Elastosonography of thyroid lesions

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Résumé
Élastographie ultrasonore des lésions thyroïdiennes
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Si l'échographie est une méthode de choix dans le diagnostic des lésions thyroïdiennes, les limites en termes de caractérisation imposent de recourir à une cytoponction afin de pouvoir décider de la conduite à tenir. La disponibilité de méthodes ultrasonores complémentaires comme l'élastographie peut affiner la caractérisation des nodules et de ce fait aider à mieux orienter la prise en charge.

Matériels et méthodes : Quatre-vingt-seize patients (11 hommes et 85 femmes ; 58 +/- 24 ans) adressés pour cytoponction de 108 nodules thyroïdiens de taille comprise entre 9 et 32 mm non majoritairement kystiques ont bénéficié d’une échographie conventionnelle puis d’une étude élastographique. Les résultats de l’élastographie ont été confrontés aux résultats de la cytoponction en prenant en compte le diagnostic proposé à savoir : caractère malin suspecté, caractère bénin suspecté, douteux, inclassable.

Résultats : Les lésions se classaient en 95 nodules à caractéristique molle (classes I et II) et 13 nodules à caractéristique dure (classes III et IV). Aucune lésion de type cancer n’a été retrouvée parmi les nodules des classes I et II alors que six cancers étaient détectés au sein des nodules de classes III et IV. Par ailleurs, la cytoponction de cinq nodules des classes I et II et de deux nodules des classes III et IV ne présentait pas les critères d’interprétation suffisants en terme de cellularité.

Conclusion : L’élastographie ultrasonore en temps réel semble être un complément intéressant de l’échographie conventionnelle réalisée pour les nodules thyroïdiens permettant de sélectionner des patients à haut risque de lésions néoplasiques pour lesquels un diagnostic histologique précis et/ou une surveillance plus grande seraient reçus.


Abstract
While ultrasound is the imaging modality of choice for diagnosis of thyroid lesions, characterization remains limited and tissue diagnosis frequently is required for management. The availability of additional tools such as elastography may improve lesion characterization and direct management.

Materials and Methods: A total of 96 patients (11 males and 85 females; 58±24 years) referred for fine needle aspiration (FNA) of mainly solid thyroid nodules 9-32 mm in diameter underwent conventional US and elastosonography. Results on elastography were correlated with histological results from FNA and classified as follows: suspected malignant lesion, suspected benign lesion, suspicious, indeterminate.

Results: The nodules were classified as follows: 95 nodules were soft (classes I and II) and 13 nodules were hard (classes III and IV). No cancers were detected in class I and II lesions and 6 cancers were detected in class III and IV lesions. FNA provided insufficient cellular material for diagnosis in 5 class I-II nodules and 2 class III-IV nodules.

Conclusion: Real-time elastosonography may be a useful adjunct to conventional US in the evaluation and characterization of thyroid nodules allowing identification of patients at high risk of malignancy for whom tissue diagnosis and/or close follow-up is required.

Key words: Elastography. US. Thyroid.


Sonography (US) is the imaging modality of choice to evaluate the thyroid gland, obtain measurements, and detect nodules. The significant improvements in both spatial and contrast resolution of current US units, due to the routine use of high-frequency transducers, has markedly improved the ability to detect nodules and characterize their echotexture. While the presence of microcalcifications, marked hypoechogenicity, irregular margins, and the absence of a hypoechoic halo around the nodule are US features of malignancy (1), uncertainties remain for lesion characterization that frequently require FNA or biopsy for definitive diagnosis. In patients with no suspicious US feature, the availability of a simple technique to determine if tissue diagnosis is required or not would be valuable given the high frequency of thyroid nodules in the general population, and low number of thyroid malignancy.

As such, it would appear to be important to have a technique that would complement conventional US findings and provide objective data to further characterize nodular lesions of the thyroid to reduce the number of biopsies and prevent unnecessary surgery. Evaluation of tissue deformability could provide valuable information given the reported differences in tissue characteristics between benign pathology that is soft and malignant pathology that is hard. Lyschik, et al. (2) demonstrated significant differences in the stiffness between normal thyroid tissue and thyroid tumors with mean values of elastic...
moduli of 10±4.2 kPa for normal thyroid tissue and 63.3±56.8 kPa for papillary carcinoma. Different techniques have been proposed to perform tissue elastography with X-rays, US and MRI (3-12). The US technique was first developed in the 1970’s but could only be truly developed in the 1980’s after B-mode sonography became available. It corresponds to an objective measurement of the subjective evaluation performed by clinicians when palpating the thyroid gland. Elastography is an objective representation from the mechanical palpation of a tissue of interest, with an image showing data with regards to the elastic modulus of the tissue (Young’s modulus). This technique was proposed to evaluate multiple organs, including breast, prostate, and liver, and, to a lesser extent, the thyroid (5, 6, 14-19).

