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Sonoelastographic evaluation for benign neck lymph nodes and parathyroid lesions

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Abstract

Aim: The aim of the study was to evaluate the performance of real-time strain sonoelastography for comparison of perithyroidal lymph nodes of Hashimoto thyroiditis patients, jugular lymph nodes of healthy individuals and parathyroid lesions. **Material and methods:** Fifty parathyroid lesions (Group 1), 52 lymph nodes in Hashimoto thyroiditis patients (Group 2) and 51 reactive jugular lymph nodes (Group 3) were examined by ultrasound, and elastography was performed for a total of 95 patients. Real-time strain sonoelastography using elasticity score (E-index) was performed. The differences in E-index between the three groups were evaluated. **Results:** The mean E-index and size of parathyroid lesions were 2.30 ± 0.91 and 13.46 ± 5.69 mm, respectively. Parathyroid hyperplasia was detected by parathyroidectomy in two patients (2/37; 5%) with a total of four lesions (4/50; 8%). The remaining lesions were considered as adenomas. The mean E-index and size in Group 2 were 2.70 ± 0.93 and 7.83 ± 3.35 mm, respectively. The mean E-index and size in Group 3 were 1.88 ± 0.59 and 11.60 ± 4.96 mm, respectively. There were statistically significant differences between the groups in terms of E-index (p <0.01). **Conclusions:** When reactive jugular lymph nodes, perithyroidal lymph nodes of Hashimoto thyroiditis patients and parathyroid lesions are compared, it seems that strain sonoelastography indices add a benefit to routine practice in the differential diagnosis of parathyroid lesions and benign neck lymph nodes.

Introduction

Parathyroid adenomas are benign tumors and are the most common causes of primary hyperparathyroidism[1]. Solitary benign adenoma (89%), double adenomas (4%), parathyroid hyperplasia (6%), and parathyroid carcinoma (<1%) are probable causes of primary hyperparathyroidism[2,3].

Hashimoto thyroiditis, a type of autoimmune thyroiditis, is one of the most common thyroid disorders. In these patients, prominent reactive cervical lymph nodes may be present especially in level VI and the "Delphian" node, just cephalic to the isthmus. These perithyroidal lymph nodes are also helpful in diagnosis[4,5].

High-resolution sonography is a sensitive imaging test for the detection of superficial masses, and currently one of the first-line imaging techniques for the evaluation of parathyroid gland lesions[1]. Doppler ultrasonography with the detection of the extrathyroidal feeding vessel has improved the determination of parathyroid adenomas[6]. Ultrasonography and technetium-99m-sestamibi scintigraphy with or without sestamibi single photon emission computed tomography (SPECT) are the dominant imaging modalities for preoperative localization of parathyroid adenomas[7,8].

As a relatively new method, sonoelastography is currently under investigation for tissue characterization of several anatomic sites. Elastography of a mass shows its elastic properties. It allows examination of changes in tissue elasticity features[9]. Strain elastography, as performed in this study, is a non-invasive method involving manual compression that provides an evaluation of tissue stiffness differences.

The aim of this study was to determine the performance and additional values of real-time strain sonoelastography

