

The role of intraoperative frozen sections for thyroid nodules

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Summary

The role of intraoperative frozen sections (FS) during thyroidectomy is controversial. **Aim:** to evaluate the role of FS for thyroid nodules management. **Patients and methods:** All patients who had thyroid surgery for nodular disease and previous USG-guided FNAB in 2006 were prospectively analyzed. They underwent intraoperative FS evaluation, and the biopsy material was classified as benign, malignant or follicular neoplasm. FNAB, FS and paraffin sections were compared. **Results:** Under the FS, 54% of the nodules were benign, 30% were follicular neoplasms, and 16% were malignant. All cases considered benign and malignant under the FS evaluation were confirmed through the histological "paraffin" analysis. Since it is not considered a definitive indication for total thyroidectomy, if the follicular neoplasms were classified as "benign" under the FS, their sensitivity, specificity, positive and negative predictive values and global diagnostic accuracy were 69%, 100%, 100%, 91,5% e 77%, respectively. Among the 42 cases classified as "follicular neoplasm" under the FNAB, in 1 case the FS conclusion was for papillary carcinoma, in 3 cases as benign (all confirmed through the "paraffin"); and 38 cases continued as "follicular pattern", being 29 follicular adenomas and 9 carcinomas through the "paraffin". **Conclusion:** The FS is only indicated when the FNAB reports "follicular neoplasm".

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INTRODUCTION

The fact that fine needle aspiration (FNA) is a highly accurate preoperative method to be used for the diagnosis of thyroid nodules in cancer detection¹, and the so-called "follicular neoplasia" still is a dilemma². The value of the intra-operative frozen section (FS) remains controversial while its potential to help the surgeon decide between hemithyroidectomy or total thyroidectomy. The method can potentially avoid a second surgery to remove the contralateral lobe should the surgical specimen reveal malignancy in the histopathology included in paraffin and, alternatively, it can avoid an unnecessary total thyroidectomy which will cause the patient to have to replace levothyroxine forever and increase the chance of the patient developing hypoparathyroidism and damage to the recurrent laryngeal nerve³.

The goal of the present investigation is to assess the value of the frozen section regarding decision making when facing a nodular disease of the thyroid gland.

MATERIALS AND METHODS

During the year of 2006, in a prospective study, 126 patients were consecutively submitted to thyroidectomy because of a thyroid nodular disease, and the nodules were previously assessed by guided FNA. All the patients were submitted to FNA performed by the same ultrasound operator and pathologist and the pathology interpretation was carried out by the same pathologist who participated in the harvesting of the material. During surgery, all the specimens were submitted to intraoperative frozen section test. The histopathology diagnosis of the material embedded in paraffin was available. The present study was approved by the Ethics in Research Committee of the local institution.

The FNA is conducted through a 20mL plastic syringe with a 21 gauge needle. Ultrasound was performed by means of a 10MHz probe and a minimum of three aspirations was normally used without local anesthesia. In case of mixed nodules, the liquid component was initially emptied, and the puncture was repeated afterwards. The material collected was assessed by the pathologist, and the liquid was previously centrifuged. All the material collected was fixed in alcohol and dyed by Papanicolaou or HE. The frozen section exam was made with one or two representative sections of the area most likely to present capsular invasion.

The cytopathology specimens were classified as inconclusive, benign (colloid nodule, cyst or thyroiditis), malignant and suspected malignant (specimens which definition of malignancy could not be established, presenting a follicular pattern). The presence of monomorphic epithelial cells or slightly pleomorphic, frequently grouped in micro-follicles or in syncytial masses and showing nuclei

with atypia or eosinophilic aspect of Hurthle cells, were all considered follicular pattern. As to the frozen sections, the surgical specimens were classified into inconclusive, benign, malignant and follicular pattern.

