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RESEARCH ARTICLE

French Brain Tumor DataBase: 5-Year Histological Results on 25 756 Cases

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Keywords
brain tumor, database, epidemiology, neuro-oncology, neuropathology, neurosurgery.

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Abstract

This work aimed to prospectively record all primary central nervous system tumor (PCNST) cases in France, for which histological diagnosis is available. The objectives were to (i) create a national registry and a network to perform epidemiological studies; (ii) implement clinical and basic research protocols; and (iii) harmonize the health care of patients affected by PCNST. For 5 years, 25 756 cases of newly diagnosed and histologically confirmed PCNST have been recorded. Histological diagnoses included glioma (48.9%), all other neuroepithelial tumors (5%), meningioma (28.8%), nerve sheath tumors (8.4%), lymphoma (3.2%) and others (5.7%). Cryopreservation was reported for 6018 PCNST specimens. Tumor resections (R) were performed in 78% cases, while biopsies accounted for 22%. Median age (MA), sex, percentage R and number of cryopreserved tumors were detailed for each histology; for example, out of 6053 glioblastomas (MA 63 years, male 59.4%, R 62%, 1611 were cryopreserved), and out of 37 atypical teratoid/rhabdoid tumors (MA 2 years, male 56.8%, R 94%, 17 were cryopreserved). This database or databank dedicated to PCNST cases contains detailed data on clinical, histological and other characteristics, such as the inclusion of data on cryopreserved specimens that are not available in other European registries. Therefore, this is a valuable resource that can be used for planning future epidemiological and clinical research.

INTRODUCTION

Primary central nervous system tumors (PCNSTs) represent a complex heterogeneous group of pathological entities that may be benign, malignant or of unpredictable evolution (2, 8, 24, 28, 30, 31, 42). These tumors represent a major public health problem (16), and the French epidemiological data are fragmentary (17, 20, 26, 32, 33), as a national registry for these tumor cases does not exist. The main objective of this project was to prospectively record all PCNST cases in France, for which histological diagnosis is available. The long-term goals in creating the French Brain Tumor DataBase (FBTDB) were to: (i) create a national registry and a national network to perform epidemiological studies; (ii) implement a new database and use it for setting up both clinical and basic research protocols; (iii) allow the evaluation of the medical practices of an area or of the entire country; and (iv) harmonize the health care of patients affected by PCNST at the higher level. The French societies involved in the management of patients diagnosed with PCNST [ie, Association des Neuro-Oncologues d'Expression Française (ANOCEF), Société Française de Neurochirurgie (SFNC), Société Française de Neuropathologie (SFNP)] were linked to initiate this work at a countrywide level through the use of a national survey on the medical practices in neuro-oncology and a census of the protocols of fundamental research existing in France (3, 21). The

methodology and initial results of the FBTDB, clinical epidemiology for childhood PCNST and a specific work concerning oncological patterns of care for patients with glioblastoma have already been published by the FBTDB (4–7, 36).

Here, we report the histological results of the FBTDB on 25 756 cases of newly diagnosed and histologically confirmed PCNST, and discuss a few perspectives of such database.

MATERIALS AND METHODS

Patients with newly diagnosed and histologically confirmed PCNSTs (since 1 January 2004) were identified in the FBTDB, and initial data were prospectively collected. All neurosurgeons and neuropathologists in France who participated in creating the FBTDB were instructed to complete a data file card for each patient that underwent surgery. Histological diagnosis was always made by experienced neuropathologists; more than 90% of these neuropathologists worked in public academic centers. The methodology for the FBTDB accrual was previously described in detail (4). In summary, the data file card was placed in all operating rooms where surgery for PCNST is performed, and was systematically sent along with the sample to the pathology lab. The easy-to-complete card contains questions on sociodemographic, clinical, radiological, surgical and pathological data (an optional question about cryopreservation of the samples was included). The first part of the card (ie, sociodemographic, clinical, radiological and surgical data) was completed by the neurosurgeon. The second part was completed by the pathologist. All completed cards were mailed to the Tumor Registry from Herault (TRH) [Registre des Tumeurs de l'Hérault (RTH), Montpellier, France], which has extensive expertise in working with tumor data and has the required authorization for recording data with personal identifiers. The TRH compiled all cards and analyzed the data in collaboration with the University Institute of Clinical Research of Montpellier-Nîmes (IURC, Institut Universitaire de Recherche Clinique, Montpellier-Nîmes, France). A new data file card has been used since 2007 (Figure 1). The data presented here include age, sex, histological diagnosis according to the ICD-0-3 [World Health Organization (WHO) classification] and Systematized Nomenclature of Medicine (SNOMED) codes from Louis *et al* (28) and French nomenclature Association for the Development of Information Technology in Cytology, Anatomy and Pathology (ADICAP) (1) (a list of included codes is presented in Table 1), cryopreservation of samples and surgery (biopsy/resection).

Note that from 2004 to 2006, pathologists used The WHO 2000 Classification (24). Since 2007, the new WHO classification (28) has been applied, and rare mesenchymal tumors of the meninges have been recorded only since 2007.

The study was approved by the French legislation, and by all the French societies involved in the neuro-oncology field: ANOCEF, SFNC and SFNP.

RESULTS

From 2004 to 2008, a total of 25 756 cases of newly diagnosed histologically confirmed PCNSTs was recorded in the FBTDB. Of the 60 participating centers (coupled neurosurgical department/pathological lab) located throughout France, 50 were public centers (45 academic centers and 5 general hospitals) and 10 were private institutions. However, with regard to the number of patients, the proportions were 94% from public centers and 6% from private institutions.