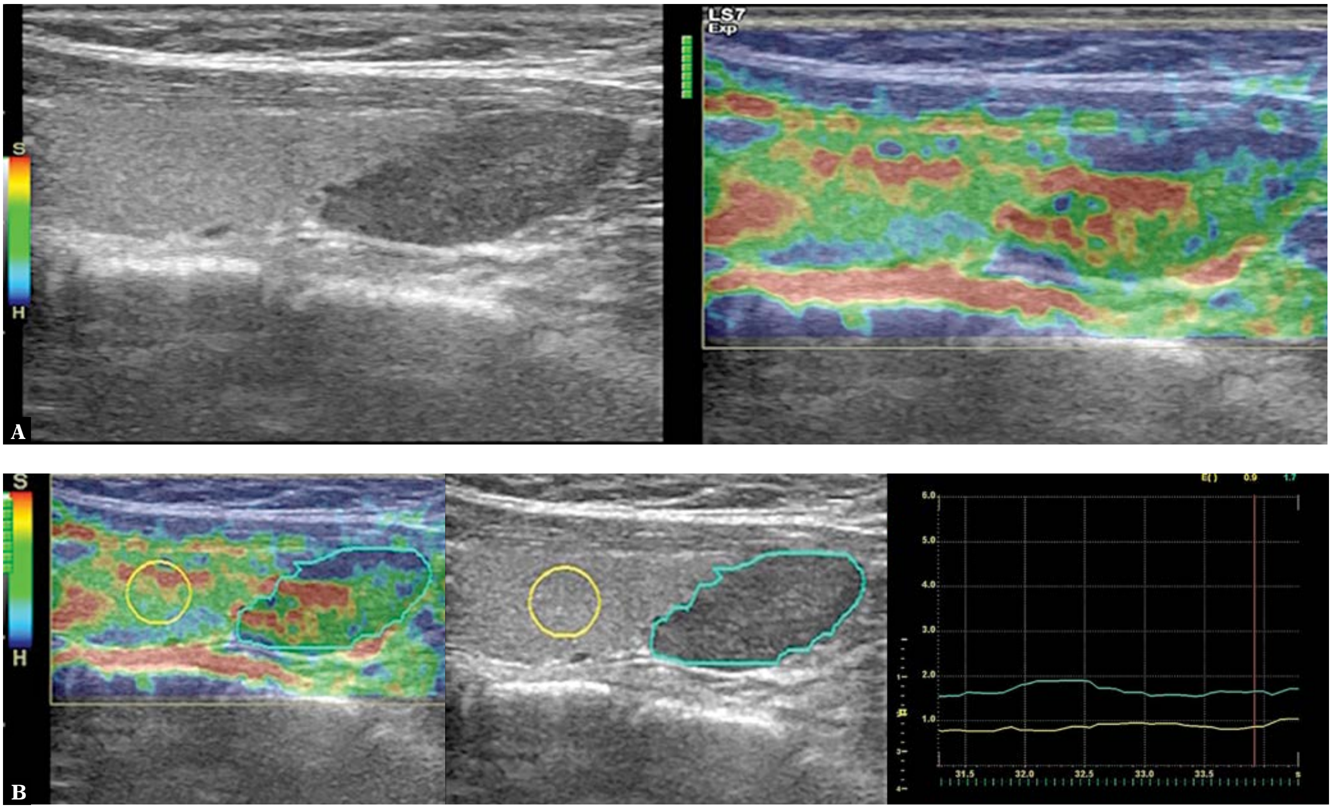


Fig. 1. *A 39-year-old woman with hyperparathyroidism and brown tumor in her left humerus. An example of a parathyroid adenoma. Diagnosis was confirmed by parathyroidectomy. Scintigraphy scan was positive. The gray-scale image shows a typical hypoechoic adenoma deep in relation to the right lower pole of the thyroid gland* **(A)**. *Elastographic examination of the lesion revealed predominantly green and red colors* **(A)** *and E-index of 1.7* **(B)**. *(E-index; elasticity score)*

in the differential diagnosis of perithyroidal reactive lymph nodes of patients with Hashimoto thyroiditis, reactive jugular lymph nodes of healthy individuals and parathyroid gland lesions.

Material and methods

Study groups

This prospective study was performed in the Department of Radiology between April 2016 and March 2018. All patients gave informed written consent for sonographic evaluation and for this work. All procedures were performed in accordance with the Declaration of Helsinki for human subjects, and our Institutional Review Board approved the study.

In total, 95 patients who had been referred to the Department of Radiology for sonographic evaluation, were included in the study. A total of 153 lesions were examined by ultrasonography, and strain sonoelastography was added.

The diagnosis in patients with parathyroid adenomas or hyperplasia was confirmed by parathyroidectomy or fine-needle aspiration biopsy with parathormone (PTH) washout or with a positive scintigraphy scan and high serum PTH level.

The diagnosis of Hashimoto thyroiditis was confirmed by demonstration of serum thyroid antibodies and antithyroglobulin antibodies. Patients with Hashimoto thyroiditis have lymph nodes around the thyroid gland like parathyroid glands. Thus, these lymph nodes located at level VI were used as one of the control groups. Patients with Hashimoto thyroiditis without district nodular lesions in the thyroid gland were included in the study to exclude probable metastatic lymph nodes. Additionally, we believe that there are insufficient numbers of level VI lymph nodes in healthy individuals to serve as a control group. Therefore, level III and IV lymph nodes of healthy individuals were used as the other control group.

