AGING STUDIES IN ATOMIC BOMB SURVIVORS

原爆被爆者における加齢の研究

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SUMMARY

Although the studies of the effect of ionizing radiation on atomic bomb survivors have not produced any evidence of radiation-induced aging, there have been studies on experimental animals and man which suggest accelerated aging after exposure to ionizing radiation. To determine if certain physiologic functions could be related to exposure to ionizing radiation, a battery of age-related tests was given at the time of the physical examinations at ABCC.

Some 11,351 persons were given these non-invasive age-related tests. The results were essentially negative. Until a satisfactory operational definition of biologic or physiologic age is developed, the administration of functional tests as a measure of aging does not seem justified.

BACKGROUND

Premature aging and death have been ascribed to whole-body radiation in experimental animals.1-4 In man, a variety of disease states associated with radiation have been reported.5 The studies of mortality experience of physicians and radiologists in the United States and the United Kingdom⁶⁻¹¹ point to the carcinogenic, including the leukemogenic, effects of ionizing radiation exposure. The excess mortality observed in these studies is primarily due to neoplastic diseases, and does not provide evidence for radiation-induced aging. In the studies of the A-bomb survivors, 12-14 the increased mortality from cancer has been observed, but there has not been a general increase in mortality from natural causes to

要約

原爆被爆者における電離放射線の後影響をみる種々の調査からは、放射線による加齢の証拠が観察されていないが、電離放射線被曝後の加齢の促進を示唆するような、動物実験による研究やヒトに関する調査は行われている。生理学的機能が電離放射線被曝と関係しているかどうかを調べるために、ABCCにおける健康診断の時に年齢と関係のある一連の検査を行った。

年齢と関係のある簡単な検査が11,351人に対して行われた。結果は本質的には陰性的なものであった。 生物学的または生理学的年齢に関して運用できる満足な定義が開発されない限り、加齢の尺度として機能検査を行うことは妥当ではないと思われる。

背 景

実験動物においては、放射線の全身照射により早期加齢及び早期死亡が起こるとされている.1-4 ヒトにおいては、放射線被曝に伴う種々の疾病状態が報告されている.5 米国及び英国の医師及び放射線科医についての死亡率調查6-11において電離放射線被曝による白血病誘発を含む発癌影響のあることが指摘されている。これらの調査に見られる死亡率の増加は主として新生物性疾患によるものであり、放射線誘発性の加齢によるという証拠はない。原爆被爆者の調査12-14では、癌による死亡率の増加がみられたが、加齢促進の仮説を裏書きするような癌以外の病死因

support the hypotheses of accelerated aging. Premature aging caused by ionizing radiation has not been documented. 4.15.16

Many physiologic processes, changed with increasing age and a number of them have been observed among Japanese exposed to a single dose of radiation from the A-bomb (Appendix Table A). The studies showing no changes associated with A-bomb exposure involved tests on Achilles tendon reflex time, electrocardiograms, ballistocardiograms, isoantibody levels, cold pressor responses (systolic pressure). ventilatory function, resting blood pressure, serum cholesterol, immunoglobulin levels, responses to glucose, and many others. 17-31 On the other hand, many functional tests are correlated with chronological age. The nature of these correlations as well as the relationship of other kinds of tests to age have been summarized by Finch and Beebe. 32 In some of the age-related observations, the survivors of heavy exposure to A-bomb radiation have revealed more intensive changes than nonexposed persons. These can be summarized as follows:

Morphologic changes in mucosal capillaries seen in Japanese exposed in childhood were similar to those found in older persons.³³

Aging and radiation independently produces increases in chromosome aberrations. It is not known if these influences are additive. ^{34,35}

Mortality from neoplasia, which generally increases with age, is more prevalent among heavily exposed A-bomb survivors.³⁶

The present study is based on a battery of tests devised by Hollingsworth et al²³ during 1958-60 as indicators of aging. It was undertaken to investigate further the relationship of age-related physiologic functions to exposure to ionizing radiation by examining the results of each test separately and linking them together in an index of aging.²⁸

MATERIAL AND METHODS

The population tested consists of survivors who have cooperated in a long-term study of possible delayed effects of the A-bomb by participating in biennial examinations at ABCC in Hiroshima and Nagasaki.³⁷ Dosimetric information is available for each member of the cohort under

による死亡率の総体的な増加はなかった。電離放射線による早期加齢はまだ報告されていない。4,15,16

多くの生理学的過程は年齢に伴って変化しており、その多くは1回の原爆放射線線量に被曝した日本人に観察された(付録、表A).原爆放射線被曝と関係のある変化を示さなかった検査としてはアキレス腱反射時間,17 心電図,18 心弾図,19 同種抗体値,20 寒冷昇圧反応(収縮期圧),21 肺換気機能,22 安静時血圧,23 血清コレステロール,23 免疫グロブリン値,24.25 ブドウ糖反応26 などその他多くの検査27-31 がある.一方,多くの機能検査は暦年齢と相関がある。これらの検査との相関の性質及びその他の検査と年齢との関係はFinch 並びにBeebe32 によって要約されている。年齢と関係のある所見の一部において、高線量の原爆放射線被曝者は非被曝者よりも強い変化を示した。これを次に要約して示す。

