Article abstract

To determine whether nervous system neoplasms are associated with primary malignancies elsewhere, we studied the frequency of multiple primary tumors in patients in whom at least one of the primary tumors was within the nervous system. The patients were Connecticut residents with tumors diagnosed between 1935 and 1964. Of 135 patients, 130 had two primary tumors, four had three primary tumors, and one had four primary tumors. Only with multiple primary tumors involving the brain and breast did the number of observed cases significantly exceed the number of expected cases; eight patients who had a meningioma associated with a breast cancer accounted for this excess. Patients with breast cancer presenting with signs or symptoms of an intracranial neoplasm should be carefully evaluated, for the intracranial lesion may be a potentially curable meningioma.

Nervous system neoplasms and primary malignancies of other sites

The unique association between meningiomas and breast cancer

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Does a cancer in a particular anatomic site increase, decrease, or have no effect on the risk that a second primary cancer will develop in the same or another site? In this paper, we attempt to answer this question in relation to tumors of the nervous system, with particular consideration of the association between neoplasms of the nervous system and primary malignancies of other sites.

A number of recently published findings prompted the present study. Of great interest was McAllister and colleagues[1] report of the isolation of viruslike particles from a brain tumor that developed after a human rhabdomyosarcoma cell line was implanted into fetal cats. The brain tumor, a sarcoma, was thought to be a metastasis of the rhabdomyosarcoma. However, no viruslike particles could be isolated from the original rhabdomyosarcoma cell line, and these investigators considered the possibility that the C-type virus particles obtained from the brain tumor represented competent human sarcoma virions capable of inducing tumors.[1] Of further interest was the recent report of several families with a high prevalence of breast cancer, soft-tissue sarcoma, leukemia, and brain tumors.[2]

Investigations dealing with multiple primary neoplasms have included (1) individual case reports documenting the occurrence of multiple primary malignancies in a single patient; (2) reports dealing with large series of such patients, with estimations of the frequency of occurrence of multiple primary tumors; and (3) reports based on population surveys attempting to compare the incidence rate or risk of development of a second primary with the corresponding risk of development of a first primary cancer in the general population. The third type of investigation is especially relevant. If a history of one cancer decreases the chance

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that a second primary cancer will develop, it would seem that the first cancer provides some degree of protection against development of a new primary malignancy elsewhere. However, if the development of one cancer increases the risk of development of a second primary cancer, one might argue that the same genetic or environmental carcinogenic factors (including oncogenic viruses) operating in the development of the first cancer were again operating in the development of the second cancer. Such investigations, together with studies of families with a high prevalence of cancer, serve to identify particular segments of the general population who should be investigated further with respect to possible environmental or genetic oncogenic factors.

A number of dysgenetic syndromes may be associated with nervous system neoplasms, including tuberous sclerosis, Lindau's syndrome, von Recklinghausen's neurofibromatosis, neurocutaneous melanosis, and Sturge-Weber-Dimitri disease. The tumors usually associated with tuberous sclerosis are astrocytomas and glioblastomas. In addition to the multiple peripheral, spinal, and cranial nerve sheath tumors that occur in von Recklinghausen's neurofibromatosis, other nervous system tumors found in individuals with this disease include meningiomas (often multiple), glial tumors of the central nervous system, and ependymomas. The cerebellar hemangioblastoma of Lindau's syndrome is associated with similar tumors of the retina (Hippel's disease), renal tumors, and congenital cysts of the pancreas and kidney. In neurocutaneous melanosis, melanotic pigmentation of various areas of the skin is associated with melanoma of the leptomeninges. Sturge-Weber-Dimitri disease is characterized by a capillary-venous malformation of one cerebral hemisphere and a homolateral port-wine stain in the area of distribution of the trigeminal nerve. All these conditions are believed to be attributable to hereditary factors, although sporadic cases have been reported.[3]

Among the more common tumors of the nervous system, meningiomas are known to occur in association with cerebral gliomas;[4–6] multiple primary neoplasms of the meninges also have been reported.[7] Depending on the series, glioblastomas have been found to have a multicentric origin in from 4.9[8] to 20 percent[9] of patients. Two instances of glioblastoma in association with colloid cysts of the third ventricle also have been reported.[3] Multiple ganglioneuromas sometimes occur[10] and have been reported in patients with von Recklinghausen's neurofibromatosis.[3] Tables 1 and 2 summarize the recent literature concerning the association of neoplasms of the nervous system with primary malignancies in other sites in individual patients and within families. The site of associated malignancies seems to have no consistent pattern.

