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Review Article

Thyroid Ultrasound Elastography: A Promising Undeniably Diagnostic Tool for Predicting the Risk of Malignancy

MH Rahman

Abstract:

Thyroid disease is of common occurrence, especially in iodine deficient areas. Thyroid nodules are common findings in the general population. It is important to distinguish the subset of thyroid nodules that are malignant, as morbidity and mortality from thyroid cancer increases with disease stage. B-mode ultrasound features are initially used to select thyroid nodules for FNA. Although FNA is considered the gold standard for diagnosis, it is yet imperfect as up to 15-30% of samples are considered non-diagnostic or indeterminate. Thyroid ultrasound elastography(USE) is a noninvasive method of assessing thyroid nodules that provides complementary information to B-mode ultrasound and FNA. The combined use of thyroid USE with B-mode ultrasound may improve the ability to discriminate benign from malignant thyroid nodules and reduce the number of needed FNAs. Thyroid USE may also aid with the difficult problem of distinguishing between malignant and benign follicular neoplasm.The elastic properties of tissue have always been of interest in clinical practice. In the past, the identification of structures that were stiffer on physical palpation would raise the suspicion. With the development and advancement of medicine, there proved to be a true correlation in the prediction of malignancy of lesion: malignant disease tends to stiffen the affected tissue, either by increased cell proliferation or fibrosis. Palpation is the oldest method for the detection of thyroid nodules, which if informed by the knowledge that malignant thyroid lesions tend to be much harder than benign ones. Palpation is dependent on the size, location and skill of the physician. Nodules are very small or located in deep regions; there detection by palpation is difficult or even impossible. Although malignant lesion differs in terms of elasticity, it may not have echogenic properties, preventing its detection by conventional ultrasound. Imaging that indicates the stiffness or deformation related to their structural formation.

Key words: Thyroid, Elastography, Ultrasound, Thyroid nodule, Malignancy.

Introduction:

Thyroid pathology including thyroid nodules and diffuse thyroid disease represents often a diagnosing challenge for clinicians. Thyroid nodules are a common finding in the general population, present in up to 67% of adults by high resolution B-mode ultrasound and in 50% of pathologic examinations at autopsy[1-3]. It is important to distinguish the subset of thyroid nodules that are malignant, as morbidity and mortality from thyroid cancer increases with disease stage. Despite the high prevalence of thyroid nodules, only 4-8% of nodules sampled by fine needle aspiration (FNA) are found to be malignant[1,4]. B-mode ultrasound features are initially used to select thyroid nodules for FNA. Features such as speculated margins, taller than wide shape, marked hypoech genicity, and micro calcifications are suggestive of malignancy[5]. FNA is then typically used for confirmation of malignancy.

1. Dr. Hafizur Rahman MBBS, M.Phil (Nuclear Medicine), Chief Medical Officer & Professor, Institute of Nuclear Medicineand Allied Sciences, Faridpur.

Address of correspondence :
Dr. Hafizur Rahman MBBS, M.Phil (Nuclear Medicine), Chief Medical Officer & Professor, Institute of Nuclear MedicineAnd Allied Sciences, Faridpur. Mob: +88-01711235280,
E-mail: mhrn08@yahoo.com

Although FNA is considered the gold standard for diagnosis, it is yet imperfect as up to 15-30% of samples are considered non-diagnostic or indeterminate[6]. Repeat FNA provides conclusive results in the majority of these nodules, but inconclusive results are again obtained for 9.9-50% of nodules with initial non-diagnostic cytology and 38.5-43% of nodules with initial in indeterminate cytology[2]. While some inconclusive FNA results are attributable to technical factors such as insufficient sampling, a subset of these results are due to the less easily remedied dilemma of follicular neoplasm, which can compromise 6.7% of total FNA results or 22% of the inclusive FNA results[4]. Follicular neoplasm is malignant 15-30% of the time, requiring a total thyroidectomy, but malignancy is difficult to determine by FNA, core biopsy, or even frozen section analysis[7].

Palpation is a practical diagnostic technique, especially for thyroid evaluation, and the presence of a hard thyroid nodule is associated with an increased risk of malignancy. However, this assessment is subjective and relies on the experience of the examining clinician. Small and deep nodules and those contained in multinodular goiters cannot be palpated reliably. The novel technology of ultrasound elastography has been referred to as electronic palpation because it provides a reproducible assessment of tissue consistency. Ultrasound elastography was first proposed in 1991 by Ophir, and was first used for thyroid applications in 2005 by Lyshchik. Moreover, the use of shear-wave elastography for diagnosing thyroid nodules was first reported in 2010 by Sebag. The stiffness of tissue is determined by the structural properties of its matrix. Pathological changes, such as the presence of a tumor or inflammation, alter the tissue composition and structure and increase the lesion stiffness.

