performance is attained when experienced operators perform the examinations. To overcome the lack of objectiveness and reproducibility associated with interpretation of grayscale US images, textural analysis providing quantitative and objective information about image patterns was recently introduced to enable differentiation between benign and malignant thyroid nodules.[17] In our study, malignant and benign thyroid nodules with PET uptake were distinguished based on grayscale US image features and histogram parameters (skewness and intensity). These results demonstrate that presumably benign thyroid nodules detected on grayscale US images do not require additional FNA, and diagnostic performance may be improved by performing histogram analysis for confirmation. However, it is also necessary to differentiate metastatic thyroid lesions from primary thyroid malignancy in cancer patients with PET-CT uptake to allow staging. To date, there have been no published studies investigating primary thyroid malignancy and metastatic thyroid lesions using grayscale US image examination. Unfortunately, our results did not show that adding textural analysis to US image evaluation aided differentiation of metastatic thyroid lesions from primary thyroid malignancies. However, the present study did find differences between metastatic thyroid nodules and primary thyroid malignancy in orientation and calcification. Our findings were similar to a previously published study that showed the most common US features in metastatic thyroid nodules were hypoechogenicity, non-circumscribed margins, solid internal composition, lack of calcification, and parallel orientation.[18] Specifically, all metastatic thyroid lesions did not contain microcalcifications representing psammoma bodies observed in primary thyroid malignancies.[19,20]

Various methods for texture analysis have been introduced. In the present study, we chose first-order texture features derived from histograms.[10,15,21] Histogram texture analysis has been