小児期に被曝した日本人に見られる粘膜毛細血管の形態的変化はより高齢の人に見られる変化に類似していた。33

加齢及び放射線はそれぞれ独自に染色体異常の 増加をもたらす。これらの影響が相加的であるか どうかは分からない。^{34,35}

新生物による死亡率は一般に年齢に伴って増加 するが,高線量の原爆放射線被曝者ではいっそう その率が高い.36

本調査は、1958-60年にかけて加齢の指標として Hollingsworth ら²³ が考案した一連の検査を基に、 各検査の結果を個々に検討すると共にそれらを一つの 加齢指標にまとめることによって、年齢と関係のある 生理学的機能と電離放射線被曝の関係²⁸ をさらに調 べるために実施された。

対象者及び方法

検査の対象となったのは、広島及び長崎 ABCCで 2年ごとに検診を受けて原爆の後影響の長期的研究 に協力している被爆者である.³⁷ 観察中のコホート の各対象者については線量推定が行われている.³⁸ observation.³⁸ The present study differs from previous ABCC studies involving aging tests because of the larger cohort on which the measurements were made.

A total of 11,351 persons exposed to varying doses of ionizing radiation from the A-bomb were given a battery of noninvasive age-related tests between July 1970 and June 1972 during the 8th cycle of biennial examinations at ABCC. The age at the time of examination (ATE), sex of the examinees, and dose distribution in the two cities are shown in Appendix Table B.

Aging Tests

The instruments and testing methods were devised by Hollingsworth et al^{23,28} and have been previously described. The following tests were used:

Hand grip strength was measured by a dynamometer in kilograms for both left and right hands. Grip strength devices were calibrated using known weights.

Skin elasticity was measured in time required for a standard pinch to flatten (Hiroshima only).

Perception of vibration was measured as the voltage intensity required for perception. An electric vibrometer was applied at the ankle.

Reaction time to a complex task was measured by the Bogitch light-extinction test. The task was to switch off randomly placed lights which suddenly appeared. Each switch-off activated the next randomly placed light (Hiroshima only).

Vital capacity (in cubic centimeters), total and 1 second was measured using a Collins spirometer in Hiroshima and the Benedict-Roth respirometer in Nagasaki. Correction was made for hesitant starts.

Auditory acuity (in decibels) was tested for each ear at 4000 cycles/sec.

Visual acuity was measured by a standard Snellen chart.

Visual accommodation was measured using Ishihara's optometer and Ishihara's International Near Vision Chart to determine the

本調査は測定を行ったコホートがより大きいという 点で、以前 ABCC で実施した加齢に関する調査と 異なる。

原爆によって種々の量の電離放射線に被曝した総数11,351名について、ABCCの2年ごとの定期検診である第8診察周期検診において、1970年7月から1972年6月までの間に一連の年齢と関係のある非観血的検査を行った。広島・長崎両市における被検者の検査時の年齢、性、及び線量の分布を付録、表Bに示す。

加齢検査

検査の器具及び方法はHollingsworth ら^{23,28} によって 考案されたもので、以前に説明されている。次の検 査を実施した。

握力は握力計を用いて左右両手についてkg単位 で測定した。握力計間の差異は既知の重量の おもりを用いて補正した。

皮膚弾性は、一定の方法でつままれた皮膚が完全に平らになるまでの時間を測定した. これは 広島だけで行った.

震動感覚は震動の感知される電圧の強さとして 測定した. 足首に電気震動計を当てて行った.

複雑な作業に対する反応時間を Bogitch の閃光 反応検査により測定した. 作業とは、電燈を配置して任意に点燈したものを順次消してゆくこと である. スイッチを切ると次の電燈が点燈する ようになっている。これは広島だけで実施した。

肺活量(cm³ 単位)は総肺活量及び1秒間の肺活量を,広島では Collins 肺活量計を用い,長崎では Benedict-Roth 肺活量計を用いて測定した.呼気開始が遅れた場合には補正を行った.

聴力(アシベル単位)は毎秒4000サイクルで左右 の耳を検査した。

視力は標準の Snellen 視力表を用いて測定した。

眼調節力は角膜頂点から近点までの距離を石原 式近点測定器及び石原式万国式近距離試視力表 distance from the anterior pole of the cornea to the near point.³¹ Vision was first corrected with lens sets using the International Hiragana Vision Chart.

The age-related tests were not administered to all who participated in the 8th Cycle examination. Tests of grip strength were given to about 9500 persons. Some of the tests, like visual accommodation and vital capacity, were not administered until later in the cycle. The measurements of skin elasticity, and the reaction time were made in Hiroshima only. The number of participants given the various tests is shown in Appendix Table C.

Dosimetry

Individual estimates of radiation exposure were made based on the dosimetry system developed jointly by the Oak Ridge National Laboratory and the Japanese National Institute of Radiological Sciences. Each dose estimate is based on a detailed interview for the collection of necessary information on the location at the time of the bomb and shielding configuration. Dose estimates relate to air dose or whole-body radiation and are expressed in rad. The total dose is the sum of the neutron and gamma components.

Dose estimates are available for about 90% of the survivors in the Adult Health Study cohort. Estimates were not made for persons whose shielding situation was complex, those who were unable to recall the shielding pattern ATB, or for whom history is incomplete.

Analytical Method

Two methods of analysis were adopted. The first was to take each aging test result separately and to examine differences, if any, between the mean test values by city, sex, age ATE, and by dose. This approach will presumably show the significance of each test with respect to aging and radiation exposure.