Of the 25 756 PCNST cases, 12 192 were men (47.3%), 13 564 were women (52.7%), 1601 were children (age: <15 years) (6.2%) and 521 were teenagers (15 ≤ age < 20 years) (2%).

Tumor localizations were specified in 17 199 cases and included supratentorial (77.7%), infratentorial (15.7%), spinal cord or cauda equina (5.3%) and mixed (1.3%). Surgery was specified in 21 997 cases. Tumor resections represented 78% of surgical operations, while biopsies represented 22%. For each histological type and subtype, percentages of biopsy and resection are detailed in Table 1.

Histological results

The distribution by each histology, sex, mean/median age (MA) at diagnosis and surgery, for the 25 756 PCNST cases, is shown in Table 1. Gliomas accounted for about half of all PCNST cases, while meningiomas accounted for about one-third. Gliomas were more frequent in men (57.6%), while meningiomas in women (73.5%). The MAs of gliomas/all other neuroepithelial tumors/meningiomas/nerve sheath tumors/lymphomas were 56, 18, 58, 53 and 66 years, respectively.

According to the new WHO classification (27, 28), the new entities encountered in our series were: three papillary glioneuronal tumors, four rosettes forming glioneuronal tumor of the fourth ventricle, two papillary tumors of the pineal region, two pituicytomas and no spindle cell oncocytoma of the ante hypophysis. Concerning the new variants, we counted four pilomyxoid astrocytomas, four anaplastic medulloblastomas and three medulloblastomas with extensive nodularity recorded over 2 years.

Formaldehyde was used as a fixative, alone or in association, in 68% of the case samples. Cryopreservation was reported for 6018 PCNST specimens.

DISCUSSION

This work detailed all histological types and subtypes for 25 756 cases of newly diagnosed and histologically confirmed PCNST in France from 2004 to 2008. This work was made possible, thanks to the cooperation of a large number of neurosurgeons and pathologists from all over France, and the methodological support of epidemiologists. Above all, this work shows the importance of multidisciplinary networks and databases that involve clinicians, pathologists and epidemiologists (8).

However, this discussion is mainly focused on: (i) methodology; (ii) comparison of our results (histological distribution, age, sex, surgery) with a small number of publications that detailed all types and subtypes of PCNST in a large population; and (iii) current applications and perspectives of such database for scientific and public communities.

Methodology

The primary difficulty in building a tumor registry is defining the type of tumor to be recorded. Recent publications (11, 12, 17, 30, 31, 41), the classification system of the WHO (24, 28) and the European recommendations for coding tumors of the brain and

Pathological, neuroradiological & Clinical Data Card in Neurosurgery

To join systematically with the pathological sample

PATIENT'S ADHESIVE LABEL
NAME :
MAIDEN NAME :
FIRST NAME :
SEX : F ☐ M ☐
DATE OF BIRTH : _ _ / _ _ / _ _ _ _
HOSPITALIZATION NUMBER :

- **Date of the sample** : _ _ / _ _ / _ _ _ _
- **Origin of the sample** :
  surgeon : **Department :**
  Hospital : **City :**
- **PATIENT** : Home postal code: _ _ _ _ _
  (if disponible) Birth city postal code : _ _ _ _ _

-Primary central nervous system tumor possible ☐ (fill the box bellow and *)**; Other** ☐ (do not fill the box bellow but *)

Familial medical history of CNS tumor or of phacomatosis: unknown☐, no ☐, **yes** ☐ **specify:**
Personal medical history of CNS tumor or of phacomatosis: unknown☐, no ☐, **yes** ☐ **specify:**

- Time between first sign and present surgery : **unknown** ☐, known : time in month _ _ _ (0 if<1 month)
- Present and past symptomatology connected with the tumor : **unknown** ☐ ;asymptomatic ☐ ;
épilepsy ☐ épilepsy 1st symptom yes ☐ , no ☐ ; headache ☐ ; raised ICP ☐
mental statut disorders ☐ ; neurologic déficit ☐ ; other ☐ specify:
Fonctional index: préopérative Karnofsky performance statut before treatment against cerebral oedema : _ _ _ / 100
ou OMS _
- Contraste enhancement(CE) on CT: **unknown** ☐ **,** no ☐ , doubt ☐ **,** yes ☐
on MRI : CE: **unknown** ☐ , no ☐ , doubt ☐ **,** yes ☐ : homogenous ☐, heterogenous ☐, punctiform ☐, ring CE ☐,
T1 and/or T2: Unifocal lesion ☐ Multifocal ☐; Median line crossing: yes ☐ no ☐; Radiological necrosis: yes ☐ no ☐
- Radiological or macroscopic principal topographic lesion (***check just one case by item in thick***):
.Cerebral hemispheres : **Side** : Right ☐ Left ☐ median ☐ **;Lesion** Extra ☐ , Intra ☐ parenchymal **;**
for intra-parenchymal lesion: superficial (only cortex) ☐, deep (WS and/or GN) ☐, cortex and WS ☐;
.Supra tentorial : Lobe : Frontal ☐ , Parietal ☐ , Temporal ☐ , Occipital ☐ , Ventricle ☐ , Deep Brain ☐, Pineal region ☐ , Intra sellar and/or Suprasellar ☐ , other ☐ specify:
.Infra tentorial : Cerebellum ☐ , Brain stem ☐ ,4th Ventricle ☐ , Other ☐ specify:
.Mixt: Supra and infra tentorial ☐ , infra tentorial and medullar ☐ , pan CNS ☐
.Spinal cord ☐, cauda equina ☐, Mixt: medular and cauda equina☐
.Meninges : intra cranial meninge ☐ , Spinal meninge: ☐ , (*for all non meningothelial lesion*)
.Nerve : Olfactif nerve ☐, Optique nerve ☐, Nerve VIII ☐, Other cranial nerve ☐, Spinal nerve ☐ (*same line above*)
.Lesion near hemisphere ☐ , **near spinal cord** ☐ , **near caudal equina** ☐
- Patient has already had surgery with histological exam for this tumor:
no ☐ **unknown** ☐ yes ☐ date(s) : place :
- Present surgery : biopsy without frame ☐ , with frame ☐ resection ☐ **unknown** ☐