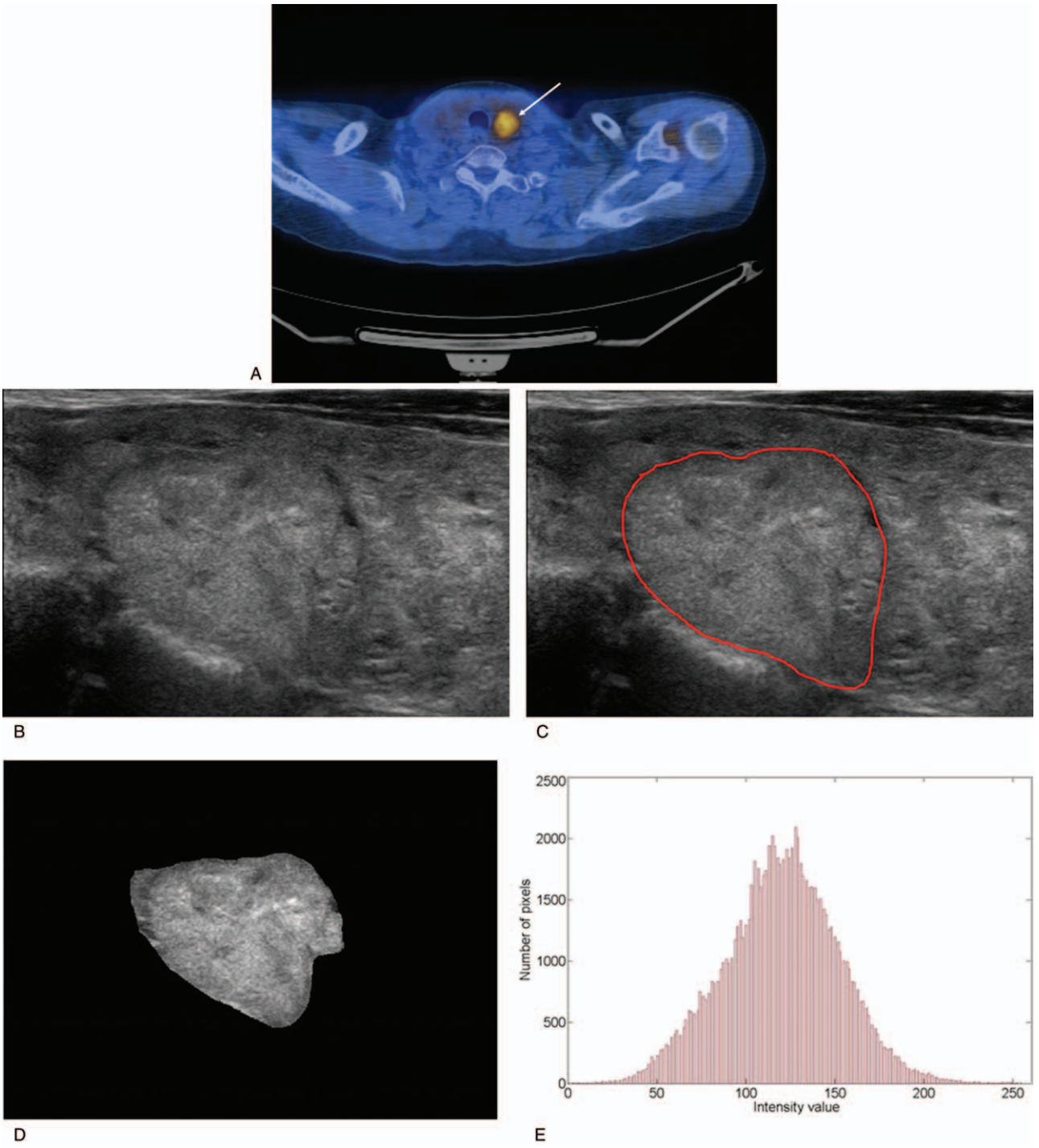

Figure 2. Positron emission tomography/ Computed tomography (PET-CT) and ultrasound (US) image of a benign follicular nodule in a 74-year-old woman. (A) Fusion Fluorine-18 fluorodeoxyglucose (18F-FDG) PET-CT shows an increased FDG uptake in the left thyroid lobe. (B) Longitudinal US image shows a 2.5 cm smooth marginated ovoid isoechoic solid nodule with parallel orientation and no calcification, in the left thyroid lobe. (C) A region of interest (ROI) was drawn on the longitudial US image and extracted (D) and (E) Histogram analysis showed the distribution of pixels (y-axis) according the pixel intensity value (x-axis) in the ROI of the nodule. Histogram parameters were as follows: skewness = -0.035: kurtosis = 3.075: uniformity = 0.014: entropy = 6.366.

applied to US images of various organs to evaluate diagnostic performance.[9,11] However, to our knowledge no studies have investigated the usefulness of texture analysis for differentiating metastatic thyroid cancer from benign nodules or primary thyroid malignancies. In this study, among the 5 histogram-based parameters that were analyzed, skewness, and intensity were significantly different between benign and malignant thyroid nodules with PET uptake. These results reveal that US image grayscales within malignant nodules were more heterogeneous and diverse than those in benign nodules, possibly due to microcalcification of the malignant nodules. Moreover, pixel intensities were significantly higher in benign nodules than in

Table 3

Comparison of histogram parameters between benign and malignant nodules.

Histogram parameters	Benign (n = 30)	Malignant (n = 41)	*P* value
Skewness	0.4 ± 0.49	0.63 ± 0.43	.046*
Kurtosis	3.62 ± 1.33	3.93 ± 1.35	.344
Intensity	28.27 ± 16.78	17.93 ± 14.3	.013*
Uniformity	0.02 ± 0.01	0.02 ± 0.03	.494
Entropy	6.18 ± 0.4	6.14 ± 0.39	.69

n = number of nodules.

Table 4

Comparison of histogram parameters between papillary thyroid carcinomas (PTCs) and metastatic thyroid nodules.

