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PRIMARY INTRACRANIAL TUMORS AMONG ATOMIC BOMB SURVIVORS AND CONTROLS, HIROSHIMA AND NAGASAKI, 1961-75

広島・長崎の原爆被爆者及び対照者の原発性頭蓋内腫瘍，1961－75年

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広島・長崎の原爆被爆者及び対照者の原発性頭蓋内腫瘍，1961－75年

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SUMMARY

An analysis was made of the relationship of radiation dose to the occurrence of primary intracranial tumors among atomic bomb survivors and nonexposed controls, Hiroshima and Nagasaki, in the fixed cohort of the Life Span Study (LSS) extended sample during the period 1961-75, or 16 to 30 years after the A-bombs.

Based on various medical sources, 104 cases of primary intracranial tumors were identified among approximately 99,000 LSS extended sample members who were alive as of 1 January 1961. Of these 104 cases, 45 had manifested clinical signs of brain tumors, but 59 cases were identified incidentally at postmortem examination. The distributions of morphologic type, age, and size of tumor were quite different for those primary intracranial tumors with and without a clinical sign of brain tumor. Glioma was the most frequent type of tumor with a clinical sign and meningioma was the most frequent type without.

In relation to radiation dose the incidence rate of primary intracranial tumors with a clinical sign showed a significant excess risk for males in the high dose group who received 100 rad or more after adjustment for age at the time of the bomb (ATB). The standardized relative risk is around 5 in this group. The data also suggest that the crude relative risk of glioma is greater in the high dose group for younger ages ATB. However, there is no increased risk in females.

要　約

1961年から1975年までの被爆後16－30年の間に，被爆者と非被爆対照者を含む広島・長崎の寿命調査拡大対象固定集団から発生した原発性頭蓋内腫瘍と被曝線量の関係を解析した．

種々の医学資料に基づき，1961年1月1日の生存者，約99,000人の寿命調査拡大集団から，104例の原発性頭蓋内腫瘍を確認した．この104例のうち，45例に脳腫瘍の臨床症状を認めたが，59例は剖検により偶然に腫瘍を確認した．脳腫瘍の臨床症状の有無によって，原発性頭蓋内腫瘍の組織型，年齢や腫瘍の大きさの分布には明らかな差異を認めた．臨床症状を認めた腫瘍では，神経膠腫が最も多く，臨床症状を認めなかった腫瘍では，髄膜腫が最も多かった．

被曝線量と臨床症状のある原発性頭蓋内腫瘍の発生率の関係をみると，100rad 以上の高線量を受けた男性では原爆時年齢を標準化した危険率は有意に高く，その標準化相対的危険率は約5倍であった．更に，神経膠腫の粗危険率は原爆時年齢が若い高線量群で高い傾向が示唆された．しかし，女性においてはかかる危険率の有意の増加は認められなかった．

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Among the 5,012 autopsy subjects in the LSS extended sample during 1961-75, there is no relationship between radiation dose and the prevalence rate of primary intracranial tumors in those identified incidentally by autopsy. The relative risk of subclinical adenoma of the pituitary gland between high dose subjects and controls was also examined for a sample of 95 sex- and age-matched pairs using Hiroshima autopsy materials for 1961-74, but no relationship to dose was observed.

INTRODUCTION

An excess risk of malignant neoplasms has been reported among patients following irradiation by therapeutic X-rays and among A-bomb survivors as a late effect of ionizing radiation exposure.[1] However, there are few reports of postradiation intracranial tumors in a human population. Significantly elevated mortality from brain tumors among children who received therapeutic X-rays for tinea capitis,[2-5] and a higher frequency of mortality from cancer of the central nervous system among children exposed prenatally to diagnostic X-ray has been reported.[6] A recent report on cancer mortality among A-bomb survivors in a fixed cohort during 1950-74, did not mention mortality from brain tumors in relation to dose, due probably to the small number of deaths.[7]

The present study analyzes the incidence of primary intracranial tumors among A-bomb survivors and controls in the LSS extended sample between 1961-75, 16 to 30 years after exposure to the A-bombs, especially, in relation to dose.

MATERIALS AND METHOD

Ascertainment of primary intracranial tumors has been conducted on the LSS extended sample[8] of 98,663 A-bomb survivors and controls, comprised of 74,355 subjects in Hiroshima and 24,308 in Nagasaki, who were alive as of 1 January 1961. Dosimetry of A-bomb survivors in this cohort was available by the T65 dose system which gives total dose as a simple sum of gamma and neutron doses in rad.[9]

Table 1 shows the distribution of the sample by dose, city, and sex. The distribution was quite different by dose and city, but there was no difference by dose and sex.

1961－75年の寿命調査拡大集団に属する剖検例5,012名の資料を用い，剖検により偶然に確認された原発性頭蓋内腫瘍と被曝線量の関係をみたが線量の効果は認められなかった．1961－74年の広島の剖検材料を用い，性と死亡時年齢を一致させた95組の剖検体を高線量群と対照群から選び，脳下垂体の潜在性腺腫の相対的危険率を検討したが，線量との関係は認められなかった．

緒　言

治療用X線を受けたことのある患者及び原爆被爆者に，電離放射線被曝の後影響として悪性新生物の危険率増加がみられることが報告されている．[1] しかし，放射線照射後の人間の頭蓋内腫瘍に関する報告は余りない．頭部白癬のために治療用X線を受けた子供の脳腫瘍死亡率が有意に高いという報告[2-5]と，出生前に診断用X線を受けた子供の中枢神経系の癌死亡率が高いという報告[6]がある．固定集団内の原爆被爆者の1950－74年における癌死亡率に関する最近の報告では，死亡数が少ないためか，線量と脳腫瘍死亡率との関係には言及していない．[7]

本調査では，1961－75年の被爆後16－30年間の寿命調査拡大集団における被爆者と対照者の原発性頭蓋内腫瘍発生率を特に線量との関係で解析した．

材料及び方法

1961年1月1日現在生存していた広島74,355人，長崎24,308人からなる98,663人の被爆者及び対照者の寿命調査拡大集団[8]について原発性頭蓋内腫瘍について確認調査を行った．この集団中の被爆者の被曝線量は，ガンマ線量と中性子線量の単純合計をrad単位で示したT65D推定線量によって得られている．[9]

表1に対象者の分布を線量，都市及び性別に示した．線量と都市別分布にはかなりの差異があったが，線量と性別分布には差はなかった．

TABLE 1 NUMBER OF SUBJECTS IN THE LSS EXTENDED SAMPLE BY DOSE, SEX, & CITY (AS OF 1 JANUARY 1961)

表1　寿命調査拡大集団中の対象者数：線量，性及び都市別（1961年1月1日現在）

City		T65 Dose in rad					Total
		NIC*	<1	1-99	100+	Unknown	
Hiroshima	No.	18711	26851	24633	2915	1245	74355
	%	76.2	86.2	69.8	53.1	56.7	75.4
Nagasaki	No.	5838	4285	10666	2570	949	24308
	%	23.8	13.8	30.2	46.9	43.3	24.6
Male	No.	10124	12470	14232	2366	992	40184
	%	41.2	40.1	40.3	43.1	45.2	40.7
Female	No.	14425	18666	21067	3119	1202	58479
	%	58.8	59.9	59.7	56.9	54.8	59.3
Total	No.	24549	31136	35299	5485	2194	98663
	%	100.0	100.0	100.0	100.0	100.0	100.0

