



# Intraoperative thyroid frozen section: indications, results and consequences

Jesper Gern<sup>1,2,3#</sup>, Michael Arbogast<sup>1,2,3#</sup>, Hakan Alakus<sup>1,3</sup>, Stefanie Brunner<sup>1,2,3</sup>, Matthias Schmidt<sup>3,4</sup>, Michael Faust<sup>3,5</sup>, Christiane Josephine Bruns<sup>1,2,3</sup>, Anne Maria Schultheis<sup>3,6</sup>, Costanza Chiapponi<sup>1,2,3</sup>

<sup>1</sup>Department of General, Visceral, Cancer and Transplant Surgery, University Hospital of Cologne, Cologne, Germany; <sup>2</sup>Department of General and Visceral Surgery, Evangelisches Klinikum Köln Weyertal, Cologne, Germany; <sup>3</sup>Medical Faculty of the University of Cologne, Cologne, Germany; <sup>4</sup>Department of Nuclear Medicine, University Hospital Cologne, Cologne, Germany; <sup>5</sup>Policlinic for Endocrinology, Diabetes and Preventive Medicine, University Hospital Cologne, Cologne, Germany; <sup>6</sup>Department of Pathology, University Hospital Cologne, Cologne, Germany

*Contributions:* (I) Conception and design: C Chiapponi, H Alakus, J Gern, M Arbogast; (II) Administrative support: CJ Bruns, M Schmidt, M Faust; (III) Provision of study materials or patients: M Arbogast, S Brunner, M Schmidt, M Faust, AM Schultheis, C Chiapponi; (IV) Collection and assembly of data: J Gern, M Arbogast, C Chiapponi, AM Schultheis; (V) Data analysis and interpretation: C Chiapponi, H Alakus, M Schmidt, J Gern, M Arbogast, S Brunner; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

#These authors contributed equally to this work.

*Correspondence to:* Prof. Dr. med. Costanza Chiapponi, MD. Department of General, Visceral, Cancer and Transplant Surgery, University Hospital of Cologne, Kerpener Str. 62, Cologne, 50937, Germany; Department of General and Visceral Surgery, Evangelisches Klinikum Köln Weyertal, Cologne, Germany; Medical Faculty of the University of Cologne, Cologne, Germany. Email: Costanza.Chiapponi@uk-koeln.de.

**Background:** Frozen section (FS) analysis is strongly influenced by the experience of surgeons and pathologists. We analyzed its performance in a secondary care hospital with surgical and pathologic experience transferred from a university hospital.

**Methods:** Indications, results, and consequences of all thyroid FS performed between January 1, 2021 and December 31, 2022 were critically reviewed.

**Results:** FS was performed in 90 (26.5%) of 340 procedures. Indications consisted in a suspicious fine needle biopsy in 28 (31.1%) cases, (99m) Technetium-Methoxy-Isobutyl-Isonitrile (MIBI) retaining hypofunctional nodules in 25 (27.8%), the intraoperative appearance in 18 (20%), the sonographic appearance in 18 (20%) and a positron emission tomography (PET) positive result in 1 case (1.1%). Malignancy was diagnosed in 21 (23.3%) and confirmed by final histology in all cases (100%). In the remaining 69 (76.7%) FS displaying no positive malignancy criteria, final histology delivered benign in 62 (89.8%) and malignant diagnoses in 7 cases (10.1%). 25% of thyroid carcinomas could not be diagnosed by FS. FS sensitivity was consequently 75% (95% CI: 55.1–89.3%). All missed malignancies were papillary thyroid carcinomas of follicular variant (fvPTC). FS sensitivity was lowest in MIBI positive hypofunctional nodules (33%) and Bethesda III (50%) as opposed to Bethesda V (92.9%) and to those cases with suspicious sonographic or intraoperative appearance (71.4%). Two-staged surgery was necessary in 10 (15.8%) of carcinomas.

**Conclusions:** Sensitivity of FS in a secondary care hospital offering surgical and pathologic experience from a specialized university center is 75% and mainly reduced by the prevalence of fvPTC. Omitting FS in Bethesda III and MIBI positive hypofunctional nodules might improve FS performance.

