CHAPTER 4
Specific tumor sites (part 2)

Contents

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Cancer of the female genital organs

Cervix

The number of cervical carcinomas in Italy is decreasing, partly as a consequence of prevention and early diagnosis activities that have spread increasingly in recent years, through spontaneous Pap smears and, more recently, the introduction of organized screening programs. In some at-risk categories (elderly women, immigrant women) screening practices, whether spontaneous or structured, are less common, when not altogether absent; in the general population, however, access to early diagnosis appears to be an increasingly consolidated cultural fact. On the other hand, only a small percentage of the premalignant lesions found by screening would have evolved into an invasive carcinoma if left to themselves for a considerable number of years. That is why, albeit infiltrating cases are decreasing, there is a clear increase in premalignant forms (substantially identifiable with CIN II and CIN III/*in situ* carcinoma), which are the true target of screening. Registration of these forms therefore plays a very important role, particularly in areas covered by screening, to monitor the potential risk of cancer in the population and its management through screening practices (program and impact assessment). Where possible, and where the registry's needs allow for it, incorporation of the following data fields in the registration of invasive forms is suggested:

INVASIVE FORMS	
Variable	**Description**
surgery date	main surgery date
surgery	type of surgery performed: ❖ conservative surgery (saturation biopsy, conization) ❖ hysterectomy ❖ total hysterectomy ❖ not performed ❖ unknown
pT	UICC 2002 TNM 6th edition extended pT coding
pN	UICC 2002 TNM 6th edition extended pN coding
total lymph nodes	number of total lymph nodes examined
positive lymph nodes	number of metastatic lymph nodes
isolated tumor cells	presence of isolated tumor cells
immunohystochemical stage N	immunohystochemical exam performed for pN staging
M	presence of distant metastasis at diagnosis (TNM 6th ed., 2002)
FIGO stage	in detail
first invitation date	date of first screening invitation
first screening test date	date first screening test was performed
date of subsequent invitations	use n data fields for n invitations to screening received by patient
date of subsequent tests	use n data fields for n screening tests taken by patient
screening status	proposed classification:: see Chapter 2, "Screening programs"

If a registry decides to include registration of premalignant forms (in particular CIN II, CIN III/carcinoma *in situ*), it may use the additional data fields listed in Table 1 (page 10). With respect to the correct classification of lesions described in pathology reports as severe dysplasia, medium dysplasia with severe traits and CIN III, as well, we recommend ascertainment at local cervical screening centers and/or independent pathology laboratories. This is important since there may be differences between centers:

- some may not consider CIN III identical to carcinoma *in situ*;
- some do not consider severe dysplasia to be identical with CIN III.

The latter aspect is more important. When encountering the terms “CIN III” or “CIN II/CIN III,” registries must always record CIN III using morphology code M-8077/2 (ICD-O-3). With respect to staging, we must stress the importance of levels of infiltration and the fact that the extension to the uterine

corpus must not be considered, but the exact origin of the neoplasm is decisive, i.e., whether arising from the corpus or cervix, in the case of adenocarcinomas found in the cervical canal. Code 179 or C55 (Uterus, NOS) should be used as rarely as possible, as it is an indicator of poor registration quality. Tables 2 (page 11) shows FIGO and 2002 TNM staging system for cervical cancer; WHO classification[1] is listed in Table 3 (page 12).

Uterus

Uterine corpus neoplasms have varying degrees of myometrial invasion; this must therefore be recorded during registration, along with extension to adjacent organs. In particular, it is important to note the status of the cervical canal, to distinguish correctly neoplasms arising in the lower uterine segment which extended to the cervical canal, neoplasms of the cervical canal that extended to the uterine corpus, and neoplasms independent of the uterine corpus and cervical canal.

Similar precautions should be adopted in the presence of presumed extensions to the bladder and rectum, for which *TNM Supplement 1993. A commentary on uniform use* introduced a significant distinction (see Table 4, page 13). For WHO classification see Table 5 (page 14).

Ovary and Fallopian tube

In the past, registration of ovary cancer and cancer of the Fallopian tube encountered problems due to the inclusion in ICD-O-2 of cystic tumors that were borderline between /3 behavior forms; with ICD-O-3, these forms were coded once again to behavior /1; this aspect must lead to consider the need to maintain registration of borderline forms, in order to verify the historical case sets of the last few years and better assess survival (Tables 6-7, pages 15-16).

Finally, it may be helpful to mention the Krukenberg tumor, a carcinoma usually located in the ovary (generally bilateral), with histological characteristics of the signet ring cell or gelatinous carcinoma (M-8490/3).

The ovary may be considered as the primary site only as an absolute exception, whereas in nearly all cases ovary location represents a metastasis originating from the stomach (and occasionally from other parts of the intestine), which registration should therefore refer to.

Female genital organs, other sites

Registries must remember to maintain registration of epithelial neoplasms of the skin of the genital area (basal cell epithelioma and squamous cell carcinoma, with all their variants), if they decided to exclude them from the other skin sites. (Tables 8-9 for WHO classification and codes, pages 18-19).

Cancer of the male genital organs

Prostate

Prostate cancer now ranks first for incidence in males, with a great geographic variability depending on the more or less widespread use of prostate specific antigen (PSA) testing in the different populations. The high increase in incidence under way seems to be connected to an increase in diagnostic sensitivity due to PSA testing, rather than to increased pressure of risk factors: in fact, mortality has for a number of years registered a slight but constant downward trend. As a consequence, there are no motivations to start organized screening programs, as supported in the literature,[2] but registries can nonetheless be asked for more careful monitoring of incident cases, to assess the impact of spontaneous screening procedures and their consequences on patient treatment and assessment of prognosis. A number of additional variables are therefore proposed for a better qualitative definition of incidence (see Table 10, page 20).

To help provide better understanding of the clinical pictures and the information found in medical reports, we present here tables describing TNM staging and grading according to Gleason score (Tables 11-13, pages 21-23). It must also be borne in mind that the 1999 ENCR rules do not allow non-microscopic diagnosis of malignant prostate cancer, and recognize PSA as a marker for values over 10 µg/l (10 ng/ml).[3]

Scientific development in this sector has led to believe that, in the absence of histological confirmation, PSA level alone is not sufficient to confirm prostate cancer diagnosis.[4] PSA increases when the glandular structures are damaged (prostate cancer, infections, benign prostatic hyperplasia): whereas PSA is therefore extremely sensitive, it has poor specificity (Table 14, page 24).

To increase diagnostic specificity, the following parameters may be used: PSA velocity, the speed at which PSA rises (suspect if ≥0.5 ng/ml/year, with PSA > 4 ng/ml; ≥0.75 ng/ml/year with PSA between 4 and 10); PSA density, or the concentration of PSA related to the size of the prostate gland; the relation between PSA and patient age and free PSA level (the lower it is, the more it is suspect, with cut-off levels at 10% and 25%).[5] However, PSA still remains an important tool for follow-up after treatment and for prognosis, and together with the clinical examination and Gleason score it is useful to establish further tests to take and the most appropriate treatment.

Therefore, cases of clinical suspicion of prostate cancer on the basis of PSA levels only, without histology confirmation, must be considered NSE cases.

In the absence of histological diagnosis[6] (Table 15, page 25), morphology classification can be performed only if

explicitly confirmed by the clinician in terms of further laboratory, clinical, and diagnostic imaging procedures, and can be supported by basis of diagnosis code 2.

Penis, scrotum, and testicle

Registries must remember to maintain registration of epithelial neoplasms of the skin of the genital area (basal cell epithelioma and squamous cell carcinoma, with all their variants), if they decided to exclude them from the other skin sites. WHO Classification[6] is listed in Table 16 (page 26).

Urinary tract neoplasms

Bladder and urinary tract

Bladder cancer is a very frequent neoplasm, particularly in males.

