THE PATHOLOGICAL SIGNIFICANCE OF CORPUS CALLOSUM INVOLVEMENT IN BRAIN SCANS

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Despite the unquestionable value of radionuclide scanning in the early detection of brain tumors, the nonspecific nature of abnormal scans remains a serious drawback in clinical practice. The differential diagnosis of a focal abnormality, as identified in static or dynamic radionuclide scanning studies, should include neoplastic, vascular, inflammatory, degenerative, traumatic, congenital, and unclassified disorders of the brain. With the exclusion of traumatic etiology, the major differential diagnosis may lie between neoplastic and occlusive cerebrovascular lesions since they are most frequently encountered and relatively easily detectable by scintillation scanning. The establishment of a specific pathological diagnosis (an infiltrating brain tumor) on the basis of an examination which utilizes a nonspecific agent (a radiopharmaceutical, such as $^{99m}TcO_4^-$) would be a desirable achievement in nuclear medicine.

Bull (*1*) in 1966 indicated the difficulties of demonstrating involvement of the corpus callosum by pneumography and angiography and advocated radioisotope scanning as the most reliable method to identify the site of neoplasm and to achieve a pathological diagnosis. In late 1966 Howieson and Bull (*2*) stated "the most convincing appearance on the gamma scan is the dumbbell-shaped zone of increased uptake produced by a tumor mass in each hemisphere and its extension through the corpus callosum." Bull (*3*) pointed out the anatomic and pathologic features of the corpus callosum which are of interest in neuroradiology and in clinical scintillation scanning. Other investigators (*4–8*) subsequently have confirmed or implied that the interhemispheric extension of focal abnormalities is a reliable sign in making the diagnosis of brain tumor on the basis of scanning alone.

The direct extension of an infiltrating cerebral neoplasm from one hemisphere into the opposite occurs frequently through the interhemispheric commisures since the cerebral falx acts as an irresistible barrier between the major portions of the brain hemispheres. Table 1 demonstrates the interhemispheric connections of the human cerebrum which are numerous, variable in size, and located at the different levels along the midline. Among these commisures, the corpus callosum stands out as the largest, connecting the cerebral hemispheres at the bottom of the longitudinal cerebral fissure (Fig. 1). The size discrepancy between the corpus callosum and the other interhemispheric connecting structures is striking. The corpus callosum, by virtue of its size and location between the cerebral hemispheres, lends itself to easier detection in brain scans when involved by abnormal foci. The objectives of this study are to further elaborate the significance of focal abnormalities crossing the midline through corpus callosum as detected in brain scans and to present a secure correlative analysis of the radionuclide scanning and pathological data.

TABLE 1. INTERHEMISPHERIC CONNECTIONS OF THE HUMAN CEREBRUM

Anterior commissure
Hippocampal commissure (fornix)
Corpus callosum
Habenular commissure
Posterior commissure
Massa intermedia (interthalamic connexus)

METHODS AND MATERIALS

All brain scans performed during the period of January 1969 through May 1971 inclusive were

Received Aug. 3, 1971; revision accepted Feb. 10, 1972.

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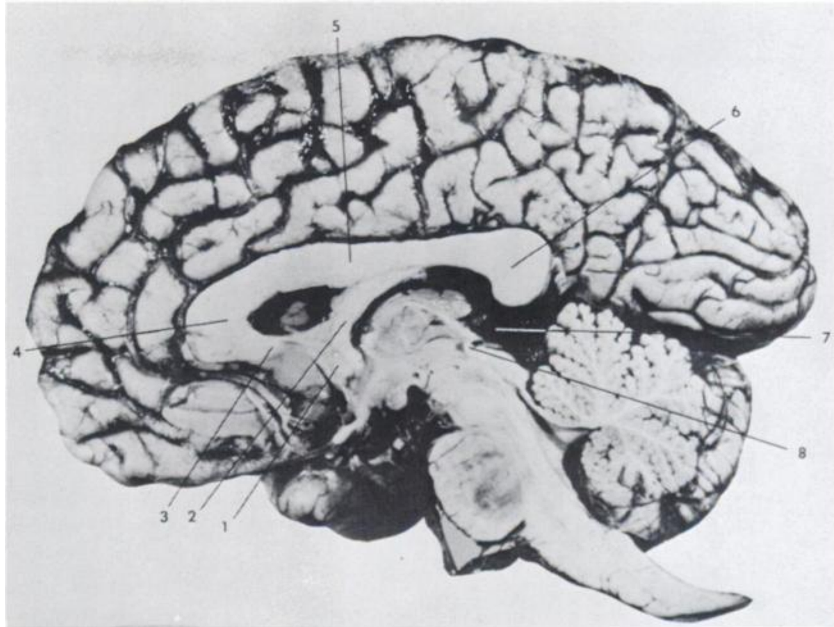