Thyroid nodules are found and pose a clinical dilemma, because only a few nodules harbor malignancy, while the majority of nodules are benign. The standard work-up of nodules consists of an ultrasound examination and fine-needle aspiration, but both have limitations. In the long-lasting search for suitable non-invasive diagnostic methods, ultrasound elastography has emerged as an additional tool in combination with ultrasound and FNA for thyroid nodule differentiation. The 2015 American Thyroid Association management guidelines stated that US elastography may be helpful tool for preoperative accurate risk assessment in patients. Nevertheless, it should not modify the recommendation made based on the gray-scale US evaluation. The 2016 American Association of Clinical Endocrinologists, American College of Endocrinology, andAssociazone Medici Endocrinologi Medical guidelines stated that US elastography provides stiffness information, which is complementary to grayscale findings, particularly in nodules with indeterminate US or cytological characteristics. Moreover, FNA is recommended for nodules with increased stiffness, an intermediate-risk factor. In addition, some specialized guidelines focusing on US elastography have been developed. The 2013 European Federation of Societies for Ultrasound in Medicine and Biology guidelines stated that US elastography could be used to guide the follow-up of lesions diagnosed as benign at FNA. In 2017, the World Federation of Societies for Ultrasound in Medicine and Biology released a guideline for the use of elastography techniques for the thyroid, with a detailed description of the procedure and its reproducibility, results, and limitations. US elastography examinations of the thyroid are easily integrated into conventional US examinations with many high-end systems. US elastography has the potential to distinguish benign from malignancy nodules, offering non-invasive complementary information to conventional US. The main role of US elastography is to indicate which nodules may be followed up without resorting to FNA or surgery because of its high NPV. It may be particularly useful in patients who have no diagnostic or indeterminate FNA cytology results. Ultrasound elastography might be used to guide the follow-up of lesions negative for malignancy at FNA. Ultrasound elastography techniques measure the elasticity of tissue in order to produce qualitative and quantitative information that can be used for diagnostic purposes in various diseases. The measurements are acquired in specialized imaging modes that can detect tissue stiffness in response to an applied mechanical force. In general, ultrasound elastography techniques can be divided into compression imaging methods, which use internal or external deformation stimuli, and shear wave imaging methods, which use ultrasound-generated shear wave stimuli.

Principle and Technique of Ultrasound Elastography:

Basically, two main approaches for elastography of the thyroid are used in clinical practice: strain and shear wave elastography[8-11]. Most of the times, offline analysis of the information is performed in experimental, work-up in progress models or on prototypes while machines for clinical applications use online signal processing. Strain elastography(SE) assess the elastic properties of tissue by analyzing tissue strain that is tissue deformation parallel to the direction of the exploratory force. Deformation may be induced by a pure mechanic force or by ultrasound. SE using mechanic force, SE with external force, Qualitative SE with external force, Semi quantitative SE with external force, SE with internal forceis used. SE using ultrasound as displacement inductor- this technique, labeled dynamic, is named acoustic radiation force impulse (ARFI) imaging and is commercially implemented by Siemens. Focused US beams may in duce axial displacement of the tissues with a few microns[8]. Therefore, no external force is applied. The result is either a single image or video sequence.

Shear-wave elastography(SWE) assess the elastic properties of tissue by analyzing the displacement of shear waves, perpendicular to the direction of the exploratory force. The information represents, essentially, the shear-wave speed. Mechanically induced external waves of excitation, often employed in liver diagnosis, are not suited for thyroid assessment. Only focused ultrasound induced shear waves are exploited for this purpose, the technique being dynamic. The information may be purely numerical or it may be represented as colors superimposed on the gray-scale imaging. Shear-wave speed measurement-ARFI quantification or point shear-wave elastography measures the average speed of the shear wave inside a region of interest (ROI). Shear-wave speed imaging-generically named shear-wave elastography, offers the information in colors.

Limitations of Thyroid Ultrasound Elastography:

Manual external compression in strain imaging leads to operator dependent variability. Nonlinearity of tissue stiffness results in greater stiffness measurements at high degree of compression. Fibrosis within both benign and malignant nodules can increase stiffness[12]. Thyroid nodules greater than 3 cm in diameter may be unable to be adequately compressed in strain imaging. Ultrasound elastography does not give meaningful information with nodules that have cystic components, as fluid movement does not reflect stiffness of the solid component of interest[13]. Ultrasound elastography cannot be performed no nodules with a calcified shell because the sound waves do not penetrate the calcifications to evaluate the central non-calcified portion of interest[14]. Coarse calcifications in benign thyroid nodules can lead to misleading measurements indicating increased stiffness, which would otherwise be characteristic of malignancy[7].

Conclusion:

Thyroid pathology including thyroid nodules and diffuse thyroid diseases represents often a diagnosing challenge for clinicians. Ultrasound, although highly accurate in identifying thyroid nodules and diffusethyroid diseases, is still not sufficiently accurate to evaluate them. Ultrasound elastography has been introduced in order to further increase ultrasound accuracy in many fields and eventually for thyroid disease. Elastography has proven useful as an ancillary tool for risk stratification in thyroid nodules. The evaluation of the technique has improved its reproducibility, and recent studies shown that 2D-SWE is a promising technique for the identification of malignant nodules, either before FNAB or after an indeterminate cytological result. Elastography is undeniably a major technological advance in thyroid imaging in recent years. The anatomic characteristics of thyroid and the frequency of nodules in the thyroid make it an ideal organ for this technique. Elastography should not be considered as an alternative to conventional ultrasound, but like an additional parameter that optimizes the ultrasound imaging.

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