The second approach was to construct the best linear equation for estimating "physiologic" age based on the various test results for the control population, that is, the population with minimal exposure to ionizing radiation. The equation so derived was then used to estimate the "physiologic" age of the population exposed to varying amounts of radiation. The hypothesis is that the difference between the estimated

を用いて測定した.31 視力はまず万国式視力表 を用いてレンズセットで矯正した。

年齡と関係のある検査は第8診察周期の受診者全員について実施したわけではない. 握力検査は約9,500名について行ったが, 眼調節力及び肺活量のような一部の検査は診察周期の後半まで行わなかった. 皮膚弾性の測定及び反応時間の測定は広島だけで行った. 各検査を受けた者の数を付録, 表Cに示す.

線量測定

各人の被曝線量推定はOak Ridge 研究所及び千葉の放射線医学総合研究所が共同開発した線量測定法に基づいて行った。各人の線量推定は原爆時の被爆地点及び遮蔽状況について必要な情報を収集するための綿密な面接に基づいて行った。線量推定は空気線量あるいは全身放射線量に関するもので、rad単位で表す。総線量は中性子線量とガンマ線量の和である。

線量推定は成人健康調査対象者のおよそ90%の被爆者について得られている. 遮蔽状況が複雑な者,被爆時の遮蔽状況を思いだせない者,又は被爆歴の不完全な者については線量推定を行っていない.

解析方法

二つの解析方法を採用した。第一の方法は、各加齢 検査の結果を個々に取り上げ、都市別、性別、診察 時年齢別、及び線量別に、検査結果の平均値間に差 があるかどうかを調べることである。この方法により 加齢と放射線被曝に関して各検査のもつ意義が分か るであろう。

第二の方法は、対照集団つまり最低量の電離放射線に被曝した集団において得られた種々の検査結果から「生理学的」年齢の推定に最も良い線型方程式を作ることである。このようにして得た方程式を用いて種々の量の放射線に被曝した対象集団の「生理学的」年齢を推定した。これは推定「生理学的」年齢と実際の暦年齢との差は放射線被曝の結果であり放射線の

"physiologic" age and the actual chronological age is the result of radiation exposure and may be taken as a measure of its aging effect.

The age-prediction formula is a multiple linear regression equation, and is limited to the age range between 35 and 74 years. This is the range in which many age dependent measurements (or transformed values) were approximately linearly related to chronological age. Log transformations were made on data for the skin elasticity and light-extinction tests.

The stepwise regression technique was used to determine the age-prediction equation based on data for the control population. However, the rules for selection were modified to exclude duplication of parameters. For example, if grip strength of the right hand was selected in the stepwise procedure, grip strength of the left hand was dropped from further consideration. This rule was applied to other variables such as audiometry, visual acuity, and vibrometer where more than one reading was taken in the age-related tests.

The stepwise regression method resulted in the selection of the following parameters:

 $X_1 = Grip strength, right hand$

 X_2 = Vital capacity, 1 second

X₃ = Audiometry, right ear

 X_4 = Vibrometer, first time

 $X_5 = Visual acuity, OD$

 X_6 = Amplitude of visual accommodation,

X₇ = Skin elasticity (log transformation), Hiroshima only

 X_8 = Bogitch light-extinction test, first time (log transformation), Hiroshima only

Using the measurements of all persons in the 0-9 rad group who were examined and given at least one out of the eight measurements, a variance-covariance matrix was used for a stepwise linear regression analysis. The order in which the variables were selected is as follows:

加齢影響の尺度とみなすことができるという仮説に 立脚している.

年齢予測式は多重線型回帰式を用い、年齢域は35歳から74歳の間に限定した。この年齢域では年齢と関係のある多くの測定値(あるいは変換値)は暦年齢とほぼ線型の関係があった。皮膚弾性及び閃光反応検査の資料については対数変換を行った。

対照群の資料を基にした年齢予測方程式を作るのに 段階式回帰法を用いた.しかし、検査項目の重複を 避ける意味で選択のための法則を修正した.例えば、 段階式回帰法で右手の握力を選択したら、左手の 握力は除外した.この法則は年齢と関係のある検査 において二つ以上の測定値を得た聴力、視力、及 び震動感覚などの変数にも適用した.

段階式回帰法の結果,次の項目が選ばれた.

 X_1 =握力,右手

X,=肺活量, 1秒

X3=聴力, 右耳

X₄ = 震動感覚検査,初回

 X_5 = 視力, 右眼

X₆=眼調節力,右眼

X₇=皮膚弾性(対数変換), 広島のみ

X₈ = Bogitch の閃光反応検査,初回(対数変 換),広島のみ

八つの検査項目のうち少なくとも一つの測定検査を 受けた0-9 rad 群の対象者全員の測定値を用いて、 分散・共分散行列を計算し、段階式線型回帰解析を 行った、変数の選択順位は次のとおりである。

	Hiros	hima 広島	Nagas	aki 長崎
	Male 男	Female 女	Male 男	Female女
1.	Χ̈́,	X_{τ}	X_6	X_4
2.	X_{6}	X_6	X_4	X_{6}
3.	X_i	X_s	X_{i}	X_i
4.	X_4	X_4	X,*	$\mathbf{X}_{\mathfrak{z}}$
5.	X ₂ *	· X ₃	X_3	X2 *
6.	X ₃	X_i	X2*	X, *
7.	X_s	X, *		
8.	X, *	X ₂ *		
R	0.901	0.888	0.813	0.786

^{*}Variable dropped. 除外した変数.