In the AIRTUM catchment area in the years 1998-2002, bladder cancer accounted for 9% of the total cancer diagnoses and 4.5% of cancer mortality for males. In females, instead, it accounted for 2.7% of incident cases and 1.7% of mortality. In Italy it is estimated that 19,313 new cases are diagnosed every year in the two sexes.[7]

The incidence trend is increasing in both genders, in particular in older age classes, while mortality is decreasing, and relative survival shows a slight improvement.[8]

The high incidence of bladder cancer, the changes in its trends, its possible occupational origin (estimated in 17% of cases),[9] make immediately obvious how important it is to have data that are certain and comparable. As already stressed in the general sections of this handbook, to obtain this kind of data it is essential to follow rigorous, standardized criteria of registration and coding; bladder cancer presents a few problems with respect to this, problems that have been long known and are generally due to the natural history and nosography of this type of neoplasm.[10-12]

Registration problems

Over 90% of bladder tumors are transitional cell carcinomas that derive from the urothelium and can present as flat or, more often, papillary neoplasms; 6-8% of cases, instead, are squamous tumors, and 2% are adenocarcinomas (morphologies which do not present registration difficulties).[13]

Adenocarcinomas can originate from the residues of the urachus or from metaplastic areas of the transitional epithelium as a consequence of chronic irritation.[14]

Registration problems with respect to urothelial tumors are caused by the numerous changes in classification over time, by the peculiar natural history of the tumor – which has a tendency to relapse – and by the presence of an intraepithelial development phase. This phase cannot always be distinguished from the invasive stage in papillary forms, especially since sometimes diagnosis is performed on minute biopsy fragments based on which it is difficult to establish with certainty the lesion's invasiveness. This problem received considerable attention in the past; following the conviction that it would be impossible for many registries to obtain exhaustive data on the invasiveness of transitional cell cancers, all tumors of the transitional epithelium were included in incidence case sets, including benign, of uncertain behavior, and *in situ* forms.

Actually, it is impossible to define invasion of the tumor at histology only for a small percentage of urothelial tumors: among the cases diagnosed in the years 1993-1994 by a pool of Italian cancer registries, the percentage was 9.6%, with a downward trend in more recent years.[15] In Turin, for cases recorded since 2000, the number has always been lower than 7%. It is therefore a false problem, at least for registries that can review the complete histology report, but it can represent a problem for registries that are completely or partially automated, since they only receive coded data.

The practice of including all transitional cell cancers in incidence, which was interrupted in the sixth edition of *Cancer Incidence in Five Continents*, was then taken up again because there was no certainty of correct coding by many registries, and it is still followed to date, especially for obvious reasons of continuity, aiding trend assessment.[16] In itself this habit would not be a problem, since incidence rates thus obtained do not represent an overestimate of infiltrating bladder cancers, but rather the overall risk of bladder cancer, *in situ* or infiltrating: however, it must always be possible to distinguish cases of invasive cancer, especially to correctly calculate survival, which must only be based on invasive tumors. It is therefore important for cases to be correctly classified and coded; however it is precisely on the method of classification that there exist ample differences between registries, to the point that comparability of survival data is compromised, leading to an overestimate which in the cited Italian case set was of 12%.

To overcome these problems, Italian registries need to have a uniform approach.

Classifications

Many classifications exist for urothelial tumors of the bladder; we cite here the two classifications published by the World Health Organization in its "blue books" of cancer classification: the historical *WHO 1973*[17] classification and the more up to date *WHO 2004* (Table 17, page 28)[18] classification

which takes into account the WHO/ISUP classification of 1998[19] (see box in the next page).
Registrars may also encounter descriptive diagnoses or diagnoses based on other classifications; to remedy these controversial situations, ENCR has planned a revision, still under way as we write (see *Newsflash ENCR,* November 2005; www.ENCR.com.fr/flash15_en.pdf) of the 1995 Recommendations, which in any case are listed below.

WHO CLASSIFICATIONS OF UROTHELIAL TUMORS OF THE BLADDER

WHO 1973

Papillary urothelial neoplasms

- Papilloma
- Grade 1 carcinoma
- Grade 2 carcinoma
- Grade 3 carcinoma

WHO 2004

Non-invasive urothelial neoplasms

- Hyperplasia (flat and papillary)
- Reactive urothelial atypia
- Urothelial atypia of unknown significance
- Urothelial dysplasia (low-grade intraurothelial neoplasms)
- Urothelial carcinoma in situ (high-grade intraurothelial neoplasm)
- Urothelial papilloma
- Inverted papilloma
- Papillary urothelial neoplasm of low malignant potential
- Low-grade non-invasive papillary urothelial carcinoma
- High-grade non-invasive papillary urothelial carcinoma

Invasive urothelial neoplasms

- with lamina propria invasion
- with invasion of the *muscolaris mucosae*

ENCR recommendations (1995)

ENCR recommends the following:

- all tumors of the bladder must be recorded, whatever the type of histology and the level of invasion;
- behavior coding must take into account both the anatomical pathology definition and the extent of invasion, therefore it is essential for registries to have access to all histology reports;
- behavior code /1 must be assigned to non-invasive low-grade papillary urothelial neoplasms with normal or slightly atypical histology, which according to the various classifications may be called:
  - benign or simple papillomas
  - papillary urothelial tumor
  - stage 1 carcinoma (Broders)
  - well-differentiated papillary carcinoma (Jewett)
  - grade 1 carcinoma (WHO 1973)
  - class I and II (CHOME) and not showing any signs of invasion;
- behavior code /2 must be assigned to both high grade papillary and flat urothelial tumors that present mitosis and more clearly atypical cells than in the previous category and that do not show any invasion;
- behavior code /3 must be assigned to tumors that present infiltration, regardless of pathology definition;
- in special cases the following codes must be used:
  - 8010/2 for *in situ* carcinomas that show clear anaplasia of the epithelium without formation of papillary structures and without invasion;
  - /1 cases in which histological examination reports the existence of a tumor, but it is not possible to determine the grade of malignancy on the examined specimen;
  - 8000/0 benign tumors without histological confirmation;
  - 8000/1 tumors of uncertain behavior without histological confirmation;
  - 8000/3 malignant tumors without histological confirmation;

We must also mention the altogether not infrequent case in which the only level of morphological information is that of a urine cytology test that is positive for cancerous cells: it being understood that the behavior code to be assigned in these cases is /1, identification of the site should entail the following:

- the case must be followed over time for improved diagnostic definition;
- if another examination (radiology, endoscopy, ECT) documented a macroscopic lesion in a specific site, the specific topography code for that site should be assigned;
- otherwise, topography code C68.9 (Urinary system, NOS) will be used.

Multiple bladder tumors

Another important issue regarding bladder tumors and, more in general, the transitional epithelium, is that of multiple primaries.
It must be noted that according to the IARC rules in force until publication of ICD-O-3, different tumors arising from two distinct organs were considered

different, considering as organ the one defined by the third digit of the ICD. According to this rule, a bladder tumor and another tumor in another area of the urinary tract (e.g., renal pelvis) were to be considered as multiple primaries, since the topography code of the bladder was 188 (then C67.) and that of the pelvis 189.1 (then C65). The new rules, instead, place all organs of the urinary tract (pelvis, ureter, bladder and other urinary organs) among the sites that must be considered single for the purpose of reporting multiple primaries, and establish that in the presence of metachronous neoplasms, the first should be reported, while for synchronous tumors code C68.9 (Urinary system, NOS) should be used.[20] This change, which is doubtless justified from a clinical and biological point of view, runs nonetheless the risk of changing incidence rates for cancer of the urinary system, causing a falsified reduction of rates and making it more difficult to interpret trends, unless the change is adequately taken into account. The only way to measure the extent of the changes (and, therefore, to assess the true trends) is to continue to register tumors as was done in the past and to compute the differences in incidence that are obtained using the two different rules. Secondary tumors can therefore be excluded or not (depending on they type of study), if possible applying the same criteria to all cases. A specific "X" code in the "TIPO CASO" data field can be used for this purpose for subsequent tumors (see Chapter 2: 2: code "X" is used for cases excluded following the 2004 IARC rules).

The same approach should be taken when the first bladder tumor has behavior /1 or /2 and a tumor with proven invasiveness is subsequently found. The second tumor must be registered (and considered, based on the criteria of the various reports), but morphology and incidence date of the first case must not be changed. Obviously, it will not be necessary to register further recurrences (whether invasive or not) of the infiltrating bladder neoplasm (while urothelial neoplasms arising in other urinary regions - renal pelvis, ureter, urethra - must be registered with the same criteria).

