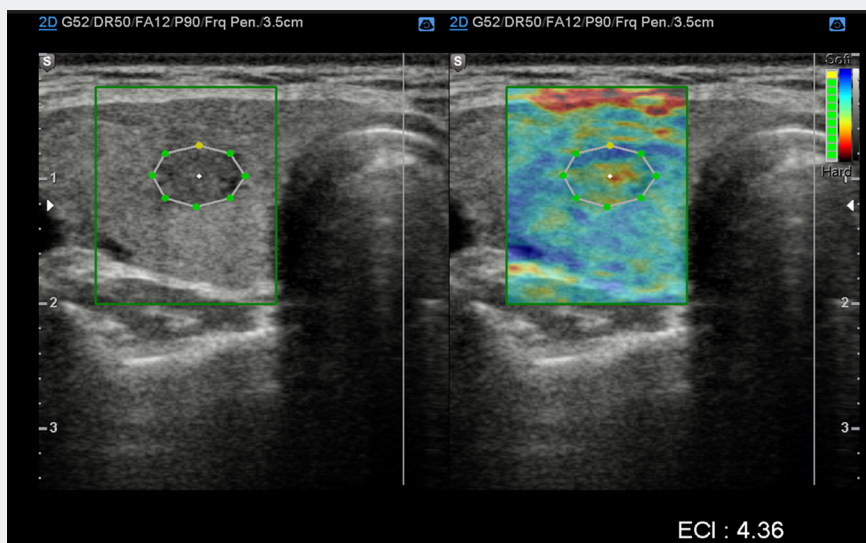# Experiences of Intrinsic Compression Ultrasound Elastography (E-Thyroid™) in Differentiating Benign From Malignant Thyroid Nodule

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"E-Thyroid effectively differentiates malignant from benign in most thyroid nodules including calcified nodule, using a validated cutoff value of ECI."

Introduction

A thyroid nodule is a very common condition which can be found among 40 to 50% of general population on ultrasound. Identification of thyroid cancer cells through fine needle aspiration (FNA) is a gold standard for diagnosis of thyroid cancer. Among all thyroid nodules, thyroid cancer occupied five to ten percent, and thus a large number of patients, even with benign thyroid nodules, are recommended to take FNA.

Although suspicious US findings can differentiate malignant nodule from benign with fair to good sensitivity and specificity, their high inter-observer variability prevents accurate diagnosis of thyroid cancer and they depend heavily on users' own experiences. Current practice especially recommends FNA if a patient is present with a calcified nodule, whether microcalcification or macrocalcification, after US examination. Thus, a non-invasive tool with high specificity is needed and should be added to routine ultrasound examination to improve diagnostic accuracy in thyroid nodule and reduce the number of unnecessary FNA.

Ultrasound elastography (USE) is an emerging non-invasive diagnostic tool based on differences of stiffness between malignant and benign lesions. Cancer shows changes of extracellular matrix with increased stiffness, which makes nodule less elastic than normal or benign lesions.[1]

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Since 2005, USE using external compression by free hands was introduced to the field of thyroid diagnosis to differentiate malignant nodule from benign,[2] but its diagnostic power has varied among studies because of lack of intra-and inter-observer agreement, subjective scoring, and biased selection of images.[2,3] Therefore, more objective and less variable USE must be implemented to obtain diagnostic reliability.

USE using carotid artery pulsation as a compression source improved intra-and inter-observer variability by removing an inherent hindrance by carotid artery pulsation and an objective scoring, based on a unique algorithm using co-occurrence matrix and an elasticity contrast within the nodule, made the users reliably obtain the degree of elasticity.[4, 5]

Methods

US and elastography examinations were performed by endocrinologists with one or two-year experience in USE, using RS80A of Samsung equipped with E-Thyroid™ software, with a 5 to 12 MHz linear transducer. To perform an elastography examination, the operator searched for a transverse plane with maximum diameter and an additional plane with different characteristics, such as echogenicity and presence of calcification, was also selected for the evaluation of elasticity. The patient was then asked to hold his or her breath for four seconds while the USE data were acquired. E-Thyroid™, a quantitative scoring method, was used to calculate elasticity contrast index (ECI). The ECI value was computed interactively and displayed on the monitor of the US machine after the nodule's boundaries were delineated by the operator. A larger ECI value suggests a stiffer nodule, indicating an increased likelihood of malignancy. The largest among multiple ECI values was selected for analysis of diagnostic accuracy.

Results

Some nodules have histological heterogeneity in nature, so initial ECI value in one axial plane obtained by the operator sometimes may not reach the value of malignancy, even though it is actually malignant (Figure 1). So, it is important to place the probe in different axial planes for repeated ECI measurements when the operator approaches a thyroid nodule with E-Thyroid™, especially when the B-mode images show suspicious findings with heterogeneous constituents. Also, in general, the highest ECI values should be counted as a representative of nodule elasticity.

