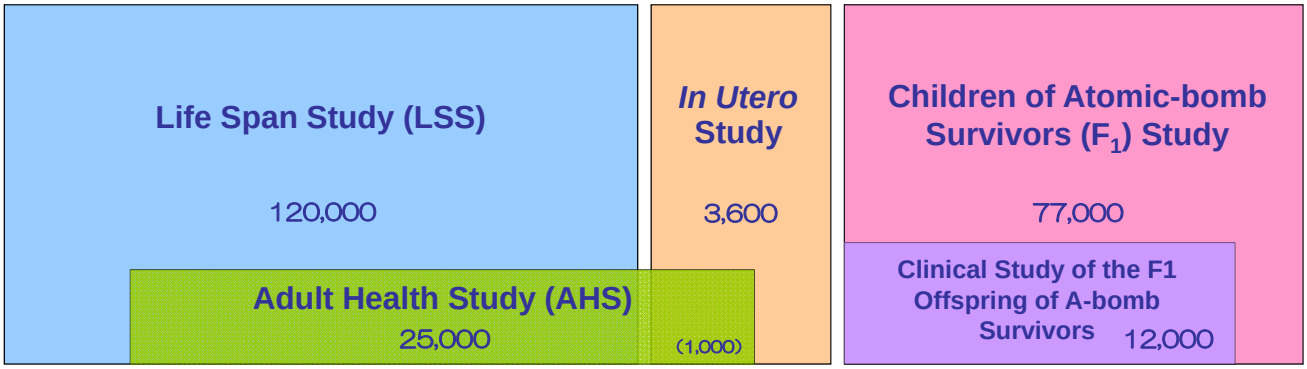
RERF Study Cohorts



■Life Span Study

The Life Span Study is an epidemiological research program investigating lifetime health effects of atomic-bomb radiation. Its major objective is to investigate long-term effects from A-bomb radiation on causes of death and incidence of cancer. About 120,000 subjects selected from among residents of Hiroshima and Nagasaki identified through the 1950 national census have been followed since that time, including about 94,000 A-bomb survivors and about 27,000 unexposed individuals.

■Adult Health Study

The Adult Health Study is a clinical study of a sub-cohort of the Life Span Study. Examinations of the A-bomb survivor subjects of the study are conducted every two years, providing a continuous health profile of this aging population. In addition, blood samples for future analysis are collected on the basis of the examinees' informed consent. This study strives to establish radiation-related risk of noncancer diseases and investigate aging- and radiation-related physiological changes. It will be continued throughout the lifetimes of the survivors to more accurately grasp radiation's association and risk in noncancer disease development. The study also provides useful information for the health management of A-bomb survivors.

■*In Utero* Study

The *In Utero* Study is designed to examine lifetime health status of about 3,600 persons who were in the womb at the time of bombing. It is known that, depending on radiation dose, persons exposed at 8–15 weeks of gestation have shown an elevated risk of microcephaly and intellectual impairment. To date, cancer incidence in individuals exposed prenatally tends to increase with radiation exposure dose at around the same level as incidence in those exposed in childhood (the period 0–5 years). It is considered that many findings will be obtained by continued follow-up of this *in utero* study cohort.

■Children of Atomic-bomb Survivors (F_1) Study

The Children of Atomic-bomb Survivors Study conducts research on such children to determine whether any genetic effects exist that could be related to parental exposure. An initial study of birth defects did not reveal any discernable effects. Subsequent studies on mortality and cancer incidence, chromosome abnormalities, and serum proteins were also conducted, but again no parental exposure effect was observed. Presently, these mortality and cancer-incidence follow-up studies are being continued, with DNA studies recently initiated. Starting in 2002, a new clinical study was initiated to investigate lifestyle-related diseases that are not observable at birth but only start to appear in middle age (e.g., hypertension, diabetes mellitus, etc.). This clinical study is still being conducted today.

