President's Cancer Panel

December 4, 2008

Charleston, SC

Environmental Factors in Cancer: Radon

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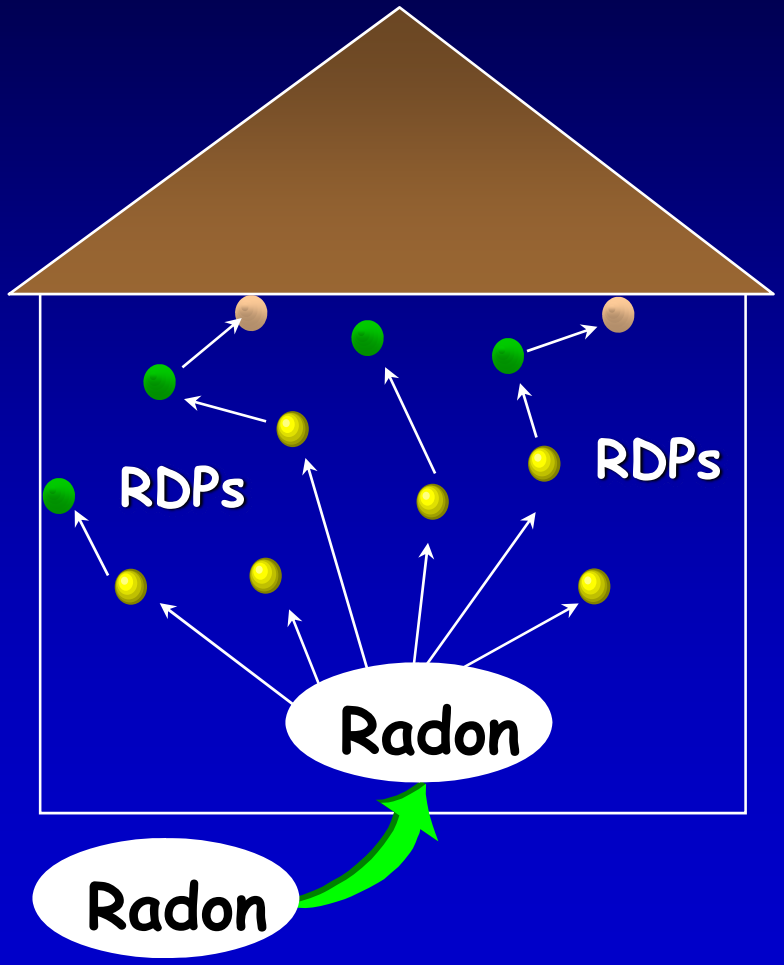
CURRENT UNDERSTANDING

