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The role of sonoelastography in the differential diagnosis of neck nodules

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KEYWORDS
Technology assessment;
Thyroid;
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Abstract Sonoelastography is an imaging technique that provides information on tissue elasticity. Its use as a diagnostic procedure is based on the premise that pathological processes like cancer alter the physical characteristics of the involved tissue. Ultrasonographic studies of the neck can reveal the nonpalpable thyroid nodules, but the nature of these lesions generally has to be established on the basis of FNAB findings. In our hands, sonoelastography displayed a diagnostic accuracy of 86.2% in identifying thyroid nodule malignancy, with positive and negative predictive values (PPV and NPV) of 64% and 94.5%, respectively. In the study of cervical lymph nodes, the results were less impressive (sensitivity 75%, specificity 80%, accuracy 77%, PPV 80%, NPV 70%), but the information obtained with this technique can in our opinion be a useful adjunct to sonographic findings. Indeed, in 5 lymph nodes with sonographic features consistent with malignancy, sonoelastography revealed diffuse elasticity that was indicative of benign disease, which was confirmed by pathological studies. Other nodular lesions of the neck can also be evaluated with sonoelastography, including enlarged parotid glands, but the data in the literature are too limited to allow hypotheses on the role of this imaging modality in this field. Sonoelastography is rapid and simple to perform, and it appears to be a potentially useful tool for the differential diagnosis of neck nodules. This is particularly true of thyroid nodules. Our experience with these lesions indicates that diffuse elasticity is strongly correlated with benign disease. If this finding is confirmed in larger studies, sonoelastography might be used to identify thyroid nodules that do not require immediate biopsy.

Sommario L'elastosonografia è una tecnica di imaging che fornisce informazioni relative alla elasticità dei tessuti e che può essere utilizzata nella pratica clinica basandosi sul presupposto che i processi patologici, come il cancro, inducono modificazioni della caratteristiche fisiche dei tessuti ammalati.
Lo studio ecografico della loggia cervicale permette di individuare formazioni nodulari non palpabili all'interno della tiroide, tuttavia l'accuratezza diagnostica di questa tecnica è scarsa e per tale motivo il ricorso alla FNAB è spesso necessario.
Nella nostra esperienza l'elastosonografia ha dimostrato, nella diagnosi differenziale dei nodi tiroidei, un'accuratezza diagnostica del 86,2% con VPN 94,5% e VPP 64%.

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Nello studio dei linfonodi cervicali i risultati ottenuti sono meno brillanti (sensibilità, specificità e accuratezza rispettivamente del 75%, 80% e 77% con VPP e VPN di 80% e 70%), ma riteniamo che le informazioni ottenibili possono in molti casi essere utili per integrare i dati ecografici; in particolare in 5 casi di linfonodi con caratteristiche morfo-strutturali indicative di malignità, l'elastosonografia ha dimostrato un pattern di completa elasticità, riconoscendo la natura benigna confermata dalle successive indagini.
Altre formazioni nodulari del collo possono essere valutate con elastosonografia, in particolare le tumefazioni parotidee, ma non esistono ancora in letteratura esperienze sufficientemente ampie da indicare l'eventuale contributo clinico in questo campo.
L'elastosonografia è una tecnica rapida e di facile esecuzione che sembra fornire un interessante contributo nella differenziazione tra formazioni nodulari del collo.
In particolare si è osservata una stretta correlazione tra noduli tiroidei totalmente elastici e quadro di benignità; se tale rapporto venisse confermato in una casistica più ampia permetterebbe di escludere in questi casi l'immediato ricorso alla FNAB.

Introduction

Ultrasound elastography, or sonoelastography, is an imaging technique that provides information on tissue elasticity. Its use in clinical practice is based on the premise that pathological processes like cancer modify the physical characteristics of diseased tissues. This principle has already been exploited for diagnostic purposes [1—4], but interest in elastography has been increased by the recent development of integrated systems that facilitate the inclusion of sonoelastographic studies in routine practice.

