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RISK OF CANCER AMONG IN UTERO CHILDREN EXPOSED TO A-BOMB RADIATION, 1950–84

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原爆放射線胎内被爆児における発癌リスク，1950-84年

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SUMMARY

This study examines the risk of cancer (incidence) over a period of 40 years among the in utero exposed survivors of the atomic bombing of Hiroshima and Nagasaki, and adds eight years of follow-up to a previous report which was confined to mortality. Only two cases of childhood cancer were observed among these survivors in the first 14 years of life; both had been heavily exposed. Subsequent cancers have all been of the adult type. Not only did the observed cancers occur earlier in the $\geq$0.30 Gy dose group than in the 0 Gy dose group but the incidence continues to increase and the crude cumulative incidence rate, 40 years after the A-bombing, is 3.9-fold greater in the $\geq$0.30 Gy group. In the observation period 1950–84, based on the absorbed dose to the mother's uterus, as estimated by the Dosimetry System 1986 (DS86), the relative risk of cancer at 1 Gy is 3.77 with a 95% confidence interval of 1.14–13.48. For the entire $\geq$0.01 Gy dose group the average excess risk per 10^4 person-year-gray is 6.57 (0.07–14.49) and the estimated attributable risk is 40.9% (2.9%–90.2%). These results, when viewed in the perspective of fetus doses, suggest that susceptibility to radiation-induced cancers is higher in pre- than in postnatally exposed survivors (at least those exposed as adults). However, definitive conclusions must await further follow-up studies.

要 約

広島・長崎の原爆胎内被爆児における40年間の発癌リスク（発生率）を調査した．死亡だけに限定した前回の報告に８年間の追跡期間を追加することになる．生後14歳までに観察された小児癌はわずかに２例だけであった．２例とも高線量に被曝している．それ以降にみられる癌はすべて成人期の癌であった．0.30 Gy 以上の線量群で観察された癌は 0Gy 線量群の症例より早期に発生しているだけでなく，増加を続けている．被爆40年後，0.30 Gy 以上の線量群の累積発生率は，0Gy 線量群の3.9倍になる．1986年線量推定方式（DS86）で推定されている母親の子宮における吸収線量によれば，1950～84年の観察期間では，1Gy 被曝線量での相対危険度は3.77で，その95％信頼区間は 1.14～13.48 になる．0.01 Gy 以上のすべての被曝線量群における10万観察人年-gray 当たりの平均過剰リスクは 6.57（0.07～14.49）で，また同群における寄与危険度は40.9%（2.9%～90.2%）である．胎児線量で評価することを考えれば，これらの結果は胎内で被曝した者のほうが出生後に被曝した者（少なくとも成人で被曝した人）に比べて放射線誘発癌に対する感受性が高いことを示唆している．しかしながら，確定的な結論を出すにはまだ追跡調査をする必要がある．

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INTRODUCTION

Much interest has centered on the relationship of abdominal or pelvic exposure of pregnant women to diagnostic radiation to the risk of cancer in their children. Bithell and Stewart[1] have reviewed the data from the Oxford Survey, showing an increase in the carcinogenic effect of prenatal x-irradiation with increasing dose within 15 years of birth and variation in the risk associated with other epidemiological factors. Recently, Harvey et al,[2] using twins, have also suggested that x-irradiation in the embryonic period increases the risk of childhood cancer (especially at ages 10–14). Among the A-bomb survivors of Hiroshima and Nagasaki, although the radiation-induced cancer risk is higher in those who were children at the time of the bomb (ATB) than older individuals,[3] no remarkable increase in cancer mortality in childhood has been seen in children exposed in utero,[4–6] nor has an increase in the incidence of leukemia in these individuals been observed.[7] This seeming disparity between the effects of exposure to medical irradiation and to that of the A-bombs has occasioned a lively, sometimes acrimonious debate (see UNSCEAR 1986 Report for a review of the evidence).[8] Suffice it here to state that the issue remains unresolved.

Earlier studies have not, however, addressed the question of whether the carcinogenic effect of prenatal radiation exposure is limited to childhood. None of the follow-up studies on radiation-induced cancer among prenatally exposed children has been longer than 15 years after birth except for those individuals exposed in utero to the A-bombing of Hiroshima and Nagasaki. There is no assurance, therefore, that cancer due to A-bomb exposure while in utero will not increase in adulthood merely because an increase in childhood cancer has not been observed. Even if stillbirths and early postnatal deaths due to A-bomb exposure modified the risk of cancer in childhood, the incidence of adult cancers may remain unaffected because of the different developmental mechanisms involved in the expression of childhood and adulthood malignancies.

It is the purpose of this study, through an eight-year extension of the observation period,[6] to review not only cancer mortality but also the postchildhood cancer-inducing effect of A-bomb exposure in the

緒　言

妊婦の腹部あるいは骨盤部への診断用放射線の被曝と，その子供における発癌リスクとの関連に多大な関心が寄せられている．Bithell と Stewart[1] は Oxford 調査資料を再検討し，15歳以下では胎内X線照射線量の増加に伴う発癌の増加がみられること，また，ほかの疫学的要因によってもその危険度に変動があることを示した．最近，双生児の調査を行った Harvey ら[2] も，胎芽期のX線照射によって小児期（特に10～14歳）の癌の危険度が高まることを示唆した．広島・長崎の原爆被爆者では，被爆時に成人であった者よりも子供であった者の放射線誘発癌の危険度が高いことが認められている[3] にもかかわらず，胎内被爆者[4-6] の小児期の癌死亡の特記すべき増加も，白血病発生率の増加も観察されていない．[7] 医用放射線と原爆放射線の間で，被曝による影響にこのような差異が認められたため，活発な，時には苛烈な議論を巻き起こしてきた（従来の知見を再検討した国連科学委員会の1986年度報告参照）．[8] ここでは，この問題は未解決であると述べるにとどめる．

しかし，これまでの研究では，胎内放射線被曝の発癌効果が小児期に限定されているかどうかの問題は取り上げられていない．広島・長崎の原爆胎内被爆者以外には，出生前に被曝した子供について放射線誘発癌の追跡調査が生後15年以上も続けられているものはない．したがって，原爆胎内被爆者に小児期の癌に増加が観察されなかったという理由のみで，今後成人期に癌の増加は起こらないという保証はない．原爆被爆による死産や出生後の早期死亡によって小児期の発癌リスクが修飾されたとしても，小児期と成人期の悪性腫瘍の発生機序が異なるため，成人期の癌発生率は影響を受けないかもしれない．

今回は8年間の観察期間を追加して，癌死亡率[6] だけでなく，広島・長崎の腫瘍登録で確認された癌

in utero exposed population, using cancer incidence data confirmed by the tumor registries in Hiroshima and Nagasaki.

MATERIALS AND METHODS

Subjects. The subjects of the present study were drawn from the 2,802 individuals constituting the RERF Mortality Study of Children Exposed In Utero (excluding 18 subjects from the original sample of 2,820 subjects determined, after the construction of the study sample, to be ineligible by the definition of the in utero exposed survivor).[9] In utero exposed survivors are defined as those individuals who were born of A-bomb exposed mothers in the period from the time of the bombing (6 August 1945 in Hiroshima and 9 August 1945 in Nagasaki) to 31 May 1946. The date of birth was obtained by interview with the individual or his or her mother (92% of these dates are consistent through year, month and day with the officially recorded birth date). The trimesters of pregnancy at which the subjects were exposed are based on the day and month of birth as follows (days in parentheses are for Nagasaki).

Trimester I: 7 (10) February 1946–31 May 1946

Trimester II: 7 (10) November 1945–6 (9) February 1946

Trimester III: 6 (9) August 1945–6 (9) November 1945

These survivors were identified from one or more of three sources, namely, birth records, the RERF Master File, and the 1960 A-bomb Survivors Survey data. Most, albeit not all, were ascertained through a search of the records on births occurring prior to 1 June 1946. The Master File contains information on all A-bomb survivors registered with the RERF. Of the 183 subjects employed in this analysis and identified by the Master File, 60.1% were derived from the supplementary schedules of the census conducted prior to 1960, 28.4% from individual investigations, and 11.5% by chance. The 1960 A-bomb Survivors Survey was based on a supplementary survey of A-bomb survivors and in utero exposed children conducted at the time of the 1960 National Census. Through this survey, all in utero exposed children resident in the two prefectures of Hiroshima and Nagasaki on 1 October 1960 were

発生率データから，胎内被爆者の原爆被爆による小児期以降の癌誘発効果をも検討することが本研究の目的である．

対象と方法

対象者． 本研究の対象者は，放影研胎内被爆者死亡調査集団2,802人から抽出された（当初の調査集団2,820名からその後18名が胎内被爆者の定義に不適格であったために除外された）．[9] 胎内被爆者とは，原爆に被爆した母親から，原爆時（広島では8月6日，長崎では8月9日）から1946年5月31日までの期間に出生した者と定義されている．出生日は，本人あるいはその母親との面接から得られた（この出生日の92%は出生記録の生年月日と一致している）．生年月日から，次のように被爆時の妊娠時期を三つの時期に区分した（括弧内の日付は長崎）．

胎内被爆者は，次の三つの資料源の少なくとも一つにより確認された．すなわち，出生記録，放影研原簿記録，及び1960年原爆被爆者調査資料である．すべてではないが，その大部分は1946年6月1日以前の出生記録から確認された．放影研に登録されたすべての原爆被爆者に関する情報が原簿記録に記録されている．今回の解析対象者で原簿記録から確認された183人のうち60.1%は1960年以前に実施された国勢調査の付帯調査票で，28.4%は個別的調査で，11.5%は偶然にその情報が得られていた．1960年の原爆被爆者調査は，1960年国勢調査時に実施された原爆被爆者と胎内被爆者についての付帯調査に基づいたものである．この調査により，1960年10月1日現在の広島・長崎両県在住の胎内被爆者全員が確認

ascertained. The study subjects identified solely by the 1960 A-bomb Survivors Survey contribute to the follow-up study for the period after 1960 only, since these individuals were necessarily alive on the date of the Survey.

された．1960年原爆被爆者調査だけで確認された者は，当然，調査時の生存者に限定されているので，1960年以降の追跡調査にのみ用いる．

The individuals included in the present study are confined to those members of the Mortality Study of Children Exposed In Utero sample (2,802 subjects) for whom estimates of A-bomb exposure doses exist. Three persons whose exposure status is unknown and 45 on whom no dose estimates exist were excluded. Individuals not present in either city ATB (NIC, 878 individuals) were also excluded. From the 1,876 prenatally exposed survivors on whom A-bomb dose estimates are available, the following were excluded: those who did not have a koseki (family register) for reasons other than stillbirth or neonatal death, foreign nationals (36 individuals), and five individuals (one cancer case) born on the day of the bombing, and where it is unclear whether they were actually born before or after the event. Six persons whose follow-up was incomplete were also excluded.

