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| **Required/**  **Recommended** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
| Recommended | Clinical information | Multi selection value list (select all that apply)  • Not provided  OR  • Previous history of penile or urethral cancer, specify  • Previous therapy, specify  • Other, specify | History of prior penile tumours and treatments, including topical treatment, radiotherapy and chemotherapy should be given particularly if the patient has been treated elsewhere.  It is good clinical practice to transcribe all clinical information from the request form on to the pathology report.1 This is a recommended rather than a required item as it is the responsibility of the clinician requesting the pathological examination of a specimen to provide information that will have an impact on the diagnostic process or affect its interpretation.  References  1 RCPath (Royal College of Pathologists) (2015). Dataset for penile and distal urethral cancer histopathology reports. Available from: https://www.rcpath.org/resourceLibrary/dataset-for-penile-and-distal-urethral-cancer-histopathology-reports.html (Accessed 1st March 2016). |  |
| Required | Operative procedure | Multi selection value list (select all that apply)  • Partial penectomy  • Radical penectomy  • Glans resurfacing  • Glansectomy  • Circumcision  • Incisional/punch biopsy  • Excisional biopsy  • Urethrectomy  • Lymphadenectomy  o Sentinel   Left, specify number of site/s   Right, specify number of site/s  o Inguinal   Left   Right  o Pelvic   Left, specify site/s   Right, specify site/s  o Other, specify   Left, specify site/s   Right, specify site/s  • Other, specify laterality and site/s  • Not specified | Operative procedure1-3  Treatment of penile carcinoma is primarily surgical. The development of supranetworks in some countries has made organ sparing techniques associated with reconstruction widely available and radical or partial penectomy is no longer the standard treatment for this disease except in advanced cases.4,5  Nodal involvement is a recognised predictor of poor prognosis. In node positive disease, the number of positive nodes, the presence of extracapsular spread (ECS) and the level of nodal involvement (pelvic versus inguinal) have been shown to influence survival by multivariate analysis and this is reflected in both TNM76,7 and TNM88 which classify any pelvic lymph node involvement or extracapsular extension of any regional lymph node (inguinal or pelvic) as pN3 in the penile but not in the urethral TNM.  Extent of inguinal node involvement and presence of ECS also predicts pelvic node involvement.6,7,9,10  The number of nodes found within an individual specimen should be specified in the report. The size of the largest nodal tumour deposit (not the lymph node size) together with presence of extranodal spread must also be recorded as there is evidence that this may affect prognosis.  Tumour presence or absence, size of tumour deposit and presence or absence of ECS are reported separately for each individual node site. Occasionally individual tumour cells are identified in the peripheral sinus. The significance of these is uncertain but they should be described within reports.  Immunohistochemistry is essential for the assessment of micrometastases in sentinel lymph nodes as small metastases under 2 mm or single isolated tumour cells may be easily missed.  References  1 RCPath (Royal College of Pathologists) (2015). Dataset for penile and distal urethral cancer histopathology reports. Available from: https://www.rcpath.org/resourceLibrary/dataset-for-penile-and-distal-urethral-cancer-histopathology-reports.html (Accessed 1st March 2016).  2 Horenblas S (2012). Sentinel lymph node biopsy in penile carcinoma. Semin Diagn Pathol 29(2):90-95.  3 Lam W, Alnajjar HM, La-Touche S, Perry M, Sharma D, Corbishley C, Pilcher J, Heenan S and Watkin N (2013). Dynamic sentinel lymph node biopsy in patients with invasive squamous cell carcinoma of the penis: a prospective study of the long-term outcome of 500 inguinal basins assessed at a single institution. Eur Urol 63(4):657-663.  4 Hakenberg OW, Comperat EM, Minhas S, Necchi A, Protzel C and Watkin N (2015). EAU guidelines on penile cancer: 2014 update. Eur Urol 67(1):142-150.  5 Lawindy SM, Rodriguez AR, Horenblas S and Spiess PE (2011). Current and future strategies in the diagnosis and management of penile cancer. Adv Urol 2011:593751.  6 International Union against Cancer (UICC) (2009). TNM Classification of Malignant Tumours (7th edition). Sobin L, Gospodarowicz M and C W. Wiley-Blackwell, Chichester, UK and Hoboken, New Jersey.  7 Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL and Trotti A (eds) (2010). AJCC Cancer Staging Manual 7th ed., New York, NY.: Springer.  8 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York.  9 Graafland NM, van Boven HH, van Werkhoven E, Moonen LM and Horenblas S (2010). Prognostic significance of extranodal extension in patients with pathological node positive penile carcinoma. J Urol 184(4):1347-1353.  10 Lughezzani G, Catanzaro M, Torelli T, Piva L, Biasoni D, Stagni S, Crestani A, Guttilla A, Raggi D, Giannatempo P, Necchi A, Pizzocaro G, Colecchia M, Salvioni R and Nicolai N (2014). The relationship between characteristics of inguinal lymph nodes and pelvic lymph node involvement in penile squamous cell carcinoma: a single institution experience. J Urol 191(4):977-982. |  |
| Recommended | Tumour focality | Single selection value list:  • Cannot be assessed  • Indeterminate  • Unifocal  • Multifocal, specify number of tumours in specimen | Some types of penile squamous carcinoma may be multifocal particularly if associated with precancerous changes (differentiated or undifferentiated penile intraepithelial neoplasia (PeIN)). There are little data for this in the literature but one text reports up to 5% of tumours are multifocal.1  References  1 Epstein JI CA, Humphrey PA (2011). Tumors of the prostate gland, seminal vesicles, penis, and scrotum. AFIP Atlas of Tumor Pathology. American Registry of Pathology, Washington DC, United States. |  |
| Required | Macroscopic tumour site | Multi selection value list (select all that apply)  • Glans penis  • Sulcus  • Foreskin  • Distal penile urethra  Single selection value list:  • No macroscopically visible tumour  • Indeterminate | Macroscopic tumour site1-5  The site(s) of primary penile and urethral tumours should be noted macroscopically. The prognosis of equivalent tumours of the foreskin may be better than that of the glans. Tumours of the urethra have a worse prognosis than those of the penis or foreskin. The presence or absence of Penile Intraepithelial Neoplasia (PeIN) or urothelial carcinoma in situ can be helpful in differentiating primary penile or urethral squamous from urothelial carcinomas.  Penile and urethral melanomas and primary skin tumours of the shaft should be handled and reported using melanoma and skin tumour datasets respectively.  References  1 RCPath (Royal College of Pathologists) (2015). Dataset for penile and distal urethral cancer histopathology reports. Available from: https://www.rcpath.org/resourceLibrary/dataset-for-penile-and-distal-urethral-cancer-histopathology-reports.html (Accessed 1st March 2016).  2 Oertell J, Caballero C, Iglesias M, Chaux A, Amat L, Ayala E, Rodriguez I, Velazquez EF, Barreto JE, Ayala G and Cubilla AL (2011). Differentiated precursor lesions and low-grade variants of squamous cell carcinomas are frequent findings in foreskins of patients from a region of high penile cancer incidence. Histopathology 58(6):925-933.  3 Tyson MD, Etzioni DA, Wisenbaugh ES, Andrews PE, Humphreys MR, Ferrigni RG, Swanson SK and Castle EP (2012). Anatomic site-specific disparities in survival outcomes for penile squamous cell carcinoma. Urology 79(4):804-808.  4 Corbishley CM, Rajab RM and Watkin NA (2015). Clinicopathological features of carcinoma of the distal penile urethra. Semin Diagn Pathol 32(3):238-244.  5 International Union against Cancer (UICC) (2009). TNM Classification of Malignant Tumours (7th edition). Sobin L, Gospodarowicz M and Wittekind C (Eds). Wiley-Blackwell, Chichester, UK and Hoboken, New Jersey. |  |