**Keywords:** Thyroid surgery; intraoperative frozen section (intraoperative FS); thyroidectomy

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## Introduction

For years the use of intraoperative frozen section (FS) has been seen as a strategy to tailor the extent of the initial surgery. The current German Guidelines recommend a total thyroidectomy with simultaneous prophylactic central lymphadenectomy in case of 曹 (PTC) larger than 10 mm diagnosed by FS (1).

However, its utility has been questioned, pointing out its low performance, the high number of deferred results, the frequent inability to adequately assess histologically defining features and its low cost-effectiveness, especially in thyroid follicular patterned lesions (2-5). It has even been stressed, that FS can jeopardize the detection of signs of capsular invasion on final pathologic examination (6).

It has been suggested, that in the future FS could be easily substituted by molecular testing of fine needle biopsy (FNB) specimens (7,8). Molecular testing and in general FNB are in Germany underused due to frequent misleading results in clinical routine and to the inadequate reimbursement for the procedure by the German health care system (9). Moreover, FNB can also produce scarring and hematoma in nodules, challenging the final histopathologic diagnosis (*Figure 1*).

### Highlight box

#### Key findings

- In the present study intraoperative frozen section (FS) in a secondary care hospital with surgical and pathological experience from a university center was used in only 26.5% of thyroidectomies.
- Malignancy was correctly diagnosed by FS in 23.3% and missed in 10% of cases, leading to a second surgery in 7.8% of carcinomas.
- All “missed diagnoses” were follicular variant papillary thyroid carcinomas (fvPTC).
- FS had a sensitivity of 75%, due to technical limitations in diagnosing fvPTC.

#### What is known and what is new?

- It has been reported that FS sensitivity is higher in specialized endocrine centers, due to more frequent and liberal use, training surgeons and pathologists.
- FS maintained its accuracy in a secondary care setting, despite more restrictive use.

#### What is the implication, and what should change now?

- FS in a secondary care setting might benefit from the experience from specialized pathology units.
- In Bethesda III and (99m) Technetium-Methoxy-Isobutyl-Isonitrile (MIBI)-retaining hypofunctional nodules beside Bethesda IV, FS appears abdicable due to low sensitivity.

Recently the University of Mainz has analyzed and compared the results of FS between their center (specialized university hospital) and the “PETS2” collective, consisting of clinics from all levels of primary, secondary, and tertiary care from Austria, Czech Republic, Germany, Norway, and Poland, with the majority of centers being in Germany (9). They described a higher sensitivity in their center, using a targeted but liberal FS analysis, compared to the PETS2 collective using FS more infrequently (35.7% *vs.* 21.8% of surgeries). They consequently documented beside a higher sensitivity (75% *vs.* 63.5%), a less frequent need for completion surgery in their center (8.1% *vs.* 20%) due to targeted use of intraoperative FS (9). The authors argument that correctly selecting nodules for FS analysis is dependent on the experience of the surgeon, that comes from having been exposed frequently to FS results during training and professional career.

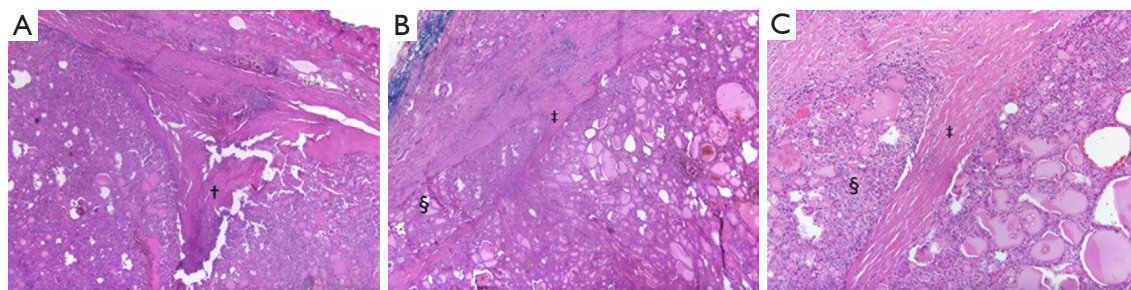
In 2018, the University Hospital of Cologne started displacing a major part of minor cervical endocrine procedures at the Evangelisches Klinikum Köln Weyertal, a nearby secondary care hospital. All procedures were performed by the same Fellow of The European Board of Endocrine Surgery in charge of the Department at the University Clinic. Since 2021 also all pathology specimens from the secondary care hospital are analyzed in the same University Pathology Department of the University Clinic, thus transferring both surgical and pathologic experience into the mentioned nearby secondary care hospital and increasing its volume to  $\geq 200$  cervical endocrine procedures yearly.

