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LUNG CANCER INCIDENCE AMONG A-BOMB SURVIVORS IN HIROSHIMA AND NAGASAKI, 1950-80
広島・長崎原爆被爆者の肺癌発生率，1950－80年

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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．

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広島・長崎原爆被爆者の肺癌発生率，1950－80年

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SUMMARY

The incidence of lung cancer during 1950-80 in a cohort of Japanese atomic bomb survivors and controls was investigated. A total of 1,057 cases were identified; 608 of these diagnoses were based on some form of histopathologic examination, and 442 were confirmed by the present investigators. The distributions of histological types varied significantly between the sexes ($p<.001$), with adenocarcinoma more frequent among women and epidermoid and small cell carcinoma more frequent among men. The distributions of primary sites did not differ significantly between the sexes. The relative risk (RR) of lung cancer increased significantly with A-bomb radiation dose ($p<.0001$); based on tentative 1965 dose estimates as revised in 1978 (T65DR) and a linear RR model, the estimated RR at 100 rad (±SE) is 1.41 ± 0.09. Among Hiroshima survivors the women experienced radiation-related excess RR nearly twice as great as men ($p=.06$). RR increased with decreasing age at the time of bombing ($p=.07$), and after allowing for this effect, there was no significant evidence that RR varied systematically with attained age. Small cell carcinoma displayed somewhat greater sensitivity to radiation than did adenocarcinoma or epidermoid carcinoma; however the variation between the histology-specific RR functions was not statistically significant ($p=.44$).

要 約

原爆被爆者とその対照者のコホートにおける1950年から1980年までの肺癌発生率について調べた．1,057症例が確認され，そのうち608例の診断は何らかの形で病理組織検査をしたもので，442例は今回調査に携わった研究員が確認したものである．組織型の分布をみると男女間に有意な差異があり（p＜.001），女性では腺癌，男性では類表皮癌，小細胞癌の発生頻度が高い．原発部位の分布には男女間に有意な差異はなかった．肺癌の相対危険度（RR）は原爆放射線量に伴って増加しており（p＜.0001），1978年に改訂された1965年暫定推定線量（T65DR）と線形RRモデルによれば，100 radでの推定RR（± SE）は1.41± 0.09である．広島の被爆者では女性の放射線による過剰RRは男性のそれのほとんど2倍に達する（p＝.06）．RRは被爆時年齢が下がるにつれて増加しているが（p＝.07），こうした効果を考慮してもRRが到達年齢に応じて系統的に変動するという有意な証拠はない．小細胞癌は腺癌や類表皮癌より放射線に対して幾分か高い感受性を示したが，組織型別RR関数の変動は統計的に有意ではない（p＝.44）．

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INTRODUCTION

In recent years, increases in lung cancer have been reported in various countries throughout the world, and Japan is no exception.[1,2] Attention has been focused on lung cancer as well as other radiation-induced cancers among A-bomb survivors since shortly after the bombings of Hiroshima and Nagasaki. Studies on clinical cases and autopsy cases during 1950-70,[3-6] and mortality during 1950-82[7] have shown that the risk of lung cancer is related to radiation dose, and that the association of anaplastic small cell carcinoma to radiation may be especially strong. The purpose of this report is to summarize the incidence rates and histopathologic characteristics of lung cancer during 1950-80 among a cohort of A-bomb survivors and nonexposed controls including as many clinical, autopsy, and death certificate cases as possible.

MATERIALS AND METHODS

Study Cohort

This study is based on the Life Span Study (LSS) extended sample, which includes about 82,000 persons exposed to the A-bombings of Hiroshima and Nagasaki and 27,000 nonexposed controls who were in neither city (NIC) at the time of the bomb (ATB). The selection of this cohort is described in detail elsewhere.[8] This is essentially the same cohort as that used in the analyses of mortality by Kato and Schull.[9] Follow-up of each member of the cohort commenced between 1 October 1950 and 1 October 1953.

The cohort was divided into categories by city (Hiroshima, Nagasaki), sex (male, female), and age ATB (0-9, 10-19, 20-29, 30-39, 40-49, 50+), data which are known for all members of the LSS-extended cohort.

As in most analyses of A-bomb survivor data in the last two decades, radiation dose is here synonymous with tissue kerma in air (sum of neutron and gamma) adjusted for shielding by man-made structures or natural objects, calculated according to the tentative 1965 dosimetry system, as revised in 1978 (T65DR dose estimates).[9,10] Survivors for whom T65DR dose estimates cannot be calculated due to complicated shielding situations or missing information were excluded from analyses of the radiation dose-response, as was the NIC group. The remaining 79,940 survivors were divided

緒　言

近年，世界各国で肺癌の増加が報告され，日本もその例外ではない．[1,2] 広島，長崎の原爆後間もなくして，被爆者の肺癌が他の放射線誘発癌同様注目を浴びている．1950－70年の臨床例及び剖検例の調査[3-6]並びに1950－82年の死亡率調査[7]により，肺癌リスクは放射線量と関連があること，また退行性小細胞癌と放射線との関連性は特に強いことが認められた．本報の目的は，できるだけ多くの臨床例，剖検例及び死亡診断書例を含め，被爆者及び非被爆対照者からなるコホートの1950年から1980年までの肺癌発生率及び病理組織学的特性を総括することである．

材料及び方法

調査コホート

本調査は，広島・長崎の原爆被爆者約82,000人と原爆時にそのいずれの都市にもいなかった(NIC)非被爆対照者27,000人を含む寿命調査(LSS)拡大標本を対象とする．このコホートの抽出については別報で詳述しており，[8] Kato 及び Schull[9] の死亡率解析で用いられたコホートとほとんど同じである．コホートの各構成員の追跡調査は1950年10月1日から1953年10月1日までの期間内に開始した．

コホートは都市別(広島，長崎)，性別(男性，女性)及び原爆時年齢別(0－9，10－19，20－29，30－39，40－49，50＋)に分類したが，そのデータは寿命調査拡大コホートの全構成員について入手されている．

過去20年の被爆者データの大部分の解析同様，本報でいう放射線量は，建造物又は地形による遮蔽について補正し，1978年に改訂した1965年暫定線量測定方式(T65DR推定線量)に従って算定した空気中の組織カーマ(中性子及びガンマ線の和)と同じものである．[9,10] 遮蔽状況が複雑なため，あるいは情報が欠如しているために，T65DR推定線量が算定できない被爆者は市内不在者群と同様放射線量反応解析から除外した．残りの79,940人は八つの線量区分，すなわち0 rad(0.5 rad以下を意味する)，

into eight dose categories: 0 rad (meaning <0.5 rad), 1-9, 10-49, 50-99, 100-199, 200-299, 300-399, and 400+.

1－9 rad，10－49 rad，50－99 rad，100－199 rad，200－299 rad，300－399 rad 及び 400＋rad に分類した．

It has been indicated that T65DR dose estimates may be seriously in error for many subjects,[11] although at the time of this writing (1986) an accepted alternative dosimetry system is not available. Revision of the dose estimates is likely to result in modification of estimates of risk of radiogenic cancer. In particular the relationship between the two cities is expected to change, since dose estimates of Nagasaki survivors are likely to change much more than those of Hiroshima survivors. Therefore, comparisons between the cities are not emphasized in this report, and some analyses are restricted to Hiroshima survivors. It is important to note that recent analyses of cancer mortality among A-bomb survivors[12] have indicated that, while estimates of radiogenic risk and intercity comparisons will be sensitive to the anticipated modification of dose estimates, other important features of the radiogenic risk such as sex differences and dependencies on age ATB or time will probably change very little.

多数の対象者について T65DR 推定線量に重大な誤りがある可能性があることが指摘されているが，[11] 本報の作成時（1986年）にはそれに代わる容認された新線量推定方式は完成されていない．推定線量の改訂によって，放射線発癌リスクの推定値も修正されることと思われる．長崎の被爆者の推定線量は広島の被爆者のそれよりも大幅に変更されそうなので，特に両市間の関係が変わることが予想される．したがって，本報では両市間の比較に重点を置かない．また，幾つかの解析を広島の被爆者に限定した．注目すべきことは，最近の被爆者癌死亡率解析[12] によれば，放射線発癌リスクの推定値と広島・長崎間の比較は推定線量修正に影響されるが，男女差や原爆時年齢又は経過期間に対する依存性など他の放射線発癌リスクの重要な特性は恐らくあまり変わらないことである．

Identification of Cases

An attempt was made to identify as many cases of lung cancer as possible using various sources available to RERF, including tumor and tissue registries in each city; records of autopsies performed at ABCC-RERF, the Schools of Medicine of Hiroshima and Nagasaki Universities, and other medical facilities in the cities; and records of certified causes of death routinely obtained by ABCC-RERF as part of its program of active follow-up of the LSS-extended cohort. Each person's follow-up began on 1 October 1950 or his/her 20th birthday, whichever was later. (No cases of lung cancer were diagnosed among persons aged less than 20 years.)