**Not in city ATB.* 原爆時市内不在

Through the ABCC-RERF pathology program, autopsies were performed on 5,012 subjects out of 17,300 deceased LSS extended sample members during 1961-75, or an autopsy rate of about 29%. Table 2 shows the distribution of autopsy subjects in the sample during 1961-75 by dose, sex, and age at death. The distribution of the autopsy subjects was not different by dose and sex, but there was significant difference by dose and age at death. The majority of these autopsy subjects were more than 60 years old in every dose category. This is characteristic of RERF autopsy data, when compared with a hospital autopsy series, because since 1961 the ABCC-RERF autopsy procurement program has focused on the fixed cohort of A-bomb survivors and controls who by definition were born before the A-bomb and are thus older than the general population.[10]

All possible cases of intracranial tumors in this cohort have been sought from RERF autopsy files, Tumor and Tissue Registries in both cities, and death certificates in the mortality study. Additional effort has been made at Hiroshima University Hospital to identify those intracranial tumor cases not reported to the Hiroshima City Tumor Registry. Pathologists reviewed all of the accumulated medical data, and recorded morphologic type and clinical signs of brain tumors. In this study the intracranial tumors were morphologically classified as glioma, meningioma, pituitary tumor, and others

ABCC－放影研の病理学調査で，1961－75年の間に死亡した寿命調査拡大集団対象者17,300人の内5,012人について剖検が行われた．すなわち，剖検率は約29％であった．表2に1961－75年に剖検を受けた対象者の線量，性及び死亡時年齢別分布を示した．剖検を受けた対象者には線量と性別分布に差異はなかったが，線量と死亡時年齢別分布との間には有意な差がみられた．剖検を受けた対象者の大部分は全線量区分で60歳以上であった．この傾向は病院での剖検調査と比較して放影研の剖検資料に特徴的なものであり，1961年以降，ABCC－放影研の剖検人手計画が，被爆者と対照者から構成されている固定集団を中心としているため，対象が原爆投下以前に生まれた者に限定されているので，一般集団より年齢が高くなっている．[10]

この集団における頭蓋内腫瘍と思われる全症例を放影研の剖検記録，両市の腫瘍，組織登録，及び死亡率調査で使用した死亡診断書から調べた．更に，広島市腫瘍登録に報告されていない広島大学病院での頭蓋内腫瘍症例を確認するため努力した．病理専門医が集められた全医学資料を検討し，脳腫瘍の組織型と臨床症状を記録した．本調査では頭蓋内腫瘍を形態学的に神経膠腫，髄膜腫，脳下垂体腫瘍，

TABLE 2 DISTRIBUTION OF AUTOPSY SUBJECTS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY SEX, AGE AT DEATH, & DOSE, 1961-75

表2　寿命調査拡大集団対象者で剖検を受けた者の分布，広島及び長崎：性，死亡時年齢及び線量別，1961－75年

Sex & Age			T65 Dose in rad					Total
			NIC*	<1	1-99	100+	Unknown	
Male		No.	561	820	945	187	60	2573
		%	52.2	52.3	48.8	53.6	73.2	51.3
Female		No.	514	748	993	162	22	2439
		%	47.8	47.7	51.2	46.4	26.8	48.7
Age	<40	No.	41	69	82	27	6	225
		%	3.8	4.4	4.2	7.7	7.3	4.5
	40-59	No.	171	202	263	79	13	728
		%	15.9	12.9	13.6	22.6	15.9	14.5
	60-69	No.	308	395	455	85	26	1269
		%	28.7	25.2	23.5	24.4	31.7	25.3
	70 +	No.	555	902	1138	158	37	2790
		%	51.6	57.5	58.7	45.3	45.1	55.7
	Total	No.	1075	1568	1938	349	82	5012
		%	100.0	100.0	100.0	100.0	100.0	100.0

Not in city ATB. 原爆時市内不在

consisting of craniopharyngioma and tumors of the blood vessels. All of the tumors of glial origin such as astrocytoma, glioblastoma, ependymoma, and ganglioglioma were classified as glioma. On the basis of clinical signs alone 54 possible cases had been diagnosed but the physical examination data were very questionable so these cases were rejected from the intracranial tumors in this study.

There were 104 cases designated as primary intracranial tumors in the LSS extended sample during 1961-75. Of these 104 cases 93 (89%) were classified for morphologic types using surgical or autopsy materials and 6 cases (6%) were designated by records of surgical operation. Only 5 (5%) of the cases were classified as primary intracranial tumors by underlying cause of death on the death certificate. Of 104 cases 45 had a clinical sign of brain tumor, but 59 cases had exhibited no clinical sign and were incidentally identified as primary intracranial tumor at autopsy. It is plain that the detection of intracranial tumor cases who were incidentally identified by autopsy depends upon the autopsy rate for the study population.

Prevalence of subclinical adenoma in the pituitary gland was examined using autopsy materials in

及び頭蓋咽頭管腫瘍と血管腫瘍からなるその他の腫瘍とに分類した．星状細胞腫，膠芽腫，上衣細胞腫，神経節膠腫等神経膠に発生する腫瘍はすべて神経膠腫として分類した．臨床症状のみで54例が頭蓋内腫瘍と診断されていたが，診察所見だけでは診断が非常に疑わしいためこれらの症例は本調査では除外した．

1961－75年の間に寿命調査拡大集団対象者中で原発性頭蓋内腫瘍とされたものが104例あった．これら104例のうち93例（89％）が外科材料若しくは剖検材料を基に組織型分類がなされ，外科手術記録によるものが6例（6％）で，死亡診断書の原死因で原発性頭蓋内腫瘍と分類された症例はわずか5例（5％）であった．104例中45例が脳腫瘍の臨床症状を有していたが，59例は臨床症状を示さず，剖検で偶然に原発性頭蓋内腫瘍が確認された．剖検で偶然に確認された頭蓋内腫瘍の探知が調査集団の剖検率に左右されることは明白である．

脳下垂体の潜在性腺腫の有病率と線量との関係を

relation to dose. The study subjects were selected from RERF autopsy materials belonging to the LSS extended sample in Hiroshima during 1961-74. Index subjects were selected from autopsy cases who received 180 rad or more and control subjects from those with less than 1 rad. Thus, 100 pairs of subjects were matched by sex and age at death. Histologic sections from the pituitary glands available in the RERF autopsy materials were restained for several sections and reviewed microscopically for subclinical adenomas, with a blind procedure for exposure dose.

The annual incidence rates of primary intracranial tumors with a clinical sign among the LSS extended sample are expressed in terms of person-years at risk in order to examine the dose effect by sex, and age ATB.[11,12] The standardized relative risk and the statistical differences were examined by the procedure of Mantel and Haenszel[13] using the risks based on the number of study subjects. The risk of primary intracranial tumors without a clinical sign was examined in autopsy subjects by sex, age at death, and dose. In the matched-sample study for subclinical adenoma in the pituitary gland, relative risk was calculated by the matched-sample procedure of Mantel and Haenszel.[13]

RESULTS

Prevalence of Primary Intracranial Tumors in the LSS Extended Sample during 1961-75

Table 3 shows the distribution of 104 primary intracranial tumors by a clinical sign of brain tumor and morphologic type. The distribution of morphologic type is quite different between symptomatic and asymptomatic primary intracranial tumors. Glioma is the most frequent type of tumor (42%) among those with one or more clinical signs, but meningioma is the most frequent type (73%) among those without such manifestations.