The technique used by our group involves the analysis of changes in radiofrequency (RF) impulses originating from the tissues before and after the manual application of gradual compression [3]. Elastographic images are produced in real time and provide color-coded maps of the different degrees of elasticity within the tissue being examined. A dedicated program known as CAM (Combinated Autocorrelation Method) rapidly elaborates changes in the RF impulses produced by compression and minimizes artifacts related to lateral displacement, furnishing a highly accurate assessment of the tissue distortion. This technique was initially used for the differential diagnosis of breast nodules. The breast is particularly suited for elastographic assessment because its structure can be compressed in a uniform manner and lesions with different degrees of elasticity within the structure are clearly revealed. More recently, ultrasound elastography has been used to study other organs as well. This article will provide an updated overview of the technique's potential contributions to the differential diagnosis of thyroid and parotid nodules and cervical lymphadenopathy.

Technique

Our sonoelastographic examinations were performed with a free-hand technique on a Logos HiVision scanner (Hitachi, Japan). The ultrasound transducer was used to produce rhythmic compression of the tissues under examination. The operator selects the size of the ROI within which the elastographic data will be represented. In general, we use a rectangular ROI large enough to include the entire structure being examined as well as a large portion of the surrounding tissue.

During the examination, the quality of the compression is evaluated in real time, and the results are expressed on the scanner panel on a scale of 1—5. A value of 3 or more is indicative of correct compression.

The elastographic image is color-coded: highly elastic tissues appear red, anelastic tissues are blue, and intermediate degrees of elasticity are shown in green. With the scanner we use, the real-time sonographic image is displayed alone on the left side of the screen and with the elastographic image superimposed upon it on the right. This allows the operator to rapidly verify that the nodule being examined remains within the scanning plane during compression.

The scanner allows real-time storage of elastographic recordings. They are considered reliable only when the color-coding within the sampled area remains constant for at least 5 s. In our experience, the structures examined with sonoelastography generally present 1 of the following 4 patterns (Figs. 1 and 2). Pattern 1: The entire surface of the formation being examined is diffusely elastic. Pattern 2: The formation appears to be largely elastic with the inconstant appearance of anelastic areas (blue) during the real-time examination. Pattern 3: Constant presence of large anelastic areas (blue) are seen at the periphery (Pattern 3A) or center (Pattern 3B) of the formation. Pattern 4: Uniformly anelastic [5]. Lesions that present pattern 1 or 2 are classified as probably benign, while patterns 3 and 4 are indicative of probable malignancy (Figs. 3 and 4).

Clinical applications

Thyroid

The incidence of nonpalpable thyroid nodules is very high (up to 50% of the population) [6—8]. A large part of the clinically silent nodules of this type are discovered on high-frequency ultrasound studies of the neck, which are being performed with increasing frequency, not only to evaluate thyroid disease but also to examine other cervical structures, such as the carotid arteries. Only a small percentage of thyroid nodules (5—6.5%) present features consistent with malignancy [9], but this