Materials and methods. *Types of tumors studied.* We studied all cases of multiple primary tumors diagnosed in Connecticut residents from 1935 through 1964 in which at least one of the primary sites was within the nervous system. The data resource was the population-based Connecticut Tumor Registry. The Registry routinely receives (1) reports on all Connecticut residents who are admitted to a hospital within the state with a diagnosis of malignant neoplasm and (2) copies of all death certificates for Connecticut residents on which cancer is mentioned.[20,21] Both benign and malignant neoplasms of the central nervous system are reportable. If the patient is known to have been admitted to a hospital outside the state, that institution is contacted for more specific information. An attempt is made to follow all patients from diagnosis to death, and it is estimated that less than 5 percent of the patients are lost to follow-up.[22]

The Registry offers many advantages for studies of multiple primary tumors. The incidence rates used to calculate the expected number of multiple primary neoplasms are obtained from the same population yielding the first primary malignancies. The Registry also has nearly complete reporting of cancer throughout the state and a large enough experience to allow meaningful comparisons between the observed and expected numbers of second primary tumors on an individual primary-site basis.

Because of close anatomic proximity, tumors of the pituitary gland, craniopharyngeal duct, and pineal gland were included with neoplasms of the nervous system. Neoplasms of the eye were not included because, although the optic nerve and retina are derived embryologically from the primary cerebral vesicle, neoplasms of the eye are, in certain instances, somewhat distinct from tumors occurring elsewhere in the nervous system. Throughout this report, the nomenclature used to describe neoplasms of the central nervous system is that suggested by Kernohan and Sayre.[23] Furthermore, the term "astrocytoma" is reserved for the grade 1 and 2 gliomas of the astrocytic series, and the term "glioblastoma" designates grade 3 and 4 gliomas of the astrocytic series.

Of tumors outside the nervous system, skin cancers were excluded from the present study because the Registry does not attempt to collect data on all skin cancer cases. Skin cancers may be treated on an outpatient basis and therefore may not be reported to the Registry.

Calculation of patient survival. In order to compare the observed and expected numbers of second primary tumors in the Connecticut population, the overall survival data for patients with a first primary malignancy were converted to person-years of exposure (PYE), that is, PYE to the risk of development of a new primary cancer. The calculation is based on the assumption that the survival experience for five patients observed for 1 year is comparable to that for one person observed for 5 years, provided the risk of development of cancer remains constant over the 5-year period. PYE were collected for each primary-site group for each year of age, starting at the first diagnosis of a neoplasm to either the individual's death or age at last follow-up. The cutoff date for follow-up was December 31, 1964.

If a patient with a recorded age of 50 years had a brain tumor and survived for 4 years, 1 month, his age at diagnosis would average 50.5 years. Such a patient would

Table 1. Association in individual patients of neoplasms of nervous system with those of other systems: Summary of literature, 1967-1971

Authors	Nervous system tumors	Associated tumors outside nervous system	Remarks
Fraumeni and Miller[11]	Astrocytoma [2] *	Adrenocortical neoplasms†	Astrocytomas developed in two of 62 children with adrenocortical neoplasms.
Li and Fraumeni[12]	Astrocytoma [1]	Rhabdomyosarcoma†	Four families had a high prevalence of cancer and an excess of multiple primary tumors. Only one person in the study group had a neoplasm of nervous system; this patient also had rhabdomyosarcoma. In other members of these families, most common tumors were soft-tissue sarcomas and breast cancers.
Li and Fraumeni[13]	Astrocytoma [1]	Rhabdomyosarcoma†	A report of 280 hospital records and 418 death certificates for children with rhabdomyosarcoma.
Gabbiani et al[14]	Cerebellar astrocytoma [1]	Synovial sarcoma† [1]	Description of ultrastructural characteristics of synovial sarcoma; review revealed history of astrocytoma 30 years prior to occurrence of sarcoma.
Jensen and Miller[15]	Brain tumor, type unspecified [2]; spongioblastoma [1]	Retinoblastoma† and tumors of several other sites	Study of 269 death certificates and 1,623 hospital records for children with retinoblastoma, and search for other primary neoplasms. Associated neoplasms in those patients who received radiation as treatment for retinoblastoma were osteosarcoma (3), Wilms' tumor (1), leukemia (1), thyroid adenocarcinoma (1), malignant melanoma (1), and embryonal neoplasm of unknown origin (1).