Pathologist : Department : City :
-Sample identity number (in the department) :

Used classification(s) Check the case(s)	OMS ☐	Sainte Anne ☐
Diagnosis in plain language		
ADICAP codification	_ _ _ _ _ _ _	_ _ _ _ _ _ _
ICD-O(WHO) codification	_ _ _ _ / _	_ _ _ _ / _

- Inclassifiable ☐ **C**linical and radiological suspicion of primary CNS tumor but non-contributive histology ☐
- Sample quality : interpretable ☐ interprétable with difficulty ☐
- **F**ixative : Formaldehyde ☐ Formaldehyde Zn ☐ Bouin ☐ AFA ☐ other ☐ specify :
- Cryopreservation of the sample (optional) : yes ☐ no ☐

Please : send this card to : Doctor Hélène Mathieu-Daudé, Registre des tumeurs de l'Hérault, Bât Recherche, Parc Euromédecine, 208 rue des Apothicaires, 34298 Montpellier cedex 5, France

Figure 1. *The pathological, neuroradiological and clinical card contains all the data asked for recording the primary central nervous system tumor (PCNST).* It is systematically filled up for each patient by the neurosurgeon in the operating room and by the pathologist if the diagnosis of PCNST is confirmed.

central nervous system (CNS) (18) include all primary benign and malignant tumors located in the CNS, including the envelopes of the CNS and the origin of the nerves localized in the skull and the spine. Second, a registry has to record all cases of the defined tumors. The ascertainment system could influence the selection of tumor types to be included in the registry definition. As our registration system was based on the neurosurgical French network, we decided to record tumors that are always seen in neurosurgery. At the beginning of this work in 2004, we did not include mesenchymal non-meningothelial tumors (except hemangiopericytoma), which were not considered as primary brain tumors by the French community at that time. Except for these differences, we selected the types of tumors that are included in the WHO 2000 (24) and Central Brain Tumor Registry of the United States (CBTRUS)

Table 1. Histological repartition of the 25 756 cases with clinical and surgical data from the French Brain Tumor Database, 2004 to 2008. Abbreviations: T = total; B = biopsy; R = resection; M = male; F = female; N = number; Med = median age at diagnosis; m = mean age at diagnosis; CRYO = cryopreservation; MPNST = malignant peripheral nerve sheath tumor.

