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PATHOLOGICAL AND EPIDEMIOLOGIC STUDY OF GASTRIC CANCER IN ATOMIC BOMB SURVIVORS, HIROSHIMA AND NAGASAKI, 1950-77

原爆被爆者の胃癌の病理学的並びに疫学的研究，広島－長崎，1950－77年

HIROO MATSUURA, M.D. 松浦博夫
TSUTOMU YAMAMOTO, M.D. 山本 務
ICHIRO SEKINE, M.D. 関根一郎
YOSHIMICHI OCHI, Ph.D. 越智義道
MASANORI OTAKE, Ph.D. 大竹正徳

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RADIATION EFFECTS RESEARCH FOUNDATION
財団法人 放射線影響研究所

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HIROO MATSUURA, M.D. (松浦博夫)[1,4]; TSUTOMU YAMAMOTO, M.D. (山本 務)[1]; ICHIRO SEKINE, M.D. (関根一郎)[2]; YOSHIMICHI OCHI, Ph.D. (越智義道)[3]; MASANORI OTAKE, Ph.D. (大竹正徳)[3]

RERF Departments of Pathology[1] and Epidemiology & Statistics[3]; Department of Pathology, Atomic Disease Institute, Nagasaki University[2]; and Department of Pathology, Hiroshima Citizens' Hospital[4]

放影研病理部[1]，疫学統計部[3]；長崎大学医学部原爆後障害医療研究施設病理部門[2]；広島市民病院病理部[4]

SUMMARY

A study to elucidate the effects of atomic bomb radiation on the incidence of stomach cancer was conducted on 79,856 A-bomb survivors whose exposure dose estimates are available. Pathological and epidemiologic reviews were conducted of 2,155 cases which during the period 1950-77 had been diagnosed, clinically or histologically, as having stomach cancer. The relationship of dose to stomach cancer incidence was assessed using total kerma dose. As a result, the following findings were obtained.

Evaluation of the dose effects (adjusted for sex and age) in each dose group showed a significant increase in the risk of stomach cancer only in the heavily exposed (200+rad) group. In the 100-199 rad group, a significant excess risk was found only in the group aged 10-19 at the time of the bomb (ATB). Especially in the case of the 200+rad group, the increased risk in stomach cancer was remarkable in the under-30-ATB age-group.

It is emphasized that the dose-response relationship for the incidence of stomach cancer, followed for 27 years, is not quadratic, but linear. Based on this finding, the estimated risk of A-bomb radiation-induced stomach cancer for both cities combined is 1.24 (0.92 in Hiroshima and 1.68 in Nagasaki) per million

要 約

胃癌発生率の原爆放射線被曝による影響を調査する目的で，被曝線量の計算されている79,856人の原爆被爆者を対象として，1950—77年の期間中に臨床的あるいは組織学的に胃癌と診断された2,155例の，病理学的及び疫学的検討を行った．線量と胃癌発生率との関係は合計kerma線量を用いて評価した．以下のような所見が得られた．

性・年齢の影響を訂正した各線量群において，胃癌リスクの有意な増加が認められたのは200 rad以上の高線量群のみであった．100—199 rad群で有意なリスクの増加がみられたのは原爆時年齢10—19歳群にすぎない．特に，200+ rad群での胃癌リスクの増加は原爆時年齢30歳未満群に顕著であった．

27年間にみられた胃癌発生率による線量反応関係は2次曲線形でなく，線形であると強調できる．この結果，原爆放射線誘発胃癌の推定リスクは，両市を合せて，100万人年rad当たり1.24（広島

person-years per rad (PYR). By sex, the risk for both cities combined is 1.46 per million PYR for males and 1.12 per million PYR for females, showing no statistical difference. However, the risks for the younger age-groups (10-19 and 20-29 ATB) adjusted for city and sex are 1.51 and 1.71 per million PYR, respectively, which are higher than the mean risk.

Stomach cancer develops at highest frequency in the lower part and on the lesser curvature of the stomach, and there are no differences in this respect between the exposed and control groups.

Histologically, the differentiated type of adenocarcinoma is frequently observed in the control and low dose groups, whereas the poorly differentiated type is seen in the high dose group.

Comparison of the differentiated and poorly differentiated types of adenocarcinoma with respect to degree of intestinal epithelial metaplasia of the gastric mucosa, showed it to be stronger in the differentiated type. There is a significant difference between these histological types in the degree of intestinal epithelial metaplasia by exposure dose.

INTRODUCTION

It has been confirmed clinically as well as by animal experiments that radiation exposure induces tumors, especially malignant tumors. Increased incidence of leukemia[1-3] and tumors of the lung,[4,5] breast,[6] thyroid,[7] and salivary gland[8,9] has been reported among the A-bomb survivors of Hiroshima and Nagasaki.

Among the malignant tumors developing in the Japanese, stomach cancer is the one with the highest incidence and mortality rate. It is of great interest to know what effect A-bomb exposure has on the incidence of stomach cancer. The issue concerning stomach cancer among A-bomb survivors has been studied in the ABCC/RERF Life Span Study (LSS) and Pathological studies. The results of studies conducted on the LSS, using information from death certificates, have indicated high stomach cancer mortality among heavily exposed survivors.[10-12] However, due to the low autopsy rate, the study using autopsy materials, has not demonstrated any statistically definite increase in stomach cancer incidence.[13-16]

0.92, 長崎1.68)である．性別では両市合せて，100万人年当たり男1.46と女1.12で統計的に差異はない．しかし，原爆時若年齢群(10－19及び20－29歳)では，両市合せて100万人年rad当たりそれぞれ1.51と1.71であり，平均リスクと比べて高かった．

胃癌発生部位は胃下部及び小彎側が最も頻度が高く，被爆群と対照群との間に差異は認められない．

組織型では，分化型腺癌は対照群及び低線量群に，低分化型腺癌は高線量群に高い頻度でみられる．

胃粘膜の腸上皮化生の程度を分化型腺癌と低分化型腺癌で比較すると，分化型腺癌により強く認められる．各々の組織型についての被曝線量別の腸上皮化生の程度に有意な差があった．

緒　言

放射線被曝により，腫瘍，殊に悪性腫瘍が発生することは動物実験を始め，臨床的にも確認されている．広島・長崎の原爆被爆者においても，白血病，[1-3] 肺癌，[4,5] 乳癌，[6] 甲状腺癌，[7] 唾液腺腫瘍[8,9] の腫瘍の発生率の増加が報告されている．

日本人にみられる悪性腫瘍中，胃癌は最も発生率及び死亡率の高い腫瘍である．この胃癌発生に対して原爆被爆がいかなる影響を及ぼしているかを知ることは極めて興味深い．この原爆被爆者の胃癌問題に関しては，ABCC・放影研の寿命調査(LSS)及び病理学的調査の両面から検索が行われている．これらの研究の結果，死亡診断書の情報を使用する寿命調査では既に高線量を受けた被爆者に胃癌死亡率が高いことが指摘されている．[10-12] しかし剖検材料を用いての調査結果では，低い剖検率の関係から，統計的に胃癌発生率の明確な増加は認められていない．[13-16]

Remarkable increase in the rate of early detection of stomach cancer due to rapid progress in stomach diagnostics and the extensive use of mass stomach screening can be mentioned as changes occurring in stomach cancer clinics over the past three decades.[17] Among cases undergoing surgery, the frequency of stomach cancer detected at an early stage has increased to more than 30% of all cases since 1970, and the surgical treatment results have improved so that the 5-year survival rate now exceeds 90%. In order to review stomach cancer among A-bomb survivors in greater detail, it seemed appropriate, in view of such changes in the clinical situation regarding stomach cancer, to pursue the association between stomach cancer and A-bomb exposure using stomach cancer cases first detected at surgery, cases detected by biopsy and diagnosed histologically, clinically diagnosed cases, and cases first identified on death certificate or at autopsy.

MATERIALS AND METHODS

The stomach cancer cases used in the present study are those pertaining to the LSS extended sample[18] during 1950-77 in Hiroshima and Nagasaki and diagnosed clinically or histopathologically. In the LSS extended sample, composed of 108,912 subjects, 152 cases whose family register (Koseki) cannot be identified, and all stomach cnacer cases with onset date prior to October 1950 were excluded from this study. Also excluded from the analysis were 26,518 subjects who were not in the city ATB, and 2,386 subjects whose dose estimates were not available. Therefore, this analysis relates to 79,856 A-bomb survivors (60,482 in Hiroshima and 19,374 in Nagasaki) among whom 2,155 (1,720 in Hiroshima and 435 in Nagasaki) were identified as stomach cancer cases during the 27 years from 1 October 1950 to 31 December 1977. Of these cases 1,148 (53.3%) were histopathologically studied. However, it is emphasized that the different sources obtained from autopsy (385 cases), surgical or biopsy (763 cases), and death certificate (1,007 cases) did not quite change systematically with increasing dose by city.