| Required | Macroscopic maximum tumour dimensions | Numeric:  • Maximum tumour width: \_\_\_ mm  • Maximum tumour thickness: \_\_\_ mm  • Cannot be assessed  • Not applicable | Macroscopic maximum tumour dimensions1-3  Measurement of the depth of invasion, measured in millimetres from the basement membrane of the adjacent epithelium to the deepest point of invasion, or the maximum thickness or size of the tumour may also give prognostic information as seen in squamous tumours of other sites such as skin. Minimal risk for metastasis is reported for tumours measuring less than 5 mm in thickness. Tumours invading deeper into penile anatomical levels are usually associated with a higher risk of nodal involvement (see MICROSCOPIC MAXIMUM TUMOUR DIMENSIONS). Thickness of penile tumours rather than depth of invasion is more readily assessed, especially in large tumours, because of the anatomical complexity of the organ.  References  1 Emerson RE, Ulbright TM, Eble JN, Geary WA, Eckert GJ and Cheng L (2001). Predicting cancer progression in patients with penile squamous cell carcinoma: the importance of depth of invasion and vascular invasion. Mod Pathol 14(10):963-968.  2 Velazquez EF, Ayala G, Liu H, Chaux A, Zanotti M, Torres J, Cho SI, Barreto JE, Soares F and Cubilla AL (2008). Histologic grade and perineural invasion are more important than tumor thickness as predictor of nodal metastasis in penile squamous cell carcinoma invading 5 to 10 mm. Am J Surg Pathol 32(7):974-979.  3 Chaux A, Caballero C, Soares F, Guimaraes GC, Cunha IW, Reuter V, Barreto J, Rodriguez I and Cubilla AL (2009). The prognostic index: a useful pathologic guide for prediction of nodal metastases and survival in penile squamous cell carcinoma. Am J Surg Pathol 33(7):1049-1057. |  |
| Recommended | Block identification key | Text | Block identification key1-4  The origin/designation of all tissue blocks should be recorded and it is preferable to document this information in the final pathology report. This is particularly important should the need for internal or external review arise and in larger more complex specimens and/or those with orientation markings. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion including accurate staging. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist.  Specimen photographs and/or annotated diagrams may be of assistance in clarification of block keys. These documents should also be retrievable as part of the pathology record.  Recording the origin/designation of tissue blocks also facilitates retrieval of blocks, for example for further immunohistochemical or molecular analysis, research studies or clinical trials.  The availability of large block technology is strongly recommended for larger specimens, such as glansectomies and penectomies as it facilitates staging with easier identification of deep structures, in particular the urethra, corpus spongiosum and corpora cavernosa.  It is recommended that a record is kept of a good representative paraffin block of tumour and if frozen tissue is stored.  References  1 RCPath (Royal College of Pathologists) (2015). Dataset for penile and distal urethral cancer histopathology reports. Available from: https://www.rcpath.org/resourceLibrary/dataset-for-penile-and-distal-urethral-cancer-histopathology-reports.html (Accessed 1st March 2016)  2 Cubilla AL, Piris A, Pfannl R, Rodriguez I, Aguero F and Young RH (2001). Anatomic levels: important landmarks in penectomy specimens: a detailed anatomic and histologic study based on examination of 44 cases. Am J Surg Pathol 25(8):1091-1094.  3 Tang V, Clarke L, Gall Z, Shanks JH, Nonaka D, Parr NJ, Elliott PA, Clarke NW, Ramani V, Lau MW and Sangar VK (2014). Should centralized histopathological review in penile cancer be the global standard? BJU Int 114(3):340-343.  4 Ebel JJ, Shabsigh A, Sharp DS and Zynger DL (2013). Whole-mount evaluation of penectomies for penile cancer: feasibility, cost and comparison to routine sectioning. Histopathology 63(1):64-73. |  |
| Required | Histological tumour type | Multi selection value list (select all that apply)  • Squamous cell carcinoma of usual subtype (NOS)  • Basaloid squamous cell carcinoma  • Warty (condylomatous) squamous cell carcinoma  • Verrucous squamous cell carcinoma  • Papillary squamous cell carcinoma  • Mixed squamous cell carcinomas, specify subtypes  • Other, specify\* | Histological tumour type1-7  The most recent World Health Organisation (WHO) book (2016)8 classifies and codes malignant squamous epithelial tumours of the penis as follows:  WHO classification of tumours of the penisa8  Descriptor ICD-O codes  Malignant epithelial tumours  Squamous cell carcinoma, NOS 8070/3  Verrucous carcinoma 8051/3  Adenosquamous carcinoma 8560/3  Sarcomatoid squamous carcinoma 8074/3  Mixed squamous cell carcinoma 8070/3  Basaloid squamous carcinoma 8083/3  Warty (condylomatous) carcinoma 8054/3  Papillary carcinoma (NOS) 8050/3  Lymphoepithelioma-like carcinoma 8082/2  Precursor lesions  Penile intraepithelial neoplasia  Low grade 8077/0  High grade 8077/2  Warty PeIN/Basaloid PeIN/Wart-basaloid PeIN  PeIN differentiated 8071/2  Paget disease 8542/3  a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.  © World Health Organisation/International Agency for Research on Cancer (IARC). Reproduced with permission  The tumours are further subclassified in the recent WHO publication into non- HPV related and HPV related tumours, however there is some group crossover particularly in Usual type squamous cell carcinomas a proportion of which are HPV positive. Mixed carcinomas may also show heterogeneity and sometimes include both HPV and non HPV associated tumour types.  A. Non–HPV-related penile squamous cell carcinomas (SCCs)  1. SCC  Usual carcinoma  Pseudohyperplastic carcinoma  Pseudoglandular carcinoma  2. Verrucous carcinoma  Pure verrucous carcinoma  Carcinoma cuniculatum  3. Papillary carcinoma, NOS  4. Adenosquamous carcinoma  5. Sarcomatoid squamous carcinoma  6. Mixed carcinoma  B. HPV-related penile SCCs  7. Basaloid carcinoma  Papillary–basaloid carcinoma  8. Warty carcinoma  Warty–basaloid carcinoma  Clear cell carcinoma  9. Lymphoepithelioma-like carcinoma  C. Other rare carcinomas  Different subtypes of penile carcinomas have been defined, which appear to be associated with different outcomes and may also therefore justify the adoption of different treatment strategies.  Over 95% of penile cancers are squamous cell carcinomas, with rare instances of sarcomas, melanomas or neuroendocrine carcinomas (including large cell and small cell neuroendocrine carcinomas). In addition to the most common, usual type of squamous carcinoma, subtypes include papillary, basaloid, warty (condylomatous), verrucous and sarcomatoid subtypes.  