Conclusions and suggestions

- All bladder tumors must be registered.
- Registries must always, when dealing with tumors of the bladder, review the entire histological diagnosis. The pathology report always records information on the invasiveness of the tumor, due to its great prognostic relevance, whether explicitly or in pT form or within the microscopic description; furthermore, in cases in which, due to the sampling conditions, it is not possible to clearly define whether the neoplasm is infiltrating, the report always states this clearly.
- Registries that do not have direct access to the diagnostic reports must declare it and must be able to verify, at least with random checks, that the coded data they receive are correct. In case of doubt, it is advisable that the data thus obtained be included in the national calculations only for incidence but not for survival, which might be overestimated.
- It is important to bear in mind that, despite the apparent complexity and great number of classifications, a correct approach in morphological coding of urothelial tumors is actually based on two very simple data items:
  - whether the neoplasm is flat or papillary (morphology code 8120 and 8130, respectively);
  - whether the neoplasm is invasive (pT 1 or higher: behavior code/3), or non invasive (pTA or pTis: behavior codes of /1 or /2).
- Naturally, ICD 9 and ICD-10 codes behavior codes must also be harmonized, remembering the following correspondences:

Behavior code	ICD-9 code	ICD-10 code
/1	236.7	D41.4
/2	233.7	D09.0
/3	188.	C67.

- For pooled data studies, it is prudent to publish pooled survival data with and without bladder cancer data, as has already been done.[21] The reason for this is that bladder cancer has high incidence, therefore any unfounded differences in survival rates for this specific disease could affect the accuracy of overall survival estimates.
- For incidence trends, the new rules on multiple primaries should be applied to the entire AIRTUM Database, so as not to alter trends artificially; it should also be clearly explained that any misalignments with previous publications are due to this reason.

Kidney

Renal parenchymal neoplasms are more difficult to diagnose compared to those of the urinary tract (including the renal pelvis), which usually present early symptoms. They are often diagnosed incidentally during ultrasound scans or X-rays performed for other reasons, and in some cases only as a consequence of the onset of metastasis. . For WHO classification see Table 18, page 29).

Central nervous system (CNS), peripheral nervous system, and intracranial-intraspinal neoplasms

Reportable cases

Registration of all **intracranial** and **intraspinal** cases is recommended, independently of their behavior (benign, uncertain, malignant), according to ENCR international guidelines, although only malignant lesions are considered for incidence estimates in *Cancer Incidence in Five Continents,* as per the criteria first established in the 7th edition.

The main reasons for this approach are as follows:

- difficulty in distinguishing benign from malignant neoplasms on the sole basis of symptoms;
- all cerebral and spinal tumors generally produce severe clinical effects, independently of their malignancy, and call for surgical removal;
- clinical syndromes associated to some benign tumors (meningiomas, pituitary gland tumors) can be particularly interesting;
- some tumors (e.g., astrocytomas) progress from low grade forms (with better prognosis) to high grade forms.

The following neoplasms are therefore reportable, independently of behavior:

- neoplasms of the central nervous system (brain and bone marrow);
- intracranial nerve neoplasms, in the intracranial and/or intradural space; optical and acoustic nerves must be considered in their entirety up to and including the peripheral organ of sense;
- spinal root tumors, with intradural location (to be classified by site using the corresponding site of the spinal cord);
- tumors of the meninges of the brain and spinal cord;
- intracranial endocrine gland neoplasms (pituitary gland, pineal body, craniopharyngeal canal, intracranial / intraosseous glomus caroticum);
- intracranial and intraspinal extranodal lymphomas;
- soft tissue and bone neoplasms, with intracranial or intraspinal development, with the exception of the following:
  - spider angiomas, angiomatosis, lymphangio-matosis, and in general congenital forms of these diseases that were present at birth;
  - Von Recklinghausen's disease with no intracranial locations (for forms initially diagnosed in peripheral sites and subsequently diagnosed as intracrianal, the date of incidence is that of the first evidence of intracranial location);
  - clearly non-cancerous lesions such as cysts, aneurysms, lesions from tuberous sclerosis, etc.; in the presence of doubt, with open differential diagnosis including these conditions, it is advisable to keep the case as NSE;
  - bone lesions from systemic diseases (e.g., multiple myeloma) or from metastasis of neoplasms with unknown site (code to C80.9).

It must be borne in mind that many intracranial neoplasms are found as clinical suspicion on the basis of diagnostic imaging alone, with no histological confirmation. Sometimes patients are diagnosed outside a hospital setting and receive palliative care at home or in a hospice facility.

It is important to pay attention to possible false positives due to errors in distinguishing multifocal primaries and metastases (hence the importance of verifying the patient's previous clinical history). Several NSE or DCI cases are thus likely to be found in this category. Access to reporting sources for palliative care and diagnostic imaging is therefore recommended, in particular with respect to the latter CT and MRI scans are essential (if possible contrast-enhanced).

To provide a complete pictures, we list here cases in which in the absence of histology data it is possible to code morphology based on the 1999 ENCR guidelines:

- gliomas M-9380/3 of the brain stem, on the basis of diagnostic imaging;
- subependymal giant cell astrocytoma, on the basis of diagnostic imaging exclusively in patients with tuberous sclerosis;
- meningiomas, on the basis of diagnostic imaging;
- eye melanoma, on the basis of diagnostic imaging and/or clinical assessment (it must be remembered that lists of patients treated abroad should be reviewed for this disease, due to the importance of proton beam radiotherapy in treatment of eye melanoma)
- melanoma of the central nervous system on the basis of diagnostic imaging and/or clinical assessment;
- craniopharyngiomas, on the basis of diagnostic imaging;
- pituitary gland neoplasms, based on diagnostic imaging associated to specific hormone changes;
- lymphomas NOS (M-9590/3) based on diagnostic imaging showing exclusive brain location.

In the presence of a diagnosis pronounced certain by a clinician using the best diagnostic imaging techniques (i.e., when there is not doubt of differential diagnosis), it is recommended to record the morphology identified with basis of diagnosis code 2 (based on the principle that an explicit diagnosis should not be refuted by registrars).

Likewise, in the presence of certain diagnosis lf malignant glial tumor, made using the best diagnostic imaging techniques, with doubt involving differential diagnosis of glioblastoma, astrocytoma, and oligoastrocytoma, it is recommended to use morphology M-9380/3 (Glioma, NOS) with basis of diagnosis code 2.
When certainty, instead, refers to a differential diagnosis of glial vs. non-glial tumors, no final decision may be made as to morphology, and therefore morphology code M-8000 should be used.
As for the biological behavior of the tumor, the clinical-radiological opinion must be followed, since even benign or borderline tumors may result in patient death.
Finally, it must be borne in mind that there is no grading for benign tumors; therefore value "9" (unknown or not applicable) should be entered in the grading data field for this type of tumors.
In incidence analysis and reports, every registry must differentiate tumors based on a behavior code, in order to offer the best possible comparability among case sets, especially to avoid artifacts in comparisons between registries and unfounded differences in subsequent analysis of survival.

WHO histology grade

Registration of grading, albeit not indispensable, is important in central nervous system neoplasms because it is essential for the interpretation of the data concerning the clinical course of the disease. Use of the new WHO classification of brain tumors solves most problems of tumor grade identification, since the grade is in many cases implicit in the tumor histotype (ICD-O 3).

Grade I: tumors with low proliferation, frequently well contained and susceptible to being resolved by surgical therapy (e.g., pilocytic astrocytoma).

Grade II: generally infiltrating tumors with low mitotic activity but potentially relapsing. Some of them tend to progress towards higher grade lesions (e.g., well-differentiated astrocytomas, oligodendro-gliomas, and ependymomas).

Grade III: histological evidence of malignancy, generally under the form of mitosis, frankly infiltrative aspects and anaplastic features.

Grade IV: presence of mitosis, necrosis, rapid evolution of disease both before and after surgical treatment.

Note that these definitions do not follow the general indications for grading listed in the ICD-O rules for assigning the sixth digit of the morphology code, which instead mainly refers to grade of differentiation.
However, ICD-O-3 rules propose that CNS tumor grade be recorded using the criteria listed in Table 19 (page 30). WHO classification[22] is listed in Table 20 (page 31).

Endocrine gland neoplasms

Pituitary gland

WHO classification[23] in Table 21 (page 34).

Thyroid, parathyroid glands

WHO classification[23] in Table 22 (page 35).

Endocrine pancreas

WHO classification[23] in Table 23 (page 36).

Adrenal gland

WHO classification[23] in Table 24 (page 37).

