What is the contribution of elastography to thyroid nodules evaluation?

Quelle est la contribution de l’élastographie dans l’évaluation des nodules thyroïdiens ?

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Résumé

La mesure de l’élasticité des nodules thyroïdiens par élastographie a été récemment proposée dans l’évaluation des nodules thyroïdiens, un index d’élasticité élevé étant corrélé avec la nature maligne des nodules. Les objectifs de cette revue sont de décrire les différentes techniques d’élastographie, d’en montrer les avantages et les limites et de faire le point sur les résultats publiés par les 11 équipes actives dans ce domaine. Des études complémentaires, de préférence multicentriques, doivent être effectuées avant de déterminer la place de l’élastographie dans l’évaluation des nodules thyroïdiens par rapport à la cytoponction à l’aiguille fine qui est l’examen de référence : diminution du nombre de cytoponctions ou au moins sélection du ou des nodules ou de la zone nodulaire à ponctionner.

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Abstract

The determination of elasticity index by elastography has been recently proposed in the evaluation of thyroid nodules, since malignancy is correlated with stiffness of the nodules. The aim of this report is to give an overview on different techniques and results reported by eleven groups active on the field. Advantages and limitations of elastography are also discussed. In our opinion, further studies, preferentially multicentric, are necessary before being able to conclude about the place of elastography in thyroid nodules evaluation, versus fine-needle aspiration cytology (FNAC), the gold standard. Indeed, elastography could reduce FNAC or at least allow to select nodule’s (or nodular zone’s) for aspirations.

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1. Introduction

Thyroid nodules that can be palpated are extremely common, with an estimated prevalence that ranges between 5.3% in women and 0.8% in men in the Whickham survey [1]. The use of ultrasound (US) imaging raises ten times this percentage of the general population with the detection of infracentimetric-nodules, this percentage increasing with age. The majority of thyroid nodules are benign (colloid nodule, follicular adenoma, cysts and thyroiditis), but 5 to 10% are malignant [2].

Clinical examination and thyroid US are the first-line procedures to help differentiate benign and malignant nodules. US features associated with malignancy include microcalcifications, hypoechogeticity, intranodular vascularity, irregular margins and absent halo sign. When these features have been combined, their specificity increases, but their sensitivity...
decreases [3]. Fine-needle aspiration cytology (FNAC) is currently the best diagnostic procedure to identify malignant thyroid tumours. In expert centers, FNAC provides useful results in 65–75% of examined nodules. Approximately 60–70% of aspirates are cytologically benign and 5% are positive for carcinoma. However, 15–25% are indeterminate or suspicious and 5-15% are inconclusive limiting the diagnostic power of FNAC [4].

Other limitations of FNAC are related to the skill of the operator, the expertise of the cytologist and the difficulty in distinguishing some benign follicular adenomas from their malignant counterparts [5].

Other ways to evaluate thyroid nodules have been proposed including molecular analysis of thyroid aspirates under development in a few centers and elastography, a technique now available that uses ultrasound to assess tissue elasticity. Indeed stiffness is usually correlated with malignancy and benign lesions are softer [6]. Different techniques of elastography have been applied to the evaluation of breast, liver, prostate and also thyroid lesions. In this report, we describe briefly these different techniques, the results published by eleven different groups and we discuss the advantages, the limitations and the place of this new diagnostic tool in the evaluation of thyroid nodules.

2. Thyroid elastography

US elastography is a newly developed technique that evaluates the degree of distortion of a tissue under the application of an external force; it is based upon the principle that the softer parts of tissues deform easier than the harder parts that allowing an objective determination of tissue consistency. Techniques of elastography applied to thyroid nodules differ according to the type of external force.


In this process the examined tissue is subjected to gradual manual compression with the US transducer. Tissue’s strain images are constructed from measurements of local displacements induced by the compressive force applied to the tissue surface. The displacement fields are estimated by tracking the echo delays in segmented waveforms recorded before and after the quasi-static compression. The US elastography display presents a color “elastogram” superimposed on the B-mode image.

Two different methods have been used:

- spatial correlation for Lyshchik et al. [7] which requires off-line strain imaging reconstruction;
- a dedicated software (combined autocorrelation method) provided by Hitachi Medical, which is more simple and fast [8–16]. The technique requires no more than 3–5 minutes of additional time examination to conventional US [10].

