

Multimodality Molecular Imaging (FDG-PET/CT, US Elastography, and DWI-MRI) as Complimentary Adjunct for Enhancing Diagnostic Confidence in Reported Intermediate Risk Category Thyroid Nodules on Bethesda Thyroid Cytopathology Reporting System

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Abstract

The potential complimentary role of various molecular imaging modalities [fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT), ultrasound (US)-elastography, and diffusion weighted imaging-magnetic resonance imaging (DWI-MRI)] in characterizing thyroid nodules, which have been designated as “intermediate risk category” on the Bethesda thyroid cytopathology reporting system (BTCRS), is illustrated in this communication. The clinical cases described (category III thyroid nodules on BTCRS) show the imaging features and the final diagnostic impressions rendered by the interpreting physicians with the modalities that have been independently compared in a tabular format at the end; of particular note is the high negative predictive value of these (specifically FDG-PET/CT), which could aid in enhancing the diagnostic confidence in the reported “intermediate risk category” thyroid nodules, a “gray zone” from the patient management viewpoint.

Keywords: Diffusion weighted imaging-magnetic resonance imaging (DWI-MRI), fine-needle aspiration cytology (FNAC), fluorodeoxyglucose-positron emission tomography/computed tomography (¹⁸F-FDG-PET/CT), ultrasound (US)-elastography

Introduction

The category III of the Bethesda thyroid cytopathology reporting system (BTCRS) is designated as “Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance.” The risk of malignancy is stated to be ~ 5-15%, and the recommended procedure

is repeating fine-needle aspiration cytology (FNAC).^[1] Similarly, the category IV thyroid nodules on BTCRS is designated as “Follicular Neoplasm or Suspicious for a Follicular Neoplasm”, the malignancy rate of these is estimated to be around 15-30%, and the suggested management approach for these is surgical lobectomy. We, herein, compare and contrast the possible adjunct role of noninvasive molecular imaging features [combining fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT), ultrasound (US)-elastography, and diffusion weighted imaging-magnetic resonance imaging (DWI-MRI)] in the reported category III thyroid nodules in two cases, illustrating how they can enhance the confidence of diagnosis due to their negative predictive value.

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Case Report

The first case was a 65-year-old female who presented with mixed echogenicity, predominantly hyperechoic lesion measuring 6.1 cm × 3.9 cm, with central macrocalcification on grayscale transverse US [Figure 1a], with internal vascularity and peripheral hallow. Ultrasonography (USG)-guided FNAC was suggestive of follicular lesion of undetermined significance (Bethesda category III) [Figure 1b]. Split-screen B-mode

US image (left) and US-elastogram (right) showed a focal stiff nodule (star) with predominantly maintained elasticity. The Rago and Asteria strain elastographic scores of the lesion were 3 and 2, respectively, which are suggestive of indeterminate nodule [Figure 1c and d]. Plain axial MRI images showed heterogeneous signal intensity on T2-weighted (T2W) [Figure 1c] and predominantly hypointensity on T1-weighted (T1W) images. The central dark hypointense area on both T2W and T1W images represents calcification (arrow) T2W and T1W images represents calcification (arrow)