In collecting stomach cancer cases, reference was made to material from the Tumor and Tissue Registries of the Hiroshima and Nagasaki City and Prefectural Medical Associations, and the

胃癌の臨床面における過去30年間の変化として，胃診断学の急速な進歩と胃集団検診の幅広い展開による早期胃癌診断率の顕著な増加を挙げることができる.[17] この早期胃癌の胃癌手術例中に占める頻度は1970年以降では全体の30%以上となり，その外科治療成績も5年生存率が90%を越えるに至っている．原爆被爆者における胃癌をより一層詳細に検討する目的で，このような胃癌の臨床的な状況を考え，外科手術において初めて探知された胃癌症例，生検により探知され組織学的に診断された症例，臨床的に診断された症例，及び死亡診断書又は剖検において初めて確認された症例を使用することにより，胃癌と原爆被爆との関連性を追求することが必要と考えられる．

材料及び方法

今回の研究に利用する胃癌症例は広島・長崎で1950—77年の間に寿命調査拡大集団[18]に属し，臨床的あるいは病理組織学的に診断されたものである．108,912人から成る寿命調査拡大固定集団のうち，戸籍不明の152人と1950年10月以前に発生した胃癌症例はこの研究から除いた．更に，原爆時市内にいなかった26,518人及び個々の線量計算ができなかった2,386人は今回の解析から除外した．したがって，本解析は原爆被爆生存者79,856人（広島60,482，長崎19,374）を対象とし，このうち，1950年10月1日から1977年12月末までの27年間に2,155例（広島1,720，長崎435）が胃癌と確認された．これらの症例中53.3%に当たる1,148例は病理組織学的に検索された症例である．しかしながら，剖検（385例），外科手術又は生検（763例）及び死亡診断書（1,007例）から得た各種資料は都市別にみて線量の増加に伴い全く系統的に変化していないという事実を強調したい．

胃癌症例の収集に当たっては広島・長崎の県・市医師会の腫瘍登録資料，組織登録資料並びに放影研の寿命調査資料を参考にした．また，腫瘍登録開始

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RERF LSS. Further, efforts were made to collect cases which occurred prior to initiation of the Tumor Registry by checking existing clinical, surgical pathology, and autopsy data at Hiroshima and Nagasaki Universities and at hospitals located in the two cities. The clinical, surgical pathology, and autopsy records of each of the 2,155 cases identified were checked as extensive as possible in order to determine the time clinical symptoms became manifest, date and method of clinical diagnosis, date of histopathological diagnosis, and date of death.

以前の症例については両市の大学及び市内の病院に残存する臨床資料，外科病理資料及び剖検資料を調査して該当症例の収集に努めた．これらの確認された2,155人の各症例については臨床，外科病理，あるいは剖検の記録を可能な範囲で調べ，臨床症状の発現時期，臨床診断の日時及びその方法，病理組織学的な診断の日時並びに，死亡日時の把握に努めた．

The exposure dose estimates used here are the tentative 1965 radiation dose estimates as revised in accordance with the recent relocation of the Nagasaki epicenter and a standardized rounding off procedure for the calculation of individual doses (T65DR).[19,20] A review of the quantity and quality of radiation received by A-bomb survivors is continuing,[21] and reassessment of the dose estimates will be made in the near future. Accordingly, in order to avoid biases which might occur from using erroneous estimates, based on T65DR, of neutrons and gamma rays separately, the relationship between stomach cancer incidence and radiation dose was reviewed using the estimated T65DR (total) received by each individual. It might be considered natural to evaluate the relationship of radiation dose to stomach cancer incidence using organ dose estimates, but since so many uncertain factors are involved in the estimates of neutron and gamma ray components of T65DR, it was decided to employ total kerma dose.

今回用いた推定被曝線量は最近の長崎の爆央の移動及び個人線量計算の標準的四捨五入手順によって改訂された1965年暫定推定線量である(T65DR)．[19,20] 原爆被爆者が受けた放射線の量及び質に関する検討は依然として続けられており，[21] 近い将来，線量推定値が再評価されることを付記する．したがって，T65DRに基づいて中性子線及びガンマ線を別々に間違った線量推定値を用いることから起こり得る偏りを避けるために，個々人が受けたT65DRの推定線量値(合計)を用いて，胃癌発生と線量との関係を検討する．胃癌発生率と被曝線量関係については臓器線量推定値による評価が当然に考慮されるべきかもしれないが，T65DRの中性子線及びガンマ線推定に対する多くの不安材料が内在するため，T65DRの合計kerma線量を用いた．

Statistical Methods

It is assumed that x_{ijk}, the observed number of stomach cancer cases indexed by sex (i=1 or 2), age (j=1, . . . , 6), and dose (k=1, . . . , 5) groups, follows the Poisson distribution with parameter $\lambda_{ijk}=R_{ijk}P_{ijk}$. Here R_{ijk} indicates the person-years at risk in the (i,j,k)th category.

統計的方法

観察胃癌症例数 x_{ijk} は，パラメータ $\lambda_{ijk}= R_{ijk}P_{ijk}$ をもってポアソン分布に従うと仮定する．ただし，性(i =1又は2)，年齢(j =1, …, 6)及び線量(k=1, …, 5)区分を表し，R_{ijk}は(i, j, k)番目の観察人年数を示す．

Two simple regression models were used in the analysis of stomach cancer incidence within city:

都市内の胃癌発生率に関する解析には二つの簡単な回帰モデルを用いる．すなわち，

$$\text{Model I: } P_{ijk} = \alpha_{ij} + \beta_1 D_{ijk}$$
$$\text{Model II: } P_{ijk} = \alpha_{ij} + \beta_1 D_{ijk} + \beta_2 D_{ijk}^2$$

where α_{ij} is the effect of sex and ATB age-groups (0-9, 10-19, 20-29, 30-39, 40-49, and 50+) at the control group level, D_{ijk} is the average total

ただしα_{ij}は対照群レベルの性及び原爆時年齢群(0－9，10－19，20－29，30－39，40－49，及び

kerma dose of the (i,j,k)th group, D^2_{ijk} the squared average of total kerma dose, with index k ranging over the five dose groups (0, 1-49, 50-99, 100-199, and 200+rad), and where β_1 and β_2 are constants expressing dose-response characteristics common to sex or age categories. Each test statistic on two dose-response estimates of parameters under the hypothesis $H_o: \beta_1 = 0$ or $\beta_2 = 0$ are $\chi^2 = \hat{\beta}_1^2/V(\hat{\beta}_1)$ or $\hat{\beta}_2^2/V(\hat{\beta}_2)$, which has approximately a χ^2 distribution with one degree of freedom, where $V(\hat{\beta}_1)$ or $V(\hat{\beta}_2)$ denotes the asymptotic variance of the maximum likelihood (ML) estimate $\hat{\beta}_1$ or $\hat{\beta}_2$ of β_1 or β_2. A test statistic for the null hypothesis ($H_o: \beta_1 - \beta_2 = 0$) of no difference in risk between two groups, say, males and females, is $\chi^2 = (\hat{\beta}_1 - \hat{\beta}_2)^2/V(\hat{\beta}_1 - \hat{\beta}_2)$ which has approximately a χ^2 distribution with one degree of freedom, where $V(\hat{\beta}_1 - \hat{\beta}_2)$ denotes the asymptotic variance of difference in two groups.

ML estimates of the parameters, based on the Poisson distribution, were obtained by the Newton-Raphson iteration method. Furthermore, a review was made of the relative risk for each dose group within strata defined by city, sex, and age, and at the same time, a risk analysis,[22,23] adjusted for the effect of city, sex, or age, was conducted.

RESULTS

Stomach Cancer Incidence

Table 1 shows by age, the annual crude incidence and relative risk of stomach cancer during 1950-77 for Hiroshima and Nagasaki combined. Stomach cancer incidence per 100,000 persons observed shows a tendency by age for cancer frequency to increase with increase of dose and markedly so in the highest dose group. The average relative risk adjusted for city, sex, and age-group was significantly different (P<.001) only in the 200+rad group, it being 1.6 times higher than the 0 rad group. When the risk was similarly observed by city (Figure 1) and sex (Figure 2), only the 200+rad group revealed a highly significant excess risk, especially in Hiroshima. There is also evidence that the excess risk for the 200+rad group is concentrated in the <30 ATB age-groups.

