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Original Article

Precision of preoperative diagnosis in patients with brain tumor – A prospective study based on "top three list" of differential diagnosis for 1061 patients

Kazunori Arita[1], Makiko Miwa[1], Manoj Bohara[1], FM Moinuddin[2], Kiyohisa Kamimura[3], Koji Yoshimoto[1]

[1]Department of Neurosurgery, Kagoshima University, [3]Department of Radiology, Graduate School of Medical and Dental Sciences, Kagoshima University, Sakuragaoka, Kagoshima, Japan, [2]Department of Neurologic Surgery, Mayo Clinic, Rochester, MN, United States.

E-mail: *Kazunori Arita - karita@m2.kufm.kagoshima-u.ac.jp; Makiko Miwa - daico@btvm.ne.jp; Manoj Bohara - boharamanoj111@gmail.com; FM Moinuddin - moin_mmc35@yahoo.com; Kiyohisa Kamimura - kiyohisa@m2.kufm.kagoshima-u.ac.jp; Koji Yoshimoto - kyoshimo@m.kufm.kagoshima-u.ac.jp

***Corresponding author:**
Kazunori Arita,
Department of Neurosurgery,
Kagoshima University,
8-35-1 Sakuragaoka,
Kagoshima 8908544, Japan.

karita@m2.kufm.kagoshima-u.ac.jp

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ABSTRACT

Background: Accurate diagnosis of brain tumor is crucial for adequate surgical strategy. Our institution follows a comprehensive preoperative evaluation based on clinical and imaging information.

Methods: To assess the precision of preoperative diagnosis, we compared the "top three list" of differential diagnosis (the first, second, and third diagnoses according to the WHO 2007 classification including grading) of 1061 brain tumors, prospectively and consecutively registered in preoperative case conferences from 2010 to the end of 2017, with postoperative pathology reports.

Results: The correct diagnosis rate (sensitivity) of the first diagnosis was 75.8% in total. The sensitivity of the first diagnosis was high (84–94%) in hypothalamic-pituitary and extra-axial tumors, 67–75% in intra-axial tumors, and relatively low (29–42%) in intraventricular and pineal region tumors. Among major three intra-axial tumors, the sensitivity was highest in brain metastasis: 83.8% followed by malignant lymphoma: 81.4% and glioblastoma multiforme: 73.1%. Sensitivity was generally low (≦60%) in other gliomas. These sensitivities generally improved when the second and third diagnoses were included; 86.3% in total. Positive predictive value (PPV) was 76.9% in total. All the three preoperative diagnoses were incorrect in 3.4% (36/1061) of cases even when broader brain tumor classification was applied.

Conclusion: Our institutional experience on precision of preoperative diagnosis appeared around 75% of sensitivity and PPV for brain tumor. Sensitivity improved by 10% when the second and third diagnoses were included. Neurosurgeons should be aware of these features of precision in preoperative differential diagnosis of a brain tumor for better surgical strategy and to adequately inform the patients.

Keywords: Brain tumor, Positive predictive value, Precision, Preoperative differential diagnosis, Sensitivity

INTRODUCTION

The precision of preoperative diagnosis of brain tumor is crucial for deciding the pertinent operative strategy and for providing adequate information to the patient. We, neurosurgical team, generally apply a preoperative differential diagnosis for the brain tumors based on clinical and image information in the preoperative case conference. In spite of several reports on the precision of preoperative neuroimaging diagnosis of brain tumor,[7,9,28] there have been no

previous reports on precision of diagnosis based on clinical and image diagnosis in the preoperative conference, as a clinical routine. To evaluate the precision of preoperative diagnosis, we investigated our own institutional experiences.

Although only one preoperative probable diagnosis is usually sufficient in most cases of brain tumor, we occasionally come across cases requiring the change of surgical strategy intraoperatively due to the incorrect preoperative diagnosis. Therefore, we have prospectively and consecutively registered "top three list" of differential diagnoses at the end of the preoperative discussion for each case of brain tumor since 2010. Based on the list, we have made surgical strategy. We here compared the "top three list" with postoperative pathology lists in 1061 brain tumors treated from 2010 to the end of 2017 to evaluate the precision of preoperative diagnosis.

MATERIALS AND METHODS

Patients

The subjects were 584 women and 477 men with initial brain tumor operated on, from January 2010 to December 2017, in which registration of "top three list" of differential diagnoses was given and postoperative pathological diagnosis was determined. Median and mean ages were 60 (ranging from 0 to 89) and 55.8 ± 18.7 (SD) years, respectively.

The location of the tumor was suprasellar intra-axial in 389 (36.7%), hypothalamo-pituitary in 251 (23.7%), supratentorial extra-axial in 170 (16.0%), infratentorial extra-axial in 114 (10.7%), infratentorial intra-axial in 68 (6.4%), supratentorial ventricular in 22 (2.1%), skull in 21 (2.0%), pineal in 14 (1.3%), and infratentorial ventricular in 12 (1.1%) [Table 1A].

The broad classification of the tumor was glioma in 282 (26.6%), meningioma in 204 (19.2%), pituitary adenoma in 183 (17.2%), metastasis in 80 (7.5%), schwannoma in 69 (6.5%), malignant lymphoma in 59 (5.6%), Rathke's cleft cyst in 26 (2.5%), hemangioblastoma in 17 (1.6%), craniopharyngioma in 17 (1.6%), cavernous angioma in 16 (1.5%), germ cell tumor in 9 (0.8), medulloblastoma in 5 (0.5%), and miscellaneous in 94 (8.9%) patients [Table 1B].