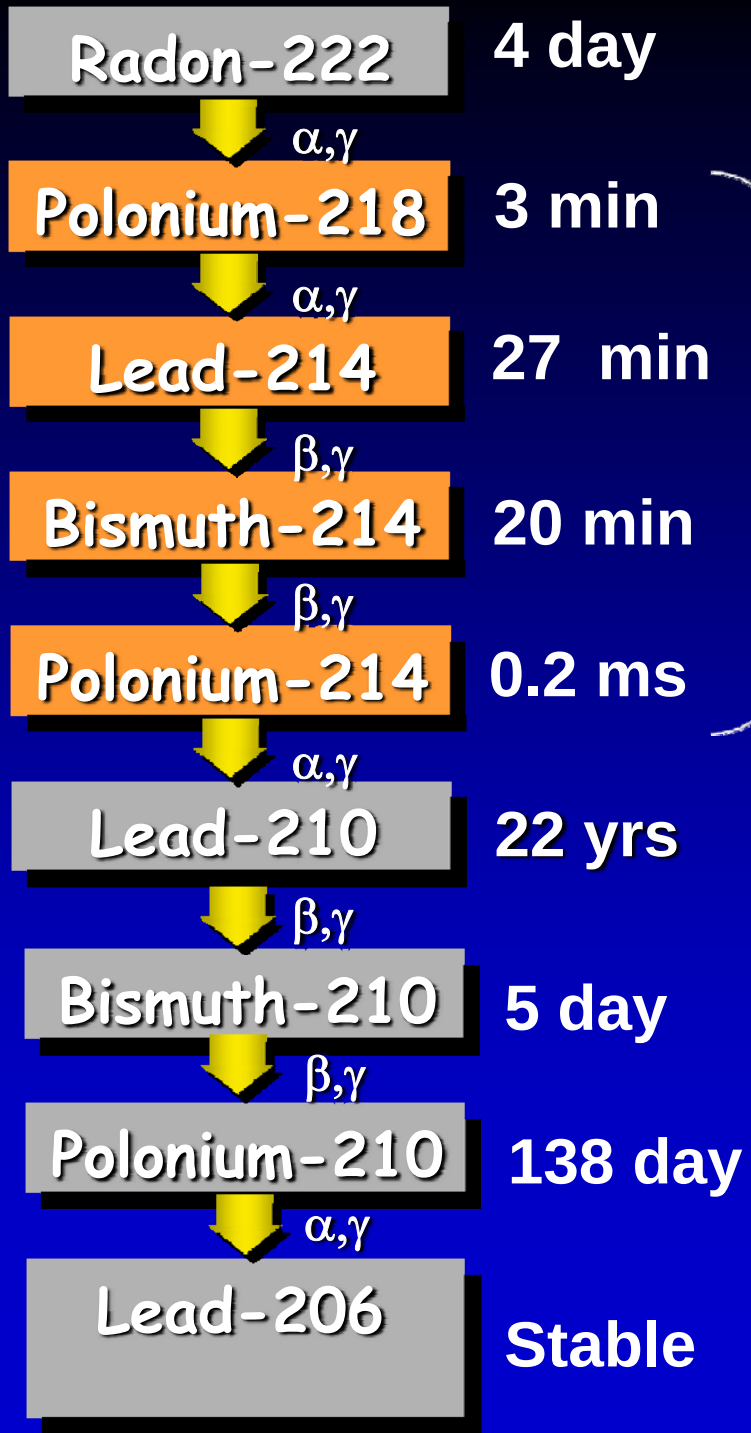
Radon –222 (radon)

- Radon is a gas
- It is naturally occurring outdoors
- In general - the primary source of radon is from the soil
- In most cases, builders do not choose to build homes radon resistant

Radon Decay Products (RDPs)