The frozen section was compared to the histopathology exam (paraffin), considered gold standard. True positive and true negative cases were defined with basis on the histopathology confirmation of the frozen section, of carcinoma or benign lesion, respectively. Thus, the disagreeing results were classified into false-positive and false-negative. Sensitivity, specificity, the predictive values of the negative and positive tests and the accuracy were calculated.

Following that, the FNA findings were compared to those from the frozen section and the impact of each one in the establishment of the surgical approach (partial or total thyroidectomy) was assessed.

RESULTS

Comparing the FS with the paraffin histopathology (Gold Standard).

In the present sample, there was no FS deemed inconclusive: 68 nodules (54%) were benign, 38 (30%) were follicular neoplasias (we must wait for the results of the paraffin study for a detailed investigation of vascular and capsular invasion) and 20 (16%) were malignant. Figure 1 compares the FS findings with the histopathology ("paraffin").

OT		histopathology	
Benign	68	→	Benign 68
Follicular pattern	38	↘	Benign 29
		↙	Malignant 9
Malignant	20	→	Malignant 20

Figure 1. Comparing the FS and the paraffin findings.

OT		histopathology	
Benign	106	↘	Benign 97
		↙	Malignant 9
Malignant	20	→	Malignant 20

Figure 2. Comparing the FS and the paraffin findings, considering the suspicious punctions (follicular pattern) as being benign.

Table 1. FS results in the assessment of thyroid nodules.

Author	n	Sensitivity	Specificity	PPV	PNV	Accuracy
Bugis et al., 1986 ⁴	198					95%
Shaha et al., 1990 ⁵	190					95%
Rosen et al., 1990 ⁶	457	53%	100%	100%	97,8%	97,9%
Shaha et al., 1990 ⁷	38					95%
Irish et al., 1992 ⁸	137					87%
Kingston et al., 1992 ⁹	395	52%	100%	100%	73%	79%
Gibbet al., 1995 ¹⁰	85					86%
McHenry et al., 1996 ¹¹	76	93%	100%			97%
Godei et al., 1996 ¹²	2470	74%	100%			
Morosini et al., 1997 ¹³	812	91,3%	100%			97,4%
Paphavasit et al., 1997 ¹⁴	1023	78%	99%	90%	98%	98%
Chang et al., 1997 ¹⁵	586			97%	95,5%	92,6%
Linder et al., 1997 ¹⁶	73	83%		95%		
Mulcahy et al., 1998 ¹⁷	66					92%
Chen et al., 1998 ¹⁸	57	23%				
Hamming et al., 1998 ¹⁹	240	67%	99%	98%	87%	89%
Tworek et al., 1998 ²⁰	68		98%			
Boyd et al., 1998 ²¹	151	86%	99%			96%
Ng SC et al., 1999 ²²	34	100%	86%			
Chow et al., 1999 ²³	84					100%
Multanen et al., 1999 ²⁴	335	74,6%				
Taneri et al.2000 ²⁵	63			28,5%	77,5%	
Piraino et al., 2000 ²⁶	85	89,4%				
Lin et al., 2000 ²⁷	63	87%				
Leteurtre et al., 2001 ²⁸	63	17%				
Tamimi et al., 2001 ²⁹	61	60%	100%			90%
Bastagli et al., 2001 ³⁰	155	42,9%	100%	100%	8,5%	92%
Lee et al., 2002 ³¹	1076					90,5%
Abboud et al., 2003 ³²	113	68%	99%			
Pisanu et al., 2003 ³³	36	33,3%				
Boutin et al., 2003 ³⁴	163	73%	99%			
Kesmodel et al., 2003 ³⁵	42	36%				
Saydam et al., 2003 ³⁶	67	100%	87%			91%
Callcut et al., 2004 ³⁷	152	67%	100%	100%		96%
Lumachi et al., 2004 ³⁸	606	83%	100%			97%
Cetin et al., 2004 ³⁹	203	87,1%	100%			97,8%
Rios et al., 2004 ⁴⁰	197	19%	100%	100%	93%	93%
Pisanu et al., 2004 ⁴¹	41	33,3%				
Furlan et al., 2004 ⁴²		56,1%				
Sahin et al., 2005 ⁴³		84%	100%			
Chao et al., 2005 ⁴⁴	135	40%	100%	100%	92%	92,9%
Dzodic et al., 2006 ⁴⁵	40	77,7%	100%	100%	94%	95%
Giuliani et al., 2006 ⁴⁶	417	56,25%	98,16%	81,81%	93,85%	
Olson et al., 2006 ⁴⁷	236	25%				
Miller et al., 2007 ⁴⁸	205	23%	99%			78%