Neuroimaging

Plain three axes preoperative computed tomographic (CT) images were in all obtained using Aquilion 64 Rows Multislice CT or Aquilion ONE 320 Rows Multislice CT (Toshiba Medical Systems, Otawara, Japan). Magnetic resonance images (MRIs) were obtained except for 9 (0.8%) patients with a pacemaker, using 3T Ingenia (Philips Healthcare, Best, the Netherlands), 3T Trio (Siemens, Malvern, PA, USA), 1.5T Magnetom Vision (Siemens, Erlangen, Germany), or Aera (Siemens, Erlangen, Germany). The basic imaging sequences for MRI were T1-weighted image (with slice thickness [ST]: 5 mm), T2-weighted image (ST: 5 mm), fluid-attenuated inversion recovery (ST: 5 mm), and diffusion-weighted image (ST: 5 mm). Gadolinium-enhanced T1-weighted images (ST: 5 mm) were obtained except for 25 (2.4%) patients with chronic renal failure. Gadolinium-enhanced 3D T1-weighted images (ST: 2 mm) were added in one-third of cases. Magnetic resonance spectroscopy (MRS) data were obtained for all intra-axial tumors. Arterial spin labeling (ASL) image was obtained in recent 3 years (2015–2017) for intra-axial tumors. ^{18}F-fluorodeoxyglucose-positron emission tomography and methionine studies were done for suspected glioma and malignant lymphoma.

Top three list

Preoperative conference based on clinical and neuroimaging information including neuroradiology report was usually conducted a week before surgery.

Table 1: Location (A) and broad pathological classification (B) of the tumors (*n*=1061).

Location (A)	*n*	%	Broad classification (B)	*n*	%
Supratentorial intra-axial	389	36.7	Glioma	282	26.6
Hypothalamo-pituitary	251	23.7	Meningioma	204	19.2
Supratentorial extra-axial	170	16.0	Pituitary adenoma	183	17.2
Infratentorial extra-axial	114	10.7	Metastasis	80	7.5
Infratentorial intra-axial	68	6.4	Schwannoma	69	6.5
Supratentorial ventricular	22	2.1	Malignant lymphoma	59	5.6
Skull	21	2.0	Rathke's cyst	26	2.5
Pineal	14	1.3	Hemangioblastoma	17	1.6
Infratentorial ventricular	12	1.1	Craniopharyngioma	17	1.6
			Cavernous angioma	16	1.5
			Germ cell tumor	9	0.8
			Medulloblastoma	5	0.5
			Miscellaneous	94	8.9

Clinical information included demographic characteristic, neurological presentation, tumor marker, clinical history, and other relevant histories. Attendees of the conference were board-certified neurosurgeons (8–12 persons) and neurosurgery residents (2–6 persons). On half of the occasions, diagnostic neuroradiology specialists (1–3 persons) attended. At the end of preoperative case discussion, one of the categories chosen from the WHO 2007 classification of tumors of the central nervous system (CNS) was registered as the most probable preoperative diagnosis, for example, anaplastic astrocytoma (Grade 3), atypical meningioma (Grade 2), or pineocytoma (Grade 1). Then, the second and third probable categories of the tumor were registered. For example, a supratentorial extra-axial tumor may be registered with meningioma Grade 2 as the first, meningioma Grade 1 as the second, and solitary fibrous tumor as the third differential diagnosis in the "top three list" for differential diagnosis. Rathke's cleft cyst, not listed in the WHO classification as it is nonneoplastic, was included in the diagnostic categories. The discontent among the attendees was further discussed to reach an agreement. If it failed, in around 5% of cases, we voted to select the diagnosis from several candidates for differential diagnosis.

The surgery was performed under the first diagnosis with heed to the following two diagnoses. For example, when the first diagnosis was glioblastoma and the second diagnosis was malignant lymphoma, the craniotomy was done for maximum safe removal, but biopsy specimen was obtained at earliest opportunity. When the preoperative diagnosis was glioma, we routinely utilized intraoperative navigation and intraoperative MRI to pursue the utmost safe removal. All the specimens acquired during surgery were submitted to pathology; the higher WHO grade pathological diagnosis was adopted as the final diagnosis when the histological features differed from place to place.

Postoperative pathology report and comparison with "top three list"

Two pathologists made a diagnosis according to the WHO categorization of CNS tumors 2007 using histological specimens stained by hematoxylin and eosin and immunohistochemical staining for related proteins. Discordance between the pathologists was further discussed in the pathology conference and the final diagnosis was endorsed by the chief of the department of pathology. In cases with low-grade glioma, information on heterozygosity at 1p and 19q was added for the differentiation between astrocytic and oligodendroglial lineage. There were 9 (0.85%) among total 1061 tumors, in which the definite pathological diagnosis was not determined even through these steps. We got the final diagnosis of these 9 cases by sending the tumor tissue to Japan Brain Tumor Reference Center, http://www.jbtrc.com, which has been pathologically diagnosing 500 or more brain tumors per year referred from all over Japan.

The "top three list" of the 1061 initial intracranial tumors was compared with the pathology reports by a coauthor (M.M.), nonattendees of neurosurgery or pathology conferences.

Statistical analysis

Calculation of values on preoperative diagnosis and statistical analyses was performed using StatFlex version 6.0 (Artech Co. Ltd., Osaka, Japan) and OpenEpi (http://www.openepi.com/Menu/OE_Menu.htm). Chi-squared test was used for the statistical comparison between unpaired variables in two or three groups. $P < 0.05$ was defined as statistical significance. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated using the program MedCalc Version 19.1.3 (Mariakerke, Belgium).

Ethical consideration

This noninterventional study was endorsed by the Medical Ethics Committee of Kagoshima University Hospital (reference No. 180119, epidemiology research). The authors certify that this study involving human subjects was conducted in accordance with the Helsinki Declaration of 1975 as revised in 2000 and the Ethical Guidelines for Medical and Health Research Involving Human Subjects (effective February 9, 2015) promulgated by the Ministry of Health, Labor and Welfare, Japan. Informed consent for the treatment and for the use of their data in general research on brain tumor was obtained from all patients. The study-specific informed consent was waived due to the noninvasive nature of our study. An opt-out approach was offered to all patients. To protect patient privacy, all data were collected and analyzed under anonymization in an unlinkable fashion.