Because the vital capacity measurements were made in connection with the cardiovascular disease study and for a more limited age group, variable X_2 was dropped. Also deleted from the derivation of the final formula was the variable X_5 , visual acuity. The deletion of these variables had little effect on the coefficient of determination (R).

The final equations derived on the basis of the control group (0-9 rad) are as follows:

肺活量測定は心臓血管系疾患の調査との関連で非常に限定された年齢群について行ったため、変数 X_2 は除外した。また、変数 X_5 つまり視力も、最終的な式から除外した。これらの変数を除外しても決定係数 (R) に対する影響はほとんどなかった。

対照群(0-9 rad)を基にして得た最終方程式は次のようになった。

Hiroshima Male:
$$Y = 51.9 - 0.155X_1 + 0.0457X_3 + 0.141X_4 + 3.57X_6 + 1.17X_7 - 2.39X_8$$
 広島 男

Female: $Y = 45.8 - 0.160X_1 + 0.0677X_3 + 0.166X_4 + 3.36X_6 + 2.57X_7 - 1.52X_8$

Male: $Y = 60.2 - 0.327X_1 + 0.0949X_3 + 0.258X_4 - 3.06X_6$

Female: $Y = 54.8 - 0.485X_1 + 0.141X_3 + 0.329X_4 - 2.19X_6$

The data, particularly for Nagasaki males, do not appear to be linear. The estimates are systematically high at the younger ages and low at older ages. Because of this, any analysis of deviations needs to be controlled on age.

By using these formulas, the individual estimated ages were calculated for each dose group. In those few cases where the measurements were missing, the mean value for the group was used.

RESULTS

Nagasaki

長崎

The results showing each age-related test taken separately are summarized in Table 1. Several highly statistically significant differences may be

資料は、必ずしも線型を示しているとは思われない。 特に長崎の男性においてはその傾向が強い、推定値 は系統的に若年齢で高く高年齢で低い、このため、 偏差についてのいかなる解析においても年齢を考慮 する必要がある。

これらの式を用いて、各線量群について個人の推定 年齢を計算した、測定を行っていない少数例につい ては、その年齢別線量群の平均値を用いた.

結 果

年齢と関係のある各検査別の結果を表1に要約して 示した. 握力では対照群(0-9 rad)と100 rad以上 seen in the grip strength between the control group (0-9 rad) and the population exposed to 100 rad or more, and in the audiometric tests between the controls (0-9 rad) and the 50-99 rad exposure group. Except for sporadic differences, there does not appear to be any consistent pattern of differences to suggest aging effects of radiation. There are other statistically significant differences, but here again they occur in some age and sex groups, and not in others. Also, except for the results of the grip strength tests and of the audiometric tests, the relationship is in the opposite direction in more than half of the differences which are statistically significant. Thus, in a large portion of the comparisons it would appear as though the control group is showing aging effects.

Simple correlation coefficients were computed between each test and chronological age for the multiple regression analysis. Table 2 shows generally high correlation between the tests and age. This is hardly surprising because the tests were specifically selected on the basis of this relationship.

There are several positive correlation coefficients in the equations. These do not mean that hearing, for example, improves with age. It merely means that the readings were used in the analysis without regard to their functional significance in relation to age. Although it might have been desirable to take the complement of the scores in these cases, they will not in any way affect the conclusions to be drawn from this study.

The multiple regression equations derived from the tests of the control group (0-9 rad) were used to estimate the chronological age ATE for each age and sex group in the two cities in the three radiation exposure groups (10-49 rad, 50-99 rad and 100+ rad). The mean differences between the estimated ages and the actual chronological ages are shown in Table 3. There was a consistent and systematic bias of the estimated age in relation to chronological age, in that the estimated ages are higher at the younger ages and lower at the older ages. But restricted to a specific age group, the mean differences were compared for each exposure group and the control group (0-9 rad), and no statistically significant increase of mean difference was found. Furthermore, the mean differences vary irregularly (sometimes higher, sometimes lower)

被曝群との間に、また聴力検査では対照群(0-9 rad)と50-99 rad 被曝群との間にいくつかの統計的に非常に有意な差がみられる。散在的に差は認められるが、放射線の加齢影響を示唆するような差の一貫した傾向はないようである。ほかにも統計的に有意な差を示すものがあるが、これも一部の性及び年齢の群に限られ他の群には見られないといった工合である。また、握力検査及び聴力検査の結果を除く他の検査結果においては、統計的に有意な差を示すもののうち半分以上においてその関係はむしろ反対の傾向を示している。つまり、比較結果の半分以上において、対照群の方があたかも加齢影響を示しているかのように見受けられる。

多重回帰解析を行うにつき、各検査と暦年齢の間の 単相関係数を計算した、表2は検査と年齢との間に 一般に高い相関のあることを示す。これは、各検査が この関係を基に選択されたのであるから何ら不思議な ことではない。

方程式中にいくつかの正の相関係数がある。これらは、例えば聴覚が年齢に伴って向上することを意味しているのではなく、単に、測定値をそのままその機能的意義と年齢との関係を考慮せずに解析に用いたことを意味している。この場合には測定値の補数を取るのが望ましかったかもしれないが、いずれにしても本調査の結論に影響を与えるものではない。

