| **Core/**  **Non-core** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
| --- | --- | --- | --- | --- |
| Core | CLINICAL INFORMATION | Multi selection value list (select all that apply)/text:  • Information not provided  OR  • Hyperparathyroidism   * Primary * Secondary * Tertiary   • Previous parathyroid surgery, specify  • Relevant familial history, *specify*  • Presence of clinical syndrome, *specify*  • Other, *specify* | Parathyroid carcinoma is a rare neoplasm representing <1% of cases of primary hyperparathyroidism.1-4 Multiple surgeries are common and may be required for initial diagnosis and/or for recurrence. Clinical syndromes which may be associated with parathyroid disease include multiple endocrine neoplasia (MEN) syndromes and familial hyperparathyroidism. In these disorders it is more likely to find parathyroid hyperplasia or adenoma although rare cases of parathyroid carcinoma have been reported.5 The hyperparathyroidism jaw-tumour (HPT-JT) syndrome involving the *CDC73* gene, is an autosomal dominant disorder that is strongly associated with parathyroid carcinoma (lifetime risk is approximately 15%).6-8 In the setting of secondary or tertiary hyperparathyroidism due to renal failure or other disorders, individual parathyroid glands may show highly atypical features that may mimic carcinoma including the presence of pseudoinvasion. Many experts are reluctant to make a diagnosis of parathyroid carcinoma in the setting of secondary/tertiary renal failure or would use more strict criteria. Therefore, knowledge of the presence of renal failure and secondary/tertiary hyperparathyroidism is important to enable proper pathological assessment. Discussion with the treating clinician (endocrinologist/surgeon, etc.) for correlative clinical information as described here and under biochemical information is important for characterizing this disease. Other relevant information may include detailed family history, imaging findings of lateralization noted on ultrasound, nuclear medicine (e.g., sestamibi) scan or 4-dimensional CT scans.9 Other information also includes any history of fine needle aspiration, since this procedure may lead to pathologic alterations important to consider during specimen interpretation.  **References**  1 Busaidy NL, Jimenez C, Habra MA, Schultz PN, El-Naggar AK, Clayman GL, Asper JA, Diaz EM, Jr., Evans DB, Gagel RF, Garden A, Hoff AO, Lee JE, Morrison WH, Rosenthal DI, Sherman SI, Sturgis EM, Waguespack SG, Weber RS, Wirfel K and Vassilopoulou-Sellin R (2004). Parathyroid carcinoma: a 22-year experience. *Head Neck* 26(8):716-726.  2 Harari A, Waring A, Fernandez-Ranvier G, Hwang J, Suh I, Mitmaker E, Shen W, Gosnell J, Duh QY and Clark O (2011). Parathyroid carcinoma: a 43-year outcome and survival analysis. *J Clin Endocrinol Metab* 96(12):3679-3686.  3 Sadler C, Gow KW, Beierle EA, Doski JJ, Langer M, Nuchtern JG, Vasudevan SA and Goldfarb M (2014). Parathyroid carcinoma in more than 1,000 patients: A population-level analysis. *Surgery* 156(6):1622-1629; discussion 1629-1630.  4 Shane E and Bilezikian JP (1982). Parathyroid carcinoma: a review of 62 patients. *Endocr Rev* 3(2):218-226.  5 Agha A, Carpenter R, Bhattacharya S, Edmonson SJ, Carlsen E and Monson JP (2007). Parathyroid carcinoma in multiple endocrine neoplasia type 1 (MEN1) syndrome: two case reports of an unrecognised entity. *J Endocrinol Invest* 30(2):145-149.  6 Carpten JD, Robbins CM, Villablanca A, Forsberg L, Presciuttini S, Bailey-Wilson J, Simonds WF, Gillanders EM, Kennedy AM, Chen JD, Agarwal SK, Sood R, Jones MP, Moses TY, Haven C, Petillo D, Leotlela PD, Harding B, Cameron D, Pannett AA, Hoog A, Heath H, 3rd, James-Newton LA, Robinson B, Zarbo RJ, Cavaco BM, Wassif W, Perrier ND, Rosen IB, Kristoffersson U, Turnpenny PD, Farnebo LO, Besser GM, Jackson CE, Morreau H, Trent JM, Thakker RV, Marx SJ, Teh BT, Larsson C and Hobbs MR (2002). HRPT2, encoding parafibromin, is mutated in hyperparathyroidism-jaw tumor syndrome. *Nat Genet* 32(4):676-680.  7 Gill AJ (2014). Understanding the genetic basis of parathyroid carcinoma. *Endocr Pathol* 25(1):30-34.  8 Weinstein LS and Simonds WF (2003). HRPT2, a marker of parathyroid cancer. *N Engl J Med* 349(18):1691-1692.  9 Christakis I, Vu T, Chuang HH, Fellman B, Figueroa AMS, Williams MD, Busaidy NL and Perrier ND (2017). The diagnostic accuracy of neck ultrasound, 4D-Computed tomographyand sestamibi imaging in parathyroid carcinoma. *Eur J Radiol* 95:82-88. |  |
| Non-core | PRE-OPERATIVE BIOCHEMICAL INFORMATION | Multi selection value list (select all that apply)/text:  • Information not provided  OR  • Calcium, *specify level with units and specimen type (serum, other)*  • Parathyroid hormone (PTH), *specify level with units*  • Other, *specify* | The highest preoperative levels of calcium and parathyroid hormone should be recorded. A clinical concern for parathyroid carcinoma is raised when a patient presents with a palpable neck mass, very high serum calcium levels (>14 mg/dl/3.5 mmol/L) and corresponding significantly elevated parathyroid hormone (PTH) levels. It remains unclear if the preoperative levels of either calcium or PTH may have a predictive role in this disease, although patients with extreme hypercalcemia are more likely to meet the criteria for the diagnosis of parathyroid carcinoma.1-4 Documenting this associated clinical information is important and may also stratify patients’ risk of recurrence.5 Different institutions may use different units for measurement of calcium. In general, standard international (SI) units are preferred which is mmol/L. However, the units used should be stated.    **References**  1 Busaidy NL, Jimenez C, Habra MA, Schultz PN, El-Naggar AK, Clayman GL, Asper JA, Diaz EM, Jr., Evans DB, Gagel RF, Garden A, Hoff AO, Lee JE, Morrison WH, Rosenthal DI, Sherman SI, Sturgis EM, Waguespack SG, Weber RS, Wirfel K and Vassilopoulou-Sellin R (2004). Parathyroid carcinoma: a 22-year experience. *Head Neck* 26(8):716-726.  2 Harari A, Waring A, Fernandez-Ranvier G, Hwang J, Suh I, Mitmaker E, Shen W, Gosnell J, Duh QY and Clark O (2011). Parathyroid carcinoma: a 43-year outcome and survival analysis. *J Clin Endocrinol Metab* 96(12):3679-3686.  3 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174.  4 Villar-del-Moral J, Jimenez-Garcia A, Salvador-Egea P, Martos-Martinez JM, Nuno-Vazquez-Garza JM, Serradilla-Martin M, Gomez-Palacios A, Moreno-Llorente P, Ortega-Serrano J and de la Quintana-Basarrate A (2014). Prognostic factors and staging systems in parathyroid cancer: a multicenter cohort study. *Surgery* 156(5):1132-1144.  5 Silva-Figueroa AM, Hess KR, Williams MD, Clarke CN, Christakis I, Graham PH, Grubbs EG, Lee JE, Busaidy NL and Perrier ND (2017). Prognostic Scoring System to Risk Stratify Parathyroid Carcinoma. *J Am Coll Surg* 224(5):908-987. |  |
| Core | OPERATIVE PROCEDURE | Multi selection value list (select all that apply)/text:  • Not specified  OR  • Parathyroidectomy, single gland  • Parathyroidectomy, en bloc with thyroid lobe  • Other parathyroid gland sampling   * Unilateral * Bilateral   • Lymph node sampling, *specify*  • Soft tissue of neck, *specify*  • Other*, specify* | For clinically suspected parathyroid carcinoma, a preoperative biopsy is not recommended. Often the presentation of parathyroid carcinoma overlaps with parathyroid adenoma and the diagnosis is not made until surgical inspection and/or histologic review of the parathyroid resection specimen.1,2 When carcinoma is suspected an en bloc resection of the concerning parathyroid gland along with the immediately adjacent or adherent structures such as the ipsilateral thyroid lobe may facilitate complete tumour resection. Advancements in preoperative imaging have reduced the need for multigland sampling and it is not recommended when a parathyroid mass is encountered.3 Similarly, lymph node sampling is generally not performed as the rate of regional nodal spread is low. If lymph node sampling is performed, the location of the resected lymph nodes should be specified. Resection of soft tissue of the neck, which may include skeletal muscle and nerve, most often will be encountered in the setting of recurrent disease. Other tissues to be specified may include oesophageal wall, thymus gland, or any structures not otherwise listed. In the unlikely scenario where more than one anatomically primary tumour occurs, a separate dataset should be completed for each tumour.  **References**  1 Quinn CE, Healy J, Lebastchi AH, Brown TC, Stein JE, Prasad ML, Callender GG, Carling T and Udelsman R (2015). Modern experience with aggressive parathyroid tumors in a high-volume New England referral center. *J Am Coll Surg* 220(6):1054-1062.  2 Ippolito G, Palazzo FF, Sebag F, De Micco C and Henry JF (2007). Intraoperative diagnosis and treatment of parathyroid cancer and atypical parathyroid adenoma. *Br J Surg* 94(5):566-570.  3 Udelsman R, Akerstrom G, Biagini C, Duh QY, Miccoli P, Niederle B and Tonelli F (2014). The surgical management of asymptomatic primary hyperparathyroidism: proceedings of the Fourth International Workshop. *J Clin Endocrinol Metab* 99(10):3595-3606. |  |
| Non-core | OPERATIVE FINDINGS | Single selection value list/text:  • Not specified  OR  • Non-adherent to surrounding structures  • Adherent to structure(s)   * Thyroid * Oesophagus * Recurrent laryngeal nerve * Skeletal muscle * Other, *specify*   • Other, *specify* | The intraoperative findings often are clues to the possible diagnosis of parathyroid carcinoma. Specifically the observation of the parathyroid mass being adherent to nearby structures (in the absence of prior fine needle aspiration or surgical procedures) is concerning for parathyroid malignancy. Recognition of involved structures and possible close margins are also important considerations when reviewing the intraoperative and pathologic information together. |  |
| Core | SPECIMEN(S)  SUBMITTED | Multi selection value list (select all that apply)/text:  • Not specified  OR  • Parathyroid   * Left * Superior * Inferior * Not specified * Right * Superior * Inferior * Not specified * Other, *specify*   • Thyroid gland   * Left * Right * Isthmus   • Lymph nodes, *specify site(s) and laterality*  • Other, *specify site(s) and laterality* | Recording each specimen submitted allows for the extent of surgery to be documented. The location of the excised parathyroid should include laterality as well as correlation with the anatomic position of superior or inferior glands. Parathyroid ‘other’ may include mediastinal locations or supernumerary glands for which laterality should be included if known/determined. Additional resected specimens may include the thyroid lobe either en bloc with the parathyroid or as a separate specimen. When lymph nodes are submitted their locations should be specified (e.g., level VI, right or left paratracheal, right or left lateral neck). If additional specimens are resected (e.g., such as additional tissue by adjacent to the recurrent laryngeal nerve, muscle, or thymic tissue) these elements are captured in the ‘other’ specimen field. | . |