Primary Intracranial Tumors with a Clinical Sign of Brain Tumors

Table 4 shows the distribution of 45 primary intracranial tumors with clinical signs by morphologic type, sex, and age at onset. Although the distribution of morphologic type is different by sex, glioma is the most frequent type of tumor in both males and females and also the most frequent type in every age

剖検材料を用いて調べた．調査対象者は広島の寿命調査拡大集団に属する1961－74年の剖検例から抽出した．指標対象者は180rad 以上で被曝した剖検例と1 rad 未満の対照者から抽出し，100組の対象者の性及び死亡時年齢を一致させた．放影研の剖検材料として保管されている脳下垂体の組織切片は数片を再染色し，被曝線量を明かさないで検鏡で潜在性腺腫があるかどうか検討した．

線量影響を性及び原爆時年齢別に調査するために寿命調査拡大集団における臨床症状を有する原発性頭蓋内腫瘍例の年間発生率を観察人年で表した．[11,12] 標準化した相対的危険率と統計的差異を，調査対象者数に基づいた危険率を用いて Mantel 及び Haenszel[13] の手法で調べた．剖検例中臨床症状を有さない原発性頭蓋内腫瘍の危険率を性，死亡時年齢及び線量別に調べた．脳下垂体の潜在性腺腫を探知するための症例－対照者を一致させた調査では，Mantel と Haenszel[13] の症例－対照者一致法で相対的危険率を計算した．

結　果

寿命調査拡大集団対象者における1961－75年の原発性頭蓋内腫瘍の有病率

表3に104例の原発性頭蓋内腫瘍の脳腫瘍の臨床症状及び組織型別分布を示した．組織型の分布は症候のあったものと無症候性のもので全く異なっていた．臨床症状を有するものの中では神経膠腫が最も多い（42%）が，症状を示さないものの中では髄膜腫が最も多かった（73%）．

脳腫瘍の臨床症状を有する原発性頭蓋内腫瘍

表4に臨床症状を有する原発性頭蓋内腫瘍45例の組織型，性及び発病時年齢別分布を示した．組織型分布は性によって異なっているが，神経膠腫は男女

TABLE 3 DISTRIBUTION OF PRIMARY INTRACRANIAL TUMORS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY MORPHOLOGIC TYPE & CLINICAL SIGNS OF BRAIN TUMORS, 1961-75

表3　寿命調査拡大集団対象者の原発性頭蓋内腫瘍の分布，広島及び長崎：組織型及び脳腫瘍の臨床症状別，1961－75年

Morphologic type	Clinical Sign of Brain Tumor					
	Yes	%	No	%	Total	%
Glioma*	19	42.2	4	6.8	23	22.1
Meningioma	8	17.8	43	72.9	51	49.0
Neurinoma	6	13.3	11	18.6	17	16.3
Pituitary tumor	4	8.9	0	0.0	4	3.9
Other**	3	6.7	1	1.7	4	3.9
Undetermined***	5	11.1	0	0.0	5	4.8
Total	45	100.0	59	100.0	104	100.0

Composed of astrocytoma, glioblastomas, ependymoma, & ganglioglioma.

**Two cases of tumor of blood vessels and two cases of craniopharyngioma.*

***Not confirmed histologically (underlying cause of death was brain tumor)*

＊星状細胞腫，膠芽腫，上衣細胞腫及び神経節膠腫より成る．

＊＊血管腫瘍２例，頭蓋咽頭管腫瘍２例．

＊＊＊組織学的に確認されていない（原死因が脳腫瘍であった）．

TABLE 4 DISTRIBUTION OF PRIMARY INTRACRANIAL TUMORS WITH CLINICAL SIGNS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY MORPHOLOGIC TYPE, SEX, & AGE AT ONSET, 1961-75

表4　寿命調査拡大集団対象者における臨床症状を有する原発性頭蓋内腫瘍の分布，広島及び長崎：組織型，性及び発病時年齢別，1961－75年

Morphologic Type		Sex		Age at Onset			Total
		Male	Female	<40	40-59	60+	
Glioma	No.	8	11	6	9	4	19
	%	50.0	37.9	42.9	47.3	33.3	42.2
Meningioma	No.	1	7	0	5	3	8
	%	6.3	24.1	0.0	26.3	25.0	17.8
Neurinoma	No.	2	4	4	1	1	6
	%	12.5	13.8	28.6	5.3	8.4	13.3
Pituitary tumor	No.	2	2	1	3	0	4
	%	12.5	6.9	7.1	15.8	0.0	8.9
Other	No.	1	2	3	0	0	3
	%	6.3	6.9	21.4	0.0	0.0	6.7
Undetermined	No.	2	3	0	1	4	5
	%	12.5	10.4	0.0	5.3	33.3	11.1
Total	No.	16	29	14	19	12	45
	%	100.1	100.0	100.0	100.0	100.0	100.0

category. Meningioma is frequently observed among those aged 40 and over. Neurinoma is frequently observed in younger ages. Pituitary tumor is observed among those whose age was less than 60.

双方，また，各年齢群において最も多くみられた．髄膜腫は40歳以上の者に多くみられた．神経鞘腫は若年者に多くみられた．脳下垂体腫瘍は60歳未満の者にみられた．

Table 5 shows the crude annual incidence rate of primary intracranial tumors with a clinical sign

表５に脳腫瘍の臨床症状を有する原発性頭蓋内腫瘍

TABLE 5 CRUDE ANNUAL INCIDENCE RATE OF PRIMARY INTRACRANIAL TUMORS WITH CLINICAL SIGNS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY MORPHOLOGIC TYPE, SEX, & DOSE, 1961-75

表 5　寿命調査拡大集団対象者における臨床症状を有する原発性頭蓋内腫瘍の年間粗発生率
広島及び長崎：組織型，性及び線量別，1961－75年

Item		T65 Dose in rad				Total
		NIC & <1	1-99	100+	Unknown	
			Male			
Person years		303590	189730	31536	13455	538311
Morphologic type (rate/100,000)						
Glioma		0.7 (2)	1.6 (3)	6.3 (2)	0.0 (0)	1.3 (7)
Meningioma		0.3 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
Neurinoma		0.3 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
Pituitary tumor		0.3 (1)	0.5 (1)	0.0 (0)	0.0 (0)	0.4 (2)
Craniopharyngioma		0.0 (0)	0.0 (0)	3.2 (1)	0.0 (0)	0.2 (1)
Undetermined		0.3 (1)	0.0 (0)	0.0 (0)	7.4 (1)	0.4 (2)
Total		2.0 (6)	2.1 (4)	9.5 (3)	7.4 (1)	2.6 (14)
90% confidence limits	Upper	3.9	4.8	24.6	35.3	4.1
	Lower	0.9	0.7	2.6	0.4	1.6
			Female			
Person years		461693	292287	43827	17307	815114
Morphologic type (rate/100,000)						
Glioma		1.9 (9)	0.7 (2)	0.0 (0)	0.0 (0)	1.3 (11)
Meningioma		0.2 (1)	1.7 (5)	0.0 (0)	5.7 (1)	0.9 (7)
Neurinoma		0.0 (0)	1.0 (3)	0.0 (0)	5.7 (1)	0.5 (4)
Pituitary tumor		0.0 (0)	0.7 (2)	0.0 (0)	0.0 (0)	0.2 (2)
Tumor of blood vessel		0.2 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.1 (1)
Undetermined		0.2 (1)	0.7 (2)	0.0 (0)	0.0 (0)	0.4 (3)
Total		2.5 (12)	4.8 (14)	0.0 (0)	11.5 (2)	3.4 (28)
90% confidence limits	Upper	4.2	7.5	–	36.4	4.7
	Lower	1.5	2.9	–	2.1	2.4

