

# Evaluation of the Nature of Thyroid Nodules by Duplex Ultrasound and Assessment of the Diagnostic Accuracy of TIRADS Classification

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## ABSTRACT

**Introduction:** Ultrasound (US) is the primary modality used to assess the thyroid glands. However, the terminology used by the radiologist is not easy for clinicians to understand. Thyroid Imaging Reporting and Data System (TIRADS) classification is the best attempt to facilitate better communication between the radiologist and clinicians.

**Aim:** To assess the Thyroid Ultrasonography (USG) characteristics which are highly suggestive of malignancy and to assess the reliability of TIRADS in the differentiation of malignant from benign thyroid nodules.

**Materials and Methods:** The present study was an observational study conducted on 200 consecutive patients presenting for thyroid swelling and underwent ultrasound of the thyroid. USG features recorded were the internal component, echogenicity, margins, calcifications, shape and vascularity. Using the modified Russ classification, each nodule was classified into a TIRADS category (I, II, III, IVA, IVB and V) based on the US features. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) was calculated for each of the suspicious US features. The risk of malignancy for each category of TIRADS classification was determined. All the

nodules underwent cytological confirmation. The threshold for statistical significance was set at 0.05.

**Results:** Among the USG characteristics, spiculated margin, microcalcification and taller-than-wide shape had highest specificity for malignant nodules. Anechoic nodule, iso or hyperechogenicity, predominantly cystic nature, macrocalcification and peripheral vascularity had a high NPV for the malignancy. The maximum number of the patients belonged to TIRADS Grade 3. The PPV was 100% for Grade V malignant nodules followed by 75% for Grade IVB malignant nodules. There was significant difference between IVA and IVB malignant nodules with IV A having very low risk for malignancy and IVB and V having significantly higher risk for malignancy.

**Conclusion:** There is no single ultrasound feature which can diagnose malignancy in thyroid nodules however, there are combinations of USG features that can strongly suggest the possibility of malignancy. TIRADS serves as a convenient classification system which can be easily understood by the clinicians and guide them to do biopsy of the TIRADS IV and V nodules, which have highest malignant risk, thus helping in better patient management.

**Keywords:** Fine needle aspiration cytology, Malignant, Thyroid nodule, Ultrasonography

## INTRODUCTION

Thyroid USG has been used in differentiating benign from malignant nodules and for guiding Fine Needle Aspiration Cytology (FNAC) for nodules suspected of being malignant [1-3]. However, fewer than 5.0%-6.5% of incidentally discovered thyroid nodules are malignant. Therefore, it is necessary according to malignancy risk, that a criteria is established for selecting thyroid nodules for FNAC [4].

There is increasing complexity of terminology used in ultrasound reporting and treating physician and surgeons face a lot of difficulty in understanding the actual meaning of those terms. So, there was a need to introduce a system through which radiologists could communicate better with the clinicians. TIRADS classification system was developed with the main goal to standardise the reporting of results of thyroid ultrasound that can be understood by clinicians and also stratify the risk of malignancy of a lesion based on the USG features of the lesion. The terminology TIRADS was first used by Horvath E et al., drawing inspiration from the "Breast Imaging and Reporting Data System" (BIRADS) of the American College of Radiology [5]. Russ G et al., proposed a TIRADS classification that was further modified and they proposed that TIRADS will be more helpful in the settings where Fine Needle Aspiration Biopsy (FNAB) is not readily available and so decisions will therefore be based to a great extent on the US features of the lesions and TIRADS classification as this implies the potential risk for malignancy [6].

This study was conducted with an aim to assess the USG characteristics which are highly suggestive of malignancy and to assess the reliability of TIRADS in the differentiation of malignant from benign thyroid nodules.