| Core | TUMOUR SITE | Multi selection value list (select all that apply)/text:  • Not specified  OR  • Parathyroid   * Left * Superior * Inferior * Not specified * Right * Superior * Inferior * Not specified * Mediastinal * Intrathyroidal, specify lobe   • Soft tissue or muscle, *specify site(s) and laterality*  • Lymph nodes, *specify site(s) and laterality*  • Other, *specify site(s) and laterality* | Parathyroid glands are paired endocrine structures with typically two glands on the right and the left. Based on patterns of embryologic development the glands may also be located in the mediastinum associated with the thymus or partially or fully within a thyroid lobe. Tumour may involve soft tissue that is further specified (i.e., adjacent to recurrent laryngeal nerve) or skeletal muscle (i.e., strap muscles). Other involved structures may include adjacent organs (i.e., thyroid, oesophagus or trachea). Regional tumour metastases to lymph nodes may also occur; the nodal level of involvement and laterality should be recorded (e.g., right paratracheal, or right level VI, etc.).1-3  **References**  1 Busaidy NL, Jimenez C, Habra MA, Schultz PN, El-Naggar AK, Clayman GL, Asper JA, Diaz EM, Jr., Evans DB, Gagel RF, Garden A, Hoff AO, Lee JE, Morrison WH, Rosenthal DI, Sherman SI, Sturgis EM, Waguespack SG, Weber RS, Wirfel K and Vassilopoulou-Sellin R (2004). Parathyroid carcinoma: a 22-year experience. *Head Neck* 26(8):716-726.  2 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174.  3 Chang YJ, Mittal V, Remine S, Manyam H, Sabir M, Richardson T and Young S (2006). Correlation between clinical and histological findings in parathyroid tumors suspicious for carcinoma. *Am Surg* 72(5):419-426. |  |
| Core | SPECIMEN WEIGHT | Numeric/text/Single select value list:  • \_\_\_ mg Parathyroid alone  OR  • \_\_\_ mg Parathyroid with other structure(s), *specify structure(s)*  • Cannot be assessed, *specify* | A normal parathyroid gland weighs approximately 40 mg. Glandular size and weight have long been utilized to aid in defining abnormal parathyroid glands in both benign and malignant conditions. Ideally the weight is of the parathyroid gland only, however soft tissue surrounding the gland should not be removed when a parathyroid atypical neoplasm or carcinoma is suspected. This allows for the microscopic evaluation of possible lesional extension into the adjacent tissues. On average parathyroid carcinomas typically weigh over 500 mg; however, there may be considerable variation in gland weight. |  |
| Core and  Non-core | TUMOUR DIMENSIONS | Numeric/text  • Maximum tumour dimension (largest tumour) \_\_\_ mm  Non-core  • Additional dimensions (largest tumour)  \_\_\_ mm x \_\_\_ mm  OR  • Cannot be assessed, *specify* | The largest dimension of the parathyroid neoplasm is recorded in millimetres (mm). The tumour dimensions may be taken from the gross examination or by microscopic examination as appropriate. Studies are conflicting as to the prognostic value of size.1-3  **References**  1 Busaidy NL, Jimenez C, Habra MA, Schultz PN, El-Naggar AK, Clayman GL, Asper JA, Diaz EM, Jr., Evans DB, Gagel RF, Garden A, Hoff AO, Lee JE, Morrison WH, Rosenthal DI, Sherman SI, Sturgis EM, Waguespack SG, Weber RS, Wirfel K and Vassilopoulou-Sellin R (2004). Parathyroid carcinoma: a 22-year experience. *Head Neck* 26(8):716-726.  2 Sadler C, Gow KW, Beierle EA, Doski JJ, Langer M, Nuchtern JG, Vasudevan SA and Goldfarb M (2014). Parathyroid carcinoma in more than 1,000 patients: A population-level analysis. *Surgery* 156(6):1622-1629; discussion 1629-1630.  3 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174. |  |
| Core | HISTOLOGICAL TUMOUR TYPE | Single selection value list:  • Atypical parathyroid neoplasm (atypical parathyroid adenoma)/neoplasm of uncertain malignant potential (UMP)a  • Parathyroid carcinoma | The histological tumour types to be included for parathyroid neoplasms are those defined in the most recent edition of the World Health Organization (WHO) Classification of Tumours of Endocrine Organs.1 Parathyroid carcinoma is diagnosed by unequivocal invasion into adjacent soft tissues, muscle or other adjacent organs (e.g., thyroid), lymphovascular or perineural invasion and/or the presence of regional or distant metastases. Parathyroid carcinoma may show a fibrotic tumour capsule as well as broad bands within the substance of the tumour. Cytologically, parathyroid carcinoma may be relatively uniform (low grade) or show high grade features including pleomorphism, macronucleoli, high-mitotic rate, and/or coagulative necrosis.2-5  Parathyroid neoplasms that show some histologically worrisome features but do not fulfil the more robust criteria of invasion or metastasis are classified as atypical parathyroid neoplasm (atypical parathyroid adenoma)/neoplasm of uncertain malignant potential (UMP). These lesions lack unequivocal invasion. Parathyroid neoplasms of UMP generally have two or more concerning features, such as fibrous bands, mitotic figures, necrosis, trabecular growth, or adherence to surrounding tissues intraoperatively. Additionally they usually have a smaller dimension, weight, and volume than carcinomas and are less likely to have coagulative tumour necrosis.6-10  **References**  1 Lloyd R, Osamura R, Klöppel G and Rosai J (eds) (2017). *WHO Classification of Tumours of Endocrine Organs, 4th ed*. IARC Press, Lyon.  2 Bondeson L, Sandelin K and Grimelius L (1993). Histopathological variables and DNA cytometry in parathyroid carcinoma. *Am J Surg Pathol* 17(8):820-829.  