Subtyping is required as verruciform carcinomas (papillary, warty or verrucous carcinomas) have better outcomes. Basaloid, pseudoglandular/acantholytic and sarcomatoid carcinomas are always high-grade with a worse prognosis than the usual type of squamous carcinoma and may more readily metastasise via the blood stream to distant sites such as the lung. Mixed patterns are frequently present and in these cases all subtypes identified should be recorded.  Different patterns of growth can also be distinguished. Vertical growth/endophytic carcinomas are associated with a higher risk of metastases than superficial spreading/exophytic carcinomas although it is not clear whether this distinction offers superior prognostic power over tumour stage.  p16 staining or assessment of HPV subtypes may also be of help in subtyping squamous tumours but are not mandatory.  Tumour subtypes of squamous cell carcinoma  • Squamous cell carcinoma of usual subtype (NOS).9,10  • Basaloid squamous cell carcinoma.11  • Warty (condylomatous) squamous cell carcinoma.12,13  • Verrucous squamous cell carcinoma.6  • Papillary squamous cell carcinoma.14  • Mixed squamous cell carcinomas (specify subtypes).6  Other rare tumour subtypes  Squamous cell carcinoma variants  • Pseudohyperplastic squamous cell carcinoma.6,15,16  • Verrucous carcinoma variant  o Carcinoma cuniculatum.15,17  • Sarcomatoid (Spindle cell) squamous cell carcinoma.18  • Pseudoglandular (Acantholytic adenoid) squamous cell carcinoma.15,19  • Lymphoepithelioma like squamous cell carcinoma.20  • Warty carcinoma variants  o Clear cell carcinoma.15  o Warty basaloid squamous cell carcinoma.21  • Adenosquamous carcinoma.22  Non squamous tumours  • High grade neuroendocrine carcinomas including large cell neuroendocrine carcinoma and small cell carcinoma.15,23,24  • Malignant melanoma.25  • Mesenchymal tumours.10  • Urothelial carcinoma of urethra.10  • Extramammary Paget’s disease.10  • Appendage tumours.10  • Metastatic tumours.8  • Lymphomas and haematological tumours.10  References  1 Cubilla AL VE, Ayala GE, Chaux A, Torres J, Reuter V (2005). Identification of prognostic pathologic parameters in squamous cell carcinoma of the penis: significance and difficulties. Pathol Case Rev 10:3-13.  2 Guimaraes GC, Cunha IW, Soares FA, Lopes A, Torres J, Chaux A, Velazquez EF, Ayala G and Cubilla AL (2009). Penile squamous cell carcinoma clinicopathological features, nodal metastasis and outcome in 333 cases. J Urol 182(2):528-534; discussion 534.  3 Chaux A, Reuter V, Lezcano C, Velazquez EF, Torres J and Cubilla AL (2009). Comparison of morphologic features and outcome of resected recurrent and nonrecurrent squamous cell carcinoma of the penis: a study of 81 cases. Am J Surg Pathol 33(9):1299-1306.  4 Chaux A, Velazquez EF, Algaba F, Ayala G and Cubilla AL (2010). Developments in the pathology of penile squamous cell carcinomas. Urology 76(2 Suppl 1):S7-s14.  5 Cubilla AL (2009). The role of pathologic prognostic factors in squamous cell carcinoma of the penis. World J Urol 27(2):169-177.  6 Chaux A and Cubilla AL (2012). 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Tumors of the prostate gland, seminal vesicles, penis, and scrotum. AFIP Atlas of Tumor Pathology. American Registry of Pathology, Washington DC, United States.  11 Cubilla AL, Reuter VE, Gregoire L, Ayala G, Ocampos S, Lancaster WD and Fair W (1998). Basaloid squamous cell carcinoma: a distinctive human papilloma virus-related penile neoplasm: a report of 20 cases. Am J Surg Pathol 22(6):755-761.  12 Cubilla AL, Velazques EF, Reuter VE, Oliva E, Mihm MC, Jr. and Young RH (2000). Warty (condylomatous) squamous cell carcinoma of the penis: a report of 11 cases and proposed classification of 'verruciform' penile tumors. Am J Surg Pathol 24(4):505-512.  13 Chaux A, Tamboli P, Ayala A, Soares F, Rodriguez I, Barreto J and Cubilla AL (2010). Warty-basaloid carcinoma: clinicopathological features of a distinctive penile neoplasm. Report of 45 cases. Mod Pathol 23(6):896-904.  14 Chaux A, Soares F, Rodriguez I, Barreto J, Lezcano C, Torres J, Velazquez EF and Cubilla AL (2010). Papillary squamous cell carcinoma, not otherwise specified (NOS) of the penis: clinicopathologic features, differential diagnosis, and outcome of 35 cases. Am J Surg Pathol 34(2):223-230.  15 Chaux A, Velazquez EF, Barreto JE, Ayala E and Cubilla AL (2012). New pathologic entities in penile carcinomas: an update of the 2004 world health organization classification. Semin Diagn Pathol 29(2):59-66.  16 Cubilla AL, Velazquez EF and Young RH (2004). Pseudohyperplastic squamous cell carcinoma of the penis associated with lichen sclerosus. An extremely well-differentiated, nonverruciform neoplasm that preferentially affects the foreskin and is frequently misdiagnosed: a report of 10 cases of a distinctive clinicopathologic entity. Am J Surg Pathol 28(7):895-900.  17 Barreto JE, Velazquez EF, Ayala E, Torres J and Cubilla AL (2007). Carcinoma cuniculatum: a distinctive variant of penile squamous cell carcinoma: report of 7 cases. Am J Surg Pathol 31(1):71-75.  18 Velazquez EF, Melamed J, Barreto JE, Aguero F and Cubilla AL (2005). Sarcomatoid carcinoma of the penis: a clinicopathologic study of 15 cases. Am J Surg Pathol 29(9):1152-1158.  19 Cunha IW, Guimaraes GC, Soares F, Velazquez E, Torres JJ, Chaux A, Ayala G and Cubilla AL (2009). Pseudoglandular (adenoid, acantholytic) penile squamous cell carcinoma: a clinicopathologic and outcome study of 7 patients. Am J Surg Pathol 33(4):551-555.  20 Mentrikoski MJ, Frierson HF, Jr., Stelow EB and Cathro HP (2014). Lymphoepithelioma-like carcinoma of the penis: association with human papilloma virus infection. Histopathology 64(2):312-315.  21 Pfannl R HM, Velazquez EF, et al. (2008). Expression of p53 and p16 in differentiated and warty/basaloid penile intraepithelial neoplasia (PeIN). Lab Invest 88:807(A).  22 Cubilla AL, Ayala MT, Barreto JE, Bellasai JG and Noel JC (1996). Surface adenosquamous carcinoma of the penis. A report of three cases. Am J Surg Pathol 20(2):156-160.  23 Landeyro J, Garcia-Fontgivell JF, Condom E and Sirvent JJ (2012). Primary large-cell neuroendocrine carcinoma of the penis: association with human papilloma virus infection. Histopathology 61(2):319-320.  24 Vadmal MS, Steckel J, Teichberg S and Hajdu SI (1997). Primary neuroendocrine carcinoma of the penile urethra. J Urol 157(3):956-957.  25 Oxley JD, Corbishley C, Down L, Watkin N, Dickerson D and Wong NA (2012). Clinicopathological and molecular study of penile melanoma. J Clin Pathol 65(3):228-231. | Value list from the WHO Classification of Tumours . Pathology and genetics of urinary system and male genital organs (2016).  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).  \* Refer to the extended list in WHO classification 2016. |