Sonographic examinations

Ultrasonography and strain elastography examinations were performed by a radiologist experienced in sonographic evaluations. Lesion dimensions on gray-scale ultrasound were evaluated and noted. Sonographic examinations were performed with a Logiq S7 Expert machine (GE Healthcare, Milwaukee, WI) equipped with a 9L-D linear-array probe. Slight repetitive manual compressions were performed, keeping the transducer perpendicular to the skin during strain elastography. The elastographic images were obtained with appropriate compression and decompression application according to a quality bar. The bar scale ranged from 1 to 7 on the screen. Images and measurements were obtained only when the optimal compression bar was in the range of 5 to 7. The elastogram was displayed as a real-time color map of relative elasticity, which was superimposed on the gray-scale image. Elastography and B-mode ultrasonography images were simultaneously presented as a two-panel image. The region of interest (ROI) was placed first on the reference tissue using a circle drawing tool and second on the mass using a free-hand drawing tool along to the lesion border. Elasticity score (E-index) was obtained by elastographic analysis. The described strain elastography method represents relative information about hardness[10]. The relation between elastogram colors and the hardness of an area is given on the elastography color bar (at the left side of each elastogram). While red color reflects less stiff tissue, blue color reflects more stiff tissue. In addition, green color reflects medium stiff tissue of the entire area undergoing elastography. When the ROI drawing is completed, the sonography machine automatically gives a value, which reflects E-index, from 0 (softest) to 6 (hardest). E-index is a semi-quantitative value which represent the strain of the ROI relative to the entire area undergoing elastography. While a low E-index indicates soft tissue, a higher E-index indicates stiff tissue. E-index from real-time strain elastography was noted. The difference in E-index and diameter between parathyroid lesions and lymph nodes was evaluated. In calculating the elasticity ratio (E-ratio), which represents how many times stiffer a lesion is, we should use a reference tissue. However, some lesions were not appropriate for this calculation. Some lesions were not in the same depth or were not at the same level with standardized reference tissue. Therefore, E-ratio was not used to compare the groups[10].

Statistical analysis

Statistical analyses were performed using SPSS version 15.0 software for Windows (IBM Corporation, Armonk, NY). Descriptive statistics of continuous variables are given as mean ± standard deviation (SD) and median (interquartile range 25–75). Kolmogorov-Smirnov test was used to test normality. To compare groups, one-way Anova test was used. $P < 0.05$ was considered statistically significant.

Results

In the study population (95 patients, 153 lesions), there were three groups. Group 1 (parathyroid lesions) had 37 patients with a total of 50 lesions. Group 2 (perithyroidal lymph nodes in Hashimoto thyroiditis patients) had 27 patients with a total of 52 lymph nodes. Group 3 (reactive jugular lymph nodes in healthy individuals) had 31 patients with a total of 51 lesions. Parathyroid hyperplasia was detected by parathyroidectomy in two patients (2/37; 5%) with a total of four lesions (4/50; 8%). The other parathyroid lesions were considered as adenomas.

The mean age of the patients was 48.7 ± 14.88 years (range 19–79), and 22% of the patients were male ($n = 21$). The mean age of the patients with parathyroid lesions was 54.38 ± 14.13 years (range 19–79), and 27% ($n = 10$) of the patients were male. The mean age of the Hashimoto patients was 39.78±11.97 years (range 20–67), and 7% ($n = 2$) of the patients were male. The mean age of the individuals with reactive jugular lymph nodes was 49.68 ± 14.77 years (range 22–72), and 29% ($n = 9$) of the patients were male. There were statistically significant differences between Group 2 and Group 1, and between Group 2 and Group 3 in terms of age (both $p < 0.05$).

The mean sizes of lesions in Group 1, Group 2 and Group 3 were 13.46 ± 5.69 mm, 7.83 ± 3.35 mm and 11.60 ± 4.96 mm, respectively. There were statistically significant differences between Group 2 and Group 1, and between Group 2 and Group 3 in terms of the diameters of the lesions (both $p < 0.001$).

The mean E-index of parathyroid lesions, lymph nodes of Hashimoto patients and jugular lymph nodes of healthy individuals were 2.30 ± 0.91, 2.70 ± 0.93 and 1.88 ± 0.59, respectively. There were statistically significant differences between the groups in terms of E-index via multiple comparisons (all $p < 0.05$).

