2nd BOSNIAN TURKISH CYTOPATHOLOGY SCHOOL

Sarajevo, Bosnia Herzegovina
6th-7th May, 2017

ORGANIZED BY:

Turkish Division of the International Academy of Pathology (TDIAP)
Turkish Society of Cytopathology
Department of Pathology, Clinical Centre of the University of Sarajevo, Bosnia and Herzegovina

BETHESDA REPORTING SYSTEM

Prof. Fernando Schmitt
Department of Pathology and Oncology, Medical Faculty of Porto University
Head of Molecular Pathology Unit, IPATIMUP
General-Secretary of the International Academy of Cytology

The Benefits of a Uniform Reporting System for Thyroid Cytopathology

- Improve communication
- Facilitate cytological-histological correlation
- Facilitate research into the epidemiology, molecular biology, pathology, and diagnosis of thyroid diseases
- Allow easy and reliable sharing of data from different laboratories for collaborative studies

TBSRTC – DIAGNOSTIC CATEGORIES

- **NONDIAGNOSTIC or UNSATISFACTORY**
- **BENIGN**
- **ATYPIA OF UNDETERMINED SIGNIFICANCE (AUS) or FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE (FLUS)**
- **FOLLICULAR NEOPLASM or SUSPICIOUS FOR A FOLLICULAR NEOPLASM (SFN)**

  - specify if Hurthle cell (oncocytic) type
- **SUSPICIOUS FOR MALIGNANCY (SM)**
- **MALIGNANT**

TBSRTC 1- Probabilistic approach and Relationship to Clinical Algorithms

Category	Risk of Malignancy (%)	Usual Management
Nondiagnostic	1-4	Repeat FNA w/ US
Benign	0-3	Follow
AUS or FLUS	10-15	Repeat FNA
SFN	15-30	Lobectomy
SM (usually papillary CA)	60-75	Lobectomy or total thyroidectomy
Malignant	97-99	Total thyroidectomy

TBSRTC 2- Probabilistic approach and Relationship to Clinical Algorithms

Category	Risk of Malignancy (%)	Usual Management
Nondiagnostic	(1-4) **0-5**	Repeat FNA w/ US
Benign	0-3	Follow
AUS or FLUS	(10-15) **10-30**	Repeat FNA, **molecular testing or lobectomy**
SFN	(15-30) **25-50**	Lobectomy or **molecular testing**
Suspicious for Malignancy (usually papillary CA)	(60-75) **50-75**	Lobectomy or total thyroidectomy
Malignant	97-99	Total thyroidectomy **(lobectomy)***

TBSRTC 2- Probabilistic approach and Relationship to Clinical Algorithms

ATA 2015, Recommendation 35B
For patients with thyroid cancer >1 cm and <4 cm without extrathyroidal extension, and without clinical evidence of any lymph node metastases (cN0), the initial surgical procedure can be either a bilateral procedure (near- total or total thyroidectomy) or a unilateral procedure (lobectomy). Thyroid lobectomy alone may be sufficient initial treatment for low-risk papillary and follicular carcinomas; however, the treatment team may choose total thyroidectomy to enable RAI therapy or to enhance follow- up based upon disease features and/or patient preferences

TBSRTC – NON DIAGNOSTIC
PPV 0-5%

- **INCIDENCE: 2-20% (<10%)**
- **SPECIMEN PROCESSED AND EXAMINED**
- **ADEQUACY CRITERION**
  - ✓ **At least 6 groups, each with at least 10 benign-appearing, well-visualized follicular cells.** **(LBC? –same criteria?)**
- **EXCEPTIONS**
  - ✓ **Chronic lymphocytic thyroiditis**
  - ✓ **Abundant colloid**
  - ✓ **Any atypia**
- **REASPIRATE 3 mo (with US)**

TBSRTC – NON DIAGNOSTIC Recommendations

- Pure acellular heavy colloid
  - ✓ *Aspirates composed only of pure heavy colloid may be followed without reaspiration*
- Cystic aspirates with watery colloid, blood and histiocytes require correlation with ultrasound findings.
- If US has "concerning features", a repeat FNA under US guidance should be performed at least 3 months later.
- If repeat FNA is "Non-diagnostic", correlation with family history and close clinical and US follow-up is appropriate.

