Thyroid

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Performance of a Raman Fingerprint in Thyroid Nodules with Indeterminate Cytology: A Prospective Blinded Monocentric Study

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Background: Molecular analysis of thyroid fine-needle aspiration biopsy (FNA) was proposed to improve indeterminate nodules management. However, sensibility and

specificity as well as the cost of molecular diagnostics require to be improved to increase their cost-effectiveness for medical practice setting. Raman spectroscopy (RS) demonstrated ability in separating benign from malignant thyroid lesions in surgically removed tissues, based on specific RS profile. This study aimed to investigate the diagnostic performance of RS on cytological samples obtained by thyroid FNA.

Methods: In this prospective, blinded monocentric study, we enrolled 123 patients with indeterminate or worse cytological diagnosis, candidate to surgery according to international guidelines, and submitted to RS analysis of FNA samples. Cytology specimens were evaluated in agreement to Italian Reporting System for Thyroid Cytology[1] as follows: TIR1 (non-diagnostic), TIR1C (non-diagnostic-cystic), TIR 2 non-malignant/benign, TIR3A (low-risk indeterminate lesion), TIR3B (high-risk indeterminate lesion), TIR 4 (suspicious of malignancy), or TIR 5 (malignant). As previously published[2], the two diagnostic subcategories referred to indeterminate nodules with low (TIR3A) and high risk (TIR3B) of malignancy, may be respectively compared to the class III and Class IV of The Bethesda System for Reporting Thyroid Cytopathology.

We compared RS, cytology and final histology, as reference standard, using various statistical approaches.

Findings: Our study population included 37 TIR3A, 32 TIR3B, 16 TIR4 and 38 TIR5; the 30.9% of patients had benign histological diagnosis after surgery. In particular, 72.9% of patients classified TIR3A and 31.3% TIR3B had benign histological diagnosis. RS analysis of FNA samples had overall specificity of 86.8% in predicting thyroid malignancy. In indeterminate cytological categories, RS specificity was 86.5%. In patients with TI-RADS score four or five, the specificity of RS increased to 87.5% for TIR3A and reached 100% in TIR3B.; if considering RS positive test, unnecessary surgery was reduced to 7.4% in the whole sample, 33.3% in TIR3A, and 6.7% in TIR 3B.

Interpretation: We demonstrated for the first time that RS represents a valuable tool for thyroid cytology and a valid alternative to molecular analyses, able to improve management and reduce unnecessary surgery in indeterminate nodules.

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1 J Endocrinol Invest. 2014;37(6): 593-599. doi: 10.1007/s40618-014-0062-0

[2]Cytopathology. 2021;32(6): 714-717.

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