RESULTS

The statistical values of the preoperative diagnoses on major 23 kinds of brain tumor, which involved more than 4 patients, are presented in Table 2.

Sensitivity in total

When the WHO classification and grading of the first preoperative differential diagnosis matched those of pathology reports, the preoperative differential diagnosis was judged to be correct. The correct diagnosis rate (sensitivity) of the first diagnosis for all 1061 tumors was 75.8% (95% confidence interval, CI: 73.1–78.3). The sensitivity

significantly improved to 86.3% (95% CI: 84.1–88.3) when the second and third differential diagnoses were included ($P < 0.0001$, Chi-squared test) [Figure 1].

When the broader categorization was permitted, for example, preoperative diagnosis of meningioma (Grade 1) was permitted for a pathologically proven atypical meningioma

Table 2: Statistical values regarding preoperative diagnosis of major brain tumor (at least 3 cases).

Pathology	Number	Sensitivity	Positive predictive value	Specificity	Negative predictive value	Accuracy
Glioblastoma	175	73.1 (65.9–79.6)	81.0 (74.8–86.0)	96.6 (95.2–97.7)	94.8 (93.5–95.9)	92.7 (91.0–94.2)
Anaplastic astrocytoma	17	17.7 (3.8–43.4)	15.8 (5.7–36.9)	98.5 (97.5–99.1)	98.7 (98.3–98.9)	97.2 (96.0–98.1)
Diffuse astrocytoma	16	56.3 (29.9–80.3)	39.1 (24.6–55.8)	98.7 (97.8–99.3)	99.3 (98.8–99.6)	98.0 (97.0–98.8)
Pilocytic astrocytoma	12	58.3 (27.7–84.8)	50.0 (29.3–70.7)	99.3 (98.6–99.7)	99.5 (99.1–99.8)	98.9 (98.0–99.4)
Anaplastic oligodendroglioma[#]	30	43.3 (25.5–62.6)	50.0 (33.7–66.3)	98.7 (97.9–99.3)	98.4 (97.8–98.8)	97.2 (96.0–98.1)
Oligodendroglioma[※]	19	26.3 (9.2–51.2)	27.8 (13.2–49.3)	98.8 (97.9–99.3)	98.7 (98.3–99.0)	97.5 (96.3–98.3)
Anaplastic ependymoma	4	0.0 (0.0–60.2)	NA	100.0 (99.7–100.0)	99.6 (99.6–99.6)	99.6 (99.0–99.9)
Ependymoma	3	66.7 (9.4–99.2)	22.2 (8.8–45.9)	99.3 (98.6–99.7)	99.9 (99.5–100.0)	99.3 (98.5–99.7)
Subependymoma	3	33.3 (0.8–90.6)	100 (NA)	100.0 (99.7–100.0)	99.8 (99.6–99.9)	99.8 (99.3–100.0)
Choroid plexus papilloma	3	33.3 (0.8–90.6)	25.0 (4.5–70.3)	99.7 (99.2–99.9)	99.8 (99.6–99.9)	99.5 (98.9–99.9)
Medulloblastoma	5	40.0 (5.3–85.3)	66.7 (17.6–94.9)	99.9 (99.5–100.0)	99.7 (99.4–99.9)	99.6 (99.0–99.9)
Meningioma[†]	204	94.6 (90.6–97.3)	98.0 (94.8–99.2)	99.5 (98.8–99.9)	98.7 (97.8–99.3)	98.6 (97.7–99.2)
Meningioma (Grade 1)	175	93.7 (89.0–96.8)	86.8 (81.7–90.6)	97.2 (95.9–98.2)	98.7 (97.8–99.3)	96.6 (95.3–97.6)
Meningioma (Grades 2 and 3)	29	17.2 (5.9–35.8)	62.5 (29.5–86.9)	99.7 (99.2–99.9)	97.7 (97.3–98.1)	97.5 (96.3–98.3)
Pituitary adenoma	183	96.2 (92.3–98.5)	93.1 (88.8–95.9)	98.5 (97.5–99.2)	99.2 (98.4–99.6)	98.1(97.1–98.8)
Metastatic brain tumor	80	83.8 (73.8–91.1)	77.9 (69.1–84.8)	98.1 (97.0–98.8)	98.7 (97.8–99.2)	97.0 (95.8–97.9)
Schwannoma	69	98.6 (92.2–100.0)	94.4 (86.5–97.8)	99.6 (99.0–99.9)	99.9 (99.3–100.0)	99.5 (98.9–99.9)
Malignant lymphoma	59	81.4 (69.1–90.3)	72.7 (62.4–81.1)	98.2 (97.2–98.9)	98.9 (98.1–99.4)	97.3 (96.1–98.2)
Rathke's cleft cyst	26	73.1 (52.2–88.4)	76.0 (58.0–87.9)	99.4 (98.7–99.8)	99.3 (98.7–99.6)	98.8 (97.9–99.4)
Hemangioblastoma	17	94.1 (71.3–99.9)	94.1 (69.2–99.1)	99.9 (99.5–100.0)	99.9 (99.4–100.0)	99.8 (99.3–100.0)
Cavernous hemangioma	16	68.8 (41.3–89.0)	55.0 (37.1–71.7)	99.1 (98.4–99.6)	99.5 (99.0–99.8)	98.7 (97.8–99.3)
Craniopharyngioma	17	76.5 (50.1–93.2)	65.0 (45.9–80.3)	99.3 (98.6–99.7)	99.6 (99.1–99.8)	99.0 (98.2–99.5)
Germ cell tumor	9	44.4 (13.7–78.8)	80.0 (33.1–97.0)	99.9 (99.5–100.0)	99.5 (99.2–99.7)	99.4 (98.8–99.8)