Among the 20 cases considered malignant at the FS, two were thyroid medullary carcinomas and all the others were papilliferous carcinoma. Among the cases classified as follicular pattern (38), 29 were benign (follicular adenomas) and nine malignant, two cases of follicular carcinoma and seven of papilliferous carcinoma - follicular variant.

If we disregard the follicular pattern punctions, the predictive values for the negative (benign puncture) and positive (malignant puncture) tests add up to 100%. However, should the FS be suspicious (follicular pattern), it is one indication to perform total thyroidectomy, for the lack of criteria to conclude for malignancy - if classified as "benign", we found a new status (Figure 2).

In this new status, considering the follicular pattern cases (wait for "paraffin" result) as "benign" in the FS, the following values were found: sensitivity = 69%; specificity = 100%; predictive value for the positive test = 100%; predictive value for the negative test = 91.5%; and accuracy = 77%.

Comparing FS with FNA

All the cases had been submitted to FNA in the preoperative test. Thus, of the 126 nodules punctured, 65 (51.6%) were benign, 42 (33.3%) were follicular neoplasia and 19 (15.1%) were malignant. Crossing these data with those obtained from the FS exam, we noticed the following:

1) the 19 cases characterized as "malignant" by the FNA were confirmed by the FS and the paraffin;

2) the 65 cases characterized as benign in the FNA were confirmed by the FS and by the paraffin;

3) considering the 42 cases reported as follicular neoplasia by the FNA, we had:

- in one case, the FS found the criteria matching those of papilliferous carcinoma (confirmed by the paraffin test);

- in three cases, FS found enough criteria to define it as being benign (confirmed by the paraffin test);

- in the remaining 38 cases, the FS kept the appearance of a follicular pattern, suggesting that one should wait for the paraffin results; of these, 29 came as follicular adenomas and nine came as carcinoma, two follicular carcinoma and seven papilliferous of the follicular variant.

DISCUSSION

Table 1 shows the study regarding the results obtained with the FNA on the assessment of thyroid nodules⁴⁻⁴⁸.

Our findings match those in the literature, with good accuracy, nonetheless, it also fails when compared to the so called "follicular pattern". Thus, specificity and positive predictive value are high. We found 100% for both, matching a good part of the data in the literature. This means

that, when the FS method points to a cancer possibility, such result is highly reliable. The "follicular pattern" results come with the pathologist's recommendation of waiting for the "paraffin" result, because the criteria necessary for the final diagnosis of malignancy were not found, thus not systematically recommending total thyroidectomy. With this, on the 2x2 Table such conclusion was classified as "benign" and this justifies the 69% sensitivity in our sample. Now, when the FNA is considered, the finding of "follicular neoplasia" is a criterion for surgical indication, thus, it must be classified as "malignant"¹.

There was a strong correlation between the benign and malignant findings among the FNA guided by ultrasound, FS and histopathology, embedded in "paraffin" (Gold Standard). Thus, when the FNA shows it is benign, or malignant, the FS did not add information. Now, within the 42 cases of "follicular neoplasia" seen at the FNA, in a FS found malignancy criteria, with an impact on the treatment decision and, in three, it was defined that it was a benign lesion.

CONCLUSION

The FS is only indicated in cases which the FNA yielded results of "follicular neoplasia".

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