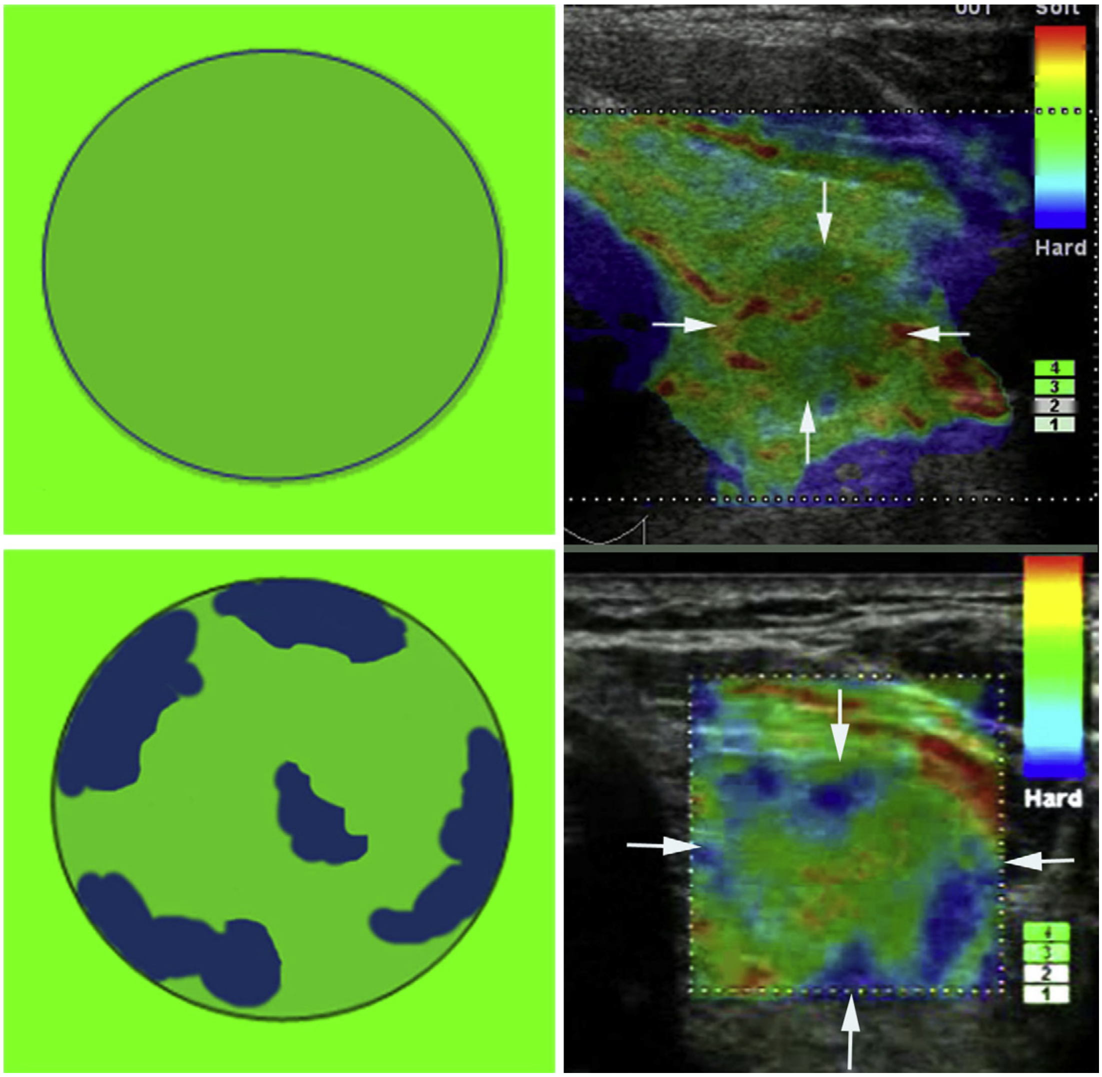

Fig. 1 Benign elastographic patterns (see text).

possibility must always be considered, even when the nodule is small. In fact, malignancy shows no correlation with nodule size, and it is not uncommon to find lymph node metastases in patients with papillary carcinomas measuring no more than a few millimeters or even those that are occult [10].

The high-frequency ultrasound transducers currently being used display high sensitivity in detecting thyroid nodules, but they are less helpful in distinguishing malignant nodules from those that are benign [10]. Currently available techniques are thus highly accurate tools for discovering thyroid nodules, and ultrasonography can also be useful in the follow-up phase to detect changes in nodule size, but it does not make any significant contribution to the characterization of these nodules, which is based exclusively on ultrasound-guided fine-needle biopsy (FNAB). In many centers, biopsies are collected for all nodules over 1 cm in diameter. For these reasons, sonoelastography has recently been used for the study of thyroid nodules. Lyshchik et al. [1] obtained promising results with an experimental technique and equipment, which were highly interesting within a research context, but the approach they used is too complex and time-consuming for routine use in clinical practice. In contrast, Bae et al. [11] have proposed an alternative to the widely used approach that involves manual compression. They showed that carotid artery pulsation can be exploited as a source of compressive stress on thyroid tissues. With this approach, they obtained diagnostic elastographic images without the artifacts caused by manual compression of the tissue by the operator.

In our experience, characterization of thyroid nodules based on the patterns described above (where patterns 1 and 2 are suggestive of benign nodules, and patterns 3 and 4 indicate malignancy) displayed a sensitivity of 82%, a specificity of 87.5%, and an overall accuracy of 86.2%. The positive and negative predictive values (PPV and NPV) were 64% and 90%, respectively [5].