In the present study, we retrospectively analyzed indication, results, and consequences of FS for this secondary care hospital, lending surgical and pathologic experience from the nearby university hospital. We present this article in accordance with the STARD reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-105/rc>).

## Methods

### *Surgical procedures*

All cervical endocrine procedures performed for nodular thyroid disease between January 1, 2021 and December 31, 2022 (24 months) at the Evangelisches Klinikum Köln Weyertal by one single surgeon were included. We selected all procedures in which a carcinoma diagnosis by FS might have influenced the extent of surgery (thyroidectomy with



**Figure 1** Hematoxylin-eosin-stained artifact caused by FNB (HE,  $\times 10$ ). (A) A collagenous scar (†) caused by the needle used for FNB procedure. The tissue has the same quality as a true capsule in a follicular tumor (B,C) with (‡) capsular invasion. The tumor cells (§) protrude through the capsule. FNB, fine needle biopsy; HE, hematoxylin and eosin.

or without lymph nodes in case of unilateral nodular disease, prophylactic central lymphadenectomy in case of bilateral nodular disease, extension of lymphadenectomy in case of lymph nodal involvement). According to the current German Guidelines pT1a PTC is treated by hemithyroidectomy, pT1b PTC and larger tumors requires a total thyroidectomy with simultaneous prophylactic resection of the bilateral central lymph node compartments (1).

#### *Indications to surgical treatment*

All indications to surgery were taken interdisciplinarily and at least based on nuclear medicine and/or endocrinologic referral. Most cases were discussed by the multidisciplinary endocrine tumor board (MTB) of the University Hospital of Cologne, which is certified by the German Cancer Society (Deutsche Krebsgesellschaft). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and performed according to the rules and regulations for retrospective analysis of the ethical committee of the University Hospital Cologne.

Indications were based on a standardized sonographic report and a Technetium scintigraphy. In some cases, MIBI scintigraphy and FNB were also performed. A MIBI mismatch in a hypofunctional nodule with worrisome sonographic features is seen as an increased risk of malignancy (10-12). Since MIBI scintigraphy has a high negative predictive value, surveillance can be offered to patients with moderately suspicious nodules willing to avoid surgery. In case of hypofunctional nodule with suspicious sonographic appearance and MIBI retention (mismatch), FNB is recommended.

All procedures were performed by the same experienced surgeon, using magnifying glasses, head light and

intraoperative neuromonitoring. The operating surgeon had a previous 12-year-experience in three university centers, performing thyroid FS.

#### *FS*

The need for intraoperative FS was sometimes assessed during MTB case discussion and sometimes suggested by the referring specialist. It was preoperatively thoroughly discussed with the patient, including the utility and the lack of use for intermediate Bethesda III and IV nodules, as documented by the current literature (2-5).

In case of intraoperative FS, the unfixed specimen was sent with a courier into the nearby university hospital. This takes approximately ten to fifteen minutes. FS is analyzed in approximately 30 minutes by the pathologist in charge of FS for the day. Results were communicated by phone to the operating surgeon. FS caused approximately a delay of 30–45 minutes for surgery, which takes in average 30–45 and 45–60 minutes for hemi- and total thyroidectomy approximately.

FS analysis begins with a gross examination of the specimen, evaluating the thyroid gland's surface and intactness. In the next step, two micro meter thick sections are cut to examine the gland, in order to identify the lesion of interest. Representative tissue of the lesion is frozen and evaluated under the microscope. The remaining tissue is fixed in formalin and paraffin embedded (FFPE) for final diagnostic evaluation.

