and “paraganglioma-like adenoma of the thyroid”, may be related to papillary carcinoma at the molecular level\(^4\), while others propose a multidirectional differentiation from pluripotent primitive cells\(^5\). Some of these controversial issues are challenged by Lloyd\(^7\) who concludes that additional studies are needed to clearly define this entity. Until then, it would seem appropriate to regard and treat hyalinizing trabecular adenoma as a benign neoplasm\(^2\). “Toxic” adenoma is a clinical rather than a pathologic entity, defining only those hyperfunctioning lesions in which clinical manifestations occur, and not any “hot” adenoma\(^3\).

### A.1.2. Follicular Carcinoma

Most authors agree that only follicular tumors that exhibit vascular and/or capsular invasion should be regarded as follicular carcinomas\(^8\). Depending on the degree of their invasiveness, follicular carcinomas have been divided into two major categories: minimally invasive or encapsulated (the most common), and widely invasive. The frequency of follicular carcinoma among thyroid malignancies ranges from 5-10% in non-iodine-deficient areas to 30-40% in iodine-deficient areas\(^2\).

Macroscopically, follicular carcinomas do not differ appreciably from follicular adenomas. The fibrous capsule surrounding the tumor tends to be thicker and more irregular than in adenomas\(^2\). Minimally invasive follicular carcinoma is an encapsulated tumor showing capsular and/or vascular invasion only on microscopic evaluation, while the widely invasive neoplasm shows lack of complete encapsulation, extensive areas of invasion to the adjacent thyroid tissue and/or widespread blood vessels infiltration\(^2\).

Immunohistochemistry, morphometry, ploidy analysis, cytogenetic and oncogene markers have failed to provide reliable information concerning the distinction between follicular carcinoma and follicular adenoma. The current diagnostic criteria for malignancy are still the histologic assessment of true capsular infiltration (the tumor must penetrate the entire thickness of the capsule) and/or invasion of blood vessels in or beyond the capsule (Figure 1B)\(^2,8-10\). It is apparent that minimally invasive follicular tumors cannot be accurately diagnosed by fine needle aspiration (FNA) cytology since the crucial diagnostic criteria are missing\(^2,9,11\). Similar problems exist in evaluating such lesions by frozen section\(^2,11,12\).

Malignant thyroid tumors composed exclusively or predominately (over 75%) of oncocytes (Hürthle cell tumors) share some similarities with follicular carcinomas as regards the clinical presentation, the architectural features and the degree of invasiveness, and therefore should be considered as a variant of follicular carcinoma\(^2,8,9\). However, some authors have suggested that the morphologic features and natural history of these tumors are distinctive enough that they be considered as a separate entity\(^13,14\).

### A.1.3. Papillary Carcinoma

Papillary carcinoma is the most common type of thyroid cancer, comprising approximately 80% of all primary thyroid malignancies\(^15\). Classical or non-otherwise specified (NOS) papillary carcinoma is characterized by the formation of papillae and a set of distinctive nuclear features (optically clear appearance, overlapping, pseudoinclusions and nuclear grooves) (Figure 1C, 1D)\(^2,16-18\). The size of papillary carcinoma is extremely variable with a mean diameter of 2-3 cm\(^2\). A clinically detected tumor is usually confined to the thyroid, is presented as a fairly well circumscribed or infiltrative neoplasm and has an indolent course. Its mode of spread is most commonly via lymphatics within the thyroid leading to “multifocal” disease and to cervical node metastases\(^2,9\). Indeed, 50% or more of papillary carcinomas have nodal metastases at initial diagnosis\(^19\).

There are several histologic variants of papillary carcinoma, some of which are associated with a more guarded prognosis (Table 3)\(^10\).

#### A.1.3.a. Variants of papillary carcinoma

**a.1. Papillary microcarcinoma:** The term refers to papillary carcinomas measuring 1cm or less in diameter and replaces the older designation of occult sclerosing carcinoma, also known as nonencapsulated sclerosing tumor and occult papillary carcinoma\(^2\). Re-