



## THYROID NODULES

### Improving needle biopsy accuracy with molecular testing

#### BACKGROUND

Thyroid nodules are very common and can be found in up to 50% of individuals that get any type of neck imaging. The concern with a thyroid nodule is whether or not it is cancerous. Fine needle aspiration biopsy (FNAB) is the best test to determine whether a thyroid nodule is cancerous outside of removing the nodule by surgery. FNAB is very accurate and comes up with a definitive diagnosis in over 80% of cases. However, in 10-15% of cases, the FNAB is described as “indeterminate” by the pathologist, meaning that they are unable to determine whether the nodule is cancerous or not by looking at the sample obtained with a microscope. This usually results in surgery being performed to obtain a definite diagnosis. Several genetic abnormalities have been identified that indicate that thyroid cancer is present in a nodule. Recently, researchers have been looking at additional methods, including genetic testing of needle biopsy specimens, to try to more accurately determine which patients have thyroid cancer.

#### THE FULL ARTICLE TITLES:

Nikiforov YE et al. Impact of mutational testing on the diagnosis and management of patients with cytologically indeterminate thyroid nodules: a prospective analysis of 1056 FNA samples. *J Clin Endocrinol Metab* 2011;96:3390-7. Epub August 31 2011.

Vriens MR et al. MicroRNA expression profiling is a potential diagnostic tool for thyroid cancer. *Cancer*. October 17, 2011. [Epub ahead of print]. doi:10.1002/cncr.26587.

#### SUMMARY OF THE STUDIES

The authors of the first study (Nikiforov, et al.) looked at 1056 indeterminate FNAB samples from 762 patients over a two year period. These samples were categorized as follicular lesion of undetermined significance (FLUS), follicular neoplasm (FN), or suspicious for malignant cells (SMC). Genetic testing was performed to determine if abnormalities suggestive of thyroid cancer were present in the needle biopsy samples. Of these patients, 479 underwent surgery (representing 513 FNAB samples). Pathologic analysis of the thyroid tissue removed at

surgery was compared to the findings of standard FNAB findings and genetic analysis. For the three categories, FLUS, FN and SMC, the cancer risk by needle biopsy alone was 14%, 27% and 52%. When the genetic testing was positive, the cancer risk increased to 88%, 87% and 95%.

In the second study (Vriens, et al.), the authors also looked at indeterminate FNAB samples to determine if they contain extra amounts of genetic proteins called microRNAs. These microRNAs have been found in thyroid cancers and control the production of other proteins within cells. The authors looked for the amount of 10 different miRNAs in 125 known cases with indeterminate FNAB results. For the miRNA which was most accurate, the authors only could predict thyroid cancers in 75% of cases.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While FNAB is very helpful in determining which patients need surgery and which can be safely observed, patients with indeterminate findings on FNAB frequently have surgery in order to make a definite diagnosis. The development of molecular genetic tests will help patients and physicians more accurately determine the chance of a nodule being cancerous or not. If the nodule is cancerous, then the appropriate surgery can be planned in advance. If the nodule is not likely to be cancerous, patients can feel more comfortable avoiding surgery and being observed for clinical changes. While the availability of this new technology is exciting and will most likely continue to improve, the costs associated with it still need to be considered.

— Ronald Koppersmith, MD

#### ATA THYROID BROCHURE LINKS

Thyroid cancer: [http://thyroid.org/patients/patient\\_brochures/cancer\\_of\\_thyroid.html](http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html)

Thyroid Surgery: [http://thyroid.org/patients/patient\\_brochures/surgery.html](http://thyroid.org/patients/patient_brochures/surgery.html)

Thyroid Nodules: [http://thyroid.org/patients/patient\\_brochures/nodules.html](http://thyroid.org/patients/patient_brochures/nodules.html)

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## THYROID NODULES, continued

### ABBREVIATIONS & DEFINITIONS

**Thyroid fine needle aspiration biopsy (FNAB):** a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

**Indeterminate thyroid biopsy:** this happens usually

when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

**microRNAs:** small pieces of genetic proteins that have been found in thyroid cancers and control the production of other proteins within cells.