The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for the histopathological reporting of carcinomas of the salivary glands

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Comments	This document replaces the 1st edition of the *Dataset for histopathology reporting of salivary gland neoplasms,* published in November 2013. In accordance with the College's pre-publications policy, this document was on the Royal College of Pathologists' website for an abridged consultation from 15 May to 12 June. Responses and authors' comments are available to view on request. **Dr Brian Rous** **Clinical Lead for Guideline Review**

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Foreword

The cancer datasets published by the Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient. Pathologists should be able to justify any variation.

Each dataset contains core data items (see Appendices C and D) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD) v9.0 in England. Core data items are those that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 95% of reports on cancer resections should record a full set of core data items. Non-core data items are also described. These may be included, with appropriate patient consent, to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholders were contacted to consult on this document:

- the British Society for Oral and Maxillofacial Pathology
- the British Association of Head and Neck Oncologists
- ENT UK
- the British Association of Oral and Maxillofacial Surgeons
- the UK and Ireland Association of Cancer Registries.

Comments from specialist and general histopathologists on the draft document that was published on the Royal College of Pathologists' website were considered as part of the review of the dataset.

The information used by the authors to develop this dataset was obtained by undertaking a search of the PubMed database from January 2010 to September 2023 (inclusive) for relevant primary research evidence and systematic reviews on salivary gland malignancies, either specifically in the oral cavity (minor glands) or generally in the head and neck (major glands) where these subsites can be separately identified. The key search term was salivary gland with additional terms (alone or in combination) including tumour, cancer, pathology, sampling, molecular, genomics, grade, size, stage, perineural invasion, lymphovascular invasion, site, multifocality, capsular invasion, metastasis, prognosis and survival. In addition, abstracts from selected conference proceedings from the American Society of Clinical Oncology (ASCO) were screened. The recommendations are in line with those of other national pathology organisations (College of American Pathologists, The Royal College of Pathologists of Australasia) and the ENT UK Consensus document for the management of patients with head and neck malignancies (www.entuk.org/publications). They incorporate the core data items and commentary from the International Collaboration on Cancer Reporting (ICCR).[1] The level of evidence for the recommendations has been summarised according to modified SIGN guidance (see Appendix E) and the grade of evidence is indicated in the text. No major conflicts in the evidence have been identified and minor discrepancies between studies have been resolved by expert consensus. Gaps in the evidence were identified by College members via feedback received during consultation.

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset.

All cancer datasets are formally revised every 3 years. However, each year, the College will ask the author of the dataset, in conjunction with the relevant subspecialty adviser to the College, to consider whether or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required. This includes all major revisions to core data items, apart from changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies, which will be implemented without further consultation. If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken whereby a short note of the proposed changes will be placed on the College website for 2 weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated

into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Professional Guidelines team, Working Group on Cancer Services and Lay Advisory Group and was placed on the College website for consultation with the membership from 15 May to 12 June 2024. All comments received from the above groups and the membership were addressed by the author to the satisfaction of the Chair of the Working Group and the Clinical Lead for Guideline Review.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Professional Guidelines team and are available on request. The authors have declared that they have no conflicts of interest.

1 Introduction

The dataset has been developed for the reporting of biopsy and resection specimens of the salivary glands. The protocol applies to all invasive carcinomas of the salivary glands, including the parotid, submandibular, sublingual and minor salivary glands. Lymphomas and sarcomas are not included. Neck dissections and nodal excisions are dealt with in a separate dataset, which should be used in conjunction with this dataset, where applicable.

The primary purpose of this document is twofold:

- to define the set of data necessary for the uniform recording and staging of the core pathological features in cancers of the salivary glands
- to describe its application in sufficient detail and clarity so that pathology reports from different departments will contain equivalent information, allowing comparison of clinical practice and outcomes.

Optimal reporting of specimens from the head and neck area requires a partnership between the pathologist and surgeon/oncologist. The surgeon can help the pathologist to provide the information necessary for patient management by the appropriate handling and labelling of the specimen in the operating theatre. The regular discussion of cases at multidisciplinary team (MDT) (and other clinicopathological) meetings and correlation with pre-operative imaging studies are important in maintaining and developing this partnership and providing optimal care to patients.[1]

The core pathological data are summarised as proformas, which may be used as the main reporting format or may be combined with free text as required. The lymph node dataset is common to all head and neck sites. Individual centres may wish to expand the detail in some sections, e.g. for sites and subsites, to facilitate the recording of data for particular tumour types.

The guidelines within this dataset should be implemented for the following reason:

- certain features of salivary gland carcinomas (type, size and grade of the primary carcinoma, the pattern of invasion and proximity of carcinoma to resection margins) have been shown to be related to clinical outcomes.[2–11]

These features may, therefore, be important:

- in deciding on the most appropriate treatment for particular patients, including the extent of surgery and the use and choice of adjuvant radiotherapy, chemotherapy or targeted therapies[12–14]
- in monitoring changing patterns of disease, particularly by cancer registries
- to allow correlation of resection specimens with preoperative imaging
- to allow the accurate and equitable comparison of surgeons in different surgical units to identify good surgical and pathological practice
- to aid the selection and comparison of patients in clinical trials.

1.1 Design of this protocol

The RCPath recognises the authority of internationally accepted guidance documents (World Health Organisation [WHO], American Joint Committee on Cancer [AJCC]/Union for International Cancer Control [UICC] TNM and ICCR) and, to promote consistent reporting practice, adopts the recommendations of these organisations. This structured reporting protocol has been developed using the framework and data items specified in the ICCR dataset on cancers of the salivary gland (published in 2018).[15] The current protocol includes all of the ICCR cancer dataset elements, as well as additional information, elements and commentary. Core ICCR references have been updated to include relevant new information from 2018 to April 2023.

ICCR dataset elements for these cancers have been included verbatim and are indicated by the blue ICCR logo. ICCR core elements are mandatory, form part of the COSD data and are, therefore, represented as standards in this document. ICCR (and RCPath) non-

core elements are recommended and may be included as guidelines or used routinely according to local practice.

1.2 Target users and health benefits of this guideline

This dataset is primarily intended for the use of consultant and trainee pathologists when reporting biopsies and resection specimens of salivary gland malignancies of the head and neck region, and it has been developed to aid a consistent approach to the reporting of these cancers. Surgeons and oncologists may refer to the dataset when interpreting histopathology reports, and core data should be available at MDT meetings to inform discussions on the management of head and neck cancer patients. The core data items are incorporated into the COSD data and are collected for epidemiological analysis by cancer registries on behalf of the National Cancer Intelligence Network.

Salivary gland tumours are diagnostically challenging, have overlapping features (even between benign and malignant tumours) and require significant experience and exposure to the analysis of these lesions. Therefore, formal double reporting by a specialist oral and maxillofacial or head and neck pathologist (who participates in the national head and neck EQA scheme and also has expertise and proficiency in salivary gland tumour diagnosis) should be considered for all lesions to ensure correct diagnosis and optimal patient outcomes.