Analysis of Nondiagnostic Results in a Large Series of Thyroid Fine-Needle Aspiration Cytology Performed over 9 Years in a Single Center

Acta Cytologica
DOI: 10.1159/000360066

Marta Almeida Ferreira[a] Rene Gerhard[b–d] Fernando Schmitt[b–d]

[a]Department of Endocrinology, Centro Hospitalar do Porto, and [b]IPATIMUP, Porto, Portugal; [c]Department of Laboratory Medicine and Pathobiology, Faculty of Medicine, University of Toronto, and [d]Department of Pathology, University Health Network, Toronto, Ont., Canada

Table 2. Comparison of nondiagnostic results between the first and second repeated FNAC

	Nondiagnostic	Diagnostic	Total	p
1st repeat	98 (43.6%)	127 (56.4%)	225 (100.0%)	0.653
2nd repeat	8 (36.4%)	14 (63.6%)	22 (100.0%)	
Total	106 (42.9%)	141 (57.1%)	247 (100.0%)	

Putting an Eye on Cytological Specimens: An Audit of the Clinical Impact of Thyroid Fine-Needle Aspiration in Different Health Care Settings

Diagn. Cytopathol. 2014

Bernardo Dias Pereira, M.D.,[1] René Gerhard, M.D., Ph.D.,[2,3,4] and Fernando Schmitt, M.D., Ph.D., F.I.A.C.[2,3,4]

Table II. Bethesda Categories of 2005 Thyroid FNA Samples, Distributed by Type of Care

	Type of Care		
Bethesda Category (n/%)	*GP[a]*	*E[a]*	*Total*
Non diagnostic[b]	115/11.6	76/7.5	191/9.5
Benign[b]	743/75	830/81.8	1573/78.5
Atypia of undetermined significance	49/4.9	36/3.6	85/4.2
Follicular tumour	69/7	57/5.6	126/6.3
Suspicious for malignancy	6/0.6	8/0.8	14/0.7
Malignant	9/0.9	7/0.7	16/0.8
Total	991/100	1014/100	2005/100

[a]General Practitioners (GP) and Endocrinologists (E).
[b,c]Non diagnostic" ($\chi^2 = 0.002$) and "Benign" categories ($\chi^2 < 0.001$).

RESEARCH ARTICLE

A Different Perspective on Evaluating the Malignancy Rate of the Non-Diagnostic Category of the Bethesda System for Reporting Thyroid Cytopathology: A Single Institute Experience and Review of the Literature

Pembegul Gunes[1☯], Sule Canberk[1☯*], Mine Onenerk[1], Murat Erkan[1], Nilufer Gursan[1], Emine Kilinc[2], Gamze Zeynep Kilicoglu[3]

1 Department of Pathology, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey, 2 Department of Interventional Radiology, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey

☯ These authors contributed equally to this work.
¤ Current address: Department of Pathology, Division of cytopathology, Acibadem pathology laboratory, Acibadem University, Istanbul, Turkey
* sule.canberk@acibadem.com

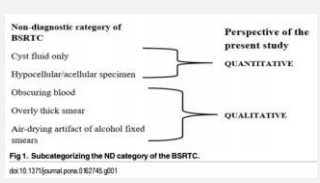


Fig 1. Subcategorizing the ND category of the BSRTC.

doi:10.1371/journal.pone.0162745.g001

Table 1. Distribution of histopathologic diagnoses.

Benign 95.3% (n = 183)	
Follicular nodular disease	*55.7% (n = 102)*
Adenomatous nodule	*14.8% (n = 27)*
Diffuse hyperplasia	*9.9% (n = 18)*
Chronic lymphocytic thyroiditis	*3.8% (n = 7)*
Follicular adenoma	*13.1% (n = 24)*
Oncocytic adenoma	*1.6% (n = 3)*
Encapsulated follicular variant of papillary thyroid carcinoma (noninvasive follicular thyroid neoplasms with papillary-like nuclear features" (NIFTP)	*1.1% (n = 2)*
Malignant 4.7% (n = 9)	
Papillary thyroid carcinoma	*33.3% (n = 3)*
Papillary thyroid microcarcinoma	*55.5% (n = 5)*
Medullary carcinoma	*11.1% (n = 1)*

doi:10.1371/journal.pone.0162745.t001

RESEARCH ARTICLE

A Different Perspective on Evaluating the Malignancy Rate of the Non-Diagnostic Category of the Bethesda System for Reporting Thyroid Cytopathology: A Single Institute Experience and Review of the Literature

Table 5. Non-diagnostic and malignancy rates for thyroid FNA in the literature.

