

# Paediatric Thyroid Nodule's Complex Cyto-Molecular Landscape

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## Description

Thyroid fine-needle aspiration (FNA) is a common diagnostic cytological procedure for triaging thyroid nodules for the detection of thyroid cancer in paediatric patients. Thyroid FNA in this setting has received more attention in recent years, including the use of more recent ultrasound score algorithms to improve accuracy and yield, particularly in light of the theoretically higher risk of malignancy of these lesions compared to the adult population, and to reduce patient discomfort. Additionally, a growing area of study is molecular genetic testing for thyroid disease, which has the potential to assist in determining the clinical management of benign from cancerous nodules. Lastly, by conducting a comprehensive analysis of all of the data that was obtained, artificial intelligence tools can be of assistance in this endeavor. These headways have prompted more prominent dependence on FNA as a first-line indicative device for pediatric thyroid infection. This review article gives an overview of these recent developments and how they will affect the way thyroid nodules in children are diagnosed and treated [1].

High-resolution ultrasonography (US)-guided fine-needle aspiration (FNA) has made it possible to detect cancer earlier, which has led to an overall rise in the incidence of thyroid cancer in recent years. FNA is regarded as the best method for evaluating thyroid nodules in order to minimize unnecessary surgeries or determine the appropriate extent of surgery, whereas US is a non-invasive imaging method that is suitable for thyroid evaluation and is well accepted by patients of all ages. Histological examination is still the gold standard for diagnosing thyroid nodules. The Surveillance, Epidemiology, and End Results (SEER) database says that thyroid cancer cases in people under 20 make up only 2.3% of all thyroid cancer diagnoses. However, these cases are still the second most common adolescent malignant neoplasms and have a mortality rate that is lower than that of adults, even in advanced forms (less than 2% worldwide), though the rarity of these conditions in children makes it difficult to collect data. The World Health Organization (19 years), the American Thyroid Association (18 years), and the American Academy of Pediatrics (21 years) all propose different age upper cutoffs for defining the pediatric group for thyroid diseases. Some studies suggest a 14- or 22-year-old cutoff for a better prognostic value [2].

The clinical, pathological, and molecular characteristics of pediatric thyroid cancers vary significantly, making their preoperative evaluation more challenging. Pediatric nodules are less common from a clinical standpoint (0.2–5% vs. 20–70%), but they have a higher risk of malignancy (mean ROM, 19–26% vs. 5–15%) and cancer prevalence (estimated to be 1.6- to 2.5-fold higher), with the highest incidence occurring between the ages of 15 and 19. In addition, pediatric patients frequently present with occult diffuse infiltrative lesions and extrathyroidal extension (such as pulmonary metastases or metastases in regional lymph nodes), highlighting the significance of non-invasive techniques

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for accurate diagnosis. They are more frequently linked to female sex, Asian origins, radiation exposure, inherited syndromes, and endocrine, metabolic, and immune differences, especially in the post-pubertal >14-year age group. Because children have a better response to radioactive iodine therapy (RAI) and a higher rate of surgical-related complications with potential long-term effects on growth and bone health, it is essential to correctly identify malignant nodules in them [3].

The commonly used US size cutoffs for risk stratification of thyroid nodules for preoperative evaluation may not be adequate for age-specific thyroid volume; Additionally, the molecular landscape of papillary thyroid carcinoma (PTC), which accounts for approximately 80–90 percent of cases, is characterized by lower BRAF p rates. V600E change and higher paces of RET/PTC movements, when contrasted with what is depicted in the grown-up partner, and 15-40% of PTC cases are of histological high-risk variations. Follicular thyroid carcinoma (FTC) and medullary thyroid carcinoma (MTC) are the second and third most common histotypes, respectively, while poorly differentiated thyroid carcinoma (PDTC) and anaplastic thyroid carcinoma (ATC) are extremely uncommon. Computer-assisted diagnosis has demonstrated reliable diagnostic performance, comparable to that of radiologists, according to a recent meta-analysis. [4].

The development of useful candidate algorithms to be applied on histology/cytology for computer-aided diagnosis is primarily limited by the relative rarity of these tumours and their intrinsic structural heterogeneity, despite the fact that the benefits and potential challenges of an AI approach are currently well known. However, this is still not the case for their pediatric counterparts, in which AI and machine learning still represent an emerging field. The use of Matrix-Assisted Laser Desorption/Ionization—Mass Spectrometry imaging (MALDI-MSI) technology to directly in situ investigate the spatial distribution of biomolecules (proteins, lipids, and metabolites) may be an additional strategy that could be used to diagnose pediatric thyroid nodules. Starting with FNA specimens, this technology has previously been utilized to investigate the proteomic data of adult indeterminate nodules, NIFTPs, and Hashimoto thyroiditis [5].

In order to accurately identify pediatric patients who would benefit from surgical intervention, it is essential to place a high priority on the creation of treatment guidelines and risk stratification tools. Thyroid nodule management and surveillance will undoubtedly be improved by the potential combination of all clinical, radiological, cytological, and molecular data merged with the assistance of artificial intelligence in the future, as well as by the comprehension of the key biomolecular pathways involved in thyroid oncogenic processes. Multicentric efforts and collaborations can further assist in increasing the number of case series describing uncommon clinical entities and molecular alterations in this group of patients, enhancing our capacity to develop AI tools for their assessment that are robust and dependable.

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## Conflict of Interest

No potential conflict of interest was reported by the authors.

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