



# The Futility of Intraoperative Frozen Section in the Evaluation of Follicular Thyroid Lesions



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## Abstract

### Educational Objective:

At the conclusion of this presentation, the participants should be able to comment on the value of obtaining intraoperative frozen section in patients with follicular thyroid lesions following publication of the 2015 American Thyroid Association guidelines.

### Objective:

Investigate the utility of intraoperative frozen section (iFS) in patients with follicular thyroid lesions following publication of the 2015 American Thyroid Association (ATA) guidelines.

### Study Design:

Single Institution Case Series

### Methods:

Patient demographics, preoperative cytology, frozen pathology and final pathology were reviewed on patients undergoing thyroid surgery at a tertiary care hospital in which iFS was utilized over a 5 year period. The test performance of iFS and the frequency of indicated completion/total thyroidectomies pre- and post-publication of the 2015 ATA guidelines were calculated.

### Results:

101 patients met inclusion criteria: 54 patients with Follicular Lesions of Undetermined Significance (FLUS) and 47 patients with a cytologic diagnosis of suspicious for follicular neoplasm/follicular neoplasm. The malignancy rate was 36%, but only 14% of malignancies were identified on iFS. A definitive benign or malignant diagnosis was given on iFS in only 21% of cases and operative management was altered in 2 cases as a result of iFS. There was a statistically significant reduction in the frequency of indicated total/completion thyroidectomies based on high risk features as a result of the 2015 ATA guidelines compared to prior recommendations (20.8% vs 5.0%,  $p < 0.001$ ). None of these patients had findings on iFS that would have altered management intraoperatively.

### Conclusions:

Intraoperative frozen section offers minimal diagnostic utility in the evaluation of follicular thyroid lesions. Updates in the 2015 ATA guidelines further diminish its potential to impact management intraoperatively. Significant improvements in its ability to identify malignancies would be needed to justify its use.

## Introduction

The role of intraoperative frozen section (iFS) for the evaluation of thyroid nodules continues to be a matter of debate.<sup>1-5</sup> In 2015 the American Thyroid Association (ATA) released updated guidelines that state that iFS can occasionally confirm malignancy at the time of lobectomy in cytologically indeterminate nodules and allow for conversion to TT (total thyroidectomy) if indicated.<sup>6</sup> They also recommend a risk-based management strategy that decreases the frequency of indicated TT/CT (completion thyroidectomy).<sup>6</sup> No known studies have described the magnitude of this reduction or the impact of the updated guidelines on the utility of iFS for nodules classified as Follicular Lesion of Undetermined Significance (FLUS) or Follicular Neoplasm/Suspicious for Follicular Neoplasm (FN/SFN). The objective of our study was to examine the utility of intraoperative frozen section (iFS) in patients with follicular thyroid lesions (FLUS and FN/SFN) following publication of the 2015 ATA guidelines. Our hypothesis was that iFS would rarely change management for nodules in these cytological categories in the context of the new guidelines, and its use is not justified.

## Methods and Materials

We performed a retrospective review of patients undergoing thyroid surgery in which iFS was utilized at the University of Missouri Hospital and Clinics after IRB approval was obtained. CPT codes were used to identify patients who underwent surgery between January 2010 and December 2015. Patient demographics, preoperative cytology, frozen and permanent pathology results were obtained from the patients' medical records, pathology reports, and operative reports. Exclusion criteria included pediatric patients, patients who underwent thyroidectomy without iFS, and cases where iFS was used to evaluate lymph nodes or parathyroid tissue. The subset of patients with a cytological diagnosis of FLUS and SFN/FN were analyzed. We then compared the frequency of indicated TT/CT before and after publication of the 2015 ATA guidelines and compared the two groups using the chi square test. We then reviewed how frequently these patients had findings on frozen section that would have altered management intraoperatively.