The diagnostic criteria of malignancy in well-differentiated follicular epithelial proliferations are based on the identification of invasion (capsular or vascular invasion) or the finding of nuclear atypia of PTC. However, the pathologist needs to be aware of the artifacts induced

by freezing, such as cytological changes mimicking PTC avoiding a false malignant diagnosis. In addition, to rule out invasive growth, the entire capsule of the lesion needs to be evaluated, which cannot be performed in the FS with the risk of a false negative diagnosis. In addition, if an entire lesion is frozen, nuclear features will be altered irreparably, as well as influencing immunohistochemical staining results rendering a final diagnosis sometimes difficult or impossible.

### Data collection and statistical analysis

Electronic and paper data of the Evangelisches Klinikum Köln Weyertal were retrospectively collected and analyzed. Data were analyzed using statistical program (IBM SPSS Statistics for Windows, v25.0. Armonk, NY, USA; RRID:SCR\_016479).

## Results

### Surgical procedures

After excluding parathyroidectomies (in which case FS is routinely performed at our institution) and non-nodular disease, in which no FS is necessary, 340 thyroid surgeries were included in the present study as possible situation in which a FS might guide the extent of surgery: 167 (49.1%) hemithyroidectomies (in which surgery can be changed into thyroidectomy with or without lymphadenectomy), 152 (44.7%) thyroidectomies (in which prophylactic lymphadenectomy can be added in case of carcinoma), 4 (1.2%) resections of recurrent multinodular goiter in the presence of bilateral rests, 9 (2.6%) isthmal resections, 5 (1.5%) partial resections and 3 (0.88%) resection of isolated sonographic suspicious rests or lymph nodes, in which the extent of resection can be extended to whole lymph node compartments.

### FS

There were 90 (26.5%) intraoperative FS analyses for 340 thyroid pathologies. In 28 (31.1%) cases, the patients had received FNB preoperatively resulting in 1 (3.5%) Bethesda I, 12 (42.8%) Bethesda III and 15 (53.6%) Bethesda V diagnoses. Additionally, in 6 (40%) cases, a BRAF mutation was diagnosed alongside with Bethesda V, warranting an almost 100% PTC diagnosis. No Bethesda II and no Bethesda IV results received FS. The other indications

for FS included 25 (27.8%) patients with sonographic suspicious MIBI-retaining hypofunctional nodules, the sonographic aspect of the nodule with/without a significant growth in 18 (20%) cases [ $\geq$  thyroid imaging reporting and database (TIRADS) IV] or the intraoperative appearance/consistency of the nodule in 18 (20%) cases and a PET positive result in 1 (1.1%) case (incidental finding during PET scan performed for other indications).

Twenty-one (23.3%) FS diagnosed malignancy intraoperatively. In all cases diagnosis was confirmed by final histology (100%). There were no false positive FS diagnoses. Sixteen (76.1%) of 21 patients received a total thyroidectomy instead of a hemithyroidectomy and 5 (23.8%) additional lymph node resection, due to a malignant FS result. All patients had classic variant PTC (*Table 1*).

In the remaining 69 (76.7%) FS analyses no positive criteria of malignancy could be identified and FS was not declared as suspicious of malignancy by the examining pathologist and for this reason the planned extent of surgery was not extended. In 62 (89.8%) cases final histology ruled out malignancy, whereas in 7 cases (10.1%) more thorough examination of the nodule including assessment of the whole nodule capsule and of the intranodular vascularization imposed a final malignant diagnosis, which had been missed by FS analysis (*Table 2*).

Thus 7 (20.6%) thyroid carcinomas diagnosed in the present study could not be diagnosed intraoperatively by FS and 5 (7.8%) of all patients with thyroid (n=64) carcinoma had to receive a second surgery to reach the recommended extent of surgery, due to a missed FS diagnosis. It follows that FS had a sensitivity of 75% (95% CI: 55.1–89.3%) in the present study. Specificity was 100% (95% CI: 94.8–100%) (*Table 3*).