These results are undeniably superior to those that can be obtained with conventional sonography, but in the group of 51 patients we examined, 2 malignant nodules were misdiagnosed. These false negative results reflect an important limitation of the technique, and caution must therefore be used in drawing conclusions on its value.

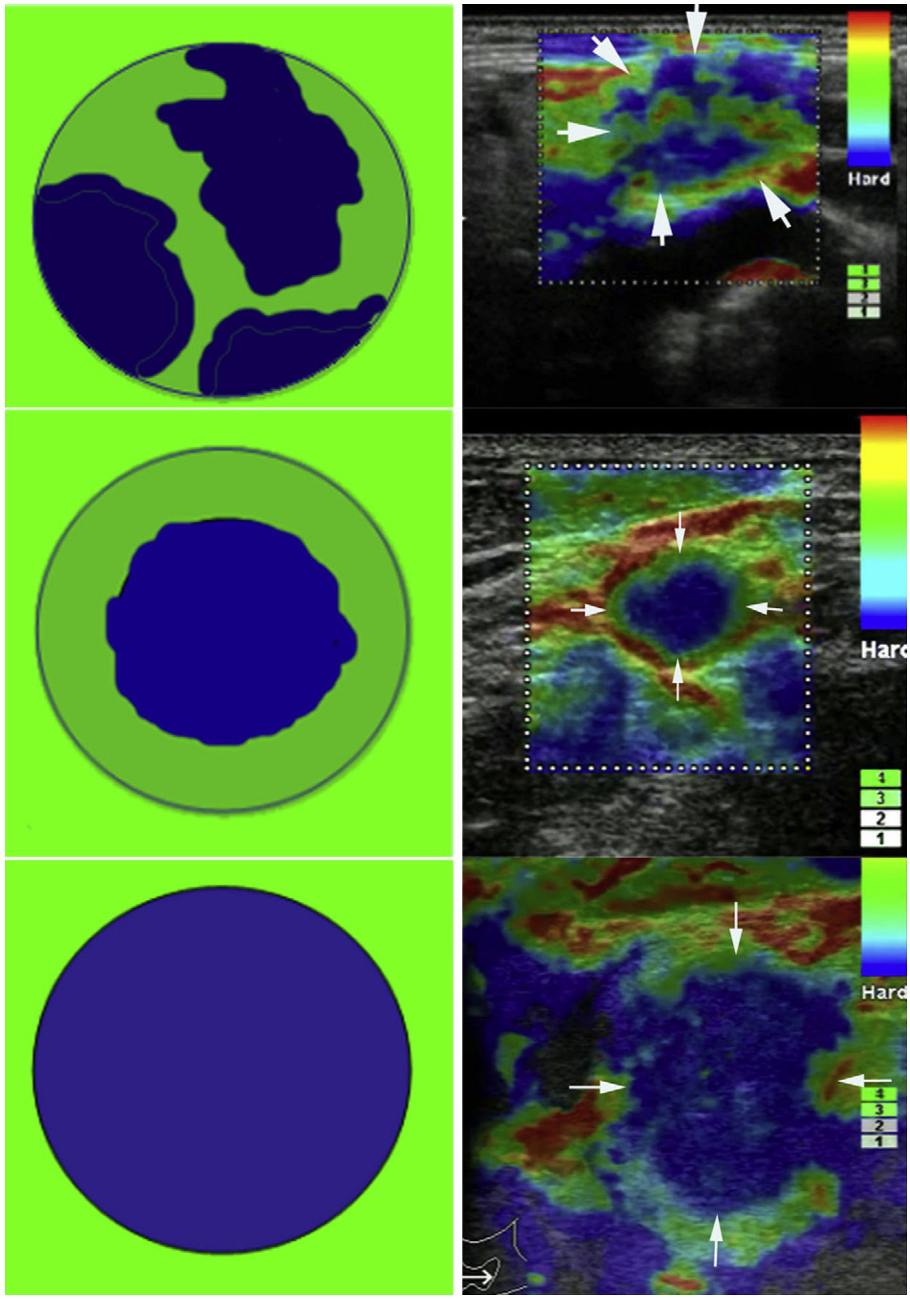

Fig. 2 Malignant elastographic patterns (see text).

