THE IOWA RADON LUNG CANCER STUDY
Phase I: RESIDENTIAL RADON GAS EXPOSURE AND LUNG CANCER

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Exposure to high concentrations of radon (222Rn) progeny produces lung cancer in both underground miners and experimentally exposed laboratory animals. The goal of the study was to determine whether or not residential radon exposure exhibits a statistically significant association with lung cancer in a state with high residential radon concentrations.

A population-based, case-control epidemiologic study was conducted examining the relationship between residential radon gas exposure and lung cancer in Iowa females who occupied their current home for at least 20 years. The study included 413 incident lung cancer cases and 614 age-frequency-matched controls. Participant information was obtained by a mailed-out questionnaire with face-to-face follow-up. Radon dosimetry assessment consisted of five components: 1) on-site residential assessment survey, 2) on-site radon measurements, 3) regional outdoor radon measurements, 4) assessment of subjects’ exposure when in another building, and 5) linkage of historic subject mobility with residential, outdoor, and other building radon concentrations. Histologic review was performed for 96% of the cases.

Approximately 60% of the basement radon concentrations and 30% of the first floor radon concentrations of study participants’ homes exceeded the U.S. Environmental Protection Agency action level of 150 Bq m⁻³ (4 pCi/L). Large areas of western Iowa had outdoor radon concentrations comparable to the national average indoor value of 55 Bq m⁻³ (1.5 pCi/L).

Excess odds of 0.24 (95% CI = -0.05 – 0.92) and 0.49 (95% CI = 0.03 – 1.84) per 11 WLM₅₋₁₉ were calculated using the continuous radon exposure estimates for all cases and live cases, respectively. Slightly higher excess odds of 0.50 (95% CI = 0.004 – 1.80) and 0.83 (CI = 0.11 – 3.34) per 11 WLM₅₋₁₉ were noted for the categorical radon exposure estimates for all cases and the live cases.

A positive association between cumulative radon gas exposure and lung cancer was demonstrated using both categorical and continuous analyses. The risk estimates obtained in this study indicate that cumulative radon exposure presents an important environmental health hazard.

Keywords: case-control studies; dose-response relationship (radiation); epidemiologic methods; epidemiologic studies; lung neoplasms; radon, smoking, women’s health

INTRODUCTION

To assess the association between radon exposure and lung cancer, we conducted a population-based case-control study of Iowa women aged 40 to 84 who lived in their current home for at least 20 years. Iowa is an excellent location to perform such a study for several reasons: 1) a substantial proportion of Iowa's population resides in the same home for 20 years or more; 2) Iowa has a high quality, National...
Cancer Institute supported Surveillance, Epidemiology, and End Results (SEER) registry for cancer reporting, which allows rapid identification of newly diagnosed lung cancer cases; and 3) Iowa homes contain the highest mean screening $^{222}\text{Rn}$ concentrations in the United States. The Iowa Radon Lung Cancer Study’s (IRLCS) unique combination of study design, enhanced dosimetric techniques, individual mobility assessment, population stability, expert histopathologic review, and high percentage of live cases provided a rare opportunity to determine whether or not residential radon exposure exhibits a statistically significant positive association with lung cancer.

METHODOLOGY

The IRLCS has four major components: 1) rapid-reporting of cases, 2) a mailed questionnaire followed by a face-to-face review and facilitated interview, 3) a comprehensive $^{222}\text{Rn}$ exposure assessment, and 4) independent histopathologic review of lung cancer tissues (1).

Case Subjects - Lung cancer cases met the following inclusion criteria: 1) newly diagnosed with a primary invasive (not in situ) lung carcinoma, without any prior primary invasive lung carcinoma; 2) female Iowa resident at time of diagnosis; 3) age ranging from 40 to 84; 4) microscopically confirmed primary lung carcinoma; and 5) residence for 20 consecutive years or more in the current home. Cases that met the eligibility criteria were identified by the Iowa Cancer Registry (ICR) between May 1, 1993 and October 30, 1996. The ICR has been a member of the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute since its inception in 1973. The consent of the case subjects’ physician was obtained prior to contacting the subjects.