Carcinoid tumors

Their coding is dealt with in the sections on single anatomic sites. It must be noted that these neoplasms underwent some of the greatest changes in the passage from the 1st to the 2nd ICD-O edition.
In the ICD-O-1 classification, Carcinoid tumor, NOS was considered of uncertain behavior and therefore to be coded as /1, while /3 was reserved for lesions explicitly defined as malignant (/1 forms were entered in incidence at the time of their conversion into malignant forms, in general manifested by the appearance of metastasis). Starting from ICD-O-2 all carcinoid tumors are instead considered malignant (behavior /3) with the exception of appendicular forms, which maintain behavior code /1 (obviously in the absence of metastasis). It is evident that this change in disease classification must be taken into account in historical studies of the disease.
It must be remembered that "carcinoid syndrome" is a paraneoplastic syndrome presenting vasomotor symptoms, intestinal hypermotility, bronchoconstriction with asthma, enlarged liver and systemic fibrosis, caused by hyperproduction of serotonin in the presence of certain carcinoids. A primary intestinal carcinoid tumor usually does not produce the syndrome, unless liver metastasis have already appeared (these are not necessary for the development of the syndrome in extra-intestinal carcinoid tumors), since the metabolic products of the tumor are inactivated by the liver. Therefore, when reviewing a clinical report on this disease, all information that may be useful in correctly identifying and coding the tumor must be collected.

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Tables

Table 1. Additional data fields to consider when registering pre-invasive cervical forms BACK

Data field	Description
multiple lesion	woman with single/multiple lesion(s) *Note: lesions arising at least 6 months after the previous are to be considered multiple*
progressive number of the cancer	in case of multiple lesions; does not include premalignant lesions when associated to a malignant tumor that has already been registered
date of histopathological examination	main surgery date
surgery	type of surgery performed: ❖ conservative surgery (saturation biopsy, conization ❖ not performed ❖ unknown
date of first invitation	date of first screening invitation
date of first screening test	date first screening test was performed
date of subsequent invitations	use n data fields for n invitations to screening received by patient
date of subsequent examinations	use n data fields for n screening tests taken by patient
screening status	proposed classification: see Chapter 2, "Screening programs"

Table 2. FIGO (1994) and TNM (2002) classification of cervical cancer BACK

FIGO 1994	Type	TNM 2002
stage 0	carcinoma in situ	TisN0
stage I	carcinoma confined to uterus	T1
stage Ia	lesion can be identified only by microscopic examination	T1a
stage Ia1	minimal stromal invasion (<5mm, horizontal spread <7 mm)	T1a1
stage Ia2	stromal invasion depth >3 and <5mm, horizontal spread <7 mm	T1a2
stage Ib	lesions larger than Ia2, confined to uterus	T1b
stage Ib1	cervix: <4 cm	
stage Ib2	cervix >4 cm	
stage II	tumor invades beyond uterus but not to pelvic wall or to lower third of the vagina	T2
stage IIA	without apparent parametrial invasion	T2a
stage IIB	with clear parametrial invasion	T2b
stage III	tumor extends to pelvic wall, involves lower third of vagina, and/or causes hydronephrosis and/or non-functioning kidney	T3
stage IIIA	tumor involves lower third of vagina	T3a
stage IIIB	❖ tumor extends to pelvic wall or causes hydronephrosis or non-functioning kidney with/without lymph node involvement	T3b, N0
	❖ all previous stages with lymph node involvement	T3b, N1 T1, N1 T2, N1
stage IV		
stage IVa	tumor invades bladder or bowel mucosa and/or extends beyond the true pelvis, with/without lymph node involvement	T4, Nx, M0
stage IVb	presence of distant metastasis, with/without lymph node involvement	Tx, Nx, M1

Table 3. WHO: histological classification of cervical cancer[1] BACK

Epithelial tumors	
8013/3	Large cell neuroendocrine carcinoma
8015/3	Glassy cell carcinoma
8020/3	Carcinoma, undifferentiated, NOS
8041/3	Small cell carcinoma, NOS
8051/3	Verrucous carcinoma, NOS
8052/3	Papillary squamous cell carcinoma
8070/2	Squamous cell carcinoma in situ, NOS
8070/3	Squamous cell carcinoma, NOS
8071/3	Squamous cell carcinoma, keratinising, NOS
8072/3	Squamous cell carcinoma, large cell, non-keratinising, NOS
8076/3	Squamous cell carcinoma, microinvasive
8077/2	Squamous intraepithelial neoplasia, grade III
	CIN III
8082/3	Lymphoepithelial carcinoma
8083/3	Basaloid squamous cell carcinoma
8098/3	Adenoid basal carcinoma
8120/3	Transitional cell carcinoma, NOS
8140/2	Adenocarcinoma in situ, NOS
8140/3	Adenocarcinoma, NOS
8144/3	Adenocarcinoma, intestinal type
8200/3	Adenoid cystic carcinoma
8240/3	Carcinoid tumor, NOS
8249/3	Atypical carcinoid tumor
8262/3	Villous adenocarcinoma
8310/3	Clear cell adenocarcinoma, NOS
8380/3	Endometrioid adenocarcinoma, NOS
8441/3	Serous cystadenocarcinoma, NOS
8480/3	Mucinous adenocarcinoma
8482/3	Mucinous adenocarcinoma, endocervical type
8480/3	Mucinous adenocarcinoma
8490/3	Signet ring cell carcinoma
8560/3	Adenosquamous carcinoma
9110/3	Mesonephroma, malignant
Mesenchymal tumors	
8805/3	Undifferentiated sarcoma
8890/3	Leiomyosarcoma, NOS
8910/3	Embryonal rhabdomyosarcoma, NOS
8931/3	Endometrial stromal sarcoma, low grade
9120/3	Hemangiosarcoma
9540/3	Malignant peripheral nerve sheath tumor
9581/3	Alveolar soft part sarcoma
Mixed epithelial and mesenchymal tumors	
8933/3	Adenosarcoma
8960/3	Nephroblastoma, NOS
8980/3	Carcinosarcoma, NOS
Melanocytic tumors	
8720/3	Malignant melanoma, NOS
Miscellaneous tumors	
9071/3	Yolk sac tumor

Table 4. FIGO (1988) and TNM (1992-2002) classification of endometrial cancer BACK

FIGO 1988	tumor limited to endometrium	TNM 1992-2002	1993 TNM notes
Ia	Tumor limited to endometrium	T1a	
Ib	tumor invades the internal half of the myometrium	T1b	
Ic	tumor invades the external half of the myometrium	T1c	
IIa	endocervical glandular involvement, with no evidence of stromal invasion	T2a	
IIb	cervical stromal invasion	T2b	including invasion of the bladder or rectum wall, excluding mucosa
IIIa	tumor involves serosa and/or adnexa; and/or cancer cells in ascites or peritoneal washings	T3a	serosa or adnexa involvement can be discontinuous
IIIb	vaginal metastasis	T3b	including clinical extension to pelvic wall
IIIc	metastasis to pelvic and/or para-aortic lymph nodes	Tx, N1	extension to bladder and bowel mucosa
IVa	tumor invades bladder and/or rectum	T4	
IVb	distant metastasis, including endoabdominal and/or inguinal lymph node metastasis	Tx, Nx, M1	

Table 5. WHO: histological classification of tumors of the uterine corpus[1] BACK

Epithelial tumors	
8020/3	Carcinoma, undifferentiated, NOS
8041/3	Small cell carcinoma, NOS
8070/3	Squamous cell carcinoma, NOS
8120/3	Transitional cell carcinoma, NOS
8262/3	Villous adenocarcinoma
8310/3	Clear cell adenocarcinoma, NOS
8323/3	Mixed cell adenocarcinoma
8380/3	Endometrioid adenocarcinoma, NOS
8382/3	Endometrioid adenocarcinoma, secretory variant
8383/3	Endometrioid adenocarcinoma, ciliated cell variant
8441/3	Serous cystadenocarcinoma, NOS
8480/3	Mucinous adenocarcinoma
8570/3	Adenocarcinoma with squamous metaplasia
Mesenchymal tumors	
8890/3	Leiomyosarcoma, NOS
8890/1	Leiomyomatosis, NOS
8891/0	Epithelioid leiomyoma(/1 in ICD-O)
8891/3	Epithelioid leiomyosarcoma
8892/0	Cellular leiomyoma(/1 in ICD-O)
8896/3	Myxoid leiomyosarcoma
8897/1	Smooth muscle tumor of uncertain malignant potential
8898/1	Metastasising leiomyoma
8930/3	Endometrial stromal sarcoma, NOS
8931/3	Endometrial stromal sarcoma, low grade
Mixed epithelial and mesenchymal tumors	
8933/3	Adenosarcoma
8934/3	Carcinofibroma
8980/3	Carcinosarcoma, NOS
Trophoblastic diseases	
9100/1	Invasive hydatidiform mole
9100/3	Choriocarcinoma, NOS
9104/1	Placental site trophoblastic tumor
9105/3	Trophoblastic tumor, epithelioid