It is also important to stress that pattern 1 (nodules that are diffusely elastic) was observed exclusively in benign nodules. If this correlation is confirmed in larger series, pattern 1 might be used as a reliable indicator of nodules that do not need immediate biopsy. The procedure can be deferred until changes are observed in the appearance or size of the nodule.

Recently, Ferrari et al. recently reported similar results in their sonoelastographic study of 23 patients with solitary thyroid nodules (PPV 72%, NPV 91%) [12].

Even better results (sensitivity 97%, specificity 100%, PPV 100%, NPV 98%) have been reported by other investigators [13]. The discrepancy can be attributed in part to the different enrolment criteria used in the studies cited above. Our sonoelastographic data are based on the study of patients who consecutively presented with ultrasound evidence of thyroid nodules and were scheduled to undergo FNAB, whereas Rago et al. [13] analyzed a more highly selected group of patients who had already been scheduled for surgery to evaluate suspicious findings that had emerged from FNAB or to relieve compressive symptoms caused by large nodules.

In conclusion, the currently available data indicate that ultrasound elastography can be a useful complement to conventional sonographic studies, which are useful in the detection and follow-up of thyroid nodules but of limited value in the characterization of these lesions.

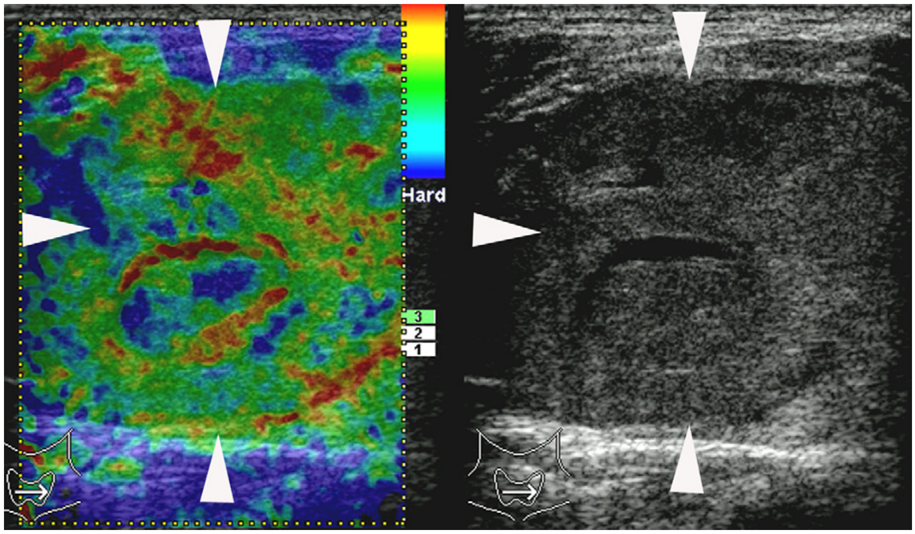

Fig. 3 This large, hyperplastic thyroid nodule appears predominantly elastic with a few small areas of anelasticity represented in blue (pattern 2).

Lymph nodes

Ultrasonography is commonly used in the differential diagnosis of cervical lymphadenopathy, and B-mode imaging is the most important component of this approach. High-definition images can be obtained with high-frequency transducers, and the scanning plane can be modified in real time to optimize visualization of the lymph node, even those measuring only a few millimeters in diameter. Additional diagnostic information can be obtained with power Doppler studies of node vascularization, but the findings are frequently ambiguous and sometimes even FNAB fails to provide a definitive answer. The only choice in these cases is lymphadenectomy and histological examination of the entire node.