FIG. 1. Midsagittal section of normal brain illustrates large size and high location of corpus callosum as compared to other interhemispheric structures. 1 shows anterior commissure; 2, fornix; 3, rostrum of corpus callosum; 4, genu of corpus callosum; 5, body of corpus callosum; 6, splenium of corpus callosum; 7, habenular commissure; 8, posterior commissure.

interpreted and analyzed. The brain scans were performed on a commercially available rectilinear scanner initially with ^{197}Hg-chlormerodrin. In August 1969, $^{99m}TcO_4^-$ became the sole radiopharmaceutical utilized. As of 1970 all scanning studies were performed on an Anger camera (Nuclear-Chicago Pho/Gamma III). Potassium perchlorate (200–400 mg) was administered orally approximately 20–40 min before the intravenous administration of the radionuclide compound. Scans were obtained in the anterior, posterior, and both lateral positions. The vertex view (*9,10*) was obtained selectively. Atropine sulfate (0.5–1 mg) was administered intramuscularly approximately 1 hr prior to the administration of $^{99m}TcO_4^-$ when a vertex view was to be taken. The study was begun immediately after intravenous injection of 15 mCi (adult dose) of $^{99m}TcO_4^-$. Delayed studies (*11*) in addition to immediate postinjection scans were obtained in a few cases. The criteria for selection of the cases are defined in Table 2. The positive superficial biopsies or radiographic studies were not considered bona fide confirmatory evidence of corpus callosum involvement. The major reasons for these precautions were to exclude the possibilities of interhemispheric herniations and displacement of midline structures without invasion of the corpus callosum (*12*). Furthermore, the existence of "collision lesions" or "collision tumors" were also given consideration (*13,14*). Because of the small number of autopsy-confirmed brain scans, it was elected to review and to follow the case material in order to secure biopsy-proven surgical evidence of corpus callosum involvement. Of 1,500 satisfactory brain scanning studies, 44 cases met the first criterion alone as outlined in Table 2,

TABLE 2. CRITERIA FOR THE SELECTION OF CASE MATERIAL

1. Satisfactory brain scans indicating corpus callosum involvement.
2. Demonstration of corpus callosum involvement at craniotomy, autopsy, or both.
3. Definitive pathological diagnosis.

TABLE 3. CALLOSAL PATTERNS IN BRAIN SCANS

1. Symmetrical patterns: Midline abnormal activities invading corpus callosum and extending into both cerebral hemispheres. (a) Falx cerebri involved, (b) falx cerebri spared.
2. Asymmetrical patterns: Predominantly unilateral abnormal activities crossing midline through corpus callosum and partly extending into opposite cerebral hemisphere.

and 12 cases met all of the criteria. The autopsy records were also reviewed for the same period in order to determine the actual incidence of callosal involvement in brain tumors.

RESULTS

In this relatively small number of cases, involvement of the corpus callosum can be divided into two major groups of abnormal patterns as detected in brain scans (Table 3). The first group was symmetrical callosal patterns in which the abnormal activity was primarily midline in the corpus callosum with symmetrical extension into the adjacent cerebral hemispheres. The second group was asymmetrical callosal patterns in which the major part of the abnormal activity was in one cerebral hemisphere,

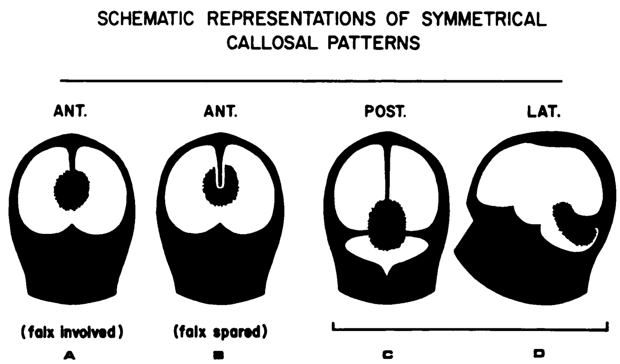

FIG. 2. Symmetrical patterns are illustrated. First two of midline patterns may look identical in which involvement or sparing of cerebral falx can be distinguished only at time of exploration. Rare symmetrical pattern, as shown in posterior and lateral views, is characterized by infra- and supratentorial components in continuity along midline. Pattern is strongly suggestive of infiltrating neoplasm.