Study questionnaires included information concerning family health history, demographics, occupational exposures, smoking history, passive smoke exposure history, previous non-malignant lung disease, diet, and a detailed section on home characteristics. Sixty-nine percent of the case subjects were alive at the time of the home visit; at which time, multiple radon detectors were placed and the questionnaires were facilitated. For the case subjects who were deceased at the time of home visit, a knowledgeable next-of-kin completed the questionnaires.

To obtain a reliable histologic diagnosis, pathologic materials were retrieved from the eligible lung cancer cases. Two surgical pathologists from the Department of Pathology at The University of Iowa Hospitals and Clinics reviewed the pathologic material upon which a diagnosis of lung cancer was made for lung cancer case subjects. The major diagnostic groups were based on the World Health Organization’s histologic typing of lung tumors and included the major categories of small cell carcinoma, squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. The reviewers were blinded to the diagnosis on the pathology report as well as to each other’s review diagnosis. When the designated histologic type of tumor differed between the two reviewers, they reviewed the pathologic material simultaneously and rendered a consensus diagnosis. To ensure comparability of data, criteria for diagnosis was made based on light microscopic observations. In some cases, special stains such as mucicarmine, PAS, or PAS after diastase were requested on the tissue blocks by the reviewing pathologists to arrive at a reliable diagnosis.
Control Subjects - Control subjects met the following eligibility criteria: 1) no prior primary invasive lung carcinoma at the time of initial contact as determined by the ICR database; 2) female Iowa resident at time of initial contact; 3) age ranging from 40 to 84; 4) alive at time of interview; and 5) residence for 20 consecutive years or more in the current home. Control subjects aged 40-64 were selected from current driver's license (DL) tapes provided by the Iowa Department of Transportation. Control subjects aged 65-84 were selected from a current tape made available through the Health Care Financing Administration (HCFA). These two databases were chosen to provide a population-based sampling frame. Both DL and HCFA controls were age-frequency matched by 5-year age groups with the lung cancer cases. Once selected, the control group was matched against the database of the ICR. If the selected control had a past diagnosis of a primary invasive lung carcinoma, she was excluded. Before contacting each HCFA control, a letter provided by the Department of Health and Human Services describing the study and the subject's rights was sent as mandated by the HCFA. With the exception of the HCFA letter, DL and HCFA informed consent was obtained in an analogous manner. Initially, a control contact letter, which described the study, was sent to the potential participant followed by a telephone call to both assess eligibility and to obtain their consent for participation in the study. The study questionnaires for controls were identical to the questionnaires completed by cases.

Radon Dosimetry - The radon dosimetry assessment consisted of five components: 1) on-site residential assessment survey, 2) on-site radon measurements, 3) regional outdoor radon measurements, 4) assessment of subjects’ exposure when in another building, and 5) linkage of historic subject mobility with residential, outdoor and other building radon concentrations. Component 1 was a residential assessment, and dosimetry placement, which was conducted in-person at the subject’s home. Upon arrival at the home, the field technician reviewed the mailed household questionnaire with the participant to check for missing or inconsistent information. Next, a home survey was performed, which documented home characteristics, location of rooms and dimensions, number of home levels, and environmental gamma radiation levels. During the home survey, the field technician recorded home floor plans, room location of detector placement, detector placement location within a room, house level of placement, time and date of placement, and detector control numbers.