Author	Year	Total FNA (n)	Total ND FNAs (n)	ND FNA/Total FNA (%)	Surgical follow-up (n)	Malignancy rate in the ND category (%)
MacDonald and Yazdi et al. [22]	1996	NA	NA	91	NA	2%
Al Maqbali et al. [23]	2014	1657	264	16%	68	(12/68) 18%
Yoon et al. [24]	2010	22754	3701	16.3%	230	(101/230) 43.9%
Schmidt et al.[25]	1997	345	59	17.1%	21	(4/21) 5.1%
Baloch et al. [8]	2003	3007	237	7%	53	(27/53) 51%
Woo et al. [15]	2015	1203	84	6.98%	51	(36/51) 70.6%
Yang et al. [19]	2007	4703	488	10.4%	46	(5/49) 10.8%
Renshaw et al. [12]	2010	7089	1671	23.5%	235	(47/235) 20%
Andre R Le et al. [14]	2015	-	197	25%	49	(6/49) 12.2%
Deandrea et al. [26]	2010	927	-	-	51	(3/51) 5.8%
Piana et al. [27]	2011	18359	2230	12%	96	(23/96) 24%
M.L. Richards et al. [28]	2008	241	51	21%	51	(7/51) 14%
Seningen JL et al. [9]	2010	1945	180	9.3%	180	(25/180) 14%
This study	2015	9020	192	6.8&	1390	(9/192) 4.7%

FNA: Fine-needle aspiration; ND: Non-diagnostic

doi:10.1371/journal.pone.0162745.t005

RESEARCH ARTICLE

A Different Perspective on Evaluating the Malignancy Rate of the Non-Diagnostic Category of the Bethesda System for Reporting Thyroid Cytopathology: A Single Institute Experience and Review of the Literature

Pembegul Gunes[1☯], Sule Canberk[1☯¤*], Mine Onenerk[1], Murat Erkan[1], Nilufer Gursan[1], Emine Kilinc[1], Gamze Zeynep Kilicoglu[2]

1 Department of Pathology, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey,
2 Department of Interventional Radiology, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey

☯ These authors contributed equally to this work.
¤ Current address: Department of Pathology, Division of cytopathology, Acibadem pathology laboratory, Acibadem University, Istanbul, Turkey
* sule.canberk@acibadem.com

Table 3. Comparison of nodule and patient characteristics in benign and malignant cases.

	Benign (n = 183)	Malignant (n = 9)
Age, years, mean (range)	50,74 (20–87)	47,22 (24–82)
Gender		
Female	81.4% (n = 149)	77.8 (n = 7)
Male	18.6% (n = 34)	22.2 (n = 2)
Consistency		
Solid	76.0% (n = 139)	77.8% (n = 7)
Cystic	24.0% (n = 44)	22.2% (n = 2)
Nodule size, mm, mean (range)	34,0 (3–95 mm)	14,0 (5–40 mm)
Number of nodules		
Solitary	35.0% (n = 64)	22.2% (n = 2)
Multiple	65.0 (n = 119)	77.8% (n = 7)

doi:10.1371/journal.pone.0162745.t003

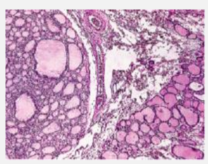
TBSRTC – BENIGN

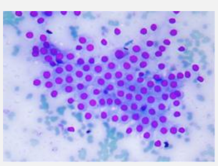
PPV 0-3%

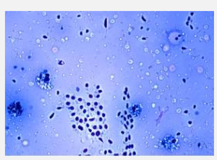
- INCIDENCE: 60-65%
- THIS CATEGORY INCLUDES
  - ✓ Hyperplastic/adenomatoid nodule.
  - ✓ Colloid nodule
  - ✓ Chronic lymphocytic thyroiditis
  - ✓ Graves´s disease
- F/U BY CLINICAL AND POSSIBLY US EXAMINATION

