TWO CASES OF ACUTE LEUKEMIA
IN HEAVILY EXPOSED A-BOMB SURVIVORS
FOLLOWING RADIO THERAPY FOR BREAST CANCER

乳癌の放射線治療後急性白血病を発症した
高線量被爆者の2例

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放射線影響研究所（元ABCC）は、昭和50年4月1日に公益法人として発足した。その経費は日米両政府の平等分担とし、日本は厚生省の補助金、米国はエネルギー省との契約に基づき米国学士院の補助金をもって充てる。
TWO CASES OF ACUTE LEUKEMIA IN HEAVILY EXPOSED A-BOMB SURVIVORS
FOLLOWING RADIOTHERAPY FOR BREAST CANCER

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SUMMARY
Two cases of acute leukemia in heavily exposed atomic bomb survivors following postoperative
⁶⁰Co radiotherapy for breast cancer are presented.

Case 1, a female who received an estimated dose of 364 rad from the A-bomb at the age of
22, was diagnosed as having left breast cancer 17 years later. At the age of 48,
about 8 years after undergoing postoperative ⁶⁰Co radiotherapy, she developed acute
monocytic leukemia.

Case 2, a female who received an estimated dose of 594 rad from the A-bomb at the age of
37, was diagnosed as having right breast cancer 22 years later. At the age of 63, 4
years after postoperative ⁶⁰Co radiotherapy, she was found to have acute erythroleukemia.

Both cases had been exposed to the A-bomb in Hiroshima and to therapeutic radiation after
developing breast cancer presumably induced by A-bomb exposure. Thus it is proposed that
acute leukemia was induced by exposure to large doses of radiation from two sources.

INTRODUCTION
There are reports of significantly elevated leukemia mortality as a late effect of radiation
exposure following localized X-ray irradiation in

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the treatment of ankylosing spondylitis patients and children with thymic enlargement.\textsuperscript{1,2} It has also been reported that the incidence of malignant tumors such as thyroid cancer,\textsuperscript{3,4} lung cancer,\textsuperscript{5} breast cancer,\textsuperscript{6,7} salivary gland cancer,\textsuperscript{5} and multiple myeloma,\textsuperscript{9} as well as leukemia,\textsuperscript{10,11} is significantly increased in A-bomb survivors who had received high doses of whole-body irradiation.

To investigate the late effects of A-bomb exposure, RERF has been conducting a follow-up study of mortality and confirmation of malignant tumors including leukemia in a fixed sample of some 109,000 subjects of A-bomb survivors and controls since 1950.\textsuperscript{12} The radiation dose received has been calculated for each exposed member of the sample according to the T65 dose estimate.\textsuperscript{13}

This report presents two cases, both A-bomb survivors belonging to this fixed sample, who developed breast cancer 17 years and 22 years after massive whole-body irradiation by the A-bomb and later developed acute leukemia following postoperative $^{60}$Co radiotherapy. They were mentioned by Russell and Antoku.\textsuperscript{14} The interrelation of A-bomb exposure, development of breast cancer, radiotherapy and development of leukemia is discussed.

CASE REPORT

\textbf{Case 1 (MF 例).} A 48-year-old female, exposed to the A-bomb 900 m from the hypocenter in Hiroshima at the age of 22. Symptoms of acute radiation illness, such as epilation and fever, persisted for 4 months and then gradual recovery followed. Her estimated exposure dose was 364 rad. Since 1953 (8 years after exposure) she had anemia with hemoglobin of 9.9 g/100 ml. Because her serum iron was low, she was treated with iron tablets for iron deficiency anemia, but her anemia persisted even when her serum iron value became normal.

In 1962 (17 years after exposure) a mass was palpated in the left breast. Biopsy revealed ductal carcinoma (Figure 1), and a radical mastectomy was performed. Postoperatively, she received $^{60}$Co radiotherapy with a total of 14,920 rad. Mild anemia persisted after surgery. In 1970, her hemoglobin had fallen to 7.0 g/100 ml, and juvenile granulocyte cells appeared in the peripheral blood; also, she had

白血病死亡率の有意な増加が認められたことが報告されている。\textsuperscript{1,2} 他方、原爆による電離放射線の全身照射を受けた被爆者においても、白血病\textsuperscript{30,31}を始め、甲状腺癌\textsuperscript{3,4}、肺癌\textsuperscript{5}、乳癌\textsuperscript{6,7}、唾液腺癌\textsuperscript{5}、多発性骨腫瘍\textsuperscript{9}などの悪性腫瘍の発生率が高線量被爆者に有意に高いことが報告されている。