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| Required | Histological grade | Single selection value list:  • Not applicable  • G1: Well differentiated  • G2: Moderately differentiated  • G3: Poorly differentiated  • Sarcomatoid areas present | Histological grade1-6  Accurate staging and grading of tumours are used to determine subsequent clinical management and follow-up. Different subtypes of penile carcinoma have been defined, which appear to be associated with different outcomes and may also therefore justify the adoption of different treatment strategies.  There is no consensus concerning grading, and the most recent World Health Organisation (WHO) classification (2016)1 recommends a three step grading system based on degree of pleomorphism and keratinisation with the overall grade determined by the worst area no matter how small the percentage of the tumour. The most recent College of American Pathologists (CAP) guidelines7 offer some outline global guidance which is applicable to usual type squamous carcinomas.  The “classical” method defines well-, moderately-well and poorly-differentiated carcinomas on the basis of the degree of cytological atypia, keratinisation, intercellular bridges and mitotic activity (see Table 1). These criteria are difficult to apply to some subtypes of penile carcinoma, for example verrucous carcinomas which are well differentiated but often show little or no keratinisation. Sarcomatoid change is a separate category, which is often combined with other tumour types and which conveys a very poor prognosis. All tumours with sarcomatoid areas should be graded as Grade 3 but this finding also needs to be noted separately as tumours with sarcomatoid areas have a worse prognosis than Grade 3 tumours generally.8  Tumours are generally graded on their worst component. Although at one time a threshold of 50% of poorly-differentiated cancer was suggested as the cut-off point most predictive of nodal metastases, it has recently been shown that any component of high-grade tumour conveys a worse prognosis so should be included in the final grade.6 Every effort should be made to assign a final grade as this is an important prognostic factor and this grade must be based on the most poorly-differentiated component, no matter how small.  References  1 World Health Organization (2016). World Health Organization (WHO) Classification of tumours. Pathology and genetics of the urinary system and male genital organs. Moch H, Humphrey PA, Reuter VE, Ulbright TM. IARC Press, Lyon, France.  2 Epstein JI CA, Humphrey PA (2011). Tumors of the prostate gland, seminal vesicles, penis, and scrotum. AFIP Atlas of Tumor Pathology. American Registry of Pathology, Washington DC, United States.  3 Velazquez EF, Melamed J, Barreto JE, Aguero F and Cubilla AL (2005). Sarcomatoid carcinoma of the penis: a clinicopathologic study of 15 cases. Am J Surg Pathol 29(9):1152-1158.  4 Slaton JW, Morgenstern N, Levy DA, Santos MW, Jr., Tamboli P, Ro JY, Ayala AG and Pettaway CA (2001). Tumor stage, vascular invasion and the percentage of poorly differentiated cancer: independent prognosticators for inguinal lymph node metastasis in penile squamous cancer. J Urol 165(4):1138-1142.  5 Velazquez EF, Ayala G, Liu H, Chaux A, Zanotti M, Torres J, Cho SI, Barreto JE, Soares F and Cubilla AL (2008). Histologic grade and perineural invasion are more important than tumor thickness as predictor of nodal metastasis in penile squamous cell carcinoma invading 5 to 10 mm. Am J Surg Pathol 32(7):974-979.  6 Chaux A, Torres J, Pfannl R, Barreto J, Rodriguez I, Velazquez EF and Cubilla AL (2009). Histologic grade in penile squamous cell carcinoma: visual estimation versus digital measurement of proportions of grades, adverse prognosis with any proportion of grade 3 and correlation of a Gleason-like system with nodal metastasis. Am J Surg Pathol 33(7):1042-1048.  7 CAP (College of American Pathologists) (2013). Protocol for the examination of specimens from patients with carcinoma of the penis. Available from: http://www.cap.org/ShowProperty?nodePath=/UCMCon/ContributionFolders/WebContent/pdf/penis-12protocol.pdf (Accessed 1st March 2016).  8 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York. |  |
| Required | Microscopic maximum tumour dimensions | Numeric:  • Maximum tumour width: \_\_\_ mm  • Maximum tumour thickness: \_\_\_ mm  • Cannot be assessed  • Not applicable | For evidence see  **MACROSCOPIC MAXIMUM TUMOUR DIMENSIONS.** | Tumour dimensions have to be determined through a combination of macroscopic and microscopic assessment, particularly if tumours are very large. |
| Required | Extent of invasion | Multi selection value list (select all that apply):  • Primary tumours of the penis and foreskin  o Cannot be assessed\*  OR  o Subepithelial/lamina propria invasion by tumour  o Invasion of corpus spongiosum of glans  o Invasion of corpus cavernosum  o Invasion of the penile urethra  o Invasion of adjacent structures, specify  • Primary tumours of the distal urethra  o Cannot be assessed\*  OR  o Subepithelial/lamina propria invasion by tumour  o Invasion of corpus spongiosum  o Invasion of corpus cavernosum  o Invasion of adjacent structures, specify | Extent of invasion1-4  Tumours invading deeper into penile anatomical levels are usually associated with a higher risk of nodal involvement. There is also a correlation between deeper infiltration and higher histological grade, although some exceptions do occur. Tumours invading corpus cavernosum are at higher risk for presenting nodal metastases than those invading only corpus spongiosum and although these are both staged as T2 in Union for International Cancer Control (UICC)1 and American Joint Committee on Cancer (AJCC)5 TNM7, TNM86 now stages corpus cavernosum invasion as T3 irrespective of urethral involvement. The tunica albuginea , which separates corpus spongiosum from corpus cavernosum is considered part of the corpora cavernosa.5  The anatomy of the penis is complex and difficulties often arise in distinguishing levels of invasion. The distinction between lamina propria and corpus spongiosum is made on the basis of vascularity. Vessels within erectile tissue are more angular and thin-walled with intervening fibromuscular tissue than those within the lamina propria, which are more variably sized and separated by loose connective tissue.  References  1 International Union against Cancer (UICC) (2009). TNM Classification of Malignant Tumours (7th edition). Sobin L, Gospodarowicz M and Wittekind C (Eds). Wiley-Blackwell, Chichester, UK and Hoboken, New Jersey.  2 Leijte JA, Gallee M, Antonini N and Horenblas S (2008). Evaluation of current TNM classification of penile carcinoma. J Urol 180(3):933-938; discussion 938.  3 Chaux A, Caballero C, Soares F, Guimaraes GC, Cunha IW, Reuter V, Barreto J, Rodriguez I and Cubilla AL (2009). The prognostic index: a useful pathologic guide for prediction of nodal metastases and survival in penile squamous cell carcinoma. Am J Surg Pathol 33(7):1049-1057.  4 Chaux A and Cubilla AL (2012). Stratification systems as prognostic tools for defining risk of lymph node metastasis in penile squamous cell carcinomas. Semin Diagn Pathol 29(2):83-89.  5 Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL and Trotti A (eds) (2010). AJCC Cancer Staging Manual 7th ed., New York, NY.: Springer.  6 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York. | \*Only applicable to biopsy specimens and resection specimens with tumours at the margins. |
