

# Relation of 18FDG-PET CT positivity with tumor cytopathology and molecular markers in malignant and benign thyroid tumors

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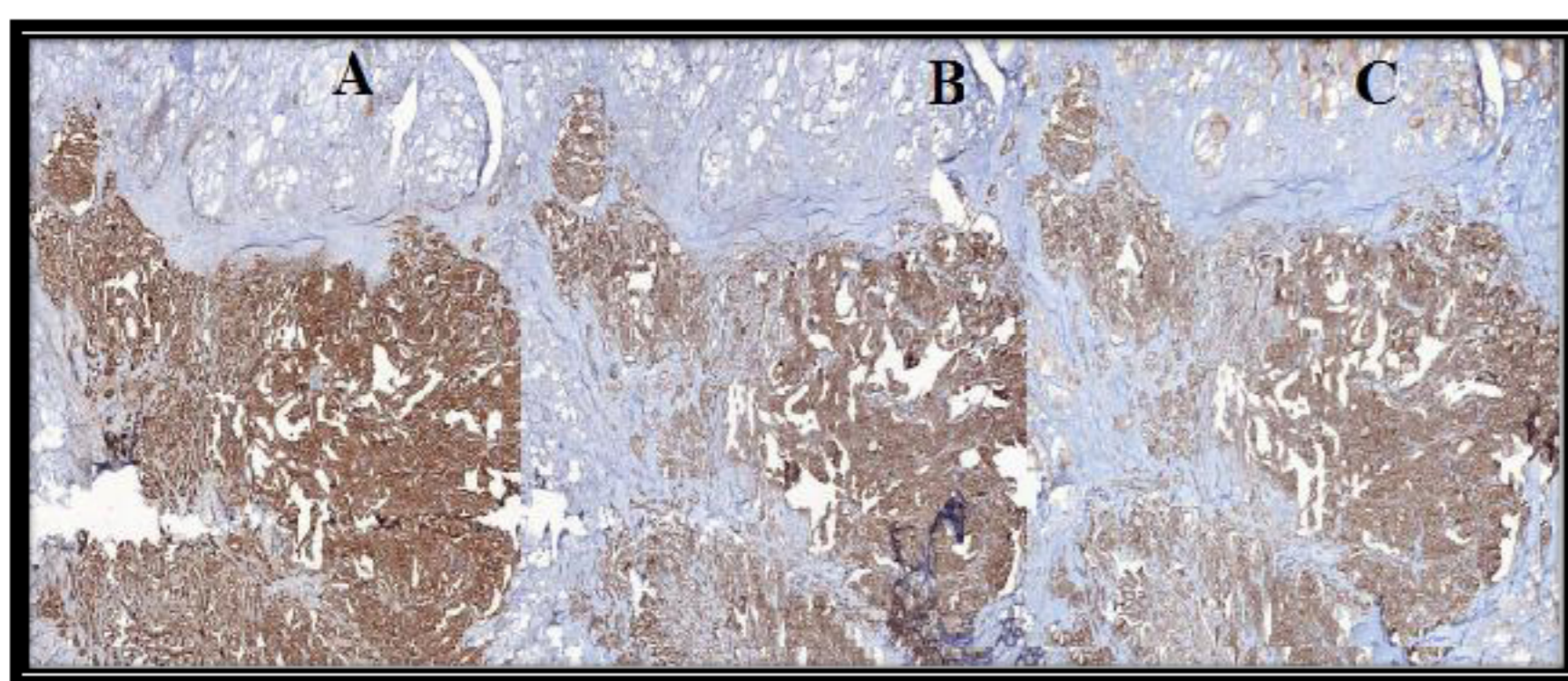
## Introduction

- Thyroid incidentalomas are found in %1.2-2.3 of FDG-PET scans and malignancy risk of these lesions is 25-50% (1,2). However, causes leading to concentration of 18F-FDG by benign or malignant lesions have not been explained yet. In our study, we aimed to investigate relationship between Ki67 proliferation index, NIS, Galectin-3, PTEN, P53 expressions, 18FDG-PET CT positivity

## Methods

- Fifteen patients with twenty seven nodules who had focal uptake in the thyroid gland on 18F-FDG PET scan and underwent total thyroidectomy between 2010 and 2014 were included in this study. Demographical characteristics, 18F-FDG PET CT and histopathology reports were assessed retrospectively. Immunohistochemical analysis for NIS, PTEN, P53, Ki67 and Galectin-3 were performed in 27 nodules (Figure 1).

**Figure 1.** PTEN (A), Galectin-3 (B) and NIS (C) strong positivity in a benign thyroid nodule.



- The demographical data of 15 patients and clinicopathological features of 27 nodules are summarized in Table.1 Neither age nor gender was associated with 18F-FDG uptake and malignancy. 18F-FDG PET positivity was not associated with malignancy (p=0.136).
- Galectin-3 staining intensity/density was not associated with age, gender, malignancy or 18F-FDG uptake (Table 2).
- Table 1.** General characteristics of patients.