対照群(0-9 rad)の検査から得た多重回帰方程式を用いて、両市の三つの被曝群(10-49 rad,50-99 rad 及び100 + rad)において、性及び年齢別に検査時の暦年齢を推定した。推定年齢と実際の暦年齢との差の平均を表3に示す。推定年齢と暦年齢との関係には一貫した系統的な偏りが認められた。つまり、推定年齢は若年者では高めであり高齢者では低めである。しかし、特定の年齢群に限定して各被曝群と対照群(0-9 rad)について差を比較したところ、その差には統計的に有意な増加は見られなかった。その上、対照群と比較したその差は被曝

表1 各検査に対する被爆集団と対照集団の平均値の有意差検定;性及び年齢別,広島及び長崎

 .			a		4	0-9:10	-49 rad					0-9:50)-99 гас	i				0-9:1	00+ ra	d	
Tes	τ	City	Sex	25-34	35-44	45-54	55-64	65-74	75 +	25-34	35-44	45-54	55-64	65-74	75 +	25-34	35-44	45-54	55-64	65-74	75 -
Vital capacity/s	sec.	Н	M											*			•				
			F																		
		N	M									*									
			F																		
	Total	H	M											*							
			F												sug						**
		N	M									*									
			F																		
Grip strength	Right	Н	M					•					*				sug			*	
	_		F		*			sug													
		N	M												sug	sug	*				
			F								*				*				*		
	Left	Н	M										*			***	*			***	
			F					sug							**						
		N	M				**									sug	*				
			F				*										*				
Visual acuity	OD	Н	M						sug			sug						•			*
			F					sug													
		N	M						sug		sug			sug							
			F																		
	OS	H	M						*			*	*	*						:	*
			F																	**	
		N	M																		
			F							**		**									

TABLE 1 Continued (表 1 続き)

	, ,		- /																		
774		City	Cav		0-9	9: 10-	19 rad					0-9: 5	0-99 ra	ad				0-9: 1	00+ ra	đ	
Test		City	SEX	25-34	35-44	45-54	55-64	65-74	75 +	25-34	35-44	45-54	55-64	65-74	75 +	25-34	35-44	45-54	55-64	65-74	75 t
Vibrometer	1st	Н	M													*					
,			F					*	sug									sug	*		
		N	M															*			
			F	*				sug							*						
	2nd	Н	M																		
			F		*			*											sug		
		N	M		_			-										*			
			F	*	sug			sug							*						
Audiometry	Right	Н	M F	•	*					*	<u>sug</u>		<u>*</u>				*				
		N	M		*									***	**		sug	sug		**	
		11	F			*		sug							*	sug		sug			
	Left	Н	M								_						sug	_			
	Lort	**	F														sug		*		
		N	M				*	**						***	*			*	_	**	
		• • • • • • • • • • • • • • • • • • • •	F			sug		sug							*						
																	*				
Amplitude of	OD	Н	M														-				
visual accom.			F			**						**					a1147	*_			
		N	M														sug				
			F										sug								
	OS	H	M										*				**				
			F			*	sug					*					*	*			
		N	M																		
			F					•						-							
Bogitch	1st	H	M					sug							*				S110	sug	
T 3-1-4			F		*					-1- 10-					*			*	sug	sug	3
Light	2nd	Н	M							**					**					υνĐ	511
						sug												*			su
extinction			F																		
		Н	 М												**		sug	*			

sug: 0.05 < P < 0.1; *: 0.01 < P < 0.05; **: 0.001 < P < 0.01; ***: P < 0.001; ---: opposite direction as dose effects 線量影響としては反対方向

TABLE 2 SIMPLE CORRELATION COEFFICIENTS BETWEEN SPECIFIED VARIABLES AND CHRONOLOGICAL AGE, 35-74 YEARS OF AGE ATE FOR THE 0-9 RAD DOSE GROUP BY SEX, HIROSHIMA AND NAGASAKI

表2 各変数と暦年齢との単相関係数,0-9 rad 線量群,診察時年齢 35-74歳;性別,広島及び長崎

			Hirosh	ima			Nagasa	aki	
Tes	st	Ma	ie	Fema	le	Ma	le	Female	
		ī	Case	r	Case	r	Case	r	Case
1. Grip strength									
Right		508	618	514	1167	473	303	454	483
Left		570	617	511	1167	457	302	344	483
2. Vital capacity/	sec	383	384	469	849	388	167	497	241
Total		266	384	466	849	360	167	525	241
3. Audiometry									
Right		+.530	582	+.547	1164	+.506	303	+.538	484
Left		+.569	582	+.564	1164	+.451	303	+.540	484
4. Vibrometer									
1st		+.611	589	+.570	1169	+.539	300	+.571	477
2nd		+.604	589	+.575	1170	+.525	300	+.567	477
5. Visual acuity									
OD		435	538	481	1079	364	277	339	452
OS		428	534	530	1091	315	277	379	455
6. Amplitude of v	risual accommodatio	n							
OD		824	308	733	665	772	112	768	238
OS		820	312	742	674	762	117	767	243
7. Skin elasticity									
Normal		+.587	582	644	1163				
Log transfe	rmation	+.826	582	810	1163				
8. Bogitch light-e		•							
First –	normal	+.429	596	+.510	1200				
-	log-trans.	+.577	596	+.620	1200				
Second -	normal	+.309	596	+.433	1200				
	log-trans.	+.487	596	+.591	1200				

among the exposure groups as compared to the control group. Thus no association could be found between estimated age and radiation in this study.