| Required | Lymphovascular invasion | Single selection value list:  • Not identified  • Present  • Indeterminate | Lymphovascular invasion1,2  Vascular invasion, lymphatic or venous, adversely affects prognosis of penile cancer. The TNM staging classification in the seventh edition of the AJCC Cancer Staging Manual3 subdivides T1 tumours into T1a and T1b based on the absence or presence of lymphovascular invasion (LVI) or poorly-differentiated tumours. This is also included in the 8th edition (TNM8)4 which also includes the additional stratifier of perineural invasion.  Embolic involvement of lymphatic vascular spaces occurs usually near the invasive tumour front, but it may also be found at a certain distance from the primary tumour in anatomical areas such as the lamina propria, penile fascia, and especially in the subepithelial connective tissues surrounding penile urethra. Venous invasion indicates a more advanced stage of the disease and is related to the compromise of the specialized erectile venous structures of corpora spongiosa and cavernosa.  Vascular invasion may be difficult to assess particularly in small biopsies and immunohistochemistry with vascular markers may be of assistance in some cases.  References  1 Slaton JW, Morgenstern N, Levy DA, Santos MW, Jr., Tamboli P, Ro JY, Ayala AG and Pettaway CA (2001). Tumor stage, vascular invasion and the percentage of poorly differentiated cancer: independent prognosticators for inguinal lymph node metastasis in penile squamous cancer. J Urol 165(4):1138-1142.  2 Ficarra V, Zattoni F, Cunico SC, Galetti TP, Luciani L, Fandella A, Guazzieri S, Maruzzi D, Sava T, Siracusano S, Pilloni S, Tasca A, Martignoni G, Gardiman M, Tardanico R, Zambolin T, Cisternino A and Artibani W (2005). Lymphatic and vascular embolizations are independent predictive variables of inguinal lymph node involvement in patients with squamous cell carcinoma of the penis: Gruppo Uro-Oncologico del Nord Est (Northeast Uro-Oncological Group) Penile Cancer data base data. Cancer 103(12):2507-2516.  3 Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL and Trotti A (eds) (2010). AJCC Cancer Staging Manual 7th ed., New York, NY.: Springer.  4 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York. |  |
| Required | Perineural invasion | Single selection value list:  • Not identified  • Present  • Indeterminate | Perineural invasion1-3  Risk groups stratification systems are available to predict the likelihood of inguinal nodal involvement and therapeutic planning and are based on a combination of histological grade and pT stage. Strongest predictive power is given by the combination of histological grade, deepest anatomical level of infiltration, and presence of perineural invasion. These factors are used for constructing the Prognostic Index. TNM8 now includes perineural invasion as a stratifier between T1a and T1b tumours in addition to lymphovascular invasion.4  Perineural invasion may be difficult to assess, especially in small and/or superficial biopsies. Immunohistochemistry with neural markers may be helpful in some circumstances.  References  1 Velazquez EF, Ayala G, Liu H, Chaux A, Zanotti M, Torres J, Cho SI, Barreto JE, Soares F and Cubilla AL (2008). Histologic grade and perineural invasion are more important than tumor thickness as predictor of nodal metastasis in penile squamous cell carcinoma invading 5 to 10 mm. Am J Surg Pathol 32(7):974-979.  2 Chaux A, Caballero C, Soares F, Guimaraes GC, Cunha IW, Reuter V, Barreto J, Rodriguez I and Cubilla AL (2009). The prognostic index: a useful pathologic guide for prediction of nodal metastases and survival in penile squamous cell carcinoma. Am J Surg Pathol 33(7):1049-1057.  3 Chaux A and Cubilla AL (2012). Stratification systems as prognostic tools for defining risk of lymph node metastasis in penile squamous cell carcinomas. Semin Diagn Pathol 29(2):83-89.  4 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York. |  |
| Recommended | Associated penile intraepithelial neoplasia | Single selection value list:  • Not identified  • Present  o Undifferentiated  o Differentiated  • Indeterminate | Associated penile intraepithelial neoplasia (PeIN)1-7  The pathological nomenclature and patterns of different forms of preinvasive lesions of the penis has been radically modified over the last few years with the abandonment of clinical terms such as Erythroplasia of Queyrat and Bowen’s disease and the adoption of the encompassing term Penile Intraepithelial Neoplasia (PeIN) in pathological reports.  The new World Health Organisation classification of PeIN distinguishes three groups: 1. Non HPV related (differentiated or simplex), 2. HPV related (undifferentiated) PeIN (basaloid, warty and warty-basaloid) and 3. Others (pleomorphic, spindle, clear cell, pagetoid).8 Undifferentiated HPV related PeIN shows full thickness warty and/or basaloid features (previously designated severe dysplasia/carcinoma in situ). Differentiated PeIN usually involves only the basal layer and is associated with architectural atypia and aberrant keratinisation with features similar to that seen in precancerous lesions of the vulva. Undifferentiated PeIN is associated with p16 positivity and warty/basaloid invasive tumours but differentiated PeIN is associated with lichen sclerosis (balanitis xerotica obliterans), more commonly seen with verrucous and pseudohyperplastic tumours, and is usually p16 negative. It should also be noted that PeIN of any type is often multifocal.  The presence and subtype of PeIN should be reported together with its margin status independent of associated invasive tumour. The splitting of PeIN into subgrades (for example I-III or low-grade/high-grade) is not recommended by the authors. Written reports should indicate the subtype and extent of PeIN and whether or not there is margin involvement.  Precancerous lesions identical to differentiated and undifferentiated PeIN are seen in the  distal penile urethra but there is no guidance on how to report them. Rather than designating these  as carcinoma in situ or severe dysplasia, it may be advisable to also use the term PeIN in  this context.  A potential problem arises when there are cytological abnormalities not thought to be severe  enough to be designated as PeIN of either subtype. Then a category such as ‘atypia falling  short of PeIN’ with a recommendation for follow up may be used, to avoid over treatment.  It is not necessary to report PeIN using the full dataset if it is the only abnormality present without invasive carcinoma.  Immunohistochemistry with p16 may be of help in subclassifying PeIN but is not regarded as mandatory. It may also be of use in identifying high-risk HPV in atypical condylomas.  References  1 Velazquez EF, Chaux A and Cubilla AL (2012). Histologic classification of penile intraepithelial neoplasia. Semin Diagn Pathol 29(2):96-102.  2 Chaux A, Velazquez EF, Amin A, Soskin A, Pfannl R, Rodriguez IM, Barreto JE, Lezcano C, Ayala G, Netto GJ and Cubilla AL (2012). Distribution and characterization of subtypes of penile intraepithelial neoplasia and their association with invasive carcinomas: a pathological study of 139 lesions in 121 patients. Hum Pathol 43(7):1020-1027.  3 Velazquez EF, Soskin A, Bock A, Codas R, Cai G, Barreto JE and Cubilla AL (2005). Epithelial abnormalities and precancerous lesions of anterior urethra in patients with penile carcinoma: a report of 89 cases. Mod Pathol 18(7):917-923.  4 Corbishley CM, Rajab RM and Watkin NA (2015). Clinicopathological features of carcinoma of the distal penile urethra. Semin Diagn Pathol 32(3):238-244.  5 Chaux A, Pfannl R, Lloveras B, Alejo M, Clavero O, Lezcano C, Munoz N, de Sanjose S, Bosch X, Hernandez-Perez M, Velazquez EF and Cubilla AL (2010). Distinctive association of p16INK4a overexpression with penile intraepithelial neoplasia depicting warty and/or basaloid features: a study of 141 cases evaluating a new nomenclature. Am J Surg Pathol 34(3):385-392.  6 Oparka R HC (2013). Pathology of the Vulva and Vagina. Precursors of vulvovaginal squamous cell carcinoma. L B. Springer.  7 Slaton JW, Morgenstern N, Levy DA, Santos MW, Jr., Tamboli P, Ro JY, Ayala AG and Pettaway CA (2001). Tumor stage, vascular invasion and the percentage of poorly differentiated cancer: independent prognosticators for inguinal lymph node metastasis in penile squamous cancer. J Urol 165(4):1138-1142.  8 World Health Organization (2016). World Health Organization (WHO) Classification of tumours. Pathology and genetics of the urinary system and male genital organs. Moch H, Humphrey PA, Reuter VE, Ulbright TM. IARC Press, Lyon, France. |  |