Dose-response Relationship

The average T65DR for each dose group by city is given in a footnote to Table 1. Table 2

50+）の効果を示し，D_{ijk} は（i，j，k）区分の合計 kerma 平均線量，D^2_{ijk} は合計 kerma の２乗平均線量であり，添字 k は五つの線量群（0，１－49，50－99，100－199及び200＋ rad ）を示し，β_1 並びに β_2 は性又は年齢区分に共通な線量反応特性を表す定数である．パラメーターの二つの線量反応推定に関する仮定 $H_o: \beta_1 = 0$ 又は $\beta_2 = 0$ のもとで各検定統計量は $\chi^2 = \hat{\beta}_1^2/V(\hat{\beta}_1)$ 又は $\hat{\beta}_2^2/V(\hat{\beta}_2)$ で近似的に自由度１の χ^2 分布に従う．ただし $V(\hat{\beta}_1)$ 又は $V(\hat{\beta}_2)$ は β_1 又は β_2 の最尤推定値 $\hat{\beta}_1$ 又は $\hat{\beta}_2$ の漸近分散を示す．二つの群，例えば，男性群と女性群の間にリスクの差異はないとする帰無仮説（$H_o: \beta_1 - \beta_2 = 0$）の検定統計量は，$\chi^2 = (\hat{\beta}_1 - \hat{\beta}_2)^2/V(\hat{\beta}_1 - \hat{\beta}_2)$ であり，近似的に自由度１の χ^2 分布に従う．ただし，$V(\hat{\beta}_1 - \hat{\beta}_2)$ は両群の差の漸近分散を示す．

ポアソン分布に基づいたパラメーターの最尤推定値は，Newton-Raphson 反復法によって求められる．更に都市，性，年齢に区分された層内の各線量群に対する相対的リスクについて検討すると同時に，都市，性，年齢の影響に対して訂正した一つのリスク分析[22,23]を実施した．

結　果

胃癌発生率

表１は広島・長崎両市合計による1950－77年の間の胃癌の年間粗発生率及び相対的リスクを年齢別に示している．10万人当たりの胃癌発生率を年齢別に観察すると線量の増加とともにその発生頻度の増加傾向が認められ，その傾向は高線量被曝群において顕著である．都市，性，年齢群により訂正した平均相対リスクは，200＋ rad 群においてのみ有意差を示し（P＜.001），0 rad 群の1.6倍であった．リスクを同様に都市別（図１）及び性別（図２）に観察すると，200＋ rad 群のみが，特に広島において有意に高い過剰リスクを示した．また，200＋ rad 群の過剰リスクは原爆時年齢が30歳未満のグループに集中していることも明らかである．

線量反応関係

各線量群の都市別の平均 T65DR 線量は表１の脚注に示すとおりである．都市及び性別の年齢効果を

TABLE 1 CRUDE ANNUAL INCIDENCE RATES AND RELATIVE RISKS OF STOMACH CANCER AMONG HIROSHIMA AND ANGASAKI A-BOMB SURVIVORS BY AGE ATB AND DOSE, 1950-77
表1　広島及び長崎原爆被爆者における原爆時年齢並びに線量別の胃癌の年間粗発生率及び相対リスク，1950－77年

Age ATB		Total	T65DR in rad				
			0	1-49	50-99	100-199	200+
0-9	Stomach cancer	32	14	12	1	1	4
	Annual incidence ($\times 10^5$)	7.8	8.6	5.8	5.2	9.4	36.4
	Relative risk	-	1.0	.7	.6	1.1	4.2*
	Person-years ($\times 10^3$)	410.7	162.5	207.0	19.5	10.7	11.0
10-19	Stomach cancer	112	30	47	9	11	15
	Annual incidence ($\times 10^5$)	24.8	17.5	22.3	38.3	45.0	67.1
	Relative risk	-	1.0	1.3	2.2*	2.6**	3.8***
	Person-years ($\times 10^3$)	452.4	171.3	210.8	23.5	24.4	22.4
20-29	Stomach cancer	147	50	65	11	8	13
	Annual incidence ($\times 10^5$)	54.2	47.5	51.6	70.2	66.5	104.7
	Relative risk	-	1.0	1.1	1.5	1.4	2.2**
	Person-years ($\times 10^3$)	271.3	105.2	126.0	15.7	12.0	12.4
30-39	Stomach cancer	417	176	183	19	17	22
	Annual incidence ($\times 10^5$)	143.9	149.8	134.7	120.0	159.2	222.9
	Relative risk	-	1.0	.9	.8	1.0	1.4
	Person-years ($\times 10^3$)	289.8	117.5	135.9	15.8	10.7	9.9
40-49	Stomach cancer	742	280	358	36	33	35
	Annual incidence ($\times 10^5$)	266.7	250.0	273.9	235.2	298.3	384.2
	Relative risk	-	1.0	1.0	.9	1.1	1.4*
	Person-years ($\times 10^3$)	279.2	112.0	120.7	15.3	11.1	9.1
50+	Stomach cancer	705	282	345	37	22	19
	Annual incidence ($\times 10^5$)	364.9	352.8	373.9	348.3	380.8	410.4
	Relative risk	-	1.0	1.1	1.0	1.0	1.1
	Person-years ($\times 10^3$)	193.2	79.9	92.3	10.6	5.8	4.6
Total	Stomach cancer	2155	832	1010	113	92	108
	Annual incidence ($\times 10^5$)	113.7	111.2	111.9	112.5	123.2	155.6
	Relative risk	-	1.0	1.0	1.0	1.1	1.6***
	Person-years ($\times 10^3$)	1895.6	748.3	902.7	100.5	74.7	69.4

Relative risk values are adjusted for city and sex and also for age in the totals.
相対リスクは，都市及び性，全体については年齢に対しても補正を加えている．
NS (P>.10), Sug (P<.10), * (P<.05), ** (P<.01), *** (P<.001).
Mean dose by dose group are 0, 10.4, 70.6, 141.9, 358.6 in Hiroshima, and 0, 10.8, 70.6, 143.0, 347.1 in Nagasaki.
線量群別の平均線量は広島において0，10.4，70.6，141.9，358.6，長崎において0，10.8，70.6，143.0，347.1である．

summarizes the dose-response coefficients of regression analysis using Model I and Model II, taking into consideration the effect of age by city and sex. Using the linear-quadratic (L-Q) dose-response represented in Model II shows no significant or definite contribution to stomach cancer incidence, but only the linear response effect on induction of stomach cancer assumed in Model I gives a highly or definitely significant difference (P<.01). In Hiroshima, the dose-response relationship suggests a significant

考慮した上でのモデルⅠとモデルⅡの回帰分析の線量反応係数は表2に要約する．モデルⅡによる線形－2次曲線形（L-Q）線量反応を用いた場合は，胃癌発生への有意なあるいは明確な寄与は認めないが，モデルⅠで仮定した胃癌誘発への線形反応効果のみが，高く明確な有意差（P＜.01）を示した．広島においては，線量反応関係は非線形の有意な可能性を示唆