	ICD-O	ADICAP	N	M	F	m	Med	CRYO	Reported surgery		
									T	R (%)	B (%)
Tumors of neuroepithelial tissue											
Glioma NOS	9380/3	N7R0	205	114	91	49.96	56.0	37	192	30.7	69.3
Astrocytic tumors											
Astrocytoma NOS	9400/3	N7S0	205	127	78	42.82	46.0	23	171	46.2	53.8
Pilocytic astrocytoma	9421/1	N0S8	718	367	351	16.26	12.0	201	617	86.7	13.3
Pilomyxoïd astrocytoma	*9425/3*	*(0001)*	4	1	3	10.50	10.0	2	2	50.0	50.0
Subependymal giant cell astrocytoma	9384/1	N0T2/3	50	24	26	16.90	16.5	25	39	92.3	7.7
Pleomorphic xantho-astrocytoma	9424/3	N7S9	56	30	26	36.73	34.0	14	50	84.0	16.0
Fibrillary astrocytoma	9420/3	N7S2	115	68	47	38.48	40.0	36	102	40.2	59.8
Gemistocytic astrocytoma	9411/3	N7S4	41	26	15	45.61	48.0	11	35	45.7	54.3
Protoplasmic astrocytoma	9410/3	N7S6	12	7	5	47.42	43.5	1	10	40.0	60.0
Anaplastic astrocytoma	9401/3	N7T6	372	204	168	57.16	60.0	105	352	35.2	64.8
Glioblastoma	9440/3	N7X0	6053	3593	2460	61.61	63.0	1611	5212	61.9	38.1
Giant cell glioblastoma	9441/3	N7X2	115	63	52	55.90	60.0	43	109	67.9	32.1
Gliosarcoma	9442/3	N7X4	62	40	22	55.77	57.0	17	54	92.6	7.4
Gliomatosis cerebri	9381/3	N7R9	25	15	10	48.08	52.0	4	21	23.8	76.2
			8033	4679	3354	55.50	60.0	2130	6966		
				58.2%	*41.8%*			*26.5%*		61.6	38.4
Oligodendroglial tumors											
Oligodendroglioma	9450/3	N7V0	1271	731	540	43.24	42.0	346	1064	61.7	38.3
Anaplastic oligodendroglioma	9451/3	N7V4	1313	733	580	52.68	54.0	456	1202	69.3	30.7
			2584	1464	1120	47.90	48.0	802	2266		
				56.7%	*43.3%*			*31.0%*		65.7	34.3
Oligoastrocytic tumors											
Oligoastrocytic tumors NOS	9382/3	N7R4	8	5	3	47.75	46.0	2	6	50.0	50.0
Oligoastrocytoma	9382/3	N7V2	416	223	193	43.92	42.0	106	370	58.9	41.1
Anaplastic oligoastrocytoma	9382/3	N7V3	831	475	356	52.24	55.0	224	771	60.7	39.9
			1255	703	552	49.42	51.0	332	1147		
				56.0%	*44.0%*			*26.5%*		60.1	39.9
Ependymal tumors											
Subépendymoma	9383/1	N0W6	57	40	17	51.81	55.0	14	46	87.0	13.0
Myxopapillary ependymoma	9394/1	N7W2	87	53	34	37.47	35.0	14	71	97.2	2.8
Ependymoma, NOS	9391/3	N7W0	388	217	171	41.46	43.0	88	305	92.5	7.5
Cellular ependymoma	9391/3	N7W1	30	16	14	33.70	33.0	9	28	92.9	7.1
Papillary ependymoma	9393/3	N7W4	15	8	7	44.67	50.0	4	12	91.7	8.3
Clear cell ependymoma	9391/3	N7W5	18	11	7	26.67	20.0	3	14	85.7	14.3
Ependymoma, anaplastic	9392/3	N7W8	128	62	66	26.33	13.5	50	112	90.2	9.8
Tanicytic ependymoma	9391/3	*(0002)*	10	8	2	40.10	42.0	3	8	50.0	50.0
			733	415	318	38.52	41.0	185	596		
				56.6%	*43.4%*			*25.2%*		91.4	8.6
Total			12 605	7261	5344	52.35	56.0	3449	10 975		
Gliomes				*57.6%*	*42.4%*			*27.4%*		63.9	36.1
Choroid plexus tumors											
Choroid plexus papilloma	9390/0	N0Z0	89	42	47	26.70	22.0	19	76	92.1	7.9
Atypical choroid plexus papilloma	*9390/1*	*(0003)*									
Choroid plexus carcinoma	9390/3	N7Z0	14	9	5	23.43	13.0	4	14	85.7	14.3
			103	51	52	26.25	20.0	23	90		
				49.5%	*50.5%*			*22.3%*		91.1	8.9
Other neuroepithelial tumors											
Astroblastoma	9430/3	N7T4	1	0	1	24.00	24.0	1	1	100.0	0.0
Chordoid glioma of the third ventricle	9444/1	*(0004)*	3	2	1	41.66	46.0	1	2	50.0	50.0
Angiocentric glioma	*9431/1*	*(0005)*									
Esthesioneuroblastoma	9522/3	B7F2	20	15	5	49.05	47.0	2	18	94.4	5.6
			24	17	7	47.08	47.0	4	21		
				70.8%	*29.2%*			*16.7%*		95.0	5.0
Neuronal and mixed neuronal–glial tumors											
Dysplastic gangliocytoma of cerebellum (Lhermitte–Duclos)	9493/0	N0L2	4	3	1	40.75	42.5	1	4	100.0	0.0
Desmoplastic infantile astrocytoma/ganglioma	9412/1	N0N0	5	1	4	16.40	2.0	0	5	100.0	0.0