All results of the study are presented in Table 1. Images of a parathyroid adenoma, a lymph node of a Hashimoto patient and a jugular lymph node of a healthy individual, including gray-scale and elastography examinations, are shown in Fig. 1, Fig. 2 and Fig. 3.

Discussion

The perithyroidal central compartment lymph nodes, as particularly prominent in patients with lymphocytic thyroiditis, can commonly be mistaken for parathyroid glands. However, several features have been described to distinguish lymph nodes from adenomas. While a benign reactive lymph node usually has an echogenic fatty hilum supplied by small hilar vessels, a parathyroid adenoma usually has a polar, peripheral vascular structure supplied by an extrathyroidal feeding vessel[1,6,11,12]. High-resolution ultrasonography findings, together with laboratory findings and other imaging methods, have an impressive value for the diagnosis of parathyroid lesions. In the current study, strain sonoelastography was found to provide additional contribution to the differential diagnosis of parathyroid lesions and lymph nodes.

In our study, parathyroid hyperplasia was detected by parathyroidectomy in two patients (2/37; 5%) with a total of four lesions (4/50; 8%). One patient had a single lesion and the other patient had three lesions. The distribution of the patients with parathyroid adenoma was as follows: a solitary lesion in 27 patients (27/35; 77%), 2 lesions in six patients (6/35), 3 lesions in one patient (1/35), and 4 lesions in one patient (1/35). Among the Hashimoto patients with lymph nodes, 15 patients

(15/27) had one lymph node, 4 patients (4/27) had 2 lymph nodes, 4 patients (4/27) had 3 lymph nodes, 3 patients (3/27) had 4 lymph nodes, and one patient (1/27) had 5 lymph nodes. Among the healthy individuals with reactive lymph nodes, 19 patients (19/31) had one lymph node, 8 patients (8/31) had 2 lymph nodes, 2 patients (2/31) had 3 lymph nodes, 1 patients (1/31) had 4 lymph nodes, and one patient (1/31) had 6 lymph nodes. Frequencies were in accordance with the frequency commonly reported in the literature[2,3].

In an article by Azizi *et al.*[13], the authors evaluated 57 parathyroid adenomas using shear wave elastography, and obtained lower elastography scores in adenomas compared with the thyroid parenchyma. However, in a study by Ünlütürk *et al.*[14], the authors evaluated 93 parathyroid lesions, using strain elastography and obtained higher elastography levels in adenomas compared with the thyroid tissue and parathyroid hyperplasia. Because of the small number of parathyroid hyperplasia lesions ($n = 4$; 8%), in accordance with the low frequency in the literature, the comparison between parathyroid adenoma and hyperplasia could not be performed in our study.

In an article by Isidori *et al.*[15], the authors evaluated 47 parathyroid lesions, 18 thyroid ectopic nodules and 14 reactive lymph nodes using quasi-static sonoelastography, and obtained higher elastography scores in adenomas compared with reactive lymph nodes. In our study, the perithyroidal reactive lymph nodes related to chronic autoimmune thyroiditis, and reactive jugular lymph nodes with more number in healthy individuals were used as control groups. Compared with the aforementioned article, we obtained a higher E-index in parathyroid lesions compared with the reactive jugular lymph nodes. Additionally, we obtained a lower E-index in jugular reactive lymph nodes when compared with perithyroidal lymph nodes of Hashimoto patients. In light of our study, these results showed that Hashimoto patients' lymph nodes are stiffer than reactive jugular lymph nodes. The sonoelastography technique is based on wide acceptation that