2 Clinical information required for the diagnosis of carcinomas of the salivary glands

The request form should include patient demographic data, which includes:

- patient name
- date of birth
- sex
- hospital and NHS number (where appropriate) or other patient identification number.

Clinical information should include:

- duration of symptoms
- details of the surgery and whether the intent is curative or palliative

- details of previous pathology reports
- core clinical data items (see section 5)
- clinical/radiological TNM stage (for correlation with pathological findings)
- history of previous biopsy (fine needle aspiration [FNA], core, etc.), resection, radiotherapy or chemotherapy, as this may influence the interpretation of the histological changes and should prompt a comment on the extent of any response to treatment.

The request form should present the opportunity for surgeons to provide annotated diagrams of specimens, either as freehand drawings or on standard diagrams (electronic request forms may not allow this in certain situations). Copies of reports that are sent to the cancer registries should include the patient's address, if possible.

The following should also be recorded:

- the name of the clinician requesting the investigation
- the date and time of the operation
- the date and time at which the specimen was fixed
- the date and time the specimen was received in the laboratory.

Details of the legal basis of data sharing with the cancer registries can be accessed here: https://digital.nhs.uk/services/national-disease-registration-service.

3 Receipt and preparation of specimens before dissection

Fixation should be in neutral buffered formalin for 24–48 hours in a container of adequate size (the volume of fixative should be 10 times that of the tissue). Resection specimens identified as a biohazard risk should be fixed for at least 48 hours (e.g. HIV, tuberculosis). If tissue is sent fresh from theatres, this should reach the pathology laboratory promptly. Refer to the COVID-19 Resources Hub for the latest COVID-19-related guidance.

Surgical specimens for salivary malignancies might be submitted without orientation. Sometimes, the superficial, deep or other aspects of parotid specimens are indicated. Accordingly, the specified aspect(s) should be painted (different colour when >1 indicated aspects). Some non-orientated parotidectomy specimens resemble a triangular pyramid,

the base and apex of the pyramid likely corresponding to the superior and inferior aspects, respectively; the longest aspect is likely to be the posterior margin/aspect. Resections of intraoral salivary gland carcinomas are more likely to be oriented (palate, floor of mouth, ventral tongue/sublingual gland, buccal mucosa or involving bone, etc.). If non-orientated, a clock-face method should be used with appropriate photographs or a diagram.

After the general description (ICCR tables 1–5), the specimen is weighed and palpated to assess for differences in texture, particularly if the tumour does not visibly extend out. The specimen is then sliced, and the cut surface of the slices is inspected (see section 4.2). Photography of the specimen can be useful to record the extent and particular features of the disease (e.g. extraglandular extension, border/growth pattern of tumour, pleomorphic adenoma 'ghost') and the sites from which tissue blocks are selected; it should be used as a standard of practice for larger specimens. The specimen, as well as the carcinoma, should be measured in 3 dimensions (including thickness/depth of invasion/maximum diameter).

If core biopsies are submitted, it is good practice to have only 1 core per block to prevent tissue exhaustion.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

4 Specimen handling and block selection

4.1 Introduction

The specimen handling and preparation protocol described below is based on contemporary practice and should be regarded as a guide only; it may need to be modified in individual cases. A detailed dissection protocol is beyond the scope of these guidelines, but a brief summary of dissection methods and block selection is included to facilitate recording of the core data items. More detail can be found in the relevant sections of the RCPath document *Tissue Pathways For Head and Neck Pathology*.[16] It is particularly important to record the macroscopic dimensions of the tumour, the closest margins and any gross capsular breach or invasion.

It is important to identify if the patient has been enrolled in clinical trials before starting to undertake a macroscopic examination of the tumour and the selection of blocks, as the clinical trial protocol may dictate specific requirements in this regard.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

4.2 Selection and recording of blocks for histology

Slices should be 3–5 mm thick and can be sequential (like a bread loaf) or cruciate. The latter includes ‘equatorial’ sections (through the maximal diameter of the specimen/tumour) and the opposite ‘polar’ sections, which are perpendicular to the former. A methodical text-based block key and/or photographic record of blocks taken should be included.

Inspection of the cut surface is centred on assessing areas of interest (AOI), largely centred on the tumour. Measurements should be taken (tumour per se, distance from margins) and other descriptors are recorded, including silhouette (e.g. circumscribed, ovoid, rounded, bosselated, encapsulated; highly asymmetrical/irregular, satellite nodules or ill-defined), colour and texture (solid, cystic, necrotic together with ratios in case of mixed pattern) and cystic contents (watery/haemorrhagic, whitish/yellowish, semisolid/pasty). The capsule/outline of the gland (for major gland lesions) should be examined macroscopically and any discontinuity or evidence of rupture recorded. Further AOI include the relationship with the facial nerve (if identified), the presence of multiple lobules or nodules, tumour extension beyond the capsule and the number/size of intra or peri-glandular lymph nodes. The presence and features of metastases in the latter should also be recorded.

The selection and number of slices to be processed depends on the size and AOI. Small specimens may be processed in their entirety. 5–8 blocks may be sufficient for moderately sized tumours, up to 2–3 cm. Mega-blocks may be used for large tumours (>5.0 cm); however, digital slide scanning, immunohistochemistry and molecular testing can be challenging on mega-blocks. Alternatively, multiple, macroscopically different areas should be sampled, particularly at the edge of the tumour; the method of sampling should be recorded to enable reconstruction. Selected blocks should include normal tissue, the relationship between the tumour and the nearest resection margin, lymph nodes within the gland or in peri-glandular soft tissue and macroscopically identified nerves. 1 block from a non-neoplastic gland should also be obtained if no normal background tissue adjacent to the tumour is evident.

Cutting up specimens from minor salivary glands follows similar principles, but special attention should be paid to those from hard palate. These may involve underlying bone and are often orientated. The bone may be anatomically dissected and subjected to

decalcification; cruciate slicing of the remainder with painting of indicated margins seems appropriate. Ideally, a single report should be issued including analysis of the decalcified specimen and results of molecular/further testing. This would avoid confusion with multiple supplementary reports and changes to the diagnosis, pathological T stage and patient management. It is, however, appreciated that decalcification and molecular testing can be time consuming. Realistically, and considering MDT discussions, when a confident diagnosis can be reached through examination of the mucosa and soft tissues, an interim report can be issued prior to completion of decalcification. Staging can then be agreed during MDT discussions based on imaging. In relatively rare cases when molecular testing is necessary, this should be explained at the MDT together with the differential to allow provisional management.

1 specified block should be designated for molecular testing, in which the tumour content should be formally assessed. It is important to ensure that this representative block is not decalcified as it may render molecular testing ineffective. It is also preferable that a mega-block is not used for this purpose as it would make immunohistochemistry, fluorescence in situ hybridisation (FISH), polymerase chain reaction (PCR) and next generation sequencing (NGS)-based techniques more challenging to perform.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

5 Core data items

We have set out to use the ICCR dataset in its current form, with appropriate qualifications and clarifications for implementation in UK clinical practice. In addition to the main dataset items, as outlined below, demographic and clinical data should be collected, as per the ICCR dataset. This includes the patient's name, date of birth, sex, hospital and NHS number (where appropriate) or other patient identification number.