放影研では、原爆被爆の後影響を調査するため、約109,000人の被爆者と対照者を含む固定サンプル\textsuperscript{12}について、1950年以降の死亡者や白血病を含む悪性腫瘍の発生の確認を行っている。このサンプルに属する被爆者の受けた放射線量はT65D方式\textsuperscript{13}によると、個々の被爆者の受けた線量が計算されている。

今回、我々はこの放影研の固定サンプルに所属する被爆者で、原爆により大量の放射線の全身照射を受けた17年後と22年後に乳癌を発症し、外科手術後$^{60}$Coの放射線治療を受けた後に急性白血病を発症した2例を報告し、原爆被爆、乳癌発症、放射線治療、白血病発症の相互関係について若干の考察を試みた。この2例はRussellとAntoku\textsuperscript{14}の報告した症例中に含まれている。

症例

\textbf{症例1 (基本疾患番号1例).} 48歳の女性で、22歳の時広島の爆心地から900 mの地点で被爆し、脱毛、発熱などの症状が4か月、その年の12月まで続いて次第に回復してきた。推定被爆線量は364 radである。1953年（被爆後8年）、ヘモグロビン9.9g/100mlと貧血を指摘された。血清鉄が低値のため鉄欠乏性貧血として治療を受けたが、貧血は血清鉄が正常化の時点でも持続していた。

1962年の検診時（被爆17年後）に左乳房の腫瘤を指摘された。胸郭切開にて分離管離（図1）と診断され、同年2月左乳房根治手術を受けた。術後、計14,920 radの$^{60}$Coによる放射線治療を受けた。術後の軽度の貧血が持続していたが、1970年10月頃より、激甚なる貧血状態が著明となり、12月の末梢血でヘモグロビンが7.0g/100mlとなり、幼若
shortness of breath. She was admitted to the Department of Internal Medicine, Research Institute for Nuclear Medicine and Biology, Hiroshima University on 8 February 1971. Peripheral blood findings at that time were: RBC 1,790,000/mm³, hemoglobin 7.0 g/100 ml, hematocrit 22.0%, WBC 4,050/mm³, white blood cell differential: staff cells 6, segmented cells 23, lymphocytes 55, monocytes 5, monoblasts 10, promyelocytes 1, and platelets 32,000/mm³. Bone marrow aspirate showed marked hypoplasia with nucleated cell count of 9,000/mm³, and only 1% blast cells, but immature monocytes and mature monocytes were increased to 10% and 27.5%, respectively. The monocytes had positive phagocytosis (Figure 2). The cells classified as monoblasts were 15 µ in diameter, nuclei showed very fine chromatin patterns with rare nucleoli, and the cytoplasm was fairly abundant and stained a pale blue. Immature monocytes had more cytoplasmic vacuoles. Nuclei were reniform or irregular. These cells shifted from monoblast to immature monocytes to mature monocyte. Chromosome examination by the bone marrow direct method showed 11 of 15 observed cells to have 45 chromosomes with no definite evidence of clone formation, with common reciprocal translocation of B group and D group chromosomes. A diagnosis of acute monocytic leukemia was made on the basis of the above findings. The patient was discharged on 23 March 1971 with follow-up as an outpatient, because there was no change in the anemia or increase in blast cells, in spite of 10%-20% immature monocytes seen on peripheral blood smears. She was readmitted on 8 April 1971 due to high fever. Bone marrow aspiration done on 8 April 1971 revealed a nuclear cell count of 22,500/mm³, immature monocytes 6.5%, and erythroid series was rare. Treatment by 6MP, corticosteroid, and endoxan was started before the patient died with the complication of infection on 1 June 1971 (Table 1). The case was considered to be acute monocytic leukemia on autopsy though a picture of modification was presented as a result of treatment.

Case 2 (MF). A 63-year-old female, exposed to the A-bomb 854 m from the hypocenter in Hiroshima at the age of 37. She had fever, hemorrhage, and epilation. Her estimated exposure dose was 594 rad. She had medical examinations at ABCC in 1949, 1951, 1952. She had an exposure of 1944, 1951, and 1952. She died of acute monocytic leukemia on 1 June 1971. The case was considered to be acute monocytic leukemia on autopsy though a picture of modification was presented as a result of treatment.