3 Asare EA, Sturgeon C, Winchester DJ, Liu L, Palis B, Perrier ND, Evans DB, Winchester DP and Wang TS (2015). Parathyroid Carcinoma: An Update on Treatment Outcomes and Prognostic Factors from the National Cancer Data Base (NCDB). *Ann Surg Oncol* 22(12):3990-3995.  4 Erovic BM, Goldstein DP, Kim D, Mete O, Brierley J, Tsang R, Freeman JL, Asa SL, Rotstein L and Irish JC (2013). Parathyroid cancer: outcome analysis of 16 patients treated at the Princess Margaret Hospital. *Head Neck* 35(1):35-39.  5 Stojadinovic A, Hoos A, Nissan A, Dudas ME, Cordon-Cardo C, Shaha AR, Brennan MF, Singh B and Ghossein RA (2003). Parathyroid neoplasms: clinical, histopathological, and tissue microarray-based molecular analysis. *Hum Pathol* 34(1):54-64.  6 McCoy KL, Seethala RR, Armstrong MJ, Nikiforova MN, Stang MT, Carty SE and Yip L (2015). The clinical importance of parathyroid atypia: is long-term surveillance necessary? *Surgery* 158(4):929-935; discussion 935-926.  7 Hundahl SA, Fleming ID, Fremgen AM and Menck HR (1999). Two hundred eighty-six cases of parathyroid carcinoma treated in the U.S. between 1985-1995: a National Cancer Data Base Report. The American College of Surgeons Commission on Cancer and the American Cancer Society. *Cancer* 86(3):538-544.  8 Shaha AR and Shah JP (1999). Parathyroid carcinoma: a diagnostic and therapeutic challenge. *Cancer* 86(3):378-380.  9 Schulte KM, Gill AJ, Barczynski M, Karakas E, Miyauchi A, Knoefel WT, Lombardi CP, Talat N, Diaz-Cano S and Grant CS (2012). Classification of parathyroid cancer. *Ann Surg Oncol* 19(8):2620-2628.  10 Kameyama K and Takami H (2005). Proposal for the histological classification of parathyroid carcinoma. *Endocr Pathol* 16(1):49-52. | a Defined as tumours that are histologically or clinically worrisome but do not fulfill the more robust criteria (i.e., invasion, metastasis) for carcinoma. They generally include tumours that have two or more concerning features, such as fibrous bands, mitotic figures necrosis, trabecular growth, or adherence to surrounding tissues intraoperatively. Atypical parathyroid neoplasms usually have a smaller dimension, weight, and volume than carcinomas and are less likely to have coagulative tumour necrosis.  Value list from the WHO Classification of Tumours: Pathology and Genetics of Tumours of Endocrine Organs (2017))  Note that permission to publish the WHO classification of tumours may be needed in your implementation. It is advisable to check with the International Agency for Research on Cancer (IARC). |
| Core | HISTOLOGICAL TUMOUR GRADE | Single selection value list:  • Low grade  • High grade  • Not determined  • Not applicable (i.e., atypical neoplasm/adenoma, UMPa) | The division of parathyroid carcinoma into low grade and high grade utilizes cytologic features including pleomorphism necrosis and mitotic activity. High grade parathyroid carcinomas are characterized by the presence of multiple concurrent histologically adverse features including sheets of cells with pleomorphic enlarged nuclei (4x the size of background parathyroid cells) often with macronucleoli, coagulative necrosis, abnormal mitoses, and/or increased proliferation rate.1,2 Focal cellular atypia or endocrine atypia may be found in benign entities including the characteristic of cells 4x as large and is insufficient to meet criteria for true nuclear pleomorphism.  **References**  1 Bondeson L, Sandelin K and Grimelius L (1993). Histopathological variables and DNA cytometry in parathyroid carcinoma. *Am J Surg Pathol* 17(8):820-829.  2 Stojadinovic A, Hoos A, Nissan A, Dudas ME, Cordon-Cardo C, Shaha AR, Brennan MF, Singh B and Ghossein RA (2003). Parathyroid neoplasms: clinical, histopathological, and tissue microarray-based molecular analysis. *Hum Pathol* 34(1):54-64. |  |
| Core | EXTENT OF INVASION | Multi selection value list (select all that apply)/text:  • Cannot be assessed  • Confined to parathyroid without invasion through tumour capsule  OR  • Invasion through tumour capsule  • Invasion into extra-parathyroidal soft tissue  • Invasion into adjacent structures, *specify*   * Recurrent laryngeal nerve * Thyroid gland * Oesophagus * Skeletal muscle * Other, *specify* | Parathyroid carcinoma and parathyroid neoplasms of uncertain malignant potential may be difficult to diagnose on histologic examination. The extent of tumour involvement has been proposed as one critical factor in diagnosis. Many, but not all, tumours show a fibrotic capsule with invasion. By definition a parathyroid neoplasm of uncertain malignant potential may not invade other structures (i.e., cannot involve adipose tissue, muscle or adjacent organs as these features are restricted to parathyroid carcinomas). Documentation of tumour extent may also imply severity of local disease however studies correlating tumour extent with prognosis are conflicting.1-5 Rarely a parathyroid carcinoma may show lymphovascular involvement, a true hallmark of a carcinoma, with minimal to no localized invasive growth. As parathyroid neoplasms are very vascular caution in making the diagnosis of carcinoma is warranted in cases where an invasive growth pattern is not encountered. Overall, the documentation of the presence and extent of local tissue involvement in parathyroid carcinomas is inconsistently presented in the literature for this rare disease. The importance of including these findings in this dataset is for data collection that may aid in future stratification of these tumours for staging and outcome.  **References**  1 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174.  2 Silva-Figueroa AM, Hess KR, Williams MD, Clarke CN, Christakis I, Graham PH, Grubbs EG, Lee JE, Busaidy NL and Perrier ND (2017). Prognostic Scoring System to Risk Stratify Parathyroid Carcinoma. *J Am Coll Surg* 224(5):908-987.  3 Erovic BM, Goldstein DP, Kim D, Mete O, Brierley J, Tsang R, Freeman JL, Asa SL, Rotstein L and Irish JC (2013). Parathyroid cancer: outcome analysis of 16 patients treated at the Princess Margaret Hospital. *Head Neck* 35(1):35-39.  4 Stojadinovic A, Hoos A, Nissan A, Dudas ME, Cordon-Cardo C, Shaha AR, Brennan MF, Singh B and Ghossein RA (2003). Parathyroid neoplasms: clinical, histopathological, and tissue microarray-based molecular analysis. *Hum Pathol* 34(1):54-64.  5 Digonnet A, Carlier A, Willemse E, Quiriny M, Dekeyser C, de Saint Aubain N, Lemort M and Andry G (2011). Parathyroid carcinoma: a review with three illustrative cases. *J Cancer* 2:532-537. |  |
| Core and  Non-core | LYMPHOVASCULAR INVASION | Single selection value list:  • Not identified  • Present  Non-core/Multiselct value list:   * Vascular invasion * Lymphatic invasion | Lymphovascular invasion is the presence of tumour cells within a lymphatic or vascular space. Identifying this feature in the tumour capsule or in peritumoural soft tissue is a diagnostic criterion to define parathyroid carcinoma. Lymphovascular invasion should not be present in an atypical parathyroid neoplasm/adenoma or parathyroid tumour of uncertain malignant potential. Vascular invasive parathyroid carcinomas have a worse prognosis than carcinomas diagnosed solely on the basis of other forms of invasive growth and appear to have a higher risk of recurrence.1 The presence of fibrin associated with the tumour cells within an endothelial lined space supports the finding of true vascular invasion.2-6 As an endocrine organ, the parathyroid glands are highly vascular, and it is important not to mistake tumour next to small vessels as representing vascular space invasion. Special stains may be utilized for further visualization/confirmation of vascular invasion though are not essential.  **References**  1 Schulte KM, Gill AJ, Barczynski M, Karakas E, Miyauchi A, Knoefel WT, Lombardi CP, Talat N, Diaz-Cano S and Grant CS (2012). Classification of parathyroid cancer. *Ann Surg Oncol* 19(8):2620-2628.  2 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174.  3 Silva-Figueroa AM, Hess KR, Williams MD, Clarke CN, Christakis I, Graham PH, Grubbs EG, Lee JE, Busaidy NL and Perrier ND (2017). Prognostic Scoring System to Risk Stratify Parathyroid Carcinoma. *J Am Coll Surg* 224(5):908-987.  4 Stojadinovic A, Hoos A, Nissan A, Dudas ME, Cordon-Cardo C, Shaha AR, Brennan MF, Singh B and Ghossein RA (2003). Parathyroid neoplasms: clinical, histopathological, and tissue microarray-based molecular analysis. *Hum Pathol* 34(1):54-64.  5 Digonnet A, Carlier A, Willemse E, Quiriny M, Dekeyser C, de Saint Aubain N, Lemort M and Andry G (2011). Parathyroid carcinoma: a review with three illustrative cases. *J Cancer* 2:532-537.  6 Yip L, Seethala RR, Nikiforova MN, Nikiforov YE, Ogilvie JB, Carty SE and Yim JH (2008). Loss of heterozygosity of selected tumor suppressor genes in parathyroid carcinoma. *Surgery* 144(6):949-955; discussion 954-945. |  |
| Core | PERINEURAL INVASION | Single selection value list:  • Not identified  • Present | The close proximity of the parathyroids with the recurrent laryngeal nerve, leads to potential invasion of this structure. Critical review is required of this parameter as close proximity without direct nerve involvement would be considered not involved. |  |
| Core | NECROSIS | Single selection value list:  • Not identified  • Present | The finding of coagulative necrosis is uncommon outside of the diagnosis of atypical parathyroid neoplasm/adenoma or parathyroid carcinoma.1 Necrosis may also be more common in high grade tumours. It is important to know if a fine needle aspiration may have been performed as this may lead to secondary necrosis in a parathyroid adenoma and should not be reported as an atypical neoplasm or carcinoma without other supporting criteria.  **References**  1 Bondeson L, Sandelin K and Grimelius L (1993). Histopathological variables and DNA cytometry in parathyroid carcinoma. *Am J Surg Pathol* 17(8):820-829. |  |