First introduced in thyroid nodules evaluation, RTE has been used in nine out of 11 studies. The main limitation of RTE is that the extent of nodule compression influences the elasticity score. There is no objective way to measure pressure during US elastography and strain variations due to changes in compression are unavoidable. Therefore, it is difficult to apply exactly the same level of pressure during examination by different radiologists. Another pitfall of RTE is the existence of carotid artery pulsations which may generate compression-decompression movements and create interfering elastographic images in nodules in close vicinity to carotid artery.

2.2. Carotid artery pulsations [17]

In this technique, the pulsatility of the carotid artery represents the thyroid compression source for elastography. Multiple scans are obtained and the corresponding strain images are generated off-line. The processing time for these data sets is approximately 24 hours [17].

2.3. Shear wave in the shear wave elastography (SWE) [18]

This technique was described in detail by Bercoff et al. [19]. It consists in the generation of a remote radiation force by focused ultrasonic beams. Several pushing beams at increasing depths are transmitted to generate a quasi-plane shear wave frame that propagates through the whole imaging area. After generation of this shear wave, an ultrafast echographic imaging sequence is performed to acquire successive radio frequency dots at a very big frame rate (up to 20,000 frames per second). Based on Young’s modulus formula, the assessment of tissue elasticity can be derived from shear wave propagation speed. A color-coded image is displayed depending on stiffness of the tissue from blue (soft) to red (hard). Quantitative information in the studied area is also delivered; elasticity index (EI) is expressed in kilo-Pascal (kPa). Both steps of SWE are achieved using a linear US probe without requiring any pressure by the operator.

3. Results

Since the first report by Lyshchik et al. [7], several groups have evaluated the usefulness of elastography to discriminate benign and malignant nodules. Recent meta-analysis based on seven RTE [7–13] and one elastography based on carotid artery pulsations [17] studies indicates that this technique can be used with a high specificity and a good sensitivity. The meta-analysis included 639 thyroid nodules of which 381 were referred to surgery and 248 characterized by FNAC. One hundred and fifty-three nodules were malignant: 135 papillary carcinomas, nine follicular carcinomas, six medullary carcinomas, two poorly differentiated metastatic carcinoma and one non-Hodgkin carcinoma. The mean sensitivity and specificity for the diagnosis of malignant thyroid nodules were 92% (confidence interval 88–96) and 90% (confidence interval 85–95), respectively, 16/153 thyroid carcinoma were overlooked by US elastography: 10/135 papillary carcinomas, 4/9 follicular carcinomas and 2/2 poorly differentiated carcinomas.

The conclusions of the meta-analysis are highly favorable [20]. Four more studies are now available, three with RTE
[14–16] and one with SWE [17]. Similar data have been obtained by the group of Vorlander et al., in a prospective study including 309 patients. These authors classified the nodules in three groups:

- softer (96 nodules, all benign);
- intermediate (15 carcinomas/132 nodules);
- harder (35 carcinomas/81 nodules).

This study includes six follicular carcinomas in the intermediate and harder groups but softer than papillary carcinomas [14]. Similarly, Gietka-Czernel et al. reported a sensitivity of 86% and a specificity of 97% in the analysis of 71 nodules [15].

In contrast with the optimistic tone of these reports, sensitivity and specificity were much lower, 75% and 64% respectively, in the study of Kagoya et al. [16].

Promising results have been obtained by Sebag et al. with SWE in 146 nodules, (29 malignant), from 93 patients. The sensitivity for detecting malignancy was 81.5% and specificity 93.9%, the latter value increasing to 97% after the addition of US features, (hypoechogenicity, microcalcifications, intranodular vascularity), to elastigraphy data [18].

4. Discussion

A number of studies published since 2005 uniformly suggest that elastography of thyroid nodules is a satisfactory technique, easy to perform with a good sensitivity and specificity to discriminate between benign and malignant nodules. However, Hegedus in one recent editorial turned one’s attention to the weakness of all these studies:

- small sample sizes, focus on patients with solitary nodules;
- inadequate account of selection criteria [21].

