

# Diagnostic Accuracy of Strain Ultrasound Elastography in Differentiating Benign and Malignant Thyroid Nodules, Taking Histopathology as the Gold Standard

Diagnostic Accuracy of Strain Ultrasound in Benign and Malignant Thyroid Nodules

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## ABSTRACT

**Objective:** To evaluate the diagnostic accuracy of strain Ultrasound elastography in differentiating malignant and benign thyroid nodules.

**Study Design:** A descriptive cross-sectional study

**Place and Duration of Study:** This study was conducted at the Radiology department of Bahawal Victoria Hospital Bahawalpur from Feb 2020 to Feb 2021 for a period of one year.

**Materials and Methods:** A total of 80 patients with palpable thyroid nodules were included after passing through selection criteria. Strain ultrasound elastography was done to distinguish benign and malignant lesions in all patients. The findings were compared with the results of histopathology testing.

**Results:** The mean age of participants was  $46.5 \pm 6.21$  years. Out of 80 patients, 43 (53.7%) were male and 37 (46.2%) were female. Mean disease duration was  $8.71 \pm 4.52$  months and mean nodular size was  $4.38 \pm 1.50$  cm. The strain USG confirmed positivity for malignancy in 40 cases while the other 40 were regarded negative for any malignancy. In comparison with histopathology findings, 3 were found to be false-positive and 2 were false negative. On adjusting the confounding variables, strain USG was found to be 95% sensitive, 90.5% specific, had PPV of 90.8%, NPV of 94.1%, and was 93% accurate in terms of differentiating benign from malignant thyroid tumors on comparison with histopathology.

**Conclusion:** Strain ultrasound elastography is a non-invasive technique with a considerable diagnostic accuracy of differentiating benign and malignant thyroid nodules when compared with gold-standard histopathology.

**Key Words:** Ultrasound Strain elastography, thyroid nodules, histopathology, malignancy

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## INTRODUCTION

Around 33% of individuals aged between 18-65 years are diagnosed with thyroid nodules while the incidence is as high as 50% in individuals older than 65 years<sup>1</sup>. Although most of thyroid nodules are benign in nature, 5-15% are reported to be malignant<sup>2</sup>. Generally the status of the thyroid gland and presence of nodules is

assessed through ultrasound which is then followed by estimation of thyroid-stimulating hormone and anti-thyroid antibodies to identify the underlying causes of benign nodules like Hashimoto's thyroiditis.<sup>2</sup>

Similarly, calcitonin is measured to detect medullary thyroid cancer. Lastly, a fine needle aspiration cytology is conducted to make a definite diagnosis.

Although ultrasound (US) accurately reports thyroid nodules, it is limited in terms of differentiating benign from malignant nodules<sup>3</sup>. The sensitivity and specificity of US in defining thyroid nodules range from 52-97% and 26.6-83%, respectively<sup>4</sup>. American thyroid association guidelines state that the US is not sufficiently sensitive or specific to diagnose all types of malignant nodules<sup>5</sup>. Recently elastography is utilized as a novel technique to evaluate thyroid nodules which compare elasticity of nodules<sup>6</sup>. Clinically, two types of Elastography: Shear and strain are in practice<sup>7</sup>. Among them, strain elastography assesses two characters of elasticity: Firstly, colors within and surrounding the nodules are assessed, and secondly compares the region of interest with the surrounding reference area. Later, the strain ratio is calculated. A raised strain ratio

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strongly predicts malignancy<sup>8</sup>. According to a study, strain elastography found malignant thyroid tumors in 40.65% of the suspected population<sup>9</sup>. Another study reported 100% sensitivity and 80.2% of specificity of strain elastography in differentiating benign from malignant thyroid nodules<sup>10</sup>. However, the literature is divided while describing the efficiency of strain ultrasound elastography in differentiating benign from the malignant thyroid nodule. Moreover, local data is scarce on this subject. Therefore, the study was designed to evaluate the diagnostic accuracy of strain US elastography in differentiating malignant and benign thyroid nodules. Moreover, a biopsy is believed as the gold standard in diagnostic testing of thyroid nodules but given its invasive nature, there is a need to introduce a non-invasive accurate technique for detecting the nature of thyroid nodules. Therefore, the results of our will significantly assist clinicians in choosing the correct treatment plan.