Table 6. WHO: histological classification of tumors of the ovary[1] BACK

Serous tumors	
8441/3	Serous cystadenocarcinoma, NOS
8442/1	Serous cystadenoma, borderline malignancy
8461/3	Serous surface papillary carcinoma
8462/1	Serous papillary cystic tumor of borderline malignancy
8463/1	Serous surface papillary tumor of borderline malignancy
9014/1	Serous adenofibroma of borderline malignancy
9014/3	Serous adenocarcinofibroma
Mucinous tumors	
8472/1	Mucinous cystic tumor of borderline malignancy
8480/3	Mucinous adenocarcinoma
9015/3	Mucinous adenocarcinofibroma
Endometrioid tumors and variants	
8380/1	Endometrioid adenoma, borderline malignancy
8380/3	Endometrioid adenocarcinoma, NOS
8381/1	Endometrioid adenofibroma, borderline malignancy
8381/3	Endometrioid adenofibroma, malignant
8805/3	Undifferentiated sarcoma
8931/3	Endometrial stromal sarcoma, low grade
8933/3	Adenosarcoma
8950/3	Müllerian mixed tumor
Clear cell tumors	
8120/3	Transitional cell carcinoma, NOS
8310/1	Clear cell tumor, borderline malignancy
8310/3	Clear cell adenocarcinoma, NOS
8313/1	Clear cell adenofibroma of borderline malignancy
8313/3	Clear cell adenocarcinofibroma
9000/1	Brenner tumor, borderline malignancy
9000/3	Brenner tumor, malignant
Squamous cell tumors	
8070/3	Squamous cell carcinoma, NOS
Mixed epithelial tumors	
8323/1	Mixed cell tumor, borderline malignancy
8323/3	Mixed cell adenocarcinoma
Undifferentiated and unclassified tumors	
8020/3	Carcinoma, undifferentiated, NOS
8140/3	Adenocarcinoma, NOS
Gonadal stromal tumors	
8593/1	Stromal tumor with minor sex cord elements
8620/1	Granulosa cell tumor, adult type
8622/1	Granulosa cell tumor, juvenile
8810/1	Cellular fibroma
8810/3	Fibrosarcoma, NOS
Sertoli cell tumors	
8631/1	Sertoli-Leydig cell tumor of intermediate differentiation
8631/3	Sertoli-Leydig cell tumor, poorly differentiated
8633/1	Sertoli-Leydig cell tumor, retiform
8634/1	Sertoli-Leydig cell tumor, intermediate differentiation, with heterologous elements
8634/3	Sertoli-Leydig cell tumor, poorly differentiated, with heterologous elements
8640/1	Sertoli cell tumor, NOS

Table 7. WHO: histological classification of tumors of the Fallopian tubes and ligaments[1] BACK

Epithelial tumors	
8020/3	Carcinoma, undifferentiated, NOS
8070/3	Squamous cell carcinoma, NOS
8120/3	Transitional cell carcinoma, NOS
8310/3	Clear cell adenocarcinoma, NOS
8380/1	Endometrioid adenoma, borderline malignancy
8380/3	Endometrioid adenocarcinoma, NOS
8441/3	Serous cystadenocarcinoma, NOS
8442/1	Serous cystadenoma, borderline malignancy
8472/1	Mucinous cystic tumor of borderline malignancy
8480/3	Mucinous adenocarcinoma
Mixed epithelial-mesenchymal tumors	
8933/3	Adenosarcoma
8950/3	Mixed Müllerian tumor
Soft tissue tumors	
8890/3	Leiomyosarcoma, NOS
Germ-cell tumors	
9080/3	Teratoma, malignant, NOS
Trophoblastic diseases	
9100/3	Choriocarcinoma, NOS
9104/1	Placental site trophoblastic tumor
Tumors of the broad ligament and other uterine ligaments	
tumors of the Müllerian epithelium	
8310/3	Clear cell adenocarcinoma, NOS
8380/3	Endometrioid adenocarcinoma, NOS
8460/3	Papillary serous cystadenocarcinoma
8480/3	Mucinous adenocarcinoma
miscellaneous tumors	
8933/3	Adenosarcoma
9110/1	Mesonephric tumor, NOS
9391/3	Ependymoma, NOS
Mixed and unclassified gonadal stromal tumors	
8623/1	Sex cord tumor with annular tubules
8632/1	Gynandroblastoma
8590/1	Sex cord-gonadal stromal tumor, NOS
Steroid cell tumors	
8650/1	Leydig cell tumor, NOS
8670/3	Steroid cell tumor, malignant
Germ-cell tumors	
9060/3	Dysgerminoma
9070/3	Embryonal carcinoma, NOS
9071/3	Yolk sac tumor
9072/3	Polyembryoma
9085/3	Mixed germ-cell tumor
9100/3	Choriocarcinoma, NOS
Biphasic or triphasic teratomas	
9080/3	Teratoma, malignant, NOS

Monodermal teratomas	
8070/3	Squamous cell carcinoma, NOS
8140/3	Adenocarcinoma, NOS
8240/3	Carcinoid tumor, NOS
8243/3	Goblet cell carcinoid
8410/3	Sebaceous adenocarcinoma
8720/3	Malignant melanoma, NOS
9090/3	Struma ovarii, malignant
9091/1	Strumal carcinoid
9391/3	Ependymoma, NOS
9440/3	Glioblastoma, NOS
9473/3	Primitive neuroectodermal tumor, NOS
9501/3	Medulloepithelioma, NOS
Germ-cell and gonadal stromal tumors	
9073/1	Gonadoblastoma
Tumors of the rete ovarii	
9110/3	Mesonephroma, malignant
Miscellaneous tumors	
8013/3	Large cell neuroendocrine carcinoma
8041/3	Small cell carcinoma, NOS
8090/1	Basal cell tumor
8200/3	Adenoid cystic carcinoma
8576/3	Hepatoid adenocarcinoma
8693/1	Extra-adrenal paraganglioma, NOS
8960/3	Nephroblastoma, NOS
9050/3	Mesothelioma, malignant
9100/3	Choriocarcinoma, NOS
9110/1	Mesonephric tumor, NOS
Tumors of the lymphatic system	
9734/3	Plasmacytoma, extramedullary (not occurring in bone)

Table 8. WHO: histological classification of tumors of the vagina[1] BACK

Epithelial tumors	
8020/3	Carcinoma, undifferentiated, NOS
8041/3	Small cell carcinoma, NOS
8051/3	Verrucous carcinoma, NOS
8070/2	Squamous cell carcinoma *in situ*, NOS
8070/3	Squamous cell carcinoma, NOS
8071/3	Squamous cell carcinoma, keratinising, NOS
8072/3	Squamous cell carcinoma, large cell, non-keratinising, NOS
8077/2	Squamous intraepithelial neoplasia, grade III VAIN III
8083/3	Basaloid squamous cell carcinoma
8098/3	Adenoid basal carcinoma
8200/3	Adenoid cystic carcinoma
8240/3	Carcinoid tumor, NOS
8310/3	Clear cell adenocarcinoma, NOS
8380/3	Endometrioid adenocarcinoma, NOS
8480/3	Mucinous adenocarcinoma
8560/3	Adenosquamous carcinoma
9110/3	Mesonephroma, malignant
Soft tissue tumors	
8805/3	Undifferentiated sarcoma
8841/1	Angiomyxoma
8890/3	Leiomyosarcoma, NOS
8910/3	Embryonal rhabdomyosarcoma, NOS
8931/3	Endometrial stromal sarcoma, low grade
Mixed epithelial and mesenchymal tumors	
8933/3	Adenosarcoma
8940/3	Mixed tumor, malignant, NOS
8980/3	Carcinosarcoma, NOS
Melanocytic tumors	
8720/3	Malignant melanoma, NOS
Miscellaneous tumors	
9071/3	Yolk sac tumor
9260/3	Ewing's sarcoma
9364/3	Peripheral neuroectodermal tumor