*Numbers in brackets indicate number of such tumors reported.
†Index tumor.

Table 2. Association within same family of neoplasms of nervous system with those of other systems: Summary of literature, 1967-1971

Authors	Nervous system tumors	Associated tumors outside nervous system	Remarks
Li and Fraumeni[13]	Brain tumor, type unspecified [2];* medulloblastoma [2]	Rhabdomyosarcoma †	Brain tumors in sibling and mother, medulloblastoma in brother.
Lynch and Krush[16]	Glioma [1]	Endometrial carcinoma † and intestinal cancers	Report of family with high prevalence of cancer of endometrium, colon, and rectum; one individual in family had glioma.
Lynch and Krush[17]	Brain tumor,† type unspecified [2]	Tumors of several sites, especially carcinoma of colon and endometrium	Occurrence of 113 malignancies in 650 members of a family with a high incidence of neoplasms; period of study, 1895-1970.
Walker et al[18]	Brain tumor, type unspecified [2]	Malignant neoplasms of stomach, bowel, breast, adrenal gland, soft tissues	Study of large kindred with high prevalence of malignant disease, especially brain tumors; actual number of total cases not given.
Bottomley et al[19]	Brain tumor, type unspecified [3]	Malignant neoplasms, especially breast cancer, sarcoma, acute leukemia	Report of kindred in which 37 of 405 family members had malignancy.
Lynch et al[2]	Brain tumor, type unspecified [5]	Breast cancer † and soft-tissue sarcoma [10], leukemia [6]	Report of 34 families in which two or more of the first-degree relatives had breast cancer. Sarcoma in 10 members of five families, leukemia in six members of four families, and brain tumors in five members of five families.

*Numbers in brackets indicate number of such tumors reported.
†Index tumor.

Table 3. Example illustrating the calculation of person-years of exposure (PYE) following first primary brain tumor

Age	Patient 1* PYE‡	Patient 1* PME§	Patient 2† PYE	Patient 2† PME	Total experience for these two patients
50		6			0.50
51	1				1.00
52	1			6	1.50
53	1		1		2.00
54		7		8	1.25

*Brain tumor diagnosed at age 50; patient survived 4 years, 1 month.
†Brain tumor diagnosed at age 52; patient survived 2 years, 2 months.
‡PYE = Person-years of exposure.
§PME = Person-months of exposure. Both patients were males.

Table 4. Association of additional primary tumors with index tumors

Index cases (patients)	Additional primary tumors per index case	Total additional tumors in index tumor cases
130	1	130
4	2	8
1	3	3
Total 135		141

contribute 6 person-months of exposure (PME) at age 50, 1 PYE at each age from 51 through 53, and 7 PME at age 54. If a second patient with a recorded age of 52 had a brain tumor and had survived for 2 years, 2 months at the date of last follow-up, he would be, on the average, 52.5 years old at diagnosis. He would contribute 6 PME at age 52, 1 PYE at age 53, and 8 PME at age 54. The PME can then be converted into PYE by dividing by 12. The total experience for these two patients would be 0.50 PYE at age 50, 1.00 PYE at age 51, 1.50 PYE at age 52, 2.00 PYE at age 53, and 1.25 PYE at age 54. Table 3 gives examples of such calculations.

The survival experience for all patients with a first primary neoplasm of the nervous system thus was collected for each age group, and the experience in each 5-year age group was totaled, giving 18 such groupings (ages 0-4, . . ., 80-84, 85, and older). Age-specific, sex-specific, and site-specific incidence rates[24,25] were then applied to the appropriate PYE in order to obtain the expected number of second primary cancers for each specific group. Thus, for each age, sex, and site grouping, the following equation could be applied to individuals who already have a malignancy at site 1: $PYE_1 \times \text{incidence}_2 = \text{expected number of new primary}$ malignancies at site 2, where PYE_1 refers to PYE in patients with cancer at one site who are exposed to the risk of development of a new primary cancer and incidence_2 refers to the probability that a new cancer will develop at a second site.

The figures for expected cancer were then summed over all age groups to obtain the total number of expected cancers at each site. Using the same methods, it was possible to determine the expected number of primary nervous system neoplasms following primary malignancies in other sites. The coded records of reported cases of second primary cancers were selected and matched by case number with the first primary cancers to obtain the observed number of second primaries.