症例の確認

広島・長崎各市の腫瘍登録及び組織登録，ABCC-放影研，広島，長崎両大学医学部，及び両市のその他の医療機関で行われた剖検の記録，並びに寿命調査拡大コホートの積極的追跡調査プログラムの一環として ABCC-放影研が通常入手する死亡診断書など利用可能な多数の情報源を用いてできる限り多くの肺癌例を確認するようにした．各対象者の追跡調査は1950年10月1日，あるいは対象者の20回目の誕生日のどちらかおそい時から開始した．（20歳以下の対象者には肺癌と診断された症例はなかった．）

Tissue specimens or slides from autopsies, biopsies, and/or surgical procedures were obtained when possible for microscopic examination by a single pathologist (T.Y.). Autopsy protocols were reviewed, and reexamination of questionable cases were conducted from paraffin blocks. Mainly H-E stain was employed, although PAS and Alcian-Blue were used as well. Histological classification was based on the Japan Lung Cancer Society's critieria,[13] which are similar and comparable to the World Health

可能な限り剖検，生検及び外科手術から組織標本又は切片を入手して，一人の病理医（山本 務）の鏡検に供した．剖検記録を検討し，また診断の疑わしい症例についてはパラフィンブロックの再検査をした．PAS とアルシアンブルー染色も用いたが，主として H-E 染色を用いた．組織学的分類は世界保健機関の分類方式[14] と類似している日本肺癌学会の

Organization's classification system.[14] In the event of even minor uncertainty, the diagnosis was established in conference with the coinvestigators.

基準[13]に基づいて行った．診断について少しでも不確実な場合には，共同研究者と協議して診断を確定した．

Statistical Methods

Accumulation of person-years (PY) at risk commenced with the beginning of each person's follow-up, or on his/her 20th birthday, whichever was later, and ceased upon onset of lung cancer, death from any cause, or 31 December 1980, whichever was earliest. Because of the variety of sources from which cases were identified, no single event could be defined as a date of onset which was known for all cases. Therefore, the recorded dates of onset for this study range between the date of first diagnosis and the date of death.

The age attained throughout the period of follow-up, 1950-80, was divided into six categories: 20-29, 30-39, ..., and 70+. The period of follow-up was also divided into four intervals ending on the last days of 1954, 1958, 1962, and 1980. For analyses of lung cancer risk, PY and cases were aggregated and cross-classified according to city, sex, age ATB, attained age, interval of follow-up, and radiation dose, using the categories defined above. For analyses as quantitative variables, the categories of age ATB and attained age were assigned as classmarks the values 5, 15, ..., 55 and 25, 35, ..., 80, respectively. The classmark values for the radiation dose categories were the average doses within each category.

For analyses of the radiation dose-response among the 79,940 exposed survivors with T65DR dose estimates, directly standardized incidence rates were calculated. These were adjusted for age ATB, attained age, interval of follow-up, and (when appropriate) city and/or sex using the distribution of PY in the 0 rad group. Further analyses of the effects of radiation were based on linear RR models. A detailed description of the use of such models is given elsewhere.[7] Let $i=1, \ldots, 224$ be an index for strata defined by the combinations of city, sex, age ATB, attained age, and interval of follow-up. Let the classmark values of dose, d, index the radiation dose categories. The numbers of lung cancer cases in the various combinations of strata and dose groups were assumed to be realizations of independent Poisson random

統計学的方法

観察人年（PY）の累算は，各対象者の追跡調査の開始時あるいは20回目の誕生日のどちらか遅いときから始まり，肺癌の発症，あらゆる原因による死亡，及び1980年12月31日のうち最も早い時期に終了した．多くの情報源により症例を確認したので，全症例についてわかるような唯一の事象を，発病年月日として決定することはできなかった．したがって，本調査については記録された発病年月日は最初の診断年月日から死亡年月日までの期間にまたがっている．

1950－80年の追跡調査期間中の到達年齢を20－29，30－39，...，70＋の六つの区分に分類した．追跡調査期間も1954年，1958年，1962年及び1980年の最終暦日を終了日とする四つの期間に分類した．肺癌リスクの解析のために，上記の区分を用いて，都市，性，原爆時年齢，到達年齢，追跡調査期間及び放射線量に従ってPYと症例を集計し，相互分類した．定量変数の解析については，原爆時年齢区分と到達年齢区分にそれぞれ5，15，...，55と25，35，...，80の階級値を割り当てた．放射線量区分の階級値は各区分内の平均線量である．

T65DR線量が推定されている被爆者79,940人の放射線量反応解析のために，直接標準化した発生率を算定した．これらは0 rad群のPY分布を用いて原爆時年齢，到達年齢，追跡調査期間並びに（適切なとき）都市又は性について調整した．線形RRモデルを用いて放射線の効果を更に解析した．このようなモデルの使用についての詳細な説明は別に記述した．[7] $i=1, \ldots, 224$を，都市，性，原爆時年齢，到達年齢及び追跡調査期間を組み合わせて定義した層の指数と仮定し，線量dの階級値が放射線量区分を示していると仮定する．層と線量群の種々な組み合わせにおける肺癌症例数は，期待値PY(d; i)×(d; i)のポアソン独立確立変数の実現であるとみなした．

variables with expected values $PY(d;i) \times (d;i)$, where $PY(\cdot)$ denotes PY at risk and $\lambda(\cdot)$ denotes the specific incidence rate. Then $RR(d;i) = \lambda(d;i)/\lambda(0;i)$ is the RR associated with dose d in stratum i. Under the linear RR model, the radiation-related excess RR is proportional to dose:

ただし $PY(\cdot)$ は観察 PY を，また $\lambda(\cdot)$ は特定発生率を示す．次に $RR(d;i) = \lambda(d;i)/\lambda(0;i)$ は層 i の線量 d と関連のある RR である．線形 RR モデルの下では，線量関連過剰 RR は線量に比例する：

$$RR(d;i) - 1 = \beta_i d \quad . \qquad [1]$$

The coefficient β_i represents excess RR per unit of radiation dose. Notice that the excess RR in [1] may depend on i, which allows modification of the dose response by factors such as sex, age ATB, etc. Because RR cannot be less than zero, the excess RR per 100 rad must be greater than $-100/d_{max}$, where d_{max} is the largest dose classmark, 526 rad. Thus, a minimum feasible value of $-.19$ is set for the excess RR per 100 rad in [1] for analyses based on all dose categories.

係数 β_i は放射線量単位当たりの過剰 RR を示す．〔1〕における過剰 RR は，性，原爆時年齢などの因子による線量反応の変更を可能にする i に左右されるかもしれないことに注目すること．RR は 0 以下であるはずがないのだから，100 rad 当たり過剰 RR は $-100/d_{max}$ 以上でなくてはならない．ただし d_{max} は最大線量階級値 526 rad である．このようにすべての線量区分に基づく解析の〔1〕の 100 rad 当たり過剰 RR について最小実行値 $-.19$ を決める．

Parameter estimation and significance testing were based on maximum likelihood analysis of the Poisson regression models described above,[15,16] which requires that the background (spontaneous) incidence rates, $\lambda(0;i)$, be estimated simultaneously with the parameters of excess risk. For most anlayses the following parametric background model was used:

パラメーターの推定及び有意性検定は，過剰リスクのパラメーターを用いてバックグラウンド（自然）発生率 $\lambda(0;i)$ を同時に推定する必要のある上記のポアソン回帰モデルの最大尤度解析に基づいて行った．[15,16] 大部分の解析については以下のパラメトリックバックグラウンドモデルを用いた．

$$\log[\lambda(0;i)] = \alpha_0^{(k)} + \alpha_1 CITY + \alpha_2 SEX + \alpha_3(ATB - 30) + \alpha_4 \ell n(ATT/50) + \alpha_5 [\ell n(ATT/50)]^2 \quad , \qquad [2]$$

where k indexes the four intervals of follow-up, CITY and SEX are indicator variables, and ATB and ATT denote the classmark values of age ATB and attained age, respectively, defined above. Allowing separate constant terms for the first three intervals of follow-up, $\alpha_0^{(1)}$, $\alpha_0^{(2)}$, and $\alpha_0^{(3)}$, was necessary to accommodate exceptionally low rates observed prior to 1963. For simplicity, estimates of the parameters in the background model [2] are not reported in the text of this report, but are summarized for selected models in Appendix Table 1. For certain analyses, which are explicitly identified below, [2] was not used; rather background rates were permitted to vary without restriction among the 224 strata. The latter approach, designated the nonparametric background model, was also used to test the goodness-of-fit for the parametric background model [2].