One small suspicious nodule close to the carotid artery showed a low ECI value of 1.06 and was considered to be benign (Figure 2). This nodule actually turned out to be Hashimoto's thyroiditis by fine needle aspiration. However, the ECI value of nodule close to the carotid artery, which is the compression source of USE, tends to have lower ECI value than other nodules within the thyroid, like the nodule in Figure 2.

Figure 1. Axial (A) and sagittal (B) B-mode ultrasonography images showed a 6 x 7 x 8 mm sized round heterogenous hypoechoic nodule on the right thyroid lobe. (C) Initial ECI value obtained by the operator in axial view of E-Thyroid mode was 2.44. (D) However, after changing the position of probe to the different plane, ECI value measured 4.36 and this indicated malignancy (over 3.1). Post-operative pathology confirmed papillary thyroid carcinoma.

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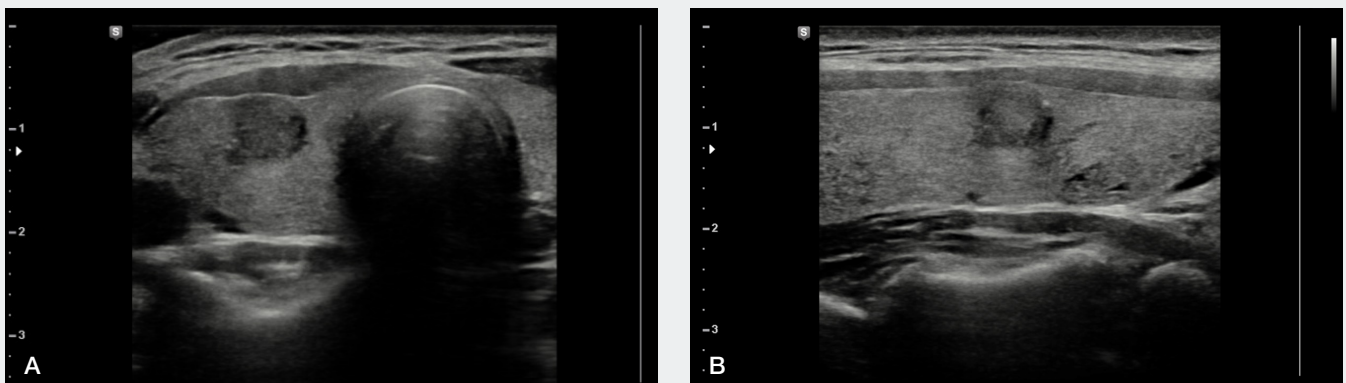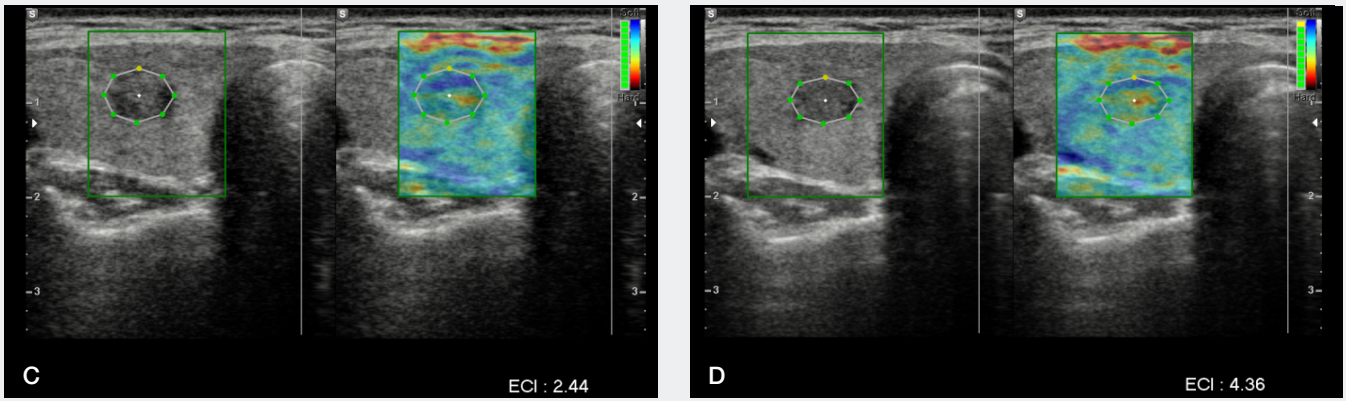
A previous study of a group of 165 patients with 154 benign and 42 malignant nodules (all papillary thyroid carcinoma), showed the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 81.0%, 63.6%, 37.8% and 92.5%, respectively, when an ECI value over 3.11 was used as a cut-off for diagnosis of malignant nodule using Accuvix XG machine with E-Thyroid™ software.[6]

Usually, most calcified nodules are considered to be potentially malignant regardless of the type of calcification present (macrocalcification or microcalcification). For 65 nodules with calcification, 45 benign and 20 malignant nodules, 23 benign calcified nodules which accounted for more than fifty percent of all benign calcified nodules, were correctly classified by E-Thyroid™, with an ECI value less than 3.11. In contrast, only 4 (8.9%) were correctly classified by B-mode US analyzed by a highly experienced radiologist.[6] Therefore, benign calcified nodules could be effectively differentiated from malignant calcified nodules by E-Thyroid™.