Since the probability of a second primary cancer is very small, the number of second primary cancers can be expected to follow a Poisson distribution. A table of significance factors for the ratio of a Poisson variable to its expectation[26] was used to test the statistical significance of the results. When the number of observed cases was zero, statistical significance was tested with the values given in a table of confidence limits for the expectation of a Poisson variable.[27] The total Connecticut population was available for the estimation of the incidence rate for the first primary cancer, whereas only those in whom a first primary cancer developed were subsequently available for the estimation of the incidence of the second primary cancer. The estimation of the incidence of first primary cancers therefore has negligible error in comparison with the estimation of the incidence of second primary cancers, since the former estimate is based on a much larger sample size.

Results. A search of a group of 185,344 records produced a subgroup of 5,022 patients with multiple primary tumors diagnosed from 1935 through 1964. A further search of the subgroup revealed 135 patients (59 males and 76 females) with multiple primary tumors in whom at least one of the primary sites was within the nervous system, as defined for the purposes of this study. As noted in table 4, 130 patients each had one primary tumor in addition to the one within the nervous system, four patients each had two additional primaries, and one patient had three additional associated neoplasms. Calculation reveals that 130 additional tumors were associated with 130 of the index tumor cases, eight additional tumors were associated with four of the index cases, and three additional tumors were associated with one of the index cases. Thus, 141 additional primary tumors were associated with the 135 index tumor cases within the nervous system.

Three patients had both first and second primary tumors within the nervous system. One patient had an astrocytoma and meningioma, another had a meningiosarcoma and glioblastoma, and the third had a meningiosarcoma in association with an oligodendroglioma. All these six separate primary tumors of the nervous system were microscopically confirmed. In the entire group of tumors, both the first and subsequent primary neoplasms were confirmed microscopically in approximately 75 percent of the 141 multiple primary tumor pairs (index case and associated primary tumor), one of the group of multiple primaries was confirmed

Table 5. Histologic confirmation of multiple primary tumor pairs

First primary neoplasm	Subsequent primary neoplasm: Microscopically confirmed Number	Microscopically confirmed Percent	Not microscopically confirmed Number	Not microscopically confirmed Percent	Total Number	Total Percent
Microscopically confirmed	106	75.2	7	5.0	113	80.2
Not microscopically confirmed	14	9.9	14	9.9	28	19.8
Total	120	85.1	21	14.9	141	100.0

Table 6. Distribution by site of the 141 multiple primary tumors associated with the 135 index tumor cases within the nervous system*

Site	No.	Percent
Digestive tract	37	26.4
Breast	22	15.6
Female genital organs	18	12.8
Prostate	15	10.6
Lymphatic and hematopoietic tissues	11	7.8
Kidney	8	5.7
Bladder	5	3.6
Thyroid	4	2.8
Skin (malignant melanoma) †	4	2.8
Respiratory system	4	2.8
Buccal cavity and pharynx	3	2.1
Brain and cranial meninges	2	1.4
Other and unspecified sites in nervous system	1	0.7
Pituitary and craniopharyngeal duct	1	0.7
Other endocrine glands	1	0.7
Connective and other soft tissue	1	0.7
Bone	1	0.7
Other and unspecified sites	3	2.1
Total	141	100.0

*And intracranial neoplasms involving the pituitary gland, craniopharyngeal duct, and pineal gland.

†Malignant melanoma was included in the study despite the fact that other skin tumors were not. Patients with malignant melanoma are usually hospitalized at some time during the course of their disease, and reporting of this neoplasm is therefore fairly complete.

microscopically in 15 percent, and none of the tumors was so confirmed in 10 percent (table 5).

In 39 patients, the multiple primary tumors were diagnosed simultaneously. The average time interval between discovery of nonsimultaneously diagnosed multiple primaries was 60.8 months.

Approximately 75 percent of the index tumor cases involved the brain and cranial meninges. Table 6 shows the distribution by site of the 141 multiple primary tumors associated with the 135 index tumor cases. The most commonly involved sites outside the nervous system, in order, were the digestive tract, breast, female genital organs, and prostate.

The distribution by histologic type of microscopically confirmed tumors involving the brain and cranial meninges in patients with multiple primaries was compared with the distribution of such neoplasms in all patients.[25] In comparison with the relative frequency in the general population, there was a distinct increase in the percentage of meningiomas and a corresponding decrease in the percentage of the astrocytoma group of tumors ($p < 0.01$) (table 7).