| Core | MITOTIC COUNT | Numeric/single selection value list:  • \_\_\_ per 2 mm2 b  • Cannot be assessed | The presence of mitoses is uncommon in benign parathyroid disorders and should raise concern for a parathyroid malignancy. However, absolute mitotic count does not definitively separate adenomas from carcinomas. The literature commonly refers to mitotic rates per 50 or 10 high power fields (HPFs) without always defining the diameter of the HPFs. For this reporting protocol mitotic count should be evaluated as number of mitoses per 2 mm2. It is recommended that reporting pathologists know their field diameter when calculating mitotic rates. The estimate of 10 HPFs equating to 2 mm2 is commonly used as this reflects many microscopes in widespread use. The area of the tumour with the highest mitotic activity, i.e., ‘hot-spot’, should be preferentially counted if identified. Limited studies to date have evaluated the prognostic significance of this histologic factor.1-3 The use of supplemental techniques such as PHH3 for identifying mitosis is not established in parathyroid neoplasms. The finding of abnormal mitoses may be remarked upon in the pathology report.  **References**  1 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174.  2 Silva-Figueroa AM, Hess KR, Williams MD, Clarke CN, Christakis I, Graham PH, Grubbs EG, Lee JE, Busaidy NL and Perrier ND (2017). Prognostic Scoring System to Risk Stratify Parathyroid Carcinoma. *J Am Coll Surg* 224(5):908-987.  3 Bondeson L, Sandelin K and Grimelius L (1993). Histopathological variables and DNA cytometry in parathyroid carcinoma. *Am J Surg Pathol* 17(8):820-829. | b 2 mm2 approximates 10 HPFs on some microscopes. |
| Core and  Non-core | MARGIN STATUS | Single selection value list/text/numeric:  • Not involved (R0)  Non-core   * Distance of tumour to closest margin \_\_\_ mm   • Involved   * Abutting tissue edge (R1 resection) * Transected, fragmented or ruptured (possible R2 resection) * *Specify if named structure/location is involved at margin(s)*   • Cannot be assessed, *specify* | Parathyroid neoplasms have a potential to locally recur if incompletely excised. Disruption of the gland intra-operatively, rupture, piecemeal removal and involved surgical margins all place a patient at increased local risk of recurrence.1-4 Such disruption of parathyroid specimens would be considered as R2 margin status when gross residual disease may remain (transected margins). Often the proximity to the adjacent nerve may lead to the tumour abutting the margin either focally or with possible circumscribed nests approximating the margin. These scenarios are consistent with a R1 microscopic surgical margin. As parathyroid masses are often without orientation the location of the margin involved may not be determined; however if known should be specified. Currently surgery is the only modality to effectively treat parathyroid tumours.  **References**  1 Erovic BM, Goldstein DP, Kim D, Mete O, Brierley J, Tsang R, Freeman JL, Asa SL, Rotstein L and Irish JC (2013). Parathyroid cancer: outcome analysis of 16 patients treated at the Princess Margaret Hospital. *Head Neck* 35(1):35-39.  2 Digonnet A, Carlier A, Willemse E, Quiriny M, Dekeyser C, de Saint Aubain N, Lemort M and Andry G (2011). Parathyroid carcinoma: a review with three illustrative cases. *J Cancer* 2:532-537.  3 Yip L, Seethala RR, Nikiforova MN, Nikiforov YE, Ogilvie JB, Carty SE and Yim JH (2008). Loss of heterozygosity of selected tumor suppressor genes in parathyroid carcinoma. *Surgery* 144(6):949-955; discussion 954-945.  4 Schulte KM, Gill AJ, Barczynski M, Karakas E, Miyauchi A, Knoefel WT, Lombardi CP, Talat N, Diaz-Cano S and Grant CS (2012). Classification of parathyroid cancer. *Ann Surg Oncol* 19(8):2620-2628. |  |
| Core | LYMPH NODE STATUS | Single selection value list/text/numeric:  • No nodes submitted or found  OR  • Number of lymph nodes examined  • Not involved  • Involved   * Number of positive lymph nodes * Number cannot be determined | Regional lymph node metastasis from parathyroid carcinoma is uncommon with involvement mostly in the central neck (levels VI or VII) and rarely lateral neck (levels II, III, and IV).1 Metastases to lymph nodes has shown a potential correlation with survival however this has not been confirmed by large database studies.2-7 Although the evaluation of lymph node metastasis for extranodal extension (ENE) is encouraged for other head and neck malignancies, there is currently limited data on ENE specific to parathyroid carcinoma and so it is not included in this dataset.  **References**  1 Schulte KM, Gill AJ, Barczynski M, Karakas E, Miyauchi A, Knoefel WT, Lombardi CP, Talat N, Diaz-Cano S and Grant CS (2012). Classification of parathyroid cancer. *Ann Surg Oncol* 19(8):2620-2628.  2 Harari A, Waring A, Fernandez-Ranvier G, Hwang J, Suh I, Mitmaker E, Shen W, Gosnell J, Duh QY and Clark O (2011). Parathyroid carcinoma: a 43-year outcome and survival analysis. *J Clin Endocrinol Metab* 96(12):3679-3686.  3 Sadler C, Gow KW, Beierle EA, Doski JJ, Langer M, Nuchtern JG, Vasudevan SA and Goldfarb M (2014). Parathyroid carcinoma in more than 1,000 patients: A population-level analysis. *Surgery* 156(6):1622-1629; discussion 1629-1630.  4 Talat N and Schulte KM (2010). Clinical presentation, staging and long-term evolution of parathyroid cancer. *Ann Surg Oncol* 17(8):2156-2174.  5 Silva-Figueroa AM, Hess KR, Williams MD, Clarke CN, Christakis I, Graham PH, Grubbs EG, Lee JE, Busaidy NL and Perrier ND (2017). Prognostic Scoring System to Risk Stratify Parathyroid Carcinoma. *J Am Coll Surg*.  6 Hsu KT, Sippel RS, Chen H and Schneider DF (2014). Is central lymph node dissection necessary for parathyroid carcinoma? *Surgery* 156(6):1336-1341; discussion 1341.  7 Lee PK, Jarosek SL, Virnig BA, Evasovich M and Tuttle TM (2007). Trends in the incidence and treatment of parathyroid cancer in the United States. *Cancer* 109(9):1736-1741. |  |