FIGURE 1 RELATIVE RISK OF STOMACH CANCER INCIDENCE BY CITY ADJUSTED FOR SEX AND AGE, 1950-77

図1　性及び年齢に対して補正を加えた都市別胃癌発生の相対リスク，1950－77年

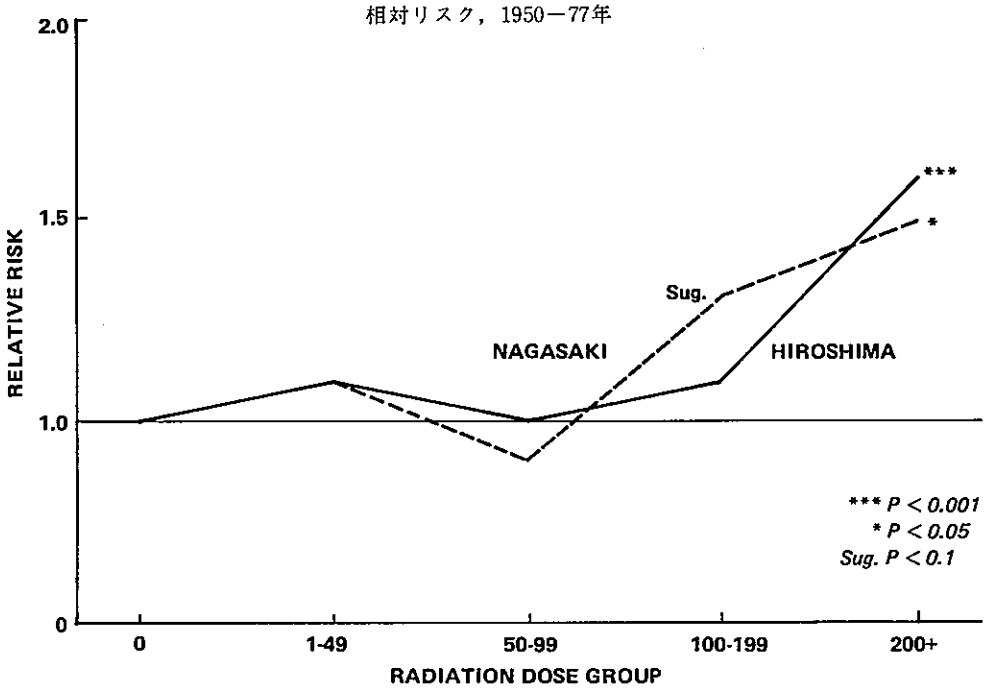

FIGURE 2 RELATIVE RISK OF STOMACH CANCER INCIDENCE BY SEX ADJUSTED FOR CITY AND AGE, 1950-77

図2　都市及び年齢に対して補正を加えた性別胃癌発生の相対リスク，1950－77年

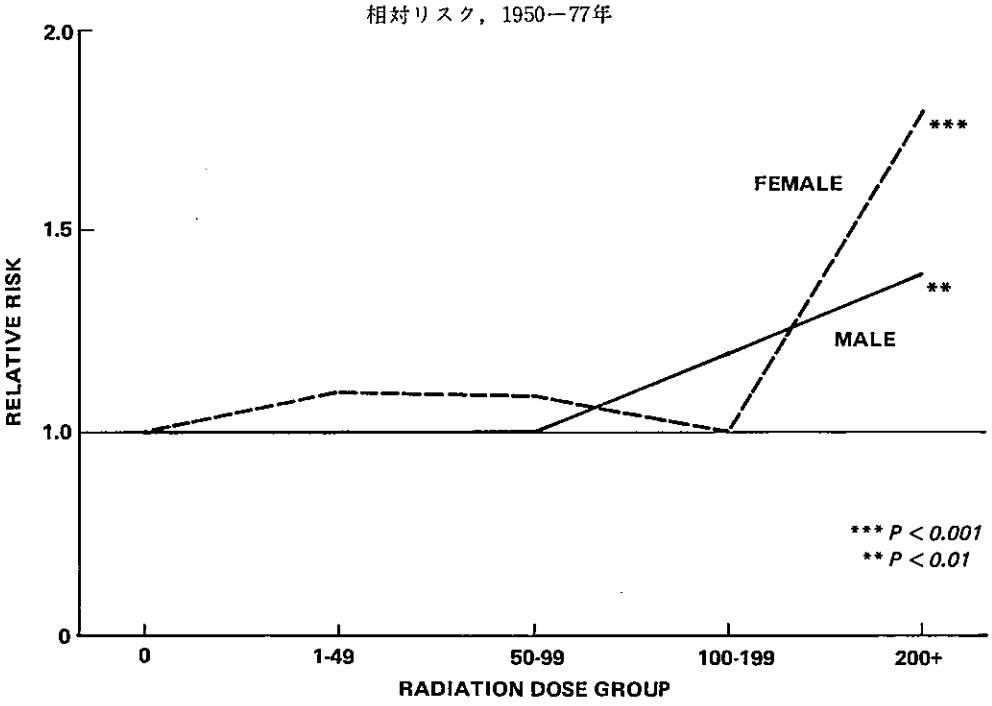

TABLE 2 DOSE-RESPONSE COEFFICIENTS ESTIMATED BY CITY, SEX, AND MODEL
表2　都市，性及びモデル別に推定した線量反応係数

Items	Total		Male		Female	
	Model I	Model II	Model I	Model II	Model I	Model II
			Hiroshima & Nagasaki			
Linear : $\beta_1 \times 10^6$	1.24***	0.84NS	1.46**	1.03NS	1.12**	0.61NS
(SD)	(0.28)	(0.72)	(0.50)	(1.35)	(0.36)	(0.96)
Quadratic : $\beta_2 \times 10^6$		1.23NS		1.27NS		1.58NS
(SD)		(2.09)		(3.69)		(2.77)
			Hiroshima			
Linear : $\beta_1 \times 10^6$	0.92**	−0.65NS	1.25*	−2.41NS	0.72Sug	−0.14NS
(SD)	(0.36)	(0.77)	(0.64)	(1.64)	(0.42)	(0.94)
Quadratic : $\beta_2 \times 10^6$		4.83*		9.94*		2.73NS
(SD)		(2.34)		(4.48)		(2.97)
			Nagasaki			
Linear : $\beta_1 \times 10^6$	1.68**	3.07*	1.72*	4.64Sug	1.66**	2.12NS
(SD)	(9.47)	(1.35)	(0.77)	(2.37)	(0.59)	(1.66)
Quadratic : $\beta_2 \times 10^6$		−4.56NS		−8.86NS		−1.43NS
(SD)		(3.76)		(6.39)		(4.74)

The estimates of the nuisance parameters except for the linear and linear-quadratic responses are not included because they are of no importance in this study. The goodness of fit is due to the Pearson's χ^2 statistic with the corresponding degrees of freedom. Note that the two groups between 0-9 and 10-19 age ATB in Nagasaki males were combined. It is noted that all models applied here showed a good fit. Significance levels are as in Table 1.

線形及び線形-2次曲線反応を除くニューサンス・パラメターの推定値は，本研究においては重要性に欠けるためこの表には含めなかった．適合度検定は，対応する自由度の Pearson の χ^2 統計量による．長崎における男性群のうち原爆時年齢0－9歳群及び10－19歳群の2群が一つにまとめられていることに注意する．ここで適用されたすべてのモデルへよい適合度を示すことは注目に値する．有意水準は表1に示すとおりである．

possibility of nonlinearity. But this significance is only for males. On the other hand, in Nagasaki a linear response model seems to give the best representation for both males and females. Therefore, from the standpoint of dose-response evaluation overall, it appears to be reasonable to conclude that radiation-induced stomach cancer response is adequately described by a linear function. Thus the average risk of stomach cancer by sex is 1.46 per million PYR for males (1.25 in Hiroshima and 1.72 in Nagasaki), and 1.12 per million PYR for females (0.72 in Hiroshima and 1.66 in Nagasaki). The difference in risk between males and females by city is not statistically significant. The influence of age is very strong. Since there is a possibility that there are differences between younger and more advanced age-groups, in their respective sensitivities in dose-response effects, it may be useful

する．しかしこの有意性は男性群においてのみ認められるにすぎない．一方，長崎においては，線形反応モデルが男女両群ともに最も適格に表現すると考えられる．したがって，線量反応評価全般からみると，放射線誘発胃癌反応は線形関数により適格に説明されると結論付けることが妥当であると考える．このように，胃癌の平均リスクを性別にみると，男性は100万人年当たり1.46（広島1.25，長崎1.72）であり，女性は100万人年当たり1.12（広島 0.72，長崎1.66）である．これらの都市別のリスクの男女差は統計的に有意でない．年齢の影響は極めて強い．若年齢群と高年齢群とでは線量反応効果における各々の感受性が異なる可能性もあるので，性，年齢別に層化して

TABLE 3 MEAN AGE AT ONSET OF STOMACH CANCER BY AGE ATB AND DOSE
表3 原爆時年齢別，線量別胃癌発病時平均年齢

Age ATB	Total	T65DR in rad				
		0	1-49	50-99	100-199	200+
0-9	31.3	30.9	32.3	37.0	31.0	28.3
	(32)	(14)	(12)	(1)	(1)	(4)
10-19	39.1	38.7	38.4	40.2	40.5	40.5
	(112)	(30)	(47)	(9)	(11)	(15)
20-29	48.6	49.1	48.7	47.0	47.6	48.4
	(147)	(50)	(65)	(11)	(8)	(13)
30-39	58.3	58.6	58.0	57.4	60.9	56.8
	(417)	(176)	(183)	(19)	(17)	(22)
40-49	65.9	66.5	65.5	65.5	64.3	65.9
	(742)	(280)	(358)	(36)	(33)	(35)
50+	75.0	74.4	75.5	74.2	75.0	76.3
	(705)	(282)	(345)	(37)	(22)	(19)
Total	64.3	64.8	64.8	62.9	61.6	58.8
	(2155)	(832)	(1010)	(113)	(92)	(108)

Number of stomach cancer cases in each category in parentheses.
括弧内の数字は各区分における胃癌症例数を表す.

to examine different effects using a linear dose-response relationship, stratified by sex and age. Review of the dose-response relationship for stomach cancer by ATB age-group is conducted here with respect to Model I only. The results of regression analysis show significant radiation effects greater than zero only in the <30 ATB age-groups adjusted for both city and sex, especially in the 10-19 and 20-29 ATB age-groups.

線形線量反応関係を用いて異なる効果を調べることは有効であるかもしれない．原爆時年齢群別の胃癌の線量反応関係は今回はモデルIについてのみ検討する．この回帰分析による結果からみると，都市及び性を補正した原爆時年齢30歳未満の年齢群，特に，10—19歳群と20—29歳群のみが0よりも有意に大きい放射線の影響を認める．

Average Age at Onset of Stomach Cancer

Table 3 shows average age at onset of stomach cancer by age ATB and dose group. Little difference with increased dose can be observed in average age at onset of stomach cancer. Moreover, for each of the ATB age-groups, comparison of the average age at onset of stomach cancer by dose shows no significant difference with increased dose. This is similarly observed to hold for both sexes by city.