Three cases with onset prior to January 1961 were excluded in calculation of incidence rate.
Number of cases in parentheses.
1961年1月以前に発病した3例は発生率計算から除外した．
（）内は症例数．

of brain tumor by morphologic type, sex, and dose. Three cases whose onset was prior to January 1961 were excluded in the calculation of the incidence rate. In males, the rate (10^{-5}) of all types of primary intracranial tumors is 9.5 in the high dose group (100 rad or more), 2.1 in the low dose group (1-99 rad) and 2.0 in the control group (less than 1 rad and not-in-city (NIC) ATB). The crude relative risk for those in the high dose group in comparison with the control group is 4.8 and the risk for those in the low dose region is 1.1, respectively, although the 90% confidence limits of the rate suggest no significant difference. The crude risk of glioma was elevated in the high dose group, but the

の年間粗発生率を組織型，性及び線量別に示した．1961年1月以前に発症した3例は発生率計算から除外した．男性では原発性頭蓋内腫瘍の全組織型の発生率（10^{-5}）は高線量群（100rad 以上）で9.5，低線量群（1－99rad）で2.1，対照群（1 rad 未満及び原爆時市内不在者）で2.0である．この比率の90%信頼限界は有意差を示唆していないが，対照群と比較した高線量群の粗相対的危険率は4.8，低線量群の危険率は1.1である．神経膠腫の粗危険率は高線量群で

TABLE 6 COMPARISON OF RISK FOR PRIMARY INTRACRANIAL TUMORS WITH CLINICAL SIGNS IN LSS EXTENDED SAMPLE MALES, HIROSHIMA & NAGASAKI, BY DOSE, & AGE ATB, 1961-75

表 6　寿命調査拡大集団対象者男性における臨床症状を有する原発性頭蓋内腫瘍の危険率の比較，広島及び長崎：線量及び原爆時年齢別，1961－75年

Item	T65 Dose category in rad		
	Control NIC & <1	Low Dose 1-99	High Dose 100 +
	Age <20 ATB		
Number of subjects	11208*	7427	1102
Person years	165592	109554	16178
Number of cases	2	1	2
Rate per 1000	1.8	1.3	18.1
Annual incidence rate (10^{-5})	1.21	0.91	12.36
Crude relative risk	1.0	0.8	10.2
	Age 20-39 ATB		
Number of subjects	5060	2800	615
Person years	70553	38844	8574
Number of cases	2	0	1
Rate per 1000	4.0	0.0	16.3
Annual incidence rate (10^{-5})	2.83	0.00	11.66
Crude relative risk	1.0	0.0	4.1
	Age 40+ ATB		
Number of subjects	6325	4005	649
Person years	67446	41332	6784
Number of cases	2	3	0
Rate per 1000	3.2	7.5	0.0
Annual incidence rate (10^{-5})	2.97	7.26	0.00
Crude relative risk	1.0	2.4	0.0
	Total		
Number of subjects	22593	14232	2366
Number of cases	6	4	3
Rate per 1000	2.7	2.8	12.7
Standardized relative risk	1.0	1.0	4.8

Mantel and Haenszel[13] test of significance after adjustment for age ATB: $\chi^2=6.56$, *d.f.* = 2, $.01 < P \leq .05$.
原爆時年齢補正後の Mantel と Haenszel [13] の有意性検定.
Standardized relative risk adjusted for 3 age ATB groups. 三つの原爆時年齢群を補正した相対的危険率
**1 case with onset before 1961 was excluded.* 1961年以前に発病した1例は除外した.

number of cases was too small to draw a definite conclusion. In females, however, no primary intracranial tumor was identified in the high dose group. The relative risk in the low dose group is 1.9 in comparison with the control group. There is, thus, no evidence for a radiation effect in the female exposed population.

高いが，症例数が少ないため明確な結論は引き出せない．しかしながら，女性では高線量群の原発性頭蓋内腫瘍は確認されなかった．対照群と比較した低線量群の相対的危険率は1.9である．したがって，女性の被爆集団には放射線影響の証拠はみられない．

Table 6 compares the risk of primary intracranial tumor with a clinical sign among the male

表6では男性集団中臨床症状を有する原発性頭蓋内

TABLE 7 DISTRIBUTION OF PRIMARY INTRACRANIAL TUMORS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY MORPHOLOGIC TYPE, & CLINICAL SIGNS, 1961-75

表7 寿命調査拡大集団対象者における原発性頭蓋内腫瘍の分布，広島及び長崎：組織型及び臨床症状別，1961－75年

Morphologic Type	Clinical sign of brain tumor			
	Yes	%	No	%
Glioma	11	64.7	4	6.8
Meningioma	3	17.6	43	72.9
Neurinoma	1	5.9	11	18.6
Pituitary tumor	2	11.8	0	0.0
Vascular tumor	0	0.0	1	1.7
Total	17	100.0	59	100.0

population by age ATB and three dose groups. Although the number of cases is small in each cell when the data are partitioned into nine different cells, including three age ATB categories and three dose categories, the standardized relative risk adjusted for age ATB is approximately 5 in the high dose group and 1.0 in the low dose group in comparison with the control group as the standard. The procedure of Mantel and Haenszel[13] reveals this difference to be significant ($.01 < P < .05$). By dose and age ATB, the crude relative risk in the high dose group is greater in the young age ATB group (less than 20) than in the middle age ATB group (20-39). In the older group the relative risk is 2.4 in the low dose region. It appears that age ATB is an important variable for radiation-induced primary intracranial tumors with a clinical sign of brain tumor. However, all three cases in the high dose group were found in Nagasaki survivors, with none in Hiroshima.

Appendix I lists the 45 primary intracranial tumors with a clinical sign by city, sex, age ATB, dose, date of onset, age at onset, morphologic type, and method of diagnosis.

Primary Intracranial Tumors in Autopsy Subjects

There were 76 cases of primary intracranial tumors identified among the 5,012 autopsy subjects in the LSS extended sample. There were 17 cases with and 59 cases without a clinical sign.