本研究の対象者は，胎内被爆者死亡調査対象群（2,802人）中，原爆放射線被曝線量推定値が得られている者に限定した．被爆状態が不明である３名及び被曝線量推定値が得られていない45名は除外した．原爆時にいずれの市にもいなかった者（NIC，878人）も除外された．原爆放射線被曝線量推定値の入手できる胎内被爆者1,876人から次の者を除外した：死産あるいは新生児死亡以外の理由で戸籍のなかった者か外国籍の者（36人），並びに原爆の日に出生したが，その出生が実際には爆発の前後のいずれであったか不明確な５人（癌１症例を含む）．更に追跡調査の不完全な６人も除外した．

In the present study the subjects to be analyzed were confined to those surviving on and after 1 October 1950; a) 37 identified solely through the Master File who had died in the interval from the time of the bombing to 30 September 1950 were excluded. Also excluded was one case recorded in the Master File who died after 1 October 1950 and was only identified as an in utero exposed child at death. b) 161 individuals identified through birth records who died between the time of the bombing and 30 September 1950 were excluded. The final count of the in utero exposed subjects in this study is 1,630 (Table 1), and those who could at least be identified by a birth record accounted for 67.6% (1,102), those ascertained through the Master File, 11.2% (183), and those recognized solely by the 1960 A-bomb Survivors Survey, 21.2% (345).

本研究の解析の対象者は，1950年10月１日以降の生存者に限定した；すなわち a）原爆時以降1950年９月30日までの期間の死亡者で，原簿記録だけで確認された37人を除外した．死亡時に胎内被爆児と初めて確認され，原簿記録に登録された1950年10月１日以降に死亡した１例も除外した．b）出生記録から確認され，原爆時から1950年９月30日までの間に死亡した161人も除外した．本研究における胎内被爆者の最終的な総数は1,630人であり（表１），そのうち少なくとも出生記録で確認した者が67.6％（1,102），原簿記録で確認した者が11.2％（183），そして1960年原爆被爆者調査でのみ確認した者は21.2％（345）である．

Confirmation of the cause of death and cancer. Death was confirmed by examination of the koseki, and the cause was transcribed from schedules based on death certificates kept in the health centers throughout Japan. Confirmation of death is 99% complete.

死因と癌の確認． 死亡は戸簿調査で確認し，死因は日本全国各地の保健所が保管する死亡診断書に基づく死亡票から転記している．死亡の確認は99％完全である．

TABLE 1 NUMBER OF SUBJECTS, OCTOBER 1950–DECEMBER 1984
表1 対象者数，1950年10月～1984年12月

A. Mortality sample (total 1,630 subjects)

DS86 dose (uterus):	0 Gy	710 (100)	≥0.01 Gy	920 (166)
City:	Hiroshima	1401	Nagasaki	229
Sex:	Male	765	Female	865
Data source:	Birth records	1102	Others	528

B. Distribution by DS86 organ (uterus) dose groups and T65DR fetus dose groups

T65DR fetus dose (Gy)	DS86 organ dose (uterus, Gy)			
	0	0.01–0.29	≥0.30	Total
0	708 (100)	108 (0)		816 (100)
0.01–0.29	2 (0)	568 (153)	70 (3)	640 (156)
≥0.30		6 (2)	168 (8)	174 (10)
Total	710 (100)	682 (155)	238 (11)	1630 (266)

Dose groups of both DS86 and T65DR are defined by total dose of neutron and gamma doses
DS86 線量群及びT65DR 線量群ともガンマ線と中性子の合計線量で区分した
( ) Number of subjects assigned temporal DS86 dose estimates for this paper
この報告書で暫定的に推定した DS86 線量を適用した対象者数

Cases of cancer were ascertained through the death schedules and the tumor registries in Hiroshima and Nagasaki. The latter registries have collected data on cancer cases in these cities since 1958 under the sponsorship of the local medical associations and with the technical assistance of RERF. Not all of the methods of ascertainment used by the registries are equally reliable. Histological confirmation by tissue examination is definite, followed in reliability by clinical findings, including findings of operations and radiography, and the statement on the death certificate. It should be further noted that it is impossible to identify systematically cancer cases among subjects who have migrated from the tumor registry reporting areas.

癌症例は，死亡票と広島・長崎の腫瘍登録で確認した．腫瘍登録は，両市医師会が放影研の技術援助により，1958年以来両市において癌症例のデータを収集してきた．登録における確認方法の信頼性はすべてが等しいわけではない．その信頼性は，まず組織検査による組織学的確認が確実であり，そして手術及びX線検査所見を含む臨床所見，最後に死亡診断書の記述という順になる．腫瘍登録届出地域から転出した対象者中の癌症例を組織的に確認することは不可能であることをつけ加えておかねばならない．

Dosimetry. The A-bomb radiation dose estimates used heretofore at RERF have been based on a dosimetric system developed at the Oak Ridge National Laboratory. Individual estimates of the gamma ray and neutron doses, taking into account the shielding status of the survivors, were computed; these estimates are often referred to as "tissue kerma in air."[10,11] Fetal absorbed doses in this system are

線量測定. これまで放影研が採用してきた原爆放射線線量推定値は，米国 Oak Ridge National Laboratory が開発した線量方式に基づいている．被爆者の遮蔽状態を考慮して，個々にガンマ線及び中性子の線量推定値が計算された．これら推定値は，しばしば“空中組織 kerma 線量”[10,11] と呼ばれている．この

merely the estimates of maternal kerma (T65DR) multiplied by transmission factors averaged over all stages of fetal development and without regard to orientation or posture at the time of exposure.[11] These transmission factors differed trivially from those associated with the uterus (see Table 9 of Reference 11).

Recently, as an outgrowth of a complete reassessment of the A-bomb radiation dosimetry, a new system has been installed. This system, known as the Dosimetry System 1986 (DS86), differs in many respects from its predecessor.[12–14] The DS86 estimates, for example, within 1,600 m in Hiroshima and 2,000 m in Nagasaki, when the requisite detailed shielding information exists, are computed directly for each individual through a modeling of the circumstances attending his or her exposure without the use of explicit, average transmission factors and take into account orientation and posture, where known. Thus, they allow better for the effects of the latter and the scattering of radiant energy that occurs within tissues. Beyond 1,600 m in Hiroshima or 2,000 m in Nagasaki, where detailed shielding histories do not exist for the majority of survivors, organ-absorbed doses are obtained indirectly. Free-in-air (FIA) kerma is estimated at the survivor's location by regression methods, and the latter estimate is then adjusted using average structural and body transmission factors. Actual fetal absorbed doses, as such, are not yet available, and may not be for some time. We have, therefore, used the mother's computed uterus-absorbed dose (doses above 6 Gy have been truncated). Phantom studies[11] have shown that the correspondence between the uterus dose and that to fetal tissues is high in the latter half of pregnancy, but may overestimate the energy absorbed by the developing tissues in the first half when more fluid surrounds the embryo or fetus.

Unfortunately, DS86 doses are not presently available on all subjects whose T65DR doses have been estimated. Indeed, for 266 subjects (16.3%) in the present sample such doses are not at hand. To these individuals we have assigned a tentative DS86 uterus-absorbed dose computed in the following manner. Women within the Life Span Study (LSS) sample who were 12 years of age or older ATB and on whom both a DS86 uterus-absorbed dose and a

線量方式では，胎児吸収線量は原爆時の母体の方向や姿勢に関係なく，母体の kerma 線量（T65DR）に胎児発育期の全過程について平均化した透過率を乗じたにすぎない.[11] この透過率は，子宮に関する透過率と大差はない（参考文献11の表 9 参照）.

近年，原爆放射線線量の完全な再評価の結果，新方式が導入された．1986年線量測定方式（DS86）と呼ばれるこの方式は，多くの点でこれまでの方式とは異なる.[12-14] 例えば，広島で 1,600 m，長崎で 2,000 m 以内では必要とする詳細な遮蔽情報が揃っていれば一定の平均透過率の代わりに各個人の被爆状況のモデル化によって体の方向や姿勢が既知の場合はこれも考慮に入れて個別的に DS86 推定値は直接計算される．このように DS86 推定値は，体位及び組織内の放射エネルギーの散乱の影響が一層よく考慮されている．広島では 1,600 m 以遠，長崎では 2,000 m 以遠の大部分の被爆者の詳細な遮蔽歴はなく，臓器吸収線量は間接的に求められている．被爆者の被爆位置での空中 kerma 線量（FIA）は，回帰法により推定され，更に構造物や身体の平均透過率を用いて補正される．実際の胎児吸収線量はまだ得られておらず，今しばらく時間がかかるかもしれない．したがって，計算されている母親の子宮吸収線量を用いた（6 Gy 以上の遮蔽 kerma 線量は 6 Gy で打ち切られている）．ファントムを用いた研究[11] によると，妊娠後期では子宮線量と胎児組織線量との一致度は高いが，前期では胎芽あるいは胎児周囲には液体が多く発達中の組織での吸収エネルギーは過大に推定されているかもしれないことが示されている．

残念ながら，T65DR 線量の推定されていたすべての対象者について現在 DS86 線量が入手できているわけではない．実際，今回の調査集団中266人（16.3%）の DS86 線量は得られていない．これら対象者には，以下の方法で計算した暫定的 DS86子宮吸収線量 を適用した．寿命調査対象集団の被爆時12歳以上の女性で，かつ，DS86 子宮吸収線量と T65DR 線量の

T65DR dose exist were distributed by their T65DR dose in 0.10 Gy intervals. Within each of these intervals, the mean DS86 uterus-absorbed dose was calculated. We then distributed those subjects in the in utero sample without a DS86 dose but on whom a T65DR kerma dose of less than 6 Gy exists in the same 0.10 Gy T65DR intervals, and to the individuals within each such interval assigned a uterus-absorbed dose corresponding to the mean DS86 organ dose calculated as described above. If the T65DR kerma dose was 6 Gy or over, since there are reasons to believe these estimates are in error, we assigned the mean DS86 uterus-absorbed dose among those women in the LSS sample who were 12 years of age or older ATB with T65DR kerma doses of 6 Gy or over. For the cancer cases, the maternal DS86 uterus-absorbed dose and T65DR fetus dose (neutron and gamma), based on Kerr's factors, are shown in Table 3, but it should be assumed that the errors are very large in the fetus doses.

Statistical methods. The expected cancer cases and total deaths from causes other than cancer were computed based on the vital statistics for all of Japan (1947–84)[15] and compared with the observed cancer cases and noncancer deaths in the years 1950–84. Since the deaths in any five-year period after 1950 are relatively few, we have used the average mortality rate in successive 5-year age-groups to calculate the expectations. For example, the average mortality rate at the 5–9 age-group in 1950–54 was used to compute the expected number of deaths in the 5–9 age-group. To obtain the number of cancer cases, the ratio 1.4 (for 1975–79)[16] of cancer cases to the number of cancer deaths was used. The cancer cases were observed mainly in the period 1960–81, and, despite the small number, they probably suffice for calculating the expected cancer cases. The two-tailed p-values for the test of the null hypothesis, that is the ratio of the observed and the expected numbers is one, were calculated based on the Poisson distribution with the mean of the expected values for cancer cases and deaths from causes other than cancer.