| Required | Margin status | Urethral margin (primary tumours of the penis and foreskin (resections and excision biopsy only))  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by PeIN only  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Proximal urethral margin (primary tumours of the urethra only)  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by PeIN only  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Distal urethral margin (primary tumours of the urethra only)  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by PeIN only  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Peri-urethral tissues  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Corpus cavernosum  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Circumferential shaft margin  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed   > 5mm  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR  Peripheral cutaneous margin  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by PeIN only  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Peripheral glans margin  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by PeIN only  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Deep soft tissue margins (NOS) (other than periurethral tissue and corpus cavernosum)  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm  Other margin, specify  Multi selection value list (select all that apply)/numeric  • Not applicable  • Cannot be assessed  • Involved by PeIN only  • Involved by invasive carcinoma  • Not involved  o Distance to invasive tumour   \_\_\_\_\_mm OR   > 5mm | Margin status1,2  Penile preserving techniques have led to closer surgical tumour resection margins and there is evidence that this does not significantly compromise local recurrence rates if tumour cells are not present at the margin itself. Positive margins must be recorded by site and microscopic distance of tumour from close margins (5 mm or less) recorded in mm. Microscopic margin positivity may be identified unexpectedly in tumours that infiltrate widely without creating a mass effect. The presence of microscopic involvement of surgical margins, however, has implications for audit of pre-operative staging and/or surgical technique. Actual measurement of linear extent of individual involved margins is a non core item but is valued by surgeons in assessing their techniques.  Staging in the presence of positive margins needs to be undertaken but made clear to clinicians. The term ‘at least’, as in pT2 at least, may be used to indicate a positive margin. It is not helpful to clinicians not to stage if margins are positive.  The deep central soft tissue margin is defined as areas of intervening tissue not identified as periurethral tissue, corpus cavernosum or circumferential shaft margins or may be used if the specific site of the deep margin is indeterminate.  Margins of resection for penile specimens (except circumcision)  Urethral  Periurethral tissues including lamina propria and corpus spongiosum  Corpus cavernosum  Circumferential margins of bare penile shaft  Peripheral skin  Deep central soft tissue margin (other than periurethral tissue, corpus cavernosum or circumferential shaft)  Margins of resection of circumcision specimens  Coronal sulcus/glans margin  Peripheral cutaneous margin  Deep central soft tissue margin  References  1 Minhas S, Kayes O, Hegarty P, Kumar P, Freeman A and Ralph D (2005). What surgical resection margins are required to achieve oncological control in men with primary penile cancer? BJU Int 96(7):1040-1043.  2 Velazquez EF, Soskin A, Bock A, Codas R, Barreto JE and Cubilla AL (2004). Positive resection margins in partial penectomies: sites of involvement and proposal of local routes of spread of penile squamous cell carcinoma. Am J Surg Pathol 28(3):384-389. |  |
| Required | Lymph node status | Multi selection value list (select all that apply)/numeric  INGUINAL NODES - SENTINEL  RIGHT  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified  LEFT  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified  INGUINAL NODES - NON SENTINEL  RIGHT  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified  LEFT  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified  PELVIC NODES  RIGHT  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified  LEFT  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified  OTHER NODES (specify laterality and site)  • Not submitted  o Number of lymph nodes examined \_\_\_\_\_  • Not involved  • Isolated tumour cells only  • Involved  o Number of positive lymph nodes \_\_\_\_\_\_OR  o Number cannot be determined  o Maximum dimension of largest deposit \_\_\_mm  o Extracapsular spread  • Present  • Not identified | Lymph node status1-8  Nodal involvement is a recognised predictor of poor prognosis. In node positive disease, the number of positive nodes, the presence of extracapsular spread (ECS) and the level of nodal involvement (pelvic versus inguinal) have been shown to influence survival by multivariate analysis and this is reflected in TNM71,9 and TNM810 which classify any pelvic lymph node involvement or extracapsular extension of any regional lymph node (inguinal or pelvic) as pN3 in the penile but not in the urethral TNM. However in penile TNM810 the number of nodes which stratifies the staging between N1 and N2 is two or more unilateral nodes rather than one or more in TNM7.1,9 The extent of inguinal lymph node involvement including number of nodes involved and presence or absence of ECS is used to determine the need for pelvic node sampling or excision.  The size of the largest nodal tumour deposit (not the lymph node size) must also be recorded as there is evidence that this may affect prognosis in penile cancer. Both TNM7 and TNM8 classify very small amounts of tumour as micrometastases (up to 0.2 mm)1,9-11 and isolated tumour cells as N0 (i+).10 However there is no evidence for a prognostic cut-off point for lymph node metastasis size in penile cancer so it is recommended in that maximum dimension of largest tumour deposit is recorded and tumour deposits over 0.2 mm staged as N1.  For urethral cancer in TNM71,9 the size of metastasis in a single regional node, if greater than 2 cm, stratifies between N1 and N2 nodes or if there are multiple nodes involved, but in TNM810 there is no metastasis size specified and the only stratifier is between single and multiple regional nodes.  