症例2（基本名簿番号）。63歳の女性で、37歳の時、広島の爆心地から854mの地点で被爆し、発熱、出血、脱毛などの急性症状を呈した。推定被曝線量は594 radである。ABCCでは1949年、1951年、1952年に、また、1959年からは2年に1回ずつ検診を
Figure 1. Case 1. Cells show ductal structure surrounded by stroma of the connective tissue typical of adenocarcinoma. (H & E ×200)

図1 症例1. 細胞は管構造を示し結合繊からなる間質により囲まれている。典型的な腺癌である。（H&E ×200）

Figure 2. Case 1. Bone marrow smear. Leukemic immature monocyte. (May-Giemsa x1000)

図2 症例1. 骨髄標本。白血病性未分化単球を示す。（May-Giemsa ×1000）
Figure 3. Case 2. Cells proliferate along inner wall of the large gland. Some cells are destroyed and are mixed with red blood cells. This is atypical comedo type carcinoma. (H & E ×200)

図3 症例2. 大きな腺管の内壁に沿って細胞が増殖している。一部の細胞は破壊され赤血球が混在する。非定型的なcomedo型の癌である。（H&E ×200）

Figure 4. Case 2. Peripheral blood smear of buffy coat. Leukemic erythroblast shows megaloblastoid features. (Wright ×1000)

図4 症例2. 末梢血 Buffy coat の標本。巨芽球様の細胞を示す。（Wright ×1000）
### TABLE 1 HEMATOLOGICAL DATA

<table>
<thead>
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<th>PERIPHERAL BLOOD</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8 February 71</td>
<td>7 April 71</td>
</tr>
<tr>
<td>White Blood Cell/mm³</td>
<td>4050</td>
<td>17250</td>
</tr>
<tr>
<td>Red Blood Cell/mm³ (×10⁶)</td>
<td>179</td>
<td>216</td>
</tr>
<tr>
<td>Hemoglobin g/100 ml</td>
<td>7.0</td>
<td>8.1</td>
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<td>Hematocrit %</td>
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<td>26.0</td>
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<td>Platelet</td>
<td>32000</td>
<td>6000</td>
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<tr>
<td>Band Neutrophil</td>
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<td>2</td>
</tr>
<tr>
<td>Segmented Neutrophil</td>
<td>23</td>
<td>26</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>55</td>
<td>22</td>
</tr>
<tr>
<td>Monocyte</td>
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<td>4</td>
</tr>
<tr>
<td>Immature Monocyte</td>
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<td>28</td>
</tr>
<tr>
<td>Monoblast</td>
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<td>9</td>
</tr>
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<td>Promyelocyte</td>
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<td></td>
</tr>
<tr>
<td>Myelocyte</td>
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<td></td>
</tr>
<tr>
<td>Metamyelocyte</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Erythroblast</td>
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<td></td>
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### BONE MARROW (CASE 1)

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<th>19 February 71</th>
<th>8 April 71</th>
<th>10 May 71</th>
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<tbody>
<tr>
<td>Nuclear Cell Count/mm³</td>
<td>9000</td>
<td>22500</td>
<td></td>
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<tr>
<td>Lymphocyte %</td>
<td>36.5</td>
<td>22.0</td>
<td>55.0</td>
</tr>
<tr>
<td>Monocyte %</td>
<td>27.5</td>
<td>49.0</td>
<td>13.5</td>
</tr>
<tr>
<td>Immature Monocyte %</td>
<td>10.0</td>
<td>6.5</td>
<td>15.5</td>
</tr>
<tr>
<td>Monoblast %</td>
<td>1.0</td>
<td>3.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Granuloid/Erythroid</td>
<td>2.3/1</td>
<td>44.3/1</td>
<td>3.3/1</td>
</tr>
</tbody>
</table>

1952, and biennially since 1959 with normal findings up to June 1967.