Besides, most studies have been performed with RTE, intra- and inter-reproducibility is not available in the reports. In a recent study, there was no inter-observer agreement in evaluation of thyroid nodules with RTE [22]. Besides, the trials suffered from methodological failures (small sample sizes, inadequate selection criteria) and locked informations about nodules consistence, size, number and topography. Serious care should also be paid to these nodules characteristics and follicular carcinoma.

4.1. Nodules characteristics

Both RTE and SWE are unreliable in the evaluation of cystic nodules; they are not helpful in the management of these lesions with a very low risk of cancer. Until now, no data are available yet on mixed thyroid nodules.

Significant artefacts are measured in nodules with coarse or rim calcifications. In RTE with probe compression, there was no tissue strain deformation and nodules with calcified shell were excluded from US elastography [10]. In shear wave elastography, the US beam crossing of the calcifications is uncertain [18]. These dystrophic calcifications have been documented of non-diagnostic value in the evaluation of thyroid nodules [23].

Recently, several reports have suggested a link between these calcifications and malignancy [24], the risk of malignancy being doubled [25]. In a retrospective study based on 2122 thyroid nodules Lu et al. found macrocalcifications in 213 nodules, 19.3% of which being malignant [26]. Clinical and US features may be suggestive of malignancy:

- their detection in solitary nodule or in less than 40 year-old-patients [27];
- interruption and thickening of the calcifications [28,29].

RTE is influenced by the volume, topography and number of thyroid nodules. Indeed, in nodules larger than 3 cm diameter, elastography with external compression of the whole nodule may not be obtained [29]. In large nodules, greater than 4 cm diameter, the accuracy of FNAC for diagnostic of carcinoma is not satisfactory [30] SWE may be more efficient in their evaluation since they allow targeting of FNAC. Besides, no information is available at the moment about the lower diameter of thyroid nodules that can be evaluated by either RTE or SWE. RTE is also limited in the evaluation of multinodular goiters because nodules must be clearly distinguishable one from the other. SWE may overcome these limitations of real-time elastography based on probe compression. This is of major interest because the group of patients with multinodular goiters represent up to 40% of all patients referred for thyroid nodules. The risk of cancer per patient in this group has been appreciated either lower [31,32] or equal [25] to that in the group of solitary nodules. The accuracy of RTE may also be altered if nodules are close to the carotid artery because arterial pulsation may create elastographic images and therefore alter the adequate acquisition and accurate interpretation of the data [29].

4.2. Subtype of thyroid carcinoma

In the meta-analysis of Bojunga et al. [20], false-negative results were observed in 10/135 (7%) of the papillary carcinomas and 4/9 (44%) of follicular carcinomas. The correct diagnosis of this subtype of carcinoma may be a difficult problem even at the histopathology level. Their gross anatomy and cellular patterns overlap with those of benign nodules. Sonographic differences between follicular adenomas and carcinomas have not been fully established [33]. Indeed, previous reports on the US features of follicular neoplasm showed variable results. Several features have been reported: presence of microcalcifications, hypoechogenicity, irregular margins [34], intranodular vascularity (Doppler patterns 3 or 4) [35].

Seo et al. on the basis of a retrospective study have reported that iso-hypoechogenicity and microcalcifications or rim calcifications are more common in follicular carcinomas than in follicular adenomas [36]. However, in one prospective study, the sensitivity of the US characteristics was found to be 86.5% for non-follicular neoplasm and 18.2% for follicular carcinomas [37]. Further studies involving more cases of follicular adenomas and carcinomas need to be done to explicit the role of
elastography in their evaluation.

5. Conclusion

Based on data from the literature between 2005 and 2010, it appears that elastography may be useful in the management of thyroid nodules. The finding of high elasticity index helps to direct FNAC more appropriately with the selection of nodules or nodular zone for aspiration. In contrast, low elasticity index is in favor of benign lesions and may reduce FNAC. Elastography may be useful in the clinical management of patients bearing nodules with non-diagnostic or indeterminate FNAC [38]. Further studies focused on nodules characteristics (size, number, topography, ...), and more cases of follicular carcinomas need to be done before broadening the use of elastography in thyroid nodules evaluation. Besides, careful evaluation of nodules with conventional US is absolutely necessary first to exclude cystic and calcified nodules from elastography, second to improve elastography performance as suggested by Sebag et al. [18]. In addition, the significance of elasticity index should be approached with the analysis of its relationship with pathological characteristics of surgical pieces.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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