- Radon enters home
- Radon decays into RDPs in the air
- Some RDPs remain in the air
- Some RDPs plate out on surfaces



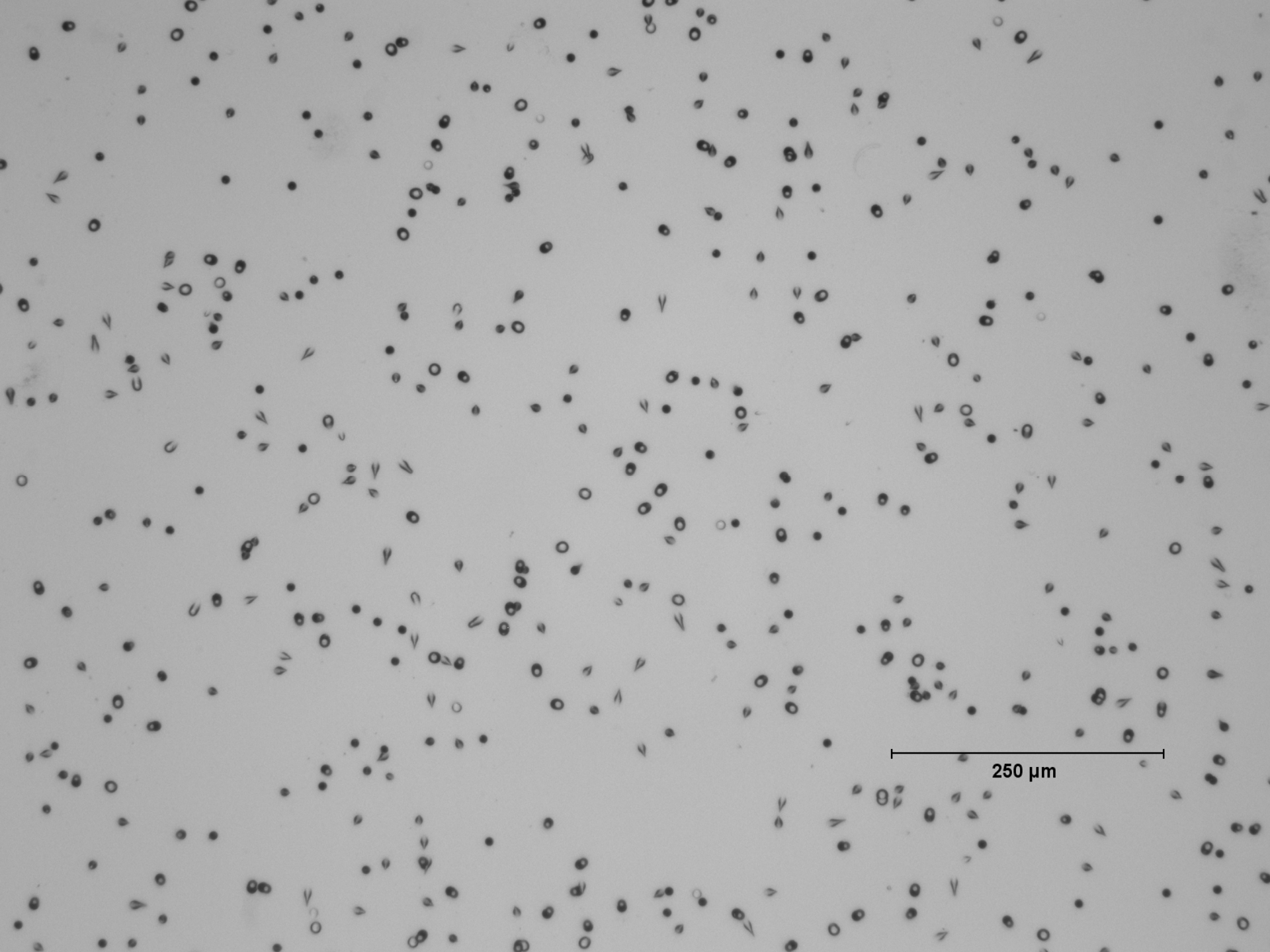
^{218}Po and ^{214}Po deliver the radiologically significant dose to the respiratory epithelium

