DIAGNOSIS

Mutation screen improves sensitivity of thyroid fine-needle aspiration cytology

Molecular testing in conjunction with fine-needle aspiration cytology (FNAC) improves the diagnosis of malignant thyroid nodules, according to a report published in the *Journal of Clinical Endocrinology and Metabolism*.

The ability to distinguish benign thyroid nodules from those that are malignant is crucial. FNAC is currently considered the 'gold standard'; however, up to 40% of nodules have indeterminate results with this test, which leads to unnecessary surgeries for some patients and missed diagnoses of malignant disease for others. Development of methods to improve diagnostic accuracy is, therefore, considered a prime objective.

Yuri Nikiforov and coworkers used a mutation-analysis approach to tackle this problem. "We developed an assay that allowed us to test a very small portion of cells collected by FNA from thyroid nodules for multiple mutations," explains Nikiforov, "this was important since the goal was not to compromise the routine cytologic

examination, and at the same time to obtain information on all major mutations known to occur in thyroid cancer."

The researchers prospectively analyzed point mutations (*BRAF* and *RAS*) and gene rearrangements (*RET-PTC1*, *RET-PTC3* and *PAX8-PPAR γ*) in 470 thyroid nodule samples from 328 patients. Mutations were detected in 32 of the aspirates, 31 (97%) of which were confirmed as malignant after surgery. The molecular analysis was most beneficial for nodules with indeterminate FNAC results, particularly those nodules in the low-risk category (follicular lesions of undetermined significance [FLUS]). "The finding of any mutation was 100% predictive of malignancy in this subgroup of nodules," Nikiforov notes, "whereas nodules with FLUS cytology and no mutations were benign after surgery."

The results of this study confirm that molecular analysis can aid diagnosis of malignancy in thyroid nodules with indeterminate

FNAC results. "The next step is to expand this panel and add additional molecular markers, such as micro RNAs," Nikiforov concludes.

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Original article Nikiforov, Y. E. et al. Molecular testing for mutations in improving the fine needle aspiration diagnosis of thyroid nodules. *J. Clin. Endocrinol. Metab.* doi:10.1210/jc.2009-0247