More specifically, FS had a sensitivity of 50% for Bethesda III nodules (95% CI: 6.7–93.2%), 92.9% for Bethesda V (95% CI: 66.1–99.82%), 33.3% for MIBI-retaining hypofunctional nodules (95% CI: 0.8–90.6%) and 71.4% (95% CI: 29–96.3%) for cases in which preoperative sonography of intraoperative appearance alone moved the surgeon to indicate FS (*Table 1*). Thus, sensitivity was lower for Bethesda III and MIBI-retaining hypofunctional nodules as compared to Bethesda V ( $P=0.001$ ;  $P=0.00001$ ) and to preoperative sonography and or intraoperative appearance (both  $P=0.42$ ).

There were no FS analyses in 250 (72.2%) thyroid surgeries and malignant histology were thus “missed” by a non-performed FS in 36 (56.2%) cases. In most cases



**Table 1** Cases of diagnosed malignancy intraoperatively due to FS

Patient No.	Gender	Age, years	pT	Variant	pN	cM	Indication for FS
1	Female	48	1a	Classic	1a	0	Bethesda V
2	Female	44	1b	Classic	0	0	Bethesda V
3	Female	73	3b	Classic	0	0	Sonography
4	Female	75	1b	Classic	1a	0	Bethesda V
5	Female	37	1b	Classic	1a	0	Bethesda V
6	Female	25	1b	Classic	0	0	Bethesda V
7	Female	61	1b	Classic	1	0	Sonography
8	Female	46	1b	Classic	0	0	Bethesda V
9	Female	51	1b	Classic	0	0	Bethesda I
10	Female	23	2	Classic	0	0	Bethesda V
11	Female	19	2	Classic	0	0	Bethesda V
12	Male	58	1b	Classic	1	0	Bethesda V
13	Female	31	2	Classic	0	0	Bethesda V
14	Female	36	1b	Classic	0	0	Bethesda III
15	Female	74	1a	Classic	x	0	Bethesda III
16	Female	31	1b	Classic	1b	0	Bethesda V
17	Male	28	2a	Classic	1a	0	Sonography
18	Male	72	1b	Classic	1b	0	Bethesda V
19	Female	36	1b	Classic	1a	0	Bethesda V
20	Female	50	1a	Classic	1	0	Sonography
21	Male	63	1a	Classic	x	0	Sonography

In 21 (75%) cases in which a malignant tumor was exposed to FS, malignancy was correctly recognized by FS impacting the extent of surgery. In all cases a classic variant PTC was confirmed by final histopathology. pT, pN, cM, TNM classification; FS, frozen section; PTC, papillary thyroid carcinoma.

histopathology revealed either incidental microcarcinomas in hemithyroidectomies (n=4, 11.1%) or pT1a and b carcinomas sufficiently treated according to the German guidelines with thyroidectomy (n=25, 69.4%) and/or the performed resection (n=4, 11.1%). In three (8.3%) cases an intraoperative diagnosis would have influenced the extent of resection and a second surgery due to postoperative diagnoses had to be recommended according to the current German guidelines (1). These included a Bethesda II nodule turning out to be a pT3a PTC of classic variant, a Bethesda IV nodule turning out to be a pT3a follicular thyroid carcinoma of oncocyctic variant (former Hürthle cell carcinoma) and an incidentally discovered pT1b classic PTC with lymph nodal metastasis (Table 4).

In conclusion 10 (15.6%) patients with thyroid carcinoma

needed a staged thyroidectomy due either to an omitted FS (n=3, 30%) or to the lack of positive criteria of malignancy by FS (n=7, 70%).

## Discussion

Preoperative diagnosis of thyroid carcinoma is still rare in Germany. FNB is still underused and often hypofunctional nodules deemed suspicious by sonography undergo upfront hemithyroidectomy (13). Intraoperative frozen section is seen by patients and referring colleagues as a reliable way to diagnose or rule out malignancy and thus avoiding a second surgery. A real-life analysis of 68 clinics from all levels of primary, secondary, and tertiary care from Austria, Czech Republic, Germany, Norway, and Poland, with the

**Table 2** Malignant cases in which FS missed malignancy

Patient No.	Gender	Age, years	pT	Variant	pN	cM	Indication for FS	FS result
1	Female	30	1am [3]	Follicular	0	0	Bethesda III	No suspicion
2	Female	51	1a	Follicular	0	0	Sonography	Unclear/malignancy possible
3	Female	49	1b	Follicular	0	0	Bethesda V	Unclear/malignancy possible
4	Female	40	2	Follicular	0	0	Sonography	No suspicion
5	Female	42	2	Follicular	0	0	MIBI mismatch	Unclear/malignancy possible
6	Female	38	2	Follicular	0	0	Bethesda III	No suspicion
7	Female	68	2	Follicular	0	0	MIBI mismatch	No suspicion

pT, pN, cM, TNM classification; FS, frozen section; MIBI, (99m) Technetium-Methoxy-Iso-butyl-Isonitrite.