Radon Decay Products

What happens when radon decay products are inhaled?

Double Strand Breaks

- **Highly radioactive particles adhere to lung tissue, where they can irradiate sensitive cells.**
- **Radiation can alter the cells, increasing the potential for cancer.**


250 µm

Radon causes lung cancer even below the U.S. EPA's radon action level of 150Bq/m^3 (4 pCi/L)

Residential Epidemiologic Study	# of studies pooled	# of lung cancer cases/controls	Increased risk per 100 Bq/m^3 (95% CI)
North American Pooled Analysis	7	3,662/4,966	11% (0% - 28%)
European Pooled Analysis	13	7,148/14,208	8% (3% - 16%)
Chinese Pooled Analysis	2	1,050/1,995	13% (1% - 36%)

Pooled risk estimates likely underestimate the true risk posed by protracted radon exposure

1. Errors in radon detector measurement
2. Failure to consider temporal and spatial radon variations within a home
3. Missing information on radon exposure from other sites, such as prior homes
4. Failure to properly link radon concentrations with subject mobility
5. Measuring radon gas as a surrogate for radon progeny exposure

Risk estimates increase with improved exposure assessment

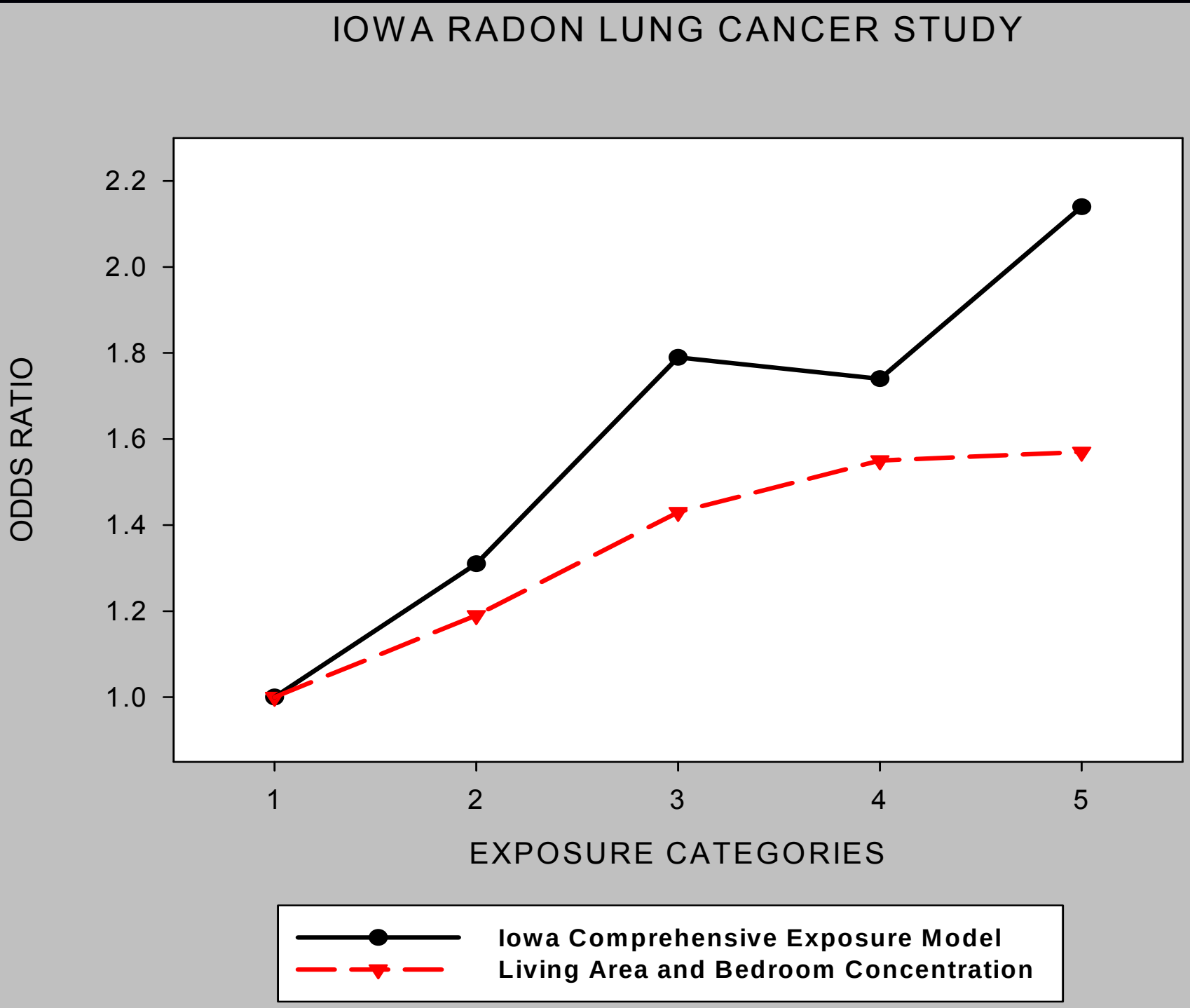
Residential Epidemiologic Study	Increased risk per 100 Bqm^{-3} (95% CI)	Increased risk at 100 Bq/m^3 Analyses based on improved radon concentration data (95% CI)
North American Pooled Analysis	11% (0% - 28%)	**18% (2% - 43%)**

Analysis restricted to individuals who resided in either one or two homes for the period 5 to 30 years prior to recruitment and also had at least 20 years covered by a year-long radon measurement.