Table 9. WHO: histological classification of tumors of the vulva[1] BACK

Epithelial tumors	
8041/3	Small cell carcinoma, NOS
8070/2	Squamous cell carcinoma in situ, NOS
8070/3	Squamous cell carcinoma, NOS
8071/3	Squamous cell carcinoma, keratinising, NOS
8072/3	Squamous cell carcinoma, large cell, non-keratinising, NOS
8083/3	Basaloid squamous cell carcinoma
8051/3	Verrucous carcinoma, NOS
8077/2	Squamous intraepithelial neoplasia, grade III VIN III
8090/3	Basal cell carcinoma, NOS
8120/3	Transitional cell carcinoma, NOS
8140/3	Adenocarcinoma, NOS
8200/3	Adenoid cystic carcinoma
8500/3	Infiltrating duct carcinoma, NOS
8542/3	Paget's disease, extramammary
8560/3	Adenosquamous carcinoma
Adnexal tumors of the skin	
8400/3	Sweat gland adenocarcinoma
8410/3	Sebaceous adenocarcinoma
Soft tissue tumors	
8804/3	Epithelioid sarcoma
8832/3	Dermatofibrosarcoma, NOS
8841/1	Angiomyxoma
8850/3	Liposarcoma, NOS
8890/3	Leiomyosarcoma, NOS
8910/3	Embryonal rhabdomyosarcoma, NOS
9581/3	Alveolar soft part sarcoma
Melanocytic tumors	
8720/3	Malignant melanoma, NOS
Miscellaneous tumors	
8247/3	Merkel cell carcinoma
9071/3	Yolk sac tumor
9260/3	Ewing's sarcoma
9364/3	Peripheral neuroectodermal tumor

Table 10. Additional data fields to consider in prostate cancer registration BACK

Data field	Description
laterality	right lobe, left lobe, both lobes
Gleason score I	primary Gleason score
Gleason score II	secondary Gleason score
grading	histopathological grading: GX, G1, G2, G3-4
vascular invasion	absent, present
perineural invasion	absent, present
PIN	absence/presence or intraepithelial prostate cancer
extension of invasive cancer	❖ right lobe up to 50%; right lobe over 50% ❖ left lobe up to 50%; left lobe over 50% ❖ bilateral
extraprostatic extension	cannot be assessed; absent; right lobe; left lobe; both lobes
surgical margins	cannot be assessed; not involved; right lobe, left lobe, both lobes
seminal vesicles	not present; not assessable, not involved; involved
adjacent structures	not involved; involved
examined pelvic lymph nodes	number of total lymph nodes examined
metastatic pelvic lymph nodes	number of metastatic lymph nodes
other lymph nodes	lymphadenectomy site
other lymph nodes examined	other total lymph nodes examined
other metastatic lymph nodes	other metastatic lymph nodes
intraoperative staging	intraoperative lymphadenectomy
pT	UICC 2002 TNM 6th edition coding
pN	UICC 2002 TNM 6th edition coding
immunohistochemistry stage N	immunohistochemical exam performed for pN staging
surgery date	date of main surgery
surgery	type of surgery performed: ❖ single needle biopsy ❖ multiple needle biopsy ❖ TURP (transurethral resection) ❖ nodulectomy ❖ prostatectomy ❖ robotic laparoscopic prostatectomy ❖ radical prostatectomy ❖ unknown
date of preoperative therapy	start date for preoperative therapy
type of preoperative therapy	unknown, no therapy, hormone therapy, radiation therapy

Table 11. 2002 TNM prostate cancer staging – Difference between pT, cT, and M staging BACK

cT		Description	pT	
TX		primary tumor cannot be assessed		
T1		clinically unapparent tumor, not palpable nor visible by imaging	not applicable	
	T1a	❖ tumor incidental histologic finding in 5% or less of tissue resected	not applicable	
	T1b	❖ tumor incidental histologic finding in more than 5% of tissue resected	not applicable	
	T1c	❖ tumor identified by needle biopsy (e.g., because of elevated PSA)	not applicable	
T2		tumor confined within the prostate (a tumor identified in one or both lobes by needle biopsy, but not palpable nor visible by imaging is classified as T1c)	T2	
	T2a	❖ tumor involves one half of one lobe or less		T2a
	T2b	❖ tumor involves more than one half of one lobe but not both lobes		T2b
	T2c	❖ tumor involves both lobes		T2c
T3		tumor extends through the prostate capsule (invasion of the apex or capsule of the prostate but not beyond is not classified as T3 but as T2)	T3	
	T3a	❖ extracapsular extension (unilateral or bilateral)		T3a
	T3b	❖ tumor invades seminal vesicle(s)		T3b
T4		tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall	T4	
MX		distant metastasis cannot be assessed		
M0		no distant metastasis		
M1		distant metastasis		
	M1a	❖ metastasis in non-regional lymph node(s)		
	M1b	❖ bone metastasis		
	M1c	❖ metastasis in other sites with or without bone disease		

Table 12. Histopathological grading vs. Gleason score in prostate cancer BACK

Grading	Description	Gleason score
GX	grade cannot be assessed	
G1	well differentiated (slight anaplasia)	2-4
G2	moderately differentiated (moderate anaplasia)	5-6
G3-G4	poorly differentiated or undifferentiated (marked anaplasia)	7-10

Table 13. Clinical staging of prostate cancer BACK

Stage I	T1a	N0	M0	G1
Stage II	T1a	N0	M0	G2, G3-4
	T1b	N0	M0	any G
	T1c	N0	M0	any G
	T1	N0	M0	any G
	T2	N0	M0	any G
Stage III	T3	N0	M0	any G
Stage IV	T4	N0	M0	any G
	any T	N1	M0	any G
	any T	any N	M1	any G

Table 14. Risk of prostate cancer based on PSA level BACK

PSA >2.5 ng/ml and ″4.0 ng/ml	20-25%
PSA between 4.1 ng/ml and 9.9 ng/ml	30-35%
PSA ≥10 ng/ml	67%*
** the risk increases if a PSA increase is documented*	

Table 15. WHO: histological classification of tumors of the urinary system and male genital organs[6]

BACK

Histological classification of prostate and seminal vesicle tumors	
Epithelial tumors	
8070/3	Squamous cell carcinoma, NOS
8082/3	Lymphoepithelial carcinoma
8120/3	Transitional cell carcinoma, NOS
8140/3	Adenocarcinoma, NOS
8147/3	Basal cell adenocarcinoma
8148/2	Glandular intraepithelial neoplasia, grade III PIN III
8201/3	Cribriform carcinoma, NOS
8230/3	Solid carcinoma, NOS
8260/3	Papillary adenocarcinoma, NOS
8290/3	Oxyphilic adenocarcinoma
8480/3	Mucinous adenocarcinoma
8490/3	Signet ring cell carcinoma
8500/3	Infiltrating duct carcinoma, NOS
8560/3	Adenosquamous carcinoma
8572/3	Adenocarcinoma with spindle cell metaplasia
Neuroendocrin tumors	
8041/3	Small cell carcinoma, NOS
8240/3	Carcinoid tumor, NOS
8574/3	Adenocarcinoma with neuroendocrine differentiation
8680/1	Paraganglioma, NOS
9500/3	Neuroblastoma, NOS
Prostatic stromal tumors	
8935/1	Stromal tumor, NOS
8935/3	Stromal sarcoma, NOS
Mesenchymal tumors	
8830/3	Malignant fibrous histiocytoma
8890/3	Leiomyosarcoma, NOS
8900/3	Rhabdomyosarcoma, NOS
9120/3	Hemangiosarcoma
9150/1	Hemangiopericytoma, NOS
9220/3	Chondrosarcoma, NOS
9540/3	Malignant peripheral nerve sheath tumor
Miscellaneous tumors	
8310/3	Clear cell adenocarcinoma, NOS
8720/3	Malignant melanoma, NOS
8960/3	Nephroblastoma, NOS
8963/3	Malignant rhabdoid tumor
9061/3	Seminoma, NOS
9071/3	Yolk sac tumor
9081/3	Teratocarcinoma
9100/3	Choriocarcinoma, NOS
Epithelial tumors of the seminal vesicles	
8140/3	Adenocarcinoma, NOS
Mesenchymal tumors of the seminal vesicles	
8830/3	Malignant fibrous histiocytoma
8850/3	Liposarcoma, NOS
8890/3	Leiomyosarcoma, NOS
9120/3	Hemangiosarcoma
9150/1	Hemangiopericytoma, NOS
Miscellaneous tumors of the seminal vesicles	
9100/3	Choriocarcinoma, NOS