In December 1967 (22 years after exposure) the patient noted a mass in the upper inner quadrant of the right breast, and biopsy at the Hiroshima Prefectural Hospital revealed ductal carcinoma (Figure 3). A right mastectomy was performed in January 1968 and postoperative radiotherapy with 12,770 rad administered. Her postoperative course was uneventful and, except for a postoperative scar, no abnormal findings were presented on examinations in 1969 and 1971. On 21 December 1971, she developed anemia and was readmitted with a suspicion of hemorrhage due to gastric ulcer. The hematologic findings were: RBC 1,400,000/mm³, hemoglobin 30% (Sahli), WBC 11,000/mm³, white blood cell

1967年12月（被曝22年後）右乳房内側上部の腫瘤に気付き、県病院で受診し、組織検査で分泌管癌（図3）と診断された。1968年1月右乳房摘出術を受け、術後12,770 radの放射線治療を受けていた。術後の経過は順調で、1969年及1971年の検診では手術痕を除き異常所見はない。1971年12月に貧血をきたし、胃潰瘍による出血を疑われて某病院に入院した。12月21日の末梢血液所見は、赤血球140×10⁴／mm³、ヘモグロビン30％（Sahli）、白血球11,000／mm³、白血球分類－単核球0.4％、中性粒細胞49、リンパ球
differential — staff cells 4, segmented cells 49, lymphocytes 38, monocytes 2, promyelocytes 1, myelocytes 1, metamyelocytes 5, erythroblasts 20/100 WBC (“highly dysplastic erythroblasts” and numerous polynucleated erythroblasts), megaloblastoid cells, and Jolly’s bodies (Figure 4). Acute erythroleukemia was suspected. She died on 5 January 1972 despite blood transfusions and prednisone treatment (Table 1).

Autopsy at ABC yielded leukemic cells in the liver, spleen, lymph nodes, heart, kidneys, and adrenal glands. The bone marrow was homogeneously pinkish-red. At least 90% of the blast cells varied in size from 20-40 μm in diameter. Nuclei showed fine chromatin pattern and nucleoli. Some cells were multinucleated. Maturing erythroid elements were nuclei or nuclear fragments. Erythroleukemia was diagnosed. Generalized hemorrhagic tendency was marked and the direct cause of death was considered to be bleeding of the digestive tract.

DISCUSSION
Newell and Kremenetz16 reported that the risk of leukemia in breast cancer patients was significantly higher in Negro women than in Caucasian women. Carey et al16 reported that among 46 cases of acute myelogenous leukemia, they found 4 cases with breast cancer less than 1 year before the onset of the leukemia, but without radiotherapy. The observed number of acute leukemia cases was 30 times greater than expected, suggesting that breast cancer is a predisposing complication to leukemia. Sakka17 reported that the incidence of leukemia in patients who had received radiotherapy following breast cancer surgery was significantly elevated.

Court Brown and Doll1 reported that ankylosing spondylitis patients who had received radiotherapy showed excess leukemia mortality which peaked 3-5 years after radiotherapy and the excess risk was evident for 6-14 years thereafter.

Leukemia developing in A-bomb survivors has gradually decreased with the peak being 6-7 years after exposure, but the incidence has not dropped to the control level 25-29 years after the bombs.18 The latent period of acute leukemia was shorter in the younger exposed and the incidence in the older exposed was increased 10 years after exposure. Chronic myelogenous leukemia reached its peak 5-10 years after
### Table 2: Leukemia Following Radiotherapy for Breast Cancer in Japanese Women

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Type of Leukemia*</th>
<th>Latent Period</th>
<th>Therapeutic Radiation Dose</th>
<th>Reference</th>
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<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>CML</td>
<td>1 7</td>
<td>4800</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>AML</td>
<td>9</td>
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<td>25</td>
</tr>
<tr>
<td>3</td>
<td>46</td>
<td>CML</td>
<td>5</td>
<td></td>
<td>25</td>
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<tr>
<td>4</td>
<td>41</td>
<td>AML</td>
<td>2 11</td>
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<tr>
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<td>57</td>
<td>AMOL</td>
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<td>6</td>
<td>40</td>
<td>Ery L.</td>
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<td>9600</td>
<td>25</td>
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<tr>
<td>7</td>
<td>58</td>
<td>AML</td>
<td>18</td>
<td>10000</td>
<td>25</td>
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<td>8</td>
<td>44</td>
<td>CML</td>
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<td>51</td>
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<td>18800</td>
<td>24</td>
</tr>
<tr>
<td>15</td>
<td>48</td>
<td>AMOL</td>
<td>8 2</td>
<td>14920 {Present}</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>63</td>
<td>Ery L.</td>
<td>4</td>
<td>12770 {Present}</td>
<td></td>
</tr>
</tbody>
</table>

*CML – Chronic myelogenous leukemia; AML – Acute myelogenous leukemia; AMOL – Acute monocyctic leukemia; Ery L. – Erythroleukemia.