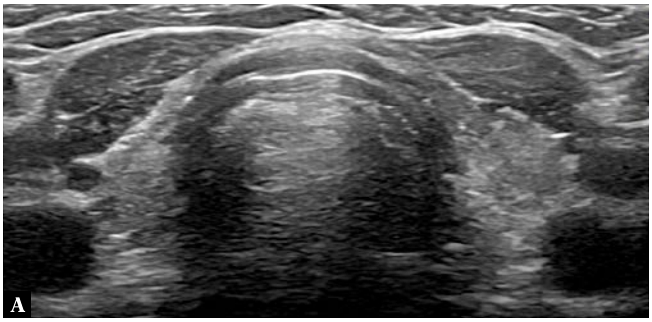
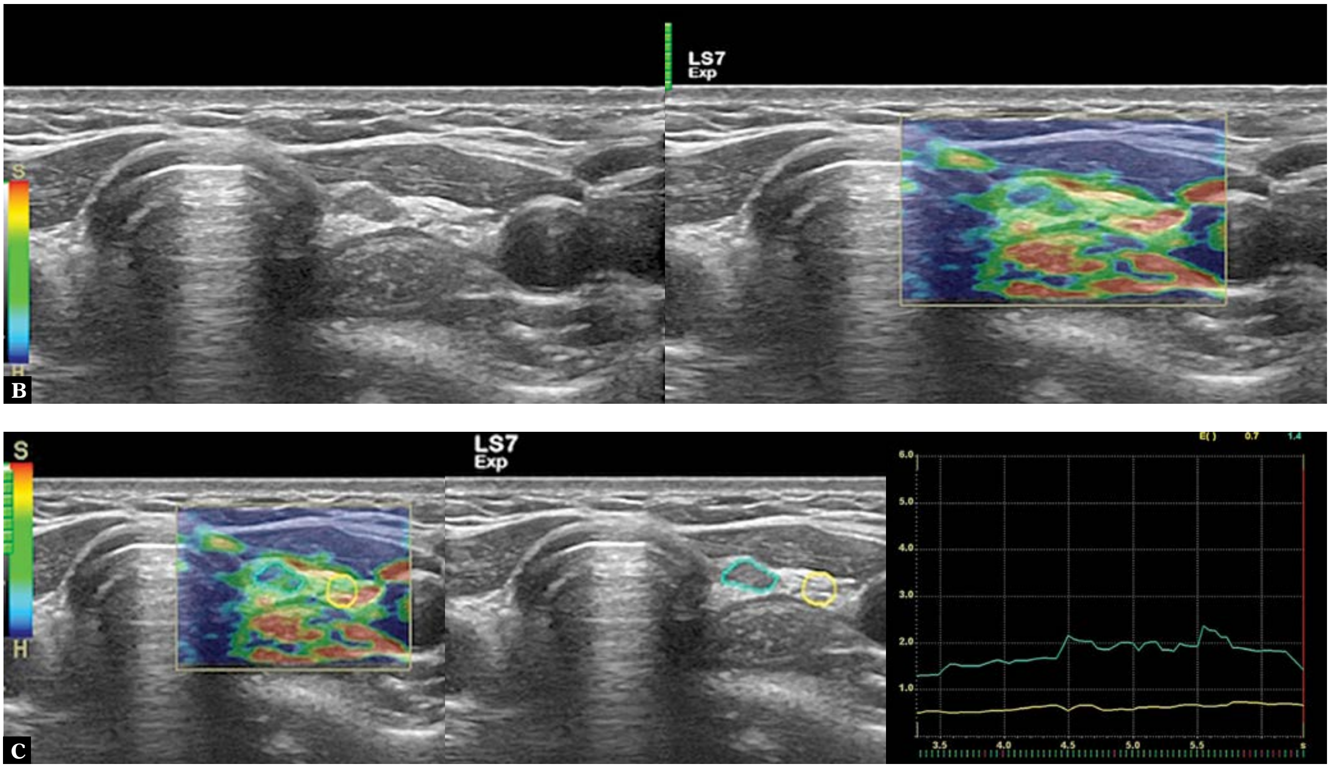


Fig. 2. *A 52-year-old woman with Hashimoto thyroiditis. The gray-scale images show heterogeneous thyroid gland parenchyma* **(A)**, *and the left lower lymph node* **(B)**. *Elastographic examination of the lesion revealed green and blue colors* **(B)** *and E-index of 1.4* **(C)**. *(E-index; elasticity score)*



	Group 1	Group 2	Group 3	*P* value
Age (mean ± SD) (min.–max.)	54.38 ± 14.13 (19–79)	39.78 ± 11.97[a] (20–67)	49.68 ± 14.77 (22–72)	<0.001
Diameter (mm) (mean ± SD) (median; IQR)	13.46 ± 5.69 13; 9.25 (8–17.25)	7.83 ± 3.35[b] 7; 3.00 (6–9)	11.60 ± 4.96 10; 4.00 (8–12)	<0.001
E-index (mean ± SD) (median; IQR)	2.30 ± 0.91[c] 2.20; 1.28 (1.7–2.98)	2.70 ± 0.93[d] 2.65; 1.58 (1.9–3,48)	1.88 ± 0.59[e] 1.80; 1.00 (1.3–2.3)	<0.001