Tumour presence or absence, size of tumour deposit and presence or absence of ECS are reported separately for each individual node site in both nodal resections and sentinel nodes. Occasionally individual tumour cells are identified in the peripheral sinus. The significance of these is uncertain but they should be described within reports. Immunohistochemistry is essential for the assessment of sentinel lymph nodes. Dynamic sentinel node biopsy, using either the blue dye technique or lymphoscintigraphy, refers to the intraoperative identification of the first node draining the tumour. It relies on the assumption that lymphatic spread is a stepwise process, so that, if the sentinel node is negative, further nodal dissection would yield negative results. This technique may be used in some centres for patients with no clinical signs of nodal involvement.  Although the N categories differ for P(p)enile and U(u)rethral primary tumours it is recommended that data items as specified in this section are recorded for tumours of both these primary sites as tumours of the distal, as opposed to proximal, urethra appear to spread in the same way to local lymph nodes as do those of the penis.  References  1 International Union against Cancer (UICC) (2009). TNM Classification of Malignant Tumours (7th edition). Sobin L, Gospodarowicz M and Wittekind C (Eds). Wiley-Blackwell, Chichester, UK and Hoboken, New Jersey.  2 Hakenberg OW, Comperat EM, Minhas S, Necchi A, Protzel C and Watkin N (2015). EAU guidelines on penile cancer: 2014 update. Eur Urol 67(1):142-150.  3 Svatek RS, Munsell M, Kincaid JM, Hegarty P, Slaton JW, Busby JE, Gaston KE, Spiess PE, Pagliaro LC, Tamboli P and Pettaway CA (2009). Association between lymph node density and disease specific survival in patients with penile cancer. J Urol 182(6):2721-2727.  4 Graafland NM, van Boven HH, van Werkhoven E, Moonen LM and Horenblas S (2010). Prognostic significance of extranodal extension in patients with pathological node positive penile carcinoma. J Urol 184(4):1347-1353.  5 Lughezzani G, Catanzaro M, Torelli T, Piva L, Biasoni D, Stagni S, Crestani A, Guttilla A, Raggi D, Giannatempo P, Necchi A, Pizzocaro G, Colecchia M, Salvioni R and Nicolai N (2014). The relationship between characteristics of inguinal lymph nodes and pelvic lymph node involvement in penile squamous cell carcinoma: a single institution experience. J Urol 191(4):977-982.  6 Horenblas S (2012). Sentinel lymph node biopsy in penile carcinoma. Semin Diagn Pathol 29(2):90-95.  7 Lam W, Alnajjar HM, La-Touche S, Perry M, Sharma D, Corbishley C, Pilcher J, Heenan S and Watkin N (2013). Dynamic sentinel lymph node biopsy in patients with invasive squamous cell carcinoma of the penis: a prospective study of the long-term outcome of 500 inguinal basins assessed at a single institution. Eur Urol 63(4):657-663.  8 Corbishley CM, Rajab RM and Watkin NA (2015). Clinicopathological features of carcinoma of the distal penile urethra. Semin Diagn Pathol 32(3):238-244.  9 Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL and Trotti A (eds) (2010). AJCC Cancer Staging Manual 7th ed., New York, NY.: Springer.  10 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York.  11 Brierley JD, Gospodarowicz MK, Wittekind C (eds) (2016). UICC TNM Classification of Malignant Tumours, 8th Edition. Wiley-Blackwell. |  |
| Required | Pathological Staging (AJCC TNM 8th edition)  TNM descriptors | Choose if applicable:  • m - multiple primary tumours  • r - recurrent  • y - post-therapy | This dataset includes the American Joint Committee on Cancer (AJCC) TNM 8th edition1 definitions. The implementation of AJCC TNM 8th edition has been deferred until January 2018 in some jurisdictions. Union for International Cancer Control (UICC) 7th edition2 or AJCC 7th edition3 may be useful in the interim. If TNM 7th edition is used the following points should be noted:  1) Perineural invasion is now included as a stratifier between T1a and T1b tumours of the penis in addition to lymphovascular invasion and high grade in TNM8.  2) The division between T2 and T3 in TNM8 of the penis is entirely dependent on whether there corpus spongiosum or corpus cavernosum invasion irrespective of urethral involvement. This is the most significant change between TNM7 and TNM8.  3) The number of unilateral nodes to indicate N2 rather than N1 of the penis has increased to 3 from 2.  4) The size of metastasis is no longer used as a stratifier between N1 and N2 in unilateral regional nodes in urethral cancer.  5) The use of TX is to be avoided if at all possible and MX is not to be used.  6) Pathological staging should not be reported if the specimen submitted is insufficient for definitive staging. This may occur with biopsies or other specimens where depth of invasion or the required anatomical features cannot be discerned/assessed.  7) Staging in the presence of positive margins needs to be undertaken but made clear to clinicians. The term ‘at least’, as in pT2 at least, may be used to indicate a positive margin. It is not helpful to clinicians omit the stage if margins are positive.  By convention, the designation T refers to a primary tumour that has not been previously treated. The symbol p refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumour or a biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesion. Pathologic staging is usually performed after surgical resection of the primary tumour.  Additional Descriptor  The m suffix indicates the presence of multiple primary tumours and is recorded in parentheses, e.g.  pTa(m)N0.    Tumours of the Penis and Foreskin (TNM7 and TNM8)2,4-7  Primary Tumour (T)  Changes between TNM7 and TNM8 are indicated and/or highlighted in bold  TX Primary tumour cannot be assessed.  T0 No evidence of primary tumour.  Tis Carcinoma in situ (Penile intraepithelial neoplasia [PeIN]).  Ta TNM7\* Non invasive verrucous carcinoma.  TNM8\* Non invasive localised squamous cell carcinoma  T1 TNM7 Tumour invades subepithelial connective tissue  TNM8 Glans: Tumour invades lamina propria  Foreskin: Tumour invades dermis, lamina propria or dartos fascia  Shaft: Tumour invades connective tissue between epidermis and corpora regardless of location  All sites with or without LVI or perineural invasion and is or is not high grade  T1a \*\*Tumour invades lamina propria or subepithelial connective tissue and is without lymphovascular or perineural invasion and is not high grade (i.e. grade 3 or sarcomatoid)  T1b \*\* Tumour invades lamina propria or subepithelial connective tissue and exhibits lymphovascular or perineural invasion and or is high grade (i.e. grade 3 or sarcomatoid)  T2 TNM7 Tumour invades corpus spongiosum or cavernosum.  TNM8 Tumour invades into corpus spongiosum (either glans or ventral shaft) with or without urethral invasion  T3 TNM7 Tumour invades urethra.  TNM8 T3 Tumour invades into corpora cavernosum (including tunica albuginea) with or without urethral invasion  T4 Tumour invades other adjacent structures.  \*The dataset authors’ view is that the category of non invasive verrucous carcinoma in TNM7 and non invasive localised squamous cell carcinoma in AJCC TNM8 is to be avoided as it is not evidence based.  \*\* AJCC TNM8 introduces Perineural invasion into the pT1 category but UICC and AJCC TNM7 do not include perineural invasion as a stratifier in the pT1 category.  Regional Lymph Nodes (N)  pNX Lymph node metastasis cannot be established.  pN0 No lymph node metastasis.  pN1 TNM7 Metastasis in a single inguinal lymph node.  TNM8 Two or more inguinal metastases without extranodal extension (ENE)  pN2 TNM7 Metastases in multiple or bilateral inguinal lymph nodes.  