DISCUSSION

Physiological tests were administered to about 10,000 persons with different levels of A-bomb exposure to ascertain the effects, if any, of radiation on age of the population. These tests included the assessment of neuromuscular function, sensory responses, and coordination. Each of these represent an integration of several component functions. The tests employed covered a range of functions as recommended by Comfort.³⁹

群間で不規則(ある時は高く,ある時は低い)に変化 している。したがって、本調査では推定年齢と放射 線との間に何の関係も認められなかった。

老 窓

対象者の年齢に何らかの放射線の影響があるかどうかを確認するために異なった量の原爆放射線に被曝した約10,000名について生理学的検査を行った.これらの検査には神経筋肉機能、感覚反応及び協調運動などの評価が含まれており、それぞれいくつかの機能の統合である。実施した検査には Comfort³⁹ の提唱する範囲の機能を含めた.

TABLE 3 THE MEAN DIFFERENCE BETWEEN PREDICTED AGE AND CHRONOLOGICAL AGE ATE BY AGE ATE, SEX, AND T65D, HIROSHIMA AND NAGASAKI

表3 予測年齢と診察時の暦年齢の差の平均;	診察時年齢、性及	及びT65線量別,	広島及び長崎
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		•			T65D Dos	e in rad			
Age	e ATE		Male				Female		
	*	0-9	10-49	50-99	100+	0-9	10-49	50-99	100+
				Hirosh	ima				
35-39	Mean	7.413	6.885	6.179	9.501	4.821	5.554	5.217	6.067
	Subjects SD	92 6.17	27 6.18	7 7.80	24 6.02	105 5.19	55 4.51	29 4.11	5.97
40-44	Mean	5.077	4.409	5.265	5.938	3.398	3.214	3.892	3.119
70 77	Subjects	190	77	40	103	259	105	64	100
	SD	5.12	4.97	5.59	5.51	4.51	4.56	5.09	4.10
45-49	Mean	5.591	2.866	4.086	3.941	3.208	1.991	2.687	2.36
	Subjects	35	24	15	33	243	129	70	11:
	ŞD	5.30	5.16	5.28	3.58	4.95	4.16	5.06	5.18
50-54	Mean	2.823	2.385	4.581	2.649	1.042	0.433	0.052	0.073
	Subjects	75	24	13	33	188	104	40	7:
	SD	4.92	6.67	5.80	5.21	5.57	5.49	6.51	5.29
55-59	Mean	0.895	1.926	0.765	0.925	-0.499	-1.171	-1.732	-0.50
	Subjects	81	51	15	43	167	109	52	6
	SD	5.32	5.81	5.87	4.42	6.18	6.51	7.14	5.19
60-64	Mean	-1.445	-1.446	-2.395	-1.325	-3.972	-3.541	-3.041	-5.14
	Subjects	106	54	20	44	183	126	32	6
	SD	6.15	5.90	6.86	4.09	7.93	8.32	6.67	7.66
65-69	Mean	-4.421	-4.772	-2.377	-4.826	-6.108	-6.590	4.995	-6.61
	Subjects	94	46	26	43	184	113	. 57	6
	SD	7.08	7.48	6.34	6.78	9.66	8.53	8.56	9.60
70-74	Mean	-5.867	-7.540	-6.580	-5.559	-8.333	-8.313	-7.945	8.70
	Subjects	84	49	23	33	152	96	26	5
	SD	7.97	9.31	8.81	8.00	9.94	9.38	10.19	10.07

The use of age-related physiologic and functional tests implies that a measure of physiologic or biologic age can be derived somehow from the test data. However, there is, as yet, no basis for the belief that these tests provide a valid measure of aging. Without this validation, the measures may not reflect much more than chronologic age plus an error term.

It was felt that when test results for the different radiation exposure groups were entered into the regression equation computed by using the control group as the base, the results might provide a closer measure of physiologic age than chronologic age. However, this may not be much better than a measure of chronological age.

It is probably not possible to separate physiological from chronological age in a cross-sectional analysis. Based on a chronological age-related

年齢に関係のある生理学的検査及び機能検査を使用することは、生理学的あるいは生物学的年齢の尺度が何らかの形でこの検査資料から得られることを意味する。しかし、これらの検査から妥当性のある加齢の尺度が得られると信ずる根拠はまだない。この妥当性がない限り、その尺度は、暦年齢と誤差項以上のものを反映するものではないであろう。

対照群を基にして計算した回帰方程式に別の被曝群の 検査結果を代入した場合、その結果は暦年齢よりも より生理学的年齢に近い値を示すだろうと考えた。 しかし、これは暦年齢の尺度以上のものではないかも しれない。

横断的な解析では、暦年齢と生理学的年齢とを区別 することはおそらく不可能であろう、暦年齢と関係の

TABLE 3 Continued (表3 続き)