1 ICCR	**Descriptor**	**Core/Non-core**	**Responses**
	Operative procedure	Core	Resection Biopsy Other
Operative procedure comments: The wide distribution of subsites that are involved by salivary gland carcinomas results in a wide complexity of procedural types and necessitates open communication between			

the operating surgeon and the pathologist. The exact type of procedure (for instance, excisional biopsy versus resection) often requires clarification, possibly in discussion with the MDT, especially since procedural nomenclature is constantly evolving.[17,18] In the context of recurrent disease, there may be nodules/soft-tissue deposits of recurrent carcinoma without any surrounding salivary gland tissue, and the best procedure designation would require dialog between pathologist and surgeon.[19]

If a neck dissection specimen is submitted, please use the separate neck dissection dataset.

RCPath comments:

None.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

2 ICCR	**Descriptor**	**Core/Non-core**	**Responses**

	Specimens submitted	Core	• Parotid gland
			  – Superficial lobe only
			  – Deep lobe only
			  – Total parotid (superficial and deep lobe)
			• Submandibular gland
			• Sublingual gland
			• Other (e.g. partial gland excision), specify

Specimens submitted comments:

The salivary sites, particularly the parotid, have a nuanced, oncologically relevant compartmentalisation into superficial and deep lobes separated by the facial nerve, which should be represented appropriately under specimen type and tumour type.[19–21]

RCPath comments:

None.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

3 ICCR	Descriptor	Core/Non-core	Responses
	Tumour site	Core	• Parotid gland – Left – Right – Laterality not specified – Superficial lobe only – Deep lobe only – Total parotid (superficial and deep lobe) • Submandibular gland – Left – Right – Laterality not specified • Sublingual gland – Left – Right – Laterality not specified • Other, specify including laterality

Tumour site comments:

The salivary sites, particularly the parotid, have a nuanced, oncologically relevant compartmentalisation that should be represented appropriately under specimen type and tumour type.[17] Tissue types and microanatomic structures encountered histologically are dependent on this specimen type and site. Thus, as with procedure type, open communication with surgical colleagues is necessary to maximise accuracy.[22]

Side and laterality are standard identifying parameters for specimen types that should rarely be left not specified.[14] Reporting of laterality provides supporting information to ensure that the correct site is recorded, provides useful demographic information and is a common quality assurance metric.[21] 'Not specified' should be used rarely and only after best efforts have been made to obtain the requisite information.

RCPath comments:

The site and laterality of minor salivary gland carcinomas should be recorded.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

4 ICCR	Descriptor	Core/Non-core	Responses
	Tumour focality	Core	Unifocal Multifocal

Tumour focality comments:

Truly multifocal salivary carcinomas are rare. The most common multifocal malignancy is acinic cell carcinoma (AciCC).[23–25] Rarely multifocality in basal cell adenocarcinoma may raise the possibility of a *CYLD*-associated syndrome (i.e. Brooke-Spiegler syndrome).[26]

RCPath additional comments:

It is uncertain whether multifocality reflects separate/independently developing tumours attributable to widespread genomic instability of salivary parenchyma, the multilobular nature of a tumour or intraglandular metastases. In addition to being academically interesting, this issue can influence the pT stage. The guidance from UICC TNM 8th edition states that "in the case of multiple primary tumours in 1 organ, the tumour with the highest T category should be classified and the multiplicity or the number of tumours should be indicated in parenthesis, e.g. T2(m) or T2(5). In simultaneous bilateral primary tumours of paired organs, each tumour should be classified independently."

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

5 ICCR	Descriptor	Core/Non-core	Responses
	Tumour maximum dimension	Core	Size (mm)

Tumour maximum dimension comments:

Tumour size, specifically the largest dimension, is a key staging element for AJCC and is prognostically critical.[6,27,28] Tumour measurement (pT) should ideally be performed macroscopically on the fresh specimen if possible, since formalin fixation may cause tumour shrinkage.[29] Occasionally, the microscopic extent of the tumour should be used to record the tumour size, for example when the size significantly exceeds macroscopic estimates.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

RCPath additional comments:

Microscopic measurement is necessary when an aggressive tumour insidiously infiltrates adjacent tissues or when there are satellite tumour elements invisible on intraoperative inspection/palpation that are invading ahead or towards the periphery of the main tumour. The influence of extratumoural perineural invasion on pT should be clarified (see Core data item 9). In carcinoma ex pleomorphic adenoma, it is unclear whether there is merit in considering the size of the whole lesion (both benign and malignant areas) for staging or the malignant component only; although, at present, the latter is the accepted practice. However, it is useful to record both. Topographic/spatial relationships (e.g. whether the benign component is in the periphery of the tumour or in the midst and surrounded by the malignant component) would influence measurements. It is usual practice to round off the histological measurement to the closest millimetre where relevant.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

6 ICCR	Descriptor	Core/Non-core	Responses
	Histological tumour type	Core	WHO subtype list

Histological tumour type comments:

Historically, the definition of salivary carcinomas depended on a characteristically distinct histo-/cytology. Currently, however, the definition of salivary carcinoma histologic type also reflects its biologic behaviour and thus influences prognosis, patterns of recurrence and clinical management, in turn.[7,30] Some carcinoma types (i.e. basal cell adenocarcinoma, conventional AciCC) are more indolent with locoregional recurrence but low nodal and distant metastatic rates.[31] Other tumour types are aggressive even at early T stage; aggressive lesions (such as conventional salivary duct carcinoma) show high rates of nodal metastasis and a worse 5-year overall survival.[32,33]

Capsular invasion

Carcinoma ex pleomorphic adenoma is subclassified by type/grade of malignant component(s) and extent of invasion. Non-invasive or intracapsular variants are completely confined within the capsule or, in case of incomplete/absent capsule, contour of the adenoma without evidence of penetration into extra-capsular/glandular tissue. The

definition for minimally invasive carcinomas varies, ranging from 1.5 mm to 6 mm (this distance should be specified when possible). Invasive variants extend beyond 6 mm. Prior to diagnosing a non-invasive carcinoma ex pleomorphic adenoma, processing of the entire lesion for histologic evaluation is recommended to exclude the presence of invasive growth. Prognosis has been linked to the degree of invasion, with non-invasive and minimally invasive variants reported to have a better prognosis than invasive variants.[9,34] For salivary duct carcinoma arising from pleomorphic adenoma, intracapsular lesions behave indolently; but, once invasive, the concept of minimal invasion may be less relevant since cases with extracapsular invasion ≤2 mm have still been reported to be clinically aggressive.[32]

Metastasising pleomorphic adenoma, despite its aggressive behaviour, is not included here since it is technically considered benign under the recent World Health Organisation (WHO) classification of tumours.[35]

Cribriform adenocarcinoma of minor salivary glands

In the 2017 WHO classification of tumours, cribriform adenocarcinoma of (minor) salivary gland origin is a subcategory of polymorphous adenocarcinoma.[36] This is a controversial area and it is desirable to describe conventional polymorphous adenocarcinoma and cribriform adenocarcinoma in the dataset to allow acquisition of prognostic information.[37,38] Unlike conventional polymorphous adenocarcinoma, cribriform adenocarcinomas of minor salivary glands are more frequently extrapalatal, commonly at the base of tongue, and have a higher propensity for nodal metastasis.[38,39] Histologically they may show different architectural patterns than the conventional polymorphous adenocarcinoma and tend to have nuclei resembling those of papillary thyroid carcinoma. They tend to demonstrate translocations involving the *PRKD* family of genes, rather than the *PRKD1* point mutations seen in conventional polymorphous adenocarcinoma.[40,41] For the purposes of reporting, differentiating between these entities may be helpful given the different behavioural profile.