TMN8 Three or more unilateral inguinal metastases or bilateral metastases  pN3 ENE of lymph node metastases or pelvic lymph node metastases.    Distant Metastasis (M)  M0 No distant metastasis (clinical category only).  M1 Distant metastasis present.  M1 includes lymph node metastasis outside of the true pelvis in addition to visceral or bone sites.  Accurate staging and grading of tumours are used to determine subsequent clinical management and follow-up.  The anatomy of the penis is complex and difficulties often arise in distinguishing levels of invasion. The distinction between lamina propria and corpus spongiosum is made on the basis of vascularity. Vessels within erectile tissue are more angular and thin-walled with intervening fibromuscular tissue than those within the lamina propria which are more variably sized and separated by loose connective tissue.  Although there is a category of non-invasive verrucous carcinoma in the primary tumour classifications (Ta) in TNM7, the criteria for the diagnosis of this entity and its distinction from verrucous hyperplasia are unclear to the authors of this dataset and use of this category is not recommended. Although verrucous carcinomas have a pushing rather than infiltrative margin, they are nevertheless invasive. Invasion is often only superficial but more deeply invasive tumours may be observed. Non invasive localised tumours of the penis of any subtype are exceptionally rare in the authors experience.  Staging of pT1 is subdivided in TN 7 into pT1a for low-risk tumours and pT1b for high-risk tumours depending on the absence or presence of high-grade tumour and/or LVI. TNM8 also includes perineural invasion as a stratifier between T1a and T1b. The number of unilateral nodes needed upstage from pN1 to N2 has increased from two to three in TNM8. Metastatic tumour in regional lymph nodes with extranodal spread is categorised as pN3.  It was initially proposed that the pT2 primary tumour classification be subdivided to distinguish between invasion into the spongiosum and cavernosum, as some reports show that risk of metastases in increased in patients with invasion of the cavernosa. The Royal College of Pathologists (RCPath) dataset published in 2015 recommend substaging of T2 penile tumours into T2a (corpus spongiosum invasion) and T2b (corpus cavernosum invasion) as this is evidence based.7 TNM8 now recommends that involvement of the corpus spongiosum is classified as T2 and involvement of corpora cavernosa is T3 irrespective of urethral involvement. The RCPath dataset is also being updated in 2017 to reflect TNM8.  In the case of multiple tumours, the tumour with the highest T category should be classified and the multiplicity or number of tumours should be indicated in parentheses, e.g. pT2 (m) or pT2.  Use of the category TX is to be avoided and the designation e.g. ‘T (numerical value) at least’ is preferable if full staging is not possible because of the nature of the specimen (e.g. small incision biopsies) or the presence of positive margins.  If deep structures are not sampled and/or the invasive tumour extends to the margins of excision staging should still be attempted but designated as ‘pT1 at least’. The designation of pTX (unstageable) even in small biopsies should be avoided as far as possible as it is clinically unhelpful.  The category M0 should not be used in pathological staging. The term MX is no longer in use.  Tumours of the Distal Penile Urethra (TNM7 and TNM8)2,8  It should be noted that the N categories differ considerably between urethral and penile tumours  and extranodal spread is not a feature of the urethral N staging (i.e. there is no N3 category). There are only minimal changes between TNM7 and TNM8.  Primary Tumour (T) of the Male Penile Urethra  TX Primary tumour cannot be assessed.  T0 No evidence of primary tumour.  Ta Non-invasive papillary carcinoma\*.  Tis Carcinoma in situ\*\*  T1 Tumour invades subepithelial connective tissue.  T2 Tumour invades any of the following: corpus spongiosum, periurethral muscle.  T3 Tumour invades any of the following: corpus cavernosum.  T4 Tumour invades other adjacent organs.  \* The dataset authors’ view is that the use of this category for non invasive squamous localised squamous cell carcinoma is to be avoided as it is not evidence based. This category includes non-invasive papillary urothelial carcinomas but these are very rare in the distal urethra.  \*\* The dataset authors recommend the use of the same terminology (PeIN) for squamous  precancerous lesions of the distal urethra as in the penis.  Regional Lymph Nodes (N)  NX Regional lymph nodes cannot be assessed.  N0 No regional lymph node metastasis.  N1 TNM7 Metastasis measuring up to 2 cm or less in greatest dimension in a single lymph node.  TNM8 Single regional lymph node metastasis  N2 TNM7 Metastasis more than 2 cm in greatest dimension in a single node, or metastases of any  size in multiple nodes.  TNM8 Multiple regional lymph node metastases  There are no different cN or pN categories in the Urethral tumour TNM which contrasts with the penile TNM.  Distant Metastasis (M)  M0 No distant metastasis\*  M1 Distant metastasis.  \* This is a clinical category, not to be used in pathological reporting.  References  1 Amin MB E, S., Greene, F.L., Byrd, D.R., Brookland, R.K., Washington, M.K., Gershenwald, J.E., Compton, C.C., Hess, K.R., Sullivan, D.C., Jessup, J.M., Brierley, J.D., Gaspar, L.E., Schilsky, R.L., Balch, C.M., Winchester, D.P., Asare, E.A., Madera, M., Gress, D.M., Meyer, L.R. (Eds.) (2017). AJCC Cancer Staging Manual 8th ed. Springer, New York.  2 International Union against Cancer (UICC) (2009). TNM Classification of Malignant Tumours (7th edition). Sobin L, Gospodarowicz M and Wittekind C (Eds). Wiley-Blackwell, Chichester, UK and Hoboken, New Jersey.  3 Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL and Trotti A (eds) (2010). AJCC Cancer Staging Manual 7th ed., New York, NY.: Springer.  4 Leijte JA, Gallee M, Antonini N and Horenblas S (2008). Evaluation of current TNM classification of penile carcinoma. J Urol 180(3):933-938; discussion 938.  5 Chaux A, Caballero C, Soares F, Guimaraes GC, Cunha IW, Reuter V, Barreto J, Rodriguez I and Cubilla AL (2009). The prognostic index: a useful pathologic guide for prediction of nodal metastases and survival in penile squamous cell carcinoma. Am J Surg Pathol 33(7):1049-1057.  6 Chaux A and Cubilla AL (2012). Stratification systems as prognostic tools for defining risk of lymph node metastasis in penile squamous cell carcinomas. Semin Diagn Pathol 29(2):83-89.  7 RCPath (Royal College of Pathologists) (2015). Dataset for penile and distal urethral cancer histopathology reports. Available from: https://www.rcpath.org/resourceLibrary/dataset-for-penile-and-distal-urethral-cancer-histopathology-reports.html (Accessed 1st March 2016)  8 Corbishley CM, Rajab RM and Watkin NA (2015). Clinicopathological features of carcinoma of the distal penile urethra. Semin Diagn Pathol 32(3):238-244. | Note that permission to publish the TNM cancer staging tables may be needed in your implementation. It is advisable to check. |
| Required | Primary tumour (T) | TNM AJCC 8th edition for Penis and foreskin |  |  |
| Required | Regional lymph nodes (N) | TNM AJCC 8th edition for Penis and foreskin |  |  |
| Required | Primary tumour (T) | TNM AJCC 8th edition for Penile urethra |  |  |
| Required | Regional lymph nodes (N) | TNM AJCC 8th edition for Penile urethra |  |  |