ただし k は四つの追跡調査期間を示し，CITY 及び SEX は指示変数であり，ATB 及び ATT はそれぞれ上に説明した原爆時年齢及び到達年齢の階級値を示す．最初の三つの追跡調査期間 $\alpha_0^{(1)}$，$\alpha_0^{(2)}$，$\alpha_0^{(3)}$ にそれぞれの定数項を付与することは，1963年以前に観察された例外的に低い発生率を順応させるために必要であった．簡単にするために，バックグラウンドモデル〔2〕のパラメーターの推定値は本報の本文には報告していないが，選択モデルについて付録表1に要約して示した．下に明示した特定の解析については，〔2〕を使用しないで，むしろ224層中で無制限にバックグラウンド率を変動させた．非パラメトリックバックグラウンドモデルと呼ぶ後者の方法は，パラメトリックバックグラウンドモデル〔2〕の適合度の検定にも用いた．

RESULTS

Description of Cases

A total of 1,057 cases of lung cancer among members of the LSS-extended cohort during the period 1950-80 were identified. Of these, 608 were based on some form of histopathologic diagnosis (Table 1), including 442 which were confirmed by histopathologic examination of tissue specimens in the current study (Table 1A). For 615 cases no histopathologic review was possible for this study. The majority of these diagnoses were based on death certificates and/or tumor registry records (Table 1B). The heavy

結　果

症例の説明

1950－80年の寿命調査拡大コホートの構成員において肺癌例総計1,057が確認された．そのうち608例は何らかの形の病理組織学的診断に基づくものであり(表1)，今回の調査で組織標本の病理組織検査により確認された442例を含む(表1A)．615例については本調査において病理組織学的検討は不可能であった．それらの診断のうち大多数は死亡診断書及び腫瘍登録記録に基づいて行われた(表1B)．死亡診断書に

TABLE 1 SUMMARY OF DIAGNOSTIC DATA
表1　診断データの要約

A. Cases confirmed by microscopic examination for the present study
今回の調査で顕微鏡検査により確認された症例数

Type of Specimen	Exposed Survivors		NIC	Total
	T65DR Known	T65DR Unknown		
Autopsy only	293	7	76	376
Autopsy, plus surgical or biopsy	7	1	1	9
Surgical	24	1	10	35
Biopsy	19	0	3	22
Total	343	9	90	442

B. Cases not confirmed for the present study　今回の調査で確認されなかった症例数

Most Definitive Diagnosis of Lung Cancer	Exposed Survivors		NIC	Total
	T65DR Known	T65DR Unknown		
	Histopathologic Diagnoses			
RERF Autopsy Program, but specimen not available	6	1	2	9
Tumor Registry Record				
Autopsy	7	0	4	11
Microscopic or cytological	105	3	38	146
Total	118	4	44	166
	Other Diagnoses			
Tumor Registry Record				
Surgical, endoscopic or radioisotopic	129	3	40	172
Death Certificate	183	5	69	257
No Autopsy Program, Tumor Registry, or Death Certificate Diagnosis	19	0	1	20
Total	331	8	110	449

reliance on death certificate diagnoses (257 cases) is a cause for concern, since the Autopsy Program recorded a confirmation rate of only 61% for death certificate diagnoses of lung cancer.[17] For 318 cases the Tumor Registries contained records of premortem diagnoses of lung cancer. None of these diagnoses were based solely on ultrasonographic, radiographic, or clinical examinations, and 46% (146) were based on cytological or microscopic examination of tumor cells. The false positive rates for those various kinds of premortem diagnoses are unknown.

記載されている肺癌の診断に関して，剖検プログラムではわずか61%の確認率しか得られていないので，死亡診断書による診断（257例）を過度に信頼するのは問題がある.[17] 318例については腫瘍登録に肺癌の臨床診断記録があった．このうち超音波検査，X線検査あるいは臨床検査だけに基づく診断は全くなく，46%（146例）は腫瘍細胞の細胞診あるいは鏡検に基づく診断であった．各種の臨床診断についての偽陽性率は不明である．

The distribution of histological types among the 442 confirmed cases are shown by sex and exposure status in Table 2. Adenocarcinoma was the most common diagnosis, accounting for 174 (40%) of the 435 cases assigned a histological type, followed by epidermoid carcinoma (148; 34%) and small cell carcinoma (72; 17%). The distributions differ significantly between the sexes ($p<.001$, based on Pearson's χ^2 test with mucoepidermoid and unclassified cases omitted). Adenocarcinoma is relatively more frequent among women (55%) than among men (33%), while the opposite is true for epidermoid carcinoma (males 38%, females 25%) and small cell carcinoma (19% and 11%).

表2に442例の組織型分布を性及び被爆状況別に示した．腺癌の診断が最も多く，組織型が判明している435例のうち174例（40%）を占め，類表皮癌（148例，34%）と小細胞癌（72例，17%）が続いた．分布は男女間で有意に異なる（粘液性類表皮癌及び分類不能症例を除いた Pearson χ^2 検定によれば $p<.001$）．腺癌は男性（33%）よりも女性（55%）の方が相対的に頻度が高いが，反対に類表皮癌（男性38%，女性25%）と小細胞癌（男性19%，女性11%）は女性よりも男性の方が頻度が高い．

TABLE 2 DISTRIBUTION OF HISTOLOGICAL TYPES AMONG 442 CONFIRMED LUNG CANCER CASES; BY T65DR STATUS AND SEX (LSS-EXTENDED COHORT, BOTH CITIES, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)

表2 確認された442肺癌症例の組織型分布，T65DR 有無別及び性別（寿命調査拡大コホート，両市，全原爆時年齢区分，到達年齢20+，1950−80年）

Histological Type	Exposed Survivors				NIC		Total	
	T65DR Known		T65DR Unknown					
	Male	Female	Male	Female	Male	Female	Male	Female
Adenocarcinoma	80 (35%)	60 (54%)	1 (17%)	2 (67%)	16 (25%)	15 (58%)	97 (33%)	77 (55%)
Epidermoid Carcinoma	78 (35%)	28 (25%)	3 (50%)	1 (33%)	32 (51%)	6 (23%)	113 (38%)	35 (25%)
Small Cell Carcinoma	43 (19%)	13 (12%)	2 (33%)	0 (0%)	11 (17%)	3 (12%)	56 (19%)	16 (11%)
Large Cell Carcinoma	12 (5%)	7 (6%)	0 (0%)	0 (0%)	3 (5%)	2 (8%)	15 (5%)	9 (6%)
Mixed Epidermoid Adenocarcinoma	13 (6%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	13 (4%)	2 (1%)
Mucoepidermoid Carcinoma	0 (0%)	1 (1%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	1 (<1%)	1 (1%)
Total Classified	226 (100%)	111 (100%)	6 (100%)	3 (100%)	63 (100%)	26 (100%)	295 (100%)	140 (100%)
Not Classified	5 -	1 -	0 -	0 -	1 -	0 -	6 -	1 -
Total	231 -	112 -	6 -	3 -	64 -	26 -	301 -	141 -

The primary site of the lung cancer was at least partially known for 445 cases (Table 3). Survivors without T65DR dose estimates and the NIC group are included in the table. Cancers were only slightly more frequent in the right lung, compared to the left, and this pattern did not differ significantly between males and females ($p=.60$, based on the χ^2 test for a 2×2 table without correction for continuity). Among 370 cancers arising in the lungs and for which the lobe of origin was known, 203 (55%) occurred in the upper lobes. This proportion was slightly higher among females (73/120; 61%) than males (130/250; 52%), but the difference was not statistically significant ($p=.11$).

肺癌の原発部位は445例について少なくとも部分的に判明している(表3)．表3にはT65DR線量が推定されていない被爆者と市内不在者群が含まれている．癌は左肺と比べて右肺の方が頻度がわずかだが高く，このパターンは男女間で有意な差異はなかった(連続性に対する訂正を行わない2×2表のχ^2検定によればp＝.60)． 肺に発生し，その原発肺葉が判明している370例のうち，203例(55%)は上部肺葉に発症した．この比率は男性(130/250例; 52%)よりも女性(73/120例; 61%)の方が多少高かったが，その差異は統計的に有意ではなかった(p＝.11)．

TABLE 3 DISTRIBUTION OF PRIMARY SITES OF LUNG CANCER AMONG 445 CASES BY SEX (LSS-EXTENDED COHORT; BOTH CITIES, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)

表3 445症例における性別肺癌原発部位分布(寿命調査拡大コホート，両市，全原爆時年齢区分，到達年齢20＋，1950－80年)

Lobe	Sex: Male	Sex: Female	Total
Left Lung			
Upper	68 (22%)	39 (28%)	107 (24%)
Lower	44 (14%)	19 (14%)	63 (14%)
Unknown	25 (8%)	9 (6%)	34 (8%)
Subtotal	137 (45%)	67 (48%)	204 (46%)
Right Lung			
Upper	62 (20%)	34 (24%)	96 (22%)
Middle	11 (4%)	6 (4%)	17 (4%)
Lower	65 (21%)	22 (16%)	87 (20%)
Unknown	24 (8%)	9 (6%)	33 (7%)
Subtotal	162 (53%)	71 (51%)	233 (52%)
Bronchus			
Subtotal	6 (2%)	2 (1%)	8 (2%)
All Sites			
Total	305 (100%)	140 (100%)	445 (100%)