In Japan, 10 cases of leukemia developing after postoperative radiotherapy for breast cancer were reported by Miyata et al.\textsuperscript{19} and Wakisaka and Kariyone.\textsuperscript{20} These cases plus 4 cases reported subsequently\textsuperscript{21-24} and the 2 cases presented here make a total of 16 cases reported. These 16 cases are listed in Table 2 with their cell type, latent period, and therapeutic radiation dose.\textsuperscript{25} Acute myelogenous leukemia was the most frequent type with 8 cases (50%), followed by chronic myelogenous leukemia and erythro-leukemia with 3 cases each (18.8%), acute monocyctic leukemia with 2 cases (12.5%), and no case of lymphocytic leukemia. The latent period was less than 3 years in 6 cases, 3-5 years in 2 cases, 6-8 years in 3 cases, 9-11 years in 2 cases, 12-14 years in 1 case, and more than 15 years or more in 2 cases. It is noteworthy that onset in less than 3 years was the most frequent, accounting for 37.5%. The latent period seems to be shorter compared with the cases of exposure regardless of age and has occurred only sporadically thereafter.

乳癌の手術後、放射線治療を受けた後に白血病を発症した事例について、我々では、行田ら\textsuperscript{19}、脇坂及び前田\textsuperscript{20} が10例を報告している。その後4症例の症例報告があり、\textsuperscript{21-24} 今回を含め2症例を加えて16例の報告が行われる。これら16例の病型、潜伏期間、治療用放射線量をリストし表2に示した。\textsuperscript{25} 病型についてみると、急性骨髄性白血病が最も多く8例（50％）、慢性骨髄性白血病と急白血病が各々3例（18.8％）、急性リンパ性白血病が2例（12.5％）であり、リンパ球性白血病は1例も認められなかった。潜伏期は3年未満6名、3-5年2名、5-8年3名、9-11年2名、12-14年1名、15年以上2名で、3年未満に発症したものが37.5％を占め最も多くかったことが注目され、慢性骨髄性白血病の放射線治療後の場合に比較し、
ankylosing spondylitis following radiotherapy. The radiotherapy doses ranged from 4,800 rad to 18,800 rad and averaged 9,900 rad. No definite relationship seems to be present between the radiotherapy dose received following surgery for breast cancer and the latent period.

Only a few papers have reported cancer in A-bomb survivors following radiotherapy. Russell and Antoku reported 5 cases of malignant neoplasms among 137 patients in the RERF Adult Health Study sample of A-bomb survivors and controls who had received radiotherapy; among the 4 who had received significant doses of A-bomb radiation, there were 2 cases of leukemia and 2 of lung cancer and it was difficult to determine whether the 2 cases of leukemia were caused by exposure to A-bomb radiation or by exposure to therapeutic radiation. Takahashi et al. reported 2 distally exposed A-bomb survivors who developed acute leukemia after receiving radiotherapy for malignant neurinoma and breast cancer. Because of their distal exposure, A-bomb radiation probably can be disregarded in these two cases.

It is evident from the reports of Shore et al. and Boice et al. that the incidence of breast cancer is high in women exposed to therapeutic or diagnostic radiation. Their reports make no mention of leukemia incidence in the group treated with X-ray.

It has already been demonstrated in a follow-up study of the RERF Life Span Study sample that breast cancer incidence is high in A-bomb survivors. Tokunaga et al. detected 360 cases of breast cancer in the females of this sample for the period 1950-74. On the basis of pathological examinations and surgical records, they classified 292 as cases of definite or probable breast cancer, 45 of whom were exposed to high doses of 100 rad or more.

On the other hand, 63 cases of leukemia were identified in the period 1950-71 among the female members of this fixed sample, and 26 of them had exposure to 100 rad or more.