In the present study, the opportunity to examine differences in cancer risk with time is limited because of the small number of cancer cases. However, the cumulative cancer incidence rates calculated by life

両方が得られている者を T65DR 線量 0.10 Gy ごとの線量群に分類し，各線量群ごとに DS86 子宮吸収線量の平均値を計算した．次に，胎内被爆者調査対象者で，DS86 線量は入手されていないが 6 Gy 未満の T65DR kerma 線量の者に，上記と同様に T65DR 0.10 Gy ごとの線量群に分類し，同一の線量群で上述のように計算した DS86 臓器線量の平均値をその者の子宮吸収線量とした．T65DR kerma 線量が 6 Gy 以上の者には，その推定値が誤りと考えられるので，両市の線量を有する被爆時12歳以上の女性で寿命調査対象群の T65DR kerma 線量が 6 Gy 以上の者の DS86 子宮吸収線量の平均値を適用した．癌症例については母親の DS86 子宮吸収線量と Kerr の係数に基づいて計算した T65DR 胎児線量（中性子とガンマ線）を表 3 に示したが，この胎児線量は大きな誤差を含むものとして理解する必要がある．

統計的解析方法． 期待癌発生数及び癌以外の死因による期待死亡総数は，日本全国の人口動態死亡統計（1947～84年）[15] から計算し，1950～84年の観察癌発生数及び癌以外の観察死亡数と比較した．1950年以降のいずれの 5 年区間でも死亡数は比較的少ないので，継続的に 5 歳区分した年齢階層の平均死亡率を期待数の計算に用いた．例えば，1950～54年の 5 ～ 9 歳の年齢階層の平均死亡率をもとに 5 ～ 9 歳の年齢階層の期待死亡数を計算した．癌発生数の計算には，癌死亡数に対する癌発生数の比率 1.4（1975～79年）[16] を用いた．癌症例は主に1960～81年に観察され，少数ではあったが，恐らく期待癌発生数を計算するには十分であろう．観察数と期待数の比率が 1 であるという帰無仮説検定には，期待癌発生数や癌以外の死因による期待死亡数を平均値とした Poisson 分布から両側検定 p 値を計算した．

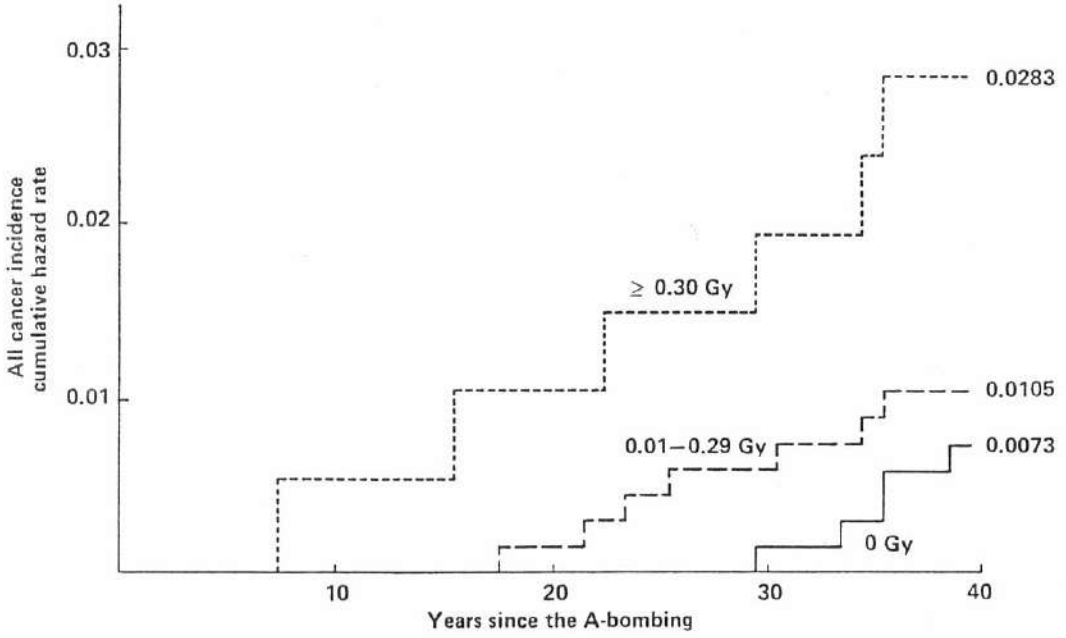
本研究では，癌症例が少数であるため発癌リスクの経時的変化について検討することに限界がある．しかし，観察期間を 1 年間隔に区切り生命表により

table methods, using an observation period divided at intervals of one year, have been calculated for three dose groups (0, 0.01–0.29, and ≥0.30 Gy), and graphically represented (Figure 1).

計算した癌累積発生率を三つの線量群(0, 0.01～0.29, そして≥0.30 Gy)について図に示した(図1).

FIGURE 1 CUMULATIVE HAZARD RATE USING LIFE TABLES AND ONE-YEAR INTERVALS FOR THREE EXPOSURE DOSE GROUPS (DS86 UTERUS-ORGAN DOSE)

図1 生命表を用い1年間隔に推定した三つの被曝線量群(DS86 子宮臓器線量)別の累積癌発生率



Estimation of cancer risks is based on an additive relative risk (RR) model in which the differences by city i (Hiroshima, Nagasaki) and sex j (males, females) in the background cancer incidence rate were stratified and the risks determined using a Poisson model[17] based on R_{ijk}, the person-years of observation in the period 1950–84 in four dose groups (k = 0, 0.01–0.29, 0.30–0.59, and ≥0.60 Gy). Under the Poisson model, it is postulated that Y_{ijk}, the number of cancer cases, follows the Poisson distribution with mean $E(Y_{ijk})$, where

発癌リスクは相加的相対危険度(RR)モデルから推定した. このモデルでは, 癌自然発生率の都市別 i (広島・長崎), 性別 j (男, 女)の差異を層化し, 四つの線量群(k=0, 0.01～0.29, 0.30～0.59, ≥0.60 Gy)別のリスクは1950～84年の観察人年である R_{ijk} に基づく Poisson モデル[17]を用いて決定した. Poisson モデルでは, 癌発生数 Y_{ijk} は Poisson 分布に従い $E(Y_{ijk})$ を平均値とする.

$$E(Y_{ijk}) = R_{ijk} g_{ij} (1 + bX_{ijk}).$$

Here g_{ij} is the background cancer incidence rate for city i and sex j per person-years of observation and X_{ijk} is the mean absorbed dose to the mother's uterus of dose group k in the stratum ij. Assuming k = 0 in the 0 Gy dose group, then the expected

ここで g_{ij} は都市 i, 性 j の観察人年当たりの癌自然発生率であり, X_{ijk} は ij 層における k 線量群の母体の平均子宮吸収線量である. 0 Gy 線量群では k=0 とすれば, この群の期待癌発生数は $E(Y_{ijo})$=

cancer cases in this group would be $E(Y_{ij0}) = R_{ij0}g_{ij}$ and the RR in the dose group k as contrasted with the 0 Gy dose group would be $1 + bX_{ijk}$. A model using mean doses is appropriate for testing a hypothesis which assumes that the cancer risk increases with dose because, although the estimated doses may be unreliable individually, the dose group-specific mean is more stable.

$R_{ij0}g_{ij}$ となり，0 Gy 線量群に対する k 線量群の相対危険度は $1 + bX_{ijk}$ となるであろう．個人別推定線量は信頼性が低いかもしれないが，線量群ごとの平均値はより安定しているので，平均線量を用いたモデルは被曝線量の増加に伴って癌危険度は増加するという仮説の検定に適切である．

RESULTS

Number of deaths. Because of the limitations imposed by the data, they have been divided into only two time periods.

結　果

死亡数． データによる限界があるため，死亡数は2期間にのみ区分した．

I. 1 October 1950–30 September 1960 (age 4–15 years)
第Ⅰ期. 1950年10月1日～1960年9月30日（4～15歳）

II. 1 October 1960–31 December 1984 (age 14–39 years)
第Ⅱ期. 1960年10月1日～1984年12月31日（14～39歳）

The numbers of deaths by cause are shown in Table 2. In period I, the subjects were 4–15 years old and deaths were few. The first cancer patient, however, was identified in these years. For period II, when the subjects were 14–39 years old, except for the ≥0.3 Gy group, about 50% of the deaths were due to accidents or suicide (44% is the expected value based on the vital statistics during the same observation period in all of Japan), and cases of cancer deaths began to increase in all dose groups as the survivors grew older.

死因別死亡数を表2に示した．第Ⅰ期では，対象者は4～15歳で死亡数はわずかしかない．しかし最初の癌患者はこの時期に確認された．第Ⅱ期では対象者は14～39歳で，≥0.30 Gy 線量群を除き死亡数の約50％は事故若しくは自殺によるものである（日本全国の同観察期間の人口動態死亡統計に基づく期待値は44％である）．被爆者の加齢に伴いすべての線量群で癌死亡数が増加し始めた．

Number of cancer cases. All identified cancer cases are listed in Table 3. Thirteen (72.2%) of the 18 cases were confirmed histologically and for 2 cases only the death certificate statements are available. In the first 10 years after birth, only one cancer death was identified, a case of liver cancer in a girl aged 6. (No cancer cases were recorded in the period August 1945–September 1950.) Her mother, aged 31 ATB, had an estimated absorbed dose to the uterus (DS86) of 1.39 Gy in Hiroshima in trimester I (delivery on 5 March 1946). The subject, the third child, weighed about 2,000 g at birth, and was reported to have had a small head and to be mentally retarded.[18] The next case to be identified was one of Wilms' tumor in a girl aged 14 (August 1960). The mother, aged 21 ATB, had an estimated uterus-absorbed dose (DS86) of 0.56 Gy in Hiroshima in trimester II. The subject, the first child, weighed about 3,300 g, a standard weight, at

癌症例数． 確認した全癌症例を表3に示した．18例中13例（72.2％）は組織学的に確認され，2例は死亡診断書の記述のみ得られている．出生後の最初の10年間では6歳女児の肝癌の癌死亡1例が確認されたのみである．（1945年8月～1950年9月の間は，癌症例の記録は1例もない．）その母親は被爆時31歳で，妊娠時期Ⅰに広島で被爆し，子宮吸収線量推定値（DS86）は1.39 Gy である（1946年5月5日出産）．本人は第三子で，出生時の体重約2,000 g，小頭症と精神遅滞であったことが報告されている．[18] 次に確認された症例は14歳の女児で，Wilms 腫瘍であった（1960年8月）．その母親は被爆時21歳で妊娠時期Ⅱに広島で被爆し，子宮吸収線量推定値（DS86）は0.56 Gy であった．本人は第一子で出生時体重は