Parentheses: 95% CI, [#]including anaplastic oligoastrocytoma, [※]including oligoastrocytoma, [†]meningioma of any grades, NA: Not applicable

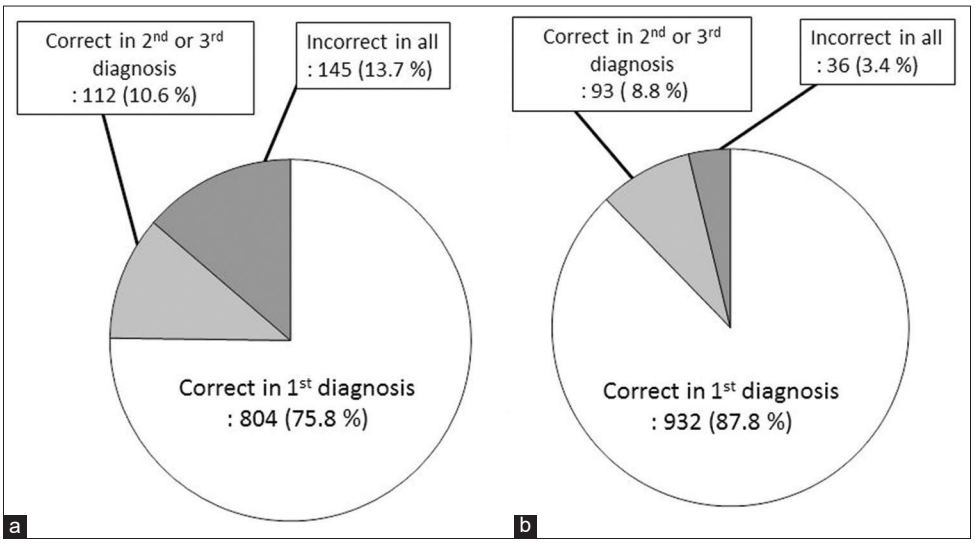

Figure 1: Sensitivity of preoperative diagnosis. (a) Sensitivity in preoperative differential diagnosis according to the WHO classification (2007) and grading (Total: 1061). (b) Sensitivity in preoperative differential diagnosis according to broader classification of brain tumor (Total: 1061).

(Grade 2), the sensitivity of the first diagnosis was 87.8% (95% CI: 85.7–89.8). It significantly improved to 96.6% (95% CI: 95.3–97.6) when the second and third diagnoses were included ($P < 0.0001$, Chi-squared test).

Sensitivity according to the location of the tumor

The sensitivity of the first differential diagnosis was high (>84%) in hypothalamic-pituitary, supratentorial extra-axial, and infratentorial extra-axial tumors. While it was low (36–42%) in supratentorial intraventricular, infratentorial intraventricular, and pineal region tumors; even with inclusion of the second and third diagnoses, the sensitivities were still <80% [Figure 2].

Sensitivity according to age groups

The sensitivity was significantly lower in 46 children (<18 years old) than in 1015 adults (≥18); 60.9% versus 76.5%, $P = 0.0158$. It was also significantly lower in children compared to two other age groups, 18–64 years and >64 years old; 60.9% versus 75.3% versus 78.2, $P = 0.0312$.

Sensitivity according to the WHO 2007 classification

Among 297 gliomas, the sensitivity of the first differential diagnosis was over 70% only in glioblastoma (73.1%). The sensitivity significantly improved up to 89.7% when the second and third differential diagnoses were included ($P = 0.0001$, Chi-squared test). In diffuse astrocytoma, ependymoma, and medulloblastoma, the sensitivity of the first diagnosis was under 70%, but it improved over 90% when the second and third differential diagnoses were included. For anaplastic astrocytoma and anaplastic ependymoma, it was still below 50% even on inclusion of the second and third differential diagnoses [Table 2 and Figures 3, 4].

In tumors other than gliomas, sensitivity was generally high. It was over 80% in metastasis, malignant lymphoma, pituitary adenoma, meningioma (overall and Grade 1), hemangioblastoma, and schwannoma; over 90% in the latter four. However, the sensitivity did not reach 20% in Grade 2 + 3 meningioma (21 in atypical, 2 in chordoid, 3 in anaplastic, and 3 in rhabdoid meningioma) [Table 2 and Figures 4, 5].

Positive predictive value (PPV)

PPV was 76.9% (95% CI: 74.5–79.1) in total. The PPV was high in extra-axial tumors (>90%) in pituitary adenoma, schwannoma, and meningioma. Among 297 gliomas, glioblastoma had high PPV of 81.0% (95% CI: 74.8–86.0). However, it did not exceed 50% in other types of gliomas. For meningioma, it was 98.0% (95% CI: 94.8–99.2) in overall and 86.8% (95% CI: 81.7–90.6) in Grade 1 meningioma, whereas it was 62.5% (95% CI: 29.5–86.9) in Grade 2 meningioma [Table 2 and Figure 4].

Specificity, negative predictive value (NPV), and accuracy

The specificity, NPV, and accuracy were generally high because of large number of true negative cases. Those were 96.6%, 94.8%, and 92.7% in glioblastoma, respectively. In other 23 kinds of tumors, those values were over 97% [Table 2].

