Original Paper

Comparing the Diagnostic Accuracy of RTE and SWE in Differentiating Malignant Thyroid Nodules from Benign Ones: a Meta-Analysis

Wuguo Tian Shuai Hao Bo Gao Yan Jiang Xiaohua Zhang Shu Zhang
Lingji Guo Jie Yan Donglin Luo

Department of Breast and Thyroid Surgery, Research Institute of Surgery, Daping Hospital, Third Military Medical University, Chongqing, China

Key Words

Real-time elastography • Shear wave elastography • Malignant thyroid nodules • Meta-analysis • Sensitivity • Specificity

Abstract

Background: Approximately 10-20 million Americans have been clinically diagnosed with thyroid nodules. Shear wave elastography (SWE) and real-time elastography (RTE) are two primary forms of elastography for identifying the status of thyroid nodules. The aim of this study is to assess the performance of RTE and SWE in identifying malignant thyroid nodules. **Methods:** Relevant articles were systematically retrieved from PubMed, Embase and Cochrane Library. In order to evaluate the overall diagnostic accuracy, we have considered pooled sensitivity (SEN), specificity (SPE), area under the curve (AUC) and partial AUC with corresponding 95% confidence intervals (95%CI). Stratified analyses by ethnicity (Caucasian, Asian), the number of malignant nodules (> 50 , ≤ 50), score system (elasticity scores: ES and strain ratio: SR) and ES (> 4 , ≤ 4) were performed to explore potential sources of heterogeneity. All statistical tests were performed using the R 3.2.1 software package. **Results:** We analyzed 80 trials from 71 studies with 16,624 subjects (12,348 for SWE, 4,276 for RTE). The pooled results suggested that RTE is more accurate than SWE in diagnosing malignant cases (RTE: SEN = 0.829, 95%CI = 0.799-0.855, SPE = 0.828, 95%CI = 0.789-0.862, AUC = 0.889; SWE: SEN = 0.784, 95%CI = 0.732-0.828, SPE = 0.824, 95%CI = 0.766-0.871, AUC = 0.859). No significant difference was found in the subgroup analyses. **Conclusion:** Our findings revealed that RTE is superior to SWE in differentiating malignant and benign thyroid nodules. Nevertheless, more studies focusing on the diagnostic accuracy of RTE and SWE during different stages of thyroid nodules development should be carried out in the future.

© 2016 The Author(s)
Published by S. Karger AG, Basel

Dr. Donglin Luo

Department of Breast and Thyroid Surgery, Research Institute of Surgery, Daping Hospital, Third Military Medical University, No. 10 Changjiangzhi Road, Yuzhong Area, Chongqing, 400042 (China); Tel. +86-023-68757950, E-Mail donglinluo@163.com

KARGER

Introduction

Thyroid nodules are frequently observed in clinical practice. Epidemiological studies demonstrate that approximately 10-20 million Americans have been clinically diagnosed with thyroid nodules, of which 4-7% of the cases were classified as malignant [1, 2]. The incidence of thyroid nodules has been increasing, leading to an increase in the demand of precise detection techniques, capable of dealing with small, incidentally discovered nodules.

Fine-needle aspiration (FNA) has long been considered as a standard procedure for differentiating benign and malignant nodules. However, this method is limited by its invasive approach of sampling [3, 4]. Elastography, as a non-invasive imaging modality, is promising in the diagnostic evaluation of thyroid nodules [5-7]. It utilizes ultrasound imaging to evaluate the tissue elasticity distribution.

The two prevalent types of elastography are real-time ultrasound elastography (RTE) and shear wave elastography (SWE). The former, also called “electronic palpation,” was firstly introduced in 1991; this technique is designed to identify malignant thyroid nodules using tissue elasticity measurements [8]. Its function bases on the mechanism that with an external force softer tissue have a high degree of deformation than hard parts; and the degree of distortion of a tissue under compression can be recorded, which leads to an objective evaluation of tissue stiffness. Nowadays, there are two primary criteria, including a qualitative assessment with the elasticity score and a quantitative assessment with the strain ratio, for assessing the diagnostic power of RTE [9]. SWE has also been found to be a promising diagnostic method [10-12]. In brief, the mechanism of SWE is that tissues are stressed by a radiation force produced by an ultrasonic beam, and the speed of shear waves were recorded by ultrafast sonographic tracking techniques. As suggested by the Young modulus formula, tissue elasticity can be reflected by the speed of shear wave propagation and the real-time color-coded elastogram in which tissues in blue are softer whereas tissues in red are comparatively stiffer [13].

So far, a large number of studies on the effectiveness of SWE and RTE in differentiating between malignant and benign thyroid nodules have been conducted. These studies, however, are limited in sample size and have reported a wide range of sensitivities and specificities. Therefore, we conducted a meta-analysis to assess the performance of RTE and SWE on identifying malignant thyroid nodules.

Materials and Methods

Search strategy

A systematical literature search for relevant articles was carried out in electronic databases, including PubMed, Embase and Cochrane Library, using the following key terms in conjunction with a complete set of their corresponding synonyms: “thyroid neoplasms or thyroid carcinoma” AND “sensitivity or specificity or diagnosis” AND “elastography or elasticity imaging techniques” (up to Sept. 9 2015). In addition to that, we conducted a manual search for relevant references contained in published articles to ensure the completeness of the selection process.

Inclusion and exclusion criteria

To start with, titles and abstracts of all retrieved articles were manually screening to exclude duplicate publications and irrelevant articles. The remaining studies were included in the meta-analysis if the following inclusion criteria were satisfied: 1) Studies evaluating the diagnostic accuracy of SWE or RTE; 2) The diagnosis of malignant and benign thyroid nodules should be confirmed by histopathological examination on samples from fine-needle aspiration biopsy or surgical resection; 3) Diagnostic accuracy statistics, including true-positive (TP), false-positive (FP), true-negative (TN), false-negative (FN), sensitivity (SEN) and specificity (SPE), should be provided; 4) Clinical studies should have gotten informed consents from each study subject and obtained approval from the local ethics committees. Furthermore, studies were excluded if: 1) Studies incorporated duplicated data; 2) Studies belonged to case reports, reviews, abstracts

and meeting reports that did not provide sufficient data for evaluation; 3) Studies that were not approved by local ethics committees or did not acquire informed consents from all the study subjects.