胃癌発病時平均年齢

表3は胃癌発病時平均年齢について原爆時年齢別，線量群別に示している．線量の増加に伴う胃癌発病時年齢の差はほとんど認められない．更に，各原爆時年齢群ごとに，線量別の胃癌発病平均年齢を比較した場合，線量の増加に伴う有意差は認められない．これは都市ごとに男女別に観察しても同様である．

Average Period Until Onset of Cancer

Average periods from A-bomb exposure to development of stomach cancer are shown in Table 4 by age and dose. When the average

発病までの平均期間

原爆被爆時から胃癌発病までの平均期間を年齢別及び線量別に表4に示す．胃癌発病までの平均期間を，全年齢群平均と比較し線量群別に調べると，

TABLE 4 AVERAGE TIME PERIOD FROM A-BOMB EXPOSURE TO ONSET OF STOMACH CANCER BY AGE ATB AND DOSE
表4　原爆時年齢別，線量別の原爆被爆時から胃癌発病までの平均期間

Age ATB	Total	T65DR in rad				
		0	1-49	50-99	100-199	200+
0-9	25.1	25.1	26.8	27.0	23.0	19.8
10-19	23.4	22.6	23.0	25.2	24.6	23.9
20-29	23.0	23.8	22.8	21.5	21.6	23.0
30-39	22.4	22.5	22.3	21.0	24.6	21.8
40-49	20.6	21.1	20.4	19.7	19.4	20.4
50+	17.8	17.7	18.0	17.4	17.5	19.6
Total	20.4	20.5	20.2	19.9	20.7	21.3

The number of stomach cancer cases in each category is given in parentheses in Table 3.
各区分における胃癌症例数は表3の括弧内に示すとおりである．

periods until onset of stomach cancer are compared with all age-group averages and examined by dose group, the 50+ ATB age-group seems to be the only one to consistently fall short of the all age-group average for all dose groups. This appears to be a competing risk phenomenon, being due to reductions in the 50+ ATB age-group due to deaths resulting from other causes. However, comparing these average time periods by dose groups, there is no suggestion of a tendency for the average period to decrease with increase of dose. The average period in the 0-9 ATB age-group appears to decrease, it being 20 years in the 200+ rad group as compared with 25 years in the control (0 rad) group. Due to the paucity of cases, however, this result is not definite. The results of follow-up studies on the average periods compared here will naturally show large-scale changes as time passes, just as follow-up studies will show that the average age at onset of stomach cancer changes. Assuming that in future research an increase of stomach cancer cases will be observed in the youngest age-group that were exposed (in which few cases of 200+rad were detected during the present study period), not only the average age at the time of onset of stomach cancer, but the average period until onset for this dose group, as well as other groups, will definitely increase.

すべての線量群に対して全年齢群平均を一様に下回るのは原爆時年齢50＋歳群のみであると考えられる．これは競合リスク現象であり，原爆時年齢50＋歳群においてほかの死因のため短縮が起きたためと考えられる．しかし，線量群別の平均期間を比べると，線量の増加に伴う平均期間の短縮傾向は全く示唆されない．原爆時年齢0－9歳群の平均期間は200＋rad群で20年で，対照（0 rad）群の25年に比べ短縮しているようである．しかし，例数も少なくこの結果は明確ではない．ここで比べた平均期間に関する追跡調査の結果は，時が経つにつれ当然大きく変化するであろうが，これは胃癌発病平均年齢が追跡調査が進むにつれ変化していくのと同様である．被爆した若年齢群（今回の調査期間で200＋rad が探知された症例はほとんど含んでいない）に今後の研究において胃癌症例の増加が観察されるとすれば，ほかの群とともにこの群の胃癌発病時平均年齢並びに発病までの平均期間も必然的に増加するであろう．

Pathological Observations

Of the present stomach cancer study material, 1,148 cases (53.3%) were diagnosed as having stomach cancer based on histopathological

病理学的観察．

今回の胃癌研究材料のうち，1,148症例（53.3%）が病理組織学的な検索から胃癌と診断されている．これらの症例は大きく二つの群，すなわち，胃癌原発

review. These cases can be classified roughly into two groups, namely, those in whom the primary focus was detected and those in whom only the infiltrative, metastatic, or local recurrent focus could be detected. Of these, the former, primary focus cases, accounts for 997 cases (86.8%). The total of 1,148 stomach cancer cases include 385 autopsy cases, 576 gastrectomy cases, 36 biopsy cases, and 151 cases in whom the primary focus could not be detected and only the infiltrative metastatic focus or local recurrent focus could be detected. Furthermore, these cases include 64 cases (6 autopsy cases, 13 gastrectomy cases, 42 biopsy cases, and 3 cases with only metastatic infiltrative focus) on whom histopathological specimens were not available for microscopic examination, and reference was made only to pathological diagnosis reports. Even among the primary focus cases detected, pathological observations of all items were not possible on some cases. So, the number of pathological observations varies according to the specimen available in each case. These cases were excluded from analysis as unexamined cases.

Location of Stomach Cancer. Tables 5 and 6 show the major locations of tumors in the stomach by four exposure dose groups. In Table 5, the locations are classified into three sites, i.e., upper part (C), middle part (M), and lower part (A), and in Table 6 into six sites, namely, lesser curvature (Min), greater curvature (Maj), anterior stomach wall (Ant), posterior stomach wall (Post), circumferential area (Circ), and other.

First, observation of the frequency of cancers by site show the highest frequency in each dose group to be in the lower part of the stomach, followed by the middle part, while the frequency of the upper part is lowest for all dose groups. By exposure dose, the frequencies for the 100-199 rad group and the 200+rad group are almost identical. On the other hand, when classifying by six sites, the frequency of cancer in the lesser curvature of the stomach shows up as highest, while that of all other sites is low. However, these particular findings are not related to radiation dose.

Histological Type. On the basis of the General Rules for Gastric Cancer Studies in Surgery and Pathology, compiled by the Japanese Research Society for Gastric Cancer,[24] the 997 cases in

病巣を検索し得た症例群と，胃癌の浸潤性病巣，転移性病巣，あるいは局所再発病巣のみを検索した病例群に分けることができる．このうち，前者の胃癌原発病巣を検索した症例が997例（86.8%）である．これらの1,148例の胃癌症例の内訳は剖検例385例，胃切除例576例，胃生検例36例，胃癌原発病巣を検索し得ず，浸潤転移巣あるいは局所再発病巣のみを検索した症例151例である．また，これらの症例中には著者らが病理組織標本を再鏡検することができず病理診断報告書のみを参考にした病例34例（剖検例6例，胃切除例13例，胃生検例42例，転移浸潤病巣のみを検索した症例3例）が含まれている．胃癌原発病巣を検索し得た症例でもすべての項目に対する病理学的観察が十分でないものもあった．したがって各症例の検討可能な標本の有無により，病理学的観察の症例数が異なる．これらの症例は，検査されなかった症例として解析から除外された．

発生部位． 表5，6は胃における腫瘍の主たる発生部位を四つの被曝線量群別に表したものである．表5は上部（C），中部（M），下部（A）の3部分に分け，また，表6は小彎側（Min），大彎側（Maj），前壁（Ant），後壁（Post），全周性（Circ），その他の六つに区分して発生部位を示している．

まず，発生部位の頻度を観察すると，いずれの線量群においても胃下部の頻度が最も高く，次いで胃中部が高く，胃上部は低い．更に，線量群別に観察すると100－199 rad 群と200＋rad 群の頻度はほぼ同一である．一方，6部位別にみると，胃小彎側の癌の頻度が最も高く，その他の部位はいずれも頻度が低い．しかしながらこれらの特定の所見は放射線量とは関係しない．

腫瘍組織型． 胃癌原発腫瘍病巣を検索した997例

TABLE 5 LOCATION OF STOMACH CANCER (1) BY DOSE
表5 線量別発生部位 (1)

Location	Total	T65DR in rad			
		0	1-99	100-199	200+
C (Upper)	135	51	68	7	9
%	13.3	12.1	13.2	20.6	20.5
M (Medium)	326	143	161	9	13
%	32.1	33.9	31.3	26.5	29.5
A (Lower)	553	228	285	18	22
%	54.5	54.0	55.4	52.9	50.0
Total	1014	422	514	34	44
%	100.0	100.0	100.0	100.0	100.0

Test statistic is $\chi^2 = 4.71$ with 6 degrees of freedom (P>0.10).
検定統計量は自由度6の$\chi^2 = 4.71$である(P>0.10).