Simultaneously diagnosed neoplasms could not be included in comparing the observed and expected numbers of second primary cancers, because it was not possible to calculate an expected number for this group of tumors. Only in the case of multiple primary tumors involving the breast and nervous system did the number of observed second primary cancers significantly exceed the number expected (18 cases observed versus 10.25 cases expected; $p < 0.05$). All these 18 patients were females. Tables 8 and 9 provide a more detailed description of the characteristics of these tumors. The patients' age at diagnosis of the breast cancer followed no consistent pattern. Of the 18 nonsimultaneously diagnosed tumor pairs, each tumor in 14 pairs was microscopically confirmed, and one of the two tumors in the remaining four pairs was so confirmed. Eight cases of a meningioma associated with a breast cancer accounted for the excess of observed-over-expected second primary cancers; only 3.37 such cases were expected ($p < 0.05$).

Discussion. Before interpreting the results, it is necessary to examine certain possibilities for bias. For many of the multiple primary tumors studied, the central nervous system is a common metastatic site for the associated tumor; metastatic disease thus may be mistaken for a new primary cancer. One therefore cannot overemphasize the importance of microscopic confirmation of both tumors or at least of the central nervous system tumor, because malignancies of the central nervous system do not commonly metastasize to distant sites outside the central nervous system. The reverse can also hold true, however.

Table 7. Distribution of histologically confirmed primary tumors of the brain and cranial meninges (Connecticut, 1935-1964)

Tumor	Patients with multiple primary neoplasms		All patients	
	Number	Percent	Number	Percent
Glioblastoma	37	43.5	1,167	52.3
Meningioma	35	41.2	402	18.0
Astrocytoma	5	5.9	271	12.1
Medulloblastoma	1	1.2	101	4.5
Neurilemoma	0	0.0	48	2.2
Hemangioma	4	4.7	50	2.2
Ependymoma	0	0.0	46	2.1
Oligodendroglioma	1	1.2	24	1.1
Other, specified	2	2.3	74	3.3
Other, unspecified	0	0.0	49	2.2
Total	85	100.0	2,232	100.0

The attending physician may believe that neoplastic disease in a second site represents metastatic spread, and therefore clinical investigations that would determine the existence of a new independent primary lesion may not be carried out.

In cases 7, 8, and 9, the development of the nervous system tumor, which was not confirmed microscopically, was followed by the development of a histologically confirmed malignancy of the breast (table 8). However, the nervous system tumors had been diagnosed 2 years, 1 year, and 4 years, respectively, before diagnosis of the breast cancers. In case 18 (table 9), a confirmed carcinoma of the breast was diagnosed more than 13½ years before diagnosis of the spinal cord tumor, which was not microscopically confirmed. Although in these four cases the tumor that was not histologically confirmed may have represented metastatic spread from the microscopically confirmed malignancy, we consider this only a small possibility.

In comparing the observed and expected numbers of second primary cancers, one must consider that since persons in whom one cancer has already developed may be more closely followed medically than those in whom a malignancy has not developed, subsequent cancers are likely to be discovered more often and at an earlier date. A person with one cancer already diagnosed may be more health-conscious or may come from areas of the state with better medical facilities than members of the general population, so that any second cancer may be diagnosed earlier.

Of particular interest is the higher percentage of meningiomas in patients with multiple primary tumors. This also holds true for the group with breast cancer and nervous system tumors. This finding has special clinical significance because meningiomas are potentially curable.

In regard to the higher percentage of meningiomas among patients with multiple primary cancers, one might argue that since a patient with a meningioma has a longer survival period than patients with other types of brain tumors, other primary tumors may become manifest. However, in the patients in the group with multiple primary tumors who had meningiomas, nine of the meningiomas were diagnosed at the same time that the other primary was diagnosed, 17 were diagnosed after the other primary, and only nine were diagnosed before diagnosis of the other primary neoplasm. Thus, for the majority of patients, the argument of longer survival cannot explain the excess of meningiomas, since most of these tumors were diagnosed at the same time or after the other primary. Furthermore, in the analysis to determine the expected number of patients with both meningioma and breast cancer, the survival experience of all patients with breast cancer and all patients with meningioma was taken into account.