## MATERIALS AND METHODS

The present study was an observational study conducted on 200 consecutive patients from December 2014 to December 2016 in the Department of Radiodiagnosis in collaboration with the Department of Pathology and Surgery in Jawaharlal Nehru Medical College and Hospital, Faculty of Medicine, AMU, Aligarh, India. The patients presenting to the surgery outpatient department for neck swelling were initially clinically evaluated for thyroid swelling. They were referred to the radiology department and underwent ultrasound of the thyroid. Colour and power Doppler were used as and when necessary. This study was approved by Institutional Ethics and Research Advisory Committee. Written informed consent was obtained from all the patients who participated in the study. The patients of any age or sex were included in the study who presented with clinically suspected thyroid nodules were included in study. Patients with diffuse thyroid disease were excluded from the study.

## Sonographic Evaluation

All US scans and power Doppler US examinations of the thyroid gland were performed using Samsung Medison Sonoace X8

with a linear-array transducer (5-12 MHz) that provides enough penetration (about 5 cm depth) and excellent resolution (0.7-1 mm) using an optimised gain. Power Doppler examinations were performed by using the standard equipment settings for thyroid ultrasound. The patient was examined in supine position with the neck hyperextended (a pillow may be placed below the shoulders to achieve neck hyperextension). US features of all of the thyroid nodules were prospectively recorded for clinical use according to the internal component, echogenicity, margins, calcifications, shape and vascularity. Using the modified Russ classification, each nodule was classified into a TIRADS category (I, II, III, IVA, IVB and V) based on the US features [Table/Fig-1] [6]. Based on the results of a previous study marked hypoechogenicity, microcalcifications, irregular margins or microlobulation, and a taller-than-wide shape were counted as suspicious US features [6].

Category	Features
TIRADS category I	Normal thyroid
TIRADS category II	Benign aspect-simple cyst, benign spongiform, isolated macrocalcification and typical subacute thyroiditis
TIRADS category III	Probably benign-nodules with none of high suspicious US feature, isoechoic or hyperechoic nodule
TIRADS category IVA	Low suspicious-Nodules with no signs of high suspicious US features* and moderately hypoechogenic nodules
TIRADS category IVB	High suspicious-Nodules with 1 or 2 suspicious US features* and no metastatic lymphadenopathy
TIRADS category V	High suspicious aspects-Nodules with $\geq 3$ suspicious US features* and/or metastatic lymphadenopathy
*USG features highly suspicious of Malignancy	taller-than-wide shape irregular or microlobulated margins, microcalcifications, marked hypoechogenicity

[Table/Fig-1]: TIRADS classification.

## USG Guided FNAC

USG-guided FNAC was performed by the same radiologists who performed the initial scans for each thyroid nodule without administration of local anaesthesia. About 3-4 smears were made for each nodule using 23-gauge needle attached to a 2 mL disposable plastic syringe. Materials obtained from aspiration biopsy were used to prepare smears, immediately placed in 95% ethyl alcohol and sent to the Department of Pathology for papanicolaou staining. Cytopathologists of the hospital interpreted the smears. Reporting of thyroid cytology, FNAC results were classified as benign, indeterminate, suspicious for papillary thyroid carcinoma, malignant, or inadequate [7,8]. Also, those patients who have undergone surgery their histopathological reports were also collected.

## STATISTICAL ANALYSIS

All statistical analysis was performed using the statistical software SPSS 22.0 (SPSS Inc, Chicago, USA) and MedCalc 12.7. Sensitivity, specificity, PPV and NPV were calculated for each of the suspicious US features that are highly suggestive of malignancy as described in USG section. The threshold for statistical significance was set at 0.05.

## RESULTS

A total of 200 patients were evaluated in present study. FNAC reports showed indeterminate result in ten cases and there was inconclusive report owing to inadequate sampling/technical error in nine patients. Thus, 19 patients were excluded from the study. The age range of the patients in the study was 11 to 75 years. The largest group of patients was in the 21-30 years age group followed by 31-40 years age groups. There were only 3 patients above 70 years. A female preponderance was noted in patients with thyroid nodules in all age groups. There were 169 female and 31 male

patients in the study.