Table 7 shows the distribution of morphologic type by cases with and without a clinical sign. It appears that significantly different distributions of morphologic type exist for tumors with

腫瘍例の危険率を原爆時年齢及び三つの線量群別に比較した．資料を三つの原爆時年齢区分と三つの線量区分の九つの区分に分割すると各区分の症例数は少なくなるが，対照群を標準として比較した原爆時年齢を標準化した相対的危険率は高線量群が約5，低線量群が1.0である．Mantel と Haenszel[13] の手法を用いると，この差は有意となる（$.01 < P < .05$）．線量及び原爆時年齢別における高線量群の粗相対的危険率は原爆時年齢が中間の群（20－39歳）より原爆時年齢が若年の群（20歳未満）の方が高い．高齢者群では低線量群の相対的危険率は2.4である．原爆時年齢は脳腫瘍の臨床症状を有する放射線誘発性原発性頭蓋内腫瘍の重要な変数であると思われる．しかし，高線量群の3例はすべて長崎の被爆者であって，広島では1例もみられなかった．

付録1に臨床症状を有する原発性頭蓋内腫瘍45例を都市，性，原爆時年齢，線量，発生年月日，発生時年齢，組織型及び診断法別に列挙した．

剖検を受けた対象者の原発性頭蓋内腫瘍

寿命調査拡大集団対象者で剖検を受けた5,012例から76例の原発性頭蓋内腫瘍が確認された．臨床症状を有するもの17例，有しないもの59例であった．

表7に組織型分布を臨床症状の有無別に示した．臨床症状を有する腫瘍と有しない腫瘍の組織型分布には

TABLE 8 PREVALENCE RATE OF PRIMARY INTRACRANIAL TUMORS WITHOUT CLINICAL SIGNS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY MORPHOLOGIC TYPE, SEX, & AGE AT DEATH, 1961-75

表8　寿命調査拡大集団対象者における臨床症状を有しない原発性頭蓋内腫瘍の有病率，広島及び長崎：組織型，性及び死亡時年齢別，1961－75年

Item	Age at Death			Total
	<60	60-79	80 +	
	Male			
Autopsies*	495	1653	419	2567
Morphologic type (rate/1000 autopsies)				
Glioma	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Meningioma	0.0 (0)	4.2 (7)	2.4 (1)	3.1 (8)
Neurinoma	2.0 (1)	1.8 (3)	4.8 (2)	2.3 (6)
Vascular tumor	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Total	2.0 (1)	6.0 (10)	7.2 (3)	5.4 (14)
	Female			
Autopsies*	446	1355	627	2428
Morphologic type (rate/1000 autopsies)				
Glioma	2.2 (1)	1.5 (2)	1.6 (1)	1.6 (4)
Meningioma	2.2 (1)	18.5 (25)	14.4 (9)	14.4 (35)
Neurinoma	4.5 (2)	2.2 (3)	0.0 (0)	2.1 (5)
Vascular tumor	0.0 (0)	0.7 (1)	0.0 (0)	0.4 (1)
Total	9.0 (4)	22.9 (31)	15.9 (10)	18.5 (45)

**17 cases of primary intracranial tumors with clinical signs were excluded.*
臨床症状を有する原発性頭蓋内腫瘍17例は除外した．
Number of cases in parentheses. ( ) 内は症例数．

and without a clinical sign. Meningioma is the most frequent type of tumor for those without a clinical sign.

Table 8 shows the prevalence rate of primary intracranial tumors without a clinical sign by sex, age at death, and morphologic type. The rate is significantly higher in females than in males in every age category, and altogether is 3.4 times greater. Meningioma is the most frequent type of tumor among females whose age at death was 60 and over.

Table 9 shows the prevalence rate of primary intracranial tumors without a clinical sign by dose and sex. There is no tendency for greater risk of primary intracranial tumors without a clinical sign in both males and females by dose. Examination of risk after adjustment for age at death in males and females showed no radiation effect though the number of cases is small in the high dose group.

The autopsy records revealed 12 cases (20.3%) of other malignant neoplasms out of 59 primary

有意差があるようである．髄膜腫は臨床症状を有しないものに最も多くみられた．

表8に臨床症状を有しない原発性頭蓋内腫瘍の有病率を性，死亡時年齢及び組織型別に示した．全年齢区分で女性の有病率が男性より有意に高く，全体で3.4倍である．死亡時年齢が60歳以上の女性では髄膜腫が最も多かった．

表9に臨床症状を有しない原発性頭蓋内腫瘍の有病率を線量及び性別に示した．線量別にみて男性，女性共に臨床症状を有しない原発性頭蓋内腫瘍の危険率が増加する傾向は認められない．男性と女性の死亡時年齢を補正して危険率を調べると，高線量群の症例数は少ないが，放射線影響はみられなかった．

剖検記録では，臨床症状を有しない原発性頭蓋内腫瘍59例中12例（20.3%）に他の悪性新生物が認めら

TABLE 9 PREVALENCE RATE OF PRIMARY INTRACRANIAL TUMORS WITHOUT CLINICAL SIGNS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, BY MORPHOLOGIC TYPE, SEX, & DOSE, 1961-75
表9　寿命調査拡大集団対象者における臨床症状を有しない原発性頭蓋内腫瘍の有病率，広島及び長崎：組織型，性及び線量別，1961－75年

Item	T65 Dose in rad				Total
	NIC & <1	1-99	100 +	Unknown	
		Male			
Autopsies*	1380	942	186	59	2567
Morphologic type (rate/1000 autopsies)					
Glioma	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Meningioma	4.3 (6)	2.1 (2)	0.0 (0)	0.0 (0)	3.1 (8)
Neurinoma	2.9 (4)	1.1 (1)	5.4 (1)	0.0 (0)	2.3 (6)
Vascular tumor	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Total	7.2 (10)	3.2 (3)	5.4 (1)	0.0 (0)	5.5 (14)
Standardized relative risk	1.0	0.4	0.8	–	–
		Female			
Autopsies*	1256	988	162	22	2428
Morphologic type (rate/1000 autopsies)					
Glioma	2.4 (3)	1.0 (1)	0.0 (0)	0.0 (0)	1.6 (4)
Meningioma	15.9 (20)	11.1 (11)	18.5 (3)	45.5 (1)	14.4 (35)
Neurinoma	1.6 (2)	3.0 (3)	0.0 (0)	0.0 (0)	2.1 (5)
Vascular tumor	0.8 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (1)
Total	20.7 (26)	15.2 (15)	18.5 (3)	45.5 (1)	18.5 (45)
Standardized relative risk	1.0	0.7	1.0	–	–

Standardized relative risk after adjustment for age at death. 死亡時年齢補正後の標準化相対的危険率.
Mantel & Haenszel[13] test by age at death shows no significant differences in both sexes.
死亡時年齢による Mantel と Haenszel[13] 検定では両性とも有意差がみられない.
**17 cases of primary intracranial tumors with clinical signs were excluded.*
臨床症状を有する原発性頭蓋内腫瘍17例は除外した.
Number of cases in parentheses. ( ) 内は症例数.

intracranial tumors without a clinical sign. The rate declined with age at death, being 50% in those under 60 years, 30.8% at 60-69 years and 14.3% at 70 years or more. Examined by dose, the rate is 20.0% in the high dose group, 11.1% in the low dose group and 25.0% in the control group. Therefore, the rate of complication of other malignant neoplasms in those primary intracranial tumor cases without a clinical sign seems unrelated to dose. The 59 primary intracranial tumors without a clinical sign were generally small and most were less than 3 cm in largest dimension.

Subclinical Adenoma in the Pituitary Gland in Autopsy Material by Dose

To examine the presence of subclinical adenoma in the pituitary gland between the high dose group and the control group, 100 matched pairs were selected from the autopsy material in the sample for 1961-74.