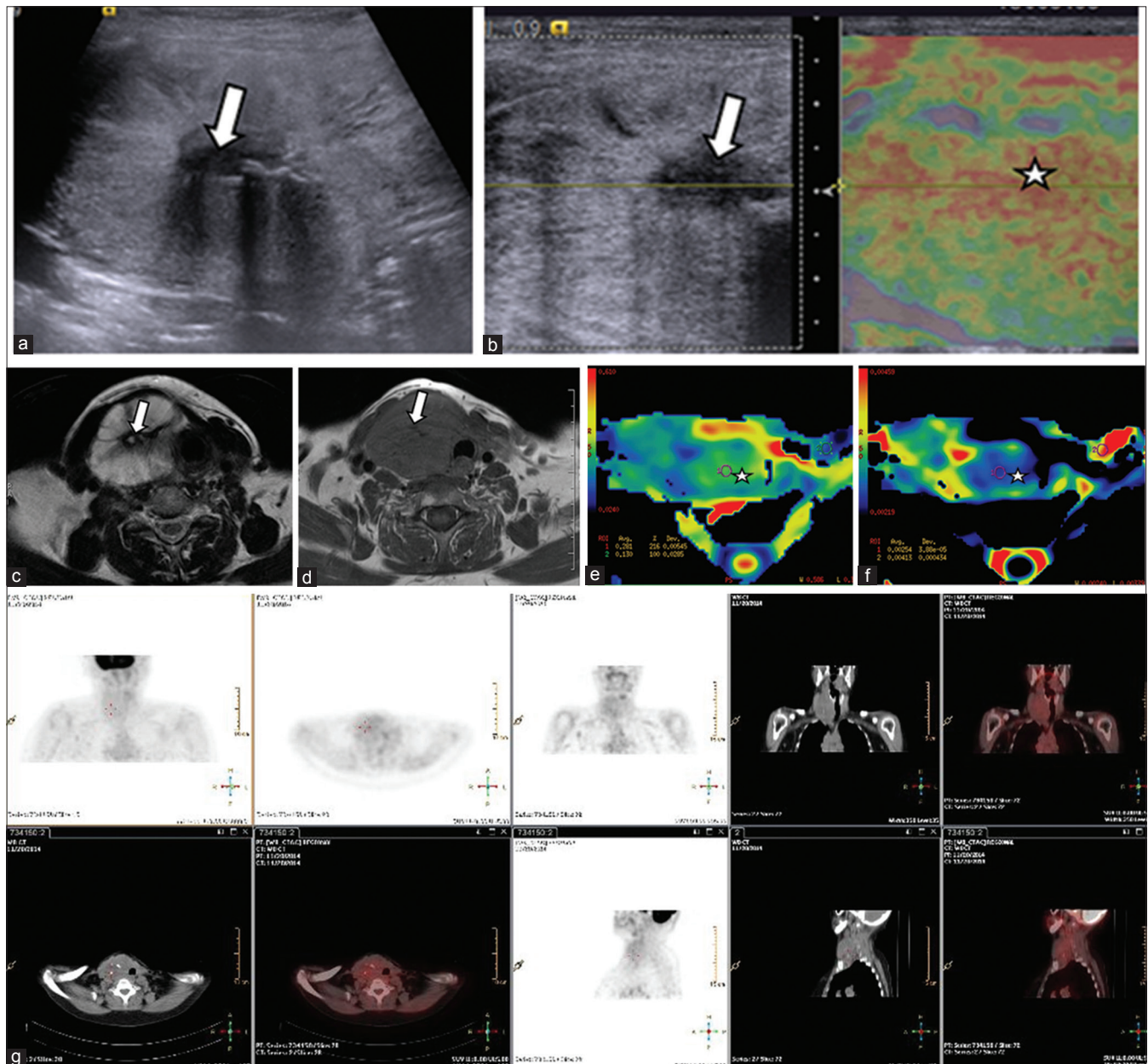


Figure 1: (a) Grey scale ultrasonography demonstrating mixed echogenicity predominantly hyperechoic lesion (6.1 × 3.9 cm) with central macrocalcification (b) Split-screen B-mode ultrasound image (left) and US elastogram (right) showing a focal stiff nodule (star) with predominantly maintained elasticity. The Rago and Asteria Strain elastographic scores of the lesion were 3 and 2 (c and d). Plain axial MRI images showing heterogeneous signal intensity on T2W and predominantly hypointensity on T1W images respectively. Also noted was central darkly hypointense area on both T2W and T1W images representing calcification (arrow) (e and f). Diffusion colored maps of EADC and ADC value obtained from ADC map with b factor 0 and 500. The ADC map shows low values of in the area of stiffness on elastogram (star) corresponds to restricted diffusion with a measured ADC value of $0.34 \times 10^{-3} \text{ mm}^2/\text{s}$. (g) FDG-PET/CT demonstrating very low grade FDG uptake in the nodule

[Figure 1e and f]. Diffusion colored maps of exponential apparent diffusion coefficient (eADC) and apparent diffusion coefficient (ADC) value obtained from the ADC map, with b-factor between 0 and 500. On elastogram (star), the ADC map showed low values in the area of stiffness that corresponds to restricted diffusion with a measured ADC value of $0.34 \text{ mm}^2/\text{s} \times 10^{-3} \text{ mm}^2/\text{s}$. The FDG-PET/CT [Figure 1g] was predominantly negative, with very low grade FDG uptake in the

nodule. A repeat FNAC is suggested for colloid nodular goitre with cystic changes.