[a] Different from both Group 1 and Group 3 (p <0.001 and p = 0.023, respectively)
[b] Different from both Group 1 and Group 3 (both p <0.001)
[c] Different from both Group 2 and Group 3 (p = 0.043 and p = 0.038, respectively)
[d] Different from both Group 1 and Group 3 (p = 0.043 and p <0.001, respectively)
[e] Different from both Group 1 and Group 2 (p = 0.038 and p <0.001, respectively)
E-index – elasticity score,
SD – standard deviation,
IQR – interquartile range 25–75

Tab. 1. *Comparison of age of the patients, size of the lesions, and elasticity score (E-index) among the groups*

most malignant lesions have a stiffer consistency than that of benign tumors or surrounding benign tissue because of desmoplastic reactions and areas of fibrosis that they contain. This change in stiffness can also be present in chronic or inflammatory diseases. Our latter result reflected this kind of change.

The patients in Group 2 were selected from among patients without nodules in the thyroid parenchyma. The limitation of the study was that no tissue sampling of the lymph nodes was performed in the Hashimoto patient group. Actually, it does not need to be confirmed histologically if no nodules are detected in this type of patient unless there are additional doubts.

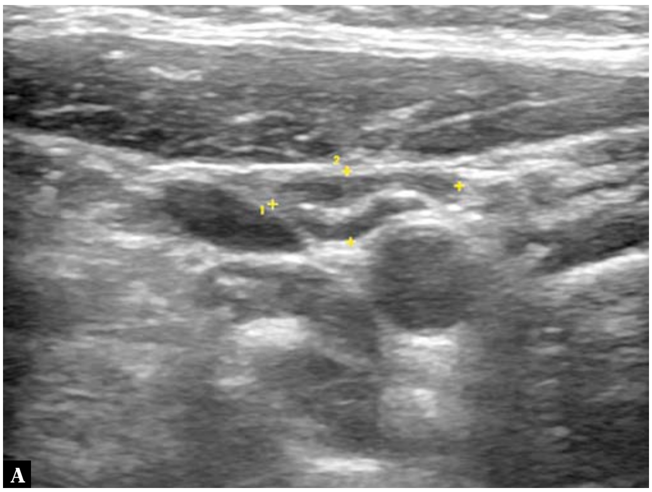
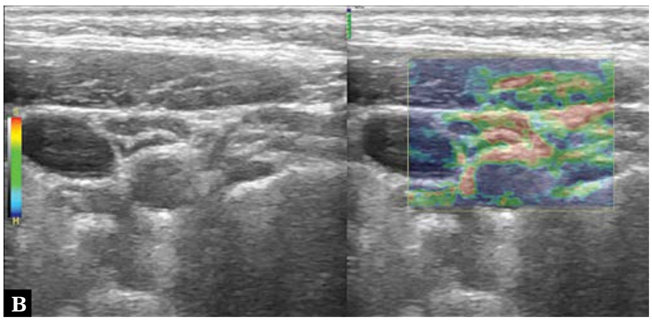
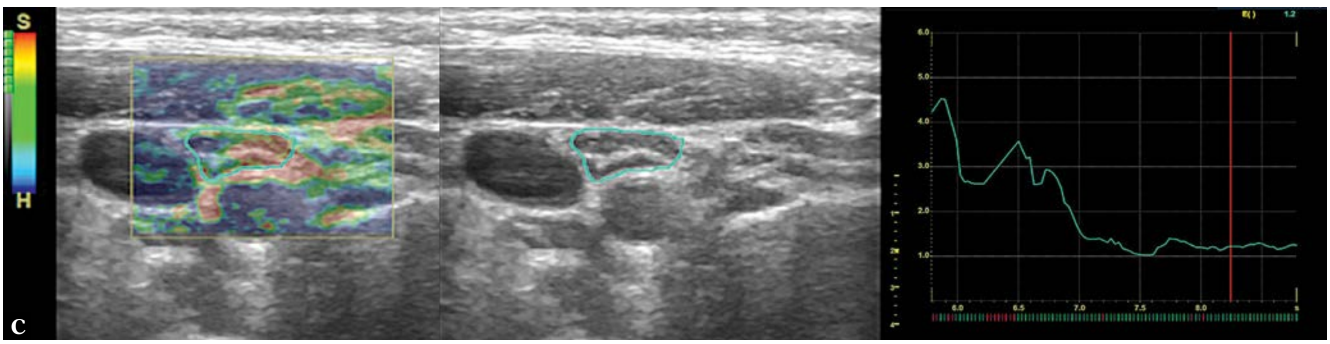