Out of 181 patients, 11 nodules (6.07%) were malignant and rest 170 (93.9%) nodules were benign. The majority of the nodules were predominantly solid in its internal content. All of the 11(100%) malignant nodules were predominantly solid and majority of the predominantly cystic nature of the nodules were benign in nature. Majority of the nodules with oval to round shape were benign 154

Characteristics		Benign Nodules	Malignant Nodules
Internal Contents	Predominantly Solid	130 (76.5%)	11 (100%)
	Predominantly Cystic	40 (23.5%)	0 (0%)
Echogenicity	Anechoic	11 (6.5%)	0 (0%)
	Hypoechoic	18 (10.6%)	7 (63.6%)
	Isoechoic	118 (69.4%)	4 (36.4%)
	Hyperechoic	23 (13.5%)	0 (0%)
Margin	Smooth	145 (85.3%)	5 (45.5%)
	Spiculated	0 (0%)	1 (9.1%)
	Lobulated	19 (11.2%)	1 (9.1%)
Calcification	Ill-defined	6 (3.5%)	4 (36.4%)
	Microcalcification	2 (1.2%)	3 (27.3%)
Shape	Macrocalcification	21 (12.4%)	0 (0%)
	Ovoid to round	154 (90.6%)	6 (54.5%)
Vascularity	Taller-than-wide	2 (1.2%)	3 (27.3%)
	Irregular	14 (8.2%)	2 (18.2%)
Vascularity	Peripheral	85 (50%)	3 (27.3%)
	Intranodular	12 (7.1%)	3 (27.3%)
	Both	40 (23.5%)	4 (36.4%)

[Table/Fig-2]: Frequency analysis of USG characteristics of benign and malignant thyroid nodules.

(90.6%). Microcalcification was more specifically associated with the malignant nodule and seen in the 27.3% cases [Table/Fig-2].

Specificity of spiculated margin, taller-than-wide shape and hypoechogenicity was 100%, 98.8% and 89.4% respectively showing they were more specifically associated with malignancy. Malignant nodules revealed highest specificity for spiculated margin, followed by microcalcification and taller-than-wide shape as some malignant USG characteristics. However, the sensitivity was low for all these features. Highest sensitivity was noted for predominantly solid nature (100%) for malignant nodules. Highest PPV was noted for spiculated margins (100%). Among the benign USG characteristics

Characteristic	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Accuracy
<b>Malignant nodule</b>					
Taller-than-wide	27.3	98.8	95.5	60	94.5
Spiculated margin	9.1	100	94.4	100	94.4
Hypoechoic	63.6	89.4	97.4	28	87.9
Predominantly solid	100	76.5	100	21.6	77.9
Micro-Calcification	27.3	98.8	95.5	60	94.8
<b>Benign nodule</b>					
Anechoic	0	93.5	93.5	0	87.8
Hyperechoic	0	86.5	93.1	0	81.22
Macrocalcification	0	87.6	93.1	0	82.3
Predominantly Cystic	0	76.5	92.2	0	71.8
Peripheral	27.3	50	91.4	3.4	48.6
Isoechoic	36.6	30.59	88.1	3.28	30.9
Smooth	45.5	14.7	80.6	3.3	16.5

[Table/Fig-3]: Diagnostic accuracy of USG findings for malignant and benign nodules.

anechoic (93.5%) nature showed the highest specificity followed by macrocalcification (87.6%), hyperechoic (86.5%) and predominantly cystic (76.5%) nature [Table/Fig-3].

In present study, TIRADS grading was done based on previously described different ultrasound characteristics used to differentiate benign and malignant nodules. Out of total 181 patients, maximum number of the patients belonged to TIRADS Grade 3 (n=147) (Benign=145 and Malignant=2). TIRADS Grade IVA and IVB had 7 and 8 patients respectively. Out of 181 nodules, the PPV was

Tirads Grading	Total (n=200)	Benign (n=170)	Malignant (n=11)	PPV (%)	NPV (%)
I	0	0	0	0	0
II	19	18	0	0	94.25
III	159	145	2	1.36	82
IVA	9	5	2	28.57	95.5
IVB	12	2	6	75	97.41
V	1	0	1	100	95.2

**[Table/Fig-4]:** Distribution of Benign and Malignant nodule in each TIRADS Category with PPV for malignancy.

100% for Grade V malignant nodules followed by 75% for Grade IVB malignant nodules [Table/Fig-4]. There was significant difference between IVA and IVB malignant nodules with IVA having very low risk for malignancy and IVB having significantly high risk for malignancy.