Table 16. WHO: histological classification of tumors of the urinary system and male genital organs[6] BACK

Histological classification of tumors of the penis	
Malignant epithelial tumors	
8041/3	Small cell carcinoma, NOS
8050/3	Papillary carcinoma, NOS
8051/3	Verrucous carcinoma, NOS
8070/3	Squamous cell carcinoma, NOS
8074/3	Squamous cell carcinoma, spindle cell
8083/3	Basaloid squamous cell carcinoma
8090/3	Basal cell carcinoma, NOS
8247/3	Merkel cell carcinoma
8310/3	Clear cell adenocarcinoma, NOS
8410/3	Sebaceous adenocarcinoma
8560/3	Adenosquamous carcinoma
Precursors	
8077/2	Squamous intraepithelial neoplasia, grade III
8080/2	Queyrat's erythroplasia
8081/2	Bowen's disease
8542/3	Paget's disease, extramammary
Melanocytic tumors	
8720/3	Malignant melanoma, NOS

Histological classification of tumors of the testicle	
Germ-cell tumors	
9064/2	Intratubular malignant germ cells
Pure forms	
9061/3	Seminoma, NOS
9063/3	Spermatocytic seminoma
9070/3	Embryonal carcinoma, NOS
9071/3	Yolk sac tumor
9080/3	Teratoma, malignant, NOS
9084/3	Teratoma with malignant transformation
9100/3	Choriocarcinoma, NOS
9104/1	Placental site trophoblastic tumor
Mixed forms	
9081/3	Teratocarcinoma
9085/3	Mixed germ cell tumor
9101/3	Choriocarcinoma combined with other germ-cell elements
Gonadal stromal tumors	
Pure forms	
8590/3	Sex cord-gonadal stromal tumor, malignant
8591/1	Sex cord-gonadal stromal tumor, incompletely differentiated
8592/1	Sex cord-gonadal stromal tumor, mixed forms
8620/1	Granulosa cell tumor, adult type
8622/1	Granulosa cell tumor, juvenile
8640/1	Sertoli cell tumor, NOS
8640/3	Sertoli cell carcinoma
8642/1	Large cell calcifying Sertoli cell tumor
8650/1	Leydig cell tumor, NOS
8650/3	Leydig cell tumor, malignant
9073/1	Gonadoblastoma

Miscellaneous tumors	
8240/3	Carcinoid tumor, NOS
8380/3	Endometrioid adenocarcinoma, NOS
8441/3	Serous cystadenocarcinoma, NOS
8442/1	Serous cystadenoma, borderline malignancy
8470/3	Mucinous cystadenocarcinoma, NOS
8680/1	Paraganglioma, NOS
8960/3	Nephroblastoma, NOS
Tumors of the vasa deferentia and the rete testis	
8140/3	Adenocarcinoma, NOS
Tumors of the paratesticular structures	
8140/3	Adenocarcinoma, NOS
8806/3	Desmoplastic small round cell tumor
9050/3	Mesothelioma, malignant

Table 17. WHO: histological classification of tumors of the urinary tract[6] BACK

Urothelial tumors	
8020/3	Carcinoma, undifferentiated, NOS
8031/3	Giant cell carcinoma
8082/3	Lymphoepithelial carcinoma
8120/0	Transitional cell papilloma, benign
8120/2	Transitional cell carcinoma in situ
8120/3	Transitional cell carcinoma, NOS
8121/0	Schneiderian papilloma, NOS
8122/3	Transitional cell carcinoma, spindle cell
8130/1	Papillary transitional cell neoplasm of low malignant potential
8130/2	Papillary transitional cell carcinoma, non-invasive
8130/3	Papillary transitional cell carcinoma
8131/3	Transitional cell carcinoma, micropapillary
Squamous neoplasms	
8051/3	Verrucous carcinoma, NOS
8052/3	Papillary squamous cell carcinoma
8070/3	Squamous cell carcinoma, NOS
Glandular neoplasms	
8140/3	Adenocarcinoma, NOS
8310/3	Clear cell adenocarcinoma, NOS
8480/3	Mucinous adenocarcinoma
8490/3	Signet ring cell carcinoma
Neuroendocrine tumors	
8041/3	Small cell carcinoma, NOS
8240/3	Carcinoid tumor, NOS
8680/1	Paraganglioma, NOS
Melanocytic tumors	
8720/3	Malignant melanoma, NOS
Mesenchymal tumors	
8830/3	Malignant fibrous histiocytoma
8890/3	Leiomyosarcoma, NOS
8900/3	Rhabdomyosarcoma, NOS
9120/3	Hemangiosarcoma
9180/3	Osteosarcoma, NOS
Tumors of the lymphatic system	
9731/3	Plasmacytoma, NOS

Table 18. WHO: histological classification of tumors of the kidney[6] BACK

Renal cell tumors	
8260/3	Papillary adenocarcinoma, NOS
8310/3	Clear cell adenocarcinoma, NOS
8312/3	Renal cell carcinoma, NOS
8317/3	Renal cell carcinoma, chromophobe type
8319/3	Collecting duct carcinoma
Metanephric tumors	
8935/1	Stromal tumor, NOS
Nephroblastic tumors	
8959/1	Cystic partially differentiated nephroblastoma
8960/3	Nephroblastoma, NOS
Mesenchymal tumors	
8830/3	Malignant fibrous histiocytoma
8890/3	Leiomyosarcoma, NOS
8900/3	Rhabdomyosarcoma, NOS
8960/1	Mesoblastic nephroma
8963/3	Malignant rhabdoid tumor
8964/3	Clear cell sarcoma of kidney
9120/3	Hemangiosarcoma
9150/1	Hemangiopericytoma, NOS
9180/3	Osteosarcoma, NOS
Mixed mesenchymal and epithelial tumors	
8959/0	Benign cystic nephroma
9040/3	Synovial sarcoma, NOS
Neuroendocrine tumors	
8240/3	Carcinoid tumor, NOS
8246/3	Neuroendocrine carcinoma, NOS
9364/3	Peripheral neuroectodermal tumor
9500/3	Neuroblastoma, NOS
Tumors of the lymphatic system	
9731/3	Plasmacytoma, NOS
Germ-cell tumors	
9080/1	Teratoma, NOS
9100/3	Choriocarcinoma, NOS

Table 19. ICD-O rules for CNS tumor grade registration BACK

Histological types to code	WHO grade	ICD-O code	ICD-O behavior code (5th digit)
Astrocytomas			
subependymal giant cell astrocytoma	I	9384	1
pilocytic	I	9421	1
low grade	II	9400	3
pleomorphic xanthroastrocytoma	II-III	9424	3
anaplastic	III	9401	3
glioblastoma	IV	9440	3
Oligodendrogliomas			
low grade	II	9450	3
anaplastic	III	9451	3
Oligoastrocytomas			
low grade	II	9382	3
anaplastic	III	9382	3
Ependymal tumors (ependymomas)			
subependymoma	I	9383	1
myxopapillary	I	9394	1
low grade	II	9391	3
anaplastic	III	9392	3
Choroid plexus tumor			
papilloma	I	9390	0
carcinoma	III-IV	9390	3
Neuronal/glial tumors			
gangliocytoma	I	9492	0
ganglioglioma	I-II	9505	1
ganglioglioma, anaplastic	III	9505	3
desmoplastic infantile ganglioglioma	I	9412	1
disembryoplastic neuroepithelial tumor	I	9413	0
central neurocytoma	I	9506	1
Pineal tumors			
pineocytoma	II	9361	1
pineal parenchymal tumor of intermediate diff.	III-IV	9362	3
pinealoblastoma	IV	9362	3
Embryonal tumors			
medulloblastoma	III	9470	3
other PNET	III	9473	3
medulloepithelioma	III	9501	3
neuroblastoma	III	9500	3
ependymoblastoma	III	9392	3
Tumors of cranial and spinal nerves			
schwannoma	I	9560	0
malignant peripheral nerve sheath tumor	III-IV	9540	3
Meningeal tumors			
meningioma	I	9530	0
atypical meningioma	II	9539	1
papillary meningioma	II-III	9538	3
hemangiopericytoma	II-III	9150	3
anaplastic meningioma	III	9530	3