**Table 3** FS results according to the diagnosis indicating the need for FS

Diagnosis leading to FS	Rate of malignancy per indication	Rate of FS	True positive results	True negative results	False negative results	Carcinomas in which FS was not performed
Bethesda I	0/1 (0%)	1/1 (100%)	1/1 (100%)	0/1 (0%)	–	–
Bethesda III	5/19 (26.3%)	12/19 (63.1%)	2/12 (16.7%)	8/12 (66.7%)	2/12 (16.7%)	1/5 (20%)
Bethesda V	15*/17 (88.2%)	15*/17 (88.2%)	13/15 (86.7%)	1/15 (6.7%)	1/15 (6.7%)	0/15 (0%)
MIBI mismatch	7*/39 (17.9%)	26*/39 (66.7%)	1*/26 (3.8%)	23/26 (88.5%)	2/26 (7.7%)	4/7 (57.1%)
Sonography and/or intraoperative appearance	38/270 (14.1%)	37/270 (13.7%)	5*/45 (11.1%)	30/45 (66.7%)	2/45 (4.4%)	31/43 (72%)
All (number of patients)	64/340 (18.8%)	90/340 (26.5%)	21/90 (23.3%)	62/90 (68.9%)	7/90 (7.8%)	36/64 (56.2%)

The highest sensitivity was for Bethesda V, as expected. In case of Bethesda III and MIBI mismatch the sensitivity was lower. Some patients had more indications for FS, like for example MIBI mismatch + Bethesda V in one case (\*). FS, frozen section; MIBI, (99m) Technetium-Methoxy-Iso-butyl-Isonitrite.

**Table 4** Malignant cases in which FS was omitted and might have spared a second surgery to reach the extent of removal recommended by the guidelines

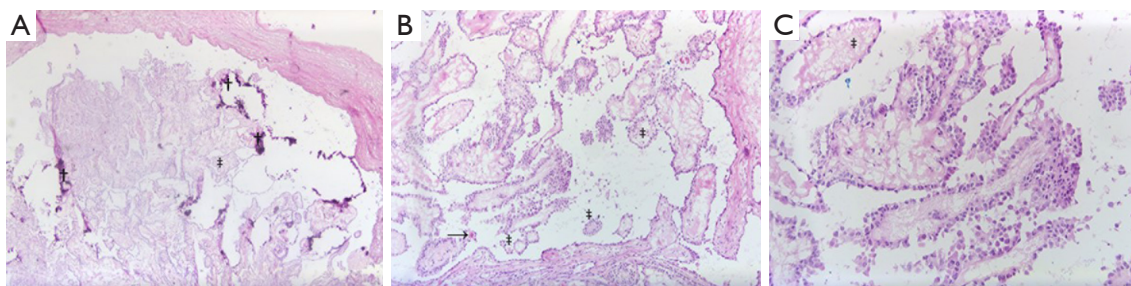
Patient No.	Gender	Age, years	pT	Variant	pN	cM	Indication for omitting FS	Second surgery
1	Female	39	1b	Classic	1	0	Symptomatic	Performed
2	Male	40	3a	Follicular oncocytic	0	0	Bethesda IV	To be performed
3	Male	31	3a	Classic	0	0	Bethesda II	To be performed

pT, pN, cM, TNM classification; FS, frozen section.

