Capsule of Follicular Cell Tumors, its Significance and Morphology

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Capsule of thyroid nodule
- NODULAR GOTHIR
- FOLLICULAR ADENOMA
- FOLLICULAR CARCINOMA
- PAPILLARY CARCINOMA
- POORLY DIFFERENTIATED CARCINOMA
- MEDULLARY CARCINOMA
- OTHERS

Capsule in Papillary Thyroid Carcinoma
- NON-ENCAPSULATED TYPE
- ENCAPSULATED TYPE
- CYSTIC TYPE

Macroscopic Types of Papillary Thyroid Carcinomas
- Encapsulated type: 6%
- Partly encapsulated type: 11%
- Non-encapsulated type: 75%
- Cystic type: 7%

Diagnosis of Follicular Variant of Papillary Thyroid Carcinoma
- CLASSICAL TYPE
- NON-ENCAPSULATED TYPE
- ENCAPSULATED TYPE

**ENCAPSULATE FOLLICULAR VARIANT OF PAPILLARY THYROID CARCINOMA**

**FOLLICULAR ADENOMA/CARCINOMA**

Perhaps the most difficult problem in thyroid pathology is the distinction of follicular carcinoma from follicular adenoma and from the follicular variant of papillary carcinoma. Evans HL. Cancer 54:535-540, 1984

**FOLLICULAR ADENOMA/CARCINOMA**

**ADENOMA**
A benign encapsulated tumour of the thyroid showing evidence of follicular cell differentiation.

**CARCINOMA**
A malignant epithelial tumour showing evidence of follicular cell differentiation and lacking the diagnostic nuclear feature of papillary carcinoma.

**Diagnostic algorithm of follicle forming thyroid nodule**

- Papillary carcinoma cell nuclei
- Nodular goiter
- Follicular a./c.
- Poorly diff. carcinoma

- Solid, trabecular, insular pattern, necrosis, mitosis
- Invasion
- Follicular c.
- Poorly diff. c.
- Follicular a.
- Nodular goiter

- Positive
- Negative
**Invasions**

- Capsular invasion
- Vascular invasion

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**My Procedure**

- Cover glass 24mm
- Longitudinal sections
- Nodule ≤ 2cm: Entire nodule
- Nodule > 2cm: 10 sections + Additional sections

*Note: Nodules are treated with nodulectomy, lobectomy, subtotal/total thyroidectomy.*

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**Invasion**

1. **Capsular Invasion (CI)**

**Patterns of Capsular Invasion (CI)**

- True CI
- Insufficient CI

Capsular invasion is defined by *tumour penetration* through the tumour capsule unassociated with the site of a previous fine needle aspiration biopsy. (WHO 2004)

**Patterns of Capsular Pseudoinvasion (CPI)**

Capsule penetration through the tumour capsule.
WHAFFT
Worrisome histologic alterations following FNA of the thyroid
LiVolsi VA, Merino MJ. Lab Invest 62, 1990

- Hemorrhage and hemosiderin
- Focal and geographic pattern of lesion

INVASION

2. VASCULAR INVASION (VI)

Patterns of Vascular Invasion (VI)

Capsular invasion is defined by the presence of intravascular tumour cells either covered by endothelium or associated with thrombus.
(WHO 2004)

True VI

Pseudo VI

Artificially dislodged tumour cell (or tissue)

Patterns of Pseudovascular Invasion (VI)

Artificially dislodged tumour cells (or tissue)

Patterns of Vascular Invasion (VI)

Capsular invasion is defined by the presence of intravascular tumour cells either covered by endothelium or associated with thrombus.
(WHO 2004)

Patterns of Pseudovascular Invasion (VI)

Diagnosis of Follicular Carcinoma

Follicular tumours

- Showing definite invasion
- PTC nuclei (-)
- Follicular tumors of uncertain malignant potential (FT-UMP)

- Showing questionable invasion
- PTC nuclei (questionable)
- Well differentiated tumour of uncertain malignant potential (WD-UMP)

**Immunohistochemical Demonstration of Lymphatic and Blood Vessels**

Elastic tissue stains: only limited use in identifying intracapsular vessels

**Immunohistochemistry**

<table>
<thead>
<tr>
<th>Vascular Markers</th>
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<tbody>
<tr>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>CD31 or CD34</td>
<td></td>
</tr>
<tr>
<td>Ulex europaeus lectin</td>
<td></td>
</tr>
<tr>
<td>Laminin</td>
<td></td>
</tr>
<tr>
<td>Type IV collagen</td>
<td></td>
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</tbody>
</table>

**Immunohistochemistry**

Lymphatic Markers

- FLT4
- Live-1
- D2-40

**Distribution of Lymphatic and Blood Vessels in the Follicular Thyroid Tumours**

Intramural lymphatic vessel density was significantly higher in the follicular variant of PTC than in either follicular adenoma or follicular carcinoma.