Histogram parameters	PTC (n = 30)	Metastatic thyroid nodule (n = 11)	*P* value
Skewness	0.6 ± 0.46	0.71 ± 0.37	.443
Kurtosis	4.05 ± 1.44	3.59 ± 1.04	.273
Intensity	20.17 ± 13.64	11.82 ± 14.91	.123
Uniformity	0.02 ± 0.03	0.02 ± 0	.458
Entropy	6.16 ± 0.4	6.09 ± 0.37	.575

n, number of nodules.
*P value < .05 was considered statistically significant.

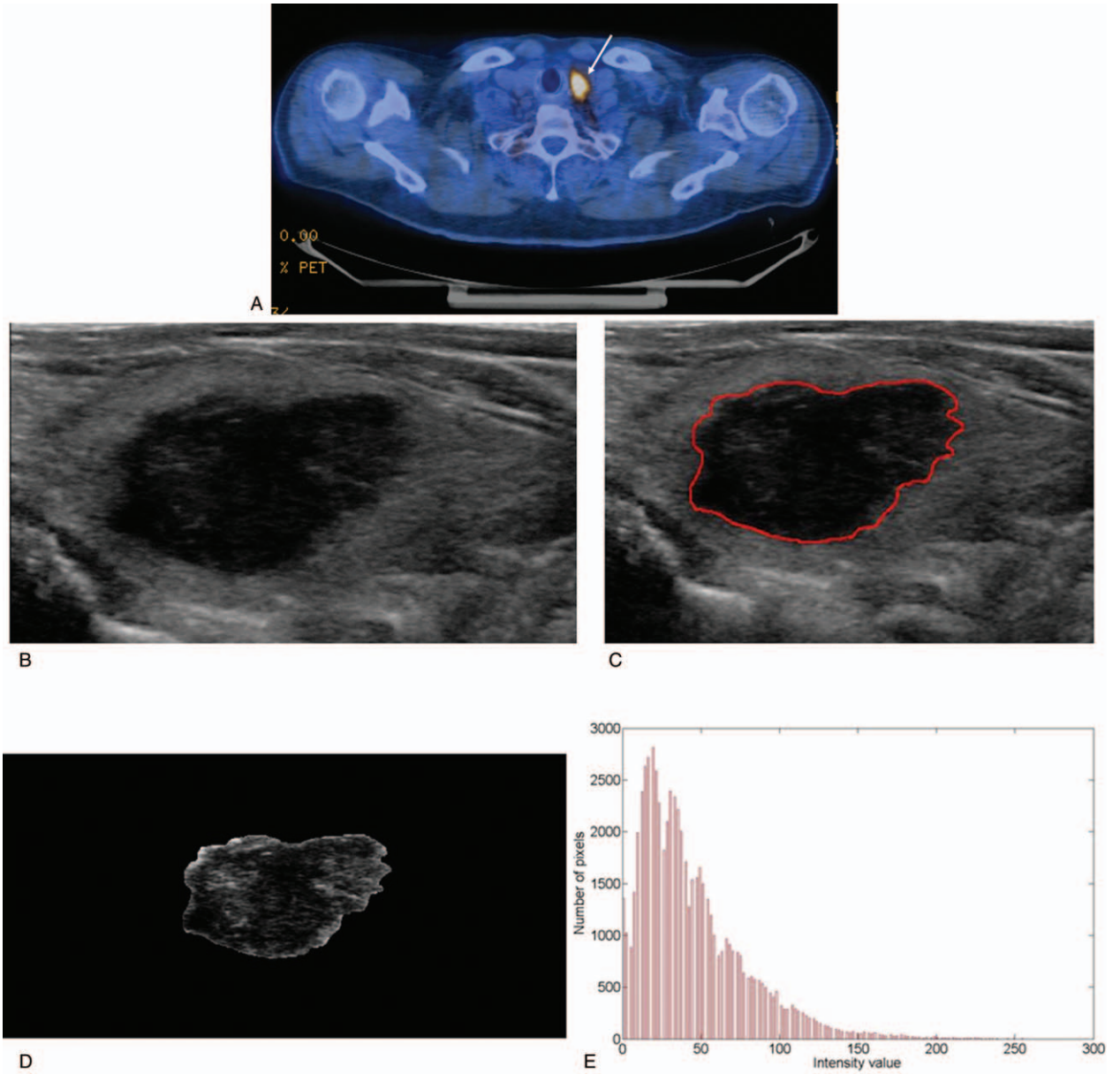

Figure 3. PET-CT and ultrasound (US) image of a metastatic adenocarcinoma from the lung of a 70-year-old man. (A) Fusion Fluorine-18 fluorodeoxyglucose (18F-FDG) PET-CT shows an increased FDG uptake in the left thyroid lobe. (B) Longitudinal US image show a 2.7 cm irregular, markedly hypoechoic nodule, with parallel orientation and no calcification.(C) An ROI was drawn on the transverse US image and extracted (D) *and* (E) Histogram analysis showed the distribution of pixels (y-axis) according the pixel intensity value (x-axis) in the ROI of the nodule. Histogram parameters were as follows: skewness = 1.397: kurtosis = 5.468: uniformity = 0.025: entropy = 5.581.

malignant nodules, indicating hypoechogenicity due to the hypercellularity of the malignant nodules.[22] Parameters derived from histograms could provide another clue to enable differentiation of tumors with similar gross US findings; however, in a pairwise comparison, histogram parameters were not significantly different between PTCs and metastatic thyroid nodules. Nonetheless, histogram parameters can be used to distinguish benign from malignant thyroid nodules, and the results may reduce unnecessary FNA for cytopathological confirmation of thyroid nodules with PET uptake. Consequently, parameters derived from histograms may serve as an additional aid to facilitate diagnostic confirmation. However, FNA cannot be avoided for differentiation of metastatic thyroid lesions from PTCs when the US features appear malignant, even if they are atypical.