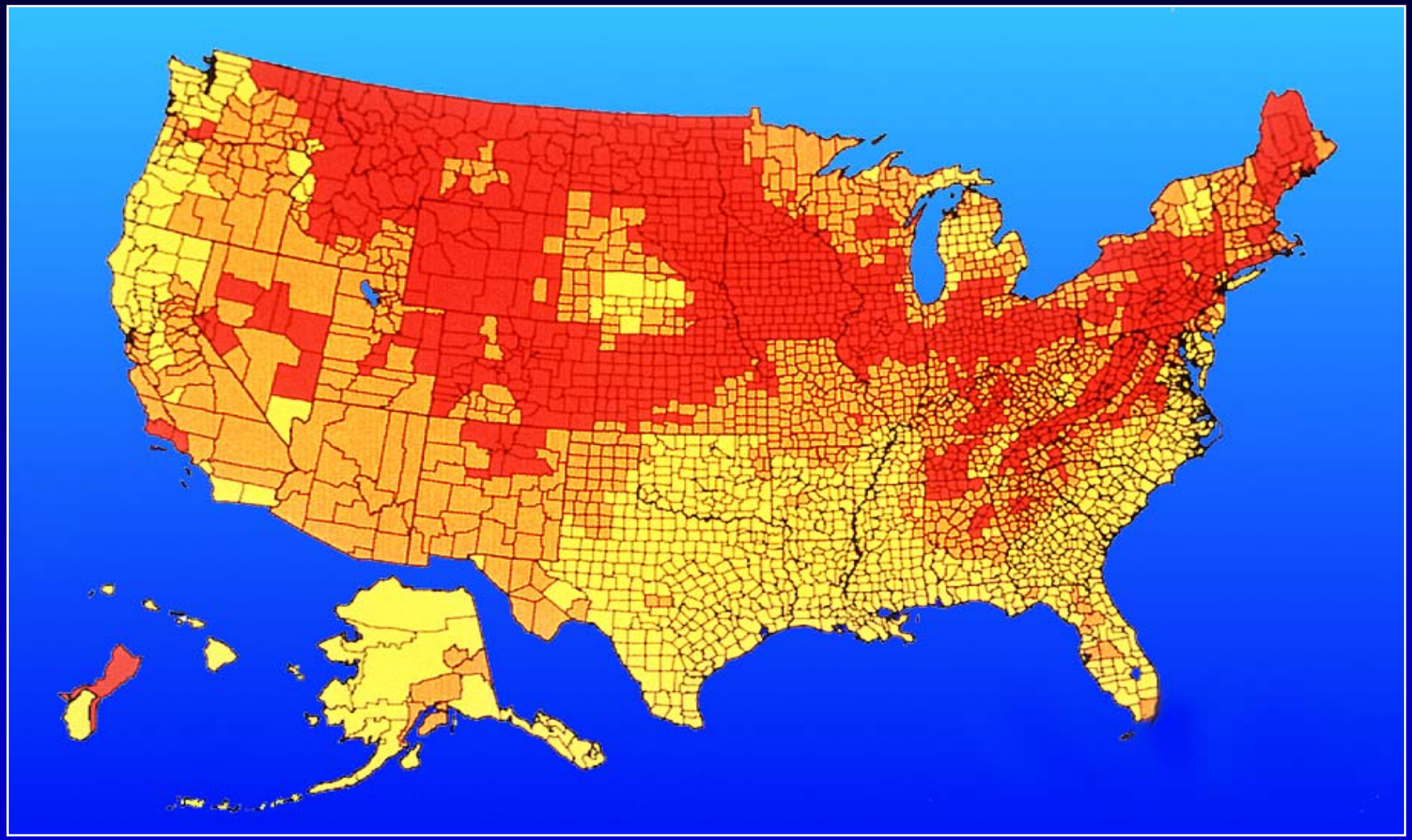
Iowa Radon Lung Cancer Study (IRLCS)

- The NIEHS\NCI funded IRLCS collected historical information on participant mobility within the home, time spent outside the home, and time spent in other buildings.
- Numerous yearlong radon measurements were performed on each level of the participant's home.
- Outdoor radon measurements were also conducted in addition to workplace radon exposure assessments.
- The spatially diverse measurements were linked to where the participant spent time, for at least the proceeding 20 years, in order to obtain a cumulative radon exposure for the individual.

Field et al. Residential radon gas exposure and lung cancer: the Iowa Radon Lung Cancer Study., *American Journal of Epidemiology*, 151 (11):1091-102, 2000.


IOWA RADON LUNG CANCER STUDY
ODDS RATIO
2.2
2.0
1.8
1.6
1.4
1.2
1.0
1
2
3
4
5
EXPOSURE CATEGORIES
Iowa Comprehensive Exposure Model
Living Area and Bedroom Concentration

Most radon-induced lung cancers occur below the U.S. EPA's radon action level



Zone 1 - Predicted average indoor screening level > than 4 pCi/L
Zone 2 - Predicted average indoor screening level between 2 and 4 pCi/L
Zone 3 - Predicted average indoor screening level less than 2 pCi/L

Protracted radon exposure increases the risk of all types of lung cancer

Residential Study	Histologic type most associated with radon exposure
North American Pooled Analysis	Small Cell
European Pooled Analysis	Small Cell
Iowa Radon Lung Cancer Study	Large Cell Squamous