TABLE 2 NUMBER OF DEATHS OBSERVED BY CAUSE AND OBSERVATION PERIOD

表 2 死因別及び観察期間別の観察死亡数

Cause of death	Obs. period Oct. 1950–Sep. 1960			Obs. period Oct. 1960–Dec. 1984			Total Oct. 1950–Dec. 1984		
	DS86 0 Gy <513>	DS86 0.01–0.29 Gy <569>	DS86 ≥0.30 Gy <203>	DS86 0 Gy <702>	DS86 0.01–0.29 Gy <677>	DS86 ≥0.30 Gy <234>	DS86 0 Gy <710>	DS86 0.01–0.29 Gy <682>	DS86 ≥0.3 Gy <238>
Total deaths	8	5	4	16	17	12	24	22	16
All known causes	8 (100.0)	3 (100.0)	4 (100.0)	16 (100.0)	17 (100.0)	12 (100.0)	24 (100.0)	20 (100.0)	16 (100.0)
Diseases									
Infective and parasitic disease	3 (37.5)	1 (33.3)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (12.5)	1 (5.0)	2 (12.5)
Malignant neoplasms	0 (0.0)	0 (0.0)	1 (25.5)	2 (12.5)	5 (29.4)	2* (16.7)	2 (8.3)	5 (25.0)	3* (18.8)
Respiratory system	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	0 (0.0)	0 (0.0)	1 (5.0)	0 (0.0)
Others except ill-defined conditions	3 (37.5)	1 (33.3)	0 (0.0)	5 (31.3)	2 (11.8)	6 (50.0)	8 (33.3)	3 (15.0)	6 (37.5)
Ill-defined conditions	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	1 (8.3)	2 (8.3)	1 (5.0)	1 (6.3)
Accidents or suicide	0 (0.0)	1 (33.3)	1 (25.5)	9 (56.3)	8 (47.1)	3 (25.0)	9 (37.5)	9 (45.0)	4 (25.0)
Cause unknown**	0	2	0	0	0	0	0	2	0

< >Number of subjects at risk 観察対象者数 ( ): % of a cause group in all known causes 全死因に占めるその死因の%

*Including the stomach cancer death suspected to have been induced by radiotherapy for Wilms' tumor

Wilms 腫瘍の放射線治療で誘発された疑いのある胃癌死亡例を含む

**Completely unknown causes of death 死因不明

TABLE 3 ALL CANCER CASES

表3 癌症例のリスト

MF No.	Dose (Gy) DS86 uterus	Dose (Gy) T65DR fetus	City and Sex	Timing ATB	Birth date Y	Birth date M	Birth date D	Onset Date Y	Onset Date M	Onset Age	Death Date Y	Death Date M	Death Age	Site	Ascertainment
[redacted]	0.00	0.00	H F	III (34)	'45	9	4	'75	1	29	'78	3	32	breast	histologically
	0.00	0.00	H F	III (26)	'45	11	02	'84	3	38		alive		breast	operation
	0.00	0.00	H F	I (3)	'46	4	12	'79	2	32		alive		breast	histologically
	0.00	0.00	H F	II (17)	'45	12	31	'80	10	34		alive		uterus	histologically
	(0.00)	0.00	H F	I (8)	'46	3	6	-	-	-	'80	10	34	uterus	death certificate
	0.01	0.00	H F	III (36)	'45	8	20	'80	7	34	'80	7	34	chorio	histologically
	0.01	0.00	H M	II (23)	'45	11	24	'68	11	22		alive		urinary	radiography
	0.01	0.00	H F	III (32)	'45	9	22	'81	3	35		alive		stomach	histologically
	0.02	0.00	H F	III (38)	'45	8	8	'63	7	18	'63	11	18	leukemia*	histologically

(Continued 続く)

Timing ATB: I = trimester I, II = trimester II, III = trimester III, and ( ) is gestational age
被爆時期: I＝妊娠時期Ⅰ，Ⅱ＝妊娠時期Ⅱ，Ⅲ＝妊娠時期Ⅲ，（ ）は胎内週齢

- Unkown 不明

*acute granulocytic 急性骨髄性　　**acute lymphocytic 急性リンパ球性

†MF No. 245977: The primary cause and onset of disease is known from surgical data. The onset might be 7 September 1952. Mental retardation and small head size also have been reported (refer to RERF TR 1-83).[18]
死因と発症時期は手術データより判明．発症時期は1952年9月7日の可能性あり．精神遅滞と小頭症も報告されている（RERF TR 1-83参照）.[18]

471020: The death certificate states that uterine cancer is the primary cause of death.
死亡診断書によれば子宮癌が死亡原因とされている．

703517: The cause of death is the recurrence of ovarian cancer.
死因は卵巣癌の再発．

857242: The death certificate indicates that this individual died of stomach cancer; however, it may have been induced radiotherapeutically in the course of the treatment of the Wilms' tumor.
死亡診断書によれば胃癌で死亡している．しかしWilms腫瘍の治療過程で放射線治療により胃癌が誘発されたのかもしれない．

TABLE 3 Continued 続き

MF No.	Dose (Gy)		City and Sex	Timing ATB	Birth date			Onset			Death			Site	Ascertainment
								Date			Date				
	DS86 uterus	T65DR fetus			Y	M	D	Y	M	Age	Y	M	Age		
[redacted]	0.04	0.02	H M	I (4)	'46	4	1	'76	3	29	'76	8	30	leukemia**	histologically
	(0.08)	0.01	H F	I (7)	'46	3	11	-	-	-	'67	6	21	colon	death certificate
	(0.21)	0.25	N F	I (3)	'46	4	13	'71	3	24	'71	10	25	stomach	operation
	0.40	0.28	H F	II (22)	'45	12	2	'80	1	34		alive		thyroid	histologically
	0.56	0.33	H F	II (15)	'46	1	17	'60	8	14	'81	12	35	Wilms'	histologically
	0.58	0.44	H M	III (36)	'45	8	25	'80	8	35		alive		hystiocytosis	histologically
	0.90	0.75	H M	II (17)	'46	1	6	'75	6	29		alive		stomach	histologically
	1.39	0.61	H F	I (8)	'46	3	5	-	-	-	'53	1	6	liver	histologically
	2.13	2.41	N F	III (36)	'45	8	23	'68	5	22	'81	7	35	ovary	histologically

birth. This individual died at age 35 of stomach cancer. No cancer was observed in the 0 Gy dose group before 30 September 1960, that is, at a time when they were still under about 15 years of age.

A further 16 cases of cancer were identified in period II. The stomach cancer in the Wilms' tumor patient is not included in these 16 cases because the cancer of which she died may have been an effect of radiotherapy. She received irradiation (probably ^{60}Co) five times during 1960–62 although the doses are unknown. In the following analysis, this case will be treated as Wilms' tumor and not as stomach cancer. A total of five cancer cases in females aged 29–38 occurred in the 0 Gy dose group (three cases of breast cancer, two of uterine cancer). The first cancer case in the 0 Gy dose group was a 29-year-old breast cancer patient. A total of 11 cases in subjects aged 18–35 occurred in the $\geq$0.01 Gy groups (seven females and four males). These include two cases of leukemia (a female aged 18 with acute myelogenous leukemia and a male aged 29 with acute lymphatic leukemia), previously reported by Ishimaru et al,[7] both of whom were exposed to low doses of A-bomb radiation (DS86 uterus-absorbed dose of 0.02 Gy in trimester III and 0.04 Gy in trimester I, respectively) in Hiroshima. In addition, there were two cases of stomach cancer (both female), and one each of urinary cancer (male), villous tumor (female), and colon cancer (female) in the 0.01–0.29 Gy dose group. There was one case each of thyroid cancer (female), malignant histiocytosis (male), stomach cancer (male), and ovarian cancer in the $\geq$0.30 Gy group.

Comparison with statistics for all of Japan. Using the vital statistics for all of Japan for 1947–84 and a cancer incidence ratio of 1.4(1975–79),[15,16] the expected numbers of cancer cases and total deaths from causes other than cancer were computed and compared with the observed numbers (Appendix Tables 1 and 2). For cancer cases occurring in subjects under 14 years of age, mortality statistics were used since the tumor registries are incomplete before 1958.

In the 0 Gy dose group, the observed results (5 cancer cases and 22 noncancer deaths at 4–39 years of age; October 1950–December 1984) differ only slightly from the expected values based on

約3,300 g，標準体重であった．胃癌のため35歳で死亡した．1960年9月30日以前，すなわち対象者がまだ15歳未満の時期には，0 Gy 線量群では癌は全く観察されなかった．

第Ⅱ期では，更に16例の癌症例を確認した．Wilms 腫瘍患者の死因である胃癌は放射線治療の影響であったかもしれないので，この16例の中にはこの胃癌は含まれていない．この患者は1960～62年に，線量は不明であるが5回の放射線照射（恐らく ^{60}Co）を受けた．以後の解析でこの症例は胃癌ではなく Wilms 腫瘍として扱う．0 Gy 線量群では29～38歳の女性で計5例の癌症例があった（3例は乳癌，2例は子宮癌）．0 Gy 線量群での最初の癌症例は29歳の乳癌患者であった．≥0.01 Gy 線量群には，18～35歳の対象者で計11例の症例があった（女性7人，男性4人）．この中には石丸ら[7]によって以前報告された白血病2例（18歳の急性骨髄性白血病の女性と29歳の急性リンパ球性白血病の男性）が含まれており，両者とも広島で低線量の原爆放射線（各々，DS86 子宮吸収線量で妊娠時期Ⅲに 0.02 Gy と妊娠時期Ⅰに 0.04 Gy）に被曝した．この2例に加えて0.01～0.29 Gy 線量群では，胃癌2例（両者とも女性）と泌尿器系癌（男性），絨毛上皮腫（女性），結腸癌（女性）が各1例ずつみられた．≥0.30 Gy 線量群では甲状腺癌（女性），悪性組織球症（男性），胃癌（男性），そして卵巣癌が各1例ずつみられた．

日本全国の統計との比較． 1947～84年の日本全国の人口動態死亡統計と癌発生比率1.4（1975～79年）[15,16]を用い，癌発生数と癌以外の死因による死亡総数について期待値を計算し，観察数と比較した（付録表1及び2）．14歳以下の癌症例に関しては，1958年以前の腫瘍登録が不完全であることから，死亡統計を用いた．

0 Gy 線量群の観察結果（4～39歳で癌5例，非癌死亡22例；1950年10月～1984年12月）は，日本全国からの期待値（期待癌発生数 3.76，期待非癌死亡数

all of Japan (3.76 expected cancer cases and 21.25 expected noncancer deaths; p-values are 0.357 and 0.761, respectively). This supports our belief that with regard to deaths, at least, the follow-up study of the in utero exposed children is complete and unbiased. Compared with the expected 3.64 cancers and 21.79 noncancer deaths at 4–39 years of age, 7 cancer cases and 17 noncancer deaths were observed in the 0.01–0.29 Gy group (p-values are 0.065 and 0.360, respectively). The 3 cancer cases at 4–39 years of age observed in the 0.30–0.59 Gy and the 3 in the ≥0.60 Gy group are significantly larger than the expected 0.68 and 0.54 cancer cases in these groups (p-values are 0.010 and 0.005, respectively). There is little difference, however, between the 3 observed noncancer deaths and the 4.28 expected in the 0.30–0.59 Gy group (p-value is 0.762).