Note: The diagnosis of primary squamous cell carcinoma of the salivary gland should be used sparingly and when a demonstrable origin from a salivary duct can be seen. In most instances it is a metastasis from another site (most commonly from head and neck skin).

RCPath additional comments:

The histological classification of salivary carcinomas is complex and has evolved with time, but it often presents difficulties for physicians, surgeons and clinical oncologists as they might not be aware of the continually changing landscape of salivary malignancies in WHO classification.[42–49] Salivary gland cancer subtyping can guide patient management, and it is good practice to provide this information as well as the grade of the tumour.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies]

7 ICCR	Descriptor	Core/Non-core	Responses
	Histological tumour grade	Core	Not applicable Low or intermediate grade High-grade transformation Cannot be assessed

Histologic tumour grade comments:

The histologic (microscopic) grading of salivary gland carcinomas has been shown to be an independent predictor of behaviour and plays a role in optimising therapy. Further, there is often a positive correlation between histologic grade, clinical stage and prognosis.[9,50–52] However, as alluded to above, most salivary gland carcinoma types have an intrinsic biologic behaviour and attempted application of a universal grading scheme is not recommended.[9] Thus, by assigning a histologic type, the tumour grade itself is often implied. Hence, a generic grading scheme is no longer recommended for salivary gland carcinomas.[27]

Carcinoma types for which grading systems exist and are relevant are incorporated into the histologic type. The major categories that are amenable to grading include adenoid cystic carcinoma, mucoepidermoid carcinoma (MEC), and adenocarcinoma not otherwise specified (NOS).[9,50,53] Additionally, polymorphous adenocarcinoma, AciCC and epithelial-myoepithelial carcinomas can be graded,[36] with the understanding that a validated grading scheme has not yet been established.

In adenoid cystic carcinoma, histologic grading is based on the growth/architectural pattern.[52] Those adenoid cystic carcinomas showing a solid growth pattern are regarded as histologically high-grade carcinomas.[54]

The histologic grading of MEC includes a combination of growth pattern characteristics (e.g. cystic, solid, neurotropism) and cytomorphologic findings (e.g. mucous:squamoid cells ratio, anaplasia, mitoses, necrosis).[55–57] Proposed systems typically distinguish low, intermediate and high-grade tumours and can be broadly classified as descriptive or score-based.[48,55,56] A comparison of the various grading systems shows that the Brandwein system is likely the best predictor of behaviour. A binary grading system (Brandwein high versus low-plus-intermediate) has been proposed to better reflect biological behaviour in MEC but is not widely used at present.[57–60]

High-grade transformation has evolved into an important concept of tumour progression in salivary gland carcinomas and should be kept in mind while attempting to grade. Historically designated as 'dedifferentiation', high-grade transformation describes progression of a typically monomorphic carcinoma into a high-grade carcinoma with pleomorphism.[61–63] Establishing this is important as cancers demonstrating high-grade transformation show an aggressive clinical course that deviates drastically from the usual behaviour for a given tumour type, thus alerting to the potential need for more aggressive clinical management. Tumours for which this phenomenon is characterised include AciCC, adenoid cystic carcinoma and epithelial-myoepithelial carcinoma.[61–68] Secretory carcinoma and polymorphous adenocarcinoma can also rarely undergo high-grade transformation.[62,63,66]

RCPath additional comments:

A 3-tier grading system for AciCC has recently been proposed based on 4 parameters including mitotic index, tumour necrosis, fibrosis at the frankly invasive front/infiltrative edge, and tumour borders.[64] The 5-year overall survival was reported to be 50% in high-grade AciCCs, and 100% in low-grade or intermediate-grade tumours. At present, there is not enough evidence for grading of AciCC, however, high-grade transformation (if present) should be reported.

Adenocarcinoma NOS does not have a formalised grading scheme and is graded intuitively based on the cytomorphologic features.[9]

The grading of polymorphous adenocarcinoma is intuitively based on cytomorphologic features, acknowledging that the majority will be low grade.[36] Nonetheless, caution should be exerted as high-grade variants (possible relationship to cribriform adenocarcinoma) could also be classified as adenocarcinoma NOS and the decision can be subjective and reflects experience and expertise.

A 2-tier grading system for secretory carcinoma has also been proposed based on mitotic count and necrosis.[66] The 5- and 10-year disease-free survival has been reported to be higher (93% and 73%) in low-grade and lower (46% and 46%) in high-grade subtypes. At present, there is insufficient evidence for grading of these tumours; however, high-grade transformation (if present) should always be reported.

Grading of epithelial-myoepithelial carcinomas can be based on assessing infiltrative pattern, perineural invasion, necrosis, cellular atypia (particularly of the myoepithelial components) and mitotic rate.[49,67] Again, caution should be exerted as higher grade variants may be difficult to distinguish from some adenoid cystic carcinomas (and vice versa); *MYB* translocation, widely regarded as characteristic of the latter, may even be detected in the former.[49] Some studies have suggested that salivary carcinomas showing a biphasic (luminal/non-luminal or 'ductal/myoepithelial') structural organisation may form part of a continuum rather than reflect distinct entities but this remains to be proved.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

8 ICCR	**Descriptor**	**Core/Non-core**	**Responses**
	Extent of invasion	Core	Macroscopic extraparenchymal extension Not applicable Cannot be assessed
		Structures involved	Bone Skin Other, specify

Extent of invasion comments:

Macroscopic extraparenchymal (extraglandular) extension is the parameter required to upstage a tumour to T3 and is thus more important than microscopic extraparenchymal extension. Bone, skin and facial nerve involvement are parameters that define stage

T4a.[27] While microscopic extraparenchymal extension is not a stage-defining parameter, in certain instances it may yield useful information for postoperative clinical management.