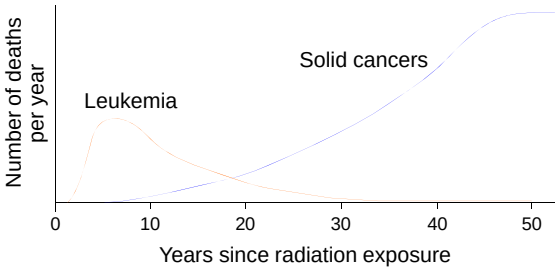
Study details	Number of study subjects	Study period
① Physical abnormalities at birth	77,000 persons	1948–1954
② Chromosome aberrations	16,000 persons	1967–1985
③ Abnormalities in blood protein	24,000 persons	1975–1985
④ Mortality and cancer incidence	77,000 persons	1946–present
⑤ Clinical examination of lifestyle diseases	12,000 persons	2002–present

Late Effects from Radiation

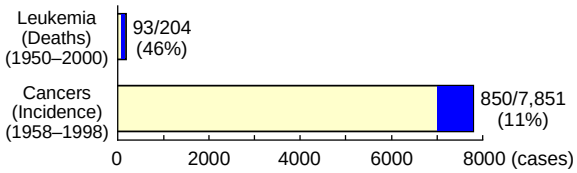
Cancer Incidence and Mortality among A-bomb Survivors

It has been found that cancer incidence and mortality are higher among A-bomb survivors than among the unexposed (see the figure at right). The largest percentage increase in cancer incidence and mortality due to radiation exposure is shown for leukemia. Leukemia started to increase two or three years after exposure, reached a peak after five to ten years, and decreased thereafter. However, incidence and mortality from leukemia still appear even now to be slightly higher in A-bomb survivors than in the unexposed. On the other hand, solid cancers (all cancers other than leukemia) started to increase about ten years after exposure and have continued to rise with time.

Extent of increase in excess leukemia and cancer mortality due to radiation exposure (schematic diagram)



Numbers of people dying of leukemia and those contracting cancer in the Life Span Study cohort

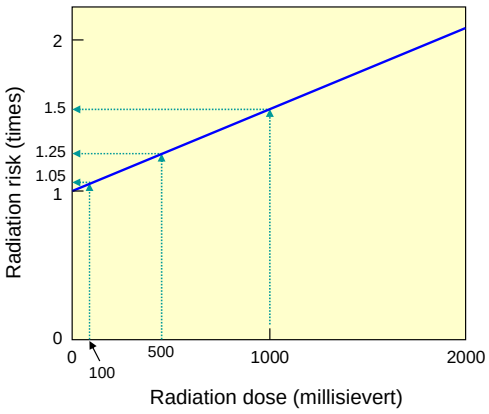


The numbers of leukemia deaths and cancer cases among A-bomb survivors exposed to at least 0.005 Sv (5 mSv) in the Life Span Study cohort are shown in the figure at left. The blue portions (about half of leukemia deaths and about 10% of cancer cases) indicate excess leukemia deaths and cancer cases attributable to radiation exposure.

Radiation Risk (at age of 70)

RERF's epidemiological research of A-bomb survivors has revealed that exposure to radiation dose of 1 Sv (1,000 mSv) at age 30 increases mortality risk from solid cancers at age 70 an average of about 1.5 times for both sexes. The risk increases in direct proportion to radiation dose above around 100 to 200 mSv. However, association remains unclear below that range. If we assume that cancer risk is proportional to radiation without "threshold" (the demarcation point above which there are effects and below which there are no effects), projections indicate that exposure to 100 mSv and 10 mSv increases cancer risk by about 1.05 and 1.005 times, respectively.

Cancer risk from radiation exposure



Radiation Risk (lifetime)

Based on the above data, exposure to radiation dose of about 100 mSv at age 30 is thought to increase the lifetime risk of cancer mortality from 20% without radiation exposure to about 21% (1 percentage point increase) on average for both sexes. A-bomb exposure was a single acute exposure, while environmental contamination represents chronic exposure. The effects from chronic exposure, even in the case of the same total dose, are thought to be smaller than the effects from acute exposure (1/2 or 1/1.5). Based on this theory, chronic exposure to about 100 mSv would increase lifetime risk by 0.5 to 0.7 of a percentage point. Based on the studies of A-bomb survivors, it is also known that risk from radiation is larger for those exposed when young as shown in the table below.

