



## THYROID CANCER

# Noninvasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTP) are similar to benign tumors

### BACKGROUND

Thyroid cancer is one of the most rapidly increasing cancers in the United States and over 90% of cases are papillary thyroid cancer. More recently it has become increasingly recognized that there are many different subtypes of papillary thyroid cancer, and that each subtype displays unique cellular features, genetic mutations and clinical behavior. Follicular variant papillary thyroid cancer, a term that was originally used to describe papillary thyroid cancers composed primarily of spherical “follicles” as opposed to the finger-like “papilla” of classical papillary thyroid cancer, is a very common subtype of papillary thyroid cancer. Despite the high incidence of the follicular variant papillary thyroid cancer, it has become a controversial and confusing entity because some cases behave similar to benign thyroid nodules called follicular adenomas whereas other cases are more aggressive cancers and can spread throughout the body.

Adding to the confusion, the term noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) was introduced two years ago to describe select slow growing and well- circumscribed cases of follicular variant papillary thyroid cancers. Unlike other forms of papillary thyroid cancer, NIFTP tumors do not seem to grow or spread, and consequently may be able to be treated like benign thyroid nodules. The purpose of the following study was to characterize the genetic make-up and clinical behavior of NIFTP tumors and to compare them to both benign tumors and more invasive forms of papillary thyroid cancer.

### THE FULL ARTICLE TITLE

Johnson DN et al 2018 Noninvasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTPs) are genetically and biologically similar to adenomatous nodules and distinct from papillary thyroid carcinomas with extensive follicular growth. Arch Pathol Lab Med. Epub 2018 Mar 27. PMID: 29582677.

### SUMMARY OF THE STUDY

Investigators reviewed pathology specimens from 61 follicular variant papillary thyroid cancers obtained between 2009 and 2016 from the University of Chicago. Based on their review they reclassified the tumors into: 32 cases (63%) of NIFTPs, 4 cases (7%) of an invasive encapsulated form of follicular variant papillary thyroid cancer, 14 cases (23%) of classic papillary thyroid cancer with extensive follicular growth and 11 cases (18%) of benign follicular adenomas. The investigators then extracted DNA from each specimen and analyzed for mutations in 50 cancer genes and finally the clinical outcome of each case was recorded.

The results showed that NIFTP tumors were similar to benign follicular adenomas. None of the 11 patients with follicular adenomas and none of the 32 cases of NIFTP tumors showed recurrence after initial treatment. All of the patients with papillary thyroid cancer with extensive follicular growth were disease free as well, whereas 3 of the 4 patients with invasive encapsulated form developed metastasis of their cancer. Mutations in the RAS cancer gene were found in 4 (36%) of follicular adenomas, 20 (62%) of NIFTP tumors and 3 (75%) of patients with the invasive encapsulated form. More importantly, no follicular adenoma and no NIFTP tumor had the BRAF V600E cancer gene mutation, a mutation that usually found in cancers that are more similar to classical papillary thyroid cancer.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While this study is limited by the relatively small number of cases, the results suggest that there is great similarity between NIFTP tumors and benign follicular adenomas. Consequently, much like benign adenomas, patients with NIFTP tumors probably do not need completion thyroidectomy surgery or radioactive iodine therapy. The need for less invasive treatment will hopefully improve patient quality of life and reduce the psychologic stress that comes with a diagnosis of cancer.

— Philip Segal, MD





## THYROID CANCER, continued

### ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <https://www.thyroid.org/thyroid-cancer/>

Thyroid Nodules: <https://www.thyroid.org/thyroid-nodules/>

### ABBREVIATIONS & DEFINITIONS

**Papillary thyroid cancer:** the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

**Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP):** a new term has been used to describe a type of papillary thyroid cancer which is non-invasive. These cancers behave less aggressively than typical papillary thyroid cancer and have been shown to have low risk for recurrence and low risk for spread outside of the thyroid.

**Follicular variant of papillary thyroid cancer:** one of the subtypes of papillary thyroid carcinoma, which has been classified to three different forms: non-invasive follicular thyroid neoplasm with papillary-like nuclear features, invasive encapsulated and infiltrative FVPTC.

**Genes:** a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

**Mutation:** A permanent change in one of the genes.

**Cancer-associated genes:** these are genes that are normally expressed in cells. Cancer cells frequently

have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC, TERT and RAS.

**BRAF gene:** this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.

**Lymph node:** bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

**Total thyroidectomy:** surgery to remove the entire thyroid gland.

**Radioactive iodine (RAI):** this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