| Non-core | COEXISTENT FINDINGS | Multi selection value list (select all that apply)/single select/text:  • None identified  • Present   * Other finding(s) in same parathyroid gland as neoplasm * Other, *specify*   • Tissue from another submitted parathyroid gland, *specify*   * Normal * Hypercellular, *specify* * Other, *specify* | Coexistent findings enables documentation of other histologic features identified in either the same parathyroid gland as the neoplasm or in other parathyroid gland tissue submitted for evaluation. As coexisting parathyroid conditions may be encounted in other parathyroid glands submitted it is important to detail whether the histology has normal, hypercellular (i.e., specifying if specific for hyperplasia or adenoma), or other features seen as relevant to this dataset. Malignant pathology identified in the thyroid would utilize the corresponding thyroid dataset. |  |
| Non-core | ANCILLARY STUDIES | Multi selection value list (select all that apply)/Numeric/text:  • Not performed  OR  • Immunohistochemistry performed   * Ki-67, specify results and method \_\_\_\_% * Parafibromin (CDC73), *specify results* * PGP9.5, *specify results* * Other immunohistochemistry, *specify*   • Molecular performed   * CDC73 (parafibromin gene) * Germline testing, *specify results* * Tumour (somatic) testing, s*pecify results* * Other molecular test(s), *specify*   • Other, *specify* | Parafibromin is the protein encoded by the *CDC73* gene (previously known as HRPT2).1 Germline mutations and deletions in the *CDC73* gene occur in the autosomal dominant HPT-JT syndrome with somatic second hits occurring in carcinomas and adenomas arising in this setting. Patients presenting with apparently sporadic parathyroid carcinoma may have occult HPT-JT syndrome.2-7 Somatic only double hit mutation/inactivation also occur frequently in parathyroid carcinomas not associated with HPT-JT.7 Immunohistochemistry for parafibromin is not widely available and may be technically difficult to perform and interpret.2 Immunohistochemical evaluation of parafibromin shows nuclear staining in normal parathyroid cells and most benign parathyroid tumours. Loss of nuclear expression of parafibromin occurs in most but not all tumours associated with biallelic *CDC73* mutation/ deletion.7-10 Loss of parafibromin expression is not completely sensitive for *CDC73* mutation but may be used to triage genetic testing for HPT-JT syndrome in patients with atypical parathyroid neoplasms and parathyroid carcinoma. Parafibromin loss may be associated with a higher likelihood of recurrence in parathyroid carcinoma.2,7-9,11-13 It has been suggested that tumours which demonstrate loss of parafibromin expression may show subtle morphological clues including sheet like growth, eosinophilic cytoplasm, perinuclear cytoplasmic clearing and nuclear enlargement.7  Ki-67 proliferative index has also been reported as elevated in parathyroid neoplasms though with some overlap with hyperplasia and adenomas.1,10,14-16 If performed, evaluation of Ki-67 immunohistochemical staining of the parathyroid neoplasm should be recorded as a percent of tumour cells staining in hot spots (the areas with greatest Ki-67 expression). The method used to calculate the Ki-67 percent should be specified (e.g., manual count and the number of cells evaluated, or automated computer assisted calculation including the number of cells counted).    Other markers might include Cyclin D and/or galectin-3 overexpression or retinoblastoma (Rb) loss of expression which has also been studied with an association in carcinomas compared to adenomas.16-18 Protein Gene Product 9.5 (PGP9.5) is also overexpressed in the majority of parathyroid carcinomas and has shown similar performance in parathyroid carcinomas as parafibromin immunohistochemical evaluation.12  **References**  1 Truran PP, Johnson SJ, Bliss RD, Lennard TW and Aspinall SR (2014). Parafibromin, galectin-3, PGP9.5, Ki67, and cyclin D1: using an immunohistochemical panel to aid in the diagnosis of parathyroid cancer. *World J Surg* 38(11):2845-2854.  2 Gill AJ (2014). Understanding the genetic basis of parathyroid carcinoma. *Endocr Pathol* 25(1):30-34.  3 Bondeson L, Sandelin K and Grimelius L (1993). Histopathological variables and DNA cytometry in parathyroid carcinoma. *Am J Surg Pathol* 17(8):820-829.  4 Yip L, Seethala RR, Nikiforova MN, Nikiforov YE, Ogilvie JB, Carty SE and Yim JH (2008). Loss of heterozygosity of selected tumor suppressor genes in parathyroid carcinoma. *Surgery* 144(6):949-955; discussion 954-945.  5 Wang O, Wang C, Nie M, Cui Q, Guan H, Jiang Y, Li M, Xia W, Meng X and Xing X (2012). Novel HRPT2/CDC73 gene mutations and loss of expression of parafibromin in Chinese patients with clinically sporadic parathyroid carcinomas. *PLoS One* 7(9):e45567.  6 Guarnieri V, Battista C, Muscarella LA, Bisceglia M, de Martino D, Baorda F, Maiello E, D'Agruma L, Chiodini I, Clemente C, Minisola S, Romagnoli E, Corbetta S, Viti R, Eller-Vainicher C, Spada A, Iacobellis M, Malavolta N, Carella M, Canaff L, Hendy GN, Cole DE and Scillitani A (2012). CDC73 mutations and parafibromin immunohistochemistry in parathyroid tumors: clinical correlations in a single-centre patient cohort. *Cell Oncol (Dordr)* 35(6):411-422.  7 Gill AJ, Lim G, Cheung VKY, Andrici J, Perry-Keene JL, Paik J, Sioson L, Clarkson A, Sheen A, Luxford C, Elston MS, Meyer-Rochow GY, Nano MT, Kruijff S, Engelsman AF, Sywak M, Sidhu SB, Delbridge LW, Robinson BG, Marsh DJ, Toon CW, Chou A and Clifton-Bligh RJ (2019). Parafibromin-deficient (HPT-JT Type, CDC73 Mutated) Parathyroid Tumors Demonstrate Distinctive Morphologic Features. *Am J Surg Pathol* 43(1):35-46.  