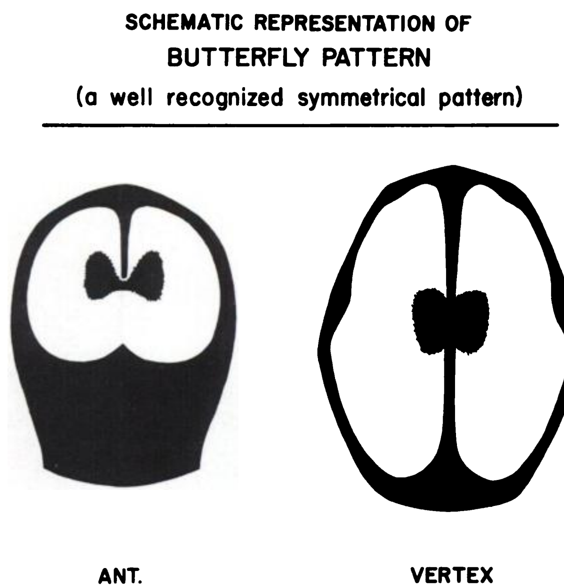

FIG. 3. Classical butterfly pattern that almost invariably indicates infiltrating tumor extending through corpus callosum into both cerebral hemispheres.

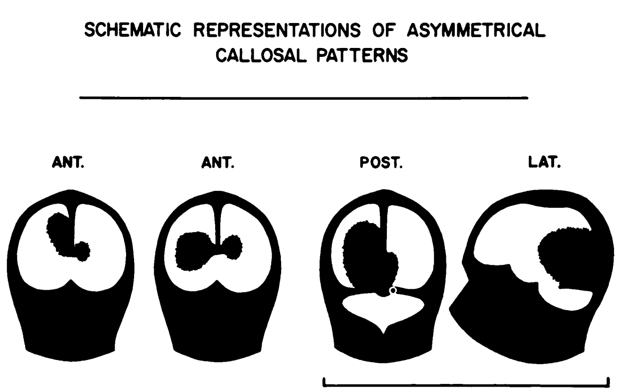

FIG. 4. Asymmetrical callosal patterns are illustrated. Interhemispheric extension of abnormal focus below inferior edge of cerebral falx is strongly suggestive of corpus callosum involvement.

but crossed the midline through the level of the corpus callosum and extended into the opposite hemisphere. Twelve cases of this series were evenly distributed in these two groups.

The schematic representations of the symmetrical callosal patterns are illustrated in Fig. 2. Of the six cases with one of these patterns, four were glioblastoma, one astrocytoma grade II, and one malignant melanoma. All tumors in this group were supratentorial with the exception of one. Involvement or sparing of the cerebral falx created two subgroups but these could be distinguished only at the time of exploration. Some of these symmetrical patterns may look identical on the scanning studies regardless of involvement or sparing of the cerebral falx (Fig. 2A and B). As illustrated in Fig. 2C and D, an unusual pattern is characterized by infra- and supratentorial involvement in the midline. This is strongly suggestive of an infiltrating neoplasm since it does not correlate with respect to any specific vascular distribution. Figure 3 demonstrates the "butterfly" pattern which is well recognized symmetrical callosal pattern. The "butterfly" pattern (*15*) has been shown to be the most characteristic pattern of a tumor mass that extends through the corpus callosum. We observed this pattern in somewhat atypical form in three cases.

The schematic representations of the asymmetrical callosal patterns are illustrated in Fig. 4. The interhemispheric crossing of the abnormal activity below the inferior edge of the cerebral falx was the most convincing sign of corpus callosum involvement in these patterns. Of the remaining six cases with asymmetrical callosal patterns, there were one astrocytoma grade II, two glioblastomas, one malignant melanoma, and two sarcomas.

REPRESENTATIVE CASES

Case 3. Figure 5 demonstrates an example of symmetrical callosal pattern. The abnormal focus was bifrontal and appeared to be in the anterior portion of the corpus callosum. In this 31-year-old white male, a left frontal craniotomy revealed a 50-gm melanoma deep in the left frontal lobe that extended along the corpus callosum to the left of the midline. The falx cerebri was free of tumor. At surgery the tumor was found to be more to the left of the midline than it appeared in the preoperative brain scans. In this case and Case 12, discrepancies can be found between the preoperative scan data and the surgical findings which may be due to the decrease of the interhemispheric displacement of tumor after reduction of an increased intracranial pressure during the neurosurgical procedure.