The 10 deaths from noncancer causes among those aged 4–39 in the ≥0.60 Gy group are significantly larger than the expected 3.42 (p = 0.002). Noncancer diseases accounted for 80.0% of the deaths in this dose group in these years (8/10, one each of meningitis, pulmonary tuberculosis, acute myelitis, nephrosis, heart failure, diabetes, acute myocardial infarction, and cerebral spastic infantile paralysis), and deaths from accidents or suicide accounted for 20.0% (2/10). Of the 22 deaths from causes other than cancer in subjects aged 4–39 in the 0 Gy dose group, 59.1% (13/22, four cases from nephritis or nephrosis, two cases each from diarrheal disease and epilepsy, and one each from meningitis, moniliasis, and heart failure, and two ill-defined causes) were from noncancer deaths and 40.9% (9/22) due to accidents or suicide. As observed, even with the exclusion of cancer, the proportion of disease-related deaths among all deaths of subjects aged 4–39 is greater in the ≥0.60 Gy than in the 0 Gy dose group.

Estimation of risk of cancer. Cumulative hazard rates for the three dose groups (0, 0.01–0.29, ≥0.30 Gy) were calculated using life table methods and one-year intervals as shown in Figure 1. The cumulative hazard rates, 40 years after the A-bombing, are 0.0073 in the 0 Gy dose group, 0.0105 in the 0.01–0.29 Gy group, and 0.0283 in the ≥0.30 Gy group. As will be noted, the rates in the low dose group and the 0 Gy group are about the same, although cancers were detected earlier in the

21.25；p値は各々0.357，0.761）と大差はない．これは，少なくとも死亡に関しては胎内被爆者の追跡調査は完全であり，偏りがないという我々の考えを裏づけるものである．0.01—0.29 Gy 群では，4～39歳の期待値癌発生数3.64及び非癌死亡数21.79に対し，癌発生数7，非癌死亡数17が観察された（p値は各々0.065と0.360）．0.30—0.59 Gy 群では4～39歳の癌発生数3，≥0.60 Gy 群では癌発生数3が観察され，両群とも各々の期待値0.68及び0.54よりも有意に多くみられた（p値は各々0.010と0.005）．しかし，0.30—0.59 Gy 群の期待値4.28に対し，観察された非癌死亡数は3で大差はない（p値は0.762）．

≥0.60 Gy 群では，4～39歳の非癌死亡数10は期待値3.42より有意に多くみられた（p値0.002）．非癌死亡数10には，癌以外の病死が80.0％を占め（8/10，髄膜炎，肺結核，急性脊髄炎，ネフローゼ，心不全，糖尿病，急性心筋梗塞，脳性痙性小児麻痺，各1例），そして事故若しくは自殺による死亡が20.0％（2/10）を占めた．0 Gy 線量群では4～39歳の癌以外の原因による死亡22例中，59.1％は癌以外の死因による病死であり（13/22，腎炎又はネフローゼ4例，下痢性疾患とてんかん各2例，髄膜炎，カンジダ症，心不全各1例，そして詳細不明2例），40.9％（9/22）は事故若しくは自殺による死亡であった．以上から分かるように，癌を除いても4～39歳の全死亡数の病死の割合は，0 Gy 線量群よりも ≥0.60 Gy 群の方が高い．

発癌リスクの推定． 図1に示すように三つの線量群（0，0.01—0.29，≥0.30 Gy）の累積発生率を1年間隔で生命表を用いて計算した．原爆投下から40年後の累積発生率は0 Gy 線量群で0.0073，0.01—0.29 Gy 群で0.0105，そして ≥0.30 Gy 群では0.0283である．低線量群と0 Gy 線量群とでは前者で癌がより早期に発生したが，その累積発生率はほぼ同じであること

former group. However, cancers not only occurred earlier in the ≥0.30 Gy group than in the 0 Gy dose group, but the incidence continues to increase and the cumulative rate is 3.9-fold greater in the former group.

In the 0 Gy dose group, there were five cancer cases, and a crude incidence rate of 23.0 per 10^5 person-years (5/21770; see Table 4). In the 0.01–0.29 Gy dose group, there were seven cancer cases, and the crude incidence rate is 32.3 per 10^5 person-years (7/21659). The seeming concentration of cancer cases in the 0.01–0.08 Gy interval in the 0.01–0.29 Gy group may be due to chance. The ≥0.30 Gy group was divided into a 0.30–0.59 Gy and ≥0.60 Gy groups. In the 0.30–0.59 Gy group, there were three cancer cases, and the crude

が分かる．しかし0.30 Gy群では0 Gy線量群より癌が早期に発生するだけでなく，発生率が増加を続け，累積発生率は0 Gy線量群の3.9倍になっている．

0 Gy線量群では癌症例が5例あり，10万人年当たりの粗発生率は23.0であった(5/21770，表4参照)．0.01—0.29 Gy群では癌症例が7，粗発生率は10万人年当たり32.3である(7/21659)．0.01—0.29 Gy群の0.01—0.08 Gyの間に癌症例が集中しているのは，偶然であると思われる．≥0.30 Gy群を0.30—0.59 Gy群と≥0.60 Gy群とに分けた．0.30—0.59 Gy群では癌症例が3，粗発生率は10万人年当た

TABLE 4 CANCER INCIDENCE, LEVEL OF PRENATAL EXPOSURE TO A-BOMB RADIATION, AND ESTIMATES OF RELATIVE RISK (RR) BY AN ADDITIVE MODEL ADJUSTING FOR CITY AND SEX. 1950–84

表4 癌発生率，胎児被曝線量，及び都市，性を訂正した相加的モデルによる相対危険度(RR)の推定値，1950—84年

	DS86 uterus organ dose (Gy)			
	0	0.01–0.29	0.30–0.59	≥0.60
Observed				
Mean DS86 uterus dose (Gy)	0.000	0.087	0.416	1.372
Mean T65DR fetus dose (Gy)	0.000	0.054	0.324	1.051
No. at risk	710	682	129	109
Person-years	21770	21659	4095	3287
Cancer cases	5	7	3	3
Crude rate ($\times 10^{-5}$)	23.0	32.3	72.3	91.3
Estimated				
Back ground cases	5.58	5.38	0.96	0.76
Excess cases	–	1.31	1.13	2.88
RR	1.00	1.24	2.18	4.78
95% CI RR	–	(1.01, 2.10)	(1.06, 6.32)	(1.19, 17.93)

Pearson χ^2 for goodness of fit: $\chi^2 = 3.96$ (df = 11, p = 0.971)

Test for H_0: all RRs = 1 (b = 0) $\chi^2 = 4.71$ (df = 1, p = 0.030)

Refer to the Statistical methods section for the model equation. The estimated coefficient b (SE) is 2.767 (2.225) for the mean DS86 uterus organ dose (Gy) by each strata.

モデルは統計的方法の項参照．各層別のDS86子宮臓器線量(Gy)の平均値に対する推定係数b(SE)は2.767(2.225)．

incidence rate is 72.3 (3/4095). Similarly, in the ≥0.60 Gy group, there were three cancer cases with a crude incidence rate of 91.3 per 10^5 person-years (3/3287). The mean DS86 uterus-absorbed doses are 0.087, 0.416, and 1.372 Gy in the 0.01–0.29, 0.30–0.59, and ≥0.60 Gy groups, respectively.

The risks of childhood and adult cancers combined, using a Poisson additive RR model based on person-years of observation from 1 October 1950 to 31 December 1984, are shown in Table 4. The fit of this model, as judged by Pearson's χ^2 is good (χ^2 = 3.96, df = 11, p = 0.971), and the null hypothesis, H_0: b = 0, that is, all RRs = 1, can be rejected statistically (χ^2 = 4.71, df = 1, p = 0.030). These results indicate statistically that the risk of childhood cancer and adult cancer combined increases with increasing dose. This finding, however, may have been influenced in part by the fact that the two cases of cancer in the 0–14 age range occurred in the ≥0.30 Gy group. The excess cases (4.01 = 1.13 + 2.88) in the ≥0.30 Gy group shown in Table 4 is greater than the two cases observed in the same group in the age range 0–14 years. An analysis similar to that in Table 4, limited to the risk of adult cancers in subjects 15 years of age or over and based on person-years of observation of subjects aged 15–39 has been made. Though, at face value, the risk of cancer tends to increase with increasing dose, the linear increasing trend with dose is not statistically significant (p = 0.164).

Summary measures of the cancer incidence risk and their 95% confidence intervals among the in utero exposed children, based on an additive RR model and using the DS86 uterus-absorbed doses, are shown in Table 5. Over the period 1950–84, the estimated RR (95% confidence interval) of cancer at 1 Gy organ (uterus)-absorbed dose is 3.77 (1.14–13.48), the estimated average excess risk per 10^4 person-year-gray (PYGy) among survivors receiving 0.01 Gy or more is 6.57 (0.47–14.49), and the estimated attributable risk is 40.9% (2.9%–90.2%). An analysis limited to the risk of adult cancers for those aged 15–39 gives estimates of the cancer RR at 1 Gy of 2.44 (0.71–9.49), of average excess risk of cancer per 10^4 PYGy of 4.80 (–1.26–14.98), and an attributable risk of 26.0% (–6.8%–81.2%).