RCPath additional comments:

Macroscopic parenchymal extension is challenging to assess in tumours of minor glands and can also be difficult in multilobular major gland lesions. Recognition is straightforward when a mass fungates out of a major gland on macroscopic inspection. However, establishing whether a gentle bulging of the gland surface reflects early extraparenchymal extension or a subcapsular tumour simulating such an extension is more challenging. Further tissue levels can be helpful to establish mushrooming of tumours and patterns of frank invasion. For histological establishment of extraparenchymal invasion, direct abutment or infiltration of tumour cells within the surrounding parenchyma (without a fibrous capsule) is needed. Reporting invasion of bone, overlying skin and nerve is important, as it can affect staging.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

9 ICCR	Descriptor	Core/Non-core	Responses
	Perineural or intraneural invasion	Core	Not identified Present Location • Intratumoural • Extratumoural Degree of extent • Focal • Extensive/multifocal

Perineural invasion comments:

Perineural invasion is diagnostically useful since it helps to establish a malignant diagnosis, and it is particularly useful in establishing a diagnosis of basal cell adenocarcinoma. The value of perineural invasion as a prognosticator varies depending on tumour type and literature,[69] and any clinically significant differences between small nerves trapped within the tumour stroma or ahead of the main tumour front are not explored. While perineural invasion has not been studied for salivary gland cancers in as much depth as for head and neck squamous cell carcinoma, much of the literature

supports the importance of recording this feature as a data element.[70–79] Involvement of a named nerve (i.e. facial nerve) is incorporated into staging and assigns a more advanced stage.[27,75,76] But even beyond this, more granular documentation including the extent of perineural invasion (e.g. number of neural sites involved, intra- or extratumoural localisation, distance between and size of involved nerves, distance of peritumoural neural invasion from the main front, and the effect of extratumoural invasion on excision margins) may also be prognostically relevant and hence be included as a core element. These features should be considered in conjunction with assessing the extent of invasion, and they could overcome difficulties arising when only the number of sites involved is assessed. For example, identifying 2 small, closely located intratumoural sites can be reasonably regarded as focal rather than multifocal. Conversely, identifying 1 intra- and 1 extratumoural site that are widely apart suggests more extensive involvement.

RCPath additional comments:

Perineural invasion is a widely known feature of adenoid cystic carcinoma, where it is regarded as an adverse prognosticator. A meta-analysis of multiple cohorts suggests that intraneural invasion might also be an independent predictor of poor prognosis.[8,58,76] However, in routine practice, pathologists use the term perineural invasion to describe both perineural and intraneural invasion; distinction between these features may be helpful. The use of S100 immunohistochemistry in assisting recognition of perineural invasion might be helpful, however caution should be exercised as it can be positive in a range of salivary tumours.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

10 ICCR	Descriptor	Core/Non-core	Responses
	Lymphovascular invasion	Core	Not identified Present Cannot be assessed

Lymphovascular invasion comments:

Lymphovascular invasion is diagnostic of malignancy in salivary gland tumours (caution: the rare intravascular tumour deposits in pleomorphic adenoma should not be misinterpreted as indicative of malignancy).[77] Existing data are limited but support its

prognostic value, although this varies by tumour type and study.[52,78–80] As with other organ sites, the significance of the distinction between vascular and lymphatic invasion as well as the extent of vascular invasion is not known.

RCPath additional comments:

Morphological criteria for establishing lymphovascular invasion (e.g. the lining of intravascular tumour aggregate by endothelium, association with thrombus, and attachment to the vascular wall) have drawn little or no attention in salivary carcinomas. CD31, CD34, ERG and podoplanin immunoreactivity can help to distinguish endothelial phenotypes if invasion is suspected.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

11 ICCR	Descriptor	Core/Non-core	Responses
	Margin status	Core	Involved (specify) Not involved (distance) Cannot be assessed Specify which margin is involved

Margin status comments:

Complete surgical excision to include cancer-free surgical margins is the primary mode of therapy for salivary gland cancers, as retrospective studies have shown an increased risk for recurrence and decreased survival with positive surgical margins.[81–85] Unlike mucosal sites, there are no data to indicate a specified critical distance of tumour from margin indicative of a prognostic difference. Indeed, this may be dependent on tumour type, type of salivary gland involved and silhouette/border as well. Based on the current level of evidence, reporting of distances to margins constitutes a non-core element.

For illustration, adenoid cystic carcinoma often has an infiltrative silhouette/border and high propensity for local recurrence. The ‘safe distance’ for this tumour will be intuitively greater than for a more indolent carcinoma such as epithelial-myoepithelial carcinoma or conventional AciCC, for instance. Limited data suggest that even with >5 mm clearance, approximately 20% of adenoid cystic carcinomas recur, which is less than the recurrence rate for close (<5 mm) and positive margins.[85,86] In contrast, almost all

epithelial- myoepithelial carcinomas are cured if margins are negative, even without a stipulation in distance to margin.[87]

Occasionally, some salivary carcinomas (e.g. AciCC) may show ‘encapsulation’ similar to that of pleomorphic adenoma. In superficial parotid gland tumours, this ‘capsule’ may rest on the facial nerve and thus, particularly when preoperative FNA is unavailable or inconclusive, be resected conservatively (i.e. via extracapsular dissection) in order to spare and minimise injury to the facial nerve. Thus, it is not uncommon for such tumours to have ‘close margins’ within the tumour capsule. It is not clear whether this scenario indicates an increased risk of local recurrence, but the presence of a capsule is thought to confer a better prognosis. Limited data on extracapsular dissection for salivary carcinomas also suggest a favourable outcome even with close margins, though this may be influenced by tumour type since most carcinomas removed this way are slow growing and low grade.[88–91]

RCPath additional comments:

The distance from the tumour to the nearest resection margin should be measured to the nearest millimetre based on macroscopic assessment and confirmed or amended histologically. If there is substantial discrepancy, an explanation, for instance intra-operatively undetectable, insidiously invading tumour elements, may be given and appreciated by the surgical team. For low and intermediate salivary carcinomas, there is evidence to suggest that close margins (variably defined as <1 mm, <3 mm or <5 mm) may not result in a poorer outcome.[88–91] However, margin status and distance for intermediate and high-grade lesions is important.[92,93]

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

To generate further evidence and in order to standardise practice, we recommend that the distance of all salivary gland cancers from margins should be recorded as a core item. If the lesion is completely encapsulated, the distance of the intracapsular tumour from the margin should also be recorded. Most intracapsular tumours have been shown to have a good prognosis. This may guide future patient management.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

12 ICCR	Descriptor	Core/Non-core	Responses
	Pathological staging (UICC TNM8)	Core	See Appendix B

Tumour staging comments:

By AJCC/UICC 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 clinical stage information supplemented/modified by operative findings and gross and microscopic evaluation of the resected specimens.[94] pT entails a resection of the primary tumour or 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 lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumour. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumour has been completely removed. If a biopsied tumour is not resected for any reason (e.g. when technically unfeasible) and if the highest T and N categories or the M1 category of the tumour can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies]

RCPath further comments:

At present, minor salivary gland tumours are staged according to the TNM of the relevant mucosal site. However, this presents some difficulties as the criteria are not entirely applicable to salivary malignancies. For example, 'depth of invasion' in oral minor salivary gland carcinomas can be confusing and can be recorded as 'tumour thickness'. Similarly, the nature of the invasive front is not relevant; it may be recorded as 'pattern of infiltration' or 'not applicable' for intracapsular tumours.