A major part of the residential assessment included a mobility review. Historical participant mobility within the home as well as time spent outside the home and in another building was ascertained by a face-to-face interview with the study participant. Beginning with the year the participant moved into the current home, the interviewer prompted the participant to go forward in time and identify periods where their mobility patterns remained relatively stable. Within these stable time periods, hours spent in another building, outside, and within the home were collected using task-linkage (e.g., retrieval of hours based on time spent involved in specific duties or activities). Each participant-reported period was identified using autobiographical memory cues and facilitated using task-linkage. Using this methodology, all time (168 hrs. per week) was accounted for from the year they moved into their current home to study enrollment (1,2).

The second component of the radon dosimetry assessment was on-site measurement of home radon gas concentrations for each case and control (1). Using the results of the mobility interview, the field technician placed radon detectors in rooms where the subject spent most of her time either the year prior to diagnosis for cases or the year prior to initial contact for controls. At least one monitor was
placed on each level of the home, current and historic bedrooms, and in home work areas (1,3). Landauer’s Radtrak Alpha Track Detector (ATD) was used to provide an integrated mean radon gas measurement of residential radon gas concentrations. The radon detectors remained within the participants’ home for one year, after which time a field technician retrieved the detectors noting any improper movement of the detectors. The IRLCS followed a strict Quality Assurance (QA) plan for proper placement and removal of radon detectors, which included telephone contacts with study subjects quarterly during the year-long dosimetry period to assure the radon detectors remained appropriately placed (4). The dosimetry QA portion of the plan was guided by Environmental Protection Agency Guidelines. Three components were used to monitor detector performance: 1) Five percent of detectors were exposed (spikes) to known quantities of radon to test the accuracy of the detector's response, 2) twelve percent of the detectors were collocated (duplicates) to monitor the precision of the detectors’ response, and 3) five percent of detectors were unexposed (blanks) to examine whether or not the detectors picked up extraneous exposures. Detectors were exposed to known radon concentrations in the U.S. Environmental Protection Agency’s Eastern Environmental Radiation Facility in Montgomery, Alabama. Electret Passive Environmental Radon Monitors (E-PERM®) detectors were also collocated with ATDs at 2% of the sites as field intercomparison detectors. A termination survey was performed at the end of the monitoring period for each placement to retrieve dosimetry; at which time the participant, or next-of-kin, was administered a final questionnaire that ascertained information on changes in home construction or behaviors that may have affected radon concentrations during the monitoring period. Movement or damage of detectors was recorded. A QA Officer from outside the study periodically reviewed all aspects of radon measurements, including field procedures, data management, data collection, laboratory correspondence, data analyses, reports, and data archives (4).

The third component of the radon dosimetry assessment was the measurement of mean outdoor radon concentrations (5). One hundred eleven geographically dispersed locations in Iowa were measured by 129 U.S. Environmental Protection Agency proficient alpha track detectors. The detectors were housed in weatherproof chambers held 1 to 2 meters above the ground and placed for 1 year at least 10 m from a home. Side-by-side duplicates, 1 and 2 meter pairs, and year-to-year pairs suggested instrumental, vertical, and annual variations of less than 15% (0.1 pCi/L). Outdoor radon concentration contour maps were generated from the outdoor radon measurements by variogram and kriging analyses. The data’s spatial distribution was analyzed through variogram modeling to determine the best functional representation and correlation vector for the complete data set. This modeling was used to construct a surface map of outdoor radon concentrations through a procedure known as kriging. Each point on the kriged surface map is a weighted local average of the direct outdoor measurements. Outdoor radon exposure was estimated using this surface map. The exposure model assumed that a subject is exposed to outdoor radon within a 20-mile radius of her home.

The fourth component of the radon dosimetry assessment was the estimation of other building (workplace, church, store, etc.) radon concentrations for each subject. The distribution of radon concentrations in work places is not well documented. We have studied the relationship between bedroom radon and workplace radon for approximately 100 women in nearby Minnesota. The results from this study suggest that the best estimate for the workplace radon is 0.5 times the bedroom radon. Thus, we also constructed a kriged surface map for the other buildings based on 0.5 times the first floor
radon concentrations within the control subjects’ homes. This map was then used to estimate other building radon exposures. The exposure model assumed that a subject is exposed to radon in other buildings within a 20-mile radius of her home.