Data extraction

Two researchers independently reviewed the full text of each selected study and the following information was extracted: first author, publication year, region, race, the number of nodules in the case and control group, diagnostic statistics such as TP, FP, FN and TN. To assess the diagnostic accuracy of RTE with different score system, the elasticity score (ES) and strain ration (SR) were also extracted from studies if they were available. Discrepancies between the two researchers with respect to data extraction and consolidation were resolved by a third reviewer. Furthermore, SEN and SPE were either calculated from the original data or, in absence of such data, estimated using the corresponding summary receiver operating characteristics (SROC). Finally, missing data in the selected studies were not removed but requested from the appropriate authors via email.

Quality assessment

The methodological quality of adopted studies was evaluated systematically by two reviewers in accordance with the rating system of Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) which is the standard quality assessment of selected studies [14]. The QUADAS-2 system concerns about 4 major aspects including the index test, patient selection, the reference standard and flow and timing. Each study was scored by ten questions with a maximum score of 10 and scores were compiled based on whether they met each of the 10 criteria: "yes" (1 score), "unclear" or "no" (0 score).

Statistical methods

The overall diagnostic accuracy of SWE/RTE was assessed by the pooled SEN, SPE, area under the curve (AUC) and partial AUC along with their corresponding 95% confidence intervals (95% CIs). Moreover, SROC curves were generated to present the estimator of diagnostic accuracy. Heterogeneity among the included studies was evaluated by the Deek's funnel plot asymmetry test, and a *P* value of less than 0.05 reveals the existence of significant heterogeneity. Subgroup analysis by ethnicity (Caucasian, Asian), the number of malignant nodules (> 50 , ≤ 50), score system (elasticity scores: ES and strain ration: SR) and ES (> 4 , ≤ 4) were carried out to explore potential sources of heterogeneity. Finally, potential publication bias was evaluated by Deeks' Funnel Plot Asymmetry Test. All the statistical analysis was performed by R 3.2.1 software. All statistical analyses were implemented by the R 3.1.2 software.

Results

Literature search

The search strategy enabled us to identify a total of 615 relevant articles from various databases; 264 of these articles were removed as they were duplicated publications. The remaining 351 articles were subject to abstract and titles review. We further removed 255 articles: 67 letters, reviews or meta-analyses and 188 were unrelated studies. Therefore, only 96 articles were eligible for full text review and data assessment. Finally, we excluded 25 studies due to unavailable data and the remaining 71 studies were included in the meta-analysis [3, 5-7, 10-12, 15-78]. The entire process of literature search, from article identification to the final stage of inclusion, is illustrated in Figure 1.

Main characteristics of the included studies

All of the included studies were carried out between 2005 and 2015 with a total number of 16,624 subjects (12,348 for SWE, 4,276 for RTE). A total of 829 malignant cases diagnosed by SWE in 20 published studies and 3,260 malignant cases by RTE in 60 published studies. The proportion of selected studies involving Caucasians and Asians was 53.75% and 46.25%, respectively. The main characteristics of selected studies for assessing RTE and SWE are indicated in Table 1 and Table 2, respectively. And the Deek's funnel plot asymmetry test did not find any heterogeneity between RTE ($P = 0.33$) or SWE ($P = 0.37$). Additionally,

the QUADAS-2 guidelines indicated that the overall quality of included studies was considered to be high.

Summary of diagnostic performance

Since there was significant heterogeneity among included studies (P -value < 0.05), a random-effects model was adopted to analyze the overall accuracy of SWE and RTE. The pooled results indicate that RTE was more accurate than SWE as suggested by higher sensitivity, specificity and AUC (RTE: sensitivity = 0.829, 95%CI = 0.799-0.855, specificity = 0.828, 95%CI = 0.789-0.862, AUC = 0.889;

SWE: sensitivity = 0.784, 95%CI = 0.732-0.828, specificity = 0.824, 95%CI = 0.766-0.871, AUC = 0.859). The estimates of sensitivity and specificity for SWE, along with their corresponding 95%CI, are presented in Figure 2A-B, respectively. Finally, the SROC curves for SWE and RTE are displayed in Figure 3A-B.

Subgroup analysis

We also carried out a subgroup analysis to investigate whether the diagnostic accuracies of the two elastography techniques significantly differed in stratified populations. Due to the presence of significant heterogeneity (P -value < 0.05), we implemented a random-effects model for the subgroup analysis. The results demonstrated that SWE for diagnosing thyroid nodules was more accurate in Caucasians than in the overall populations and Asians (SEN: 0.795 > 0.784 > 0.787, SPE: 0.855 > 0.824 > 0.803, AUC: 0.876 > 0.859 > 0.856, partial AUC: 0.786 > 0.765 > 0.751). Additionally, subgroup analysis by the number of malignant nodules revealed that SWE was more powerful for diagnosing those thyroid nodules with more than 50 malignant nodules than those with at most 50 malignant nodules (specificity: 0.84 > 0.82, AUC: 0.881 > 0.855). However, the subgroup of thyroid nodules with at most 50 malignant nodules had the highest sensitivity compared to that in the overall analysis and the subgroup of Asians (sensitivity: 0.797 > 0.784 > 0.782). Subgroup analysis of SWE for thyroid nodules diagnostic accuracy was illustrated in Figure 4A-B.

Since there was just one study involving Africans in the meta-analysis of RTE, subgroup analysis by ethnicity was carried out for Caucasians and Asians only. RTE for diagnosing thyroid nodules appeared to be more powerful in Caucasians than that in Asians with respect to sensitivity, AUC and partial AUC (sensitivity: 0.845 > 0.82, AUC: 0.899 > 0.887, partial AUC: 0.894 > 0.842). On the other hand, the subgroup of Asians had slightly higher specificity compared to the overall analysis and the subgroup of Caucasians (specificity: 0.835 > 0.828). In addition, subgroup analysis by the number of malignant nodules indicated that RTE was more appropriate in diagnosing thyroid nodules with more than 50 malignant nodules compared to those with at most 50 malignant nodules (sensitivity: 0.832 > 0.83, specificity: 0.854 > 0.812, AUC: 0.908 > 0.873).

Since the difference between score systems used in RTE may have a significant impact on the evaluation of diagnostic accuracy, subgroup analysis by score systems was also performed. It appeared that RTE with SR had higher sensitivity and specificity than RTE with

Fig. 1. Literature selection flow chart.