Lung Cancer Incidence and Radiation Dose

The incidence of lung cancer among exposed survivors with T65DR dose estimates is summarized by city, sex, and radiation dose in Table 4, and the standardized incidence rates are illustrated in Figure 1. Two remarkable features are apparent in the figure. The first is the relatively low rates among Nagasaki males exposed to 1-99 rad and Nagasaki females

肺癌発生率と放射線量

T65DR線量が推定されている被爆者における肺癌発生率を表4に都市，性及び放射線量別に要約し，標準化発生率を図1に示した．注目すべき二つの特徴が図1にみられる．第一の特徴は，1－99 rad線量で被爆した長崎の男性と10－99 rad線量で被爆した長崎の女性においては，発生率が比較的低い

exposed to 10-99 rad. The second feature is the absence of any obvious increasing trend with dose above 100 rad. City-specific standardized incidence rates and RRs for both sexes combined are summarized in Table 5; the two features mentioned above are clearly seen in this sex-pooled data. The standardized incidence rates (± one approximate SE) for all doses of 100+ rad are 87.8 ± 10.5 per 10^5 PY and 71.9 ± 12.9 per 10^5 PY for Hiroshima and Nagasaki, respectively. The corresponding standardized rate ratios (100+ rad vs 0 rad) are 2.4 and 1.5, respectively.

ことである．第二の特徴は，100 rad 以上の線量では明らかな増加傾向がないことである．男女合計の都市別標準化発生率と RR を表5に要約した．上述の二つの特徴がこの男女合計データに明確にみられる．100 rad 以上の線量の標準化発生率（±1近似標準誤差）は，広島では10^5 PY 当たり87.8±10.5，長崎では10^5 PY 当たり71.9±12.9である．その対応する標準化発生率比（100＋rad 対 0 rad）はそれぞれ 2.4と1.5である．

TABLE 4 LUNG CANCER INCIDENCE AMONG EXPOSED SURVIVORS WITH T65DR DOSES; BY CITY, SEX, AND T65DR RADIATION DOSE (LSS-EXTENDED COHORT, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)

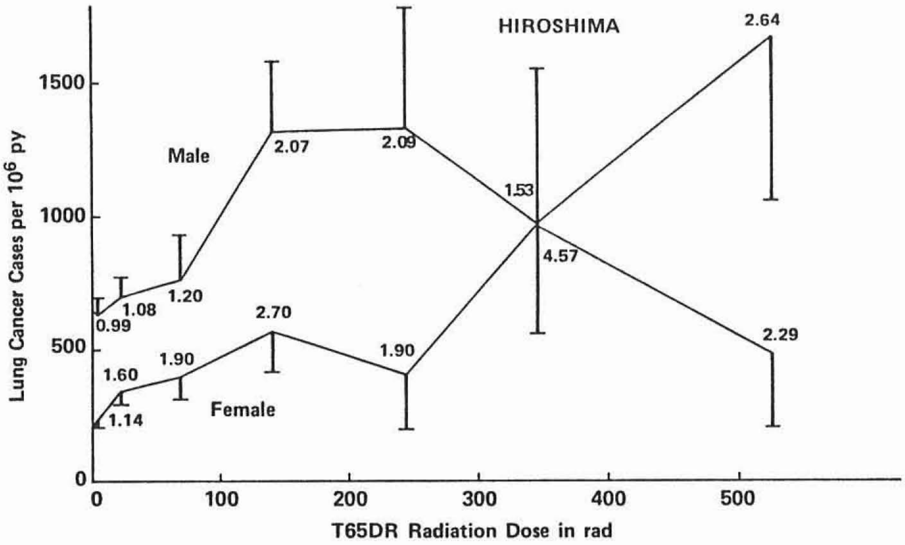
表4 T65DR 線量が推定されている被爆者における肺癌発生率；都市，性及び T65DR 放射線量別（寿命調査拡大コホート，全原爆時年齢区分，到達年齢20＋，1950－80年）

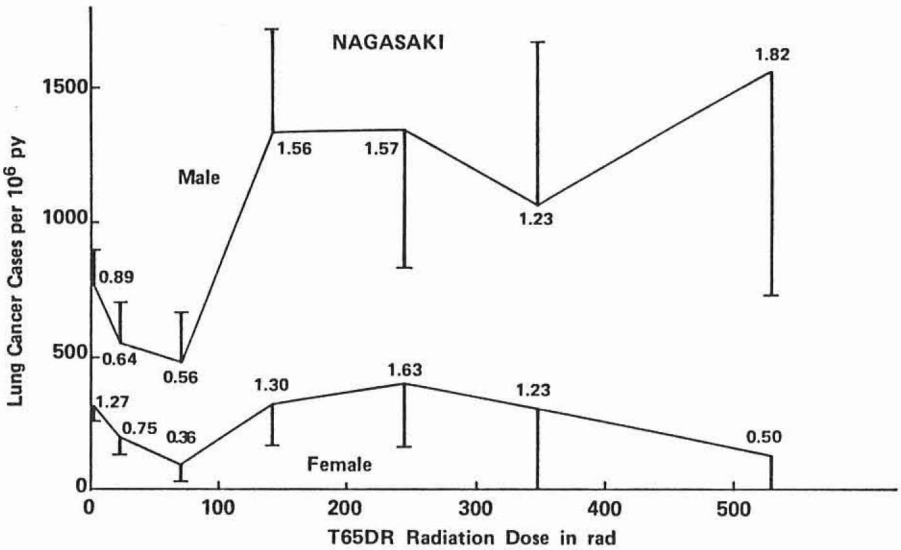
	T65DR Radiation Dose in rad								Total[a]
	0	1-9	10-49	50-99	100-199	200-299	300-399	400+	
				All Exposed Survivors					
Number	31618	22614	14819	4187	3115	1370	635	1582	79940
Mean Dose	0	3	22	71	142	244	345	526	32
				Males, Hiroshima					
Person-Years	244305	153794	91507	22155	16584	6369	3147	5231	543092
Cases	151	89	66	19	25	8	3	8	369
Rate (per 10^5PY)[b]	63.3	62.6	68.5	75.8	131.2	132.3	96.9	167.1	-
Relative Risk	1.00	0.99	1.08	1.20	2.07	2.09	1.53	2.64	-
				Males, Nagasaki					
Person-years	41548	65496	36041	15338	15182	7697	2979	4018	188298
Cases	30	34	15	7	13	7	3	4	113
Rate (per 10^5PY)	85.8	76.1	54.9	48.1	133.6	134.7	105.8	155.8	-
Relative Risk	1.00	0.89	0.64	0.56	1.56	1.57	1.23	1.82	-
				Females, Hiroshima					
Person-Years	399982	220315	163914	42932	24415	9337	5578	6814	873289
Cases	89	55	60	19	14	4	6	3	250
Rate (per 10^5PY)	21.0	23.8	33.4	39.9	56.7	39.8	95.9	47.9	-
Relative Risk	1.00	1.14	1.60	1.90	2.70	1.90	4.57	2.29	-
				Females, Nagasaki					
Person-Years	54261	101935	56140	19853	20044	10541	3777	4606	271158
Cases	11	27	9	2	6	3	1	1	60
Rate (per 10^5PY)	24.8	31.4	18.6	9.0	32.1	40.5	30.5	12.4	-
Relative Risk	1.00	1.27	0.75	0.36	1.30	1.63	1.23	0.50	-

(a) Person-years may not sum to Total due to rounding.
人年は四捨五入のため単純合計ではない．

(b) Directly standardized to adjust for age ATB, attained age, and time since exposure, using the distribution of PY in the 0 rad group for both cities and both sexes combined. Approximate standard errors for rates are shown in Figure 1.
両市及び男女合計の 0 rad 群の PY 分布を用いて，原爆時年齢，到達年齢，被爆後経過期間について調整するために直接標準化した．図1に発生率の近似標準誤差を示す．

FIGURE 1 STANDARDIZED LUNG CANCER RATES BY CITY, SEX, AND RADIATION DOSE (LSS-EXTENDED COHORT, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)
図1 肺癌の標準化率；都市，性及び放射線量別（寿命調査拡大コホート，全原爆時年齢区分，到達年齢20＋，1950－80年）





Adjusted for age ATB, attained age, and time since exposure by direct standardization, based on the distribution of PY in the 0 rad group with both cities and both sexes combined. The numerical values shown in the figure are the ratios of rates in each dose category to the rate for the 0 rad group.