The considerably higher percentage of meningiomas found in the patients with multiple primary tumors might reflect the fact that the rate of postmortem examinations is higher in patients dying of cancer than in those dying of other causes with no known neoplasm. Meningiomas that may be asymptomatic during life therefore would be detected at autopsy. In order to test this hypothesis, the percentage of all meningiomas of the central nervous system first diagnosed at autopsy (15 percent) was compared with the corresponding percentage in cases of multiple primary tumors (56 percent). This suggests that the above hypothesis explains the higher percentage of meningiomas in patients with multiple primary neoplasms. This was not the case in the eight patients with both a meningioma and a breast cancer. Six of these patients had symptoms suggesting an intracranial neoplasm prior to death. In only two asymptomatic patients was the totally unsuspected meningioma first discovered at autopsy. The figure of 25 percent (two of eight patients) is not very different from the overall figure of 15 percent.

The association of breast cancer and meningiomas raises some interesting etiologic possibilities, especially when they are considered in conjunction with other epidemiologic features of meningiomas. First, meningiomas are the only common primary intracranial neoplasm with a higher incidence in females.[25] Second, several authors have reported the rather abrupt appearance of meningiomas during pregnancy, and there is general agreement that these tumors enlarge during pregnancy.[28] Whether this is due to an acceleration in the growth of the tumor or an increase in the fluid content of the tumor has not been elucidated. The association of breast cancer and meningiomas demonstrated in the present study may be related to hormonal factors.

Only in the case of nervous system tumors and breast cancer did the number of observed second primary neoplasms significantly exceed the expected number. This agrees with the findings of Lynch and associates,[2] who reported a similar association in members of the

Table 8. Association of neoplasms of the nervous system* and breast cancer
Nonsimultaneously diagnosed cases: First primary tumor in the nervous system

Case number	First primary tumor			Subsequent primary tumor			Months between diagnoses	Age at diagnosis of breast cancer
	Site	Microscopically confirmed?	Histologic type	Site	Microscopically confirmed?	Histologic type		
1	Cranial meninges	Yes	Meningioma	Breast	Yes	Adenocarcinoma	5	69
2	Cranial meninges	Yes	Meningioma	Breast	Yes	Carcinoma, NOS†	53	49
3	Cranial meninges	Yes	Meningioma	Breast	Yes	Carcinoma, NOS	306	86
4	Brain	Yes	Glioblastoma	Breast	Yes	Carcinoma, NOS	1	48
5	Brain	Yes	Glioblastoma	Breast	Yes	Carcinoma, NOS	31	48
6	Brain	Yes	Astrocytoma	Breast	Yes	Carcinoma, NOS	196	30
7	Unspecified nervous system site	No	-------	Breast	Yes	Adenocarcinoma	24	53
8	Brain or cranial meninges	No	-------	Breast	Yes	Ductal carcinoma	12	69
9	Brain or cranial meninges	No	-------	Breast	Yes	Adenocarcinoma	48	56
10	Pineal	Yes	Pinealoma	Breast	Yes	Carcinoma, NOS	73	57

*Including tumors of the pineal and pituitary gland.
†NOS = Not otherwise specified.

Table 9. Association of neoplasms of the nervous system* and breast cancer
Nonsimultaneously diagnosed cases: First primary tumor outside the nervous system

Case number	First primary tumor			Subsequent primary tumor			Months between diagnoses	Age at diagnosis of breast cancer
	Site	Microscopically confirmed?	Histologic type	Site	Microscopically confirmed?	Histologic type		
11	Breast	Yes	Anaplastic carcinoma, NOS†	Cranial meninges	Yes	Meningioma	13	79
12	Breast	Yes	Carcinoma, NOS	Cranial meninges	Yes	Meningioma	16	60
13	Breast	Yes	Carcinoma, NOS	Cranial meninges	Yes	Meningioma	44	41
14	Breast	Yes	Carcinoma, NOS	Cranial meninges	Yes	Meningioma	148	70
15	Breast	Yes	Carcinoma, NOS	Brain	Yes	Astrocytoma	12	60
16	Breast	Yes	Carcinoma, NOS	Brain	Yes	Benign brain tumor, NOS	119	43
17	Breast	Yes	Carcinoma, NOS	Spinal meninges	Yes	Meningioma	269	52
18	Breast	Yes	Carcinoma, NOS	Spinal cord	No	------	163	62

*Including tumors of the pineal and pituitary gland.
†NOS = Not otherwise specified.

same kindreds. Patients or families with this group of tumors should be more intensively studied in an attempt to identify the genetic or environmental factors responsible for this association. With this relationship in mind, physicians should evaluate carefully any patient with breast cancer who presents with signs or symptoms of an intracranial neoplasm, for if a new independent primary tumor is discovered, there is a good chance it is a potentially curable meningioma.

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