Table 1. Main characteristic of the selected studies of real-time elastography in the meta-analysis. TP: true positive, FP: false positive, FN: false negative, TN: true negative; ES: elasticity score; SR: strain ratio

Study	Region	Race	No. of Nodules		Score System		Diagnostic Power			
			Case	Control	ES scale	SR cutoff	TP	FP	FN	TN
Akcay, 2014 [15]	Turkey	Caucasian	10	93	4		10	6	0	87
Asteria, 2008 [3]	Italy	Caucasian	17	69	4		16	13	1	56
Azizi, 2013 [16]	USA	Caucasian	86	826	4		57	99	29	727
Bhatia, 2011 [18]	China	Asian	28	57	4		21	16	7	41
Bojunga, 2012 [19]	Germany	Caucasian	21	137	4		16	38	5	99
Çakal, 2015 [20]	Turkey	Caucasian	29	572		3.75	24	28	5	544
Cakir, 2011 [21]	Turkey	Caucasian	125	266	5		73	77	52	189
Cakir, 2014 [22]	Turkey	Caucasian	81	189	5		80	7	1	182
Cantisani, 2012 [27]	Italy	Caucasian	40	100		2.05	35	8	5	92
Cantisani, 2012 [24]	Italy	Caucasian	37	60		2	36	5	1	55
Cantisani, 2013 [25]	Italy	Caucasian	58	89		2	54	10	4	79
Cantisani, 2014 [26]	Italy	Caucasian	112	232		2.02	104	19	8	213
Cappelli, 2012 [28]	Italy	Caucasian	15	144	3		12	9	3	135
Ciledag, 2012 [30]	Turkey	Caucasian	9	65		2.31	8	12	1	53
Ding, 2011 [32]	China	Asian	56	69		2.73	50	18	6	51
Ferrari, 2008 [33]	Italy	Caucasian	9	14	4		8	3	1	11
Friedrich-Rust, 2010 [35]	USA	Caucasian	7	46	4		6	6	1	40
Friedrich-Rust, 2012 [34]	Germany	Caucasian	3	57	4		3	7	0	50
Gietka-Czernel, 2010 [37]	Poland	Caucasian	22	31	5		19	1	3	30
Guazzaroni, 2014 [38]	Italy	Caucasian	52	316		3.28	43	55	9	261
Hong, 2009 [5]	China	Asian	49	96	6		43	10	6	86
Hong, 2012 [40]	China	Asian	121	208	6		106	21	15	187
Kagoya, 2010 [41]	Japan	Asian	11	36	4		8	13	3	23
Kagoya, 2010 [41]	Japan	Asian	11	36		1.5	10	18	1	18
Ko, 2014 [43]	Korea	Asian	121	246	5		108	46	13	200
Lippolis, 2011 [44]	Italy	Caucasian	36	66	4		32	62	4	4
Liu, 2014 [46]	China	Asian	19	45	5		16	9	3	36
Lyshchik, 2005 [6]	Japan	Asian	22	30	4		8	4	14	26
Magri, 2015 [47]	Italy	Caucasian	21	197	5		19	59	2	138
Mansor, 2012 [48]	Egypt	Caucasian	4	42	4		4	6	0	36
Mehrotra, 2013 [49]	UK	Caucasian	10	137	5		9	28	1	109
Merino, 2011 [50]	Spain	Caucasian	10	96	6		10	57	0	39
Moon, 2012 [51]	Korea	Asian	217	486	4		141	204	76	282
Ning, 2012 [52]	China	Asian	32	67		4.23	26	11	6	56
Ning, 2012 [52]	China	Asian	32	67	4		26	19	6	48
Ragazzoni, 2012 [53]	Italy	Caucasian	40	92	4		34	15	6	77
Rago, 2007 [7]	Italy	Caucasian	34	58	4		33	0	1	58
Rago, 2010 [54]	Italy	Caucasian	31	111	3		30	9	1	102
Reginelli, 2014 [55]	Italy	Caucasian	71	422	4		67	135	4	287
Rivo-Vazquez, 2013 [56]	Spain	Caucasian	28	164	5		21	89	7	75
Rubaltelli, 2009 [57]	Italy	Caucasian	11	40	4		9	5	2	35
Sahin, 2014 [58]	Turkey	Caucasian	23	267	5		19	131	4	136
Shao, 2015 [59]	China	Asian	203	309	5		169	28	34	281
Shuzhen, 2012 [60]	China	Asian	66	225	4		59	35	7	190
Shweel, 2013 [61]	Egypt	Caucasian	16	50	5		12	7	4	43
Stoian, 2012 [62]	Romania	Caucasian	11	58	5		10	1	1	57
Tatar, 2014 [65]	Turkey	Caucasian	9	141		1.94	8	19	1	122
Trimboli, 2012 [66]	Italy	Caucasian	126	372	4		102	141	24	231
Unluturk, 2012 [67]	Turkey	Caucasian	58	179	3		27	36	31	143
Wang, 2010 [71]	China	Asian	19	32	5		17	3	2	29
Wang, 2012 [70]	China	Asian	32	99	4		28	8	4	91
Wang, 2013 [68]	China	Asian	52	116		3.86	42	10	10	106
Wang, 2013 [68]	China	Asian	52	116	5		44	25	8	91
Wang, 2014 [69]	China	Asian	375	112		3.65	325	16	50	96
Xie, 2011 [72]	China	Asian	27	33	4		26	5	1	28
Xu, 2014 [74]	China	Asian	116	325	4		93	20	23	305
Xu, 2014 [73]	China	Asian	66	117	6		49	10	17	107
Yan, 2013 [75]	China	Asian	163	184		4	137	19	26	165
Zhan, 2013 [76]	China	Asian	21	37	5		16	15	5	22
Zhang, 2014 [77]	China	Asian	77	142	6		67	6	10	

ES (sensitivity: 0.865 > 0.818, specificity: 0.866 > 0.817). By contrast, the estimates of AUC and partial AUC favored RTE with ES (AUC: 0.879 > 0.864, partial AUC: 0.873 > 0.86). Finally, subgroup analysis by ES indicated that RTE with ES greater than 4 is more accurate than RTE with ES less or equal to 4 with respect to the thyroid nodules diagnosis and detection (sensitivity: 0.824 > 0.809, specificity: 0.825 > 0.811, AUC: 0.879 > 0.874). All RTE subgroup analyses are illustrated in Figure 5A-B and Figure 6A-B.