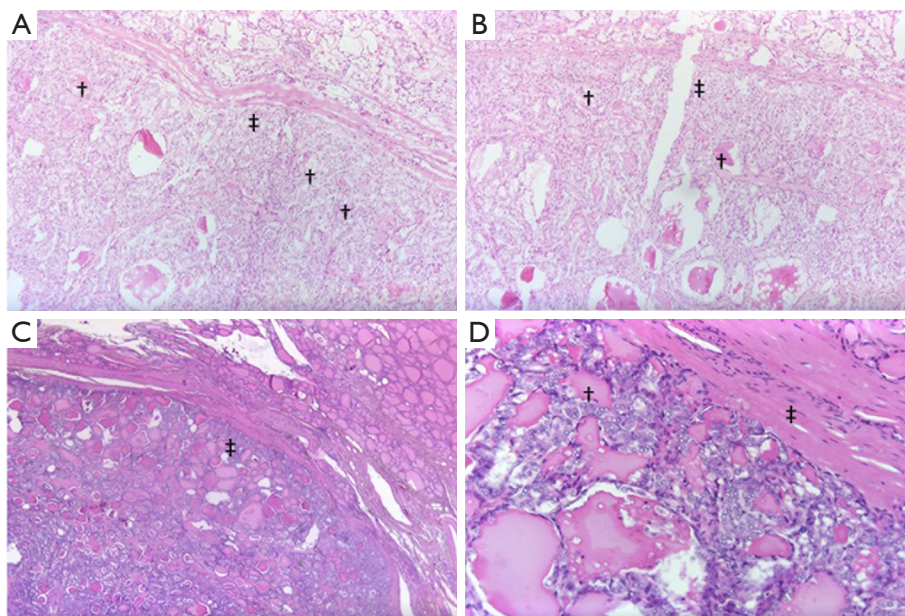
majority of centers being in Germany (PETS2 collective) recently described FS use in 21.8% of surgeries, as opposed to 35% in a university center practicing targeted liberal use (9). FS's utility, however, has been controversially discussed during the last years, especially concerning indeterminate nodules (6,14). Since the sensitivity of FS have been said to be influenced by the experience of the

indicating surgeon's and the FS performing pathologist (9), we decided to analyze our initial experience in a secondary health care center acquiring surgical and pathological experience from a university hospital.

The collective of procedures transferred to the secondary care hospital have a malignancy rate of 18.8% and FS analysis was performed in 26.5% of surgeries performed



**Figure 2** Hematoxylin-eosin-stained frozen section of a PTC (classic variant). The figures depict frozen sections of a PTC (A:  $\times 2.5$ ; B:  $\times 10$ ; C:  $\times 20$ ). A cystic lesion with a solid component with multiple calcifications (†), including psammomatous calcifications (→) and true papillae (‡) with a central stromal core covered by epithelium. As known for the technique, high power magnification (C) of the frozen tissue does not allow the identification of nuclear features of PTC, yet the diagnosis of PTC can be made. PTC, papillary thyroid carcinoma.



**Figure 3** Technical limitations of frozen section of follicular variant papillary thyroid carcinoma. (A,B) Frozen section (HE,  $\times 2.5$ ). (C,D) Formalin-fixed paraffin embedded (HE,  $\times 5$  and  $\times 10$ ). (A-C) A lesion entirely composed of follicles (†), surrounded by a fibrous capsule (‡) with no visible papillae. Nuclear atypia cannot be assessed in the frozen section as freezing modifies typical nuclear features of PTC. In the definite tissue sections (C,D) instead, typical nuclear features of PTC (nuclei with cleared chromatin, overlapping nuclei, nuclear grooves) are clearly visible. HE, hematoxylin and eosin; PTC, papillary thyroid carcinoma.

for pathologies, in which FS might have any influence on the extent of resection. The use of FS was thus lower than that reported for the university of Mainz and similar to that of the PETS2 collective (9). FS sensitivity was similar to that reported for the University Hospital of Mainz (75%) and thus higher than that reported for the secondary care hospitals of the PETS group (63.5%).

All malignant pathologies, which were not recognized

by FS, were follicular variant of PTC (fvPTC). There are several reasons as explanation for this fact. First of all, a diagnosis of invasive growth requires the assessment of the entire lesion, which cannot be performed in the frozen section. Secondly, the nuclear features for PTC are not reliably identified in the FS of fvPTC (Figures 2,3).

Since fvPTC has been currently reported to make up 11.8–53.3% of all PTC cases (15) and is approximately 12%

at our German institution (16), it is probably difficult to further improve the sensitivity of our FS.