Table 1. *Continued*

	ICD-O	ADICAP	N	M	F	m	Med	CRYO	Reported surgery		
									T	R (%)	B (%)
Dysembryoplastic neuroepithelial tumor	9413/0	N0N2	128	71	57	20.52	18.0	37	117	92.3	7.7
Gangliocytoma	9492/0	N0L0	12	4	8	33.25	32.5	3	11	81.8	18.2
Ganglioglioma	9505/1	N7N0	287	159	128	22.83	18.0	87	212	87.7	12.3
Anaplastic ganglioglioma	9505/3	N7N1	34	19	15	45.56	50.0	10	28	89.3	10.7
Central neurocytoma	9506/1	N4L0	74	37	37	35.16	31.0	23	62	90.3	9.7
Extraventricular neurocytoma	*9506/1*	*(0006)*									
Cerebellar liponeurocytoma	*9506/1*	*(0007)*									
Papillary glioneuronal tumor	*9509/1*	*(0008)*	3	2	1	22.00	16.0	2	3	100.0	0.0
Rosette-forming glioneuronal tumor of the fourth ventricle	*9509/1*	*(0009)*	4	2	2	35.50	30.0	2	3	100.0	0.0
Paraganglioma	8680/1	P0A0	22	10	12	47.77	44.0	4	17	100.0	0.0
Paraganglioma malignant	8680/3	P7A0	3	1	2	52.66	55.0	0	2	50.0	50.0
			576	309	267	26.72	23.0	169	464		
				53.6%	*46.4%*			*29.3%*		89.9	10.1
Tumor of the pineal region											
Pinealoma, NOS	9360/1	P7P0	11	9	2	39.73	44.0	3	11	36.4	63.6
Pineocytoma	9361/1	P7P2	28	11	17	48.93	47.5	4	25	80.0	20.0
Pineal parenchymal tumor of intermediate differentiation	9362/3	P7P6	3	2	1	26.33	28.0	2	3	33.3	66.7
Pineoblastoma	9362/3	P7P4	24	12	12	23.08	18.0	5	21	61.9	38.1
Papillary tumor of the pineal region	*9395/3*	*(0010)*	2	1	1	53.00	53.0	0			
			68	35	33	37.44	39.5	14	60		
				51.5%	*48.5%*			*20.6%*		63.3	36.7
Embryonal tumors											
Medulloblastoma, NOS	9470/3	N7P0	314	186	128	17.90	11.5	111	290	90.0	10.0
Desmoplastic medulloblastoma	9471/3	N7P2	53	35	18	12.23	9.0	22	45	93.3	6.7
Medulloblastoma with extensive nodularity	*9471/3*	*(0011)*	3	1	2	10.33	7.0	1	2	100.0	0.0
Anaplastic medulloblastoma	*9474/3*	*(0012)*	4	4	0	19.00	15.5	1	3	100.0	0.0
Large-cell medulloblastoma	9474/3	*(0013)*	1	1	0	2.00	2.0	1	1	100.0	0.0
CNS primitive neuroectodermal tumor	9473/3	N7M2	68	33	35	22.25	12.5	16	63	79.4	20.6
CNS Neuroblastoma	9500/3	N7M0	14	9	5	16.36	5.0	6	13	76.9	23.1
CNS Ganglioneuroblastoma	9490/3	N7M1	8	4	4	34.50	36.5	0	6	100.0	0.0
Medulloepithélioma	9501/3	N7Q0	3	0	3	2.66	3.0	1	2	50.0	50.0
Ependymoblastoma	9392/3	N7X8	1	0	1	25.00	25.0	0			
Atypical teratoid/rhabdoid tumor	9508/3	X7R8	37	21	16	9.32	2.0	17	32	93.8	6.3
			506	294	212	17.33	10.0	176	457		
				58.1%	*41.9%*			*34.8%*		88.8	11.2
Tumors of the cranial and paraspinal nerves											
Schwannoma (neurilemnoma, neurinoma)	9560/0	N0A0	1894	900	994	51.75	53.0	360	1634	97.9	2.1
Schwannoma (neurofibromatosis type1)	9560/0	N0B0	101	50	51	53.55	55.0	6	87	97.7	2.3
Cellular schwannoma	9560/0	N4A0	16	8	8	46.62	52.5	2	13	76.9	23.1
Plexiform schwannoma	9560/0	N0A6	8	2	6	47.25	48.5	0	7	100.0	0.0
Mélanotic schwannoma	9560/0	N0C4	5	2	3	52.60	47.0	0	4	100.0	0.0
Neurofibroma	9540/0	N0C0	78	40	38	39.89	39.0	8	65	100.0	0.0
Plexiform neurofibroma	9550/0	N0C1	9	5	4	35.11	29.0	1	6	100.0	0.0
Granular cells neurofibroma	9540/0	N0C8	3	0	3	57.66	62.0	1	2	100.0	0.0
Neurofibroma (neurofibromatosis type 1)	9540/0	N0D0	13	7	6	34.70	29.0	2	10	100.0	0.0
Neurofibrosarcoma (SAI)	9540/3	N7C0	6	3	3	43.83	38.5	2	6	83.3	16.7
Perineurioma	9571/0	N0G0	3	1	2	58.33	59.0	0	2	100.0	0.0
Intraneural perineurioma	9571/0	N0G4									
Malignant perineurioma	9571/3	*(0014)*									
Malignant peripheral nerve sheath tumor	9540/3	N7A0	16	4	12	44.44	40.0	2	8	100.0	0.0
Epithelioid MPNST	9540/3	N7A3									
MPNST with mesenchymal differentiation	9540/3	N7H0									
Melanotic MPNST	9540/3	N7A5	1	0	1	35.00	35.0	0	1	100.0	0.0
MPNST with glandular differentiation	9540/3	N7A6	1	1	0	28.00	28.0	0	1	100.0	0.0
			2154	1023	1131	51.07	53.0	384	1846		
				47.5%	*52.5%*			*17.8%*		97.8	2.2