**Distribution of Lymphatic Vessels in Encapsulated Follicular Tumours**

Intracapsular lymphatic vessels: scant or none
**Distribution of Blood Vessels in Encapsulated Follicular Tumors**

CD34 staining

**Distribution of Lymphatic and Blood Vessels**

CD34 staining for blood vessels (○) + D2-40 staining for lymphatic vessels (○)

Follicular carcinomas tend to give rise to hematogenous spread and do not usually show lymphatic spread possibly due to lymphatic and blood vessel distributions.

**Thickness of Tumor Capsule**

The capsule of follicular carcinoma tends to be thicker and more irregular than that of adenoma.

Evans, HL. Cancer 54:535-540, 1984
Yamasaki H. Ann J Surg Pathol 16:392-400

**Capsule Thickness**

Follicular adenomas (20 cases)
Minimally invasive follicular thyroid carcinomas (48 cases)

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>Capsule thickness (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>20</td>
<td>174 ± 30.9</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>48</td>
<td>407 ± 33.8</td>
</tr>
</tbody>
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The follicular carcinoma tends to be surrounded by a wide thick capsule.

**Subtypes of FTC and Recurrence and/or Metastasis**

Minimally invasive FTC
Widely invasive FTC
Inc. poorly

<table>
<thead>
<tr>
<th>Subtypes of FTC</th>
<th>No. of cases</th>
<th>No. of cases with recurrence and/or distant metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimally invasive FTC</td>
<td>48</td>
<td>11 (23%)</td>
</tr>
<tr>
<td>Widely invasive FTC</td>
<td>14</td>
<td>11 (79%)</td>
</tr>
</tbody>
</table>

**No. of Vascular Invasion in Subtypes of FTC**

Minimally invasive FTC
Widely invasive FTC (INCL. POORLY)

<table>
<thead>
<tr>
<th>No. of vascular invasion</th>
<th>No. of cases</th>
<th>No. of cases with vascular invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 1-3 4+</td>
</tr>
<tr>
<td>Minimally invasive FTC</td>
<td>14</td>
<td>1 2 11</td>
</tr>
<tr>
<td>Widely invasive FTC</td>
<td>16</td>
<td>1 2 11</td>
</tr>
</tbody>
</table>
NO. OF VASCULAR INVASION AND RECURRENCE AND/OR METASTASIS IN MINIMALLY INVASIVE FTC

<table>
<thead>
<tr>
<th>No. of vascular invasion (VI)</th>
<th>With recurrence and/or metastasis</th>
<th>Without metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI&lt; 4</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>VI&gt;= 4</td>
<td>64%</td>
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![Table showing number of cases with vascular invasion and metastasis](image)

SIGNIFICANCE OF INVASION

Follicular carcinoma

- Encapsulated
  - With capsular invasion only
  - With limited (<4) vascular invasion
  - With extensive (>=4) vascular invasion
- Widely invasive

There is a prognostic difference depending on the number of vessels involved.

STI PATTERN IN MINIMALLY INVASIVE FTC

- Solid
- Trabecular
- Insular

<table>
<thead>
<tr>
<th>STI pattern</th>
<th>No. of case</th>
<th>With metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>35</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>Present</td>
<td>18</td>
<td>5 (33%)</td>
</tr>
</tbody>
</table>

DISTANT METASTASIS IN MINIMALLY INVASIVE FTC

- Tumour size
- Gender
- Capsule thickness
- Capsular invasion
- Vascular invasion
- Solid, Trabecular, and Insular patterns

- Not significant for metastasis
- The capsule of MI-FTC is thicker than that of adenoma
- Not significant for metastasis
- Number of VI could be important
- With extensive (>=4) vascular invasion
- Possible significant marker

![Diagram showing STI pattern and metastasis](image)