り72.3である（3/4095）．同様に≥0.60 Gy群では癌症例が3，粗発生率は91.3である（3/3287）．DS86子宮吸収線量の平均値は，0.01—0.29，0.30—0.59，≥0.60 Gy群で各々，0.087，0.416，1.372 Gyである．

1950年10月1日から1984年12月31日までの観察人年に基づくPoisson相加的相対危険度モデルによる小児期の癌及び成人期の癌を合わせたリスクを表4に示した．Peasonのχ^2によればこのモデルの適合性は良好であり（χ^2=3.96，df=11，p=0.971），帰無仮説H_0：b=0，すなわち全相対危険度=1，は統計的に棄却される（χ^2=4.71，df=1，p=0.030）．これらの結果は，線量の増加に伴い小児期の癌と成人期の癌とを合わせた発生率が増加していることを統計的に示している．しかし，≥0.30 Gy群の0～14歳年齢階層で発生した2例の癌症例によりこの結果は幾分影響を受けたかもしれない．表4に示す≥0.30 Gy群の過剰発生数（4.01＝1.13＋2.88）は，同群の0～14歳年齢階層で観察された2例より大きい．15歳以上の成人期の発癌リスクに限定し，15～39歳の観察人年に基づき表4と同様の解析を行った．線量増加に伴い発癌リスクが増加する傾向があるように見えるが，この線形増加傾向は統計的に有意ではない（p=0.164）．

DS86子宮吸収線量と相加的相対危険度モデルから，胎内被爆児における癌発生リスクの総括的指標とその95％信頼区間を表5に示した．1950～84年の臓器（子宮）吸収線量1 Gyでの癌の推定相対危険度（95％信頼区間）は3.77（1.14～13.48），0.01 Gy以上に被曝した被爆者の1万人年Gy（PYGy）当たりの推定平均過剰発生数は6.57（0.47—14.49），また推定平均過剰危険度は40.9％（2.9％～90.2％）である．15～39歳での成人期の発癌リスクに限定した解析によると，1 Gyでの癌の相対危険度は2.44（0.71～9.49），1万PYGy当たりの癌の平均過剰発生数は4.80（−1.26～14.98），また寄与危険度は26.0％（−6.8％～81.2％）と推定される．

TABLE 5 SUMMARY MEASURES OF CANCER INCIDENCE (1950–84) IN RELATION TO PRENATAL EXPOSURE TO A-BOMB RADIATION BY AN ADDITIVE MODEL BASED ON MOTHER'S ESTIMATED DS86 UTERUS ORGAN DOSE

表5 母親のDS86推定子宮臓器線量を用いた相加的モデルによる，胎内被曝線量と癌発生率（1950—84年）に関する総括的指標

	Estimated RR (at 1 Gy)	Average excess risk (per 10^4 PYGy†)	Attributable risk (%)
Follow-up 1950–84 all ages*			
Estimated values	3.77	6.57	40.9
95% lower	1.14	0.47	2.9
95% upper	13.48	14.49	90.2
Follow-up over age range 15–39 years**			
Estimated values	2.44	4.80	26.0
95% lower	0.71	−1.26	−6.8
95% upper	9.49	14.98	81.2

†person-year-gray 人年-gray

*Significant, p = 0.030 in the test for H_0: all relative risks = 1 (b = 0)
有意，H_0：全相対危険度＝1（b＝0）の検定で p＝0.030

**Not significant, p = 0.164 in the test for H_0: all relative risks = 1 (b = 0)
有意でない，H_0：全相対危険度＝1（b＝0）の検定で p=0.164

DISCUSSION

No investigation, heretofore, has examined the relationship of radiation exposure in the embryonic or fetal period to risk of adult cancer in a human population. This study, which includes cancer incidence up to 40 years following exposure, suggests an increase of cancer in individuals who were prenatally exposed. The observation of two cases of childhood cancer in children aged 0–14 in only the ≥0.30 Gy dose group may have influenced, to some degree, these results. At present, although the risk of adult cancers in subjects 15 years of age or older, excluding the two cases of childhood cancer, shows a tendency to increase with increasing A-bomb radiation dose, the increase is not statistically significant.

The cumulative cancer incidence rate with childhood and adult cancers combined, 40 years after A-bomb exposure, is 0.0283 in the ≥0.30 Gy group as against 0.0073 in the 0 Gy group and 0.0105 in the 0.01–0.29 Gy group. Although cancers tended to occur earlier in the 0.01–0.29 Gy group than in the 0 Gy dose group, the crude cumulative cancer incidence rates differ little. As seen in Table 5, during the observation period 1950–84, the estimated

考　察

ヒトにおける胎芽若しくは胎児期の放射線被曝と成人期の発癌リスクとの関連についての調査は，これまで全く行われていない．原爆後40年までの癌発生率を含めた今回の研究は，胎内被爆者に癌発生の増加がみられることを示唆している．0～14歳の小児期の癌の症例2例が≥0.30 Gy群のみに観察されることが，調査結果に多少影響を及ぼしたかもしれない．現在，小児期の癌2例を除いた15歳以上の成人期の発癌リスクは，原爆放射線被曝線量に伴って増加する傾向を示すが，この増加は統計的に有意ではない．

原爆被爆後40年の小児期の癌と成人期の癌とを合わせた累積癌発生率は，0 Gy線量群0.0073，0.01–0.29 Gy群0.0105に対して≥0.30 Gy群では0.0283である．0 Gy線量群に比べて0.01—0.29Gy群に癌は早期に発生した傾向があるが，粗累積癌発生率は両群で差はほとんどない．表5に示すように1950～84年の観察期間中，1 Gyでの癌の推定相対危険度は

RR of cancer at 1 Gy is 3.77 (1.14–13.48). Among the ≥0.01 Gy dose groups the estimated average excess risk per 10^4 PYGy is 6.57 (0.47–14.49), and the estimated attributable risk to A-bomb radiation is 40.9% (2.9%–90.2%). These summary indexes are 30%–40% lower if the calculation is limited to the risk of adult cancer in the subjects 15–39 years of age. In the future, as the observation period becomes longer, the average excess risk will increase and the RR and the attributable risk will decrease as the incidence of spontaneous cancer increases.

To determine whether these risks are higher than those of postnatally exposed children, the risk of all cancers among A-bomb survivors aged 0–9 ATB has been compared with those of children in utero ATB in Table 6. For A-bomb survivors aged 0–9 ATB, the data were derived from Part 2 of Report 11 of the RERF LSS.[19] It should be noted that the period of observation differs between the A-bomb survivors aged 0–9 ATB and the in utero exposed, and one risk estimate is based on cancer mortality while the other is based on cancer incidence. However, nearly identical average excess risks are seen; these are based on the uterus-absorbed dose of the mothers of the in utero exposed children, in the one instance, and the kerma dose received by the A-bomb survivors aged 0–9 ATB, in the other. It is well known that the RR of cancer is higher the younger the age ATB. Comparison of in utero exposed children with exposed adults shows the cancer risk (including adult cancers) to be higher in fetuses than in adults. This raises the possibility that radiation-induced cancers will increase as the in utero exposed children become older. Since the incidence of adult cancers originally is higher than the incidence of childhood cancer, the future may show more clearly an increase in cancer incidence due to radiation exposure. At present, it remains to be resolved why the risk of leukemia in the prenatally exposed survivors is not commensurate with that seen in the A-bomb survivors aged 0–9 ATB.

In the analysis thus far described, the cancer incidence rate is based on cancers occurring after 1 October 1950. The reasons for this limitation are: a) because of the confusion in the official vital statistics system immediately after the war,

危険度3.77(1.14～13.48)である．≥0.01 Gy 群では，1万 PYGy 当たりの推定平均過剰発生数は6.57(0.47～14.49)，そして原爆放射線による推定寄与危険度は40.9%(2.9%～90.2%)であった．これらの総括的指標は，15～39歳の成人期の発癌リスクに限定して計算すると30%～40%低下する．将来，観察期間が長くなるにつれて癌の自然発生率が増加するため，平均過剰発生数は増加し相対危険度及び寄与危険度は減少するであろう．

これらの値が出生後に被曝した子供のリスクより高いか否かを被爆時0～9歳の原爆被爆者と胎内被爆児との間で全部位の発癌リスクを比較し表6に示した．被爆時0～9歳の原爆被爆者については，放影研寿命調査第11報第2部[19]からデータを得た．被爆時0～9歳の原爆被爆者と胎内被爆者とでは観察期間が異なることに留意したい．前者の推定リスクは癌死亡率に基づき，後者では癌発生率に基づいている．しかし，両者で平均過剰危険度はほぼ等しい．一方は胎内被爆児の母体の子宮吸収線量に，他方は被爆時0～9歳の原爆被爆者の kerma 線量に基づいている．癌の相対危険度が被爆時年齢の若いほど高くなることはよく知られている．胎内被爆児と被爆時成人であった者とを比較すれば，発癌リスク(成人期の癌を含む)は被爆時成人であった者よりも胎児であった者の方が高い．これは胎内被爆児が加齢するにつれて放射線誘発癌は増加する可能性を示している．成人期の癌発生率は本来，小児期の癌発生率より高いので，将来，放射線被曝に起因した癌発生率の増加がより明確に認められるかもしれない．胎内被爆児の白血病のリスクがなぜ被爆時0～9歳の被爆者のそれと同様でないのか，現在のところ未解決である．

以上の解析では，1950年10月1日以降に発生した癌に基づいて癌発生率を求めた．このように限定した理由は，a)終戦直後の人口動態死亡統計の混乱の

TABLE 6 COMPARISON OF CANCER RISK BETWEEN "IN UTERO EXPOSED" AND "EXPOSED AT 0–9 AGE ATB"

表 6 "胎内被爆児"と"被爆時年齢 0 ～ 9 歳の被爆者"との発癌リスクの比較

		In utero (1950–84) DS86 uterus dose		0–9 Age ATB (1950–85) DS86 tissue kerma
No. of cancer		18 (2)		142 (31)
RR at 1 Gy	all cancer	3.77	leukemia	17.25
			other cancer	2.23
Average excess risk /10^4 PYGy	all cancer	6.57	leukemia	2.93
			other cancer	2.27

( ) Number of leukemia cases 白血病の症例数

the death certificates for some deaths within one year after birth, 1945–46, were not available and the cause of those deaths are unknown, b) it should reduce the possibility of bias in ascertaining subjects through the Master File where they may have been identified as in utero exposed shortly after their death notice prior to October 1950, and c) it makes more exact comparison of the magnitude of the risk in the in utero exposed with the risk among A-bomb survivors of 0–9 years of age ATB since the risk in the latter group is based on cases of cancer death occurring after 1 October 1950.

As previously stated, 161 and 37 deaths occurring before 1 October 1950 among the subjects identified through the birth records and Master File, respectively, were excluded from the present analysis. None of these 198 deaths was attributed to cancer. However, since the risk of cancer from birth to the present is of interest, and the restriction of the observation period to cancers occurring after 1 October 1950 provides information only on the risk after approximately 4 years of age, the risk was estimated for the entire period from birth to December 1984 based on the subjects identified through birth records. Individuals so ascertained represent 67.6% (1102/1630) in Table 1 and 161 individuals were died from birth to 30 September 1950. An increasing trend in cancer incidence with dose similar to that shown in Table 4 is observed among these 1,263 (1,102 + 161) subjects, though the increasing trend is not statistically significant because of the smaller sample size (Appendix 3). The estimated RR at 1 Gy within this group is 3.19

ため，1945～46年の生後1年以内の死亡診断書の一部が入手できなかったので，死因が不明の者があったこと，b) 1950年10月以前においては，死亡届によって初めて胎内被爆児であったと原簿記録で確認したことによって生じる偏りの可能性を排除する必要があること，c) 被爆時 0 ～ 9 歳の被爆者のリスクも1950年10月 1 日以降に発生した癌死亡例に基づいているので，胎内被爆児と被爆時 0 ～ 9 歳の原爆被爆者とのリスクをより正確に比較することができるためである．

前述のように，出生記録又は原簿記録により確認した者で1950年10月 1 日以前の死亡例，各々161例と37例は本解析から除外した．これら198の死亡例はいずれも癌に起因したものではなかった．しかし，出生時から現在までの癌の発生リスクに注目すれば，1950年10月 1 日以降の癌発生に観察期間を限定すると，約 4 歳以降の危険度についての情報しか得られないことになるので，出生記録から確認した対象者について，出生時から1984年12月までの全期間にわたるリスクを推定した．出生記録で確認した者は，表 1 の67.6％(1,102/1,630)を占めており，出生時から1950年 9 月30日までに死亡した者が161人であった．表 4 で示したのと同様に，線量に伴う癌発生率の増加傾向がこれら1,263人(1,102 + 161)の対象者でも観察された．ただし，集団が小標本であるためにこの増加傾向は統計的に有意ではない(付録 3)．この集団内の 1 Gy での推定相対危険度は3.19(0.74～

(0.74–16.03), the average excess risk per 10^4 PYGy is 4.67 (–0.77–12.78), and the attributable risk is 30.3 (–5.5–91.2). These values are somewhat lower than those shown in Table 5 (1950–84).