Staging for intra-osseous MECs should be interpreted with caution. Due to their inherent intra-osseous location, these are likely to fall under the pT4 category in the current TNM;

however, this is likely to be an overestimate, which may lead to over-treatment. It might be worth considering the size of the lesion through macroscopic, pathological and/or radiological correlation for clinical decision making as most are histologically low grade.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

6 Non-core data items

NC1 ICCR	Descriptor	Core/Non-core	Responses
	Ancillary studies 1	Non-core	Individual tumour markers/tests

Ancillary studies comments:

A detailed description of the use of histochemical, immunohistochemical and molecular techniques in salivary gland cancers is beyond the scope of this document. However, the following comments may be useful.

Ancillary studies include special stains, histochemistry, immunohistochemistry, in situ hybridisation and molecular analysis (FISH, PCR, NGS, etc.). These techniques are applied when the routine histology is not sufficient to make diagnosis, to narrow the differential diagnosis and eventually assist in establishing or refining diagnosis.[95,96]

Mucosubstance histochemistry (Alcian Blue followed by Periodic acid-Schiff) is valuable in assessing secretory products (e.g. in acinic cell and MECs) and stromal material (e.g. in adenoid cystic carcinoma).[56–58,96] In addition, elastic van Gieson can be useful in demonstrating elastosis in salivary cancers of a biphasic structural organisation (e.g. adenoid cystic carcinoma) and the hyalinised 'ghost' of a pre-existing pleomorphic adenoma; phosphotungstic acid haematoxylin is useful to highlight mitochondria in oncocytic carcinoma.[95]

The selection of antibodies for diagnostic or investigative immunohistochemistry of salivary carcinomas conventionally centres on markers of luminal ('ductal') or abluminal (modified 'myoepithelial') cell differentiation. A basic immunohistochemical panel for assessing salivary cancers with dual-cell populations should include markers for abluminal and luminal cells; the first abluminal group could include: CK5/6, CK14, SMA, calponin, p63, p40 and S100 protein; the second luminal group might include: CK7, Cam5.2 and EMA/CEA to establish whether multiple cell populations exist.[96–98]

Salivary myoepithelia are regarded as members of the broad family of basal epithelial cells.[99,100] Immunoreactivity for p63 and podoplanin in non-luminal phenotypes and basal keratinocytes likely reflects this. Traditionally, S100 was regarded as a good marker for myoepithelial differentiation, however it is now well established as a sensitive (but not very specific) myoepithelial marker and should always be used in conjunction with other markers. It is important to be mindful of the fact that S100 expression can be seen in several malignant salivary tumours lacking myoepithelial cells (such as polymorphous adenocarcinoma, secretory carcinoma, microsecretory adenocarcinoma, etc.).

S100 protein, together with mammaglobin and DOG-1, has been used to distinguish members of the acinic-intercalated ductal carcinoma family of tumours but caution should be exerted. S100 protein and mammaglobin expression in secretory carcinomas is established,[101] but patchy or focal DOG-1 expression may also be seen. Immunohistochemistry for tyrosine receptor kinase (*NTRK*) genes seems promising; 64% of secretory carcinomas usually show nuclear immunoreactivity, whereas AciCCs are negative.[102] Further confirmation of *NTRK* immunohistochemistry and validation for diagnostic use are desirable.

The Ki67/MIB-1 index is reported to be an independent prognosticator for salivary malignancies,[58,87,88] but values differ between different types. In MEC, for instance, indices <10% and >10% suggest favourable and unfavourable prognosis, however this should be interpreted with caution as some low-grade MECs can show an index of <5%. In AciCC a Ki-67 index >5% is an adverse prognosticator. In AciCC with high-grade transformation, the proliferation index can reach up to 60%.[57,95,96]

Androgen receptors, epidermal growth factor receptor 2 (HER2/neu, ErbB-2) and *NTRK* testing may be requested by oncology colleagues for therapeutic purposes.[103] Immunohistochemistry for androgen receptors and HER2/neu is straightforward and widely available, but validation of the latter for salivary cancers is still awaited.

In the context of diagnosing frank salivary cancers, the use of in situ hybridisation seems confined to the detection of EBV-encoded small RNA in lymphoepithelial carcinoma.[104]

[Level of evidence C – The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

NC2 ICCR	Descriptor	Core/Non-core	Responses
	Co-existent pathology	Non-core	None identified Present • Sialadenitis • Tumour-associated lymphoid proliferation (TALP) • Benign tumour(s), specify • Other, specify

Co-existent pathology comments:

For salivary epithelial malignancies, co-existing benign salivary pathology ranging from adenosis to various benign tumours[105] is of interest and suggestive of instability of salivary parenchyma, but it is not currently oncologically relevant overall.

The notion of tumour-associated lymphoid proliferation (TALP) is considered here for convenience, though TALP may be induced by the tumour rather than merely being co-existing benign salivary pathology.[106] In some tumours (e.g. MEC, AciCC) TALP may be mistaken for remnants of a lymph node and this distinction is important for staging. For AciCCs, tumours with prominent TALP may actually be more indolent.[107]

[Level of evidence D – The basis in evidence for inclusion is expert opinion.]

NC3 ICCR	Descriptor	Core/Non-core	Responses
	Tumour focality	Non-core	Specify number of tumours/foci in specimen

Number of tumour foci comments:

If possible, the number of tumours/foci should be provided in addition to dimensions of the largest focus.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

7 Reporting of small biopsy specimens

The data that can be obtained from small biopsy specimens will be determined, in part, by the size of the specimen. The type of carcinoma is the minimum data, as it may determine treatment. Intraoral biopsies can be small and fragmented; similarly, core biopsy and/or FNA may yield limited material but, where possible, a diagnosis and an estimated

histological grade should be given.[108] It is recognised that, in large tumours, the grade in superficial biopsy material may not be representative of the most aggressive part of the lesion. There is also significant heterogeneity and morphological diversity within salivary gland cancers; therefore, the eventual grade and sometimes even the diagnosis on the excision specimen might be different. It is not realistic to assess tumour size, extracapsular extension or vascular or neural invasion in small biopsies, but if obvious vascular or neural invasion is present it should be mentioned. Infiltration into other tissues, such as fat, muscle and background acini, might also be difficult to establish, but if present it should be recorded. When limited tissue is available, it should be used sparingly for further testing and a more experienced salivary gland pathologist consulted to ensure an appropriate diagnosis, to guide patient treatment and to avoid tissue exhaustion.

[Level of evidence – GPP. Recommended best practice based on the clinical experience of the authors of the writing group.]