TABLE 6 LOCATION OF STOMACH CANCER (2) BY DOSE
表6 線量別発生部位 (2)

Location	Total	T65DR in rad			
		0	1-99	100-199	200+
Min	356	143	180	17	16
%	35.1	33.9	35.0	50.0	36.4
Maj	70	25	39	0	6
%	6.9	5.9	7.6	0.0	13.6
Ant	146	54	77	4	11
%	14.4	12.8	15.0	11.8	25.0
Post	178	79	88	6	5
%	17.6	18.7	17.1	17.6	11.4
Circ	79	35	40	3	1
%	7.8	8.3	7.8	8.8	2.3
Other	185	86	90	4	5
%	18.2	20.4	17.5	11.8	11.4
Total	1014	422	514	34	44
%	100.0	100.0	100.0	100.0	100.0

Test statistic is $\chi^2 = 19.37$ with 15 degrees of freedom (P>0.10).
検定統計量は自由度15の$\chi^2 = 19.37$である(P>0.10).

whom the primary focus of stomach cancer was detected were classified in advance into the following 11 histological types: 1) papillary adenocarcinoma, 2) well-differentiated type tubular adenocarcinoma, 3) moderately differentiated type tubular adenocarcinoma, 4) poorly differentiated adenocarcinoma, 5) mucinous adenocarcinoma, 6) signet-ring cell carcinoma, 7) adenosquamous carcinoma, 8) squamous cell

については，胃癌研究会編の胃癌臨床病理規約[24]に基づいてあらかじめ11の組織型，すなわち，1) 乳頭腺癌，2) 高分化型管状腺癌，3) 中分化型管状腺癌，4) 低分化腺癌，5) 膠様腺癌，6) 印鑑細胞癌，7) 腺扁平上皮癌，8) 扁平上皮癌，9) カルチノイド

carcinoma, 9) carcinoid tumor, 10) undifferentiated carcinoma, and 11) type unknown. Of these, the type unknown group includes autopsy cases with remarkable degeneration due to postmortem autolysis, autopsy and surgical resection cases for which repeat microscopic examination of histopathological samples was not possible, and the tumor histological types which could not be ascertained through pathological diagnosis reports.

Of the tumor histological types classified above, papillary adenocarcinoma, well-differentiated type tubular adenocarcinoma, and moderately differentiated type tubular adenocarcinoma were reclassified as differentiated type adenocarcinoma; and poorly differentiated type adenocarcinoma and signet-ring cell carcinoma were reclassified as poorly differentiated type adenocarcinoma, and adenosquamous carcinoma, squamous cell carcinoma, carcinoid tumor, and undifferentiated carcinoma were reclassified as other histological types. For analysis by exposure dose, the following five groups of histological type were employed: 1) differentiated type adenocarcinoma, 2) poorly differentiated type adenocarcinoma, 3) mucinous adenocarcinoma, 4) other histological types, and 5) type unknown.

Table 7 shows histological types of all stomach cancer cases for both cities combined by exposure dose. The percentage of differentiated type adenocarcinoma are high in the 0 rad group and 1-99 rad group, showing 48.8% and 46.8%, respectively, which exceeds the 31.5% and 35.5% observed for poorly differentiated type adenocarcinoma. On the other hand, in the 100-199 and 200+rad groups, the percentage of differentiated type adenocarcinoma is decreased to 17.1% and 25.9%, respectively, whereas those for poorly differentiated type adenocarcinoma are increased to 46.3% and 40.7%, respectively. This finding suggests that the differentiated type of adenocarcinoma is frequently observed in the control and low dose groups whereas the poorly differentiated type is seen in the high dose group. Actually, a statistically significant relation can be observed between the histological type group and the dose group. As it may be assumed that the increase in the frequency of type unknown carcinoma cases in the 100+rad group as compared with that in the 0 rad group brings about a decrease in frequency of differentiated

腫瘍，10）未分化癌，11）組織型不明の各組織型に分類した．このうち，組織型不明群には死後の自己融解による変性の顕著な剖検症例，病理組織標本の再鏡検が不可能な剖検症例並びに外科切除症例，及び病理診断報告書から確かめられなかった腫瘍組織型の症例を含めた．

上記のごとく分類した腫瘍組織型のうち，乳頭腺癌，高分化型管状腺癌及び中分化型管状腺癌を分化型腺癌に，低分化腺癌と印鑑細胞癌を低分化型腺癌に，また腺扁平上皮癌，扁平上皮癌，カルチノイド腫瘍及び未分化癌をその他の組織型に再分類した．被曝線量別の腫瘍組織型の解析に当たっては，組織型を 1) 分化型腺癌，2) 低分化型腺癌，3) 膠様腺癌，4) その他の組織型，5) 組織型不明の 5 群に分類した．

表 7 は，両市を合せた全症例についての被曝線量別の胃癌組織型を示したものである．0 rad 群及び 1－99 rad 群では分化型腺癌の比率は各々 48.8%，46.8% と高く，低分化型腺癌の 31.5%，35.5% を上回っている．一方，100－199 rad 群及び 200＋rad 群では分化型腺癌の比率はそれぞれ 17.1%，25.9% と低く，低分化型腺癌は 46.3%，40.7% と増加している．この所見は，分化型腺癌は対照群及び低線量被曝群に多く観察され，低分化型腺癌は高線量被曝群に見られるということを示唆する．確かに，組織型分類群と線量群との間には統計的に有意な関係が認められる．0 rad 群に比べ 100＋rad 群の組織型不明癌症例の頻度が増加していることが，分化型腺癌の頻度の減少をもたらしているかもしれないために，低分化型腺癌に有意な増加が認められると結論し難い．

TABLE 7 HISTOLOGICAL TYPE OF STOMACH CANCER BY DOSE
表7　線量別組織型

Histological type		Total	Radiation Dose (T65DR)			
			0	1-99	100-199	200+
Differentiated adenocarcinoma	Observed	451	189	241	7	14
	%	45.2	48.8	46.8	17.1	25.9
Poorly differentiated adenocarcinoma	Observed	346	122	183	19	22
	%	34.7	31.5	35.5	46.3	40.7
Mucinous adenocarcinoma	Observed	57	28	21	3	5
	%	5.7	7.2	4.1	7.3	9.3
Other	Observed	8	3	4	0	1
	%	0.8	0.8	0.8	0.0	1.9
Type unknown	Observed	135	45	66	12	12
	%	13.5	11.6	12.8	29.3	22.2
Total	Observed	997	387	515	41	54
	%	100.0	100.0	100.0	100.0	100.0

Test statistics with and without the type unknown carcinoma are $\chi^2 = 34.59$ with 12 degrees of freedom ($P<.001$) and $\chi^2 = 23.44$ with 9 degrees of freedom ($P<.01$), respectively.

組織型不明の癌を含めた検定統計量は自由度12の$\chi^2 = 34.59$（$P<.001$）で，組織型不明の癌を含めない場合は自由度9の$\chi^2 = 23.44$（$P<.01$）である．

type carcinoma cases, it is difficult to conclude that a significant increase can be recognized for the poorly differentiated type carcinoma.

It must be emphasized that the 997 cases confirmed by autopsy, gastrectomy, and biopsy were classified histopathologically without knowledge of exposure dose. Accordingly, the distribution of type unknown carcinoma cases under each histological classification is considered to be random, and was excluded from subsequent analyses.

Degree of Extension of Cells Into the Gastric Wall. Cell extension into the gastric wall by exposure dose is classified into five stages: 1) tunica mucosa (M), 2) tela submucosa (SM), 3) tunica muscularis propria (PM), 4) tela subserosa (SS), and 5) tunica serosa (S). More than 70% of the cases in each dose group show extensions into the SS and S. Thus, no statistical differences by dose could be demonstrated between the degree of extension into the gastric wall.

Volume of Tumor Stroma. Stomach carcinoma can be classified into three types: medullary,

剖検例，胃切除例及び胃生検例の997例は被曝線量の情報を関知しない状態で病理組織学的に分類されたということは重要である．したがって，各組織学的分類における組織型不明癌は無作為的に起こったものであるとみなし，以後の解析から除外した．

胃壁内深達度． 被曝線量別の腫瘍の胃壁内深達度は1)粘膜層（M），2)粘膜下組織層（SM），3)固有筋層（PM），4)漿膜下組織層（SS）及び5)漿膜層（S）の5段階に分類される．いずれの線量群でも壁内深達度が漿膜下組織層及び漿膜層に至っている症例が70%以上を占めている．このように各胃壁内深達度段階の間には線量別にみて統計的な差は認められない．

腫瘍間質量． 間質結合織の多寡によって，胃癌は

intermediate, and scirrhous depending on the amount of stromal connective tissue. The tumor stroma volume can be classified by exposure dose into two histological types: differentiated type carcinoma and poorly differentiated type carcinoma. Most differentiated type carcinoma is either of the medullary type or the intermediate type, whereas poorly differentiated type carcinoma is mostly of the intermediate type or scirrhous type, and the frequency of scirrhous type is high in the 200+ dose group. There was a tendency in both histological types for the tumor stroma in the 200+rad group to have increased volume, but a statistical increase for linear trend was noted (P<.05) in the poorly differentiated type carcinoma only.