Fatal cancers within this study group can be ascertained almost completely because a copy of the death certificate is available. If the cancer subjects are still living, we must depend on the tumor registry, but since the latter registries were not begun until 1958, ascertainment of incident cases of cancer occurring before 1960 is incomplete. If cancer cases occurred after 1960, since the subjects may have migrated from the tumor registry reporting areas, cancer deaths can be identified, but living cancer cases cannot. Although the migration rates in the Adult Health Study do not differ by radiation category, migration is higher in the younger than in the older age-groups and higher in Nagasaki than in Hiroshima,[20] and a correspondingly high migration rate in the in utero exposed survivors from the tumor registry reporting areas is to be expected. Our evaluation assumes that migration of the in utero exposed children is independent of their radiation dose levels. The validity of this assumption is testable, at least crudely. The proportions of prefectures other than Hiroshima and Nagasaki among the last addresses available for our subjects provides information on this issue. Based on these addresses, the migration rate in the 0 Gy group is around 15% and may have increased with the level of exposure, reaching 20% in the 0.30 Gy or more (Appendix 4). As a consequence, the absolute risk of cancer incidence may be underestimated by around 15%–20%, and the risks actually higher than we compute. Subjects whose mothers were not in either Hiroshima or Nagasaki city ATB (NIC) were selected in the original sample[9] as a potential comparison group. Their last addresses also indicate that the migration rate in the NIC is especially high (33.3%) when compared to other groups. In the 0 Gy dose group (710 subjects alive in October 1950), there were two cancer deaths and one in the NIC group (795 subjects alive in October 1950); in addition, three cancer cases have been reported to the tumor registry for the 0 Gy dose group but none for the NIC group. Thus the total observed cancer cases are five for the 0 Gy dose group (this number is close to the expected number, 3.76, derived from the statistics for all of Japan) and one for the NIC

16.03)，1万PYGy当たりの平均過剰発生数は4.67(−0.77～12.78)，寄与危険度は30.3(−5.5～91.2)である．これらの値は表5(1950～84年)に示した値より幾分低い．

本研究対象群の致死性癌は，死亡診断書の写しが入手できるのでほぼ完全に確認できる．癌患者が生存している場合は腫瘍登録に頼らざるをえない．しかしこの登録は1958年に開始されたため，1960年以前の癌発生症例の確認は不完全である．癌症例が1960年以降に発生し，対象者が腫瘍登録届出地域から転出した場合は，癌死亡例の確認はできるが癌の生存例の確認はできない．成人健康調査対象者の転出率は放射線線量群間で差はないが，高年齢階層より低年齢階層で，広島より長崎で転出率が高い．[20] したがって，胎内被爆者の腫瘍登録届出地域からの転出率もそれに対応して高いと予想される．我々の解析では，胎内被爆者の転出率はその放射線線量とは無関係であると仮定している．少なくともおおまかにはこの仮定の妥当性について検証が可能である．知り得る対象者の最新の住所が広島・長崎県外で占める割合をみれば，この問題についての情報を得ることができる．これらの住所に基づく転出率は0 Gy群では約15%で，被曝線量に伴う増加傾向を示し，0.30 Gy以上の群では20%に達している(付録4)．その結果，癌発生の絶対危険度は約15%～20%過小評価されているかもしれない．したがって，その危険度は実際には我々が計算した値より高いのかもしれない．母集団[9]には，母親が原爆時に広島市あるいは長崎市に不在であった者(NIC)が潜在的対照群として選ばれている．また彼らの最新の住所から，NIC群の転出率が他の集団と比較して特に高い(33.3%)ことを示している．0 Gy線量群(1950年10月に生存していた者は710人)では癌死亡が2例，NIC群(1950年10月に生存していた者は795人)では1例あった．加えて0 Gy群では3例の癌症例が腫瘍登録に報告されていたが，NIC群では全くなかった．したがって，0 Gy群での全観察癌症例は5例で(この数は日本全国の統計からの期待数，3.76に近い)，NIC群

group. Since the high migration from the tumor registry reporting areas among the NIC group could have influenced the results, the NIC group were excluded from our analysis.

As listed in Table 3, the 16 cancer cases, excepting the two childhood ones, consist of adult cancers, such as breast (3), stomach (3), leukemia and related diseases (3), uterus (2), colon, thyroid, ovary, urinary bladder, and villous tumors. Thus, no increase has as yet been observed in any particular site of cancer. Neither of the two cases of childhood cancer (liver cancer and Wilms' tumor), observed only in the $\geq$0.30 Gy group of in utero exposed children of Hiroshima and Nagasaki A-bombs, can be unequivocally assigned to radiation. In the liver cancer case, however, mental retardation and small head size,[18] both of which are increased in the in utero exposed children, was reported.

The number of children under 15 years of age identified by birth records in whom the risk of cancer could be followed completely from birth is 1,263 and the mean DS86 organ (uterus) absorbed dose is 0.184 Gy. For this cohort, as described in a previous paper,[4] only one case of childhood cancers developed under 10 years of age, and the maximum, 95% upper limit of the estimated excess risk is far less than that estimated from the Oxford Survey.[1] Since one other individual, exposed to 0.56 Gy, developed cancer at age 14 in the same cohort, the risk estimates for childhood cancer under 15 years of age was calculated anew. The upper limit of the 95% confidence interval in a two-sided test based on a Poisson distribution of expected values for the two observed cases of cancer is 7.22, and the number of cancer cases that would be expected from the statistics for all Japan is at most 0.73 (0.52, the expected cancer deaths in the entire birth record sample multiplied by 1.4, an adjustment for mortality to incidence rate,[16] data not shown). Hence, a rough estimation of the increased risk of childhood cancer in children aged 0–14 gives a maximum of 279 ($[7.22 - 0.73]/[1{,}263 \times 0.184] \times 10^4$) as the number at risk per 10^4 population-gray. The results observed in children exposed in utero to A-bomb radiation are not strikingly at variance in terms of the magnitude of the risk with the results (an estimated risk of 572 ± 133 per 10^4 population-fetal-gray) observed among the children

では1例である．NIC群の腫瘍登録届出地域からの転出率が高いことが結果に影響を与えているかもしれないので，NIC群は本解析から除外した．

表3に記載したように，2例の小児期の癌を除く16例の癌症例は成人期の癌であり，その内訳は，乳癌3，胃癌3，白血病関連疾病3，子宮癌2，結腸，甲状腺，卵巣，膀胱，及び絨毛上皮腫各1例である．このように，特定部位の癌の増加はまだ観察されていない．広島・長崎の原爆胎内被爆児の$\geq$0.30 Gy群でのみ観察された小児期の癌の2例（肝癌とWilms腫瘍）のいずれにおいても，その原因が放射線であるとは明確に言えない．しかし肝癌の症例では，胎内被爆児で増加のみられる精神遅滞と小頭症が認められたと報告されている．[18]

出生記録で確認され15歳以下の発癌リスクを出生時から完全に追跡可能であった子供の数は1,263人で，そのDS86臓器（子宮）吸収線量の平均値は0.184 Gyである．このコホートに関しては，前回の報告書[4]で述べたとおり，10歳以下でわずか1例の小児期の癌が発生しただけで，推定過剰危険度の95%上限値，つまり最大値はOxford調査[1]による推定値よりはるかに低い．このほかに同コホートで0.56 Gyの線量を被曝した者1人に14歳で癌が発生したので，15歳以下の小児期の癌の推定危険度を新たに計算した．観察した癌2例のPoisson分布に基づく期待値の両側95%信頼区間の上限値は7.22であり，また，日本全国の統計からの期待癌発生数は最大で0.73である（データは示していないが，死亡率を発生率に補正するために，[16]出生記録からの集団全体での期待癌死亡数0.52を1.4倍する）．したがって，0～14歳での小児期の癌発生リスクの増加は，概算すると1万人Gy当たりの過剰発生数の最大値は279となる（$[7.22-0.73]/[1{,}263 \times 0.184] \times 10^4$）．原爆放射線に胎内で被曝した子供における観察結果は，医用放射線に胎内で被曝した子供について行われたOxford調査[1]の10歳以下の子供の観察結果（推定過剰発生

under 10 years of age in the Oxford Survey[1] of children exposed in utero to medical radiation.

Kneale and Stewart[21] have attributed the seeming disparity between the Oxford Survey and the A-bomb experience to children whose reticuloendothelial system was damaged through exposure and who died at a young age of infectious diseases due to a decrease or loss of their immunologic competence. Undoubtedly, mortality of children who were less than 1 year of age was high in the high dose group (around 10 excess deaths were estimated in the $\geq$0.60 Gy group), though an excess in mortality was observed only for children who were exposed in the third trimester where mechanical injury may also have played a role in their deaths. Regrettably, nothing definite is known in this regard because deaths in this age-group often have no apparent cause. There is no evidence, however, that infectious diseases were increased and resulted in an increased death of children under 1 year of age. Because there is a tendency in Japan to report early neonatal deaths as stillbirths,[22] the number of excess deaths of children under 1 year of age may have been greater. Furthermore, since our data are based almost entirely on birth records, it is not clear whether stillbirths were increased in prenatally exposed children as a result of A-bomb exposure. Yamazaki et al[23] have reported that fetal mortality was 10.2% (10/98) if the mother was within 2,000 m of the hypocenter in Nagasaki compared to a fetal mortality of 2.7% (3/113) if she was within 4,000–5,000 m of the hypocenter.

Since the number of cancer cases in the present analysis is small, we have failed to identify statistically significant differences in the risk of radiation-related cancer associated with exposure in different gestational periods. The results of other human population studies have been inconsistent in this regard.[1,24,25] Further careful follow-up of this cohort will be required if this issue is to be resolved.