8 Kim HK, Oh YL, Kim SH, Lee DY, Kang HC, Lee JI, Jang HW, Hur KY, Kim JH, Min YK, Chung JH and Kim SW (2012). Parafibromin immunohistochemical staining to differentiate parathyroid carcinoma from parathyroid adenoma. *Head Neck* 34(2):201-206.  9 Lim S, Elston MS, Gill AJ, Marsh DJ and Conaglen JV (2011). Metastatic parathyroid carcinoma initially misdiagnosed as parathyroid adenoma: the role of parafibromin in increasing diagnostic accuracy. *Intern Med J* 41(9):695-699.  10 Fernandez-Ranvier GG, Khanafshar E, Tacha D, Wong M, Kebebew E, Duh QY and Clark OH (2009). Defining a molecular phenotype for benign and malignant parathyroid tumors. *Cancer* 115(2):334-344.  11 Gill AJ, Clarkson A, Gimm O, Keil J, Dralle H, Howell VM and Marsh DJ (2006). Loss of nuclear expression of parafibromin distinguishes parathyroid carcinomas and hyperparathyroidism-jaw tumor (HPT-JT) syndrome-related adenomas from sporadic parathyroid adenomas and hyperplasias. *Am J Surg Pathol* 30(9):1140-1149.  12 Howell VM, Gill A, Clarkson A, Nelson AE, Dunne R, Delbridge LW, Robinson BG, Teh BT, Gimm O and Marsh DJ (2009). Accuracy of combined protein gene product 9.5 and parafibromin markers for immunohistochemical diagnosis of parathyroid carcinoma. *J Clin Endocrinol Metab* 94(2):434-441.  13 Kruijff S, Sidhu SB, Sywak MS, Gill AJ and Delbridge LW (2014). Negative parafibromin staining predicts malignant behavior in atypical parathyroid adenomas. *Ann Surg Oncol* 21(2):426-433.  14 Ozolins A, Narbuts Z, Vanags A, Simtniece Z, Visnevska Z, Akca A, Wirowski D, Gardovskis J, Strumfa I and Goretzki PE (2016). Evaluation of malignant parathyroid tumours in two European cohorts of patients with sporadic primary hyperparathyroidism. *Langenbecks Arch Surg* 401(7):943-951.  15 Lloyd RV, Carney JA, Ferreiro JA, Jin L, Thompson GB, Van Heerden JA, Grant CS and Wollan PC (1995). Immunohistochemical Analysis of the Cell Cycle-Associated Antigens Ki-67 and Retinoblastoma Protein in Parathyroid Carcinomas and Adenomas. *Endocr Pathol* 6(4):279-287.  16 Stojadinovic A, Hoos A, Nissan A, Dudas ME, Cordon-Cardo C, Shaha AR, Brennan MF, Singh B and Ghossein RA (2003). Parathyroid neoplasms: clinical, histopathological, and tissue microarray-based molecular analysis. *Hum Pathol* 34(1):54-64.  17 Hemmer S, Wasenius VM, Haglund C, Zhu Y, Knuutila S, Franssila K and Joensuu H (2001). Deletion of 11q23 and cyclin D1 overexpression are frequent aberrations in parathyroid adenomas. *Am J Pathol* 158(4):1355-1362.  18 Vasef MA, Brynes RK, Sturm M, Bromley C and Robinson RA (1999). Expression of cyclin D1 in parathyroid carcinomas, adenomas, and hyperplasias: a paraffin immunohistochemical study. *Mod Pathol* 12(4):412-416. |  |
| Core | HISTOLOGICALLY CONFIRMED DISTANT METASTASES | Single selection value list/text:  • Not identified  • Not assessed  • Present, *specify site(s)* | The presence of histologically confirmed distant metastases is a critical component of pathological staging.1  **References**  1 Amin MB, Edge S, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed*. Springer., New York. |  |
| Core | PATHOLOGICAL STAGING (AJCC TNM 8th edition)c  TNM descriptors | Choose if applicable:  • m - multiple primary tumours  • r - recurrent  • y - post-therapy | A prognostic staging system has not been formally adopted for parathyroid carcinomas. The rarity of this disease has limited standard review and comparison for meaningful stratification. However, it is recognized that standardized data collection as proposed here and outlined in the 8th edition of American Joint Committee on Cancer (AJCC) Staging Manual will begin the process of systematically gathering data for this rare entity.1 It is with this goal that the parathyroid dataset is established.  **References**  1 Amin MB, Edge S, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed*. Springer., New York. | Note that permission to publish the TNM cancer staging tables may be needed in your implementation. It is advisable to check.  c Used with the permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2016) published by Springer Science+Business Media. |
| Core | Primary tumour (pT)d | Single selection value list:  • TX Primary tumour cannot be assessed  • Tis Atypical parathyroid neoplasm (neoplasm of UMP)a  • T1 Localised to the parathyroid gland with extension limited to soft tissue  • T2 Direct invasion into the thyroid gland  • T3 Direct invasion into recurrent laryngeal nerve, oesophagus, trachea, skeletal muscle, adjacent lymph nodes, or thymus  • T4 Direct invasion into major blood vessel or spine |  | a Defined as tumours that are histologically or clinically worrisome but do not fulfill the more robust criteria (i.e., invasion, metastasis) for carcinoma. They generally include tumours that have two or more concerning features, such as fibrous bands, mitotic figures necrosis, trabecular growth, or adherence to surrounding tissues intraoperatively. Atypical parathyroid neoplasms usually have a smaller dimension, weight, and volume than carcinomas and are less likely to have coagulative tumour necrosis. |
| Core | REGIONAL LYMPH NODES (PN) | Single selection value list:  • NX Regional lymph nodes cannot be assessed  • N0 No regional lymph node metastasis  • N1 Regional lymph node metastasis  • N1a Metastasis to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes) or superior mediastinal lymph nodes (level VII)  • N1b Metastasis to unilateral, bilateral, or contralateral cervical (level I,II,III,IV, or V) or retropharyngeal nodes |  |  |