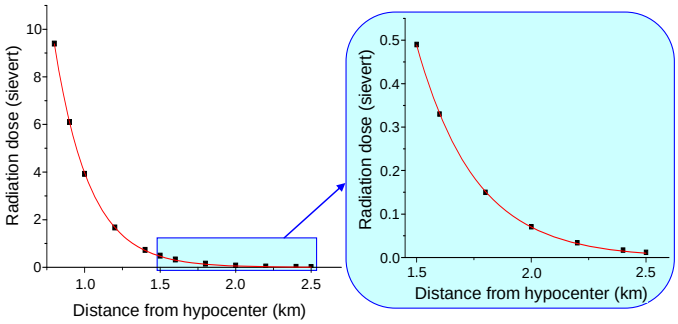
Cancer risk after single 100 mSv exposure

Age at time of exposure	Sex	Lifetime excess risk (%)	Lifetime risk without exposure (%)
10 years of age	Males	2.1%	30%
	Females	2.2%	20%
30 years of age	Males	0.9%	25%
	Females	1.1%	19%
50 years of age	Males	0.3%	20%
	Females	0.4%	16%

Estimation of Radiation Dose

Physical Dosimetry

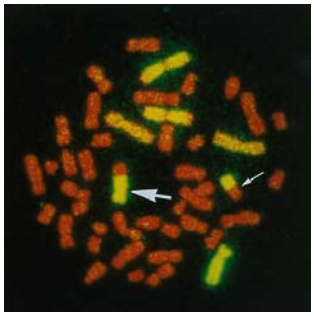
With the introduction of an A-bomb radiation dosimetry system, it became possible to estimate individual doses based on information concerning each survivor's location and shielding status at the time of bombing. The current dosimetry system was introduced in 2002 and is therefore called DS02. DS02 was created employing the latest data from nuclear physics. DS02 estimates are consistent with measurements obtained from exposed materials collected after the bombings, including bricks and tiles.



This figure shows relationship between distance from the hypocenter and air dose (without shielding), according to DS02. When a person is exposed to radiation in a typical Japanese house, radiation decreases to half of the doses presented here.

Biological Dosimetry

In addition to the radiation dosimetry system DS02, we use a method utilized since the 1960s for studying chromosomes. One cc of blood contains a few million lymphocytes (one kind of white blood cell). When cells start dividing after being cultured for two days, chromosomes can be observed. Microscopic examination of abnormalities called translocations that occur in the chromosomes will reveal roughly how much radiation someone was exposed to (see the image at right). It is also possible to estimate radiation dose by using a technique called electron spin resonance (ESR) on the enamel of an extracted tooth.

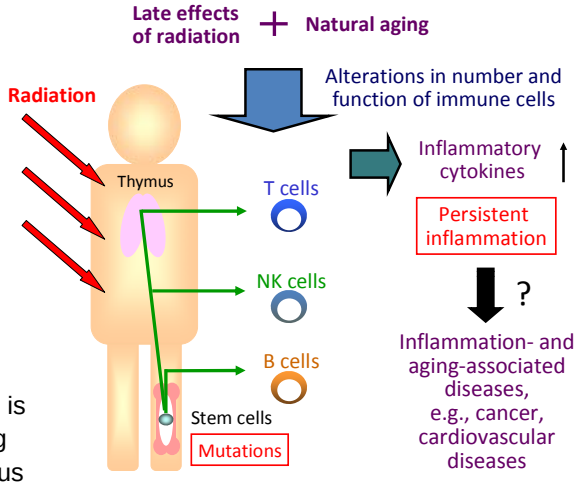


The image shows a dividing cell with abnormalities, as indicated by the arrows. Abnormal chromosomes (translocations) shown in two colors were produced by exchange between segments of two different chromosomes.

Mechanistic Studies of Radiation's Effects on the Body

Immunological Study

Alterations in the immune system associated with aging and A-bomb radiation dose have been observed in A-bomb survivors. By analyzing the numbers and functional changes of various types of immune cells, we study whether aging of the immune system, a process that appears to be accelerated by radiation, may be related to the increased risk of several aging-associated diseases among A-bomb survivors including cardiovascular disease and selected cancers (see the figure at right).



Genome Study

It is said that tendency to develop radiation-related diseases varies with each person. One of the reasons for this difference is believed to be slight variations in the structure of genes among individuals. Association between risks of development of various diseases and the entire gene structure (the genome) is being studied worldwide, with the aim of using such knowledge for prevention of diseases as well as development of related drugs. At RERF, we use some of the blood samples from our clinical study participants for genome studies, with their consent, for understanding the mechanisms that explain how radiation causes diseases for the purpose of preventing future radiation-related diseases and developing treatments for such diseases.

Radiation-related Carcinogenesis Study

We study at the molecular level characteristics of cancers developing from radiation exposure. Normal cells develop into cancer cells as a result of an accumulation of various gene abnormalities. Many cancers have several patterns in terms of types of related genes and their abnormalities. Our studies of thyroid and colon cancers suggest that particular patterns (accumulation of characteristic abnormalities in specific genes) are frequently observed in radiation-related cancers.