Original Article:

Application of Society of Radiologists in Ultrasound recommendations for fine needle aspiration of thyroid nodules

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ABSTRACT

Background: The Society of Radiologists in Ultrasound (SRU) recommendations on thyroid nodules are intended to "diagnose thyroid cancers that have reached clinical significance,while avoiding unnecessary tests and surgery in patients with benign nodules."

Methods: This prospective observational study was conducted on 193 consecutive patients undergoing ultrasonography (USG) guided thyroid FNA. Nodules were categorized as "SRU-positive"and "SRU-negative" based on USG features. The sensitivity and specificity of the SRU recommendations and of various US features for thyroid malignancy were calculated.

Results: Of 193 patients subjected to FNA, 83 patients of Bethesda class I,III,IV,V were excluded. Among 110 nodules subjected to FNA, 79 were SRU positive and 31were SRU negative. There were 24 malignancies in 110 FNA (22% malignancy prevelance). There was significant difference between the malignancy rates of SRU positive and negative groups (p=0.0192). The sensitivity, specificity, PPV, NPV of thyroid malignancy in our cohort was 91.6%, 33.7%, 27.8% and 93.5% respectively.

Conclusions: The application of SRU recommendations reduces the number of benign nodules that undergo workup. Potentially missed malignancies in SRU negative nodules are less aggressive by histologic type and stage compared to SRU-positive malignancies.

Key words: *Ultrasonography, Thyroid, Fine needle aspiration cytology*

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INTRODUCTION

Thyroid ultrasonography (USG) is the most common radiological diagnostic modality used for evaluating thyroid nodules. Many sonological features like irregular margins, micro calcifications, taller than wider shape, marked hypoechogenicity have been shown to have predilection for malignancy.[1-7] However, there is also overlap in the appearance of benign and malignant thyroid nodules. Due to inconsistent predictive value of USG features, fine needle aspiration and cytopathological examination (FNAC) of thyroid nodule is required before patients undergo resection for possible thyroid malignancies.

The easy availability of USG in recent days has led to the detection of many incidental thyroid nodules. Thus, there has been an increased tendency to carry out FNAC from these nodules so that malignancy is not missed. Though, early identification of malignancy carries a good prognosis in other cancers, this is not the case with thyroid malignancy where majority of early detected cancers are papillary microcarcinomas.[8,9]

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There are different guidelines with regard to use of USG to detect risk of malignancy in thyroid nodules. Examples of these include The Society of Radiologists in Ultrasound (SRU) recommendations,[8] criteria proposed by Kim et al[10] and American Association of Clinical Endocrinologists Criteria.[11] The SRU issued the criteria in the year 2005 for management of thyroid nodules. SRU is an American society which developed the criteria after taking opinion from a panel of experts from various medical disciplines.[8] SRU recommendations emphasises that the work up of incidentally detected thyroid nodules should not be to diagnose all thyroid cancers but to diagnose cancers which reach clinical significance, thus, avoiding unnecessary FNA in patients with incidentally detected nodules. The criteria[8] were based on nodule size and USG characteristics to determine which nodule should undergo FNAC and which need not. The aim of this study was to analyse the diagnostic accuracy of USG in differentiating benign and malignant nodules by applying SRU recommendations for selection of nodule to undergo FNAC and to compare malignancy rate in SRU-positive and SRU-negative nodules. Our hypothesis was that malignancy in SRU-negative nodules are uncommon and are less aggressive.

MATERIAL AND METHODS

The study was conducted after approval from Institutional Ethics committee. This prospective observational study was conducted in 193 consecutive patients undergoing USG- guided thyroid FNAC in the Department of Radiology at our institute during a 6 months period from January 2015 to June 2015 (Figure 1). All these patients were followed up till availability of FNAC test result.

All patients (n=193), presenting with both solitary and multiple thyroid nodules for USG guided FNAC characterisation of each nodule was done using SRU criteria (Table 1).[8]

Applications of SRU recommendations

Diagnostic ultrasound (Voluson Pro 400, General Electric Health care, Austria) images were obtained before FNAC using 7.5 MHz transducer. SRU recommendations[8] were met if nodule had any one of the following characteristics: size of 10 mm or larger with microcalcifications; size of 15 mm or larger with solid composition or coarse calcifications; size of 20 mm or larger with mixed solid-cystic composition or substantial growth since the prior USG. Because the SRU consensus statement does not explicitly define the requirements for "substantial growth", a nodule was considered to show substantial growth if interval growth was the reason for the FNAC and the nodule possessed no other criteria meeting SRU recommendations.[8] Past USG studies preceding the last diagnostic thyroid USG were not reviewed specifically for substantial change.