Table 1: Patient Characteristics

	FLUS (n= 54)	SFN/FN (n=47)	Total (n= 101)
<b>Age</b>			
Mean Age +/- SD, y	49 +/- 15	50 +/- 15	49 +/- 14
Age Range, y	23-82	24-74	23-82
<b>Sex</b>			
Male, n (%)	8 (15%)	7 (15%)	15 (15%)
Female, n (%)	46 (85%)	40 (85%)	86 (85%)
<b>Race</b>			
White, n (%)	52 (96%)	46 (98%)	98 (97%)
African-American, n (%)	2 (4%)	0	2 (2%)
Asian, n (%)	0	1 (2%)	1 (1%)
<b>Clinical Risk Factors</b>			
Family Hx Thyroid Cancer, n (%)	1 (2%)	5 (11%)	6 (6%)
XRT exposure, n (%)	1 (2%)	0	1 (1%)

## Results

Table 2: Summary of Frozen Section and Final Pathology Results

	FLUS (n= 54)	SFN/FN (n= 47)	Total (n= 101)
<b>Frozen Section Results</b>			
Definitive, n (%)	16 (30%)	5 (11%)	21 (21%)
Benign, n (%)	12 (22%)	4 (9%)	16 (16%)
Malignant, n (%)	4 (7%)	1 (2%)	5 (5%)
Non-definitive, n (%)	38 (70%)	42 (89%)	80 (79%)
Likely Benign, n (%)	6 (11%)	9 (19%)	15 (15%)
Follicular Lesion, n (%)	31 (57%)	32 (68%)	63 (62%)
Suspicious, n (%)	1 (2%)	1 (2%)	2 (2%)
<b>Final Pathology Results</b>			
Benign, n (%)	34 (63%)	31 (66%)	65 (64%)
Malignant			
PTC, classical, n (%)	2 (4%)	0	2 (2%)
Papillary microcarcinoma, n (%)	7 (13%)	8 (17%)	15 (15%)
PTC, FV, n (%)	5 (9%)	1 (2%)	6 (6%)
Hurthle cell carcinoma, n (%)	4 (7%)	4 (9%)	8 (8%)
Follicular carcinoma, n (%)	2 (4%)	3 (6%)	5 (5%)

Table 3: Comparison of the Frequency of Indicated Total/Completion Thyroidectomies Pre and Post Publication of the 2015 ATA guidelines

	n	Percentage
Pre Publication	21	20.8%
Post Publication	5	5.0%

\*P value = < 0.001

Table 4: Comparison of the Frequency of Altered Operative Management Based on iFS Findings Before and After Publication of the 2015 ATA guidelines

	n	Percentage
Pre Publication	2	2%
Post Publication	0	0%

\*P value = unable to obtain

## Discussion

While iFS has been shown to reliably identify papillary thyroid cancers, allowing conversion to a TT intraoperatively<sup>5</sup>; multiple studies have demonstrated that iFS has limited ability to identify follicular carcinomas intraoperatively<sup>1,2,4</sup>. Although others have more recently found more favorable results that the authors conclude may justify its use.<sup>7</sup> The 2015 ATA guidelines do not formally recommend for or against the use of iFS, although they comment that it is most useful in papillary thyroid cancers.<sup>6</sup> We present the largest recent review in North America investigating the utility of iFS for follicular lesions as well as the first study to report on the potential magnitude of the reduction of indicated CT/TT as a result of the 2015 ATA guidelines. We found that iFS only identified a minority (14%) of malignancies, and a definitive diagnosis on frozen section was given in 21% of cases. Additionally, there were only 2 cases in which operative management was altered based on iFS findings according to the operative reports. Neither of these patients had high risk features according to the 2015 ATA guidelines in which conversion to a TT would have been indicated.

Our review contributes additional evidence to the current literature on this topic regarding the futility of obtaining iFS for follicular lesions. It also demonstrates that the updates in the 2015 ATA guidelines further reduce the value of iFS to guide intraoperative management. Limitations of our review include its retrospective nature and relatively small study population (101 patients), although it is larger than most of the similar reviews on the topic. Finally, while consideration of performing molecular studies to help direct surgical management of indeterminate lesions could also be given, none of the patients in this study were evaluated with this testing.

## Conclusions

Intraoperative frozen section offers minimal diagnostic utility in the evaluation of follicular thyroid lesions. Updates in the 2015 ATA guidelines further diminish its potential to impact management intraoperatively. Significant improvements in its ability to identify malignancies would be needed to justify its use.

## Contact

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