## MATERIALS AND METHODS

A cross-sectional descriptive study was conducted at the radiology department of Bahawal Victoria Hospital Bahawalpur from 17<sup>th</sup> February 2020 to 17<sup>th</sup> February 2021. The study considered all the patients aged between 30-70 years, with clinically noticeable thyroid nodules and who had been diagnosed with the disease since the diagnosis of the disease. Where the participants with a record of thyroid surgery and histopathologically confirmed cases of thyroid cancer were excluded from the study. All the enrolled were asked for informed consent while ethical approval was sought from the ethical committee of the hospital. The qualified participants were enrolled through a non-probability consecutive sampling technique. Afterward, all patients underwent strain ultrasound elastography through a high-resolution unit, carrying a linear array probe. The evaluation of benign and malignant tumors was based on pre-operational definitions of two types of tumors. The findings of strain US elastography were then compared with results of histopathology testing, conducted side-by-side. Besides, baseline data included age, gender, size of the nodule, and disease duration.

SPSS (version 18.0) was used for statistical evaluation. All continuous variables were presented as mean along with standard deviation whereas categorical variables were as frequency and percentage. Considering histopathology as the gold standard, sensitivity, specificity, diagnostic accuracy, negative predictive value (NPV), and positive predictive value (PPV) of strain ultrasound elastography in terms of its differentiating capacity was calculated. The effect of confounding variables was controlled through stratification.

## RESULTS

A total of 80 patients were included in the study. The mean age of participants was  $46.5 \pm 6.21$  years. Out of 80 patients, 43 (53.7%) were male and 37 (46.2%) were female. Mean disease duration was  $8.71 \pm 4.52$  months and mean nodular size was  $4.38 \pm 1.50$  cm. Table 1 states that strain USG confirmed positivity for malignancy in 40 cases while the other 40 were regarded negative for any malignancy. In comparison with histopathology findings, 3 were found to be false-positive and 2 were false negative (Table I).

On adjusting the confounding variables, strain USG was found to be 95% sensitive, 90.5% specific, had PPV of 90.8%, NPV of 94.1%, and was 93% accurate in terms of differentiating benign from malignant thyroid tumors on comparison with histopathology.

Table II and III present the diagnostic data after stratifying it according to disease duration and size of the nodule, respectively.

**Table No.1: Diagnostic accuracy of strain accuracy as compared to histopathology**

	Positive cases as per histopathology	Negative cases as per histopathology	P-value
Positive cases as per strain USG	37 (true positive)	3 (false positive)	.001
Negative cases as per strain USG	2 (false negative)	38 (true negative)	.01

**Table No.2: Stratification of findings as per disease duration and diagnostic characteristics of strain USG**

	Positive cases as per histopathology	Negative cases as per histopathology						P-value
<b>Disease duration <math>\leq 12</math> months</b>			<b>Sensitivity</b> 94.9%	<b>Specificity</b> 90%	<b>PPV</b> 90.1%	<b>NPV</b> 94.7%	<b>Diagnostic accuracy</b> 92%	
Positive cases as per strain USG	27	2						0.01
Negative cases as per strain USG	2	30						0.01

Disease duration > 12 months			Sensitivity 100%	Specificity 91%	PPV 90.8%	NPV 100%	Diagnostic accuracy 98%	
Positive cases as per strain USG	10	1						0.02
Negative cases as per strain USG	-	8						0.01

**Table No.3: Stratification of findings as per the size of nodule and diagnostic characteristics of strain USG**

	Positive cases as per histopathology	Negative cases as per histopathology						P-value
Size of module < 5cm			Sensitivity 90.6%	Specificity 89%	PPV 88%	NPV 91.9%	Diagnostic accuracy 92%	
Positive cases as per strain USG	22	2						0.01
Negative cases as per strain USG	2	26						0.01
Size of module > 5cm			Sensitivity 100%	Specificity 92%	PPV 94.5%	NPV 100%	Diagnostic accuracy 97%	
Positive cases as per strain USG	15	1						0.01
Negative cases as per strain USG	-	12						0.01