髄様型，中間型，硬性型の三つに分類できる．腫瘍間質量は被曝線量別に分化型腺癌と低分化型腺癌の二つの組織型に分類される．分化型腺癌のほとんどは髄様型あるいは中間型であり，一方，低分化型の腺癌では中間型ないしは硬性型が大部分であり，200＋rad の線量群では硬性型の比率が高い．分化型腺癌並びに低分化型腺癌のいずれの組織型においても，200＋rad の線量群で腫瘍間質量がより増加する傾向を認めるが，直線傾向の統計的増加は，低分化型癌においてのみ認められる（P＜.05）．

Infiltrative Growth Pattern of Tumor. Infiltrative (INF) growth patterns (INFα – expansive growth of the cancerous focus, INFβ – intermediate growth between α and γ, and INFγ – infiltrative growth of the focus) of tumor into its surrounding tissue by histological type (differentiated type or poorly differentiated type carcinoma) and exposure dose were examined.

腫瘍の浸潤増殖様式． 周囲組織に対する腫瘍の浸潤（INF）増殖様式（INFα — 癌巣の膨脹性発育，INFβ — αとγの中間的浸潤，INFγ — 癌巣の浸潤性発育）について組織型別（分化型腺癌又は低分化型腺癌），被曝線量別に検索した．

Most of the differentiated type carcinoma was of either the INFα or INFβ pattern, while the poorly differentiated type carcinoma was most of the INFγ pattern. Neither the differentiated type nor poorly differentiated type carcinoma showed a significant relation between INF growth pattern and radiation dose.

分化型腺癌ではINFα，INFβが，また低分化型腺癌ではINF —γが大部分を占める．分化型及び低分化型両腺癌ともに腫瘍の浸潤増殖様式と線量との間には有意な関係は認められない．

Invasion into Lymph Duct and Vein and Metastasis. The degree of invasion in the lymph duct and vein was approximately the same and unrelated to exposure dose. Also, presence of metastatis to the lymph node and distant organ was of the same rate and unrelated to exposure dose.

リンパ管並びに静脈浸襲及び転移． リンパ管及び静脈への浸襲の程度は両者とも，被曝線量にかかわりなく同様である．また，リンパ節及びほかの遠隔臓器への転移の有無は被曝線量にかかわりなく同率である．

Intestinal Epithelial Metaplasia of the Gastric Mucosa. Intestinal epithelial metaplasia of the gastric mucosa, especially, in the gastric mucosa surrounding the tumor, classified by exposure dose, histological type, and degree of differentiation are given in Table 8. The frequency of moderate-to-severe cases in each dose group of the differentiated type was always higher than that of none-to-mild cases. The degree of intestinal epithelial metaplasia of the gastric mucosa by histological type gives a significant linear trend with increase of dose.

胃粘膜の腸上皮化生． 胃粘膜の腸上皮化生，殊に腫瘍周辺胃粘膜の腸上皮化生を，被曝線量別，組織型別及び分化の程度別に示すと表8のようになる．分化型腺癌では，いずれの線量群においても中等度以上の症例の頻度は軽度以下の症例頻度より常に高い．組織型別の胃粘膜の腸上皮化生の程度は線量の増加に伴う有意な直線傾向を示す．

TABLE 8 MUCOSAL INTESTINAL METAPLASIA BY DOSE
表8　線量別腸上皮化生

Histological type	Mucosal intestinal metaplasia		Total	T65DR in rad				Linear trend	
				0	1-99	100-199	200+	$\hat{b}$ ($\times 10^4$)	$\hat{SE}$ ($\times 10^4$)
Differentiated adenocarcinoma	None to mild	Observed	94	41	50	1	2		
		%	30.1	30.8	30.3	20.0	22.2	4.00*	1.85
	Moderate to severe	Observed	218	92	115	4	7		
		%	69.9	69.2	69.7	80.0	77.8		
	Total	Observed	312	133	165	5	9		
		%	100.0	100.0	100.0	100.0	100.0		
Poorly differentiated adenocarcinoma	None to mild	Observed	149	48	84	8	9		
		%	62.9	64.9	64.6	57.1	47.4	7.46**	0.78
	Moderate to severe	Observed	88	26	46	6	10		
		%	37.1	35.1	35.4	42.9	52.6		
	Total	Observed	237	74	130	14	19		
		%	100.0	100.0	100.0	100.0	100.0		

The estimate of parameters from a linear trend model was obtained by a weighted least square approach. Significant level are as in Table 1.
線形傾向モデルからのパラメーターの推定値は加重最小2乗法により求めた．有意水準は表1に示すとおりである．

DISCUSSION

The LSS based on death certificate information and the pathological study of autopsy cases, have been heretofore employed in investigating the development of stomach cancer in A-bomb survivors.[10-16] Epidemiologic studies of stomach cancer in A-bomb survivors in the LSS sample were conducted by Kato et al[10] (1950-66), Nakamura[11] (1950-73), and Beebe et al[12] (1950-74). The results of these studies have indicated a significant increase in stomach cancer mortality in the heavily exposed survivors.[11,12]

On the other hand, pathological research on stomach cancer includes a study by Murphy and Yasuda[13] conducted during 1948-57 using autopsy and surgical material in Hiroshima, and studies by Yamamoto et al[14-16] conducted during 1961-68, 1961-69, and 1961-74 using autopsy material in Hiroshima and Nagasaki. However, none of these pathological studies revealed a significant correlation between stomach cancer incidence and exposure.

As described in the introduction, a remarkable increase in the rate of early stomach cancer

考　察

従来から，原爆被爆者胃癌の研究に際しては，死亡診断書による寿命調査，並びに剖検症例を用いての病理学的調査が用いられてきた．[10-16] 寿命調査集団に含まれる被爆者の胃癌の疫学的研究は，加藤ら[10] (1950—66年)，中村[11] (1950—73年)，Beebe ら[12] (1950—74年) によって行われている．その結果，高線量被爆者に胃癌死亡率の有意な増加があることが指摘されている．[11,12]

一方，病理学的調査による胃癌の研究としては，1948—57年の広島の剖検材料及び外科手術材料による Murphy 及び安田[13]の研究，1961—68年，1961—69年，及び1961—74年の各期間中の広島，長崎の剖検材料を用いての山本ら[14-16]の研究を挙げることができる．しかしながら，これらの病理学的研究のいずれにおいても，胃癌発生率と被爆との間に有意な相関は認められていない．

緒言で述べたごとく，過去30年間の日本における

detection due to advancements achieved in gastric diagnostics and the popularization of mass stomach screening in Japan during the past three decades has greatly changed the clinical picture of stomach cancer.[17] It has now become almost impossible to adequately pursue the association between A-bomb exposure and the incidence of stomach cancer using the conventional procedures of the LSS and pathological study alone.

In this study, aiming to make up for deficiencies in research methods employed heretofore, the association between A-bomb exposure and stomach cancer was investigated using as study subjects all cases of stomach cancer including surgical and pathological cases and clinical cases as well as cases identified by death certificate or autopsy.

As a result, when the risk was corrected for the effects of sex and age, the effects of radiation were evident only in the 200+rad group. When the effect of dose is reviewed in relation to age-group, a significant increase in risk is observed in all three age-groups under 30 ATB who were exposed to 200+rad. However, the risk of those in the 50+ ATB age-group is not significant, it being 1.1, which is of the same level as the control group. Since those who are in the under 30 ATB age-groups are now showing a higher incidence of stomach cancer, and are now approaching the age of greatest cancer risk (50-70), it will be of great interest to conduct follow-up studies of future trends in stomach cancer incidence.

So far, an increased frequency among A-bomb survivors of leukemia,[1-3] and tumors of lung,[4,5] breast,[6] thyroid,[7] salivary gland,[8,9] and malignant lymphoma,[25] and multiple myeloma[26] have been observed. The increase in incidence of these tumors is generally observed in the heavily exposed, 100+rad groups.[3-6,9,25,26] In the present study, a significant increase in the incidence of stomach cancer was also evident in the 100+rad groups, especially 200+rad group. This tendency was similar to those for the other types of tumors mentioned above.

The finding that tumors develop at a high frequency in those exposed at a young age was pointed out by Jablon et al[27] based on their study of the 100+rad group in Hiroshima and

胃診断学の進歩と胃集団検診の普及による早期胃癌発見率の顕著な増加によって胃癌臨床像は大いに変貌を遂げており,[17] 従来の寿命調査並びに病理学的調査のみでは被爆と胃癌発生との関連性を十分に追求することができなくなってきているのが現状である.

今回は，従来行われてきた胃癌研究における研究方法の不備を補う目的で，死亡診断書又は剖検による症例に加えて，外科病理学的に診断された胃癌症例，更には胃癌臨床症例をも含めた全胃癌症例を対象として，被爆との関連性を追求する方法をとった.