					T65D Do	se in rad			
Aş	ge ATE		Male	;			Female	;	
		0-9	10-49	50-99	100+	0-9	10-49	50-99	100+
				Nagasa	ki				
35-39	Mean Subjects	10.009 66	10.128 12	11.305 10	10.393 37	7.671 83	7.103 17	6.440 10	8.648 39
	SD	7.92	6.23	9.74	7.75	6.96	6.56	5.99	7.47
40-44	Mean Subjects	10.582	12.011	12.349 27	10.425	5.861 133	6.340	6.154	6.764 211
	\$D	6.84	5.55	6.62	7.39	5.40	7.09	5.88	6.16
45-49	Mean Subjects	11.571 26	5.403 4	12.440 13	10.581 21	4.697 89	6.778 16	4.505 29	5.211 121
	SD	4.18	8.44	6.07	4.59	5.63	4.79	5.01	5.03
50-54	Mean Subjects	7.990 33	10.304 10	4.789 7	5.749 31	3.058 66	3.430 22	3.704 16	4.433 76
	SD	4.60	6.71	7.73	5.04	4.65	5.13	5.30	5.00
55-59	Mean Subjects SD	5.544 43 5.91	6.330 15 4.74	4.266 12 5.96	4.659 43 5.58	0.311 35 4.85	0.803 22 5.57	1.782 12 6.60	0.515 35 6.53
60-64	Mean Subjects SD	0.527 38 5.07	1.835 14 4.04	3.913 6 3.28	1.418 32 3.85	-1.421 39 5.92	-2.317 18 5.74	-1.421 10 4.22	-2.829 33 4.93
65-69	Mean Subjects	-2.009 38	-1.767 7	0.122 6	-1.077 40	-5.204 34	-2.873 13	-3.878 16	-3.199 33
	SD	6.25	8.73	5.23	4.60	6.53	5.80	6.04	6.94
70-74	Mean Subjects	-5.132 24	-3.180 5	-2.878 6	-3.126 24	-7.288 26	-3.954 13	-6.683 8	-6.702 22
	SD	5.69	12.54	5.07	6.77	5.90	5.80	7.95	6.86

cohort, would changes in physiologic test results over time reflect effects of change in physiological or biological age? This must be so if these functional tests have meaning. However, how can one demonstrate that a set of measurements are, in fact, related to physiological age?

The results of the present study are essentially negative, that is, no consistent differences were found in any age or sex group or city. A cross-sectional analysis in which certain physiologic or functional tests are correlated with age and used to construct by a regression method an estimator of chronological age also failed to yield effects of aging.

A similar lack of correlation between test of aging and exposure to radioactive fallout was reported by Conard et al⁴⁰ for a Marshall Island population. All that can be claimed in the present study is that there is no effect of radiation on these functions, or, if present, it

あるコホートを基にした場合,生理学的検査結果の 経時的変化は生理学的あるいは生物学的年齢の変化 の影響を反映するものであろうか.もしこれらの機能 検査が意味のあるものであればそのはずである.しか し,一連の測定が実際に生理学的年齢と関係がある ということをどのようにして証明できるだろうか.

本調査の結果は本質的に陰性的なものである. つまり,いずれの性,年齢群及び都市においても一貫した差はみられなかった. 横断的な解析により,ある種の生理学的検査,あるいは機能検査は年齢との相関があることが示され,回帰法により暦年齢を推定するのに用いたが,これによっても加齢影響を示すことはできなかった.

Marshall 群島の人々について調査を行った Conard ら⁴⁰ の報告でも、加齢検査と放射性降下物被曝との相関はみられなかった。本調査で言えることは、これらの機能に対する放射線の影響はないこと、あるいはあるとしても本調査で用いた方法では探知できない

cannot be detected by the means used. However, these results do not necessarily rule out the effects of radiation on cellular function or even on higher integrative steps. On the other hand, it seems clear that the use of these physiologic tests to estimate "biologic age" is not warranted until the methodology is validated.

ということである。しかし、これらの結果は細胞機能あるいはより高度の統合的な機能への放射線の影響の存在を必ずしも否定するものではない。一方、これらの生理学的検査を用いて「生物学的年齢」を推定することは、その方法論を妥当化しない限り意味がないことは明白のようである。

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APPENDIX TABLE A STUDIES ON AGE-RELATED FUNCTIONS IN A-BOMB SURVIVORS 付録表 A 原爆被爆者における年齢と関係ある機能についての調査

Function		No. Examined
Skin elasticity ²⁷	皮膚弾性	609
Systolic blood pressure ²³	収縮期血圧	437
Vital capacity ²³	肺活量	429
Grip Strength ²⁸	捏 力	2567
Light-extinction ²⁸	閃光反応	827
Perception of vibration ²⁸	農動感覚	831
Visual acuity ²³	視 力	433
Auditory acuity ²³	聴 力	436
Serum cholesterol ²³	血清コレステロール	426
Amplitude of visual accommodation ³¹	眼調節力	1974
Achilles tendon reflex time ¹⁷	アキレス腱反射時間	2100
Isoantibody levels ²⁰	同種抗体值	1042
Response to oral glucose ²⁶	プドウ糖反応	1481
Electrocardiogram 18	心電図	3174
Ballistocardiogram ¹⁹	心弾図	1025
Immunoglobulin levels ^{24,25}	免疫グロブリン値	803, 2043
Ventilatory functions ²²	肺换気機能	1132
Cold pressor response ²¹	寒冷昇圧反応	1156
Cardiac lipofuscin ³⁰	心臓におけるリポフスチン沈着	54 (Autop

APPENDIX TABLE B THE NUMBER EXAMINED IN ANY OF THE 8 TESTS IN HIROSHIMA OR ANY OF THE 6 TESTS IN NAGASAKI BY AGE ATE, SEX, AND T65D