Publication bias

The results of the Deeks' funnel plot asymmetry test presented that there was no significant publication bias in the meta-analysis with the *P*-value of 0.25.

Table 2. Main characteristics of the selected studies of shear wave elastography in the meta-analysis. TP: true positive, FP: false positive, FN: false negative, TN: true positive

Study	Region	Race	NO. of Nodules		Diagnostic Power			
			Case	Control	TP	FP	FN	TN
Azizi, 2015 [17]	USA	Caucasian	82	625	65	178	17	447
Bhatia, 2012 [11]	China	Asian	17	45	13	13	4	32
Bojunga, 2012 [19]	Germany	Caucasian	21	137	12	21	9	116
Calvete, 2014 [23]	Spain	Caucasian	28	129	24	5	4	124
Choi, 2015 [29]	Korea	Asian	12	90	7	2	5	88
Deng, 2014 [31]	China	Asian	56	119	45	19	11	100
Fukuhara, 2014 [36]	Japan	Asian	28	84	24	32	4	52
Fukuhara, 2014 [36]	Japan	Asian	28	84	24	32	4	52
Hamidi, 2015 [39]	Turkey	Caucasian	33	62	33	11	0	51
Kim, 2013 [42]	Korea	Asian	21	78	16	28	5	50
Liu, 2014 [46]	China	Asian	19	45	16	14	3	31
Liu, 2015 [45]	China	Asian	101	230	67	36	34	194
Sebag, 2010 [10]	France	Caucasian	29	117	25	7	4	110
Szczepanek-Parulska, 2013 [63]	Poland	Caucasian	22	371	16	58	6	313
Szczepanek-Parulska, 2014 [64]	Poland	Caucasian	22	371	21	110	1	261
Veyrieres, 2012 [12]	France	Caucasian	35	262	28	25	7	237
Xu, 2014 [74]	China	Asian	116	325	83	54	33	271
Xu, 2014 [73]	China	Asian	66	117	45	27	21	90
Zhan, 2013 [76]	China	Asian	24	34	23	5	1	29
Zhuo, 2014 [78]	China	Asian	69	122	66	5	3	117

Fig. 2. The forest plot of SWE's (A) sensitivity and (B) specificity in thyroid nodules diagnosis with the corresponding heterogeneity. The sensitivity and specificity from each study are represented by circle, and the confidence interval (CI) is indicated by error bars.

Discussion

Diagnostic differentiation of malignant thyroid nodules from benign ones has long been considered as a clinical barrier due to the invasive nature or rather low differentiation efficacy of conventional ways, such as FNA and classical sonography [79-81]. Elastography, a novel method utilizing tissue stiffness imaging, for identification of malignant and benign nodules, has gained popularity in recent years. RTE and SWE, the main practical applications of this method, are of our interest.

In this meta-analysis, studies were included in order to examine whether the two approaches displayed discrepant sensitivities and to decide which one was more useful in identifying malignant and benign thyroid nodules. The results suggest that both elastography methods were valuable in differentiating malignant from benign nodules with their considerable pooled sensitivity (82.9% for RTE, 78.4% for SWE) as well as specificity (82.8% for RTE, 82.4% for SWE), further confirming the application prospects of elastography in

Fig. 3. The summary receiver operator characteristic (SROC) curves based on overall analysis. (A) SWE; (B) RTE.

Fig. 4. The summary receiver operator characteristic (SROC) curves based on subgroup analysis of SWE. (A) Ethnicity; (B) Number of malignant nodules.

Fig. 5. The summary receiver operator characteristic (SROC) curves based on subgroup analysis of RTE. (A) Ethnicity; (B) Number of malignant nodules.

this field.

It can be seen that RTE was slightly more powerful than SWE. With a slightly lower negative likelihood compared to that of SWE, RTE may have better chances to identify malignancies. The strong malignancy predicting capacity of RTE was first reported using a

Fig. 6. The summary receiver operator characteristic (SROC) curves based on subgroup analysis of RTE. (A) Score System; (B) Elasticity Score.

US scanner modified for that research, with 82% sensitivity and 96% specificity [6], followed by a retrospective study reporting 81% sensitivity and 94% specificity [3]. A meta-analysis comprising both abovementioned studies by Bojunga et al. further conformed the high performance of RTE with sensitivity and specificity approaching to 88-96% and 85-95%, respectively [82]. With the evidence of case control study and meta-analysis, the results of RTE in our study was verified to be coincide with the current evaluation of the diagnostic efficiency of RTE in differentiating malignant nodules from benign ones. However, apart from the strict requirements for high-end and expensive devices, RTE still faces significant issues; for instance, it is nearly impossible to adequately examine multinodular goiters in order to identify follicular thyroid carcinoma [83]. The diagnostic drawbacks could be attributed to the specific soft textures of follicular carcinomas, which differ from the substantial firmness of other malignant nodules [84]. The differentiation of nodules, however, is strictly dependent on the stiffness of the tissue under compression [85].

SWE seems to have one prominent advantage over RTE. As was stated in a previous study [60], SWE allows to evaluate the elasticity of thyroid nodules in presence of autoimmune thyroiditis while it is unfeasible for RTE to do so. RTE is a method that evaluates tissue elasticity relative to the surrounding environment, which means several confounding factors may be involved.

According to the study by Zhang et al., the pooled sensitivity, specificity and AUC for the diagnosis of malignant thyroid nodules by SWE were 0.84, 0.90 and 0.92 [13]. Meantime, Lin et al. revealed that the ability of SWE for detecting malignant thyroid nodules has a high pooled sensitivity, specificity and area under the summary receiver operating characteristic curve (SEN = 0.843, SPE = 0.884, AUC = 0.93) [86]. When compared with the previous studies, our results shown that SWE has a slightly lower diagnostic power in differentiating malignant nodules from benign ones. The reason for this results is that our study included 20 published articles about SWE, while there only 5 included studies in the article of Zhang et al. [13] and 15 in the article of Lin et al. [86]. Then, contrasting with these included studies, our study not only contained the case control studies which have high sensitivity and specificity, like Zhuo et al. [78] and Sebag et al. [10] (SEN = 0.963, SPE = 0.962; SEN = 0.852, SPE = 0.939), but also incorporated those with poor results, like Xu et al. [73] and Szczepanek-Parulska et al. [63] (SEN = 0.682, SPE = 0.769; SEN = 0.761, SPE = 0.641). Hence, SWE have a slight lower, but a more robust result based on our abundant included studies.