Methods

Examination protocol

The examinations were performed using Hitachi’s Elite Doppler ultrasound unit with a 13 MHz L54M transducer. A standardized manual palpation scale, grades 1 to 4, controlling the degree of compression applied by the operator was used to avoid insufficient or excessive compression, which would alter results. Radiofrequency signals were acquired during the tissue compression-decompression cycle allowing comparison of signals obtained in similar planes for the target tissue. An online decorrelation algorithm was used to then obtain correlation data of signals during tissue deformation as a representation of tissue deformability. A color-coded image from blue (hard) to red (soft) showing tissue stiffness was generated and displayed next to a real time US image of the target tissue.

Phantom Validation

The protocol was validated using the breast elastography phantom CIROS 059 (CIROS USA) containing several solid masses 3 times stiffer than background tissue. Lesions 5-10 mm in size were evaluated with the proposed protocol in order to validate the examination protocol and assess lesion detection with the elastography mode. The phantom study revealed that nodules 4.5 mm in diameter or larger were more clearly depicted compared to conventional US due to the high contrast. Smaller nodules could not be detected. The smallest nodules in our phantom corresponded to our detection threshold. The visibility of phantom nodules was superior to B-mode US in all cases.

Clinical Study

Ninety-six consecutive patients, with a total of 108 nodules, referred for FNA of mainly solid thyroid nodules underwent conventional US for biometric and morphological characterization followed by elastography. The nodules ranged between 9 and 32 mm in size. Fifty-two percent involved the right thyroid lobe and 48% the left thyroid lobe. Ninety-four percent were solid while 6 nodules had a cystic component corresponding to less than 30% of the size of the lesion. Doppler signal was present at the periphery of 85% of nodules, and at the center of 22% of nodules.

After consent was obtained, elastography was performed. A series of 8 compression-decompression cycles were performed using the compression scale available on the unit. Only the cycles with compression values of 2 or 3 were considered. Color-coding of elastographic data was classified into 4 grades as follows:
- grade I: uniformly soft (homogeneously green);
- grade II: soft with presence of very soft peripheral zones (green with peripheral red color-coding);
- grade III: heterogeneous with soft and hard zones (areas of green and blue color-coding);
- grade IV: uniformly hard (mainly blue color-coding).

Results from elastography were correlated to results from FNA performed in all patients according to the recommendations by the National Agency for Accreditation and Evaluation in Health (ANAES) based on the presumptive diagnosis: malignant, benign, insufficient, and indeterminate.

Patients with malignant or indeterminate lesions on FNA underwent surgery. Patients with insufficient material underwent repeat FNA.

Results

All 96 patients underwent elastography without difficulty or discomfort. The examination time was less than 3 minutes per nodule. A total of 95 nodules were classified as grade I and II (88%) (fig. 1 to 3) and 13 nodules as grade III and IV (12%) (fig. 4 and 5). Nodules classified as grade I and II showed no malignancy. Of nodules classified as grade III and IV, 6 were malignant and 2 were indeterminate, corresponding to 62% of nodules in these groups. Cancers included 3 papillary carcinomas, 9 to 22 mm in size, 2 medullary carcinomas (13 and 15 mm in size) and 1 follicular carcinoma (16 mm). One of the indeterminate nodules was a microfollicular lesion and the other one was benign.

FNA provided material with insufficient cellularity for 5 grade I and II nodules and 2 grade III and IV nodules. Repeat FNA at six months provided sufficient material for diagnosis in six cases, all benign lesions, and was again insufficient in one case.

Discussion

The availability of a reproducible method complementing conventional Doppler US evaluation of thyroid nodules and allowing improved characterization of lesions is a significant advance for appropriate planning of FNA or surgery. Unlike CT and MRI which are more expensive modalities with limited usefulness for the evaluation of thyroid nodules, US elastography is easy to perform following conventional US evaluation of thyroid nodules and could be advantageous and easily implemented in centers with expertise in the evaluation and management of thyroid pathology.