付録表B 広島で八つの検査,長崎で六つの検査中一つ以上の検査を受けた 対象者の数;診察時年齢,性及びT65線量別

C	4 4 MP	Total	T65 Dose in rad									
Sex	Age ATE	Total	NIC	0-9	10-49	50-99	100+	Unk				
		 -	Hiroshima	ı + Nagasal	ki							
Total	Total	11351	2700	3562	1667	846	2125	451				
	<35	863	207	271	139	44	182	20				
	35-44	3101	695	978	340	225	676	187				
	45-54	2550	640	755	333	203	502	117				
	55-64	2219	540	692	409	159	353	66				
	65-74	1981	465	636	342	168	317	53				
	75 ÷	637	153	230	104	47	95	8				

Appendix Table B Continued (付録表B 続き)

Carr	Acc ATE	Total		•	T65 Dose	in rad		
Sex	Age ATE	Total	NIC	0-9	10-49	50-99	100 +	Unk
			Hiroshir	na + Nagas	saki			
Male	Total	4085	978	1269	533	278	823	204
	<35	371	87	106	64	18	87	9
	35-44	1222	270	398	135	84	275	60
	45-54	601	162	169	62	48	118	42
	55-64	870	207	268	134	53	162	46
	65-74	779	189	240	107	61	140	42
	75 +	242	63	88	31	14	41	5
emale	Total	7266	1722	2293	1134	568	1302	247
	<35	492	120	165	75	26	95	11
	35-44	1879	425	580	205	141	401	127
	45-55	1949	478	586	271	155	384	75
	55 - 64"	1349	333	424	275	106	191	20
	65-74	1202	276	396	235	107	177	11
	75 +	395	90	142	73	33	54	3
				shima			٠.	_
Cotal	Total	7769	1906	2602	1379	590	1090	202
	<35	507	123	172	97	25	87	3
	35-44	1826	425	646	264	140	278	73
	45-54	1717	442	541	281	138	253	62
	55-64	1658	417	537	340	119	210	35
	65-74	1549	376	514	304	132	198	25
	75 +	512	123	192	93	36	64	4
Male	Total	2668	673	894	- 418	179	426	78
.1010	<35	203	52	61	40	10	40	
	35-44	747	172	282	104	47	127	15
	45-54	379	112	110	48	28	66	15
	55-64	585	146	187	105	35	87	25
	65-74	557	139	178	95	49	76	20
	75 +	197	52	76	26	10	30	3
emale	Total	5101	1233	1708	961			124
emale	<35	304	71	111	57	411	664	
	35-44					15	47	3
		1079	253	364	160	93	151	58
	45-54	1338	330	431	233	110	187	47
	55-64	1073	271	350	235	84	123	10
	65-74	992 315	237	336	209	83	122	5
	75 +	313	71	116	67	26	34	1
2-4-1	T-4-1	3582	Nag 794	asaki	288	256	1025	240
otal	Total ≤35	356	84	960 99	42	236 19	1035	249
		1275	270	332	76	85	95 398	17
	35-44 45-54	833	198	214	52	65	249	114 55
		561	123	155	69	40		
	55-64	432	89	122	38	36	143	31
	65-74	125		38			119	28
folo	75 + Total	1417	30 305	375	11 115	11 99	31 397	126
fale		168	305 35	373 45	115 24			126
	<35	475				8	47	9
	35-44		98 50	116	31	37	148	45
	45-54	222	50	- 59	14	20	52	27
	55-64	285	61	81	29	18	75	21
	65-74	222	50	62	12	12	64	22
	75 +	45	11	12	5	4	11	2

Appendix Table B Continued (付録表B 続き)

	A ATE	m t	T65 Dose in rad										
Sex	Age ATE	Total	NIC	0-9	10-49	50-99	100 +	Unk					
			Naga	saki									
Female	Total	2165	489	585	173	157	638	123					
	<35	188	49	54	18	11	48	8					
	35-44	800	172	216	45	48	250	69					
	45-54	611	148	155	38	45	197	28					
	55-64	276	62	74	40	22	68	10					
	65-74	210	39	60	26	24	55	6					
	75 +	80	19	26	6	7	20	2					

APPENDIX TABLE C
THE NUMBERS EXAMINED IN EACH TEST BY SEX: HIROSHIMA AND NAGASAKI
付録表C 各検査の被検者数;性別,広島及び長崎

T	est		Total		J	Hiroshi	ma	Nagasaki			
		Total	Male	Female	Total	Male	Female	Total	Male	Female	
Grip Strength	Left	9504	3527	5977	6129	2175	3954	3375	1352	2023	
	Right	9500	-3523	5977	6128	2172	3956	3372	1351	2021	
Visual Acuity	OD	8671	3182	5489	5503	1900	3603	3168	1282	1886	
	os	8696	3187	5509	5526	1901	3625	3170	1286	1884	
Skin Elasticity		5998	2065	3933	5998	2065	3933	_	_	_	
Light-extinction	1st	6178	2115	4063	6178	2115	4063	_	_		
	2nd	6177	2115	4062	6177	2115	4062	-	_	_	
Vital Capacity/sec		5449	1920	3529	3921	1281	2640	1528	639	889	
	Total	5449	1920	3529	3921	1281	2640	1528	639	889	
Audiometry	Left	9380	3413	5967	6005	2065	3940	3375	1348	2027	
	Right	9382	3414	5968	6004	2063	3941	3378	1351	2027	
Vibrometer	1st	9379	3415	5964	6042	2081	3961	3337	1334	2003	
	2nd	9378	3414	5964	6041	2080	3961	3337	1334	2003	
Visual Accom.	OD	4847	1612	3235	3265	1047	2218	1582	565	1017	
	os	4909	1613	3296	3302	1050	2252	1607	563	1044	