COLLOID NODULE

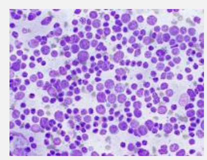
- Sparsely to moderately cellular
- Abundant colloid
- Benign follicular cells (nuclear features of papillary CA absent)
- Predominantly macrofollicles

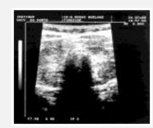


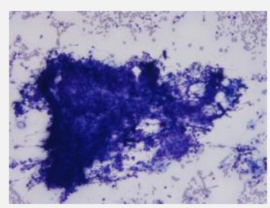


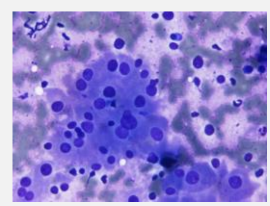


Hashimoto thyroiditis





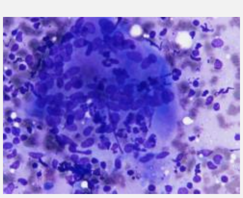


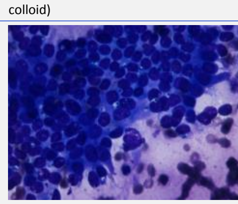


Subacute thyroiditis (de Quervain)

- viral etiology, heredity (antigen HLA-B35)
- follows acute respiratory infection
- may be unilateral (single lobe)
- solitary nodule!

- moderate cellularity
- cellular debris, small amounts of colloid, regressive changes of follicular cells
- lymphocytes, PMNs and macrophages
- multinucleated giant cells (reaction to colloid)





TBSRTC – AUS/FLUS

PPV 10-30%

- DO NOT FIT EASILY INTO BENIGN OR SUSPICIOUS CATEGORIES
- RECOMMENDED MANAGEMENT: REPEAT FNA
- AVOID OVERUSE OF THIS CATEGORY (10% USEFUL BENCHMARK OR RELATION AUS:M: 1-3)
- A SINGLE DIAGNOSIS CARRIES A LOW RISK
- IMPACT OF NEW MOLECULAR TESTS
- POST-AUS DIAGNOSIS: 50% - BENIGN AND 50% - MORE SIGNIFICANT LESION (FOLLICULAR NEOPLASM OR ABOVE) OR REPEAT AUS

Why some specimens are classified as AUS/FLUS ?

- Something is wrong with the specimen-poor preservation, drying, etc.
- There are disturbing features in the cells (nuclear enlargement, irregularity, clearing, rare grooves) but the amount of material is insufficient for diagnosis.
- Diffuse but mild nuclear clearing with incipient irregularities of the nuclear membrane, some crowding and pseudostratification.

TBSRTC – SUSPICIOUS FOR A FOLLICULAR NEOPLASM OR FOLLICULAR NEOPLASM

PPV 25-50%

- **INCIDENCE: 7-18%**
- **SIGNIFICANT ARCHITECTURAL ATYPIA**
  - ✓ **A predominance of microfollicles and/or trabecula**
- **RAISING THE POSSIBILITY OF FOLLICULAR CARCINOMA**
- **DISTINCTION BETWEEN FOLLICULAR ADENOMA AND CARCINOMA**
- **SURGERY (usually lobectomy) IS NEEDED FOR DEFINITIVE DIAGNOSIS**

TBSRTC – SUSPICIOUS FOR A HURTHLE CELL NEOPLASM

- **COMPOSED EXCLUSIVELY OF HURTHLE CELLS**
- **DIFFERENTIAL DIAGNOSIS IS DIFFERENT (MEDULLARY CA)**
- **DISTINCTION BETWEEN HCA AND HCC**
- **SURGERY (usually lobectomy) IS NEEDED FOR DEFINITIVE DIAGNOSIS**
- **FOLLICULAR NEOPLASM, HURTHLE CELL TYPE (ONCOCYTIC VARIANT)**

WHO Blue Book, Endocrine Pathology, May 2017

TBSRTC – SUSPICIOUS FOR MALIGNANCY

PPV 65-75%

- **SUSPICIOUS FOR PTC**
- **SUSPICIOUS FOR MEDULLARY CARCINOMA**
  - ✓ **Serum calcitonin level**
- **SUSPICIOUS FOR MALIGNANT LYMPHOMA**
  - ✓ **Recommendation to repeat FNA with flow cytometry**
- **SUSPICIOUS FOR METASTATIC CANCER**