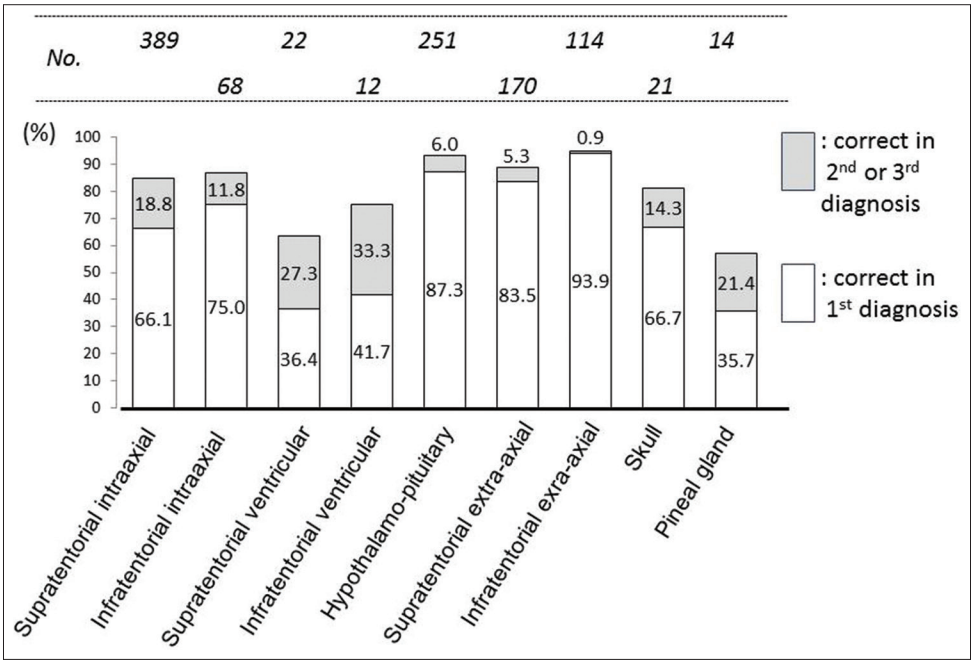

Figure 2: Sensitivity of preoperative differential diagnosis of brain tumor in each location ($n = 1061$).

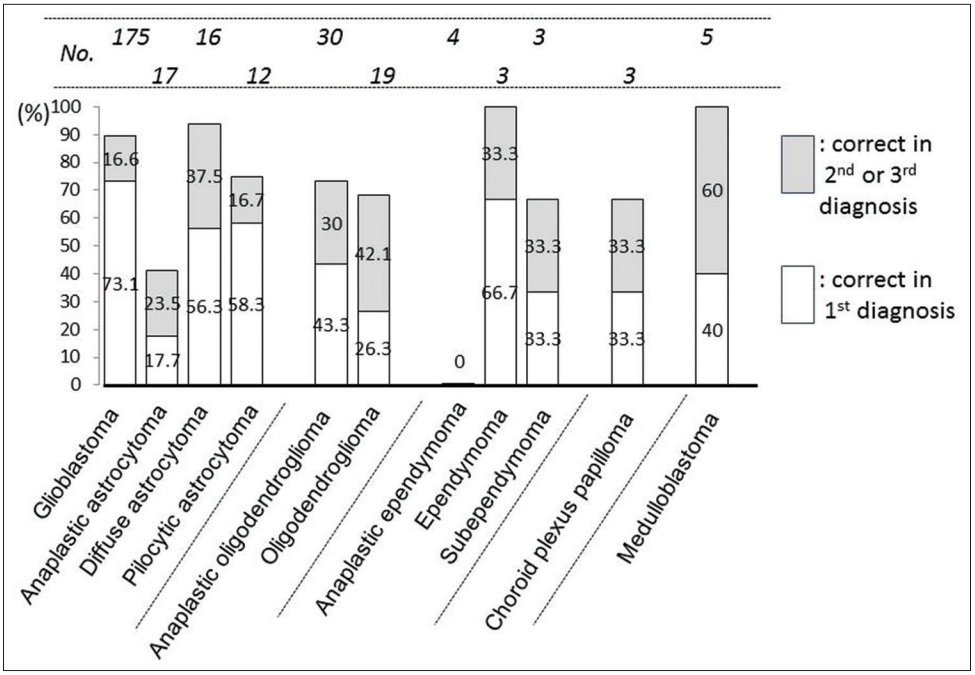

Figure 3: Sensitivity of preoperative differential diagnosis according to the WHO classification (2007) and grading in major glial tumors (n = 282).