Table 1. *Continued*

	ICD-O	ADICAP	N	M	F	m	Med	CRYO	Reported surgery		
									T	R (%)	B (%)
Tumors of the meninges											
Tumors of meningothelial cells											
Meningioma, NOS	9530/0	N0J0	1507	374	1133	57.19	57.0	264	1337	97.5	2.5
Meningothelial meningioma	9531/0	N0K2	2397	626	1771	57.46	57.0	517	2029	97.8	2.2
Fibrous (fibroblastic) meningioma	9532/0	N0J4	754	144	610	57.67	58.0	141	628	97.1	2.9
Transitional (mixed) meningioma	9537/0	N0K4	1168	267	901	57.24	57.0	218	1013	97.3	2.7
Psammomatous meningioma	9533/0	N0K8	302	39	263	62.29	63.0	44	246	96.7	3.3
Angiomatous meningioma	9534/0	N0J2	151	61	90	58.96	58.5	29	136	96.3	3.7
Rare variety meningioma (NOS)	9530/0	N0K9*	65	14	51	57.71	57.0	7	64	89.1	10.9
Microcystic meningioma	9530/0	N0K9	71	17	54	55.23	56.0	19	62	100.0	0.0
Secretory meningioma	9530/0	N0K9	89	13	76	58.23	57.0	11	70	97.1	2.9
Lymphoplasmacyte-rich meningioma	9530/0	N0K9									
Clear-cell meningioma	9538/1	N0K9	38	11	27	51.39	50.5	11	35	100.0	0.0
Chordoid meningioma	9538/1	N0K9	58	17	41	52.92	52.5	8	53	98.1	1.9
Rhabdoid meningioma	9538/3	N0K9	5	2	3	64.40	66.0	2	4	100.0	0.0
Metaplastic meningioma	9530/0	N0K3	40	10	30	56.25	54.0	3	33	93.9	6.1
Atypical meningioma	9539/1	N4J0	624	299	325	59.60	62.5	128	482	97.5	2.5
Papillary meningioma	9538/3	N7K6	8	5	3	47.12	45.0	3	7	100.0	0.0
Anaplastic meningioma	9530/3	N7J0	134	66	68	61.23	62.5	22	101	99.0	1.0
Meningiomatosis	9530/1	N4J9	8	4	4	51.00	53.5	3	7	100.0	0.0
			7419	1969	5450	57.76	58.0	1430	6307		
				26.5%	*73.5%*			*19.3%*		97.4	2.6
Mesenchymal tumors											
Benign mesenchymal tumor (NOS)		X0H0									
Lipoma	8850/0	L0L0	19	14	5	31.79	30.0	1	16	93.8	6.3
Angiolipoma	8861/0	L0P1	5	3	2	53.20	55.0	1	3	100.0	0.0
Hibernoma	8880/0	L0M4									
Liposarcoma	8850/3	L7L0	2	2	0	49.50	49.5	0	2	100.0	0.0
Solitary fibrous tumor	8815/0	F0A1	33	14	19	54.00	57.0	11	30	93.3	6.7
Fibrosarcoma	8810/3	F7A0									
Histiocytome fibreux malin	8830/3	F7M0									
Leiomyoma	8890/0	L0A0									
Leiomyosarcoma	8890/3	L7A0	3	1	2	62.66	57.0	1	3	100.0	0.0
Rhabdomyoma	8900/0	R0C0									
Rhabdomyosarcoma	8900/3	R7C0	3	1	2	11.66	13.0	0	3	100.0	0.0
Chondroma	9220/0	C0A0	4	3	1	20.75	16.0	0	2	100.0	0.0
Chondrosarcoma	9220/3	C7A0	14	5	9	38.50	36.5	1	11	90.9	9.1
Osteoma	9180/3	Q0A0	14	3	11	40.14	37.5	1	11	100.0	0.0
Osteosarcoma	9180/3	Q7A0	6	5	1	32.33	31.5	2	5	100.0	0.0
Osteochondroma	9210/0	C0G0	6	2	4	37.67	40.0	0	4	100.0	0.0
Hemangioma	9120/0	V0A0	251	125	126	39.57	41.0	13	190	96.3	3.7
Epithelioid hemangioendothelioma	9133/1	V7N0	3	1	2	68.33	69.0	0	3	100.0	0.0
Hemangiopericytoma benign	9150/1	V0K0	30	16	14	53.27	54.5	8	26	100.0	0.0
Uncertain malignancy hemangiopericytoma		V4K0	19	11	8	55.31	58.0	5	11	100.0	0.0
Infantile hemangiopericytoma		V0K1									
Anaplastic hemangiopericytoma	9150/3	V7K0	29	15	14	57.21	56.0	3	26	96.2	3.8
Angiosarcoma	9120/3	V7A0	3	3	0	49.00	44.0	0	2	100.0	0.0
Kaposi sarcoma	9140/3	V7R0									
Ewing's sarcoma—PNET	9364/3	X7L0	8	5	3	23.75	23.5	2	8	100.0	0.0
			452	229	223	42.49	45.0	49	356		
				50.7%	49.3%			10.8%		96.6	3.4
Primary melanocytic lesions											
Diffuse melanocytoma	8728/0	*(0015)*									
Melanocytoma	8728/1	*(0016)*									
Malignant melanoma	8720/3	M7A0	11	6	5	65.00	69.0	1	7	100.0	0.0
Meningeal melanomatosis	8728/3	*(0017)*									
			11	6	5	65.00	69.0	1	7		
										100.0	0.0
Other neoplasms related to the meninges											
Hemangioblastoma	9161/1	V0G0	394	208	186	45.91	45.0	81	342		
				52.8%	*47.2%*			*20.6%*		98.2	1.8