両市及び男女合計の 0 rad 群の PY 分布に基づき，直接標準化により原爆時年齢，到達年齢及び被爆後経過期間を調整した．図に示された数値は 0 rad 群の発生率に対する各線量区分の発生率の比である．

TABLE 5 STANDARDIZED RATES OF LUNG CANCER INCIDENCE AMONG EXPOSED SURVIVORS WITH T65DR DOSES; BY CITY AND T65DR RADIATION DOSE (LSS-EXTENDED COHORT, BOTH SEXES, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)

表5 T65DR線量が推定されている被爆者における肺癌発生の標準化率；都市及びT65DR線量別（寿命調査拡大コホート，男女合計，全原爆時年齢区分，到達年齢20＋，1950－80年）

	T65DR Radiation Dose in rad							
	0	1-9	10-49	50-99	100-199	200-299	300-399	400+
				Hiroshima				
Rate (per 10^5PY)(a)	36.4±2.4	37.8±3.2	45.7±4.1	53.1±8.7	84.3±13.9	76.1±22.1	97.6±33.4	91.9±28.2
Relative Risk	1.00	1.04	1.25	1.46	2.32	2.09	2.68	2.52
				Nagasaki				
Rate (per 10^5PY)	48.3±7.7	48.0±6.2	32.5±6.7	24.5±8.3	68.5±17.7	73.0±24.1	61.2±31.7	69.7±33.2
Relative Risk	1.00	0.99	0.67	0.51	1.42	1.51	1.27	1.44

(a) Cases per 10^5PY ±one approximate SE; directly standardized to adjust for sex, age ATB, attained age, and time since exposure, using the distribution of PY in the 0 rad group for both cities pooled.

10^5 PY当たり症例数±1近似標準誤差；両市合計0 rad群のPY分布を用いて，性，原爆時年齢，到達年齢及び被爆後経過期間について調整するため直接標準化した．

Results of fitting linear RR models of the form [1] for the effect of radiation exposure are summarized in Table 6. The estimates in that table are adjusted for age ATB, attained age, follow-up interval, and, as appropriate, city and/or sex by the use of the parametric background model [2]. For both cities and both sexes combined, the estimated RR at 100 rad is 1.41±0.09. For comparing dose-responses among subsets of the cohort, it is useful to consider the excess RR. Calculated as one less than the estimated RR at 100 rad, this gives the rate at which RR increases for each dose increment of 100 rad. As indicated in Table 6, the excess RR for Hiroshima (0.56±0.12 per 100 rad) is nearly three times larger than that for Nagasaki (0.19±0.11). Moreover, among Hiroshima survivors, the excess RR for females (0.83±0.24 per 100 rad) is nearly twice that for males (0.43±0.14), although the difference is only marginally significant (one-sided p=.06). The excess RR for Nagasaki females is slightly lower than that for Nagasaki males: 0.15±0.19 vs 0.20±0.13 per 100 rad, respectively; however, due to the unusual shape of the Nagasaki dose-response, this was not analyzed in further datail. Appendix Table 1 gives the full set of parameter estimates for the model with city-by-sex-specific dose-responses.

放射線被曝の影響について型式〔1〕の線形RRモデルを適合させた結果を表6に要約した．表6の推定値はパラメトリックバックグラウンドモデル〔2〕を用いて，原爆時年齢，到達年齢，追跡調査期間並びに適切なとき都市又は性について調整した．両市と男女を合計した場合，100 radの推定RRは14.1± 0.09である．このコホートの各群間の線量反応の比較には，過剰RRを考慮すると有益である．100 radでの推定RRよりも小さいRRとして算定すれば，線量100 radの増加に対するRRの増加の割合がわかる．表6に示されるように，広島の過剰RR(100 rad当たり0.56± 0.12)は長崎の過剰RR(0.19± 0.11)の約3倍である．更に，広島の被爆者においては，女性の過剰RR(100 rad当たり0.83± 0.24)は男性の過剰RR(0.43± 0.14)の約2倍であるが，その差はごくわずかに有意である(片側検定p=.06)．長崎の女性の過剰RRは長崎の男性の過剰RRより若干低く，それぞれ100 rad当たり0.15± 0.19，0.20± 0.13であるが，長崎の線量反応の形が異常だったため更に詳しく解析しなかった．付録表1は性及び都市別線量反応モデルのパラメーター推定値一式を示している．

TABLE 6 RADIATION DOSE-RESPONSE[a] FOR LUNG CANCER INCIDENCE AMONG EXPOSED SURVIVORS WITH T65DR DOSES; BY CITY, SEX, AND RADIATION DOSE RANGE (LSS-EXTENDED COHORT, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)
表6 T65DR線量が推定されている被爆者における肺癌発生率に関する放射線量反応[a]；都市，性及び放射線量範囲別(寿命調査拡大コホート，全原爆時年齢区分，到達年齢20＋，1950－80年)

City	Sex		
	Male	Female	Both
	All Radiation Doses		
Hiroshima	1.43 ± .14[b]	1.83 ± .24	1.56 ± .12
Nagasaki	1.20 ± .13	1.15 ± .19	1.19 ± .11
Both	1.34 ± .10	1.56 ± .17	1.41 ± .09
	Only Doses Less than 100 rad		
Hiroshima	1.30 ± .37	2.59 ± .61	1.78 ± .33
Nagasaki	0.46 ± .36	0.18 ± .44	0.38 ± .29
Both	1.01 ± .28	1.90 ± .47	1.32 ± .25

(a) Based on T65DR dose estimates. T65DR推定線量に基づく.

(b) Estimated RR at 100 rad ± one approximate SE, based on linear RR model [1].
線形RRモデル[1]に基づく100 rad推定RR±1近似標準誤差.

The estimated number of excess cases induced by A-bomb radiation (calculated as described by Preston et al[7]) is 76.2, which corresponds to an absolute excess risk of 1.5 cases per 10^6 PY-rad. Since these radiogenic cases are necessarily included among the 511 cases in survivors exposed to 1+rad, the estimated attributable risk is 15% (76.2/511).

Figure 1 indicates that even for Hiroshima the RR may not increase linearly over the entire range of radiation doses. Since accurate estimation of risks associated with exposures to low doses is of particular importance, Table 6 also gives results based only on doses less than 100 rad. For both sexes combined, the excess RR for Hiroshima increases to 0.78 ± 0.33 per 100 rad, while the apparent dose-response is negative for Nagasaki. Also the difference between the sexes in Hiroshima becomes even more pronounced; 1.59 ± 0.61 for females vs 0.30 ± 0.37 for males ($p=0.03$).

Table 7 gives the radiation dose-response by categories of age ATB and/or attained age. The entries in Table 7 are based on the parametric background model [2], and common linear RR functions are estimated for both cities and both sexes. Categories with age ATB less than

原爆放射線誘発の過剰症例の推定数(Prestonら[7]が報告したように算定された)は76.2で，これは10^6 PY-rad当たり1.5例の絶対過剰リスクに相当する．これらの放射線関連症例は1＋rad線量の被爆者の511例に必ず含まれているので，推定帰因危険度は15%(76.2/511)である．

図1は，広島でさえもRRは放射線量全範囲にわたり線形に増加しないかもしれないことを示す．低線量被曝領域におけるリスクの正確な推定が特に重要であるので，表6は100 rad以下の線量のみに基づいて得られた結果も示した．男女合計で，広島の過剰RRは100 rad当たり0.78± 0.33まで増加する一方，長崎では見かけ上の線量反応は負である．また広島の男女差はもっと顕著になり，女性1.59± 0.61に対し男性は0.30± 0.37(p＝0.03)である．

表7は原爆時年齢及び到達年齢区分別放射線量反応を示す．表7の記載事項はパラメトリックバックグラウンドモデル[2]に基づき，両市及び男女についても共通線形RR関数を推定した．原爆時年齢が9歳以下

9 years or attained age less than 40 years are excluded from Table 7. This was done to eliminate categories for which the dose-response cannot be estimated precisely; only 10 cases occurred in those categories. Notice that the overall estimated RR at 100 rad, when limited to persons 10+ years old ATB and after the fifth decade of life, is 1.42 ± 0.09, which is almost identical to the corresponding value in Table 6.