Our study had several limitations. First, the retrospective design caused unavoidable selection bias in the analysis of thyroid nodules diagnosed by FNA or core needle biopsy. Second, radiologists with various degrees of experience in thyroid imaging analyzed the US images. Third, 2 readers reviewed all US imaging findings independently, but interobserver reliability was not evaluated. Finally, we evaluated only 5 main parameters for textural analysis. Possibly, the results might have improved if the effectiveness of other useful parameters for differentiating thyroid nodules with PET uptake were evaluated. However, the application of multiple parameters might lower the practical value of our approach.

5. Conclusion

Texture analysis of grayscale sonograms enables differentiation between benign and malignant thyroid nodules in patients with PET uptake. However, primary and metastatic thyroid malignancies detected on grayscale sonograms do not exhibit differences based on texture analysis. Therefore, cytopathological confirmation of nodules appearing malignant on US images cannot be avoided for an ultimate diagnosis of metastasis.

Author contributions

Conceptualization: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Data curation: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Formal analysis: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Funding acquisition: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Investigation: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Methodology: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Project administration: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Resources: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Software: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Supervision: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Validation: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Visualization: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Writing – original draft: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.
Writing – review & editing: Ko Woon Park, Jung Hee Shin, Jae-Hun Kim, Soo Yeon Hahn, Yaeji Lim, Joon Young Choi.