れた．有病率は死亡時年齢とともに低下し，60歳未満では50%，60—69歳では30.8%，70歳以上では14.3%であった．線量別に調べると，高線量群では20.0%，低線量群では11.1%，対照群では25.0%であり，他の悪性新生物を併発した臨床症状を有しない原発性頭蓋内腫瘍例の有病率は線量と関係がないようである．臨床症状を有しない59例の原発性頭蓋内腫瘍は一般的に小さく，そのほとんどが最大径3cm以下であった．

線量別にみた剖検材料における脳下垂体の潜在性腺腫

高線量群と対照群の間の脳下垂体の潜在性腺腫の有無を調べるために1961－74年の剖検材料から100組の対応させた症例を抽出した．

TABLE 10 AVAILABILITY OF PITUITARY GLAND IN AUTOPSY SUBJECTS FOR 100 SEX- & AGE-MATCHED PAIRS BETWEEN INDEX CASES & CONTROLS, HIROSHIMA

表10 性と年齢を一致させた100組の剖検例中，指標例と対照例の脳下垂体入手状況，広島

Control*	Availability of Pituitary Gland		
	Index Case**		Total
	Yes	No	
Yes	95	2	97
No	3	0	3
Total	98	2	100

**T65 dose 0 rad*
***T65 dose 180+ rad*

TABLE 11 SUBCLINICAL ADENOMA IN PITUITARY GLAND IN AUTOPSY SUBJECTS FOR 95 MATCHED PAIRS BETWEEN INDEX CASES & CONTROLS, HIROSHIMA

表11 互いに一致させた95組の剖検例中指標例と対照例の脳下垂体内における潜在性腺腫，広島

Control*	Subclinical Adenoma		
	Index Case**		Total
	Yes	No	
Yes	1	8	9
No	5	81	86
Total	6	89	95

Relative risk : 5/8 = 0.6 (Mantel and Haenszel[13])
$\chi^2 = 0.31$, *d.f.* = 1, $P > .10$
**T65 dose 0 rad*
***T65 dose 180+ rad*

Table 10 shows the availability of pituitary glands for matched pairs by index and control. There were 95 pairs available for review. Table 11 shows the distribution of subclinical adenoma by index and controls. The relative risk for index cases is 0.6 and is not statistically significant. Therefore, no radiation effect was observed for prevalence of subclinical adenoma in the pituitary gland.

表10に脳下垂体の入手状況を指標群及び対照群の組み合せ別に示した．検討に利用できたのは95組であった．表11に潜在性腺腫の分布を指標群及び対照群別に示した．指標群の相対的危険率は0.6で，統計的に有意差はない．したがって，脳下垂体の潜在性腺腫の有病率に放射線影響はみられなかった．

DISCUSSION

An excess mortality of brain tumors was reported in follow-up studies of children irradiated by therapeutic X-ray for tinea capitis of the scalp.[2-5] In the United Nations Scientific Committee 1977 report[1] a radiation-induction rate of brain tumors was estimated at ap-

考　察

頭部白癬のために治療用X線照射を受けた子供の追跡調査で脳腫瘍による死亡率の増加が報告された．[2-5] 国連科学委員会の1977年報告[1]では放射線による

proximately 20 (9-39) per million per rad per year in one series[3] and approximately 5 (2-10) per million per rad per year per unit absorbed dose in another series.[4] The mean doses of therapeutic radiation were estimated at about 140 rad[3] and about 120 rad,[4] respectively. In a study of 14,554 adults with ankylosing spondylitis, no excess mortality from brain tumors was observed after X-ray treatment.[14]

The experience of A-bomb survivors provides evidence on the relationship between incidence of primary intracranial tumors and a single whole body exposure of mixed ionizing radiation composed of gamma rays and neutrons.

The present analyses demonstrate that a significant excess risk of primary intracranial tumors with a clinical sign of brain tumors occurred in the high dose group (100 rad or more) after adjustment for age ATB in the male population during the period between 16-30 years after exposure. There were firm findings on relative susceptibility by sex for radiation oncogenesis. Greater susceptibility for radiation-induced breast cancer and thyroid carcinoma in female A-bomb survivors has been reported.[15,16] Shore et al[5] reported a male predominance for radiation-induced brain tumors in irradiated children with all six of the intracranial neurogenic tumors in their study having occurred in males alone. The present evidence among A-bomb survivors of radiation-induced primary intracranial tumors is consistent with the experience of Shore et al[5] in their follow-up study of children treated by X-ray for tinea capitis with respect to sex differences.

Age sensitivity of radiation-induced intracranial tumors is also interesting. Shore et al[5] reported that no differential age sensitivity was observed for brain tumor induction related to radiation among the irradiated children whose age at treatment was less than 15 years. Nor was an excess observed in the irradiated adults followed by Court Brown and Doll.[14]

In the present study the follow-up of incidence of primary intracranial tumors among A-bomb survivors for the whole lifetime of the study subjects is incomplete, but the analysis suggests that sensitivity of radiation-induced primary intracranial tumors with a clinical sign is greater for younger ages ATB than for the older ages ATB 16-30 years after exposure. A firm

脳腫瘍誘発率は一つの調査で10^6年rad当たり約20（9－39）例で，[3] 別の治療法では単位吸収線量当たり10^6年rad当たり約5（2－10）例であった．[4] 治療用放射線の平均線量はそれぞれ約140rad[3]と約120rad[4]であった．成人の強直性脊椎炎患者14,554人の調査ではX線治療後，脳腫瘍の死亡率増加はみられなかった．[14]

原爆被爆者からは原発性頭蓋内腫瘍発生率とガンマ線及び中性子線から成る混合電離放射線への1回の全身被曝との関係に関する資料が提供されている．

本解析では，被爆後16－30年間の男性被爆者の原爆時年齢を補正したところ，脳腫瘍の臨床症状を有する原発性頭蓋内腫瘍の危険率は高線量群（100rad以上）が有意に高いことが明らかになった．放射線誘発性の腫瘍には性別による相対的危険率に差が認められた．女性の被爆者に放射線誘発性乳癌及び甲状腺癌に対する罹患性が高いことが報告されている．[15,16] Shoreら[5]は，その調査で6例の頭蓋内神経性腫瘍のすべてが男子のみに発現したことから，放射線療法を受けた子供の放射線誘発性脳腫瘍は男子に多くみられると報告した．被爆者における放射線誘発性原発性頭蓋内腫瘍に関する本資料はShoreら[5]による頭部白癬に対してX線治療を受けた子供の追跡調査の資料と性による差異のある点で一致している．

放射線誘発性頭蓋内腫瘍の年齢による感受性も興味深い．Shoreら[5]は，15歳未満で放射線治療を受けた子供では放射線誘発の脳腫瘍については年齢による感受性の差はみられなかったと報告した．また，Court BrownとDoll[14]の放射線治療を受けた成人についての追跡調査でも増加はみられなかった．

本調査では，被爆者の原発性頭蓋内腫瘍発生率について調査対象者の全生涯にわたる追跡調査は未完であるが，解析結果から臨床症状を有する放射線誘発性原発性頭蓋内腫瘍の感受性は，被爆後16－30年間では原爆時年齢が高い者より若い者の方が高いことが示唆される．この問題に関する明確な結果は，放

conclusion on this issue must await a complete follow-up investigation when the study would show disappearance of radiation-induced brain tumors among the irradiated survivors.