Our experience with lymph-node sonoelastography includes 53 patients, 28 of whom had malignant forms of lymphadenopathy (metastatic in 21 cases, non-Hodgkin lymphomas in 7). The remaining 25 had benign disease. Compared with cytological and/or histological diagnosis, sonoelastography displayed a sensitivity of 75%, specificity of 80%, and accuracy of 77% with positive and negative predictive values of 80% and 70%, respectively. These results are somewhat inferior to those obtained in the characterization of thyroid nodules, and the difference is partly related to technical factors. The thyroid parenchyma can be compressed uniformly, and in general the elastic characteristics of focal lesions in this gland can easily be compared with those of the adjacent normal tissue. In contrast, the sonoelastographic study of lymph nodes is affected by the position of the node (superficial or deep) and its relation to nearby structures such as muscles, superficial bones, or large blood vessels. In our opinion, however, this approach often provides information that is

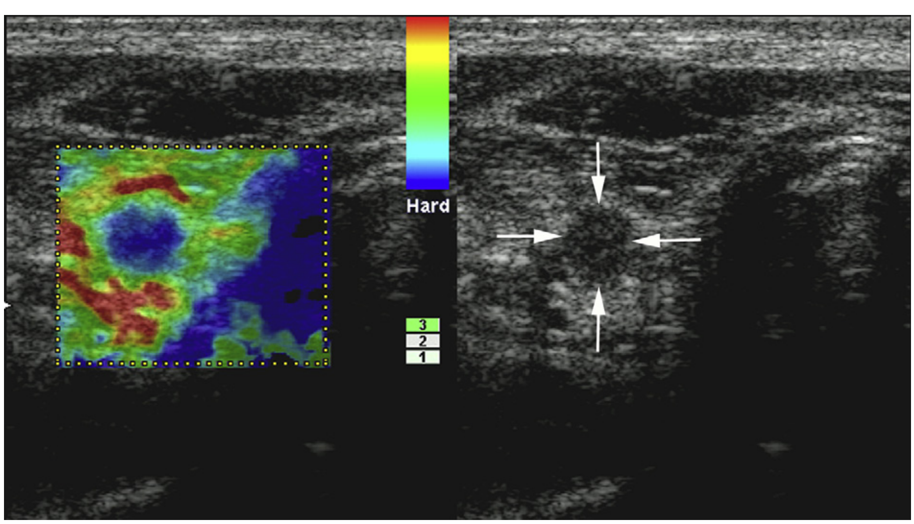

Fig. 4 A small, hypoechoic nodule in the right lobe of the thyroid displayed diffuse anelasticity (pattern 4) and was histologically diagnosed as papillary carcinoma.

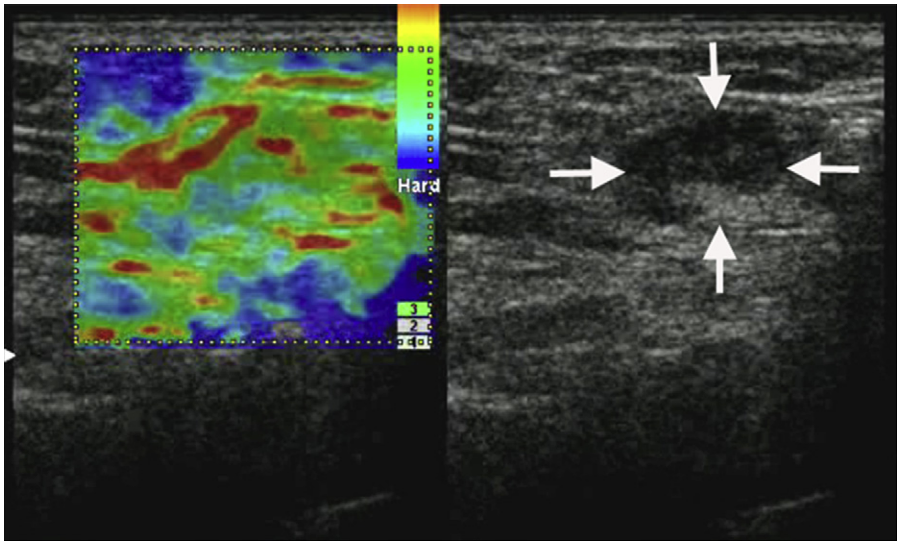

Fig. 5 This reactive lymph node (arrow) was almost completely elastic, with a pattern (green and red) similar to that of the surrounding tissues.

useful for determining whether or not the node is malignant (Figs. 5 and 6). In fact, in 5 cases in which the lymph nodes presented morphostructural features indicative of malignancy, the elastographic study revealed diffuse elasticity (pattern 1) that was consistent with benign lymphadenopathy, and this diagnosis was confirmed by the results of subsequent studies (Fig. 7).