The second case, a 29-year-old female presenting with $2.3 \text{ cm} \times 1.4 \text{ cm}$ solitary nodule of left lobe lower pole on grayscale transverse US showed a heterogeneous, predominantly iso to hypoechoic, lesion that measures $3.7 \times 1.9 \text{ cm}$ [Figure 2a] and was cold on $^{99\text{m}}\text{TcO}_4$ scintigraphy. The USG- guided

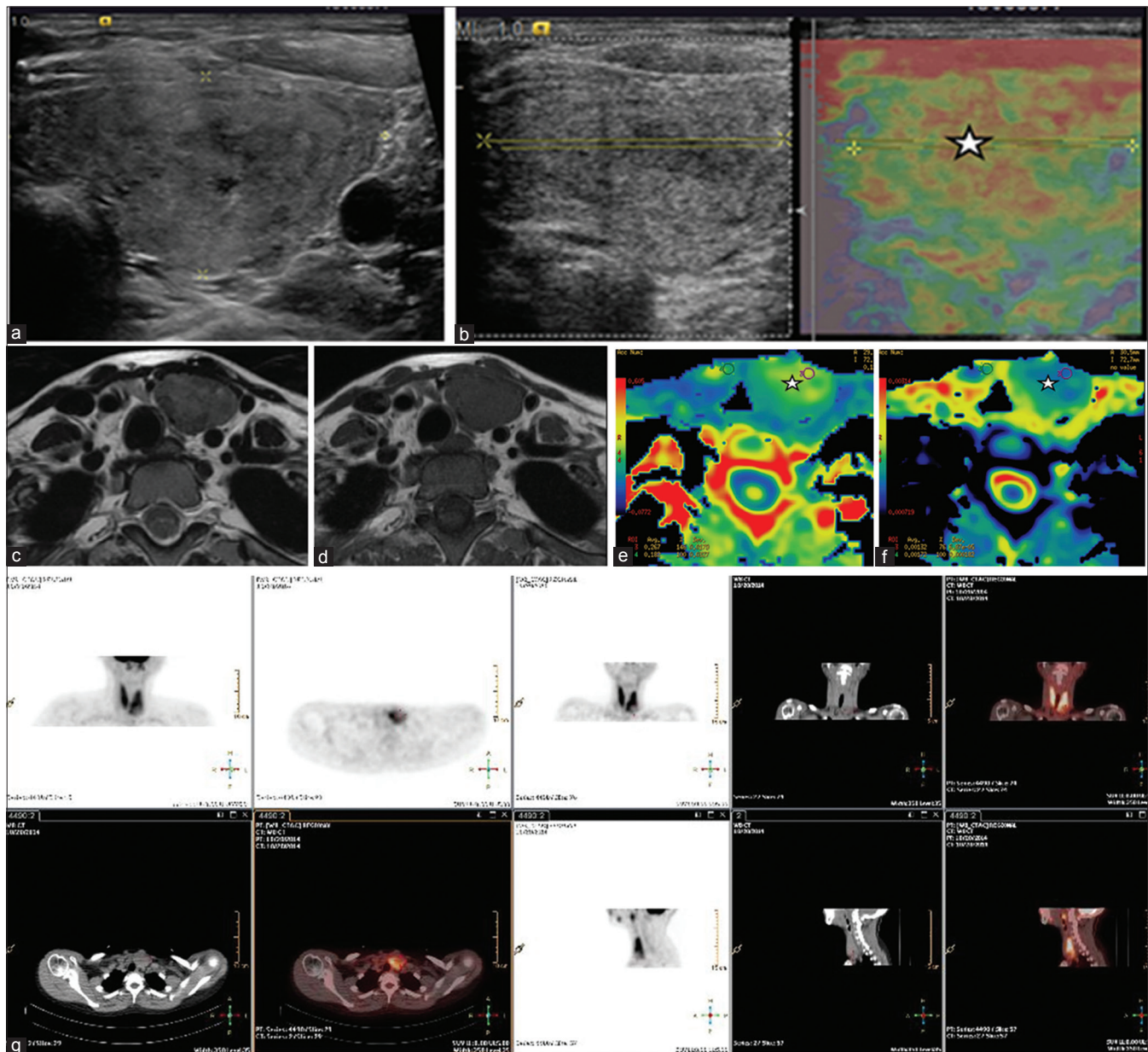


Figure 2: (a) Grey scale transverse ultrasound showing a heterogeneous predominantly iso to hypoechoic lesion ($3.7 \times 1.9 \text{ cm}$) that was cold on $^{99\text{m}}\text{TcO}_4$ scintigraphy. (b) Split-screen B-mode ultrasound image (left) and US elastogram (right) showing a predominant stiff nodule (star). The Rago and Asteria Strain elastographic scores of the lesion were 3 and 3 respectively. (c and d) Plain MRI showing a predominantly iso-to hypointense on both T2W images and T1W images respectively. (e and f). Diffusion colored maps of EADC and ADC value obtained from ADC map with b factor 0 and 500. The ADC map of the left side nodule (star) showed diffusion pattern similar to the normal parenchyma the right lobe of thyroid with a measured ADC value of $1.82 \times 10^{-3} \text{ mm}^2/\text{s}$ which represented area of stiffness on elastogram. (g) FDG-PET/CT demonstrating a predominantly to be FDG non-avid nodule in a background of diffuse uptake indicating associated thyroiditis like picture in the rest of the thyroid gland

Table 1: Final impression rendered by the interpreters of various molecular imaging modalities

	Gray scale USG	Elastography	DWI-MRI	FDG-PET/CT
Nodule 1- right side	Benign	Indeterminate	Indeterminate (restriction due to colloid material)	Benign
Nodule 2- left side	Indeterminate	Favors malignancy	Benign (favors final FNA* as gland shows a diffusion pattern similar to normal parenchyma on the other side)	Benign

*FNA: Fine-needle aspiration

FNAC was reported to be “Follicular Lesion of Undetermined Significance (Bethesda category III)” [Figure 2b]. Split-screen B-mode US image (left) and US-elastogram (right) showed a predominant stiff nodule (star). The Rago and Asteria strain elastographic scores of the lesion were 3 and 3, respectively, [Figure 2c and d]. Plain axial MRI images showed a predominantly iso-hypointense on both T2W and