の区分あるいは到達年齢が40歳以下の区分は表7から除外した．線量反応を正確に推定できない区分を削除するためにこのような除外を行ったが，これらの区分に10症例だけ発生した．100 rad の総推定 RR は，原爆時年齢10歳以上で到達年齢40歳以上の人に限定すれば，1.42± 0.09であり，表6の対応する値とほぼ同じである．

TABLE 7 RADIATION DOSE-RESPONSE[(a)] FOR LUNG CANCER INCIDENCE AMONG EXPOSED SURVIVORS WITH T65DR; BY AGE ATB AND ATTAINED AGE (LSS-EXTENDED COHORT, BOTH CITIES, BOTH SEXES, 1950-80)

表7 T65DR 線量が推定されている被爆者における肺癌発生率に関する放射線量反応，[(a)] 原爆時年齢及び到達年齢別（寿命調査拡大コホート，両市，男女合計，1950－80年）

Age ATB	Attained Age				
	40-49	50-59	60-69	70+	All 40+
10-19	1.99 ± .58 (19)[(b)]	2.37 ± .95 (8)			2.08 ±.50 (27)
20-29	1.74 ± .68 (8)	2.02 ± .48 (32)	1.67 ±.76 (9)		1.87 ±.36 (49)
30-39	0.81 (6)[(c)]	1.05 ± .22 (38)	1.29 ±.22 (83)	1.56 ±.50 (23)	1.23 ±.15 (150)
40-49	- (0)[(d)]	1.95 ± .63 (21)	1.36 ±.20 (118)	1.27 ±.16 (178)	1.35 ±.12 (317)
50+		5.3 ± .61 (3)	1.56 ±.47 (30)	1.34 ±.16 (206)	1.38 ±.16 (239)
All 10+	1.70 ±.39 (33)	1.66 ± .24 (102)	1.37 ±.14 (240)	1.32 ±.12 (407)	1.42 ±.09 (782)

(a) Based on T65DR dose estimates.
T65DR 推定線量に基づく．

(b) Estimated RR at 100 rad ± one approximate SE, based on linear RR model [1]. Number of cases is given in parentheses.
線形 RR モデル〔1〕に基づく100 rad における推定 RR ±1近似標準誤差．症例数を括弧内に示す．

(c) Minimum feasible value of RR at 100 rad, based on linear RR model.
線形 RR モデルに基づく100 rad における RR 最小実行値

(d) Not estimable, since no cases occurred.
症例がなかったので推定不可能

As shown in Table 7, RR tends to increase with decreasing age ATB, although the trend is only marginally significant (one-sided p=.04, based on a test for loglinear trend in age ATB). A similar effect is observed for attained age (p=.07) if age ATB is ignored. The two age variables are highly correlated in these data, however, so after allowing for the loglinear trend of excess RR in relation to age ATB, there is no significant additional effect of attained age (p=.46). Moreover, although the excess RR appears, very generally, to increase with attained age among the three youngest ATB groups and to decrease with attained age among the two oldest ATB

表7に示されているように，RR は原爆時年齢が下がるにつれ増加する傾向があるが，その傾向はごくわずかに有意である（原爆時年齢における対数線形傾向検定によれば p＝.04）．原爆時年齢を考慮しなければ到達年齢にも同様な影響が観察される（p＝.07）．二つの年齢変数はこれらのデータでは高い相関性があるが，原爆時年齢に関連した過剰 RR の対数線形傾向を考慮したら，到達年齢の有意な相加的な影響はない（p＝.46）．更に，過剰 RR は，ごく一般的ではあるが，三つの最も低い原爆時年齢群では到達年齢に伴い増加し，二つの最も高い原爆時年齢群では到達年齢に伴い減少するように思わ

groups, the interaction between the effects on the excess RR of age ATB and attained age is not statistically significant, after allowing for the effect of age ATB ($p=.88$).

The differences between Hiroshima and Nagasaki; between the sexes for Hiroshima survivors; and between the categories of age ATB are illustrated in Figure 2. The estimated RR at 100 rad is consistently largest for Hiroshima females, and smallest for Nagasaki survivors. The RRs are also largest in each case for persons 10-29 years old ATB. There is also a suggestion in Figure 2 that the RRs increase slightly with increasing age ATB above the age of 30 years ATB, however, the data are quite adequately fit by a loglinear model, according to which the RRs decrease monotonically with increasing age ATB. This loglinear effect of age ATB does not vary significantly among the three groups in Figure 2 ($p=.47$). Parameter estimates for the model corresponding to Figure 2, but with the loglinear effect of age ATB on excess RR, are given in Appendix Table 1.

Dose-Response by Histological Type

To examine the effect of exposure to A-bomb radiation on the risks of specific histological types of lung cancer, attention was restricted to the 343 confirmed cases among exposed survivors with T65DR dose estimates (Table 2). The proportion of the cases which were confirmed for this study tended to be higher in the high radiation dose categories: 205/486 (42%), 110/255 (43%), and 28/51 (55%) for the 0-9, 10-199, and 200+ rad groups, respectively. Therefore, analyses based only on confirmed cases will be subject to bias in the estimation of the radiation dose-response. For example, the estimated RR at 100 rad based on the 343 confirmed cases is 1.56 ± 0.15, which is greater than the corresponding estimate, 1.41 ± 0.09, based on all 792 cases (Table 6).

If it is assumed that these biases affect all histological types equally, then comparisons among histology-specific effects of radiation will be unbiased. Figure 3 displays the RRs associated with each dose category for the three major histological types; adenocarcinoma, epidermoid carcinoma, and small cell carcinoma. These RRs are adjusted for city, sex, age ATB, attained age, and interval of follow-up by the nonparametric background model, rather than

れるが，原爆時年齢と到達年齢の過剰 RR に対する影響は原爆時年齢の影響を考慮したら統計的に有意ではない（p＝.88）.

広島・長崎間の差異，広島の被爆者の男女間の差異，並びに原爆時年齢区分間の差異を図2に示した．100 rad での推定 RR は一貫して広島の女性で最大であり，長崎の被爆者で最小である．RR はまた原爆時年齢10－29歳の対象者ではどの場合でも最大である．図2では，RR が原爆時年齢30歳以上で原爆時年齢が上がるにつれて多少増加することを示唆しているが，原爆時年齢が上がるにつれ RR が単調に減少する対数線形モデルによるとデータはよく適合している．原爆時年齢のこの対数線形効果は図2の三つのグループではさほど有意な差異はない（p＝.47）．図2に対応するモデルで，過剰 RR に対して原爆時年齢の対数線形影響を有するモデルのパラメーター推定値を付録表1に示した．

組織型別線量反応

肺癌の組織型別のリスクに対する原爆放射線被曝の影響を調べるために，対象を T65DR 線量が推定されている被爆者のうち肺癌の確認された343症例に限定した（表2）．本調査のために確認された症例の比率は，0－9 rad 群，10－99 rad 群，200＋rad 群でそれぞれ 205/486（42%），110/255（43%），28/51（55%）のように，放射線量の高い区分の方が高い傾向があった．したがって，確認症例のみに基づいて行われる解析は放射線量反応の推定において偏りを生じやすい．例えば，343の確認症例に基づく 100 rad での推定 RR は1.56±0.15で，これは 792の全症例に基づく推定 RR 1.41± 0.09（表6）よりも大きい．

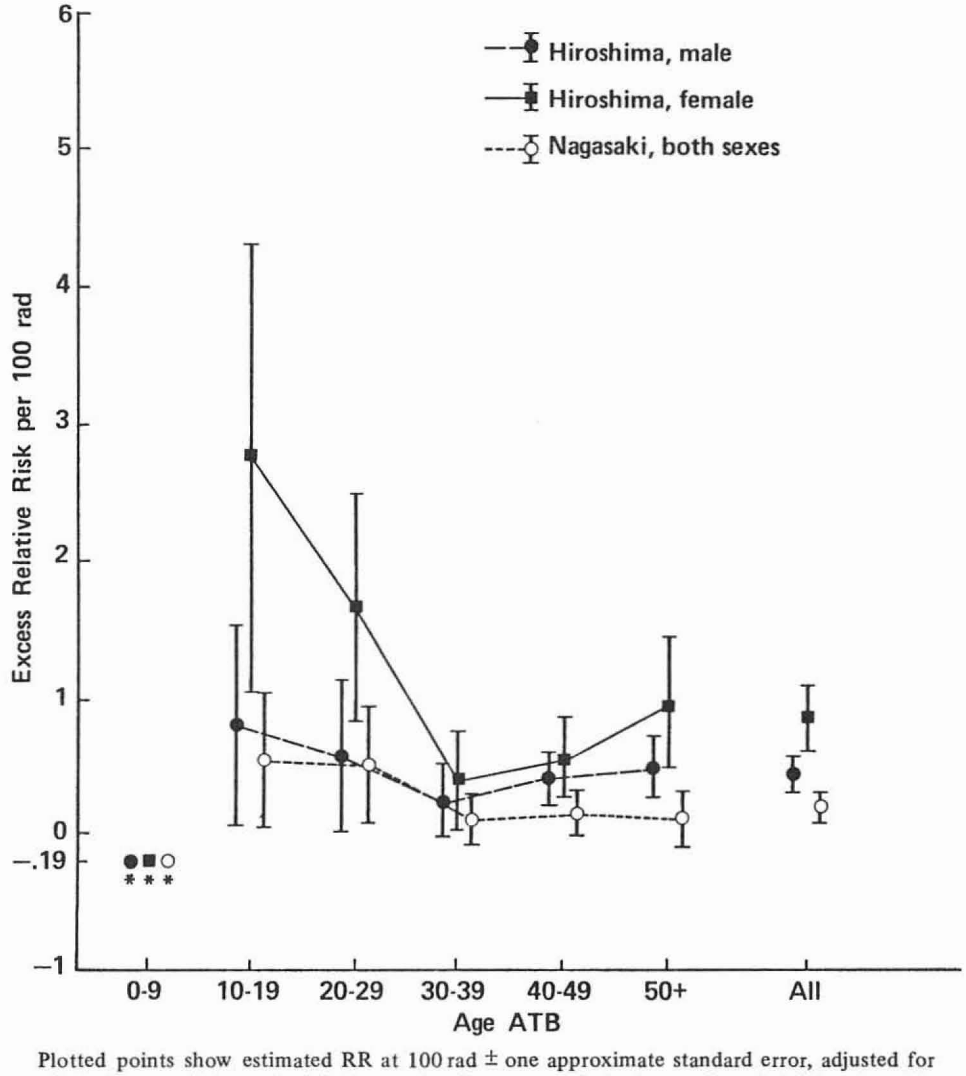
これらの偏りがすべての組織型に等しく影響を及ぼすと考えられるなら，放射線の組織型別影響の比較には偏りがないはずである．図3は三つの主要組織型である腺癌，類表皮癌及び小細胞癌について各線量区分に関連した RR を示した．これらの RR は，〔2〕よりむしろ非パラメトリックバックグラウンドモデルを用いて，性，都市，原爆時年齢，到達年齢及び追跡調査期間について調整されている．〔1〕によれ