The crude annual incidence rates of leukemia developing among breast cancer cases and among the fixed sample are compared in Table 3 classified by total sample and dose of 100 rad or more. The rate during 1950-71 in the females of the total sample is 5.2 (95% confidence limit:

潜伏期が短いようである。放射線治療による線量は 4,800 rad - 18,800 rad によ或多、平均 9,900 rad であった。乳癌手術後の治療用放射線量と潜伏期の間に明らかに関係は認められないようである。

原爆被爆者における放射線治療後の癌の発生についての報告は少ない。Russell 及び Antoku は放射線照射の被爆者と対照を含む成人被爆者調査対象者で、放射線治療を受けた137名から5名の悪性新生物を報告した。原爆により有意の線量を受けた4例のうち白血病・肺癌が各自2例あったが、白血病の2症例は、原爆によるもの、治療用放射線被曝によるかを決めることは難しいと述べている。高橋らは遠距離被爆者の報告で悪性神経腫瘍と乳癌の診断後、放射線治療を受け急性白血病を発症した2例を報告した。この2例は遠距離で被爆していた者で原爆放射線の影響は無視してよいであろう。

治療又は診断用の放射線を受けた女子に乳癌の発生率が高かったことは、Shore および Boice の報告である。彼らの報告では X 線治療群からの白血病の発生については報告していない。

原爆被爆者に乳癌の発生率が高いことは、放射線の寿命調査サンプルの追跡調査で明らかにされている。徳永ら 7 は1950-74年の観察で、このサンプルの女子から360名の乳癌を発症させ、治療又は診断又は治療の症例と分類した。うち45名の乳癌患者は100 rad 以上の高線量被曝者であった。

他方、この放射線研究の固定サンプルから発症した白血病は、白血病登録による完全にスクリーニングされ、1950-71年間に女子では63名の白血病が確認され、25名が100 rad 以上の高線量被曝の症例であった。

そこで、乳癌患者並びにこの固定サンプルからの白血病の発症率を、全サンプルと100 rad 以上の高線量とに分けて比較したのが表 3 である。女子の全サンプルからの1950-71年間の乳癌発症率は5.2(95%信頼区間：6.6-1.7)
TABLE 3 COMPARISON OF RISK OF LEUKEMIA AMONG BREAST CANCER CASES, FEMALE A-BOMB SURVIVORS AND CONTROLS IN THE RERF EXTENDED LIFE SPAN STUDY SAMPLE

<table>
<thead>
<tr>
<th></th>
<th>Number in LSS Sample</th>
<th>Number who received 100+ rad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite and probable breast cancer cases, 1950-74 (Tokunaga et al)[7]</td>
<td>292</td>
<td>45</td>
</tr>
<tr>
<td>Person years for follow-up of breast cancer cases from diagnosis until 1974</td>
<td>1898</td>
<td>325</td>
</tr>
<tr>
<td>Leukemia cases from these breast cancer cases following breast cancer diagnosis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Crude annual incidence rate per 100,000 population among these breast cancer cases</td>
<td>105.4</td>
<td>615.4</td>
</tr>
<tr>
<td>95% confidence limit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>330.0</td>
<td>1931.0</td>
</tr>
<tr>
<td>Lower</td>
<td>18.7</td>
<td>109.3</td>
</tr>
<tr>
<td>Leukemia cases during 1950-71</td>
<td>63</td>
<td>26</td>
</tr>
<tr>
<td>Person years (1950-71)</td>
<td>1210650</td>
<td>66063</td>
</tr>
<tr>
<td>Crude annual incidence rate per 100,000 population of this sample during 1950-71</td>
<td>5.2</td>
<td>39.4</td>
</tr>
<tr>
<td>95% confidence limit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>6.5</td>
<td>53.1</td>
</tr>
<tr>
<td>Lower</td>
<td>1.7</td>
<td>26.3</td>
</tr>
</tbody>
</table>

6.6-1.7) per 100,000 population, compared to 105.4 (95% confidence limit: 330.0-18.7) for the cases that developed after onset of breast cancer. With regard to only the group exposed to 100 rad or more, the crude annual incidence rate of leukemia developing after the diagnosis of breast cancer was made is 615.4 (95% confidence limit: 1931.0-109.3) per 100,000 population compared to 39.4 (95% confidence limit: 53.1-26.3) for leukemia developing in the sample as a whole. This suggests that the risk of leukemia in cases of breast cancer after A-bomb radiation is statistically higher than the risk in the heavily-exposed group as a whole. Since it can be assumed most of the breast cancer patients received postoperative radiotherapy, they can be considered to have been exposed to large radiation doses twice: A-bomb radiation and in postoperative radiotherapy. Thus, it is suggested that the risk of leukemia is higher with exposure to either of these two sources alone. Age at the time of the bomb and the number of years after exposure must also be considered as factors in the leukemia relative to these two radiation exposure experiences, but the availability of only two cases precluded a detailed study of these factors.
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