T1W images [Figure 2e and f]. Diffusion colored maps of EADC and ADC value obtained from the ADC map with B-factor between 0 and 500. The ADC map of the left side nodule (star) showed a diffusion pattern similar to the normal parenchyma of the right lobe of thyroid with a measured ADC value of $1.82 \text{ mm}^2/\text{s} \times 10^{-3} \text{ mm}^2/\text{s}$, which represented an area of stiffness on elastogram. FDG-PET/CT [Figure 2g] predominantly demonstrated the nodule to be FDG nonavid in a background of thyroiditis-like picture for the rest of the glands. A follow-up repeat FNAC at 3 months suggested chronic thyroiditis.

The overall impressions by the interpreting physicians have been tabulated in Table 1, along with the impression in gray scale USG.

Discussion and Conclusion

The primary aim of the Bethesda system for reporting thyroid cytopathology (BSRTC) reported in 2009 was to standardize the terminology for interpreting FNA specimens of the thyroid nodules.^[1] In addition to the standardization and systematization, it was observed that its implementation in routine settings helped in improving the diagnostic accuracy, with higher rates of detection of malignancy despite lower rates of thyroidectomies.^[2] The intermediate category nodules designated by BSRTC is a “gray zone” area where further enhancement of diagnostic confidence would aid in

better management and reduce unnecessary procedures including thyroidectomies.^[3]

The presented illustrations in this communication demonstrate the imaging features of the promising molecular imaging approaches and impressions rendered with each [Table 1], along with grayscale USG. The illustrations demonstrate the probable clinical utility that could be employed for characterizing these intermediate category nodules on USG-guided FNAC.^[2] We hypothesize that their combined application could also be potentially extended to category IV (“Follicular Neoplasm or Suspicious for a Follicular Neoplasm”) nodules as well, only around 15-30% of which turn out to be malignant.^[1] This would, however, need to be examined in prospective studies encompassing both categories of the intermediate category (III and IV) nodules for defining their definitive place.

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