A latent period for radiation-induced primary intracranial tumors is another important factor in the incidence rate for irradiated subjects. Shore et al[5] reported that an excess mortality of brain tumors became apparent 20 years after X-ray therapy. In the UN Scientific Committee 1977 report[1] an average latent period for radiation-induced brain tumors studied by Munk et al[17] was calculated as about 27 years. In the present study, the average period between exposure and onset for the three high dose cases was 25 years. Jablon et al[18] reported that children of A-bomb survivors who received radiation doses of 100 rad or more began to develop an excessive number of malignant neoplasms except leukemia after a latent period of about 15 years from exposure. Otake[19] reported that a significant excess mortality of cancer except leukemia was observed in heavily exposed survivors in Hiroshima after 1960 or 15 years after exposure. Beebe et al[7] recently reported that the probable onset of excess cancer mortality except leukemia among heavily exposed survivors could be observed after 1958 other than for cancer of the lung. The previous mortality reports of A-bomb survivors suggest that it was improbable an excess risk of primary intracranial tumors began among heavily exposed survivors before 1960,[7,8,18-20] although the present study did not examine the incidence of primary intracranial tumors among A-bomb survivors until after 1960 or 15 years after exposure.

Morphologic type specificity for radiation-induced primary intracranial tumors is another interesting subject. The present analyses suggest that the crude relative risk of glioma in the high dose group is about nine times greater than the control, although the group is small. Excess risk of meningioma with a clinical sign of brain tumors was not observed in the high dose group. Shore et al[5] reported 6 neurogenic tumors in their second follow-up study of 2,215 children irradiated for tinea capitis; there were 3 cases of glioma, 2 cases of meningioma, and 1 case of neurinoma. Modan et al[4] reported eight malignant and eight benign neoplasms of the brain including four meningioma among irradiated children, but they did not indicate the

射線を受けた者に放射線誘発性脳腫瘍が見られなくなり，完全な追跡調査が終了するまで待たねばならない．

放射線誘発性原発性頭蓋内腫瘍の潜伏期間は放射線を受けた対象者の発生率におけるもう一つの重要な因子である．Shore ら[5]は脳腫瘍の死亡率増加はX線治療20年後から明らかになってきたと報告した．国連科学委員会の1977年報告[1]では，Munk ら[17]の調査した放射線誘発性脳腫瘍の潜伏期間は約27年と算出された．本調査では高線量被爆群に認められた3症例の被爆から発病までの平均期間は25年であった．Jablon ら[18]は，100rad 以上の放射線量を受けた原爆被爆者の子供は被爆後約15年の潜伏期間の後白血病を除く悪性新生物の発現数が増加したと報告した．大竹[19]は広島の高線量被爆者に1960年以降，すなわち，被爆後15年以降，白血病以外の癌に有意な死亡率増加がみられたと報告した．Beebe ら[7]は最近，高線量被爆者の白血病以外の癌の死亡率増加の始まりは肺癌を除いて1958年からみられたと報告した．本調査では，被爆15年後の1960年までは被爆者の原発性頭蓋内腫瘍発生率を調査していないが，被爆者に関する先の死亡率報告は，高線量被爆者の原発性頭蓋内腫瘍の危険率増加が1960年以前に始まった可能性がほとんどないことを示唆している．[7,8,18-20]

放射線誘発性原発性頭蓋内腫瘍の組織型の特徴も興味を引く課題である．本解析では，対象が少数ながらも，高線量群における神経膠腫の粗相対的危険率は対照群に比べて約9倍であることが示唆される．脳腫瘍の臨床症状を有する髄膜腫の危険率増加は高線量群ではみられなかった．Shore ら[5]は頭部白癬のために放射線治療を受けた子供2,215人の第2回の追跡調査で6例の神経性腫瘍が認められたと報告し，3例は神経膠腫，2例は髄膜腫，1例は神経鞘腫であった．Modan ら[4]は放射線治療を受けた子供に認められた4例の髄膜腫を含む8例の悪性脳新生物と8例の良性脳新生物を報告したが，悪性

morphologic types of the malignant brain tumors. Munk et al[17] reported five cases of radiation-induced primary intracranial tumors and all were meningiomas. A number of case reports exist of brain tumors after irradiation by large amounts of X-ray therapy to the head; most of these were meningiomas and sarcomas of the brain.[21-28]

In the present study all three cases in the high dose group were in Nagasaki survivors, with none identified in Hiroshima. This city difference may reflect the difference in the radiation characteristics. Hiroshima survivors received both gamma rays and neutrons from low dose to large total dose, but Nagasaki survivors received gamma rays alone in the low dose range and a few neutrons and a large dose ot gamma rays in the high total dose range.[9] The Oak Ridge National Laboratory group has studied various organ dose estimates for A-bomb survivors,[29] but organ dose for the brain has not yet been estimated, however, it appears from the tissue kerma dose conversion factor that the absorbed dose is much more reduced for the neutron kerma than the gamma kerma dose. Therefore, it is believed that the organ dose for the brain is lower in Hiroshima survivors than in Nagasaki survivors in the same total dose categories. This fact may explain the inter-city difference of radiation-induced primary intracranial tumors with a clinical sign.

Based on the autopsy materials for 1961-75, the relationship between prevalence of primary intracranial tumors without a clinical sign and dose was examined. Although the autopsy rate in our study cohort shows a serious bias by dose, cause of death, etc.,[10] it does not seem likely that such bias introduces a statistical problem in examining the prevalence of primary intracranial tumors detected incidentally at autopsy in relation to dose. Although cases are few in the high dose group of autopsy subjects, there is no radiation effect on the occurrence of incidentally detected primary intracranial tumors. Meningioma is the most frequent type of primary intracranial tumor without a clinical sign, especially, in females. About 20% of the cases had malignant neoplasms other than intracranial tumors and incidentally detected primary intracranial tumors had no apparent relationship with coincidence of malignant neoplasms and dose.

脳腫瘍の組織型は報告していない．Munk ら[17]は5例の放射線誘発性原発性頭蓋内腫瘍を報告したが，すべて髄膜腫であった．頭部のX線治療として大量の照射を受けた後，発生した脳腫瘍について多くの症例報告がなされているが，これらの多くは髄膜腫と脳肉腫であった．[21-28]

本調査において高線量群中に認められた3例はすべて長崎の被爆者で，広島では1例も認められなかった．この都市による差異は放射線の線質による差異を示すかもしれない．広島の被爆者は低線量から高線量までガンマ線と中性子線の双方を受けたが，長崎の被爆者は低線量域ではガンマ線のみを受け，高総線量域では少量の中性子線と大量のガンマ線を受けた．[9] 米国 Oak Ridge 研究所では原爆被爆者の種々の臓器の推定線量を調査したが，[29] 脳に対する線量はまだ推定されていない．しかしながら，組織 Kerma 線量変換係数から判断すると吸収線量はガンマ Kerma 線量より中性子 Kerma 線量の方がずっと低いようである．したがって，脳に対する臓器線量は同じ総線量区分であっても長崎の被爆者より広島の被爆者の方が低いと考えられる．このことは臨床症状を有する放射線誘発性原発性頭蓋内腫瘍の都市別差異を説明するかもしれない．

1961－75年の剖検材料を基に臨床症状を有しない原発性頭蓋内腫瘍の有病率と線量との関係を調べた．本調査集団の剖検率は線量，死因等によって大きな偏りを示しているが，[10] そのような偏りが剖検で偶然に探知された原発性頭蓋内腫瘍の有病率と線量との関係を調べる上で統計的に問題を生じることはないと思われる．高線量群で剖検を受けた症例はほとんどないが，偶然に探知された原発性頭蓋内腫瘍の発現に対する放射線影響はみられない．髄膜腫は特に女性の臨床症状を有しない原発性頭蓋内腫瘍に最も多く見られる．症例の約20％は頭蓋内腫瘍以外の悪性新生物で，偶然に探知された原発性頭蓋内腫瘍は，悪性腫瘍や線量とは明確な関係を示さなかった．

In addition to the pituitary tumors which produce clinical symptoms, subclinical adenomas of microscopic size or larger have for many years been recognized at autopsy in the pituitary gland.[30-32] Therefore, the presence of subclinical pituitary adenoma was examined in relation to dose using sex- and age-matched pairs of autopsy subjects in Hiroshima, but no radiation effect was observed. An increased prevalence of pituitary adenoma has been reported in irradiated mice.[33,34] There may be different mechanisms for development of pituitary adenoma in mice and subclinical adenoma in the pituitary gland in man after exposure to ionizing radiation.

