

Methodological and clinical progress in thyroid tumor markers

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ISO 9001



**Fine-needle aspiration has two major limitations:
non-diagnostic results and suspicious or indeterminate
results .**

H. Gharib and J. R. Goellner

'Annals of Internal Medicine' 1993

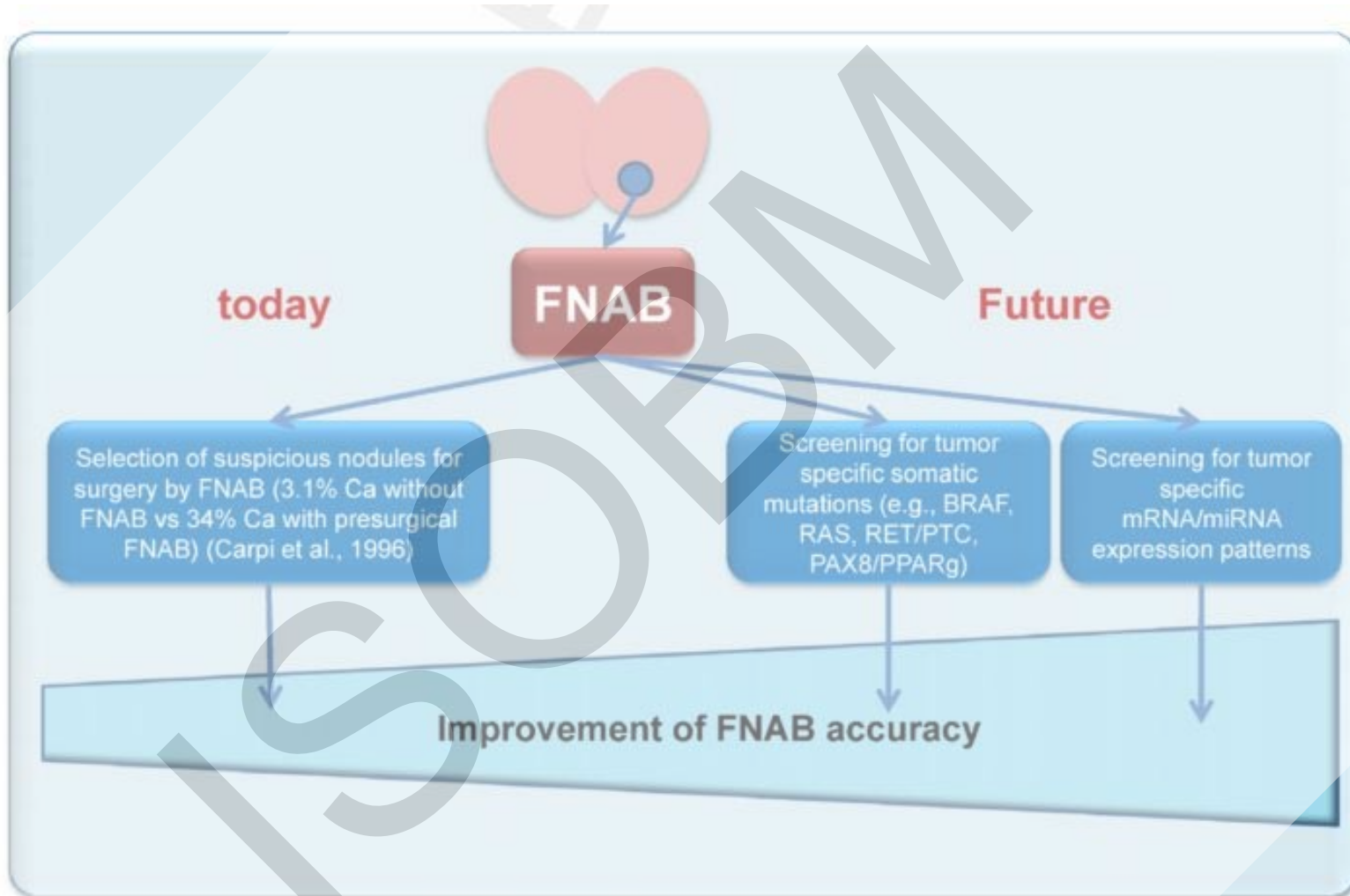


Fig. 3. FNAB diagnosis of thyroid nodules today and in the future.