Table 1. *Continued*

	ICD-O	ADICAP	N	M	F	m	Med	CRYO	Reported surgery		
									T	R (%)	B (%)
Lymphomas and hematopoietic neoplasms											
Malignant lymphoma	9590/3	K7G0	321	172	149	62.09	66.0	57	178	25.3	74.7
Diffuse large B cell lymphoma	9680/3	K7G7	513	263	250	64.67	67.0	106	394	20.3	79.7
Plasmacytoma	9731/3	J7D8	16	7	9	55.87	56.0	1	9	100.0	0.0
Granulocytic sarcoma	9930/3	*(0018)*									
			850	442	408	63.05	66.0	164	581		
				52.0%	*48.0%*			*19.3%*		23.1	76.9
Germ cell tumors											
Germinoma	9064/3	G7K0	54	46	8	20.39	17.5	9	48	37.5	62.5
Embryonal carcinoma	9070/3	G7H5	1	1	0	14.00	14.0	0	1	100.0	0.0
Yolk sac tumor	9071/3	G7H6	1	1	0	15.00	15.0	0	1	0.0	100.0
Choriocarcinoma	9100/3	T7C0									
Teratoma (NOS)	9080/1	D0V0	2	2	0	20.50	20.5	0	2	100.0	0.0
Mature teratome	9080/0	G0G0	27	15	12	25.11	17.0	4	23	95.7	4.3
Immature germ cell tumors (NOS)	9080/3	G7H0	4	2	2	19.00	18.0	0	4	75.0	25.0
Immature teratoma	9080/3	G7H1	7	4	3	8.71	8.0	2	6	100.0	0.0
Teratoma with malignant transformation	9084/3	G7G0									
Mixed germ cell tumor	9085/3	T7H0									
Immature teratoma and seminoma	9080/3	G7M6	1	0	1	8.00	8.0	0	1	100.0	0.0
Malignant germ cell tumors (NOS)	9064/3	G7A0	9	8	1	15.22	13.0	3	9	55.6	44.4
			106	79	27	20.10	17.0	18	95		
				74.5%	*25.5%*			*17.0%*		61.1	38.9
Tumors of the sellar region											
Craniopharyngioma	9350/1	D0N2	255	144	111	35.64	36.0	26	225	92.4	7.6
Adamantinous craniopharyngioma	9351/1	*(0019)*	37	19	18	38.46	35.0	5	22	100.0	0.0
Papillary craniopharyngioma	9352/1	*(0020)*	3	1	2	49.66	45.0	0	2	100.0	0.0
Granular cell tumor	9582/0	*(0021)*									
Pituicytoma	*9432/1*	*(0022)*	2	1	1	59.00	59.0	0	1	100.0	0.0
Spindle cell oncocytoma (adenohypophysis)	*8291/0*										
			297	165	132	36.29	36.0	31	250		
				55.6%	*44.4%*			*10.4%*		93.2	6.8
Miscellaneous											
Chordoma	9370/3	D4N4	61	40	21	50.88	56.0	10	50	92.0	8.0
Uncategorized			130	64	66	46.26	52.0	15	97	41.2	58.8
			191	104	87	47.74	53.0	25	147		
				54.5%	*45.5%*			*13.1%*		58.5	41.5
Total			25 756	12 192	13 564	52.15	56.0	6018	21 997		
				47.3%	*52.7%*			*23.4%*		77.9	22.1

The italicized ICD-O numbers are provisional codes proposed for the fourth edition of ICD-O.

classification schemes. In addition, we used the French nomenclature (1) in combination with the WHO (24).

Since 2007, all the codes included in the WHO 2007 (28) have been used in the FBTDB, and we started to record pituitary tumors. However, we still had some difficulties recording some cases of pituitary tumors. So, we decided to exclude pituitary tumors in the present work.

In the future, we could adopt a complementary strategy. It has been established by the Brain Tumor Epidemiology Consortium (BTEC) that glioblastomas and meningiomas have enough general agreement over time, across regions and between individual pathologists that one can consider using existing diagnostic data without further review [ie, as long as uniform guidelines, such as those provided by the WHO, are used (15)]. This would limit the number of cases to review and would mainly concern the rare PCNSTs. Moreover, some specific studies on rare PCNSTs will soon begin in France, and in these cases, the review will be part of the projects.

Comparison of our results

To our knowledge, there is no publication that detailed the distribution of all histological types and subtypes of PCNST according to the WHO 2007 Classification, by number of cases, sex, MA, number of cryopreserved samples and surgery for all ages in a large population.

First, in most countries, brain tumor registration is restricted to malignant tumor types (13). Only a few countries (eg, USA, Canada, Scandinavian countries, Austria) report incidence rates on benign and borderline brain tumors (9, 10, 12, 38, 39, 41). These tumors constitute approximately 45.5% to 70% of all brain tumors (11). However, benign and borderline lesions may be associated with significant neurological deficits, and may show malignant biological progression over time. Therefore, increasing attempts to register all brain tumor cases have been made. In the USA, it has already become legally mandatory to report all brain tumor types (Benign Brain Tumor Cancer Registries Amendment Act; Public

Law 107-260). Second, even in publications that included primary nonmalignant tumors, the details of all histological types and subtypes are very rarely presented. Therefore, our results are mainly compared to the CBTRUS results.

The sex ratios (male/female) for the CBTRUS (11) and for the FBTDB are very similar (eg, all neuroepithelial tumors: 1.28/1.34, all gliomas: 1.29/1.36, glioblastomas: 1.37/1.46, pilocytic astrocytomas: 1.14/1.05, oligodendrogliomas: 1.21/1.35, all ependymomas: 1.13/1.30, nonmalignant and malignant neuronal/glial tumors: 1.24/1.16, embryonal/primitive/medulloblastoma: 1.46/1.39, tumors of cranial and spinal nerves: 0.94/0.91, meningiomas: 0.35/0.36, lymphomas: 1.19/1.08, etc., for CBTRUS/FBTDB, respectively).

For many tumors, the MA at diagnosis is similar in the CBTRUS (11) and in the FBTDB (eg, pilocytic astrocytoma: 13/12, oligodendroglioma: 41/42, glioblastoma: 64/63, choroid plexus tumors: 17/20, nonmalignant and malignant neuronal/glial tumors: 26/23, embryonal tumors: 9/10, tumors of cranial and spinal nerves: 53/53, craniopharyngioma: 38/36, lymphoma: 63/66 years old for CBTRUS/FBTDB, respectively). In addition, it is important to note that the MA at diagnosis is often lower in clinical trials (eg, for glioblastoma, 56 years in Stupp *et al* (37) and 53 years in Westphal *et al* (40)) and in some single-institution studies (eg, 58 years in Filippini *et al* (19)). Age is an important prognostic factor for most of all PCNSTs; this underlines the importance of population studies to compare oncological management and survival between two different countries or areas.