Patients were divided into two groups: Group 1 patients had one or more nodules with at least one SRU positive nodule (n=149). Total number of SRU positive nodules was 182. Twenty four patients had more than one SRU positive nodule. Group 2 had one or more

Table 1: SRU recommendations as proposed by the Society of Radiologists in Ultrasound[8]

Ultrasound feature	Recommendations
Microcalcifications	Consider USG-guided FNAC if ≥ 1 cm
Solid or coarse calcifications	Consider USG-guided FNAC if ≥ 1.5 cm
Mixed solid and cystic or almost entirely cystic with solid mural component	Consider USG-guided FNAC if ≥ 2 cm
Substantial growth since prior ultrasound	Consider USG-guided FNAC

SRU = Society of Radiologists in Ultrasound; USG = ultrasonography; FNAC = fine needle aspiration cytology

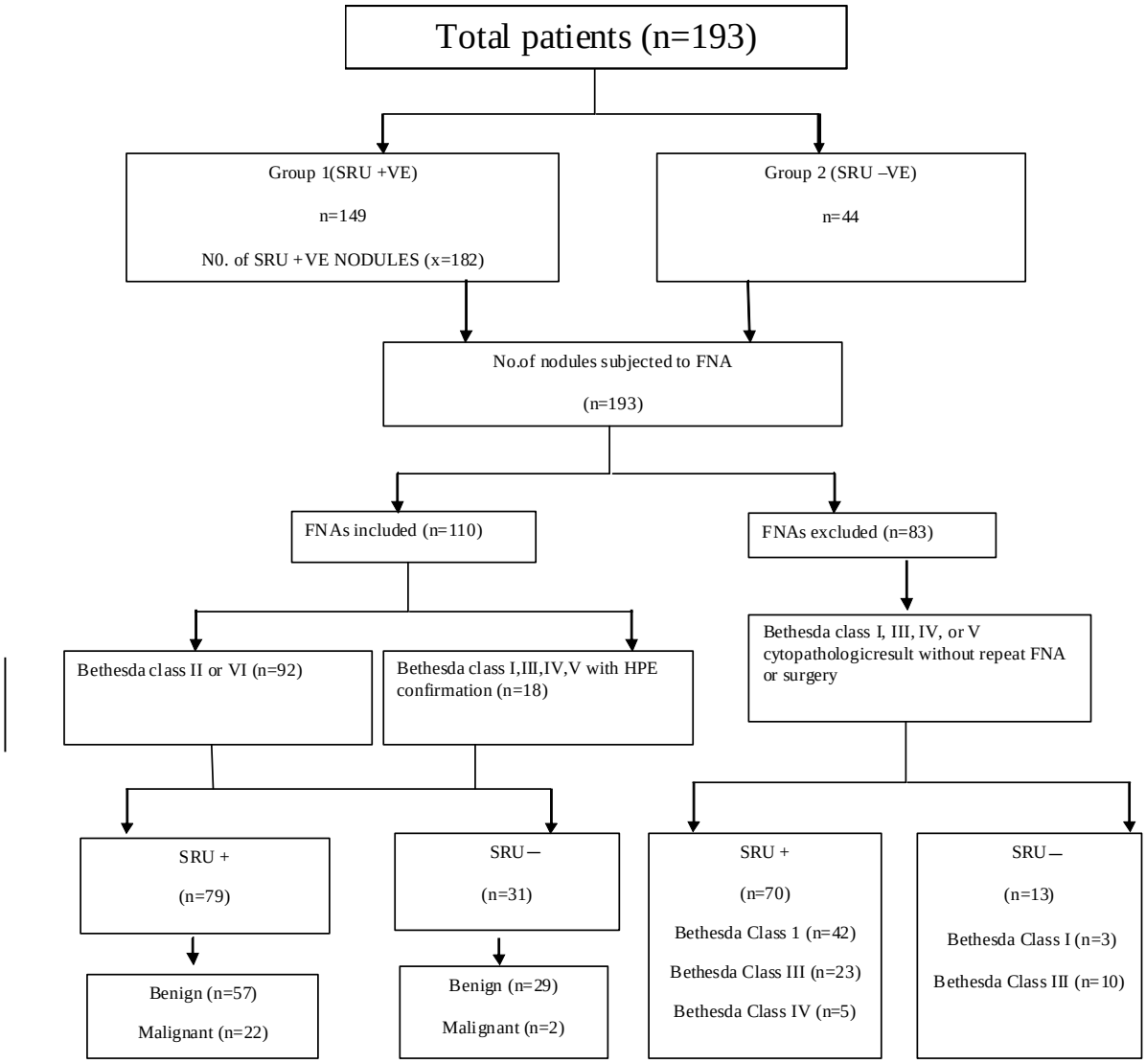

Figure 1: Study plan. Nodules were categorized on basis of USG findings as having met SRU recommendations for biopsy ("SRU +") or as not ("SRU –'')
SRU = society of radiologists in ultrasound; + = positive; – = negative; FNA = fine needle aspiration; HPE = histopathological examination

nodules but none were SRU-positive (n=44). In group 1 patients with SRU-positive nodules only the largest SRU-positive nodule was subjected to FNAC. In SRU-negative control group also, the largest nodule was subjected to FNAC.

FNAC was performed using a 22 gauge needle and non-aspiration technique was used. FNAC reports were characterised by the Bethesda System for reporting thyroid cytopathology.[12] (Table 2).

Patients were further categorized based on FNAC reports. Bethesda category II and VI nodules were included in the study (n=92). Bethesda category I,III,IV, and V nodules were either excluded from study (n=83) or were included only if histopathology report was available (n=18) as Bethesda system[12] recommends repeat FNAC for classes I and III and diagnostic surgery for classes IV and V.

Statistical analysis

Nodules in SRU-positive and-negative group were compared for their characteristics and size. SRU-positive and-negative nodules were compared for their malignancy rate. The sensitivity and specificity of categorization into

Table 2 : Bethesda system for reporting thyroid cytopathology[8]