Case 4. The study in Fig. 6 illustrates a midline

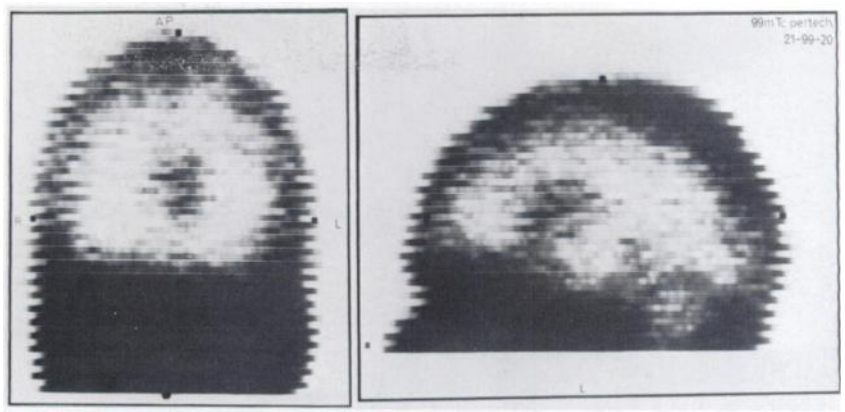

FIG. 5. Case 3. Example of symmetrical callosal pattern which appears to be occupying anterior portion of corpus callosum. In lateral view, configuration of focal lesion probably corresponds to anterior curved portion (genu) of corpus callosum. Case proved to be metastatic melanoma deep in left frontal lobe extending along corpus callosum.

abnormality that has both infra- and supratentorial components in the midline. This 60-year-old woman had a subtotal resection of a large meningeal sarcoma which appeared to arise from the tentorium. Surgery demonstrated that the tumor was extended far anteriorly and involved the splenium of the corpus callosum.

Case 10. The scan in Fig. 7 shows a large asymmetrical hemispheric abnormality that involves the left occipital lobe and the adjacent parietal lobe in a 61-year-old woman. A small portion of this large lesion crosses the midline in the posterior view. After this study was performed the patient received preoperative irradiation (2,000 rads) to the tumor. Surgery revealed glioblastoma multiforme with marked sarcomatous degeneration. At autopsy a large infiltrating tumor was found that invaded the dura and extended far anteriorly. The coronal section taken from the most anterior portion of the brain specimen (Fig. 8) verified both involvement and displacement of the corpus callosum and septum pellucidum.

Case 12. Figure 9 is an example of asymmetrical callosal pattern in the region of the genu of the corpus callosum. The medial margin of this large abnormal focus is sharply defined along the cerebral falx and its extension across the midline is far below the inferior edge of the cerebral falx. This pattern is believed to represent an infiltrating lesion, although its interhemispheric extension may not necessarily be through the corpus callosum. Occasionally, interhemispheric herniations of tumor masses or gyri containing tumor may simulate callosal patterns. This 61-year-old male had a right frontal craniotomy with subtotal removal of a glioblastoma multiforme. Surgery demonstrated that the tumor had invaded

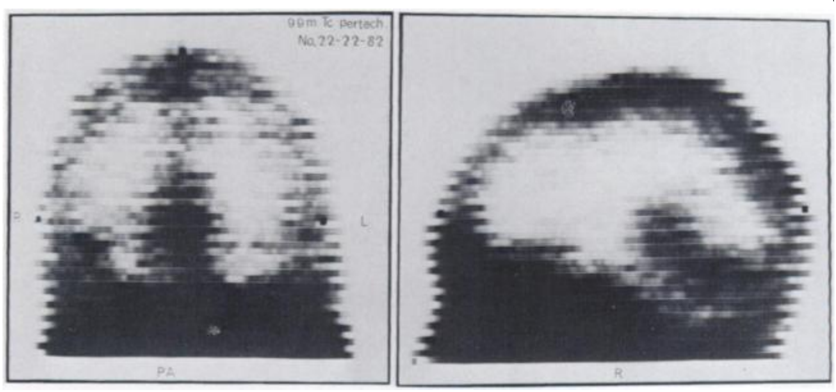

FIG. 6. Case 4. Symmetrical callosal pattern with both infra- and supratentorial components in continuity along midline. Case proved to be meningeal sarcoma that probably arose from tentorium and extended anteriorly to splenium of corpus callosum.