## DISCUSSION

Thyroid USG is now increasingly being used to evaluate thyroid diseases to characterise the morphology of the lesion and suggest a pathologic diagnosis. The role has expanded to assess the local extent of the lesions, any nodal involvement and guide FNAC wherever indicated.

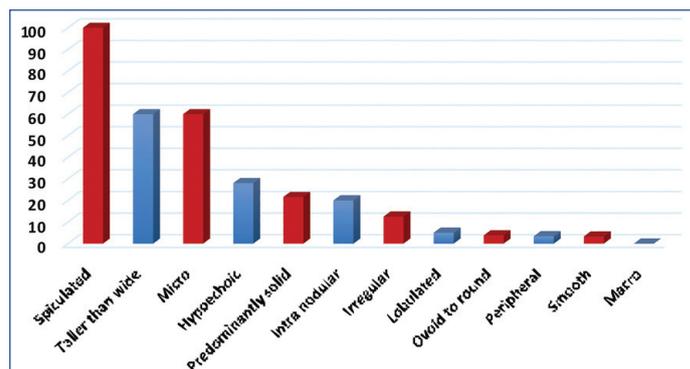
In present study, 27.3% of malignant thyroid nodules were of taller-than-wide shape. The sensitivity and specificity of taller-than-wide shape in the detection of malignant lesions were 27.3% and 98.8% respectively. This shows that the taller-than-wide shape has a high specificity for malignancy. In present study irregular shape of the nodule also shows high specificity (98.8%). Result of current study is in consistent with the study conducted by Moon WJ et al., [9].

Gaitini D et al., described that the risk of malignancy was more with solid nodule [10]. Our experience shows that all the malignant nodules were solid and all the cystic nodules were benign in nature. however, 3/4<sup>th</sup> of the benign nodules were also solid in consistency. Thus in solid lesions, we need to see other feature which might suggest malignancy. In the present study, there was one case of intracystic papillary carcinoma which had cystic internal consistency with large internal solid component. FNAC was taken from the solid area and diagnosed to be a malignant intracystic papillary neoplasm. Hypoechoogenicity was noticed in 63.6% of the malignant nodule with the sensitivity and specificity of 63.6% and 89.4% respectively whereas hypoechoogenicity seen in 10.6% cases of benign nodules. Hypoechoogenicity was more specifically associated with the malignancy. Moon WJ et al., and Gaitini D et al., in their study reported that the frequency of hypoechoogenicity was significantly different between benign and malignant nodules and hypoechoogenicity was highly specific for diagnosing malignant nodules [9,10].

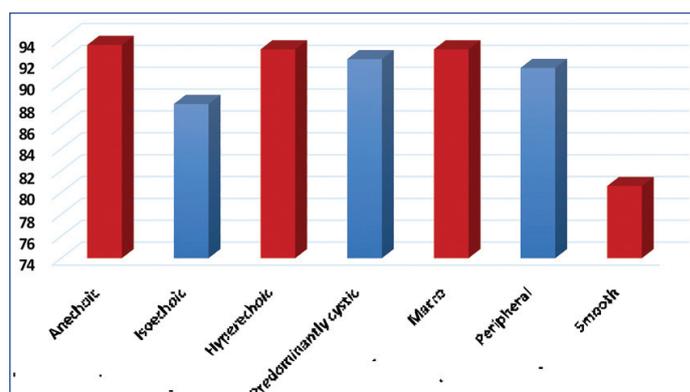
Out of the 11 proven malignant nodules, 5 (45.5%) had smooth margin followed by ill-defined margin which was seen in 4 cases (36.4%). However, sensitivity and specificity of spiculated margin in the detection of malignant nodule was 9.1% and 100% respectively. This shows that spiculated margin is highly specific feature of a malignant nodule. Moon WJ et al., reported similar result with sensitivity of 48.3% and specificity of 91.8% for spiculated margin

in the detection of malignant nodule [9].