The fifth component of the radon dosimetry assessment was the linkage between the various radon concentrations and both the subject’s temporal and spatial mobility (1-3). A time-weighted average radon exposure for each subject was calculated based on average year-long radon measurements performed in the current bedroom (and historic bedroom, if applicable); each level of the home; and in-home work area (if applicable). The average year-long radon measurement was linked to percent time spent in bedroom (and historic bedroom, if applicable); each level of the home; in-home work area (if applicable); outdoors; in another building; and on vacation for each subject. The current average year-long radon measurement was assumed to be constant over the years the participant lived in the home; however, the temporal and spatial activity (time spent in the bedroom, each level of the home, etc.) was allowed to vary for each subject by individual season and period of time as recorded in the mobility interview. The mobility interview accounted for 168 hours per week allowing for differences between weekdays and weekends, seasons (warm weather and cold weather, etc.) and employment outside of the home or work in the home. Adjustments to this formula were made for subjects who were away from the home for a short time because of military duty or extended vacations. Dose assessment included exposure for all years the subject lived in the current home. Temporal and spatial mobility information was collected in a way that allowed for the estimation of radon exposures over a wide variety of temporal windows.

RESULTS AND DISCUSSION

Approximately 60% of the basement radon concentrations and 30% of the first floor radon concentrations of study participants’ homes exceeded the U.S. Environmental Protection Agency action level of 150 Bq m⁻³ (4 pCi/L). Large areas of western Iowa had outdoor radon concentrations comparable to the national average indoor value of 55 Bq m⁻³ (1.5 pCi/L).

Excess odds of 0.24 (95% CI = -0.05 – 0.92) and 0.49 (95% CI = 0.03 – 1.84) per 11 WLM⁻¹ were calculated using the continuous radon exposure estimates for all cases and live cases, respectively. Slightly higher excess odds of 0.50 (95% CI = 0.004 – 1.80) and 0.83 (CI = 0.11 – 3.34) per 11 WLM⁻¹ were noted for the categorical radon exposure estimates for all cases and the live cases. Large cell carcinoma exhibited a statistically significant trend for both the continuous (p = 0.04) and categorical (p = 0.03) risk estimates. A suggestive dose response trend was also observed for the squamous cell carcinoma subset (categorical p-trend = 0.06). However, the differences in the linear excess odds between histologic types was not statistically significant (continuous p = 0.58, categorical p = 0.65).

CONCLUSIONS

The study found that the increased risk for individuals exposed to 11 WLM⁻¹ (roughly equivalent to a 15-year exposure at an average radon exposure of 4 pCi/L) was approximately 40%-50%. This risk estimate is substantially higher than those reported in previous residential radon studies. The enhanced
dosimetry techniques used in the IRLCS, which reduced exposure misclassification, likely contributed to the higher risk estimates. However, the IRLCS risk estimates are in general agreement with the National Academy of Science’s predicted cancer risk associated with indoor radon exposure.

The IRLCS uniquely combined enhanced dosimetric techniques, individual mobility assessment, and expert histologic review, within a population characterized by stability, high percentage of live cases, and potential for high radon exposure to examine the relationship between cumulative radon exposure and lung cancer. Our findings suggest that the ability to detect an association between cumulative radon exposure and lung cancer requires 1) a rigorously designed study minimizing radon exposure misclassification and 2) a study location with relatively high radon concentrations. Overall, the risk estimates obtained in this study indicate that cumulative radon exposure is significantly associated with lung cancer risk. The study data are currently in the final process of peer review. A detailed paper describing the findings should be available by the summer or fall of 1999.

Phase II of the IRLCS is planned. Phase II will use a new retrospective radon detector to assess the risk posed by residential radon progeny exposure.

REFERENCES