Before comparing the percentages of each PCNST between the CBTRUS and the FBTDB, it is important to note few important points. First, CBTRUS reported more than 10% of pituitary tumors (10.7% in the 2009–2010 CBTRUS statistical report in 18 states in 2002–2006 (11), and 12.7% in CBTRUS statistical report in the USA in 2004–2006 (12)), whereas FBDTB did not include pituitary tumors in the present report. Second, unspecified neoplasm accounted for 5.1% in the CBTRUS (11), while it accounted for only 0.5% in the FBTDB. This difference could be explained by the fact that in the FBTDB, histological coding comes directly from pathologists, while the CBTRUS includes cases without histological diagnosis. Third, the percentage of meningioma is smaller in the FBTDB (28.8%) than in the CBTRUS (37.7%, when considering without pituitary tumors) (11). This difference could also be explained by the fact that in the FBTDB, only cases with histological confirmation have been recorded. In 2011, reporting of all cases of PCNST is still a challenge, specifically for nonmalignant tumors and tumors without histological confirmation. In the last report of the CBTRUS, it was stated that "the cancer registry incidence rates for the malignant tumors (cancer registry range: 4.62 to 8.69 per 100 000 person-years) are again seen as being much less variable than the reported incidence rates for the non-malignant tumors (cancer registry range: 6.13 to 16.74 per 100 000 person–years)" (12).

When we take into account these three points, we can consider that our results (Table 1) show a distribution by histology, MA at diagnosis and sex comparable to the recent literature (11, 12, 17, 41), even by specific histology (23, 35). The distribution of the different subtypes of PCNST is similar in France and in the USA, except for oligodendroglial tumors. Two main reasons may explain this difference: (i) the US data were collected between 2002 and 2006 (11), while the French data were collected between 2004 and 2008. Indeed, most studies (for a review, see (22)) have reported a recent increase of oligodendroglial tumors in comparison to astrocytic tumors. (ii) French neuropathologists are more influenced by the classification proposed by Daumas-Duport *et al* (14) than American neuropathologists.

New entities and variants have been published by the last WHO classification in 2007 (28). As our work included the year 2008, French pathologists included few such cases. These new entities began to be described in 2008, 1 year after the new classification has been published. But, it is too early to be representative of a population study. Moreover, only few specific cases have been reported in the literature.

To our knowledge, this work is the first in Europe, and probably in the world, that specifies the surgery (biopsy or resection) for all histological types and subtypes of PCNST in a large population. Over 97% of tumors of the meninges, and cranial and paraspinal nerves are resected. Regarding gliomas, the proportion of biopsy appears to vary by country and/or studies. For example, the Glioma Outcomes Project described a biopsy rate for glioblastoma of 20% (25), and in the San Francisco Bay Area SEER registry, during the period 1991–2001, 27.3% of glioblastoma patients had a biopsy (43). In an Italian single-institution study, biopsy was performed in 12% of all the glioblastoma cases (19), and in an Italian consortium study, the percentage of biopsies was 25% for all astrocytoma grades that were treated with RT (29). In France, the biopsy rate for glioblastoma was 44% in the year 2004 (7), and now it decreases. For the years 2004 to 2008, the biopsy rate was 38%.

Current applications and perspectives

Epidemiological data from the FBTDB already helped to build two ongoing French Hospital Clinical Research Programs (PHRCs) (one randomized multicenter phase II trial for patients with *de novo* unresectable glioblastoma, and one national, prospective phase II study for adult patients with medulloblastoma). The FBTDB also helped to identify and recruit patients for two other ongoing "PHRCs" (one for children with craniopharyngioma, and one for adult patients with intracranial ependymoma). Other specific projects are in progress (eg, oncological management and survival for all French glioblastoma patients newly diagnosed and histologically confirmed in 2008 in all French territory; histologically confirmed grade II glioma distribution in all French territory).

To contribute to a better completeness of reported cases, a second source for recording histologically confirmed PCNST is in progress. In agreement with the French Society of Neuropathology (SFNP), a comprehensive annual listing of all cases analyzed by each pathology lab will be sent securely to the RTH. A clinical research technician will track the missing listings, verify the registered cases, complete the database and check discordant cases with each lab. Then, the clinical research technician will complete the main clinical data for cases not registered yet, by contacting the relevant department of neurosurgery. The FBTDB recently received grants from the French cancer institute [Institut National du Cancer (INCa)] to analyze and compare oncological management and survival between the different French areas.

Apart from some specific cases, the causes of PCNST are unknown (8, 26, 34). Epidemiological studies of PCNST have examined many risk factors over the past several decades; however, there are few consistent findings. The inconclusive results may be

caused by small sample sizes in individual studies and differences between studies in patients, tumor types and methods of classification. That is why the FBTDB would like to collect a huge number of cases, and study each histological type and subtype separately, and then participate in international studies with, for example, the BTEC and the International Agency for Research on Cancer (IARC).

Virtual tumor bank is one of the major interests of such database. Recording cryopreservation of samples, to our knowledge, has not been previously reported and is original in our study. More than 6000 identified PCNSTs are cryopreserved. For these cryopreserved tumors, we know the histological diagnosis, and the main clinical and radiological features. This represents the first virtual tumor bank of PCNST in Europe, and holds great potential for future biological and clinical investigations. Many specific retrospective or prospective studies will use the FBTDB to identify patients and get initial data. Collaborative studies have already been initiated.

CONCLUSION

This database or databank dedicated to PCNST contains detailed data on clinical, histological and other characteristics, such as availability of cryopreserved specimens that are not available in other European registries. Thus, it is a valuable resource that can be used for planning future epidemiological and clinical research.

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