数1万人年Gy当たり572 ±133)と，リスクの程度には顕著な差異はみられない．

Kneale と Stewart[21] は，被曝によって網内皮系が障害され，免疫能の減退若しくは喪失に起因した感染症で若年に死亡する子供がいることが，Oxford調査と原爆調査との間でみられる相違の原因であるとしている．確かに高線量群では1歳未満の子供の死亡率は高かった（≥0.60 Gy群では約10例の過剰死亡数があると推定される）．ただし，この死亡率の増加は，母親の受けた物理的傷害もその死亡に何らかの影響を与え得る妊娠時期Ⅲに被曝した子供においてのみ観察された．1歳未満では死亡原因が不明の場合がしばしばあるため，この点に関しては残念ながら確定的なことは分からない．しかし，感染症が増加し，その結果として1歳未満の子供の死亡増加となったという証拠はない．日本では早期の新生児死亡を死産として報告する傾向があるため，[22] 1歳未満の子供の過剰死亡数はもっと多かったかもしれない．更に，我々のデータは大部分出生記録に基づいているので，胎内被爆児の死産が原爆被爆の結果増加したか否かは明らかではない．山崎ら[23]は，長崎で母親が爆心地から4,000～5,000 m以内にいた場合の死産率2.7%（3/113）に対し，母親が爆心地から2,000 m以内にいた場合の死産率は10.2%（10/98）であったと報告している．

本解析の癌症例数は少なく，被爆時の妊娠時期によって放射線誘発癌リスクが統計的に有意に異なっているとは確認できなかった．この点に関して，他の人間集団の研究結果[1,24,25]では食い違いがみられる．この問題の解決には，このコホートを更に慎重に追跡調査する必要がある．

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APPENDIX TABLE 1 AVERAGE ANNUAL MORTALITY RATE ($\times 10^{-5}$) FOR ALL DEATHS AND FOR ALL DEATHS FROM MALIGNANT DISEASES BASED ON ALL JAPAN, 1947–84

付録表1　日本全国による全死亡と悪性新生物死亡の平均年間死亡率（10万対），1947－84年

Age at risk	All deaths		All malignant neoplasms		Calendar year basis for calculation
	Male	Female	Male	Female	
0	8759.2	7663.0	5.3*	3.0*	1947
1–4	1744.4	1697.4	3.4*	2.1*	1947
5–9	182.1	160.4	3.2	2.2	1950–54
10–14	68.8	54.3	4.2	3.3	1955–59
15–19	112.9	62.2	6.8	5.4	1960–64
20–24	140.1	74.1	8.6	7.7	1965–69
25–29	129.2	75.0	12.3	13.5	1970–74
30–34	118.2	71.2	18.6	23.0	1975–79
35–39	148.6	85.3	30.1	34.9	1980–84

*The numbers of cancer deaths at age 0–4 in 1947 of 1984 volume and the proportion of cancer deaths at age 0 in 1947 of 1947 volume were used. The statistics of cancer deaths at age 0–4 in 1947 of 1984 volume are different from those of 1947 volume.

1947年0～4歳の癌死亡数は1984年版，1947年0歳の癌死亡の割合は1947年版からの数字を用いた．1947年0～4歳の癌死亡統計は84年版と47年版とでは異なる．

APPENDIX TABLE 2 OBSERVED NUMBERS OF CANCER CASES AND CANCER DEATHS AND OF ALL DEATHS EXCLUDING CANCER AND THE CORRESPONDING EXPECTED NUMBERS DERIVED FROM DATA FOR ALL JAPAN

付録表 2　癌発生例（及び癌死亡）の観察数と癌以外の全観察死亡数，及び日本全国のデータから得られた各々の期待数

DS86 uterus dose group in Gy		Aug. 1945–Sept. 1950				Oct. 1950–Dec. 1984			
		Age at risk 0		Age at risk 1–4		Age at risk 4–14		Age at risk 15–39	
		Cancer cases	All deaths except cancer	Cancer cases	All deaths except cancer	Cancer cases	All deaths except cancer	Cancer cases	All deaths except cancer
0	Obs.	0 (0)	34	0 (0)	28	0 (0)	8	5 (2)	14
	Exp.	? (0.02)	39.8	? (0.05)	29.4	? (0.16)	7.5	3.6 (2.6)	13.7
	O/E	-	0.85	-	0.95	-	1.06	1.39	1.02
	p	-	0.404	-	0.892	-	0.690	0.311	0.796
0.01–0.29	Obs.	0 (0)	43	0 (0)	20	0 (0)	5	7 (5)	12
	Exp.	? (0.02)	41.7	? (0.05)	31.2	? (0.18)	8.3	3.5 (2.5)	13.5
	O/E	-	1.03	-	0.64	-	0.60	2.02	0.89
	p	-	0.766	-	0.043	-	0.329	0.050	0.822
0.30–0.59	Obs.	0 (0)	9	0 (0)	6	1 (1)	2	2 (0)	1
	Exp.	? (0.00)	8.8	? (0.01)	6.3	? (0.03)	1.6	0.6 (0.5)	2.6
	O/E	-	1.03	-	0.95	-	1.21	3.11	0.38
	p	-	0.761	-	0.890	-	0.458	0.055	0.522
≥0.60	Obs.	0 (0)	18	0 (0)	3	1 (1)	3	2 (1)	7
	Exp.	? (0.00)	6.9	? (0.01)	5.1	? (0.03)	1.3	0.5 (0.4)	2.1
	O/E	-	2.60	-	0.59	-	2.30	3.88	3.32
	p	-	0.000		0.510		0.088	0.031	0.003

Aug. 1945–Sept. 1950 (age 0–4 at risk); birth record sample only
1945年8月～1950年9月（0～4歳）；出生記録のみ

Oct. 1950–Dec. 1984 (age 4–39 at risk); the subjects to be analyzed in the paper
1950年10月～1984年12月（4～39歳）；この報告書で解析される対象者

( ) cancer deaths 癌死亡数

p two-tailed p-value for the test H_0: O/E = 1 based on the poisson distribution with the mean of the expected value.

H_0 検定：O/E＝1 のための両側検定の p 値．期待値を平均値とする Poisson 分布に基づく．

APPENDIX TABLE 3 CANCER INCIDENCE (birth–1984), LEVEL OF PRENATAL EXPOSURE TO A-BOMB RADIATION, AND ESTIMATE OF RELATIVE RISK (RR) BY AN ADDITIVE MODEL ADJUSTING FOR CITY AND SEX : Birth record sample only

付録表 3 癌発生率(出生時～1984年), 胎児被曝線量, 及び都市, 性を訂正した相加的モデルによる相対危険度(RR)の推定値:
出生記録標本のみ

	DS86 uterus organ dose (Gy)			
	0	0.01–0.29	0.30–0.59	≥0.60
Observed				
Mean DS86 uterus dose (Gy)	0.000	0.085	0.403	1.426
Mean T65DR fetus dose (Gy)	0.000	0.056	0.309	1.095
No. at risk	510	542	112	99
Person-years	17202	18380	3690	2891
Cancer cases	3	6	2	2
Crude rate ($\times 10^{-5}$)	17.4	32.6	54.2	69.2
Estimated				
RR	1.00	1.19	1.91	3.98

Pearson χ^2 for goodness of fit: $\chi^2 = 6.59$ (df = 11, p = 0.831)

Test for H_0: all RRs = 1 (b = 0) $\chi^2 = 2.49$ (df = 1, p = 0.115)

Summary measures:

	Estimated RR (at 1 Gy)	Average excess risk (per 10^4 PYGy†)	Attributable risk (%)
Follow-up: birth–1984			
Estimated values	3.19	4.67	30.3
95% lower	0.74	–0.77	–5.5
95% upper	16.03	12.78	91.2

Refer to the Statistical methods section for the model equation.
モデルは統計的方法の項参照.

The estimated coefficient b(SE) is 2.19(2.223) for the mean DS86 uterus organ dose (Gy) by each strata.
各層別の DS86 子宮臓器線量(Gy)の平均値に対する推定係数 b(SE)は 2.19(2.223).

†person-year-gray
人年-gray

APPENDIX TABLE 4 LAST ADDRESS* AVAILABLE OF SUBJECTS WHO WERE ALIVE IN OCTOBER 1950
付録表4 1950年10月生存者についての知り得る最新の住所*

DS86 uterus dose group		Total		Prefecture in Japan: Hiroshima or Nagasaki		Prefecture in Japan: Other prefectures		Foreign** country		Unknown	
		Subjects	C	Subjects	C	Subjects	C	Subjects	C	Subject	C
0 Gy	Total	710(100.0)	5	604(85.1)	4	104(14.6)	1	2(0.3)	0	0(0.0)	0
	Male	316(100.0)	0	266(84.2)	0	49(15.5)	0	1(0.3)	0	0(0.0)	0
	Female	394(100.0)	5	338(85.8)	4	55(14.0)	1#1	1(0.3)	0	0(0.0)	0
0.01–0.29	Total	682(100.0)	7	560(82.1)	5	119(17.4)	2	3(0.4)	0	0(0.0)	0
	Male	323(100.0)	2	268(83.0)	2	55(17.0)	0	0(0.0)	0	0(0.0)	0
	Female	359(100.0)	5	292(81.3)	3	64(17.8)	2#2	3(0.8)	0	0(0.0)	0
≥0.30	Total	238(100.0)	6	189(79.4)	5	47(19.7)	1	2(0.8)	0	0(0.0)	0
	Male	126(100.0)	2	107(84.9)	2	19(15.1)	0	0(0.0)	0	0(0.0)	0
	Female	112(100.0)	4	82(73.2)	3	28(25.0)	1#3	2(1.8)	0	0(0.0)	0
NIC	Total	795(100.0)	1	516(65.0)	1	265(33.3)	0	13(1.6)	0	1(0.1)	0
	Male	398(100.0)	1	251(63.3)	1	137(34.4)	0	9(2.3)	0	1(0.3)	0
	Female	397(100.0)	0	265(66.8)	0	128(32.2)	0	4(1.0)	0	0(0.0)	0

( )% C Cancer cases 癌症例 NIC Not in city ATB 被爆時市内不在者

*The dates of last address available are different among individuals and are up to December 1986.
知り得る最新の住所の日時は対象者によって異なり1986年12月までである.

**The death in a foreign country can be confirmed if they have Japanese nationality.
外国での死亡はその本人が日本国籍であれば確認可能である.

#1This cancer case was identified only by death certificate.
この癌症例は死亡診断書のみで確認された.

#2The present address of one cancer case was Aichi Prefecture, but she was hospitalized in Nagasaki Prefecture. The other cancer case was identified only by death certificate.
1例の現住所は愛知県であったが, 本人が長崎県の病院に入院した. 他の1例の癌症例は死亡診断書のみで確認された.

#3This cancer case died of stomach cancer in Kyoto but she was in Hiroshima Prefecture when she got Wilms' tumor.
この癌症例は胃癌のため京都で死亡しているが, Wilms腫瘍を発病したのは広島にいたときであった.