The results of subgroup by ethnicity and nodules number indicated that there were not potential heterogeneity in RTE and SWE. Furthermore, we conducted a stratified

analysis by evaluation methods, including strain ratio and elastography score system. And there no significant difference was found in evaluating tissue stiffness, which in accordance with previous studies by Xing et al. and Ning et al. Hence, the assessments of RTE cannot produce discrepancy in diagnostic efficacy [52, 87]. However, there were several limitations in this meta-analysis. First of all, we included only English publications, which may cause a certain loss of relative studies. Secondly, ultrasound elastography, as a new technique for evaluating the elasticity of thyroid nodules, would be affected by subtle variations in the technical performance. Naturally, the diagnostic efficacy would be influenced, which may cause heterogeneity. In our meta-analysis, only 4 studies assessed inter observer variability and gained a superior concordance rate. Therefore, inter observer variability should be assessed in more studies. Thirdly, the clinical machines applied in SWE were Siemens or SuperSonic Imagine, and these two kind machines have different reconstruction techniques for the shear wave speed map. This difference may impact the results of SWE.

In summary, this comprehensive meta-analysis demonstrated that both SWE and RTE show good sensitivity and specificity in differentiating malignancy from benignancy. Moreover, though RTE might display a higher overall diagnostic performance, its weakness lies in its inability to evaluate multinodular goiters and its strict requirements for costly high-end devices. Hence, SWE could be considered as an additional important method with significant clinical utility for thyroid nodules diagnosis.

Acknowledgements

It's funded by Chongqing Science and Technology Committee (No. CSTC2016jcyjA0579).

Disclosure Statement

None.

References

- 1 Cramer H: Fine-needle aspiration cytology of the thyroid: an appraisal. *Cancer* 2000;90:325-329.
- 2 Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, Panunzi C, Rinaldi R, Toscano V, Pacella CM: Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. *J Clin Endocrinol Metab* 2002;87:1941-1946.
- 3 Asteria C, Giovanardi A, Pizzocaro A, Cozzaglio L, Morabito A, Somalvico F, Zoppo A: US-elastography in the differential diagnosis of benign and malignant thyroid nodules. *Thyroid* 2008;18:523-531.
- 4 Sheth S: Role of ultrasonography in thyroid disease. *Otolaryngol Clin North Am* 2010;43:239-255, vii.
- 5 Hong Y, Liu X, Li Z, Zhang X, Chen M, Luo Z: Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules. *J Ultrasound Med* 2009;28:861-867.
- 6 Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ, Pellot-Barakat C, Insana MF, Brill AB, Saga T, Hiraoka M, Togashi K: Thyroid gland tumor diagnosis at US elastography. *Radiology* 2005;237:202-211.
- 7 Rago T, Santini F, Scutari M, Pinchera A, Vitti P: Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. *J Clin Endocrinol Metab* 2007;92:2917-2922.
- 8 Ophir J, Cespedes I, Ponnekanti H, Yazdi Y, Li X: Elastography: a quantitative method for imaging the elasticity of biological tissues. *Ultrason Imaging* 1991;13:111-134.
- 9 Sun J, Cai J, Wang X: Real-time ultrasound elastography for differentiation of benign and malignant thyroid nodules: a meta-analysis. *J Ultrasound Med* 2014;33:495-502.
- 10 Sebag F, Vaillant-Lombard J, Berbis J, Griset V, Henry JF, Petit P, Oliver C: Shear wave elastography: a new ultrasound imaging mode for the differential diagnosis of benign and malignant thyroid nodules. *J Clin Endocrinol Metab* 2010;95:5281-5288.