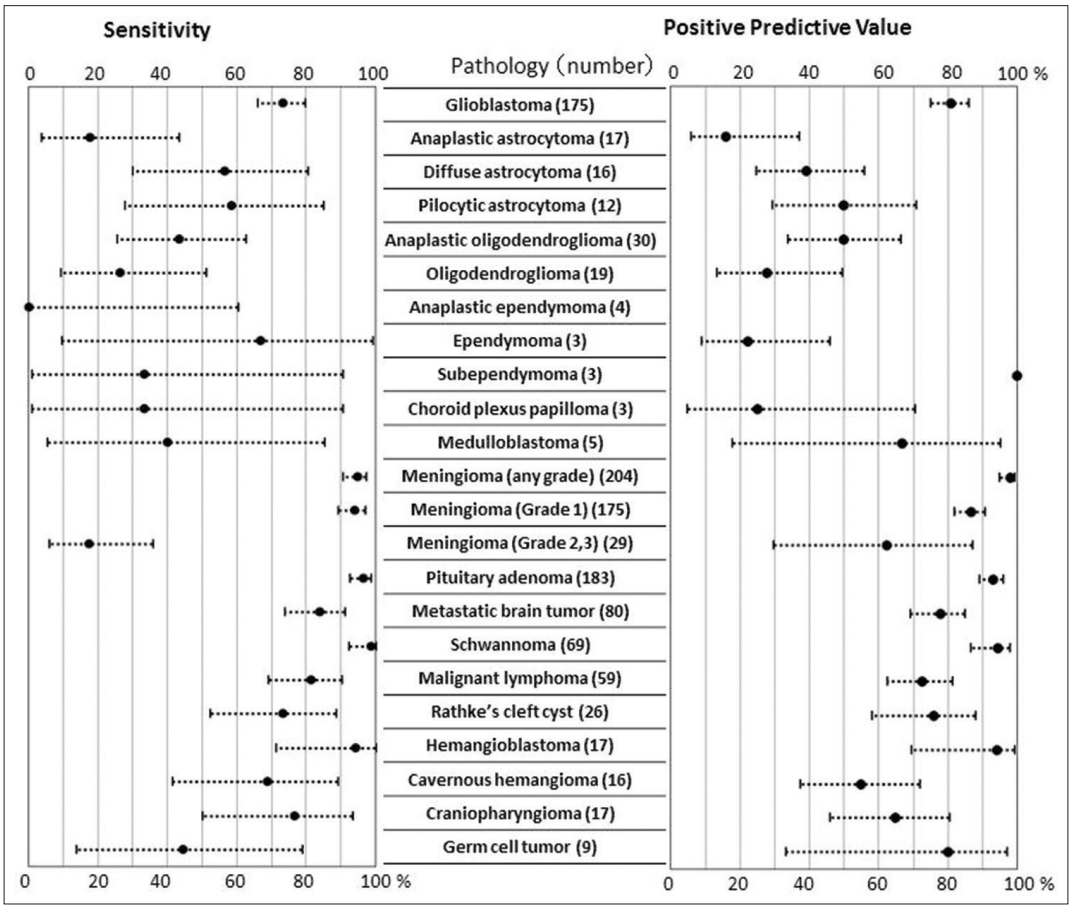

Figure 4: Sensitivity and positive predictive value of the first preoperative differential diagnosis in 23 major species of brain tumors.

Differential diagnosis of three major intra-axial tumors

Three major malignant neoplasms composed of 68.7% (314/457) of all intra-axial tumors. Sensitivity of the first diagnosis in glioblastoma (175), malignant lymphoma (59), and metastasis (80) was 73.1%, 81.4%, and 83.8%, respectively. PPV was 81.0%, 77.9%, and 72.7%, respectively [Table 3]. Specificity was 96.6%, 98.1%, and 98.2%, respectively. Incorrect diagnosis for the 175 glioblastomas included malignant lymphoma (13) and metastasis (7). For the 59 malignant lymphomas, glioblastoma (4) and metastasis (4) were incorrectly assigned as preoperative diagnosis. For the 80 metastases, glioblastoma (7) was incorrectly assigned as the preoperative diagnosis. Other false-negative diagnoses are listed in Table 3.

Strikeout lesions

When all three preoperative differential diagnoses for a lesion were incorrect, even broader categorizations were permitted we called the lesion as "strikeout lesion," consisting 3.4% (36/1061) of all. The frequent "strikeout" lesions included 5 (8.5% of total) malignant lymphomas, 3 (1.7%) glioblastomas, 3 (100%) cerebral inflammatory masses, 3 (12.0%) Rathke's cleft cysts, and 3 (75%) sellar xanthogranulomas (not registered in the WHO 2007). Following were also "strikeout" lesions; metastasis, pituitary adenoma, cavernous angioma ("hemangioma" in the WHO 2007), hemangioblastoma, craniopharyngioma, malignant melanoma, meningioma, IgG4-related hypophysitis, lymphocytic hypophysitis, schwannoma, teratoma,

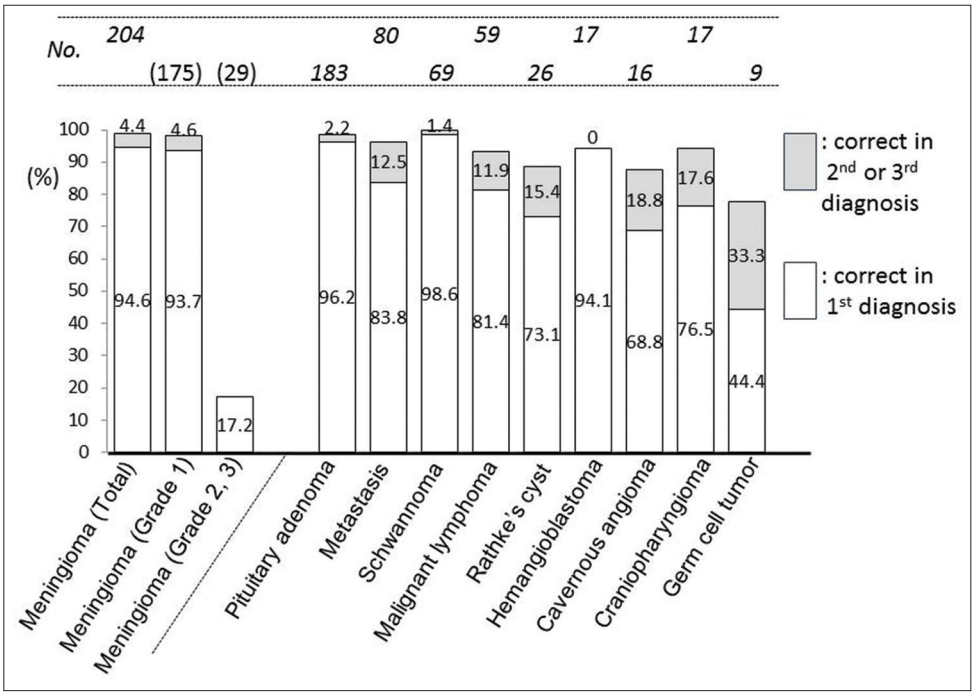

Figure 5: Sensitivity of preoperative differential diagnosis according to the WHO classification (2007) and grading in major nonglial tumors (n = 680).

Table 3: Accuracy of the preoperative diagnosis of three major intra-axial pathologies.