Class	Interpretation
I	Nondiagnostic or unsatisfactory
II	Benign
III	Atypia of undetermined significance/ Follicular neoplasm of undetermined significance
IV	Follicular neoplasm
V	Suspicious of malignancy
VI	Malignant

SRU status positive or negative, or presence/ absence of hypoechogenicity, microcalcification and coarse calcification for thyroid malignancy was calculated. The malignancy rates in SRU-positive and-negative groups were compared using Fisher's Exact test. The sensitivity and specificity of SRU recommendations for thyroid malignancy were calculated considering FNAC report and histopathology report (wherever available) as the "gold standard" and where there was a discordance between the two, the histopathology report was taken as final. Statistical analysis was done using SPSS software.

RESULTS

One hundred and ninety three patients were subjected to FNAC of which 83 patients of class I,III,IV,V(43%) were excluded of which 70 were SRU positive and 13 were SRU-negative. The final study group consisted of 110 patients (91 females) with a mean age of 45.5 years (range 12-78 years). Patients with malignant nodules were significantly older compared to those with benign nodules (mean age 50 Vs 44.3 years; p = 0.02). Malignant nodules were significantly larger in size compared to benign nodules (mean size 41 mm Vs 27mm; p=0.00015). Of the 110 FNAC that were done, malignancy was confirmed in 24 (22%) (Table 3).

Among 110 nodules subjected to FNAC 79 were SRU-positive and 31were SRU-negative. HPE reports were available in 38/110 patients. In SRU-positive group 57 (72%) were benign and 22 (28%) were malignant. Further subdivision of SRU-positive nodules, by the SRU criteria is shown in Figure 2. In SRU-negative group 29 (93.5%) were benign and 2 were malignant (Table 4) (p=0.0192). These two false-negative malignancies (Figure 3) on follow-up were found to be localised papillary carcinomas less than 1.5 cm in diameter. The SRU-positive thyroid malignancies included localised papillary carcinoma (n=13) (Figure 4), papillary carcinoma with nodal metastasis (n=6), multicentric papillary carcinoma (n=2) and one medullary carcinoma with lymph node metastases.