- 11 Bhatia KS, Tong CS, Cho CC, Yuen EH, Lee YY, Ahuja AT: Shear wave elastography of thyroid nodules in routine clinical practice: preliminary observations and utility for detecting malignancy. *Eur Radiol* 2012;22:2397-2406.
- 12 Veyrieres JB, Albarel F, Lombard JV, Berbis J, Sebag F, Oliver C, Petit P: A threshold value in Shear Wave elastography to rule out malignant thyroid nodules: a reality? *Eur J Radiol* 2012;81:3965-3972.
- 13 Zhang B, Ma X, Wu N, Liu L, Liu X, Zhang J, Yang J, Niu T: Shear wave elastography for differentiation of benign and malignant thyroid nodules: a meta-analysis. *J Ultrasound Med* 2013;32:2163-2169.
- 14 Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM: QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529-536.
- 15 Akcay MA, Semiz-Oysu A, Ahiskali R, Aribal E: The value of ultrasound elastography in differentiation of malignancy in thyroid nodules. *Clin Imaging* 2014;38:100-103.
- 16 Azizi G, Keller J, Lewis M, Puett D, Rivenbark K, Malchoff C: Performance of elastography for the evaluation of thyroid nodules: a prospective study. *Thyroid* 2013;23:734-740.
- 17 Azizi G, Keller JM, Mayo ML, Piper K, Puett D, Earp KM, Malchoff CD: Thyroid Nodules and Shear Wave Elastography: A New Tool in Thyroid Cancer Detection. *Ultrasound Med Biol* 2015;41:2855-2865.
- 18 Bhatia KS, Rasalkar DP, Lee YP, Wong KT, King AD, Yuen HY, Ahuja AT: Cystic change in thyroid nodules: a confounding factor for real-time qualitative thyroid ultrasound elastography. *Clin Radiol* 2011;66:799-807.
- 19 Bojunga J, Dauth N, Berner C, Meyer G, Holzer K, Voelkl L, Herrmann E, Schroeter H, Zeuzem S, Friedrich-Rust M: Acoustic radiation force impulse imaging for differentiation of thyroid nodules. *PLoS One* 2012;7:e42735.
- 20 Cakal E, Sahin M, Unsal IO, Gungunes A, Akkaymak E, Ozkaya EC, Bozkurt NC, Ozbek M, Delibasi T: Elastography in the differential diagnosis of thyroid nodules. *Ultrason Imaging* 2015;37:251-257.
- 21 Cakir B, Aydin C, Korukluoglu B, Ozdemir D, Sisman IC, Tuzun D, Oguz A, Guler G, Guney G, Kusdemir A, Sanisoglu SY, Ersoy R: Diagnostic value of elastosonographically determined strain index in the differential diagnosis of benign and malignant thyroid nodules. *Endocrine* 2011;39:89-98.
- 22 Cakir B, Ersoy R, Cuhaci FN, Aydin C, Polat B, Kilic M, Yazgan A: Elastosonographic strain index in thyroid nodules with atypia of undetermined significance. *J Endocrinol Invest* 2014;37:127-133.
- 23 Calvete AC, Mestre JD, Gonzalez JM, Martinez ES, Sala BT, Zambudio AR: Acoustic radiation force impulse imaging for evaluation of the thyroid gland. *J Ultrasound Med* 2014;33:1031-1040.
- 24 Cantisani V, D'Andrea V, Biancari F, Medvedyeva O, Di Segni M, Olive M, Patrizi G, Redler A, De Antoni EE, Masciangelo R, Frezzotti F, Ricci P: Prospective evaluation of multiparametric ultrasound and quantitative elastosonography in the differential diagnosis of benign and malignant thyroid nodules: preliminary experience. *Eur J Radiol* 2012;81:2678-2683.
- 25 Cantisani V, D'Andrea V, Mancuso E, Maggini E, Di Segni M, Olive M, Lodise P, Palermo S, De Antoni S, Redler A, Patrizi G, Porfiri A, Panzironi G, Ricci P: Prospective evaluation in 123 patients of strain ratio as provided by quantitative elastosonography and multiparametric ultrasound evaluation (ultrasound score) for the characterisation of thyroid nodules. *Radiol Med* 2013;118:1011-1021.
- 26 Cantisani V, Grazhdani H, Ricci P, Morteale K, Di Segni M, D'Andrea V, Redler A, Di Rocco G, Giacomelli L, Maggini E, Chiesa C, Erturk SM, Sorrenti S, Catalano C, D'Ambrosio F: Q-elastosonography of solid thyroid nodules: assessment of diagnostic efficacy and interobserver variability in a large patient cohort. *Eur Radiol* 2014;24:143-150.
- 27 Cantisani V, Ulisse S, Guaitoli E, De Vito C, Caruso R, Mocini R, D'Andrea V, Ascoli V, Antonaci A, Catalano C, Nardi F, Redler A, Ricci P, De Antoni E, Sorrenti S: Q-elastography in the presurgical diagnosis of thyroid nodules with indeterminate cytology. *PLoS One* 2012;7:e50725.
- 28 Cappelli C, Pirola I, Gandossi E, Agosti B, Cimino E, Casella C, Formenti A, Castellano M: Real-time elastography: a useful tool for predicting malignancy in thyroid nodules with nondiagnostic cytologic findings. *J Ultrasound Med* 2012;31:1777-1782.
- 29 Choi WJ, Park JS, Koo HR, Kim SY, Chung MS, Tae K: Ultrasound elastography using carotid artery pulsation in the differential diagnosis of sonographically indeterminate thyroid nodules. *AJR Am J Roentgenol* 2015;204:396-401.
- 30 Ciledag N, Arda K, Aribas BK, Aktas E, Kose SK: The utility of ultrasound elastography and MicroPure imaging in the differentiation of benign and malignant thyroid nodules. *AJR Am J Roentgenol* 2012;198:W244-249.