CANCER MORTALITY

CANCER TYPE	ESTIMATED U.S. DEATHS/YR
1. Lung and Bronchus	**161,840**
2. Colon and Rectum	49,960
3. Breast Cancer	40,930
4. Pancreas	34,290
5. Prostate	28,660
6. Leukemia	21,710
7. Non-Hodgkin Lymphoma	19,160
8. Liver and Bile Duct	18,410
9. Ovary	15,520
10. Esophagus	14,280
11. Urinary Bladder	14,100
12. Kidney and Renal Pelvis	13,010
13. Stomach	10,880
14. Myeloma	10,690
15. Melanoma	8,420

Radon is one of our major environmental toxicants in the United States

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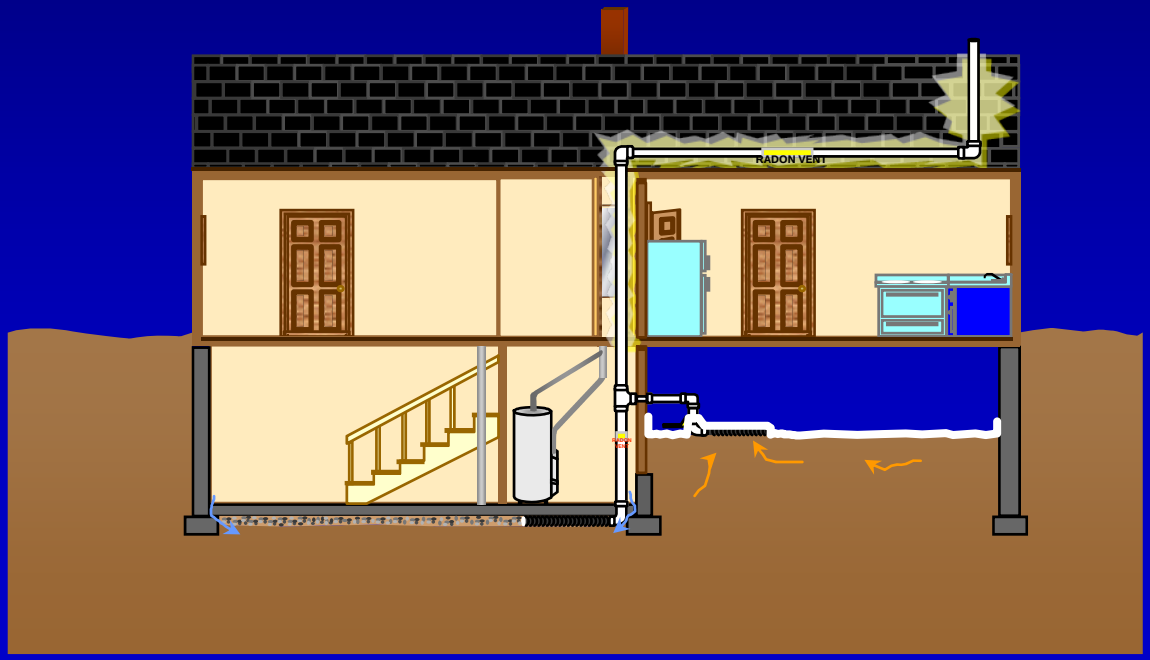
Mitigation and Radon Resistant New Construction (RRNC) methods are available to reduce the risk

For example, a recent study reported that the pre-mitigation radon concentrations in a survey of 166 homes averaged 380 Bq/m^3 (10.3 pCi/L), while post mitigation radon concentrations averaged 44 Bq/m^3 (1.2 pCi/L).



Steck DJ. Post-mitigation radon concentrations in Minnesota homes. Proceedings of the American Association of Radon Scientists and Technologists 2008 International Symposium Las Vegas NV, September 14-17, 2008, available at http://aarst.org/radon_research_papers.shtml