[2]. Based on [1], the estimated RRs at 100 rad are 1.58±0.25, 1.48±0.26, and 2.14±0.54 for these three types, respectively. Although the excess RR for small cell carcinoma is twice as large as that for adenocarcinoma, the dose-response does not differ significantly among the three histological types (p=.44).

ば，これら三つの組織型の100 radでの推定RRはそれぞれ1.58±0.25，1.48±0.26，2.14±0.54である．小細胞癌の過剰RRは腺癌の過剰RRの2倍であるが，三つの組織型では線量反応に有意な差はない(p=.44)．

FIGURE 2 RADIATION DOSE-RESPONSE BY CITY, AGE ATB, AND, SEX FOR HIROSHIMA (LSS-EXTENDED COHORT, ATTAINED AGE 20+, 1950-80)

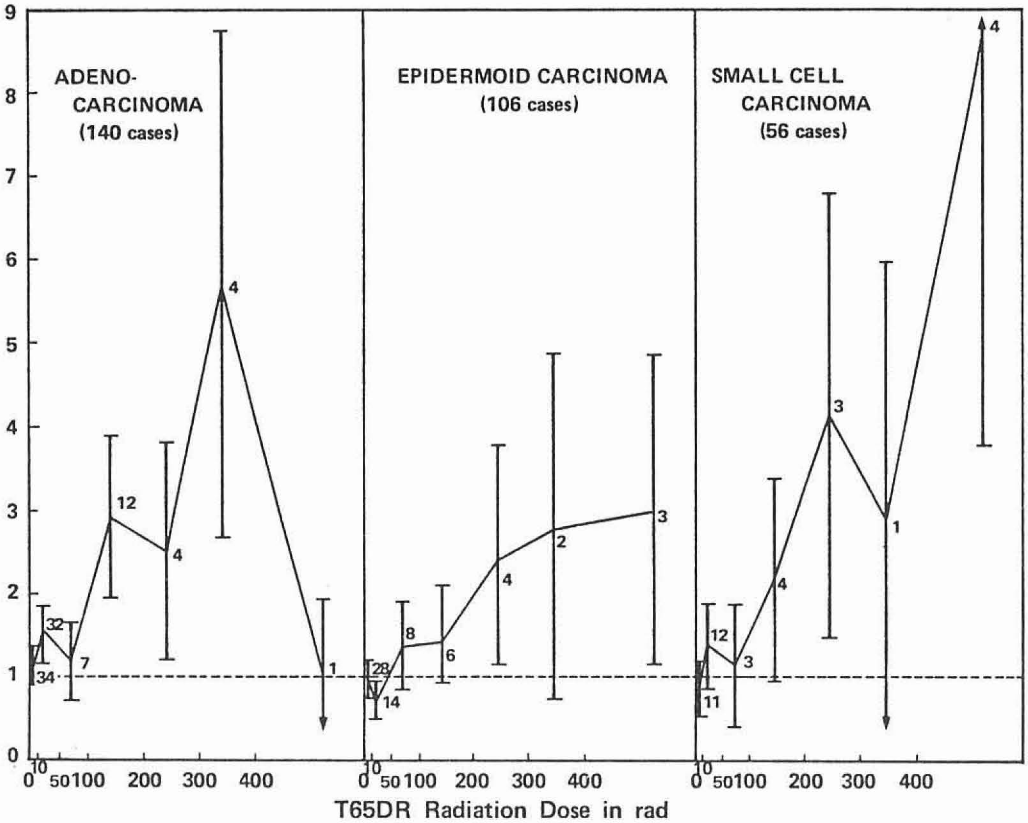
図2 放射線量反応，都市，原爆時年齢及び性別，広島(寿命調査拡大コホート，到達年齢20+，1950−80年)



Plotted points show estimated RR at 100 rad ± one approximate standard error, adjusted for attained age and interval of follow-up by the parametric background model [2]. Asterisks indicate that RR or lower end of standard error bar is set at the minimum feasible value.

記入された点は，パラメトリックバックグラウンドモデル[2]を用いて，到達年齢及び追跡調査期間を調整した100 radにおける推定RR±1近似標準誤差を示す．星印はRR，すなわち標準誤差棒の下端が最小実行値でセットされていることを示す．

FIGURE 3 RELATIVE RISK OF LUNG CANCER INCIDENCE BY RADIATION DOSE CATEGORY AND HISTOLOGICAL TYPE (LSS-EXTENDED COHORT, BOTH CITIES, BOTH SEXES, ALL AGES ATB, ATTAINED AGE 20+, 1950-80)
図3 肺癌発生率の相対危険度，放射線量区分及び組織型別（寿命調査拡大コホート，両市，男女合計，全原爆時年齢区分，到達年齢20＋，1950－80年）



Adjusted for city, sex, age ATB, attained age, and interval of follow-up by use of the stratified background model [2]. Points are plotted at average doses given in Table 4. Bars indicate ± one approximate standard error; arrows indicate when error bars extend beyond the range of the RR axis. Numbers of cases in each dose category above 0 rad are indicated in the figure.
層化バックグラウンドモデル〔2〕を用いて都市，性，原爆時年齢，到達年齢，追跡調査期間を調整した．表4に示した平均線量を用いて描記した．棒は±1近似標準誤差を示し，矢印は誤差棒がRR軸の範囲を越えることを示す．0 rad 以上の各線量区分の症例数を図中に示した．

DISCUSSION

The purpose of this report is to provide an overview of lung cancer in the LSS-extended cohort during 1950-80. Examination of the histopathologic features of the cancers in this cohort has necessarily been limited to less than half of the 1,057 cases detected, since tissue specimens were not available for 615 cases (Table 1). Among the 442 cases from which specimens were examined for this study, the

考　察

本報の目的は，1950年から1980年までの寿命調査拡大コホートにおける肺癌を全般的に検討することである．このコホートにおける癌の病理組織学的特徴の検討は，615例について組織標本が入手されていなかったので必然的に，検出された1,057例の半分以下に限られた（表1）．本調査のために組織標本を検査

pathological findings were generally consistent with those reported for other populations. For example, the predominance of adenocarcinoma among histological types has been reported for Japanese in Tokyo[18] and for Japanese women in Hawaii.[19] This contrasts with the predominance of epidermoid carcinoma in western populations. Ives et al[20] summarized sex-specific distributions of histological types of lung cancer in their Table 3 (derived from a review by Modan[21] of studies done in 10 different nations, mostly European and not including Japan). The patterns of histological types in their summary was similar to that shown here in Table 2. However, some variations between populations do exist. For example, Vincent et al[22] in a review of lung cancer patients seen at Roswell Park Memorial Institute (RPMI) during 1962-75 found that small cell carcinoma was relatively more frequent among women than men, while the opposite is true for the LSS-extended cohort (Table 2). However, in the RPMI series, epidermoid carcinoma and adenocarcinoma were the predominant types among males and females, respectively,[22] which is consistent with the present results (Table 2). Such variations may be attributable to genetic differences between Japanese and US populations, to differences in patterns of etiology, and/or to differences in diagnostic criteria and practice (42% of the RPMI[20] series were based on confirmation of autopsy data, compared to 85% (376/442) in the present study). It is interesting that the overall relative frequencies of small cell carcinoma were roughly comparable between the two series (19% for RPMI, 17% for the LSS extended), although it has been suggested that small cell carcinoma is reported more frequently from autopsy diagnoses, compared to surgical, biopsy, or cytological diagnoses.[20]