TBSRTC – MALIGNANT

PPV 97-99%

- **PAPILLARY CARCINOMA (including variants)**
- **MEDULLARY CARCINOMA**
- **POORLY DIFFERENTIATED CARCINOMA**
- **ANAPLASTIC CARCINOMA**
- **LYMPHOMA**
- **METASTATIC CANCERS**
- **OTHERS**

ACTA CYTOLOGICA
Fine Needle Aspiration

New Concept of the Encapsulated Follicular Variant of Papillary Thyroid Carcinoma and Its Impact on the Bethesda System for Reporting Thyroid Cytopathology: A Single-Institute Experience

Canberk S.[a] · Gunes P.[a] · Onenerk M.[a] · Erkan M.[a] · Kilinc E.[a] · Kocak Gursan N.[a] · Kilicoglu G.Z.[b]
Author affiliations

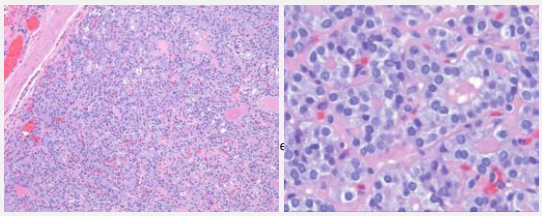
Keywords: The Bethesda System · Malignancy ratio · Fine-needle aspiration cytology · Encapsulated follicular variant of papillary thyroid carcinoma

Acta Cytologica 2016;60:198-204
https://doi.org/10.1159/000447990

If EFV-PTC were considered as a non-malignant entity, what would be the alterations in malignancy ratios of each TBSRTC categories?

	TBSRTC	Malignancy ratio with EFV-PTC in our institute	Malignancy ratio without EFV-PTC in our institute	% of relative decrease in Strickland et al	% of relative decrease in Faquin et al	% of relative decrease in Canberk et al
ND	1-4%	13%	6.5%	10%	5.5%	50%
B	0-3%	7%	6%	59%	37.6%	14%
AUS/FLUS	5-15%	45%	30%	45%	43.6%	33%
FN/SFN	15-30%	30%	10%	18%	45.5%	66%
SFM	60-75%	72%	48%	48%	28.3%	33%
M	97-99%	98%	87%	5%	3.3%	11.2%

NIFTP



Histopathologic Diagnostic Criteria for NIFTP

1. Encapsulation or clear demarcation[a]
2. Follicular growth pattern[b] with <1% papillae, no psammoma bodies & 30% solid/trabecular/insular growth pattern
3. Nuclear score of 2 or 3
4. No vascular or capsular invasion[c]
5. No tumour necrosis
6. No high mitotic activity[d]

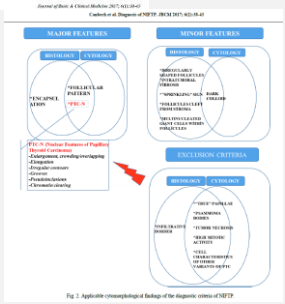
[a]thick, thin, or partial capsule or well circumscribed with a clear demarcation from adjacent thyroid tissue
[b]including microfollicular, normofollicular, or macrofollicular architecture with abundant colloid
[c]Requires adequate microscopic examination of the tumour capsule interface = COMPLETE BAMP ING
[d]High mitotic activity defined as at least 3 mitoses per 10 high powered fields (400x)

http://www.niftp.org/Criteria_for_NIFTP.html

Journal of Basic & Clinical Medicine

Diagnosis of Non-invasive Follicular Tumor with Papillary-like Nuclear Features (NIFTP): A Practice Changer for Thyroid Fine-needle Aspiration Interpretation

Sule Canberk[1*], Zubair W. Baloch[2*], Umit Ince[3], Fernando Schmitt[4,5]



TBSRTC – Risk of Malignancy (Anticipated changes due to NIFTP)

	ROM with NIFTP (%)	Optional Note
▪Nondiagnostic	0-5 * (* No significant change)	None
▪Benign	0-3 *	None
▪AUS	10-30 (6-18)	None
▪SFN	25-50 (10-40)	Yes
▪SFM	50-75 (45-60)	Yes
▪Malignant	97-99 (94-96)	Yes