In the current study, 3 cases (27.3%) of malignant nodules showed microcalcification whereas (1.2%) benign nodules showed microcalcification. Microcalcification was more specifically associated with the malignant nodule and seen in the 27.3% cases



**[Table/Fig-5]:** Positive predictive value (PPV) for malignancy of various USG characteristics.



**[Table/Fig-6]:** Negative predictive value (NPV) for malignancy of various USG characteristics.

with sensitivity and specificity of 27.3% and 98.8% respectively. Moon WJ et al., reported that the microcalcifications have a high PPV (41.8%-94.2%) but a low sensitivity (26.1%-59.1%) in the detection of malignant nodule [9]. In present study the PPV of microcalcification for the diagnosing malignant nodule was 60.0% and macrocalcification showed high NPV of 93.1% [Table/Fig-5,6]. Kim BM et al., previously reported the same result that hypoechoogenicity, marked hypoechoogenicity, and taller-than-wide shape were the ultrasound features which best predicted the chance of malignancy in thyroid nodules [8]. These features were considered to be suspicious for malignancy in study conducted by Kwak JY et al., Nam-Goong IS et al., Salmaslioglu A et al., and Tae HJ et al., [7,11-13].

Some investigators suggest a combination of these features is known to provide better diagnostic accuracy than a single feature alone. However, considerable variation in the sensitivity and specificity of the US findings for malignant thyroid nodules are reported. Factors that may affect the findings reported in previous studies include the use of different USG equipment, operator's experience and the different US criteria for identifying a malignancy.

Comparing the diagnostic performance of TIRADS in the present study with other studies [Table/Fig-7]. The studies done by Hovarth E et al., Kwak JY et al., Kim BM et al., Park JY et al., Moifo B et al., and Chandramohan A et al., show that the risk of malignancy increases as we advance the grading of TIRADS from Grade III to Grade V [5,7,8,14-16]. The result shows that present study for TIRADS Grade II, IVA, IVB and V is correlating with the other studies while present study for TIRADS Grade III is correlating with the study of Kwak JY et al., [7]. In present study, it was also noted that there is substantial increase in the risk of malignancy (i.e., from 28.57% to

TIRADS Category	Horvath E et al., [5]	Kwak JY et al., [7]	Kim BM et al., [8]	Park JY et al., [14]	Moifo B et al., [15]	Chandramohan A et al., [16]	Current Study
TIRADS 2	0	0	0	1.8	0	0	0
TIRADS 3	14.1	1.5	0	9.6	2.2	6.6	1.36
TIRADS 4A	45.0	3.9	34.1	31.1	5.9	32	28.57
TIRADS 4B		69.3	83.9	76.8	57.9	36	75
TIRADS 5	89.6	74.9	99.4	100	100	64	100

**[Table/Fig-7]:** Comparison of the diagnostic performance of the present study with other studies on the performance of TIRADS showing percentage risk of malignancy with various TIRADS categories.

75%) was noted from TIRADS Grade IVA to Grade IVB and V. Any lesion with Grade IV and V should always be biopsied because the overall risk of malignancy is very high.

## LIMITATION

The major limitation of the study was that in present study we encountered only 11 confirmed nodules of malignancy. However, the results are consistent with the few published papers. The benign lesions were not operated because of consent and ethical issues.

## CONCLUSION

USG is the best diagnostic tool in the assessment of thyroid nodules. The number of diagnosed non palpable thyroid nodules is increasing as a consequence of the widespread use of USG. Among all the clinically palpable lesions, incidence of malignancy is low. Therefore, it becomes very important to differentiate benign from malignant nodules and to guide FNAC of nodules suspected for malignancy. There are combinations of USG features that can suggest the possibility of malignancy. TIRADS serves as a convenient classification system which can guide the clinicians to biopsy the TIRADS IV and V nodules, thus helping in better patient management.

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