Deep lymph nodes in the mediastinum or abdomen can be subjected to elastographic studies during endoscopic ultrasound examinations [14,15]. Săftoiu et al. [14] proposed a quantitative assessment based on the analysis of histograms, in which the color gradations within the ROI (automatically acquired in all frames of a 10-s recording) were represented as numerical values. In the characterization of abdominal and mediastinal nodes, endoscopic elastography performed with this software displayed a sensitivity of 85.4%, specificity of 91.9%, and accuracy of 88.5% [14].

Parotid nodules

Ultrasonography is commonly used for differential diagnosis of nodular lesions in the parotid glands. The morphostructural features of these lesions can provide a general guide, but in most cases accurate characterization requires FNAB. Ultrasound elastography could prove useful in this field, but the data in the literature on this subject is currently quite limited. Our personal experience is also limitated. It is based on the study of 12 patients with parotid nodules that were ultimately diagnosed as pleomorphic adenomas or mixed tumors ($n = 7$), oncocytoma ($n = 1$), adenolymphomas (also known as Warthin's tumors) ($n = 2$), and

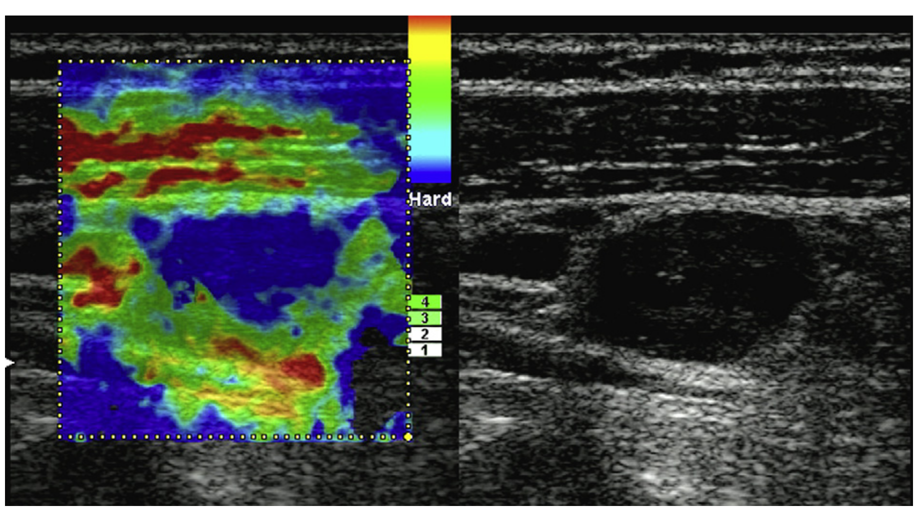

Fig. 6 This moderately enlarged, round lymph node without an echogenic hilum appeared almost completely anelastic. The histological diagnosis was melanoma metastasis.

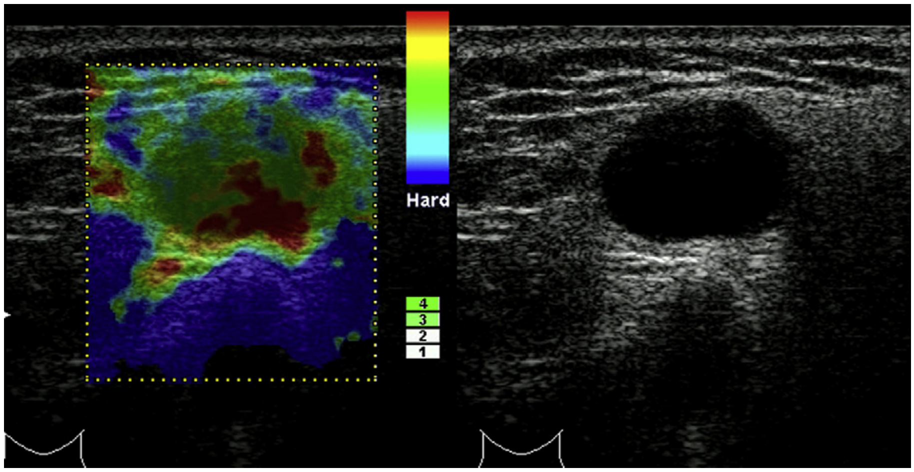

Fig. 7 Lymph node with sonographic features indicative of malignancy: hypoechoic structure, roundness, absence of hilar echogenicity. Sonoelastography revealed diffuse elasticity (green and red). The histological diagnosis was nonspecific lymphadenitis.