## DISCUSSION

Thyroid nodules are prevalent worldwide; however, the prevalence rate varies in different populations and according to the method used. For instance, the prevalence is reported to be 2 to 6% by palpation, 19-35% by the US, and up to 65% according to autopsy reports <sup>11</sup>. Undoubtedly, palpation plays a significant role during physical examination but the US is mandatory for an accurate diagnosis regarding the presence of disorder <sup>11</sup>. However, it is also true that histology testing's are required to distinguish between benign and malignant nodules. In cases of non-diagnostic cytology, high-resolution thyroid ultrasonography and real-time elastography are employed for conclusive findings <sup>12</sup>. Elastography is a novel diagnostic method that compares tissue elasticity to evaluate nodules <sup>13</sup>.

Our study was based on strain ultrasound elastography. The results found that USG confirmed positivity for malignancy in 40 cases while the other 40 were regarded negative for any malignancy. In comparison with histopathology findings, 3 were found to be false-positive and 2 were false negative. Moreover, strain USG was found to be 95% sensitive, 90.5% specific, had PPV of 90.8%, NPV of 94.1%, and was 93% accurate in terms of differentiating benign from malignant thyroid tumors on comparison with

histopathology. In contrast to the 50% positivity rate in our study, another study reported a 40.65 % diagnosis rate of strain ultrasound elastography and specificity and sensitivity of 93% and 88%, respectively, in the differentiation of malignant and benign thyroid lesions<sup>9</sup>. Another study reported 100% and 80.2% sensitivity and specificity of strain elastography (SE), respectively, in differentiating benign and malignant nodules <sup>10</sup>.

However, few studies have also disregarded strain elastography in distinguishing malignant lesions. For instance, Moon et al. Evaluated 703 thyroid nodules by SE and reported inferior sensitivity (65.4%) and NPV (79.1%). Therefore, the study didn't recommend SE as an accurate diagnostic modality <sup>14</sup>. Similarly, in 2012, another study evaluated 237 thyroid nodules and concluded lower efficiency of ultrasound elastography when compared with US gray-scale <sup>15</sup>.

However, in 2013, another study used a four-grade elasticity score to evaluate 912 nodules and found a PPV of 36.1% which was insignificantly raised than micro calcification (35.9%) but significantly higher than isthmus location (16.9%) and hypo echogenicity (13.6%). Whereas, the NPV of 92.75 was higher than the compared predictors of malignancy. The results of this study are noticeable since it evaluated the highest number of nodules that have ever been systematically assessed through SE and the study also had no selection bias <sup>16</sup>.

Another aspect was discussed by Ko et al. who reported that findings of SE done by experienced physicians had higher specificity in terms of distinguishing benign lesions from malignant lesions as compared to inexperienced physicians<sup>17</sup>. In another, the highest Cohen's kappa coefficient was reported for the strain ratio (0.95) and the lowest coefficient for the echogenicity score (0.83)<sup>18</sup>.

Asari et al. explained that the underlying principle of real-time USE stating that softer tissue parts are more vulnerable to deformation than harder parts under stress. Thus, allowing a relatively accurate assessment of tissue diameter than the conventional US. The authors reported 94%, 81%, 55.2%, and 98.2% sensitivity, specificity, PPV, and NPV, respectively, of the USE<sup>19</sup>.

The present study was limited in terms of a smaller sample size and study design. Therefore, longer studies with a larger sample size are advised to compare other aspects of USE with the gold standard.

## CONCLUSION

Strain ultrasound elastography is a non-invasive technique with a considerable diagnostic accuracy of differentiating benign and malignant thyroid nodules when compared with gold-standard histopathology.

### Author's Contribution:

Concept & Design of Study: Malik Mudasir Hassan  
 Drafting: Kamran Naseem, Tanzeela Akram  
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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