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<i>Differentiation</i>	<i>Dedifferentiation</i>	
Thyroid peroxidase (TPO)	Telomerase	PCNA
Thyroglobulin	Galectin-1 and 3	c-myc
TSH receptor	Ki-67	RAR β
Sodium iodide symporter	Oncofetal fibronectin	Cyclin D1
Pax 8	Pax 8—PPAR fusion	glut-1
TTF-1	PKC	laminin
Deiodinase	Leu 7, Leu M1	cytokeratin
	Ras	VEGF
	p53	mucl
	p21	p27
	Rb	oesitrogen receptor
	EGF-R	c-met
	DNA ploidy	E-cadherin
	Somatostatin receptor	High mobility group 1
	FGF-R	RET/PTC
	CA-19	CD44v
	CD97	CD34
	β -catenin	TGF β
	c-erbB	ETS-1
	bcl-2	MDM2
	TRK	RXR α
	Dipeptidyl diaminopeptidase IV	

Tab.1 Potential molecular markers for thyroid carcinoma. Markers that have been studied by several investigators are shown in bold. The most promising markers are discussed in detail in the text.

Galectin-3-expression analysis in the surgical selection of follicular thyroid nodules with indeterminate fine-needle aspiration cytology: a prospective multicentre study

A. Bartolazzi et al. Lancet Oncology 2008 (9); 543-549

465 follicular thyroid proliferations that were candidates for surgery, and its diagnostic accuracy

The paucity of cells obtained from thyroid FNA is an important limitation for cell-block preparation and galectin-3 immunostaining...

Galectin-3 is not useful in thyroid FNA

L.J. Mills et al. Cytopathology 2005 (16); 132-138

Many thyroid aspirates are (23%) of low cellularity and are not suitable for cell block immunohistochemistry (galectin-3)

Is galectin-3 a good method for the detection of malignancy in patients

With thyroid nodules and a cytologic diagnosis of 'follicular neoplasm'?

A critical appraisal of the evidence

A.Sanabria et al. Head Neck 2007 (11); 1046-54

Available information has methodological flaws that precludes a definitive answer about galectin-3 (on FNAB) utility in the clinical setting.

Galectin-3-expression analysis in the surgical selection of follicular thyroid nodules with indeterminate fine-needle aspiration cytology: a prospective multicentre study

A. Bartolazzi et al. Lancet Oncology 2008 (9); 543-549

The paucity of cells obtained from thyroid FNA is an important limitation for cell-block preparation and galectin-3 immunostaining...

The diagnostic performance of the galectin-3 thyrotest on LNAB-derived substrates is excellent.

Furthermore, LNAB-derived cell-block preparations allow a comparative immunocytochemical assessment, on the same cytological slides, of different antigens associated with thyroid cancer.

A prospective study: diagnostic performance of concurrent FNA

LNAB histology and galectin-3 immunodetection on LNAB specimens (A. Carpi, Ann. Med.,2010)

All examined nodules: distribution of each FNA diagnostic category within the LNAB or galectin-3 on LNAB categories

FNA	Total	LNAB				Gal-3 on LN			
		INAD	NEG	INDET	POS	INAD	NEG	INDET	POS
INAD	83°	20	55	8	0	9	72	0	2
NEG	120*	7	112	1	0	1	119	0	0
INDET	38'	1	14	21	2	1	26	0	11
POS	4	0	0	2	2	0	0	0	4
total	245	28	181	32	4	11°	217*	0'	17

Key messages

- Galactin-3 immunodetection on large needle aspiration biopsy histology from thyroid nodules provided specificity values higher than fine-needle aspiration biopsy.
- It can be used to avoid many unnecessary surgical interventions for benign thyroid lesions.

A.Carpi et al. Annals of Medicines, 2009-2010

TABLE 3. Thyroid tumor markers used or validated for clinical practice.

Thyroid tumor marker	Determination site	Determination Time	Cancer type	Clinical use
Thyroglobulin	Blood	Postoperative	Differentiated	Indicator of recurrence
Thyroglobulin	Lymphnode tissue	Preoperative	Differentiated	Diagnosis of metastases
Calcitonin	Blood	Postoperative	Medullary	Diagnosis
Germ line RET mutation	Blood	Postoperative	Medullary	Prevention, diagnosis
Galectin-3	Nodular tissue	Preoperative	Differentiated	Increases diagnostic specificity
BRAF	Nodular tissue	Preoperative	Papillary	Surgical extension, prognosis

Conclusions

- preoperative determination of tumor markers (TM) in thyroid tissue is expected to improve preoperative diagnosis of thyroid nodules
- large needle aspiration biopsy (LNAB) reduces indeterminate plus inadequate diagnoses at FNA and is a better substrate than FNA for TM determination
- galectin-3 determination on LNAB shows higher diagnostic specificity than FNA
 - gal-3 determination on LNAB improves preoperative selection of thyroid nodules