The possibility for real time correlation of US and elastography findings is mandatory to ensure adequate interpretation of collected elastographic data of target nodules and identify pitfalls that could cause the studies to be technically inadequate (4, 14-16).

A known pitfall of free hand elastography is the possibility of lateral displacement of tissues introducing errors in stiffness measurements. This is not a limiting factor for thyroid imaging be-
cause the regional anatomy allows satisfactory probe positioning. The position of the nodule relative to the carotid artery has been more problematic due to movements. Arterial pulsations may generate compression-decompression movements that may in turn create elastographic images. The carotid artery pulsation has been used in other protocols as the compression source for thyroid elastography (20, 21). It is thus important to be aware of this phenomenon to ensure technically adequate acquisition and accurate interpretation of elastographic data. Also, nodules located anterior to the common carotid artery may not be adequately compressible due to the absence of a solid structure to compress against, hence falsely suggesting nodular stiffness. Nodule diameter larger than 30 mm may also be a limitation since it may not be possible to achieve adequate compression and simultaneous evaluation of normal tissue and nodule (fig. 6).

The use of elastography for thyroid nodules has been less extensively developed than for other tissues such as breast, prostate and liver, probably because of the greater ease of implementation for breast and prostate and need for an alternative to biopsy for liver lesions. In addition, the presence of a rigid structure posterior to the target tissue allowing adequate compression, especially for the breast, has had a great impact on the acquisition of satisfactory elastographic data. Tardivon et al. (15) have reported a high specificity of US elastography (86.9%) for the diagnosis of breast cancer compared to the BI-RADS classification (47.5%) even though the sensitivity was reduced (78.7% versus 98.4% respectively). The proportion of malignancy is higher for breast nodules compared to thyroid nodules (5%) partly explaining the heightened interest in developing complementary techniques for non-thyroid lesions. While it remains true that FNA is a first line procedure in the evaluation of thyroid nodules, a number of FNA are non-diagnostic (less than 8% in experienced hands) and the number of surgical procedures remains high. The availability of a simple non-invasive easily quantifiable technique could be valuable to identify patients requiring further work-up or only follow-up. Our results indicate that US elastography could be performed at the time of conventional thyroid US prior to FNA, without added risk to patients. Our results show that hard nodules on elastography are strongly associated with the likelihood of finding malignancy on FNA. The increased stiffness of malignant thyroid nodules compared to benign nodules and normal thyroid tissue was previously reported by Lyshchick, et al. (2). It should be noted

Fig. 1: Slightly heterogeneous solid isoechoic nodule (right) with homogeneous green color-coding on elastography (left) with benign FNA.

Fig. 2: Solid echogenic nodule with hypoechoic halo (right) with homogeneous green color-coding on elastography (left) with benign FNA.

Fig. 3: Heterogeneous mixed isoechoic nodule with small cystic component (right) with mixed green (soft) color-coding over the solid components and blue (hard) color-coding over the cystic component on elastography (left): benign FNA.
that we have not assessed patients with multinodular goiter. The demonstration of hard nodules could lead physicians to performed FNA of multiple nodules, and even surgery for such nodules in spite of negative FNA. If surgery is not performed, hard nodules would undergo short interval time follow-up with FNA. On the other hand, nodule softness is highly predictive of benign lesions. Our results are similar to those by Rago, et al. (19) and Lyshchick, et al. (18) who reported a high prevalence of malignant lesions in hard nodules (with respective sensitivities of 97% and 82% and specificity values of 100% and 97%). Even though these results need to be confirmed in larger trials, elastography findings could prevent surgery for patients with soft nodules and non-diagnostic FNA. In conclusion, even though US elastography of thyroid nodules is in its infancy, it appears to be an excellent complement to conventional US and may help direct management of patients with thyroid nodules. These promising early results should be confirmed with larger multi-center studies to determine the role of US elastography in the management of thyroid pathology.

Fig. 4: 

a Well-defined solid hypoechoic nodule with mostly blue (hard) color-coding on elastography except for a green (soft) center: Follicular carcinoma on FNA.

b Well-defined solid hypoechoic nodule with green (soft) color-coding on elastography: benign adenoma on FNA.

Fig. 5: Solid hypoechoic nodule with microcalcifications (right) with homogeneous blue (hard) color-coding on elastography (left): medullary carcinoma on FNA.

References

Fig. 6: Large solid nodule with non-visualized margins causing artifactual heterogeneous blue-green color-coding on elastography secondary to inadequate compression (excluded from our study).