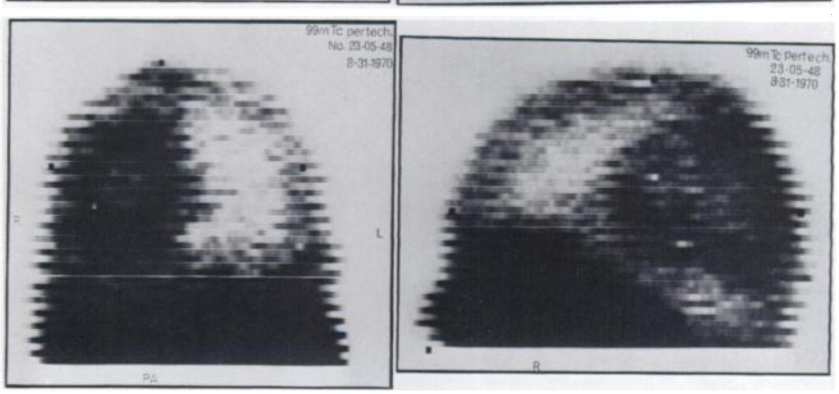

FIG. 7. Case 10. Large asymmetrical callosal pattern that involved entire right occipital lobe and adjacent parietal lobe. Interhemispheric crossing of large focus is identifiable on posterior projection.

FIG. 8. Gross brain specimens of Case 10 confirmed infiltrating necrotic tumor that invaded dura and involved corpus callosum and septum pellucidum. This was glioblastoma multiforme (courtesy of Samuel M. Chou).

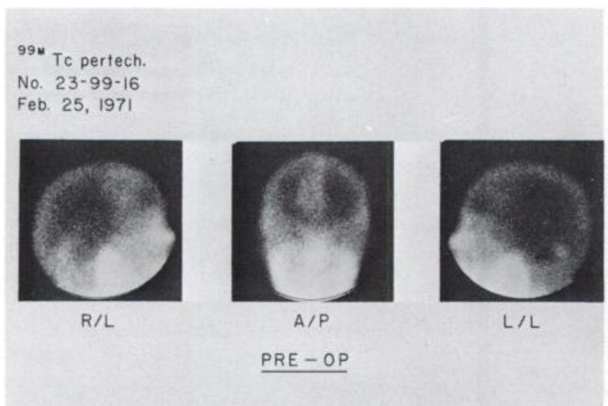

FIG. 9. Case 12. Preoperative camera images of asymmetrical focal abnormality in right frontal lobe with extension into opposite cerebral hemisphere through genu of corpus callosum. Medial margin of lesion is sharply defined along cerebral falx, but its interhemispheric extension is seen in region immediately below inferior edge of cerebral falx. Occasionally, interhemispheric herniations of tumor masses or supracallosal gyrus, if invaded by tumor, may simulate this type of callosal pattern.

the anterior portion of the corpus callosum and part of the medial aspect of the opposite left hemisphere.

DISCUSSION

Table 4 summarizes the histological types and the frequency of callosal involvement with 153 consecutive brain tumor cases. The minimal incidence of corpus callosum involvement was found to be 18.6% in gliomas, 11.1% in metastatic tumors, and 23% in primary sarcomas. These figures were considered minimal and did not necessarily reflect the true incidence of callosal involvement in this series of brain tumors since autopsy or surgical confirmation was not available in many cases. Varying figures concerning the incidence of corpus callosum involvement in brain tumors have been reported in the literature (*16–22*) and its incidence varies with the specific histological type. Bull (*1*) reported that the corpus callosum was involved in 36% of supratentorial astrocytomas and Maxwell reported 75% in glioblastomas. Malignant tumors of the brain often extend by infiltrating the adjacent normal brain structures, and this is particularly true of gliomas and sarcomas. Diffuse infiltration may occur occasionally in metastatic tumors of the brain.

