

## 75. Parathyroid

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### Authors

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### Emerging Prognostic Factors for Clinical Care

#### Ki-67 Index

Defined as <5% versus ≥5%. Ki-67 PI typically is elevated in carcinomas. However, in primary tumors, an elevated Ki-67 PI is not sufficiently sensitive or specific for distinction from benign disease, because not all parathyroid carcinomas have an elevated Ki-67 PI and Ki-67 may be increased in parathyromatosis (seeding of parathyroid cells into surrounding tissue via rupture of capsule or cystic component) and some parathyroid adenomas.<sup>1</sup> However, elevated Ki-67 is noted more frequently (up to 80%) in metastatic disease.<sup>1</sup> One small study did not find Ki-67 to be predictive of survival.<sup>2</sup> AJCC Level of Evidence: III

#### Growth Pattern

##### *Solid Growth Pattern*

Defined as present or not present. *Solid* is best defined as a confluent proliferation of tumor cells without intervening stroma.

##### *Trabecular Growth Pattern*

Defined as present or not present. A trabecular growth pattern is composed of long ribbons of tumor cells with intervening fibrosis. Peripheral palisading often is present. AJCC Level of Evidence: IV

#### Genetic Mutations

Defined as presence of germline or somatic mutation. AJCC Level of Evidence: IV

##### *Germline Mutations*

Hereditary HPT-JT

Familial isolated primary hyperparathyroidism

##### *Somatic Mutations*

Sporadic parathyroid carcinomas are often associated with a somatic mutation of the *RB* and *CDC73* genes and cyclin D1 overexpression, although some may have a p53 mutation.<sup>3</sup>

## 75. Parathyroid

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### Intraoperative Tumor Rupture

Defined as rupture of the primary tumor during the first operation. One study demonstrated that intraoperative tumor rupture is predictive of worse survival.<sup>4</sup> AJCC Level of Evidence: III

### Presence of Fibrous Bands

Defined as present or not present. There is conflicting and limited evidence showing that the presence of fibrous bands is predictive of overall survival.<sup>4,5</sup> AJCC Level of Evidence: III

### Parafibromin Staining

Defined as present or not present. Parafibromin, the protein encoded by *CDC73*, is retained in parathyromatosis, adenomas, hyperplasias, and most atypical parathyroid adenomas.<sup>1,6</sup> This marker is lost in up to two thirds of parathyroid carcinomas and thus may be diagnostically useful.<sup>1,7</sup> However, some studies suggest that loss of parafibromin may occur in some atypical parathyroid adenomas, especially if associated with HPT-JT syndrome.<sup>7-9</sup> Furthermore, the rare parathyroid carcinomas arising in the setting of secondary/tertiary hyperparathyroidism do not have *CDC73* alterations and will not show parafibromin loss.<sup>10</sup> AJCC Level of Evidence: IV

### Perineural Invasion

Defined as present/not present. AJCC Level of Evidence: IV

### Necrosis

Defined as present/not present. AJCC Level of Evidence: IV

### Type of Hyperparathyroidism

Defined as primary versus secondary versus tertiary hyperparathyroidism

## Risk Assessment Models

The AJCC recently established guidelines that will be used to evaluate published statistical prediction models for the purpose of granting endorsement for clinical use.<sup>11</sup> Although this is a monumental step toward the goal of precision medicine, this work was published only very recently. Therefore, the existing models that have been published or may be in clinical use have not yet been evaluated for this cancer site by the Precision Medicine Core of the AJCC. In the future, the statistical prediction models for this cancer site will be evaluated, and those that meet all AJCC criteria will be endorsed.

## Recommendations for Clinical Trial Stratification

The authors have not provided any recommendations for clinical trial stratification at this time.

## 75. Parathyroid

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## 75. Parathyroid

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