As 2 of 24 patients who were SRU-negative had malignancy the false-negativity rate for malignancy was 8.3%. The sensitivity, specificity, positive predictive value, negative predictive value of categorisation into SRU-status positive or-negative for thyroid malignancy were 91.6%, 33.7%, 27.8% and 93.5% respectively. In malignant nodules sensitivity, specificity, PPV and NPV were 87.5%, 81.3%, 56.7%, 95.8% respectively for hypoechogenicity; 16.6%, 96.5%, 57.1%, 80.58% respectively for microcalcification; and

Table 3: Study subject and nodules

	Benign (n=86)	Malignant (n=24)	p-value
Gender: (male:female)	12:74	7:17	0.0813
Mean age (Years)*	44.3±13	50.1±13	0.0283
Nodule Size (mm)*	27±11	41±28	0.0002

*data are expressed as mean ± standard deviation

Table 4: Categorization of biopsies, pathological results of nodules that met SRU recommendations for biopsy (SRU-positive) and Nodules that did not (SRU-negative)

Characteristic	SRU+	SRU–	P-Value
Size of nodule (mm)	33±12	21±11	0.000353
Pathological result			
Benign	57	29	
Malignant	22	2	0.0192

SRU = society of radiologists in ultrasound
+ = positive; – = negative

41.6%, 81.4%, 38.4%, 83.3% respectively for coarse calcification.

DISCUSSION

According to the SRU recommendations,[8] thyroid lesions detected on US with size 1 cm or more with microcalcifications, lesions 1.5 cm or more with solid or coarse calcifications, lesions 2 cm or more with mixed solid and cystic or almost entirely cystic with solid mural component should selectively undergo FNAC rather than subjecting all incidentally detected nodules on sonography to FNAC.[8]

On applying the SRU recommendations[8] in selection of nodules for FNAC, we found that there was significant difference in malignancy rates between the SRU-positive and-negative groups ($p<0.05$). Of the various recommendations in SRU criteria,[8] nodules which were more than 20 mm with mixed solid and cystic or almost entirely cystic with solid mural component was the most commonly encountered USG feature (Figure 2). We found that, if SRU recommendations[8] were applied before FNAC, 31 (28%) nodules would not have been subjected to FNAC. Our observation suggest that by targeting nodules which meet SRU criteria, we can reduce unnecessary FNAC procedures. On applying SRU criteria and dividing the nodules into SRU-positive and-negative groups, there were only two malignancies in negative group (Table 4); suggesting SRU-negative malignancies are uncommon. If SRU recommendations[8] were