Individual susceptibility to radon-induced lung cancer

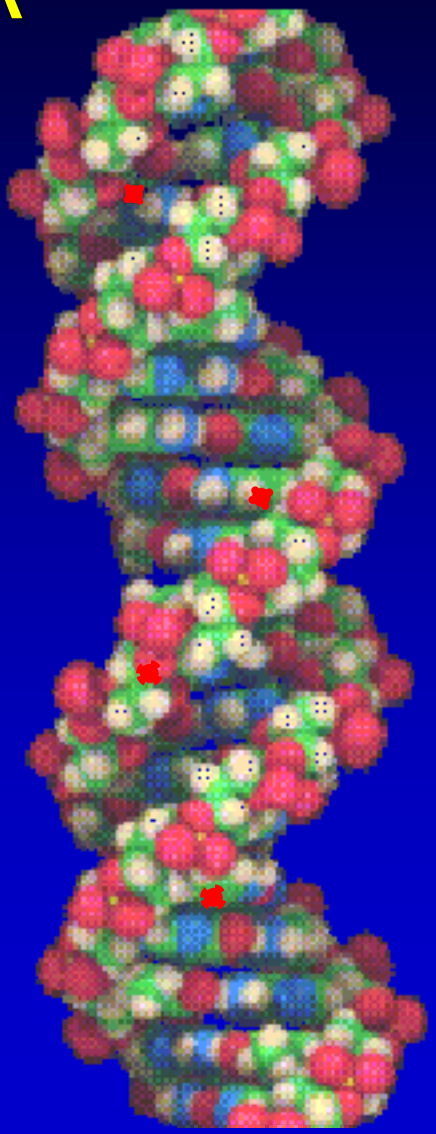
- Smokers and ex-smokers
- Individuals with lower socioeconomic status
- Infants and Children ?
- Individuals who have mixed exposures to lung carcinogens
- Individuals who have a history of medically-related radiation exposure (x-ray therapy, etc.)
- Variation by genotype

Ionizing radiation can directly and indirectly damage DNA

Alpha Particle

Free radical formation

Double –strand DNA breaks



Defects in tumor suppressor genes – p53

At risk individuals–$GSTM_1$

(glutathione S-transferase M1)

Adverse health outcomes related to protracted radon exposure other than lung cancer

Miner-based epidemiologic studies*

Suggestive evidence for stomach cancer, liver cancer, skin cancer, and leukemia

Recent miner-based incidence study of leukemia**

Incidence of all leukemia combined as well as chronic lymphocytic leukemia (CLL) was positively associated with cumulative radon exposure

Non-statistically significant increases were also noted for myeloid leukemia and Hodgkin's lymphoma

*Darby et al (1995), Kreuzer et al. (2008) ** Řeřicha et al. (2007)

Radiation Exposure and Leukemia

A recent methodologically advanced study in Iowa using the Iowa SEER cancer registry also noted an increased risk for CLL, and CML, at the geographic level.

Several other recent studies have also suggested a potential association with radiation exposure and CLL . Until recently, CLL was the only subtype of leukemia not thought to be radiogenic.

Smith et al. (2007); Linet et al. (2007)

RESEARCH NEEDS
Epidemiologic Studies

1. Assess risk factors affecting individual susceptibility (e.g., genetic polymorphisms) to radon-induced lung cancer

2. Assess the possible associations between radon exposure and extrapulmonary cancers (e.g., leukemia, lymphoma, chronic myeloid neoplasms, stomach, melanoma, etc.)

Radon could be included as an exposure of interest under future funding for understudied rare cancers

National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov

Epidemiology and Genetics Research
Cancer Control and Population Sciences

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EGRP Hosts Workshop on Understudied Rare Cancers

2nd NCI Epidemiology Leadership Workshop:
Understudied Rare Cancers
Boston, MA • September 11-13, 2005

Left to right: Dr. Robert Croyle, DCCPS Associate Director; Dr. Nancy Mueller, Professor, Harvard University; and Dr. Ed Trapido, EGRP Associate Director.

The Epidemiology and Genetics Research Program (EGRP) sponsored its second leadership workshop bringing together investigators to identify ways to stimulate research on understudied rare cancers on September 11-13, 2005, in Boston. EGRP is responsible for managing NCI's extramural epidemiology research portfolio.

EGRP-funded investigators conducting research on understudied rare cancers were invited to the workshop to identify gaps in epidemiologic and genetic research on the cancers, and to discuss ways to foster collaborations and partnerships among basic, clinical, and population scientists within the extramural and intramural communities. The National Institutes of Health's Office of Rare Diseases also cosponsored the workshop.

"The four major cancers, lung, breast, prostate, and colorectal cancer, comprise the lion's share of our portfolio, but there are other cancers – some of them highly lethal – that need more study," said Ed Trapido, Sc.D., EGRP Associate Director. "We sought the help of our investigators to identify the gaps and stumbling blocks and suggest new approaches to move forward epidemiologic research on these diseases."