MacMahon[6] reported that an excess mortality of leukemia and cancer of the central nervous system was observed among children who were prenatally exposed to diagnostic X-ray and suggested that the fetal brain was sensitive to radiation-induction of brain tumors. Jablon and Kato[35] reported that no excess risk of mortality from leukemia and other cancers including brain tumors occurred during childhood among children exposed prenatally to the A-bomb. In the present study, we also sought possible intracranial tumors in a cohort of 2,457 in utero exposed persons and controls in RERF mortality follow-up subjects. However, none were found in the period 16-30 years after exposure. Among 183 in utero children examined at ABCC up until 1965, one case of meningioma with psammoma bodies of the brain was reported in a boy who was in the 12th week of gestation ATB.[36] His estimated exposure dose was 29 rad in gamma rays and 4 rad in neutron dose. The record indicated that the tumor was surgically removed in 1954.

臨床症候を示す脳下垂体腫瘍のほかに顕微鏡的大きさ又はそれ以上の潜在性腺腫も数年来剖検時に脳下垂体に認められていた.[30-32] したがって，潜在性脳下垂体腺腫の有無と線量との関係を，性と年齢を一致させた広島の剖検例について調べたが，放射線影響はみられなかった．放射線を照射したマウスに脳下垂体腺腫の有病率が増加することが報告されている.[33,34] 電離放射線に被曝したマウスの脳下垂体腺腫と人間の脳下垂体の潜在性腺腫の発現機序の上で差異があるかもしれない．

MacMahon[6] は出生前に診断用X線に被曝した子供に白血病と中枢神経系の癌の死亡率増加がみられたことを報告し，胎児の脳は放射線の脳腫瘍誘発効果に対して感受性が高いことを示唆した．Jablon と加藤[35] は出生前に原爆に被爆した子供の小児期に白血病と脳腫瘍を含む他の癌の死亡率増加はみられなかったと報告した．本調査では放影研死亡率追跡調査対象者中の胎内被爆児及び対照者2,457人の集団について頭蓋内腫瘍があるか否かを調べた．しかし被爆後16—30年の期間内では，症例が発見されなかった．1965年までに ABCC で検査を受けた胎内被爆児183人のうち，原爆時に妊娠第12週であった少年1 人に，脳に砂腫体のある髄膜腫が認められたことが報告されている.[36] この少年の推定被曝線量はガンマ線29rad，中性子線 4 rad であった．記録によると腫瘍は1954年に外科的に切除されている．

APPENDIX I
PRIMARY INTRACRANIAL TUMORS WITH CLINICAL SIGNS IN THE LSS EXTENDED SAMPLE, HIROSHIMA & NAGASAKI, 1961-75

付録 1
寿命調査拡大集団対象者における臨床症状を有する原発性頭蓋内腫瘍，広島及び長崎，1961－75年

Case	MF No.	City & Sex	Age ATB	T65 Dose in rad	Onset Yr.	Onset Mo.	Age at onset	Diagnosis: Morphologic Type	Diagnosis: Method**	Diagnosis: Institution
1	[redacted]	N M	1	Unk	58	5	14	Astrocytoma	Autopsy	A
2		H M	14	0	59	7	28	Neurinoma	Autopsy	A
3		N F	3	27	59	8	17	Craniopharyngioma	Operation	E
4		N F	13	1	61	3	29	Neurinoma	Operation	G
5		H F	28	7	62	6	45	Meningioma	Surgical	B
6		H F	14	8	62	7	31	Pituitary tumor	Autopsy	B
7		H F	42	25	63	1	60	Meningioma	Surgical	C
8		N M	40	7	63	2	58	Pituitary tumor	Autopsy	E
9		H M	45	Unk	63	2	62	Undetermined	Death certificate	F
10		H F	49	12	63	6	67	Glioblastoma	Autopsy	A
11		H F	38	0	63	6	55	Astrocytoma	Autopsy	A
12		H M	8	NIC	63	6	26	Astrocytoma	Surgical	B
13		H M	41	NIC	63	7	59	Pituitary tumor	Surgical	B
14		H F	46	8	64	12	65	Neurinoma	Operation	H
15		H F	19	37	65	3	39	Neurinoma	Autopsy	A
16		N F	5	NIC	65	3	25	Glioblastoma	Autopsy	A
17		H M	28	0	66	1	48	Meningioma	Operation	H
18		H F	38	NIC	66	3	59	Astrocytoma	Autopsy	A
19		H F	1	NIC	66	5	22	Astrocytoma	Surgical	B
20		H F	42	0	66	7	63	Undetermined	Death certificate	F
21		N F	2	Unk	66	7	23	Neurinoma	Surgical	E
22		H F	54	15	66	10	75	Undetermined	Death certificate	F
23		H F	18	0	67	1	39	Glioblastoma	Autopsy	A
24		H F	34	63	68	1	56	Meningioma	Autopsy	A
25		H F	33	1	68	6	56	Undetermined	Death certificate	C
26		N M	2	182	68	12	25	Craniopharyngioma	Surgical	E
27		H F	19	0	69	1	43	Glioblastoma	Autopsy	A
28		H F	44	4	69	4	68	Meningioma	Autopsy	A
29		H M	59	30	69	10	83	Astrocytoma	Autopsy	A
30		H F	20	NIC	70	9	45	Glioblastoma	Autopsy	A
31		N M	31	187	70	12	56	Glioblastoma	Autopsy	A
32		H F	4	0	71	5	30	Ependymoma	Surgical	B
33		N M	16	113	71	12	42	Astrocytoma	Operation	E
34		H F	25	0	72	9	52	Glioblastoma	Surgical	C
35		H F	9	NIC	72	10	37	Tumor of blood vessel	Surgical	D
36		H M	47	5	72	11	74	Glioblastoma	Autopsy	A
37		H F	22	Unk	73	12	50	Meningioma	Surgical	C
38		N F	28	8	73	9	57	Meningioma	Operation	E
39		H F	20	23	73	10	48	Pituitary tumor	Surgical	B
40		H M	37	0	74	2	66	Glioblastoma	Surgical	C
41		H F	26	40	74	9	55	Glioblastoma	Surgical	C
42		H M	42	0	74	9	72	Undetermined	Death certificate	F
43		H F	31	NIC	74	10	60	Meningioma	Surgical	C
44		H M	17	0	75	5	47	Neurinoma	Surgical	B
45		H M	13	1	75	10	43	Ganglioglioma	Surgical	B

Institution: A – RERF; B – Hiroshima University Medical School; C – Hiroshima Citizen's Hospital; D – Hiroshima Prefectural Hospital; E – Nagasaki University Medical School; F – Private Physician or Hospital; G – Kurume University Medical School; H – Okayama University Medical School.

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