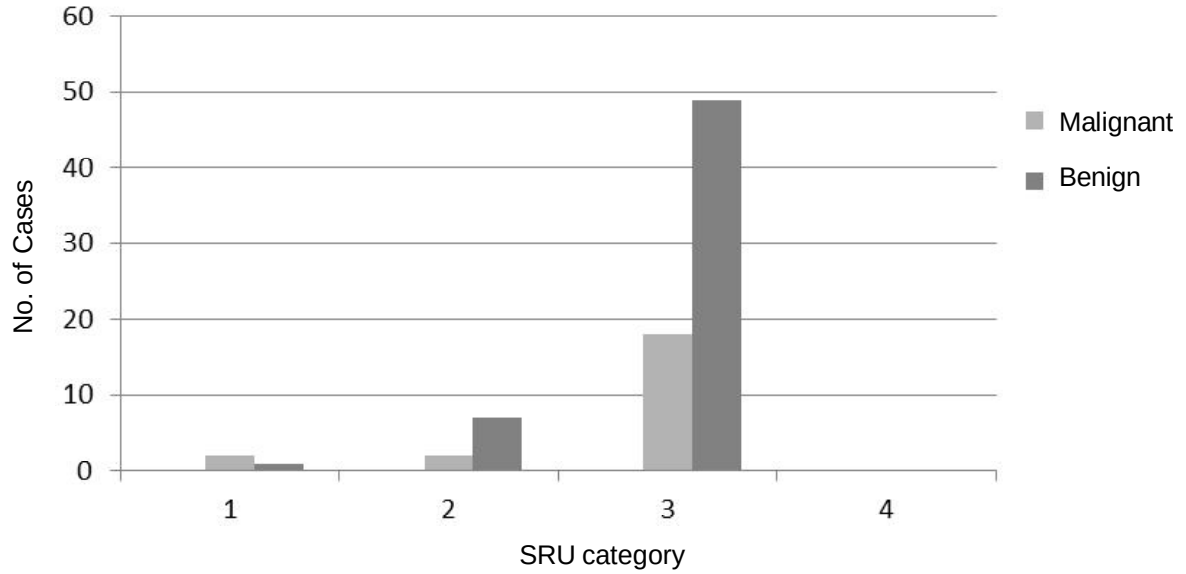

Figure 2: Various SRU-positive categories, benign and malignant nodules in each SRU-positive category. Category 1 = nodules ≥ 1cm with microcalcifications; category 2 = nodules ≥ 1.5 cm with solid or coarse calcification; category 3 = nodules ≥ 2 cm with mixed solid or cystic or entirely cystic with solid mural component. Category 4 = substantial growth since prior ultrasound

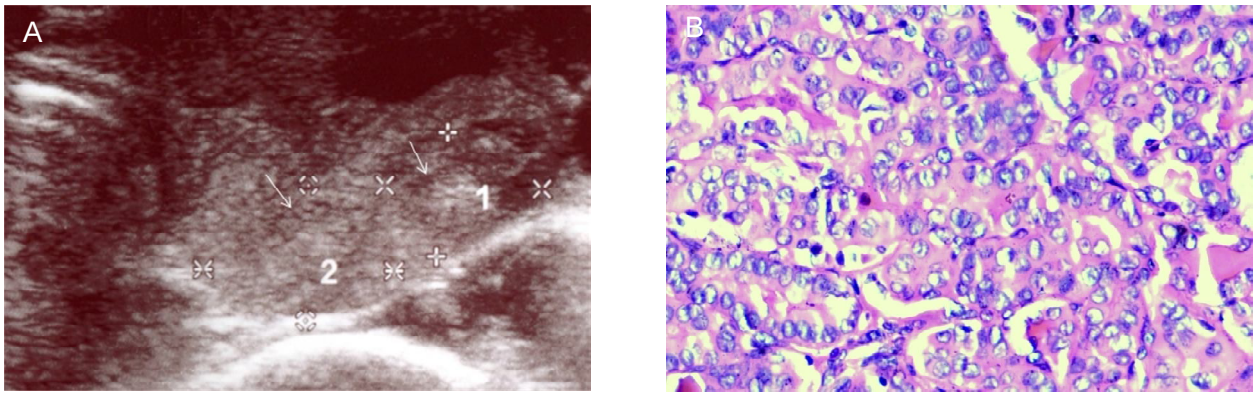

Figure 3: Ultrasonography showing two SRU-negative isoechoic nodule (white arrows) <1 cm with no evidence of calcification (A). FNAC revealed adenomatous goitre (Bethesda II). Patient underwent completion thyroidectomy Photomicrograph of left thyroidectomy specimen shows many microfollicles lined by neoplastic follicular cells displaying nuclear clearing and inclusions, suggestive of follicular variant of papillary carcinoma (B) (Haematoxylin and eosin × 200).
SRU = society of radiologists in ultrasound; FNAC = fine needle aspiration cytology.

applied, these 2 nodules would not have been subjected to FNAC. These two malignancies which were falsely-negative on SRU criteria[8] on follow-up were found to be localised papillary carcinomas less than 1.5 cm in diameter, suggesting that SRU-negative malignancies are less aggressive.