Sensitivity was lowest if FS was indicated due to MIBI-retaining hypofunctional nodules (33%). And in fact, MIBI imaging seems to be particularly suitable to detect fvPTC and FTC (17). Therefore, FS should possibly be omitted in MIBI positive nodules since its sensitivity is rather low. Also, for Bethesda III (50%) as opposed to Bethesda V (92.3%) it was low, as reported in the literature previously (4).

Adding intra operative cytology (IC), including touch imprint (TI) and crush preparations (CP) to thyroid FS might help increasing the rate of intraoperative diagnosis of fvPTC (18), however it is not routinely performed at our institution.

fvPTC seems to more often arise in Hashimoto's thyroiditis, compared to classic PTC and tends to be isoechoic by sonography, while most nodules of classic PTC result hypoechoic or very hypoechoic (18). Some reports have described lower percentages of a taller-than-wide shape and less frequently lobulated or irregular margin, a higher percentage of extrathyroidal extension, with more frequently macro- as opposed to microcalcifications and thus lower mean TI-RADS score than classic PTC (19-20). It must be concluded that nodules with lower grade of suspicion and MIBI retention might include this PTC variant and probably do not benefit of intraoperative FS analysis.

In this study the targeted use of FS, required by an experienced surgeon trained in university centers regularly practicing thyroid FS and performed by a pathology institute from a university center influenced the extent of 21 (23.3%) surgeries performed for a malignant diagnosis and 75% of surgeries, in which it was requested. FS analysis was useless in 25% of cases and was not requested in three cases in which it might have influenced resection. This caused 10 (15.6%) two-staged surgeries for thyroid carcinoma beside 54 (84.4%) sufficient primary resections. Although this rate is between those of the university of Mainz and the PETS2 collective (8.1% and 20.8%) (8), it needs to be considered that two-staged resections have no negative prognostic impact for patients with differentiated thyroid cancer, according to the literature (21). Moreover, beside one incidental pT1b PTC and a Bethesda II nodule, all remaining 8 (80%) cases were follicular nodules, for which currently both preoperative and intraoperative diagnostic remain highly problematic, as discussed above.

It also needs to be mentioned that according to other guidelines outside from Germany hemithyroidectomy is

seen as sufficient for T1 and T2, cN0 PTCs and minimally invasive follicular thyroid carcinomas up to 4 cm in size according to the ATA guidelines (22), the ESMO guidelines (23) and the Japanese guidelines (24). Therefore, FS might not play such an important role in other settings. However, there are other situations in which FS can play an important role such as transplantation: donors show the same prevalence of thyroid nodules as the general population. Although recent literature showed a higher accuracy for FNB based on the current techniques (25), digital pathology will possibly help in the future reducing FS time and increase precision (26,27).

Although the number of cases included is not large enough for formulating general recommendations, the data presented are in line with previous reports and are representative for the experience collected during this project of "experience-transfer" from a university to a secondary care hospital. Even though it is a single-center-experience, it shows an interesting possibility which might be extended in the future to other centers, maintaining the quality and the performance of a specialized university hospital and leading to a general benefit for both patients and care givers.

## Conclusions

Sensitivity of FS in a secondary care hospital offering surgical and pathologic experience from a specialized university center is 75% and mainly reduced by the prevalence of fvPTC. Omitting FS in Bethesda III and MIBI positive hypofunctional nodules might improve FS performance.

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## Footnote

*Reporting Checklist:* The authors have completed the STARD reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gS-23-105/rc>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-105/coif>). The authors have no other conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was also performed according to the local Research Ethics Guidelines according to the ethical committee of the University Hospital Cologne (IRB statement registered as nr. 23-1115-retro) and to § 15 paragraph 1 of the professional regulations for North Rhine-Westphalian physicians, retrospective chart reviews is exempted from institutional review board approval. In addition, according to § 6 paragraph 2 of the “Law on the Protection of Personal Data in Healthcare (Health Data Protection Act - GDSG NRW)”, the university staff is allowed to use clinical information to which they have access for scientific activity without patients consent, as long as personal rights are preserved.

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