8 Molecular diagnostics

The discovery of genomic alterations in salivary cancers, particularly rearrangements, has excited great interest. Alterations in carcinoma ex pleomorphic adenoma, basal cell adenocarcinoma, cribriform adenocarcinoma and polymorphous adenocarcinoma have been mentioned above and in ICCR Table 6. More widely known examples include MEC (*MAML2*), adenoid cystic carcinoma (*MYB-NFIB*), secretory carcinoma (*ETV6-NTRK3*) and hyalinising clear cell carcinoma (*EWSR1-ATF1*).[109,110–112] Other examples include AciCC (*NR4A3*)[113] and salivary duct carcinoma (*HER2-neu, TP53, PI3CA, HRAS)*, and the list is expected to expand.[114–117] Molecular analysis has been regarded as the way forward, is expected to refine diagnosis/classification and effect personalised treatment, and can facilitate development of immunohistochemical markers, *NR4A3*[113,118] being a typical example of the latter. However, as is often the case with new technologies, acquisition of further data has shifted the original excitement to cautious optimism.

A positive test confirming the presence of a molecular event can be helpful; however, a negative test does not always rule out a diagnosis because some genetic alterations are not seen in 100% of cases of a particular tumour. For example, the *MAML2* rearrangement is seen in up to 70% of MECs,[88,100] and it can be negative in a significant proportion of cases (see ICCR Table 6 for further reservations). Molecular testing and FISH are useful in cases with diagnostic uncertainty and extremely helpful in positive cases. Due to cost and turnaround time implications, it may not be possible to perform molecular testing on

each case, but it should be considered if circumstances allow. In poorly differentiated or high-grade carcinomas that cannot be classified using a haematoxylin and eosin stain or with immunohistochemistry, a panel of markers or NGS and RNA sequencing are worth consideration. A list of some of the more commonly known and used molecular alterations is provided in Table 1.

The National Genomic Test Directory for cancer specifies the genomic tests commissioned by the NHS in England for cancer, the technology by which they are available and the patients eligible to access to a test (further details and the full list is available at https://www.england.nhs.uk/publication/national-genomic-test-directories/).

Table 1: Overview of some of the common molecular alterations in salivary gland cancers (modified from Hanson *et al*., 2022[88]). Please note that this is not an exhaustive list, owing to the continually developing understanding of the molecular landscape of these cancers.

Tumour	Molecular alterations
Acinic cell carcinoma	*NR4A3*
Secretory carcinoma	*ETV6-NTRK3* fusions
Adenoid cystic carcinoma	*MYB-NFIB* fusions, *NOTCH-1* mutations
Polymorphous adenocarcinoma/CAMSG	*PRKD1-3*
Hyalinising clear cell carcinoma	*EWSR1-ATF1, EWSR1-POU5F1* (*EWSR1* rearrangement also reported in a subset of myoepithelial carcinomas)
Mucoepidermoid carcinoma	*CRTC1-MAML2*, *CRTC3-MAML2*
Salivary duct carcinoma	*HER2-neu*, *TP53, PI3CA, HRAS*
Intraductal carcinoma	*RET* fusion (intercalated duct, mixed/hybrid and oncocytic subtypes), *HRAS* (apocrine subtype)
Carcinoma ex pleomorphic adenoma	*PLAG1, HMGA2*
Basal cell adenocarcinoma	*CYLD1, CTNNB1*
Microsecretory carcinoma	*MEF2C-SS18*
Mucinous adenocarcinoma	*AKT1 E17K* and *TP53*

9 Frozen section diagnosis

On occasions, intra-operative frozen section diagnosis of the nature of a neoplasm will be requested. While it might be possible to identify the presence of neoplastic tissue, the

precise diagnosis or nature of a salivary gland cancer, or even differentiation from a benign tumour, may not be possible due to the significant morphological heterogeneity as well as overlapping features between lesions.

The report on the frozen section specimen(s) should normally form part of, or accompany, the final diagnostic report on the case.

Note: although there have been some reports on the potential usefulness of frozen sections in salivary cancer intra-operative assessment, there is limited quality evidence for their usefulness and they should be avoided, if possible.

10 Support of research and clinical trials

It is important to be aware of local protocols for tissue banking and engagement with national initiatives for the further classification of tumours (such as was implemented in the 100,000 Genomes Project). This could include receipt of non-fixed tissue and selection/storage of sufficient frozen material for downstream molecular analysis. Other features, such as assessment of the effects of biological therapy/immunotherapy, may be important but are currently beyond the remit of this dataset.

11 Criteria for audit

The following are recommended by RCPath as key assurance indicators and key performance indicators:[119,120]

- cancer resections should be reported using a template or proforma, including items listed in the English COSD, which are, by definition, core data items in RCPath cancer datasets. NHS trusts are required to implement the structured recording of core pathology data in the COSD
  - standard: 95% of reports must contain structured data
- histopathology cases must be reported, confirmed and authorised within 7 and 10 calendar days of the procedure
  - standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days
- the inclusion of SNOMED or SNOMED-CT codes:
  - standard: 95% reports should have T, M and P codes

- the availability of pathology reports and data at MDT meetings:
  - standard: 90% of cases discussed at MDT meetings where biopsies or resections have been taken should have pathology reports/core data available for discussion
  - standard: 90% of cases where pathology has been reviewed for the MDT meeting should have the process of review recorded.

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Appendix A SNOMED coding

SNOMED topography should be recorded for the site of the tumour. SNOMED morphology codes should be recorded for the diagnosis/tumour morphology.

Versions of SNOMED prior to SNOMED CT will cease to be licenced by the International Health Terminology Standards Development Organisation from 26 April 2017. It is recognised that versions of SNOMED 2, SNOMED 3/RT and SNOMED CT are in use in the UK; these are, therefore, currently considered acceptable.

SNOMED procedure codes (P codes in SNOMED 2/3/RT) should be recorded for the procedure. P codes vary according to the SNOMED system in use in different organisations, therefore local P codes should be recorded and used for audit purposes.

A list of applicable SNOMED morphology and topography codes should be provided.

Morphological item	SNOMED code	SNOMED CT terminology	SNOMED CT code
Acinic cell carcinoma	M-85503	Acinar cell carcinoma	45410002
Mucoepidermoid carcinoma	M-84303	Mucoepidermoid carcinoma	4079000
Adenoid cystic carcinoma	M-82003	Adenoid cystic carcinoma	11671000
Polymorphous adenocarcinoma	M-82003	Polymorphous low-grade adenocarcinoma	128702009
Epithelial-myoepithelial carcinoma	M-85623	Epithelial-myoepithelial carcinoma	9618003
Basal cell adenocarcinoma	M-81473	Basal cell adenocarcinoma	34603009
Sebaceous carcinoma	M-84103	Sebaceous adenocarcinoma	54734006
Papillary/Cystadenocarcinoma	M-84503	Cystadenocarcinoma	21008007
Mucinous adenocarcinoma	M-84803	Mucinous adenocarcinoma	72495009
Oncocytic carcinoma	M-82903	Oxyphilic adenocarcinoma	57596004
Salivary duct carcinoma	M-85003	Salivary duct carcinoma	397082006
Adenocarcinoma	M-81403	Adenocarcinoma	1187332001
Myoepithelial carcinoma	M-89823	Malignant myoepithelioma	128884000
Carcinoma in pleomorphic adenoma	M-89413	Carcinoma ex pleomorphic adenoma	17264009
Squamous cell carcinoma	M-80703	Squamous cell carcinoma	1162767002
Small cell carcinoma	M-80413	Small cell carcinoma	74364000
Undifferentiated carcinoma	M-80203	Carcinoma, undifferentiated	38549000

		Mammary analogue secretory carcinoma	734058001

Note: This is not a comprehensive list of all malignancies and other codes should be used as necessary.