In our study, there was no significant difference in malignancy rate between males and females (p=NS). The mean size of nodule was larger in malignant nodules than in benign nodules (p<0.05). The patients with malignant nodules were of older age than those with benign nodules (p<0.05). The mean size of SRU-positive nodule was larger than SRU-negative nodule (p= 0.0004). The sensitivity, specificity, PPV and NPV for SRU recommendations in detecting malignancy was 91.6%, 33.7%, 27.8 % and 93.5% respectively. Similar results were observed in a study[13] with values of 83% and 25% for sensitivity and specificity respectively. However, lower sensitivity (35%) and specificity (54.3%) were reported in another study.[14] These authors[14] further suggested that criteria proposed by Kim et al,[10] and American Association of Clinical Endocrinologists Criteria[11] were more accurate than SRU criteria.[8]

In a study[13] of 360 biopsy procedures the authors concluded that application of SRU recommendations[8] reduces the number of benign nodules that undergo work-up. The

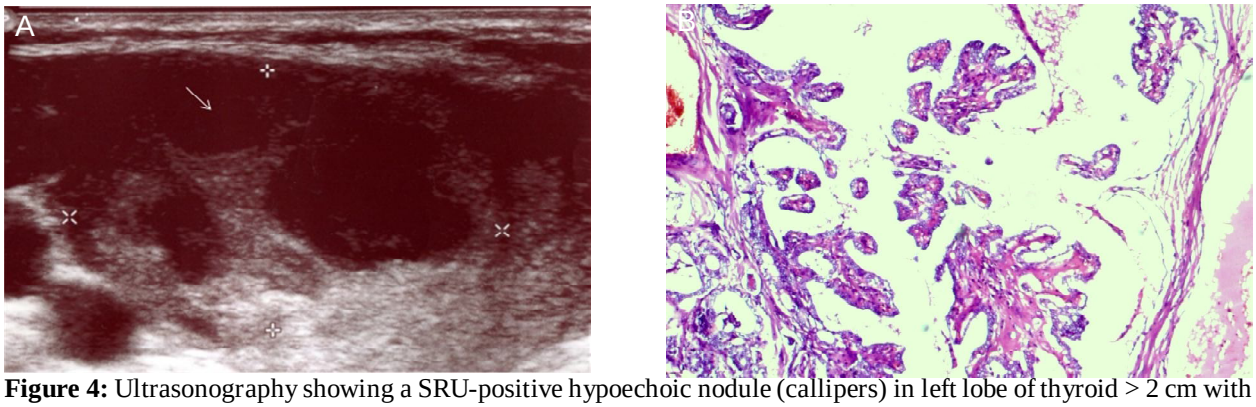

Figure 4: Ultrasonography showing a SRU-positive hypoechoic nodule (callipers) in left lobe of thyroid > 2 cm with solid and cystic areas (white arrow) with no calcification (A). Multiple nodules were there. Largest nodule FNAC revealed suspicious of papillary carcinoma (Bethesda V). Total thyroidectomy was done. Photomicrograph showing multicentric papillary carcinoma (B) (Haematoxylin and eosin × 40)

authors suggested that with the current practice, work-up of one in four thyroid biopsy procedures can be reduced. However difference between malignancy rates between the two groups was not significant in this study.[13]

We found that USG feature of hypo-echogenicity had both high sensitivity (87.5%) and specificity (81.3%) for malignancy detection. Similar findings (sensitivity and specificity of 65.9% and 87.2% respectively) were reported in another study.[1] We also found that hypoechogenicity had a high negative predictive value of 98.8% indicating that nodules which were not hypoechoic are likely to be malignant in only 4.2% of cases. We observed that US feature of microcalcification had a high specificity (96.5 %) and less sensitivity (16.6%). Similar observations have been documented in other studies[4-6,10,15] where sensitivity ranged from 85.8%-95%; specificity ranged from 26.1% to 59%. There were a few limitations to this study. First, this study was conducted at a single centre over a limited period of 6 months. Our results may not be generalisable to different practice types and referral patterns. Secondly, only the largest of SRU-positive or-negative nodules in the patient was subjected to FNAC. Thirdly, USG were done by different radiologists present in our institute, and that could have yielded slightly different results in the performance of SRU recommendations[8] because of interreader variability. We also did not review all past USG studies for the criterion of "substantial growth" because what constitutes substantial growth has not been specifically defined by the SRU.[8] Substantial growth was considered if interval growth was the reason for FNAC in one study[13] study and increase in diameter of 3 mm was the reason for FNAC in another study.[10]

We conclude that, the SRU recommendations[8] achieve the goal of diagnosing cancers that have reached clinical significance, while avoiding unnecessary tests and surgery in patients with benign nodules. Using SRU recommendations[8] can result in reduced workup in thyroid FNAC compared with current practice without strict guidelines.

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