- 31 Deng J, Zhou P, Tian SM, Zhang L, Li JL, Qian Y: Comparison of diagnostic efficacy of contrast-enhanced ultrasound, acoustic radiation force impulse imaging, and their combined use in differentiating focal solid thyroid nodules. *PLoS One* 2014;9:e90674.
- 32 Ding J, Cheng H, Ning C, Huang J, Zhang Y: Quantitative measurement for thyroid cancer characterization based on elastography. *J Ultrasound Med* 2011;30:1259-1266.
- 33 Ferrari FS, Megliola A, Scorzelli A, Guarino E, Pacini F: Ultrasound examination using contrast agent and elastosonography in the evaluation of single thyroid nodules: Preliminary results. *J Ultrasound* 2008;11:47-54.
- 34 Friedrich-Rust M, Romenski O, Meyer G, Dauth N, Holzer K, Grunwald F, Kriener S, Herrmann E, Zeuzem S, Bojunga J: Acoustic Radiation Force Impulse-Imaging for the evaluation of the thyroid gland: a limited patient feasibility study. *Ultrasonics* 2012;52:69-74.
- 35 Friedrich-Rust M, Sperber A, Holzer K, Diener J, Grunwald F, Badenhop K, Weber S, Kriener S, Herrmann E, Bechstein WO, Zeuzem S, Bojunga J: Real-time elastography and contrast-enhanced ultrasound for the assessment of thyroid nodules. *Exp Clin Endocrinol Diabetes* 2010;118:602-609.
- 36 Fukuhara T, Matsuda E, Fujiwara K, Tanimura C, Izawa S, Kataoka H, Kitano H: Phantom experiment and clinical utility of quantitative shear wave elastography for differentiating thyroid nodules. *Endocr J* 2014;61:615-621.
- 37 Gietka-Czernel M, Kochman M, Bujalska K, Stachlewska-Nasfeter E, Zgliczynski W: Real-time ultrasound elastography - a new tool for diagnosing thyroid nodules. *Endokrynol Pol* 2010;61:652-657.
- 38 Guazzaroni M, Spinelli A, Coco I, Del Giudice C, Girardi V, Simonetti G: Value of strain-ratio on thyroid real-time sonoelastography. *Radiol Med* 2014;119:149-155.
- 39 Hamidi C, Goya C, Hattapoglu S, Uslukaya O, Teke M, Durmaz MS, Yavuz MS, Hamidi A, Tekbas G: Acoustic Radiation Force Impulse (ARFI) imaging for the distinction between benign and malignant thyroid nodules. *Radiol Med* 2015;120:579-583.
- 40 Hong YR, Wu YL, Luo ZY, Wu NB, Liu XM: Impact of nodular size on the predictive values of gray-scale, color-Doppler ultrasound, and sonoelastography for assessment of thyroid nodules. *J Zhejiang Univ Sci B* 2012;13:707-716.
- 41 Kagoya R, Monobe H, Tojima H: Utility of elastography for differential diagnosis of benign and malignant thyroid nodules. *Otolaryngol Head Neck Surg* 2010;143:230-234.
- 42 Kim H, Kim JA, Son EJ, Youk JH: Quantitative assessment of shear-wave ultrasound elastography in thyroid nodules: diagnostic performance for predicting malignancy. *Eur Radiol* 2013;23:2532-2537.
- 43 Ko SY, Kim EK, Sung JM, Moon HJ, Kwak JY: Diagnostic performance of ultrasound and ultrasound elastography with respect to physician experience. *Ultrasound Med Biol* 2014;40:854-863.
- 44 Lippolis PV, Tognini S, Materazzi G, Polini A, Mancini R, Ambrosini CE, Dardano A, Basolo F, Seccia M, Miccoli P, Monzani F: Is elastography actually useful in the presurgical selection of thyroid nodules with indeterminate cytology? *J Clin Endocrinol Metab* 2011;96:E1826-1830.
- 45 Liu B, Liang J, Zheng Y, Xie X, Huang G, Zhou L, Wang W, Lu M: Two-dimensional shear wave elastography as promising diagnostic tool for predicting malignant thyroid nodules: a prospective single-centre experience. *Eur Radiol* 2015;25:624-634.
- 46 Liu BX, Xie XY, Liang JY, Zheng YL, Huang GL, Zhou LY, Wang Z, Xu M, Lu MD: Shear wave elastography versus real-time elastography on evaluation thyroid nodules: a preliminary study. *Eur J Radiol* 2014;83:1135-1143.
- 47 Magri F, Chytiris S, Zerbini F, Capelli V, Gaiti M, Carbone A, Fonte R, Malovini A, Rotondi M, Bellazzi R, Chiovato L: The Maximal Stiffness Evaluation by Real Time Ultrasound Elastography, An Improved Tool for the Differential Diagnosis of Thyroid Nodules. *Endocr Pract* 2015;10.4158/ep14504.or1-22.
- 48 Mansor M, Okasha H, Esmat S, Hashem AM, Attia KA, El-din Hussein H: Role of ultrasound elastography in prediction of malignancy in thyroid nodules. *Endocr Res* 2012;37:67-77.
- 49 Mehrotra P, McQueen A, Kolla S, Johnson SJ, Richardson DL: Does elastography reduce the need for thyroid FNAs? *Clin Endocrinol (Oxf)* 2013;78:942-949.
- 50 Merino S, Arrazola J, Cardenas A, Mendoza M, De Miguel P, Fernandez C, Ganado T: Utility and interobserver agreement of ultrasound elastography in the detection of malignant thyroid nodules in clinical care. *AJNR Am J Neuroradiol* 2011;32:2142-2148.
- 51 Moon HJ, Sung JM, Kim EK, Yoon JH, Youk JH, Kwak JY: Diagnostic performance of gray-scale US and elastography in solid thyroid nodules. *Radiology* 2012;262:1002-1013.

- 52 Ning CP, Jiang SQ, Zhang T, Sun LT, Liu YJ, Tian JW: The value of strain ratio in differential diagnosis of thyroid solid nodules. *Eur J Radiol* 2012;81:286-291.
- 53 Ragazzoni F, Deandrea M, Mormile A, Ramunni MJ, Garino F, Magliona G, Motta M, Torchio B, Garberoglio R, Limone P: High diagnostic accuracy and interobserver reliability of real-time elastography in the evaluation of thyroid nodules. *Ultrasound Med Biol* 2012;38:1154-1162.
- 54 Rago T, Scutari M, Santini F, Loiacono V, Piaggi P, Di Coscio G, Basolo F, Berti P, Pinchera A, Vitti P: Real-time elastosonography: useful tool for refining the presurgical diagnosis in thyroid nodules with indeterminate or nondiagnostic cytology. *J Clin Endocrinol Metab* 2010;95:5274-5280.
- 55 Reginelli A, Urraro F, di Grezia G, Napolitano G, Maggialetti N, Cappabianca S, Brunese L, Squillaci E: Conventional ultrasound integrated with elastosonography and B-flow imaging in the diagnosis of thyroid nodular lesions. *Int J Surg* 2014;12 Suppl 1:S117-122.
- 56 Rivo-Vazquez A, Rodriguez-Lorenzo A, Rivo-Vazquez JE, Paramo-Fernandez C, Garcia-Lorenzo F, Pardellas-Rivera H, Casal-Nunez JE, Gil-Gil P: The use of ultrasound elastography in the assessment of malignancy risk in thyroid nodules and multinodular goitres. *Clin Endocrinol (Oxf)* 2013;79:887-891.
- 57 Rubaltelli L, Corradin S, Dorigo A, Stabilito M, Tregnaghi A, Borsato S, Stramare R: Differential diagnosis of benign and malignant thyroid nodules at elastosonography. *Ultraschall Med* 2009;30:175-179.
- 58 Sahin M, Cakal E, Ozbek M, Gungunes A, Arslan MS, Akkaymak ET, Ucan B, Unsal IO, Bozkurt NC, Delibasi T: Elastography in the differential diagnosis of thyroid nodules in Hashimoto thyroiditis. *Med Oncol* 2014;31:97.
- 59 Shao J, Shen Y, Lu J, Wang J: Ultrasound scoring in combination with ultrasound elastography for differentiating benign and malignant thyroid nodules. *Clin Endocrinol (Oxf)* 2015;83:254-260.
- 60 Shuzhen C: Comparison analysis between conventional ultrasonography and ultrasound elastography of thyroid nodules. *Eur J Radiol* 2012;81:1806-1811.
- 61 Shweel M, Mansour E: Diagnostic performance of combined elastosonography scoring and high-resolution ultrasonography for the differentiation of benign and malignant thyroid nodules. *Eur J Radiol* 2013;82:995-1001.
- 62 Stoian D, Cornianuz M, Dobrescu A, Lazar F: Nodular thyroid cancer. Diagnostic value of real time elastography. *Chirurgia (Bucur)* 2012;107:39-46.
- 63 Szczepanek-Parulska E, Wolinski K, Stangierski A, Gurgul E, Biczysko M, Majewski P, Rewaj-Losyk M, Ruchala M: Comparison of diagnostic value of conventional ultrasonography and shear wave elastography in the prediction of thyroid lesions malignancy. *PLoS One* 2013;8:e81532.
- 64 Szczepanek-Parulska E, Wolinski K, Stangierski A, Gurgul E, Ruchala M: Biochemical and ultrasonographic parameters influencing thyroid nodules elasticity. *Endocrine* 2014;47:519-527.
- 65 Tatar IG, Kurt A, Yilmaz KB, Dogan M, Hekimoglu B, Hucumenoglu S: The role of elastosonography, gray-scale and colour flow Doppler sonography in prediction of malignancy in thyroid nodules. *Radiol Oncol* 2014;48:348-353.
- 66 Trimboli P, Guglielmi R, Monti S, Misischi I, Graziano F, Nasrollah N, Amendola S, Morgante SN, Deiana MG, Valabrega S, Toscano V, Papini E: Ultrasound sensitivity for thyroid malignancy is increased by real-time elastography: a prospective multicenter study. *J Clin Endocrinol Metab* 2012;97:4524-4530.
- 67 Unluturk U, Erdogan MF, Demir O, Gullu S, Baskal N: Ultrasound elastography is not superior to grayscale ultrasound in predicting malignancy in thyroid nodules. *Thyroid* 2012;22:1031-1038.
- 68 Wang H, Brylka D, Sun LN, Lin YQ, Sui GQ, Gao J: Comparison of strain ratio with elastography score system in differentiating malignant from benign thyroid nodules. *Clin Imaging* 2013;37:50-55.
- 69 Wang H, Zhao L, Xin X, Wei X, Zhang S, Li Y, Gao M: Diagnostic value of elastosonography for thyroid microcarcinoma. *Ultrasonics* 2014;54:1945-1949.
- 70 Wang HL, Zhang S, Xin XJ, Zhao LH, Li CX, Mu JL, Wei XQ: Application of Real-time Ultrasound Elastography in Diagnosing Benign and Malignant Thyroid Solid Nodules. *Cancer Biol Med* 2012;9:124-127.
- 71 Wang Y, Dan HJ, Dan HY, Li T, Hu B: Differential diagnosis of small single solid thyroid nodules using real-time ultrasound elastography. *J Int Med Res* 2010;38:466-472.
- 72 Xie P, Xiao Y, Liu F: Real-time ultrasound elastography in the diagnosis and differential diagnosis of subacute thyroiditis. *J Clin Ultrasound* 2011;39:435-440.
- 73 Xu JM, Xu HX, Xu XH, Liu C, Zhang YF, Guo LH, Liu LN, Zhang J: Solid hypo-echoic thyroid nodules on ultrasound: the diagnostic value of acoustic radiation force impulse elastography. *Ultrasound Med Biol* 2014;40:2020-2030.