The corpus callosum is the largest of the interhemispheric commissures and provides an easy bridge that can be crossed by infiltrating tumors. It is about 10 cm in length. Its anterior end, the genu, lies 4 cm from the frontal poles and its thickest posterior portion, the splenium, approaches the incisural margin of the tentorium cerebelli and lies 6 cm from the occipital poles (*23–28*). The corpus callosum is composed of crowded interconnecting transverse fibers extending from one cerebral cortex into the identical portion of the opposite cortex which fan out into the white matter of the cerebral hemispheres. The midline position of the corpus callosum make the detection of abnormal foci readily identifiable in

TABLE 4. HISTOLOGICAL CLASSIFICATION OF 153 CONSECUTIVE BRAIN TUMOR CASES AND MINIMAL INCIDENCE OF CORPUS CALLOSUM INVOLVEMENT

Histological diagnoiss	No. of cases	No. of cases with callosal involvement (surg. or autop. proof)	Minimal incidence of corpus callosum involvement
Gliomas	59	11	18.6%
Metastatic tumors	36	4	11.1%
Primary sarcomas	13	3	23.0%
Meningiomas	26		
Pituitary tumors and craniopharyngiomas	8		
Acoustic neurofibromas, cholesteatomas, and unclassified tumors	11		
Total	153	18	11.7%

Period of January 1969 through May 1971 inclusive.

radionuclide scanning studies provided that the abnormal foci reach a certain size (1.5–2 cm) and sufficiently concentrate the radiopharmaceuticals.

Interhemispheric extension of an abnormal focus as detected in brain scans may not necessarily indicate involvement of the corpus callosum since interhemispheric herniation or displacement of tumor masses could mimic callosal extension.

SUMMARY AND CONCLUSIONS

All tumors were supratentorial in location with the exception of one case (Case 4) which had both supra- and infratentorial components in continuity along the midline. In all cases confirmation of the pathology was determined by surgery and in one case autopsy evidence was also obtained. The clinical data of twelve cases in this series are summarized in Table 5. The following conclusions are submitted:

1. The corpus callosum, by virtue of its size and interhemispheric location, lends itself to easy detection in brain scans when involved by focal abnormalities.
2. The corpus callosum is frequently involved by infiltrating tumors of the brain, such as gliomas, sarcomas, and occasional metastatic tumors. Its incidence of involvement varies with the histological differentiation of tumors and the criteria utilized in any study. The relatively low incidence of corpus callosum involvement, as determined in this study (25% in primary sarcomas, 18% in gliomas, and 11% in metastatic tumors), is partially explained by the low autopsy rate (*29*) and very strict criteria which necessitated surgery or autopsy confirmed brain scans with callosal patterns.
3. The callosal patterns of abnormal activity as seen in brain scans are indicative of an infiltrating brain tumor based on this study. Some discrepancy in regard to interhemispheric extension can be observed between the preoperative scanning data and the surgical findings. This may be due to intracranial pressure changes that occur during the neurosurgical procedure.

ACKNOWLEDGMENTS

I would like to thank G. Robert Nugent, Professor and Chairman of the Division of Neurosurgery, West Virginia

TABLE 5. SUMMARY OF CLINICAL DATA

Cases	Age (yr) and sex	Diagnosis and location	Demonstration of corpus callosum involvement
1 #20-76-50	61 W.F.	Astrocytoma, grade II Corpus callosum	Right parietal craniotomy
2 #19-33-59	62 W.M.	Glioblastoma Bifrontal (lobes)	Right frontal craniotomy
3 #21-99-20	31 W.M.	Metastatic melanoma Posterior frontal lobe	Left frontal craniotomy
4 #22-22-82	60 W.F.	Primary sarcoma Tentorium	Suboccipital craniectomy
5 #21-62-19	54 W.M.	Glioblastoma Frontal lobe, deep-medial	Right fronto-parietal craniectomy
6 #22-10-21	3 W.F.	Primary sarcoma Bifrontal (falx)	Bifrontal craniotomy
7 #22-80-62	73 W.M.	Glioblastoma Corpus callosum	Right parietal craniotomy
8 #22-91-64	54 W.F.	Metastatic melanoma Bifrontal (lobes)	Bifrontal craniotomy
9 #21-93-30	50 W.F.	Astrocytoma, grade II Temporal lobe, deep	Left temporal craniectomy X2
10 #23-05-48	61 W.F.	Glioblastoma Occipito-parietal	Right parietal craniotomy autopsy
11 #23-63-17	79 W.M.	Glioblastoma Fronto-parietal lobes	Right parietal craniotomy
12 #23-99-16	69 W.M.	Glioblastoma Bifrontal (lobes)	Right fronto-temporal craniotomy

University Medical Center, School of Medicine, for allowing me to observe and photograph his neurosurgical procedures and Samuel M. Chou, Professor of Neuropathology, West Virginia University Medical Center, School of Medicine, for allowing me to review some of his autopsy records and to photograph some of the brain specimens included in this study.

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