Topography item	SNOMED code	SNOMED CT terminology	SNOMED CT code
Salivary gland, not otherwise specified	T-55000	Salivary gland structure	385294005
Parotid gland	T-55100	Parotid gland structure	45289007
Submandibular gland	T-55200	Submandibular salivary gland structure	385296007
Sublingual gland	T-55300	Sublingual gland structure	88481005
Minor salivary gland	T-55400	Minor salivary gland structure	87626005

Procedure codes (P)

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure. Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

Appendix B TNM classification

This provides updated information on staging using UICC TNM 8, which should be used for all tumours diagnosed after 1 January 2020.

Major salivary glands

Tx Primary tumour cannot be assessed

T0 No evidence of primary tumour

T1 Tumour 20 mm or less in greatest dimension without extraparenchymal extension

T2 Tumour more than 20 mm but not more than 40 mm in greatest dimension without extraparenchymal extension

T3 Tumour more than 40 mm and/or tumour with extraparenchymal extension

T4a Tumour invades skin, mandible, ear canal or facial nerve

T4b Tumour invades base of skull, pterygoid plates or encases carotid artery

Notes

- Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve except those listed under T4a or b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.
- If there is doubt as to which category a tumour should be allocated to, then the lower (less extensive) category should be used.
- For minor gland carcinomas, please refer to the dataset for lip and oral cavity carcinomas.
- For regional lymph nodes, refer to the dataset for histopathological reporting of nodal excisions and neck dissection specimens associated with head and neck carcinomas.

Distant metastasis (M)

pM1 Distant metastasis confirmed microscopically

Note that pM0 and pMX are no longer valid categories.

Appendix C Reporting proforma for salivary gland carcinomas

Surname……	Forenames……	Date of birth…… Sex.....
Hospital……	Hospital no……	NHS/CHI no……..
Date of receipt……	Date of reporting……	Report no…….....
Pathologist……	Surgeon……	

Type of specimen: Biopsy □ Resection □ Other □

Specimen and tumour site

Site: Parotid □ Submandibular □ Sublingual □ Other site □(Specify)……

If parotid: Superficial lobe □ Deep lobe □ Total parotid □

Laterality: Left □ Right □ Not specified □

Maximum tumour dimension……(mm)

Histological type: ……..

Histological grade: Not applicable □ Low grade □ High grade □ Cannot be assessed □

Tumour focality: Unifocal □ Multifocal □

Extraglandular extension – macroscopic: Yes □ No □ Cannot be assessed □

Extraglandular extension – microscopic: Yes □ No □

If present, estimate distance (mm) ……..

Perineural invasion – Present □ Not identified □

Perineural invasion location – Intratumoural □ Extratumoural □

Degree of perineural invasion – Focal □ Extensive/Multifocal □

Lymphovascular invasion: Present □ Not identified □ Cannot be assessed □

Bone invasion: Present □ Not identified □ Cannot be assessed or not applicable □

Margins: Involved □ Not involved □ Cannot be assessed □

Specify margin(s), if possible: ……..

Distance of tumour from closest margin……..….. mm

Comments/additional information:

Summary of pathological data

Tumour site…….……

Tumour type……

pTNM stage pT …... pN…….

SNOMED codes

T……. M…….

T……. M…….

Resection of primary tumour: Clear (>5 mm) □□ Close (>1 mm) □□ Involved □

Signature: ..... Date: .....

Pathological staging (Core) (UICC TNM 8th edition, only if applicable)

pTNM stage pT.....

- m – multiple primary tumours
- r – recurrent
- y – post-therapy

Appendix D Reporting proforma for salivary gland carcinomas in list format

Element name	Values	Implementation notes
Operative procedure	Biopsy Resection Other	
Specimen submitted	Parotid • Superficial lobe • Deep lobe • Total parotid (superficial and deep lobe) Submandibular Sublingual Other site (e.g. partial gland excision) (specify)	*If a neck dissection is submitted, then a separate dataset is used to record the information.
Tumour site	Parotid • Left • Right • Laterality not specified Superficial lobe only Deep lobe only Total parotid (superficial and deep lobe) Submandibular • Left • Right • Laterality not specified Sublingual • Left • Right • Laterality not specified Other site (specify including laterality)	.
Tumour focality	Core • Unifocal • Multifocal Non-core • Specify number of foci in specimen	

Tumour dimensions	Core: Maximum tumour dimension ___ mm Non-core: Other tumour dimensions in mm	
Histological type	WHO subtype list	Value list from WHO Classification of Head and Neck Tumours (2022/23). 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 on Cancer research (IARC).
Histological grade	Not applicable Low grade High grade (or high-grade transformation) Cannot be assessed	
Extent of invasion	Core • Macroscopic extraparenchymal extension • Not applicable • Cannot be assessed Non-core • Bone • Skin • Facial nerve • Other, specify	
Perineural invasion	Core (single selection value list) • Present • Not identified Location • Intratumoural • Extratumoural • Degree of extent • Focal • Extensive/multifocal Non-core • Nerve size, if known ___ mm	

Lymphovascular invasion	Core (single selection value list) • Present • Not identified • Cannot be assessed, specify	
Bone invasion	Core (single selection value list) • Present • Not identified • Cannot be assessed or not applicable, specify	
Margin status	Core (single selection value list/text/numeric) • Involved • Not involved • Cannot be assessed • Specify margin(s), if possible • Distance of tumour from closest margin ___ mm Non-core • Specify margin(s), if possible • Specify extent/distance (mm)	
Pathological staging (UICC TNM 8th edition) TNM descriptors	Core (choose if applicable) • m – multiple primary tumours • r – recurrent • y – post-therapy	
Primary tumour (pT)	Core: free text	

Appendix E Summary table – Explanation of grades of evidence

(Modified from Palmer K *et al. BMJ* 2008;3371832)

Grade (level) of evidence	Nature of evidence
Grade A	At least 1 high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal, and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high- quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal, and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix F AGREE II guideline monitoring sheet

The cancer datasets of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Introduction
2 The health question(s) covered by the guideline is (are) specifically described	Introduction
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	Introduction
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword and Introduction
12 There is an explicit link between the recommendations and the supporting evidence	All sections
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	All sections
16 The different options for management of the condition or health issue are clearly presented	All sections
17 Key recommendations are easily identifiable	All sections

Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	Section 12
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interests of guideline development group members have been recorded and addressed	Foreword