Parameter	No (%)
<60 years	6 (40%)
≥60 years	9 (60%)
Female	11 (73.3%)
Male	4 (26.7%)
18FDG Uptake +	21 (78%)
18FDG Uptake -	6 (22%)
Benign	8 (30%)
Malign	19 (70%)

**Table 2.** Association between Galectin-3 staining intensity and nodule characteristics.

	Galectin3 negative	<%50 staining	≥%50 staining	p
Female (n=24)	11 (45.8)	0 (0)	13 (54.2)	NS
Male (n=3)	2 (66.7)	0 (0)	1 (33.3)	
Age <60 (n=15)	8 (53.3)	0 (0)	7 (46.7)	NS
Age >60 (n=12)	5 (41.7)	0 (0)	7 (58.3)	
PET- (n=6)	3 (50)	0 (0)	3 (50)	NS
PET+ (n=21)	10 (47.6)	0 (0)	11 (52.4)	
Benign (n=8)	6 (75)	0 (0)	2 (25)	NS
Malignant (n=19)	7 (36.8)	0 (0)	12 (63.2)	

There was no association between age, gender and NIS staining intensity/density. NIS staining was significantly frequent in older patients ( 11 vs. 6 respectively; p=0.019)

**Table 3.** Association between NIS staining intensity and nodule characteristics.

	NIS negative	<%50 staining	≥%50 staining	p
Female	10 (41,7)	5 (20,8)	9 (37,5)	NS
Male	0 (0)	2 (66,7)	1 (33,3)	
<60 years	9 (60)	3 (20)	3 (20)	0.01
>60 years	1 (8,4)	4 (33,3)	7 (58,3)	
PET-(n=6)	3 (50)	0 (0)	3 (50)	NS
PET+ (n=21)	7 (33,3)	7 (33,3)	7 (33,3)	
Benign (n=8)	2 (25)	5 (62,5)	1 (12,5)	0.01
Malignant (n=19)	8 (42,1)	2 (10,5)	9 (47,4)	

- Ki-67 proliferation index was not associated with age, gender and malignancy. One out of six nodules (16.7%) without 18F-FDG uptake had Ki-67 index higher than 3% and eight out of nineteen nodules (38.1%) with pathological 18F-FDG uptake had Ki-67 proliferation index higher than 3%.

- PTEN was negative in eight of 19 malignant nodules (42.1%) whereas only one (12.5%) benign nodule was negative. PTEN staining intensity was not associated with age or gender of patients. Association between PTEN staining intensity and nodule characteristics are summarized in Table 4.

- P53 staining was negative in all nodules.

**Table 4.** Association between PTEN staining intensity and nodule characteristics.

	PTEN negative	<%50 (%)	≥%50 (%)	p
Female	9 (%37,5)	7 (29,2)	8 (33,3)	NS
Male	0 (%0)	2 (66,7)	1 (33,3)	
<60 years	7 (46,6)	4 (26,7)	4 (26,7)	NS
>60 years	2 (16,6)	5 (41,7)	5 (41,7)	
PET- (n=6)	3 (50)	0 (0)	3 (50)	0.06
PET+ (n=21)	6 (28,6)	9 (42,8)	6 (28,6)	
Benign (n=8)	1 (12,5)	6 (75)	1 (12,5)	0.01
Malignant(n=19)	8 (42,1)	3 (15,8)	8 (42,1)	

**Table 5.** Galectin-3, NIS, PTEN and Ki67 immunostainings, according to malignancy and FDG uptake.

	Benign and PET +	Malignant and PET +	Malignant and PET -	p
Galectin-Negative	6 (46.2%)	4 (30.8%)	3 (23.1%)	0,1
Positive	2 (14.3%)	9 (64.3%)	3 (21.4%)	
NIS Negative	2 (20%)	5 (50%)	3 (30%)	0,6
Positive	6 (35.3%)	8 (47.1%)	3 (17.6%)	
PTEN Negative	1 (11.1%)	5 (55.6%)	3 (33.3%)	0,2
Positive	7 (29.6%)	8 (44.4%)	3 (16.7%)	
Ki-67	1.75±1.16	2.46±1.19	2±1.09	0,3

## Conclusions

- Factors which have influence on FDG uptake of thyroid nodules have not been determined yet. In our study we investigated the relationship between 18F-FDG uptake and molecular markers.
- 18F-FDG uptake was not associated with Ki67, Galectin-3, PTEN or NIS expression in tumor tissue. Importance of PET positivity in thyroid nodules may be explained by identification of molecular markers related to FDG uptake.

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