した442例では，病理学的所見は他の集団について報告された所見と大体一致していた．例えば，組織型のうち腺癌が優勢であることが東京の日本人[18]とハワイの日本人女性[19]について報告されている．これは欧米人の間で類表皮癌が優勢であることと対照的である．Ivesら[20]は肺癌の組織型の性別分布を彼らの報告の第3表にまとめた(主としてヨーロッパの国で日本を含まない10か国で行われた調査をModan[21]が検討したものを資料としている)．彼らのまとめた第3表の肺癌組織型様式は表2に示された様式と類似していた．しかし，調査集団間には若干差異がある．例えば，Vincentら[22]が1962－75年のRoswell Park Memorial Institute(RPMI)で観察された肺癌患者を検討したとき，小細胞癌の発生頻度は男性よりも女性の方が比較的高かったが，寿命調査拡大コホートではその逆である(表2)．しかし，RPMI症例では男性では類表皮癌，女性では腺癌が優勢組織型であった．[22] これは本報の結果と一致する(表2)．このような差異は，日本人集団とアメリカ人集団との遺伝的差異，病因の様式の差異又は診断基準及びその実際面での差(本調査の85%(376/442)と比較して，RPMI症例[20]では42%が剖検データの確認に基づいていた)によるかもしれない．小細胞癌の相対頻度は全般的に二つの集団間でおおよそ等しい(RPMIは19%，寿命調査拡大は17%)が，外科診断，生検診断あるいは細胞診断と比較して剖検診断から報告される小細胞癌の頻度が高いことが示唆されていることは興味深いことである．[20]

Exposure to A-bomb radiation significantly increased the risk of lung cancer among the 79,940 exposed survivors with T65DR dose estimates. This is consistent not only with other studies of A-bomb survivors,[3-7] but with studies of patients with ankylosing spondilitis as well.[23,24]

T65DR線量が推定されている被爆者79,940人において原爆放射線被曝により肺癌リスクが有意に増加した．これは被爆者の他の調査[3-7]のみならず強直性脊椎炎患者の調査[23,24]とも一致している．

The differences between the radiation dose-responses of the two cities (Figures 1 and 2) is partly attributable to the use of T65DR dose estimates. Preliminary results based on an

放射線量反応の両市間の差(図1及び図2)の原因の一部はT65DR推定線量を使用したことにある．改訂推定線量の暫定値に基づく予備結果[12]は，日米線量

interim set of revised dose estimates[12] suggest that such city differences will be largely eliminated by the eventual adoption of a revised dosimetry upon completion of the US-Japan dose reassessment project. Still the exceptionally low lung cancer rates among Nagasaki survivors exposed to 1-100 rad remains unexplained.

再評価が完了し，最終的に改訂線量が採用されれば，このような都市間の差は大部分なくなることを示唆している．しかし，1－100 rad の線量に被曝した長崎の被爆者における例外的に低い肺癌率は説明されないままである．

Among Hiroshima survivors, women experienced significantly greater RR of radiogenic lung cancer incidence than men. In a recent survey of cancer mortality, a similar sex effect was observed for lung cancer.[7] The effect was shown to arise because women experienced absolute (additive) excess risks similar to those of men, but background rates substantially lower than men.[7] This is also seen in the parameter estimates for [2] given in Appendix Table 1. The background rate for women is only about $\exp(-1.01) \times 100 = 36\%$ of the background rate for men, a highly significant difference ($p<.0001$). This difference is most likely largely attributable to differences in smoking habits. Since smoking data were available for only a subset of the LSS-extended cohort, an analysis of the joint effects of smoking and A-bomb radiation on the incidence of lung cancer is given in a separate report.[25]

広島の被爆者においては，男性よりも女性の方に放射線誘発肺癌発生率の RR が有意に高い．最近の癌死亡率調査において，肺癌について同様な性差が観察された．[7] 女性の絶対（相加）過剰リスクは男性と同じであるが，バックグラウンド発生率は男性よりも相当低いので，この性差が生じた．これは付録表1に示されている〔2〕のパラメーター推定値にもみられる．女性のバックグラウンド発生率は男性のわずか約 $\exp(-1.01) \times 100 = 36\%$ であり，これは大きな有意差である($p < .0001$)．この差異は大部分喫煙習慣の差に起因すると考えられる．喫煙習慣データは寿命調査拡大コホートのうちの一群についてのみ入手されていたので，肺癌発生率に対する喫煙と原爆放射線の合同影響の解析を別の報告書に示した．[25]

Based on cases diagnosed during 1950-80, those exposed at young ages ATB have experienced greater RR of radiogenic lung cancer than those who were older. This pattern has been observed for mortality from several nonleukemic cancers.[7] Further follow-up of the cohort will be necessary in order to determine the effect that exposure in youth to radiation will have on the full lifetime risk of lung cancer; at the end of 1980, persons aged 0-20 ATB were no older than 56.

1950－80年に診断された症例によると，低年齢時被爆者の方が高年齢時被爆者よりも放射線誘発肺癌 RR が高い．この傾向は幾つかの白血病を除いた癌による死亡に観察されている．[7] 低年齢時の放射線被曝が肺癌の終身リスクに及ぼす影響を調べるためにコホートを引き続いて追跡観察する必要がある．原爆時年齢0－20歳の人は1980年の末に56歳に達していない．

The radiation dose-responses of the three major histological types of lung cancer (Figure 3) were not significantly different, although small cell carcinoma appeared to be slightly more radiosensitive than adenocarcinoma or epidermoid carcinoma. This lack of statistical significance may derive from the comparatively small numbers of cases of each type and the consequent lack of statistical power, a common weakness of studies seeking to compare the radiosensitivities of specific types of lung cancer.[20] The present data, while not conclusive in this regard, support a tentative conclusion that all three histological types are susceptible to induction by radiation.

肺癌の三つの主要組織型の放射線量反応（図3）には有意な差異はなかったが，小細胞癌は腺癌や類表皮癌よりも多少放射線感受性が高いようであった．このように統計的に有意な差が見られなかったのは各組織型の症例数が比較的少ないことと，その結果，統計検定力が弱いためかもしれない．これは特定組織型の肺癌の放射線感受性の比較を目的とする調査に共通してみられる弱点である．[20] この点に関して現在のデータは決定的なものではないが，三つの組織型はすべて放射線によって誘発しやすいという暫定的結論を支持している．

APPENDIX TABLE 1 MAXIMUM LIKELIHOOD ESTIMATES FOR SELECTED MODELS OF LUNG CANCER INCIDENCE AMONG EXPOSED SURVIVORS WITH T65DR DOSES

付録 表1 T65DR線量が推定されている被爆者における肺癌発生率の選択モデルの最大尤度推定値

Variable	Coefficient	Model #1	Model #2
		Background Incidence Rates: model [2]	
Constant (1950-54)	$\alpha_0^{(1)}$	3.828 ± 0.281 [(a)]	3.791 ± 0.283
Constant (1955-58)	$\alpha_0^{(2)}$	4.552 ± 0.200	4.516 ± 0.203
Constant (1959-62)	$\alpha_0^{(3)}$	5.457 ± 0.137	5.422 ± 0.141
Constant (1963-80)	$\alpha_0^{(4)}$	6.033 ± 0.094	5.999 ± 0.099
City (H=0, N=1)[(b)]	α_1	0.163 ± 0.101	0.155 ± 0.100
Sex (M=0, F=1)[(b)]	α_2	-1.006 ± 0.085	-1.008 ± 0.082
ATB − 30	α_3	0.020 ± 0.006	0.023 ± 0.006
ℓn (ATT/50)	α_4	5.098 ± 0.499	5.132 ± 0.503
$[\ell n\ (\mathrm{ATT}/50)]^2$	α_5	-2.793 ± 0.803	-2.851 ± 0.810
		Radiation-Related Excess RR: $RR(d;i) = \beta d \exp[\beta_1(\mathrm{ATB}-30)]$	
Dose (H, M)[(b)]	β	0.427 ± 0.136	0.548 ± 0.199
Dose (H, F)[(b)]	β	0.832 ± 0.236	1.056 ± 0.331
Dose (N, M)[(b)]	β	0.197 ± 0.131	- (c)
Dose (N, F)[(b)]	β	0.149 ± 0.186	- (c)
Dose (n, M+F)[(b)]	β	- (c)	0.256 ± 0.145
ATB − 30	β_1	- (c)	-0.026 ± 0.016

(a) Parameter estimate ± one approximate SE
パラメーター推定値±1近似標準誤差

(b) H=Hiroshima, N=Nagasaki, M=Male, F=Female
広島 長崎 男性 女性

(c) Variable omitted from model
変数をモデルから省略した

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