Figure 2. (A) B-mode images of the right lobe showed a 4 x 5 x 8 mm sized, ovoid to round, well-defined speculated, homogeneous, hypoechoic nodule close to the carotid artery, indicating suspicious malignant feature. (B) Doppler US image showed peri-nodular color pattern. (C) The ECI value of this nodule was 1.06. The fine needle aspiration confirmed Hashimoto's thyroiditis and the nodule turned out to be benign.

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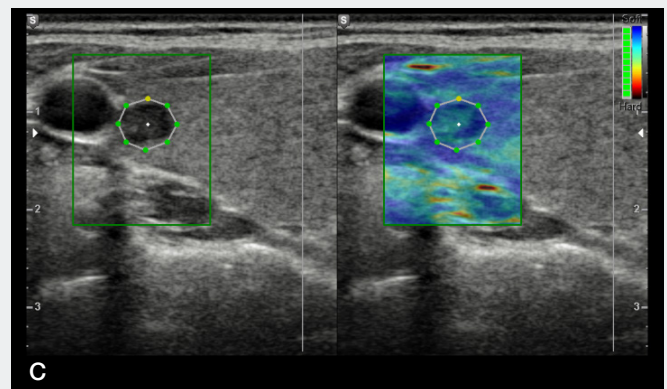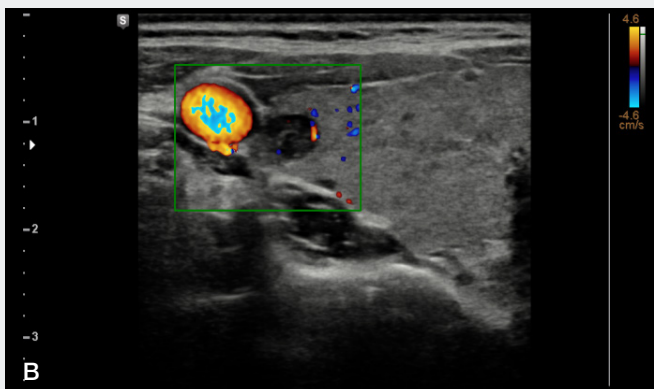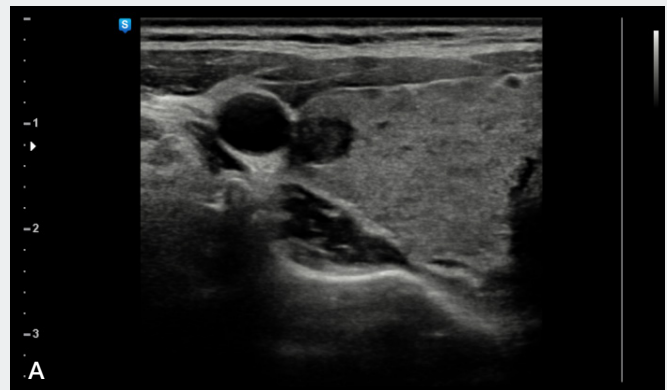
Discussion

The USE using E-Thyroid™ and resulting ECI values is valuable in that 1) it uses carotid artery as a compression source, which has been a major irritant in obtaining the elasticity data from nodule when external compression is used, 2) it shows intuitive digits and objective scoring system in elasticity measurement, and 3) it proved to be, therefore, less variable in intra-observer and inter-observer agreement.[6]

Our recent small data showed the diagnostic accuracy of US thyroid elastography was significantly associated with a nodule's distance to the carotid artery (our unpublished data). That is, a thyroid nodule which is very close to the carotid artery has a tendency to have lower ECI value than other nodules inside the thyroid lobe. Therefore, the US elastography users should also keep in mind that ECI value may have unexpected values if a thyroid nodule is too far from or too close to the compression source (i.e. carotid artery). Even though the software algorithm of US machine can be adjusted to address this issue, nodules with exceptionally low ECI values indicating benignity must be considered for repeated measurements.

Current clinical practice along with a few previous studies and experiences with calcified nodules suggest not to use elastography on calcified nodule because of false positive nature of calcification, which makes the nodule stiffer.

In fact, the amount of calcification did have a direct correlation to the value of ECI; the more calcification presented, the higher the ECI value.[6] However, according to this study, some proportion of nodules showing low ECI value could be safely categorized as benign nodules without FNA.

Conclusion

The USE using E-Thyroid™ effectively differentiates malignant from benign in most thyroid nodules including calcified nodule, using a validated cutoff value of ECI. However, it should also be kept in mind that the extreme location of a nodule in the thyroid can affect the results as it will interact differently with the compression source (i.e. carotid artery).

Supported Systems

- RS80A
- RS80A with Prestige
- WS80A
- WS80A with Elite
- Accuvix A30

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