- 74 Xu JM, Xu XH, Xu HX, Zhang YF, Zhang J, Guo LH, Liu LN, Liu C, Zheng SG: Conventional US, US elasticity imaging, and acoustic radiation force impulse imaging for prediction of malignancy in thyroid nodules. *Radiology* 2014;272:577-586.
- 75 Yan CX, Luo ZY, Liu XM, Huang PT, Mo GQ, Hong YR, Wen Q, Pan MQ, Weng HF: [Ultrasonic scores of conventional ultrasound and ultrasound elastography in the diagnosis of thyroid nodular lesions]. *Zhonghua Yi Xue Za Zhi* 2013;93:1630-1633.
- 76 Zhan J, Diao XH, Chai QL, Chen Y: Comparative study of acoustic radiation force impulse imaging with real-time elastography in differential diagnosis of thyroid nodules. *Ultrasound Med Biol* 2013;39:2217-2225.
- 77 Zhang YF, He Y, Xu HX, Xu XH, Liu C, Guo LH, Liu LN, Xu JM: Virtual touch tissue imaging on acoustic radiation force impulse elastography: a new technique for differential diagnosis between benign and malignant thyroid nodules. *J Ultrasound Med* 2014;33:585-595.
- 78 Zhuo J, Ma Z, Fu WJ, Liu SP: Differentiation of benign from malignant thyroid nodules with acoustic radiation force impulse technique. *Br J Radiol* 2014;87:20130263.
- 79 Hegedus L, Bonnema SJ, Bennedbaek FN: Management of simple nodular goiter: current status and future perspectives. *Endocr Rev* 2003;24:102-132.
- 80 Takashima S, Fukuda H, Nomura N, Kishimoto H, Kim T, Kobayashi T: Thyroid nodules: re-evaluation with ultrasound. *J Clin Ultrasound* 1995;23:179-184.
- 81 Gharib H, Goellner JR: Fine-needle aspiration biopsy of the thyroid: an appraisal. *Ann Intern Med* 1993;118:282-289.
- 82 Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M: Real-time elastography for the differentiation of benign and malignant thyroid nodules: a meta-analysis. *Thyroid* 2010;20:1145-1150.
- 83 Alexander EK: Approach to the patient with a cytologically indeterminate thyroid nodule. *J Clin Endocrinol Metab* 2008;93:4175-4182.
- 84 Cipriani NA, Nagar S, Kaplan SP, White MG, Antic T, Sadow PM, Aschebrook-Kilfoy B, Angelos P, Kaplan EL, Grogan RH: Follicular Thyroid Carcinoma: How Have Histologic Diagnoses Changed in the Last Half-Century and What Are the Prognostic Implications? *Thyroid* 2015;25:1209-1216.
- 85 Thomas A, Fischer T, Frey H, Ohlinger R, Grunwald S, Blohmer JU, Winzer KJ, Weber S, Kristiansen G, Ebert B, Kummel S: Real-time elastography--an advanced method of ultrasound: First results in 108 patients with breast lesions. *Ultrasound Obstet Gynecol* 2006;28:335-340.
- 86 Lin P, Chen M, Liu B, Wang S, Li X: Diagnostic performance of shear wave elastography in the identification of malignant thyroid nodules: a meta-analysis. *Eur Radiol* 2014;24:2729-2738.
- 87 Xing P, Wu L, Zhang C, Li S, Liu C, Wu C: Differentiation of benign from malignant thyroid lesions: calculation of the strain ratio on thyroid sonoelastography. *J Ultrasound Med* 2011;30:663-669.