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Cancer mortality of Rockwell workers exposed to external low-level ionizing radiation and internally-deposited radionuclides

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Epidemiology

by

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To Julian, Leo and Steven

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PUBLICATIONS AND PRESENTATIONS

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ABSTRACT OF THE DISSERTATION

Cancer mortality of Rockwell workers
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by

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Professor Hal Morgenstern, Chair

We conducted a historical cohort study examining cancer mortality of employees of Rockwell/Atomics International. All cohort members were assigned to the company's health physics radiation monitoring program and monitored for external-ionizing radiation exposure and/or for internal radiation exposure due to radionuclides (4518 and 2294 workers respectively) between 1950 and 1993. About 95% of these workers were male. Please note that the following results are preliminary because the mortality follow-up of the cohort was incomplete when the analyses for this dissertation were conducted (about 10% of all causes of deaths were unknown). External comparisons suggested an increased cancer mortality

from leukemia for male Rockwell employees compared to the male US population (SMR=1.62, 95%CI=0.94-2.60). An external comparison of male Rockwell employees with male National Institute of Occupational Safety and Health (NIOSH) cohort members by salary type showed an increased mortality for Rockwell managerial and technical employees from cancers of the esophagus (SMR=3.61 95%CI= 0.97, 9.23) and the stomach (SMR=3.26 95%CI= 1.05, 7.60), the respiratory system and lung (SMR=1.87 95%CI= 1.35, 2.53), the bladder (SMR= 9.53 95%CI= 1.92, 27.8), the brain (SMR= 4.59 95%CI= 1.68, 9.99), leukemias (SMR=4.95 95%CI= 2.37, 9.10), and all hemato- and lymphopoietic cancers (SMR=2.32 95%CI= 1.35, 3.71). We employed logistic regression models for cohort data matching non-cases to cases by time of case occurrence and conducted dose-response analyses for radiation exposures. We found increases in mortality with increasing external-radiation dose for total cancers, hemato- and lymphopoietic cancers and solid tumors of radiosensitive organs. We also observed an increasing trend for hemato- and lymphopoietic cancers with internal exposure to alpha-emitting radionuclides. Our data furthermore suggested a stronger effect of external radiation exposure for solid tumors after age 40. Our results are based on small numbers of exposed cases, but find effects for the same cancer sites as implicated previously in A-bomb survivor and nuclear cohorts studies. However, the size of the effect for external radiation exposure on total cancer mortality found in this study is about 10-fold greater than expected according to extrapolations from A-bomb survivor data.

CHAPTER 1

Introduction and Background

Please note that all of the following results are preliminary because the mortality follow-up of the cohort was incomplete when the analyses for this dissertation were conducted (about 10% of all causes of deaths were unknown).

Much controversy remains concerning the carcinogenic potential of chronic exposure to low-level ionizing radiation encountered in occupational settings. Studies of nuclear workers over the past 20 years have yielded conflicting findings (Stewart 1990). Among A-bomb survivors, single whole-body exposures of less than 200 mSv have not resulted in an increased cancer rate (Shimizu et al. 1990, see Table 1.1). Traditional radiobiologic theory suggests that the fractionated doses (doses spread over time) characteristic of occupational and diagnostic radiation exposures should be less harmful than the same amount of radiation concentrated in a single dose. Thus, fractionation is thought to give the tissue a chance to repair damages caused by the irradiation (BEIR V, 1990). On the other hand, the repeated repair of even minor but recurrent injuries to the cell-DNA could theoretically increase the likelihood for repair mechanisms to fail or miss.

Extrapolations from the A-bomb-survivor data to low-dose external radiation exposure based on a linear no-threshold model suggest an excess relative risk for all cancers of 0.41% (90%CI 0.32-0.52) per 10 mSv of external whole-body exposure. In contrast, the corresponding estimates derived from radiation-worker studies range from 0% to 4.94%, depending on assumptions about lag periods and the models used to estimate risk (Gribbin et al. 1993, Wing et al. 1993). Thus, the results obtained from some nuclear-worker cohort studies raise

the possibility that risk estimates for all cancers extrapolated from the A-bomb-survivor data might underestimate the carcinogenic effect of low-level radiation by as much as 10-fold. On the other hand, results from occupational studies are also consistent with the possibility of no effect at the levels and rates of exposure studied (see also Tables 1.2 - 1.4).

Internal radiation exposure is caused by deposition of radioactive particles in the human body after inhalation, ingestion, or entry through wounds. In animal experiments, high levels of internal exposure to alpha- and beta/gamma-emitting radionuclides have resulted in immuno-suppressive and carcinogenic effects to the organs in which these particles concentrate (ICRP, 1980). Recently, reduced DNA-repair response capabilities of cells have been found in long-term residents of communities 1.5 mile downwind from uranium mining facilities (Au et al. 1995). These residents were considered potentially exposed to radionuclides contaminating soil and water from these mining operations. The carcinogenic potential of internally deposited radionuclides has been confirmed in heavily exposed human populations like uranium miners and millers and radium dial painters and patients treated with Thorotrast and 224-Ra (Mays 1988). The cancer sites implicated coincided well with radionuclide-distribution patterns throughout the body, with increases in the incidence of lung, liver, and head-sinus carcinomas, as well as of leukemias and bone sarcomas.

These populations have experienced carcinogenic effects of internal radiation exposure in the high-dose range, specifically greater than 1 Sv to organ systems through which the radionuclides pass or in which they accumulate. EPA

recommendations for the amount of radon allowable in drinking water are based on the results from studies of these high-dose human exposures (BEIR IV, 1988).

Twenty-six white male workers who had been exposed to airborne plutonium during World War II were followed for 42 years, to 1986 (Voelz and Lawrence, 1991). At that time, the mean age of the workers followed was 66 years. By 1990, seven subjects had died. Three of these 7 deceased individuals were diagnosed with lung cancer, one with osteosarcoma, and another with fatal chronic respiratory disease. The individual who died from osteosarcoma had received an estimated average skeletal dose of only 16 mSv just half a year before his death. In contrast, the lowest average skeletal dose received by individuals who died of bone sarcomas among the radium dial painters was 800 mSv. Some animal experiments support the low-dose estimate: osteosarcomas developed in beagle dogs irradiated with only 20 mSv from 229-PU.

Evidence about lower-dose internal exposure to less than 1 Sv has been obtained from studies of predominantly alpha-emitting radionuclides in the nuclear industry. These studies suggest increased rates of lung cancer among workers exposed to uranium, of lung and hemato- and lymphopoietic cancers among workers exposed to plutonium and of prostate cancers among employees exposed to tritium (Checkoway et al. 1988, Wilkinson et al. 1987, Beral et al. 1988, Beral et al. 1985, Wiggs et al. 1994). However, these studies have not been conclusive with respect to the carcinogenic potential of such low-dose levels since the estimates were based on very small numbers of cases and the confidence limits did not consistently exclude the null value of one.

The inconsistencies in results across studies could be attributable to random error, selection biases resulting in healthy worker effects, differences in length of follow-up, lag assumptions and exposure distributions, as well as residual confounding. The present study will add to the discussion and the pool of information about the cancer-causing potential of occupational low-level ionizing external and internal radionuclide radiation exposures.