Table 20. WHO: histological classification of tumors of the nervous system[22] BACK

Neuroepithelial tumors	
Astrocytic tumors	
9384/1	Subependymal giant cell astrocytoma
9400/3	Astrocytoma, NOS
9401/3	Astrocytoma, anaplastic
9410/3	Protoplasmic astrocytoma
9411/3	Gemistocytic astrocytoma
9420/3	Fibrillary astrocytoma
9421/1	Pilocytic astrocytoma
9424/3	Pleomorphic xanthroastrocytoma
9440/3	Glioblastoma, NOS
9441/3	Giant cell glioblastoma
9442/3	Gliosarcoma
Oligodendroglial tumors	
9450/3	Oligodendroglioma, NOS
9451/3	Oligodendroglioma, anaplastic
Mixed gliomas	
9382/3	Mixed glioma
Ependymal tumors	
9383/1	Subependymoma
9391/3	Ependymoma, NOS
9392/3	Ependymoma, anaplastic
9393/3	Papillary ependymoma
9394/1	Myxopapillary ependymoma
Choroid plexus tumors	
9390/0	Choroid plexus papilloma, NOS
9390/3	Choroid plexus carcinoma
Glial tumors of uncertain origin	
9381/3	Gliomatosis cerebri
9430/3	Astroblastoma
9444/1	Chordoid glioma
Neuronal and mixed glial-neuronal tumors	
8680/1	Paraganglioma, NOS
9412/1	Desmoplastic infantile astrocytoma
9413/0	Dysembryoplastic neuroepithelial tumor
9492/0	Gangliocytoma
9493/0	Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
9505/1	Ganglioglioma, NOS
9505/3	Ganglioglioma, anaplastic
9506/1	Central neurocytoma
Neuroblastic tumors	
9500/3	Neuroblastoma, NOS
9522/3	Olfactory neuroblastoma
9523/3	Olfactory neuroepithelioma
Pineal gland tumors	
9361/1	Pineocytoma
9362/3	Pineoblastoma

Embryonal tumors

9392/3	Ependymoma, anaplastic
9501/3	Medulloepithelioma, NOS
9470/3	Medulloblastoma, NOS
9471/3	Desmoplastic nodular medulloblastoma
9472/3	Medullomyoblastoma
9473/3	Primitive neuroectodermal tumor, NOS
9474/3	Large cell medulloblastoma
9490/3	Ganglioneuroblastoma
9500/3	Neuroblastoma, NOS
9508/3	Atypical teratoid/rhabdoid tumor

Peripheral nerve tumors

9540/0	Neurofibroma, NOS
9540/3	Malignant peripheral nerve sheath tumor- MPNST
9550/0	Plexiform neurofibroma
9560/0	Neurilemmoma, NOS
9571/0	Perineurioma, NOS

Meningeal tumors

Meningothelial tumors

9530/0	Meningioma, NOS
9530/3	Meningioma, malignant
9531/0	Meningothelial meningioma
9532/0	Fibrous meningioma
9533/0	Psammomatous meningioma
9534/0	Angiomatous meningioma
9537/0	Transitional meningioma
9538/1	Clear cell meningioma
9538/3	Papillary meningioma
9539/1	Atypical meningioma

Non-meningothelial mesenchymal tumors

8810/3	Fibrosarcoma, NOS
8815/0	Solitary fibrous tumor
8830/3	Malignant fibrous histiocytoma
8850/0	Lipoma, NOS
8850/3	Liposarcoma, NOS
8861/0	Angiolipoma, NOS
8880/0	Hibernoma
8890/0	Leiomyoma, NOS
8890/3	Leiomyosarcoma, NOS
8900/0	Rhabdomyoma, NOS
8900/3	Rhabdomyosarcoma, NOS
9120/0	Hemangioma, NOS
9120/3	Hemangiosarcoma
9133/1	Epithelioid hemangioendothelioma, NOS
9140/3	Kaposi's sarcoma
9150/1	Hemangiopericytoma, NOS
9180/0	Osteoma, NOS
9180/3	Osteosarcoma, NOS
9220/0	Chondroma, NOS
9220/3	Chondrosarcoma, NOS
9210/0	Osteochondroma

Primary melanocytic lesions

8720/3	Malignant melanoma, NOS
8728/0	Diffuse melanocytosis
8728/1	Meningeal melanocytoma
8728/3	Meningeal melanomatosis

Tumors of uncertain histogenesis

9161/1	Hemangioblastoma

Tumors of the lymphatic system	
9590/3	Malignant lymphoma, NOS
9731/3	Plasmacytoma, NOS
9930/3	Myeloid sarcoma (see also M-9861/3)

Germ-cell tumors	
9064/3	Germinoma
9070/3	Embryonal carcinoma, NOS
9071/3	Yolk sac tumor
9080/1	Teratoma, NOS
9080/0	Teratoma, benign
9084/3	Teratoma with malignant transformation
9085/3	Mixed germ-cell tumor
9100/3	Choriocarcinoma, NOS

Tumors of the sellar region	
9350/1	Craniopharyngioma
9351/1	Craniopharyngioma, adamantinomatous
9352/1	Craniopharyngioma, papillary
9582/0	Granular cell tumor of the sellar region

Table 21. WHO: histological classification of tumors of the endocrine glands[23] BACK
Pituitary gland

Adenomas	
8272/0	Pituitary adenoma, NOS
8272/1	Atypical pituitary adenoma
Carcinoma	
8272/3	Pituitary carcinoma, NOS

Table 22. WHO: histological classification of tumors of the endocrine glands[23] BACK
Thyroid and parathyroid glands

Thyroid carcinomas	
8020/3	Carcinoma, undifferentiated, NOS
8070/3	Squamous cell carcinoma, NOS
8260/3	Papillary adenocarcinoma, NOS
8330/3	Follicular adenocarcinoma, NOS
8345/3	Medullary carcinoma with amyloid stroma
8346/3	Mixed medullary-follicular carcinoma (C73.9)
8430/3	Mucoepidermoid carcinoma
8480/3	Mucinous adenocarcinoma
8588/3	Spindle epithelial tumor with thymus-like differentiation (SETTLE)
8589/3	Carcinoma showing thymus-like differentiation (CASTLE)
Other thyroid tumors	
9080/1	Teratoma, NOS
8580/1	Thymoma, NOS
9120/3	Hemangiosarcoma
8693/1	Extra-adrenal paraganglioma, NOS
9758/3	Follicular dendritic cell sarcoma
9751/1	Langerhans cell histiocytosis, NOS
Parathyroid gland tumors	
8140/3	Adenocarcinoma, NOS

Table 23. WHO: histological classification of tumors of the endocrine glands[23] BACK
Endocrine pancreas

Well differentiated endocrine tumors	
8150/1	Islet cell tumor, NOS
8150/3	Islet cell carcinoma
8151/1	Atypical insulinoma
8151/3	Insulinoma, malignant
8152/1	Glucagonoma, NOS
8152/3	Glucagonoma, malignant
8153/1	Gastrinoma, NOS
8153/3	Gastrinoma, malignant
8155/1	Vipoma, NOS
8155/3	Vipoma, malignant
8156/1	Somatostatinoma, NOS
8241/3	Enterochromaffin cell carcinoid
Poorly differentiated endocrine carcinomas	
8041/3	Small cell carcinoma, NOS
Mixed exocrine-endocrine carcinomas	
8154/3	Mixed islet cell and exocrine adenocarcinoma

Table 24. WHO: histological classification of tumors of the endocrine glands[23] BACK
Adrenal gland

Adrenal cortical tumors	
8370/3	Adrenal cortical carcinoma
Adrenal medullary tumors	
8700/3	Phaeochromocytoma, malignant
Extra-adrenal paragangliomas	
8690/1	Glomus jugulare tumor, NOS
8691/1	Aortic body tumor
8692/1	Carotid body tumor
8693/1	Extra-adrenal paraganglioma, NOS
8693/1	Extra-adrenal paraganglioma, NOS
Other adrenal tumors	
8590/1	Sex cord-gonadal stromal tumor, NOS
9080/1	Teratoma, NOS
9120/3	Hemangiosarcoma