	The first preoperative differential diagnosis				
	Glioblastoma (%)	**Malignant lymphoma (%)**	**Metastasis (%)**	**Other false-negative diagnoses**	**Cumulative correct diagnosis rate[#] (%)**
Pathology					
Glioblastoma (n=175)	128 (correct: 73.1)	13 (7.4%)	7 (4.0)	Other gliomas 23, PPTID 2, misc. 2	89.7
Malignant lymphoma (n=59)	4 (6.8)	48 (correct: 81.4)	4 (6.8)	Misc. 3	96.2
Metastasis (n=80)	7 (8.8)	0	67 (correct: 83.8)	Meningioma 2, misc. 4	96.3

Misc.: Miscellaneous, PPTID: Pineal parenchymal tumor with intermediate differentiation, Correct: Correct diagnosis rate. [#]Accumulation of correct diagnosis rate in the first, second, and third preoperative diagnoses

Table 4: "Strikeout lesions" in which all top three preoperative diagnoses were incorrect even with broader classification.

Pathology	Strikeout cases	Total number	Strikeout rate (%)
Malignant lymphoma	5	59	8.5
Glioblastoma	3	175	1.7
Cerebral inflammation	3	3	100.0
Rathke's cyst	3	25	12.0
Sellar xanthogranuloma	3	4	75.0
Metastasis	2	81	2.5
Pituitary adenoma	2	183	1.1
Cavernous angioma	2	18	11.1
Miscellaneous (13 pathologies[#])	1 for each pathology	NA	NA

NA: Not applicable, [#]see the result

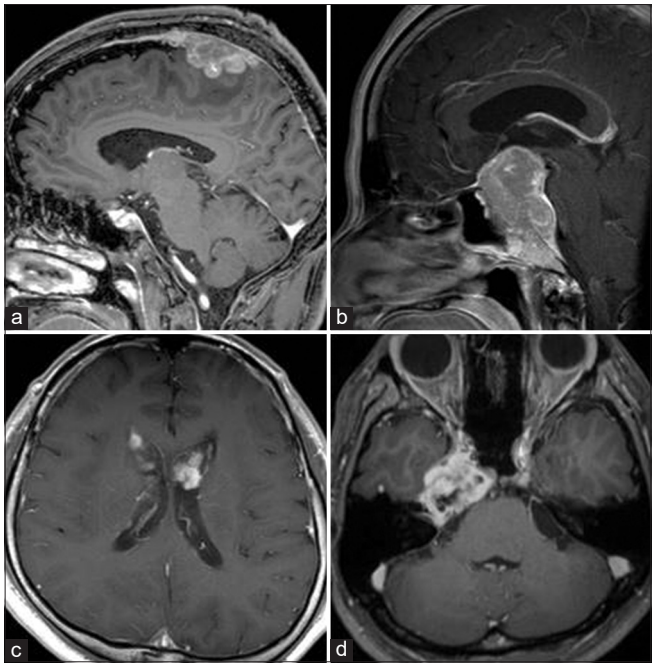

Figure 6: Representative cases of "strikeout" lesion. Pathological diagnosis and top three preoperative diagnoses. (a) Malignant lymphoma, 1: Grade 1 meningioma, 2: Grade 2 meningioma, 3: Metastasis. (b) Neuroblastoma, 1: Pituitary adenoma, 2: Atypical meningioma, 3: Atypical pituitary adenoma. (c) Subependymoma, 1: Metastasis, 2: Glioblastoma, 3: Choroid plexus carcinoma. (d) Schwannoma, 1: Chordoma, 2: Chondrosarcoma, 3: Plasmacytoma.

choriocarcinoma, neuroendocrine tumor, fibrous dysplasia, and cerebellar venous infarction [Table 4 and Figure 6].

DISCUSSION

Our prospective registration study of preoperative differential diagnosis of brain tumor showed that the sensitivity and PPV of the first diagnosis were around 75% in total. The sensitivity improved about 10% when the second and third diagnoses were included. Our study seems very unique because it included all kinds of the intracranial tumors, a total of 1061, and based on not only neuroimaging but also clinical information, eventually testing the efficiency of the preoperative conference as a clinical routine. In addition, this study assessed the significance of the second- and third-tier diagnoses.

We did not have any cases needing reoperation due to inaccuracy of preoperative diagnosis. This is partly because we selected an approach and craniotomy considering the second and third diagnoses could be correct. Moreover, this partly owes to routine intraoperative frozen tissue diagnosis which occasionally corrected surgical strategy during surgery.

It was also noteworthy that there were 3.4% of cases, in which all the three preoperative differential diagnoses were off-targeted.

The previous reports on precision of preoperative diagnosis of brain tumor were mainly from the viewpoint of diagnostic neuroradiologist. In 1995, Hangen *et al*. reported 76% of sensitivity in preoperative diagnosis of a small series of brain tumors, 173, in their prospective neuroradiologic study.[9] The sensitivity of extra-axial tumors, such as pituitary adenoma, meningioma, and schwannoma, was high (94–100%), in agreement with our study. However, the sensitivity was 50% in astrocytomas (WHO I–WHO IV) and 71% for metastatic tumors.

Julià-Sapé *et al*. also assessed the neuroimaging diagnosis in six European institutes and found high specificity, 85.2–100%, and variety of sensitivity depending on the tumor type.[11] Using broader criteria like "glial tumor," the sensitivity was as high as 86.7%, but it was very low by applying the categorization based on cell origin and grading, for example, sensitivity for low-grade astrocytoma was 14.3%.

Yan *et al*., a neurosurgeons' team, assessed the MRI reports from neuroradiology section and found sensitivity of 72.0–90.7% and PPV of 91.9–95.4% in 762 patients.[30] The values are a little higher than ours because they accepted broad categorization like glioma, not the cell origin and grading based. Again, sensitivity for extra-axial tumors was higher than that for glioma, 82.6–100.0% versus 47.8–82.8%.