その結果，性・年齢の影響のためリスクが訂正され，200＋rad 群にのみ放射線効果が明らかにされた．この線量の影響を年齢群別に考察すると，200＋rad 群において，原爆時年齢30歳未満の三つのすべての年齢群にリスクの有意な増加を認める．しかし原爆時年齢50歳以上のリスクは1.1と対照群レベルと同じ程度で有意でない．現在高い胃癌発生率を示している原爆時年齢が30歳以下の群は胃癌の好発年齢（50—70歳）に達しつつあるため，今後この胃癌発生率がどのような傾向を示すかを追跡調査することは極めて興味ある課題である.

現在までに原爆被爆者に発生頻度の増加が指摘されている腫瘍には，白血病,[1-3] 肺癌,[4,5] 乳癌,[6] 甲状腺癌,[7] 唾液腺腫瘍,[8,9] 悪性リンパ腫,[25] 多発性骨髄腫[26] がある．これらの腫瘍の発生率の増加は概して100＋rad の高線量被曝群でみられている.[3-6,9,25,26] 今回の調査では，胃癌における有意な発生率の増加も100＋rad 群，殊に200＋rad 群でより明瞭となっており，上述の他の腫瘍群における傾向と同様であった.

若年時被爆者に腫瘍の発生頻度が高いという所見は，被爆時10歳以下の広島，長崎の100＋rad 群についての検討から Jablon ら[27] によって指摘された．また

Nagasaki who were less than age 10 ATB. Also similar findings have been reported subsequently for leukemia,[3] salivary gland tumor,[8,9] and breast cancer.[6] More particularly, it has been reported that leukemia develops at the highest frequency in the heavily exposed group under age 15 ATB, and salivary gland tumor in the proximally exposed group of age 0-19 ATB, and the highest risk of breast cancer is observed in the 100+rad group who were age 10-19 ATB.

Based on the dose-response relationship obtained using total kerma dose in conjunction with the present data on the incidence of stomach cancer, it must be stressed that the dose response of stomach cancer development is definitely not quadratic, but linear, at least when results based on the T65DR are used. It should be noted, however, that only the results for males in Hiroshima suggest a quadratic dose response. Conducting observations by age-group, a significant linear response was observed in the 10-19 and 20-29 ATB age-groups. The 10-19 ATB age-group showed the most significant increase in risk, but their estimated risks of stomach cancer adjusted for both city and sex were 1.5 and 1.7 per million PYR, respectively. These values, as compared with 1.2, the average risk adjusted for all city-sex-age factors, indicate that the younger ATB age-groups have a higher risk per million PYR. Furthermore, the 0-9 ATB age-group, only a part of whom are now reaching the age of higher cancer risk, were still 32-41 years of age at the time of the 1977 survey, and a significant linear response could not be observed at that time. The dose response for this younger age-group will become known through follow-up studies continued on the fixed population.

Sites of stomach cancer are similar regardless of dose, with the frequency being highest in the lower-to-middle portions, especially on the lesser curvature. The same finding had been reported by Yamamoto et al,[14] and the above locations generally correspond with the main locations of tumors in typical stomach cancer cases.[17,28-30]

In the present analysis of stomach cancer by histological type, classification was made roughly into five types: 1) differentiated type adenocarcinoma, 2) poorly differentiated type adenocarcinoma, 3) mucinous adenocarcinoma,

その後，同様の所見が白血病，[3] 唾液腺腫瘍，[8,9] 乳癌[6]でも報告されている．すなわち，白血病では原爆時年齢が15歳未満の高線量被曝群で，唾液腺腫瘍でも0－19歳で被爆した近距離被爆者で発生率が高く，また乳癌でもその最大のリスクは原爆時年齢が10－19歳の100＋rad群にみられると報告されている．

今回の胃癌発生頻度資料に対して合計kerma線量を用いて得た線量反応関係によると，胃癌発生の線量反応は2次曲線形でなく，少なくともT65DRに基づく結果を使用する場合には，線形であると明確に強調することができよう．しかしながら，広島の男性群における結果だけは2次曲線形線量反応を示唆していることにも留意する必要がある．年齢群別観察結果から，有意な線形反応を認めたのは原爆時年齢10－19歳と20－29歳であった．原爆時年齢10－19歳群において最も有意なリスクの増加が認められたが，両年齢群の都市及び性による補正を加えた胃癌の推定リスクは100万人年当たり各々1.5及び1.7であった．これらの値は都市，性，年齢のすべての要因による補正を加えた平均リスクの1.2と比べて原爆時に若年であった群における100万人年当たりのリスクが高いことを示している．更に，ようやく一部が癌の好発年齢に達したばかりの原爆時年齢0－9歳群は1977年の調査時年齢がまだ32－41歳であり，その際には有意な線形反応は認められなかった．継続されている固定集団の追跡調査によってこの若年齢群の線量反応も明らかにされるであろう．

胃癌病巣の発生部位は線量にかかわりなく同様であり，胃下部から中部，しかもその小彎側の頻度が高い傾向を認めた．この所見は山本ら[14]の研究でも同様に報告されており，また典型的な胃癌における腫瘍の主発生部位ともおおむね一致する．[17,28-30]

今回の胃癌組織型の検討に当たっては，組織型を1)分化型腺癌，2)低分化型腺癌，3)膠様腺癌，4)その他の組織型，5)組織型不明の五つに大別

4) other histological types, and 5) type unknown. There was a tendency in the 200+rad group for the frequency of poorly differentiated type adenocarcinoma to increase, while on the other hand, the differentiated type adenocarcinoma decreased. However, since there was good agreement between the observed and expected number of the poorly differentiated type, it could not be concluded that there is a significant relationship between dose and histological type, because the possibility exists that the decrease in the frequency of differentiated type cases is due to the increase in the frequency of type unknown ones.

Generally, the radiation-induced cancers developing among A-bomb survivors have failed to exhibit predominance of any specific histological type for leukemia, breast cancer, and salivary gland tumors.[1-3,6,8,9] The exception is lung cancer, in which there has been shown to be a high frequency of small cell carcinoma.[4,5] Accordingly, it is considered necessary that a larger number of cases be accumulated in the future, so that a more comprehensive review can be made of histological types of stomach cancer.

Intestinal epithelial metaplasia is considered important as the mother tissue of stomach cancer, especially in the case of differentiated type carcinoma.[28,31,32] However, pathological studies of stomach cancer in A-bomb survivors conducted heretofore have made no mention of the degree of intestinal epithelial metaplasia. It is assumed that this is probably because the degree of intestinal epithelial metaplasia could not be determined due to the severe postmortem degeneration of the autopsy material.

The present study revealed that the degree of intestinal epithelial metaplasia is greater and its frequency is higher in the differentiated than poorly differentiated type carcinoma. This finding supports the theory that differentiated type carcinoma develops from intestinal epithelial metaplastic mucosa as its mother tissue. Review of cases of various histological types by exposure dose demonstrated a significant trend only in the degree of intestinal epithelial metaplasia. That is, there was evidence that the degree in intestinal epithelial metaplasia increases with dose.

した．200＋rad 群での低分化型腺癌の頻度が増加し，一方，分化型腺癌は減少する傾向があった．しかし，低分化型は観察数と期待数がよく一致していることから，分化型腺癌頻度の減少は組織型不明症例の頻度の増加のためであるという可能性もあり，線量と組織型との間に有意な関係があると結論付けることはできなかった．

一般に，被爆者にみられる放射線誘発癌のうち，白血病，乳癌，唾液腺腫瘍では特有な組織型の優勢は認められていない．[1-3,6,8,9] 肺癌は例外であり，小細胞癌の頻度が高いことが示されている．[4,5] したがって，今後更に多くの症例を集積した上で，胃癌組織型についてより包括的な検討をする必要があるように思われる．

腸上皮化生は，胃癌，殊に分化型腺癌の発生母地として重視されている．[28,31,32] しかしながら，今までに行われた被爆者の胃癌の病理学的な研究では，腸上皮化生の程度についての記載は全くなされていない．これは恐らく，剖検材料の死後変化が高度であったため，腸上皮化生の程度を決定することができなかったことによると推察される．

本研究の結果，低分化型腺癌と比較して分化型腺癌では腸上皮化生の程度が強く，且つその頻度も高いことが明らかになったが，この所見は，分化型腺癌が腸上皮化生性粘膜を母地として発生するという説を支持するものである．被曝線量別の各種組織型症例の検討により，腸上皮化生の程度においてのみ有意な傾向が認められた．すなわちこれは，線量に伴い腸上皮化生の程度が増加することを証拠付けるものである．

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In the continued interest of accurately defining the late effects of the atomic bombs, the qualitative and quantitative characteristics of the A-bomb radiation exposure doses are periodically refined. If warranted by future dose assessments, the data reported here will be reanalyzed and subsequently reported.

原爆の後影響を引き続いて正確に究明する目的をもって，原爆放射線被曝線量の質的・量的特質について定期的に改良を加えている．今後線量評価によって，その必要性が起これば，本報の資料を再解析の上，改めて報告する．