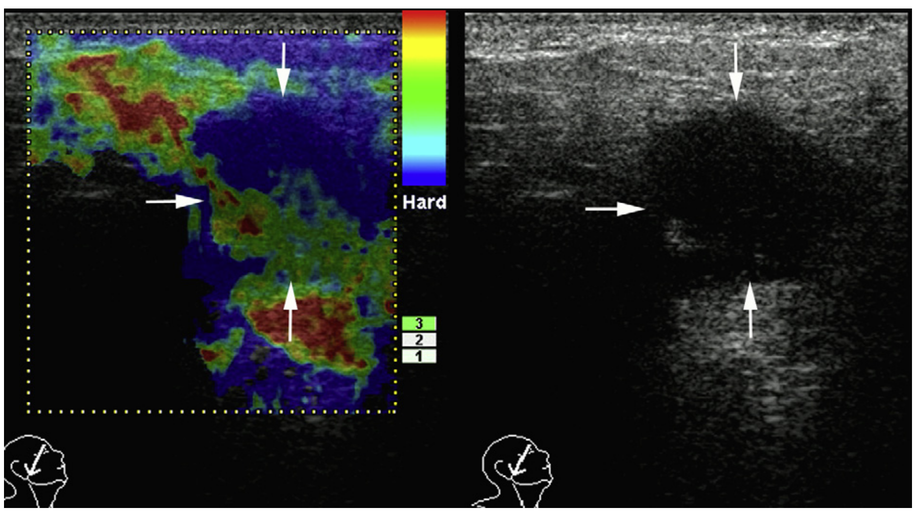

Fig. 8 This solid, hypoechoic nodule in the right parotid was largely anelastic on sonoelastography (Mucoepidermoid carcinoma).

mucoepidermoid carcinomas ($n = 2$) based on surgical histology.

Elastographic studies of the parotids have certain technical limitations that are related to location of these glands, in particular their proximity to the mandibles, the mastoid processes of the temporal bones, and the auricles of the ears. These structures can interfere with attempts to compress the parotids. In fact, our experience (albeit limited) suggests that sonoelastography can probably be used correctly only for assessment of the superficial lobe of the parotid.

Both of the mucoepidermoid carcinomas we examined proved to be largely anelastic (Fig. 8). The 2 adenolymphomas contained large cystic areas documented by ultrasound, and the elastographic appearance of these lesions was characterized by chromatic stratification, which is typical of cystic lesions and added nothing to the basic ultrasound findings. The other 8 cases involved benign lesions, 7 of which were predominantly (or uniformly) elastic. The eighth was largely anelastic and incorrectly classified as malignant on the basis of this finding.

In the absence of data from larger studies, it is difficult to define indications for elastography in the study of parotid lesions. Our initial impression is that this technique might represent a useful adjunct to conventional sonography for analyzing lesions in the superficial lobe of the parotid.

Conclusions

Ultrasound elastography was initially used with good results in the characterization of breast nodules [3,4]. Breast tissue can be uniformly compressed without difficulty, and this feature facilitates the visualization of areas with altered consistency. Numerous studies are being conducted on the use of this method for the assessment of other organs, superficial and deep [11—17]. Elastographic characterization of thyroid nodules seems to be particularly useful in clinical practice, since conventional sonography provides very little information on the benign or malignant nature of these lesions [5,11,13]. Use of this technique for studying other structures in the neck (lymph nodes, salivary glands) has not been extensively studies, and additional data based on the analysis of larger series are needed. For patients with lymphadenopathy, this approach could be useful for identifying benign forms characterized by preserved elasticity and sonographic features similar to those found in malignant nodes. It should also be stressed that elastography is simple to perform (compression maneuvers can be learned in a brief training period). It provides a rapid, painless method for reducing the number of unnecessary biopsies.

Conflict of interest statement

The authors have no conflict of interest.

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