Fig. 3. *A 22-year-old healthy woman. The gray-scale image shows a level IV reactive jugular lymph node* **(A)**. *Elastographic examination of the lymph node revealed predominantly green and red colors* **(B)** *and E-index of 1.2* **(C)**. *(E-index; elasticity score)*





Conclusions

High-resolution ultrasonography has become a valuable diagnostic tool in the evaluation of superficial structures, such as parathyroid glands and lymph nodes. This study focused on one of ultrasonography techniques, i.e. real-time strain sonoelastography. The results, based on Hashimoto's lymph nodes, jugular reactive lymph nodes and parathyroid lesions, show that this method could add additional value to differential diagnosis of parathyroid lesions and benign neck lymph nodes.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

References

1. Johnson NA, Tublin ME, Ogilvie JB: Parathyroid imaging: technique and role in the preoperative evaluation of primary hyperparathyroidism. AJR Am J Roentgenol 2007; 188: 1706–1715.
2. Ruda JM, Hollenbeak CS, Stack BC Jr: A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. Otolaryngol Head Neck Surg 2005; 132: 359–372
3. Kaplan EL, Yashiro T, Salti G: Primary hyperparathyroidism in the 1990s. Choice of surgical procedures for this disease. Ann Surg 1992; 215: 300–317.
4. Chaudhary V, Bano S: Thyroid ultrasound. Indian J Endocrinol Metab 2013; 17: 219–227.
5. Yamashiro I, Saito OC, Chammas MC, Cerri GG: Ultrasound findings in thyroiditis. Radiol Bras 2007; 40: 75–79.
6. Lane MJ, Desser TS, Weigel RJ, Jeffrey RB Jr: Use of color and power Doppler sonography to identify feeding arteries associated with parathyroid adenomas. AJR Am J Roentgenol 1998; 171: 819–823.
7. Scheiner JD, Dupuy DE, Monchik JM, Noto RB, Cronan JJ: Pre-operative localization of parathyroid adenomas: A comparison of power and colour Doppler ultrasonography with nuclear medicine scintigraphy. Clin Radiol 2001; 56: 984–988.
8. Kebapci M, Entok E, Kebapci N, Adapinar B: Preoperative evaluation of parathyroid lesions in patients with concomitant thyroid disease: role of high resolution ultrasonography and dual phase technetium 99m sestamibi scintigraphy. J Endocrinol Invest 2004; 27: 24–30.
9. Yerli H, Eski E, Korucuk E, Kaskati T, Agildere AM: Sonoelastographic qualitative analysis for management of salivary gland masses. J Ultrasound Med 2012; 31: 1083–1089.
10. Altinbas NK, Gundogdu Anamurluoglu E, Oz II, Yuce C, Yagci C, Ustuner E *et al.*: Real-time sonoelastography of parotid gland tumors. J Ultrasound Med 2017; 36: 77–87.
11. Ahuja A, Ying M, King A, Yuen HY: Lymph node hilus: gray scale and power Doppler sonography of cervical nodes. J Ultrasound Med 2001; 20: 987–992.
12. Altinbas NK, Oz I, Ustuner E, Gulpinar B, Peker E, Akkaya Z *et al.*: Intranodal palisaded myofibroblastoma: radiological and cytological overview. Pol J Radiol 2016; 81: 342–346.
13. Azizi G, Piper K, Keller JM, Mayo ML, Puett D, Earp KM *et al.*: Shear wave elastography and parathyroid adenoma: A new tool for diagnosing parathyroid adenomas. Eur J Radiol 2016; 85: 1586–1593.
14. Ünlütürk U, Erdoğan MF, Demir O, Culha C, Güllü S, Başkal N: The role of ultrasound elastography in preoperative localization of parathyroid lesions: A new assisting method to preoperative parathyroid ultrasonography. Clin Endocrinol (Oxf) 2012; 76: 492–498.
15. Isidori AM, Cantisani V, Giannetta E, Diacinti D, David E, Forte V *et al.*: Multiparametric ultrasonography and ultrasound elastography in the differentiation of parathyroid lesions from ectopic thyroid lesions or lymphadenopathies. Endocrine 2017; 57: 335–343.