In our study, the sensitivities for supra- and infratentorial ventricular tumors were unsatisfactory; 36–42%. The major reason of the low value seems to be wide variety of pathologies in the restricted area, for example, 22 supratentorial intraventricular tumors included glioblastoma, central neurocytoma (Grade 1), atypical central neurocytoma (Grade 2), malignant lymphoma, subependymal giant cell astrocytoma, subependymoma, metastasis, cavernous angioma, choroid plexus papilloma (Grade 1), atypical choroid plexus papilloma (Grade 2), simple hematoma, and

chordoid glioma. The sensitivity of the pineal gland tumor was also low, 35.7%, for pineal gland tumors which included wide variety of germ cell tumor, glioma, and metastasis.

Sensitivity for tumors in children was significantly lower than in adults in our series. This low sensitivity could be due to the greater population of intraventricular and pineal tumors in children than in adults; 15.2% versus 2.8% and 6.5% versus 1.3%, respectively. The actual sensitivity was 33.3% for both intraventricular and pineal gland tumors in the children. Moreover, another reason may be the absolutely small number of pediatric brain tumors, only 6.6 cases/year, in our institute. This paucity might have hindered the learning curve for our team's diagnostic ability.

Correct differentiation of the main three intra-axial tumors, malignant lymphoma, metastasis, and glioblastoma, is crucial to make an adequate surgical strategy, ranging from stereotactic biopsy, minimally invasive tumorectomy, and utmost safe resection including resection of nonenhanced but T2-hyperintense lesion and sometimes including lobectomy.[3,7,17,23-25] Past reported sensitivity was 36–43% for malignant lymphoma,[11,30] 35.7–68.0% for metastasis,[11,30] and 42.5% for glioblastoma.[30] The sensitivity for these three was much better, 81.4%, 83.8%, and 73.1%, respectively, in our series.

Perfusion, spectroscopic, and recently developed texture analyses of peritumoral edema may ease the differentiation between glioblastoma and solitary metastasis.[15,26] Utilization of other MRI parameters such as regional cerebral blood flow, fractional anisotropy, and permeability parameters gained from dynamic contrast-enhanced imaging may also enhance the ability to differentiate these three intra-axial malignancies.[2,21,28]

Compared to acceptable rate of sensitivity and specificity in diagnosis of glioblastoma, preoperative diagnosis of the low-grade glioma is challenging, sensitivity of 56.3% and PPV of 50%, in accordance with the previous report.[13] Sensitivity for anaplastic astrocytoma (Grade 3) was also low; 17.7%. A previous report described the sensitivity was 42.5% for "high-grade" astrocytomas which included a large proportion of glioblastoma.[9] Combination of conventional MRI features with advanced MR parameter including relative cerebral blood volume (rCBV) and MRS has reportedly improved the preoperative grading of gliomas.[8,16,18] However, the significance of accurate preoperative differential diagnosis among low-grade gliomas, such as oligodendroglioma, oligoastrocytoma, and diffuse astrocytoma may be limited because surgical strategy, utmost safe resection, is same in any of these pathologies.

In extra-axial tumors of our series, the sensitivity for high-grade meningioma (Grades 2 and 3) was remarkably lower (17.2%) compared to that for benign meningioma (Grade 1). The most common misdiagnosis for these 29 high-grade meningiomas was Grade 1 meningioma (22 cases) followed by glioblastoma (2 cases). Previously reported sensitivity for high-grade meningioma was also very low.[11] The surgical strategy for meningioma may be largely influenced by the preoperative prediction of the grade of meningioma.[18] Again, the combination of conventional imaging features on MRI and recently introduced MRI parameters may facilitate the better diagnosis of high-grade meningioma.[12,18,19,22,27]

Limitation of this study

Recently, it is recommended to use integrated classification system which combines histologic classification and genetic information, such as 1p/19q chromosomal codeletion, IDH-1 mutation, EGFR amplification, and BRAF mutation.[5,6,10,20] The new imaging modalities for preoperative differentiation of brain tumor according to the new classification have been introduced recently. The future study on precision should be based on these new classifications and utilizing these modern imaging modalities.[1,4,14,29]

We reviewed radiology reports before the conference and the attendance of diagnostic neuroradiology specialists was obtained in half of the cases in this series. Retrospectively, the discussion with neuroradiologists seemed not to be sufficient, considering some correct diagnoses in neuroradiology reports were dismissed and even some "strikeout" lesions were mentioned in the neuroradiology reports. Moreover, radiology reports were often not based on the WHO classification and grading, like "high-grade astrocytoma," and often equivocal. Radiology reports will be more useful when the final diagnosis becomes more categorical and systematically listed like our three-tier differential diagnosis list.

Strength of this study

In spite of aforementioned limitations, for the first time, this report provides the "real-world" data on efficiency of our preoperative diagnosis in our daily clinical practice. The similar study should be conducted to know the validity of our finding by other high-volume brain tumor centers. The comparison of the value of the precision and routine procedures for preoperative diagnosis between the institutes may widen chance to reach the correct preoperative diagnosis.

CONCLUSION

Our data showed that sensitivity and PPV of our differential diagnosis of the intracranial tumors in the routine preoperative conference were around 75%. It means that the diagnosis has possibility of false positive and false negative in 25%. The second and third diagnoses improved the sensitivity by 10% in general. However, the values varied considerably according to pathologies. The data on tumors of each location and pathology may give us important

information for establishing an adequate surgical strategy including the application of stereotactic biopsy, prediction of possible intraoperative alternation of approach, and proper use of intraoperative pathological diagnosis. In addition, these data may be conducive to adequately informing the patients and families. We are now planning the next stage study to investigate whether the routine use of advanced neuroimaging modalities, such as ASL, dynamic contrast-enhanced MRI, and rCBV parameters, improves the precision of our preoperative diagnosis.

Disclosures

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We declare that each of us participated sufficiently in the work to take public responsibility for this paper content. Moreover, we declare that there are no conflicts of interest that could be perceived as prejudicing the impartiality of the paper reported.

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Declaration of patient consent

Patients consent not required as patients idenity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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