References

[1] Iyer NG, Shaha AR, Silver CE, et al. Thyroid incidentalomas: to treat or not to treat. Eur Arch Otorhinolaryngol 2010;267:1019–26.
[2] Are C, Hsu JF, Schoder H, et al. FDG-PET detected thyroid incidentalomas: need for further investigation? Ann Surg Oncol 2007;14:239–47.
[3] Choi JY, Lee KS, Kim HJ, et al. Focal thyroid lesions incidentally identified by integrated 18F-FDG PET/CT: clinical significance and improved characterization. J Nucl Med 2006;47:609–15.
[4] Cohen MS, Arslan N, Dehdashti F, et al. Risk of malignancy in thyroid incidentalomas identified by fluorodeoxyglucose-positron emission tomography. Surgery 2001;130:941–6.
[5] Yi JG, Marom EM, Munden RF, et al. Focal uptake of fluorodeoxyglucose by the thyroid in patients undergoing initial disease staging with combined PET/CT for non-small cell lung cancer. Radiology 2005;236:271–5.
[6] Makis W, Ciarallo A. Thyroid Incidentalomas on (18)F-FDG PET/CT: clinical significance and controversies. Mol Imaging Radionucl Ther 2017;26:93–100.
[7] Barrio M, Czernin J, Yeh MW, et al. The incidence of thyroid cancer in focal hypermetabolic thyroid lesions: an 18F-FDG PET/CT study in more than 6000 patients. Nucl Med Commun 2016;37:1290–6.
[8] Shin JH, Baek JH, Chung J, et al. Ultrasonography diagnosis and imaging-based management of thyroid nodules: revised korean society of thyroid radiology consensus statement and recommendations. Korean J Radiol 2016;17:370–95.
[9] Chen SJ, Yu SN, Tzeng JE, et al. Characterization of the major histopathological components of thyroid nodules using sonographic textural features for clinical diagnosis and management. Ultrasound Med Biol 2009;35:201–8.
[10] Lerski RA, Straughan K, Schad LR, et al. MR image texture analysis–an approach to tissue characterization. Magn Reson Imaging 1993;11:873–87.
[11] Sucharda P, Smutek D, Sara R. Texture analysis of ultrasonograms–a new method in the diagnosis of thyroid diseases? Cas Lek Cesk 2004;143:15–20.
[12] Koprowski R, Korzynska A, Wrobel Z, et al. Influence of the measurement method of features in ultrasound images of the thyroid in the diagnosis of Hashimoto's disease. Biomed Eng Online 2012;11:91.
[13] Kim TY, Kim WB, Ryu JS, et al. 18F-fluorodeoxyglucose uptake in thyroid from positron emission tomogram (PET) for evaluation in cancer patients: high prevalence of malignancy in thyroid PET incidentaloma. Laryngoscope 2005;115:1074–8.
[14] Materka A, Strzelecki M. Texture Analysis Methods – A Review. Technical University of Lodz, Institute of Electronics, COST B11 Report, Brussels 1998.
[15] Smutek D, Sara R, Sucharda P, et al. Image texture analysis of sonograms in chronic inflammations of thyroid gland. Ultrasound Med Biol 2003;29:1531–43.
[16] Kwon MR, Shin JH, Hahn SY, et al. Histogram analysis of greyscale sonograms to differentiate between the subtypes of follicular variant of papillary thyroid cancer. Clin Radiol 2018;73:591e1-e7.
[17] Kim SY, Kim EK, Moon HJ, et al. Application of texture analysis in the differential diagnosis of benign and malignant thyroid nodules: comparison with gray-scale ultrasound and elastography. AJR Am J Roentgenol 2015;205:W343–51.
[18] Yoon JH, Kim EK, Kwak JY, et al. Sonographic features and ultrasonography-guided fine-needle aspiration of metastases to the thyroid gland. Ultrasonography 2014;33:40–8.
[19] Khoo ML, Asa SL, Witterick IJ, et al. Thyroid calcification and its association with thyroid carcinoma. Head Neck 2002;24:651–5.
[20] Robinson PC, Rifkin MD, Price A. Papillary carcinoma of the thyroid gland in a young child. Ultrasound Q 2004;20:101–3.
[21] Bartolotta TV, Midiri M, Galia M, et al. Qualitative and quantitative evaluation of solitary thyroid nodules with contrast-enhanced ultrasound: initial results. Eur Radiol 2006;16:2234–41.
[22] Na DG, Baek JH, Sung JY, et al. Thyroid imaging reporting and data system risk stratification of thyroid nodules: categorization based on solidity and echogenicity. Thyroid 2016;26:562–72.