Focus of Workshop

The workshop focused on cancers of the brain, eye, oral cavity, pharynx, head, neck, endometrium, ovary, testis, digestive and urinary systems, larynx, bones, joints, soft tissues, thyroid, and other cancers of the endocrine systems, non-Hodgkin's lymphoma, Hodgkin's disease, leukemia, myeloma, and Kaposi's sarcoma. Pancreatic cancer was excluded because it is addressed in a trans-NCI Program Announcement that EGRP currently is cosponsoring (PA for Pilot Studies in Pancreatic Cancer (PA 05-116)).

Nancy Mueller, Sc.D., of Harvard University and Dana-Farber Cancer Institute, gave the keynote address on lessons that she has learned in studying Hodgkin's lymphoma over the past 30 years. Dr. Mueller has been an EGRP grantee for 28 years. She has found the research experience richly rewarding but spoke of times when funding for epidemiologic research was a problem, and there were few advocates for such research, few epidemiologists with whom to share data, and few basic scientists interested in collaboration. The reward of rare cancer research lies in the opportunity to make a difference, she said. "It's really a labor of love...you do it because you care."

Assembled at Harvard Medical School Conference Center

Consortia and Transdisciplinary Science

Working groups discussed advancing research on understudied rare cancers in the context of consortia and transdisciplinary science. The consortia approach is an emerging paradigm in which large interdisciplinary teams of scientists think and work collaboratively using common questions, protocols and methods, and perform coordinated parallel or pooled analyses. EGRP currently is supporting or assisting in the development of epidemiological research consortia on 15 types of cancer. Technology and team science are changing the landscape of research, said Dr. Trapido.

Cost effectively include radon exposure assessment as a component of on-going prospective cohort studies

Last Reviewed: 10/3/2008
Last Updated: 10/3/2008

IN THE SPOTLIGHT

Today the National Children's Study announced the 2008 Study Centers that will manage operations in 39 additional locations... Read More

What's New

National Children's Study Announces New Centers

National Children's Study Response to the NAS Review of the Study's Research Plan (August 2008)

National Children's Study Tour Pages

Study Locations

Find out more about the Study locations. View maps and lists of locations... Read More

What is the National Children's Study?

The National Children's Study will examine the effects of environmental influences on the health and development of 100,000 children across the United States, following them from before birth until age 21. The goal of the Study is to improve the health and well-being of children.

Watch this video and learn more about the Study.

The Study defines "environment" broadly, taking a number of natural and man-made environmental, biological, genetic, and psychosocial factors into account. By studying children through their different phases of growth and development, researchers will be better able to understand the role these factors have on health and disease. Findings from the Study will be made available as the research progresses, making potential benefits known to the public as soon as possible.

Ultimately, the National Children's Study will be one of the richest research efforts geared towards studying children's health and development and will form the basis of child health guidance, interventions, and policy for generations to come. For more details on the Study, see the Study Overview.

The National Children's Study is led by a consortium of federal partners including: the U.S. Department of Health and Human Services (including the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Environmental Health Sciences, of the National Institutes of Health and the Centers for Disease Control and Prevention), and the U.S. Environmental Protection Agency.

Agricultural Health Study

Iowa
Study Update 2008

The Agricultural Health Study seeks to identify factors that promote good health

AHS Scientists Begin Study of Lung Health

Agricultural Health Study (AHS) scientists have begun a large study of asthma and respiratory health among participants, including applicators and their spouses.

The Lung Health Study was developed because research shows that farmers and their families may be more likely than the general population to have asthma and other respiratory problems.

In the AHS, for example, farmers and commercial pesticide applicators who used specific pesticides or raised animals were more likely than others to report wheezing, which is a common symptom of asthma.

For women who grew up on farms, there are two interesting findings: 1) they report less asthma than women who didn't grow up on farms. 2) if they applied chemicals, they report more allergic asthma than others in the group.

"We hope to find out if specific pesticides contribute to asthma, as well as to evaluate the role of other farming exposures" said Dr. Jane Hoppin, the scientist who is leading this study.

The Lung Health Study will look at lung function, allergic status, and genetic characteristics associated with asthma and other respiratory illnesses.

"This study will give us better information about the onset of asthma and whether there are any associations with the use of pesticides," said Dr. Hoppin.

"If you are one of the 6,000 AHS participants we contact over the next four years, we hope you will agree to take part in the Lung Health Study."

What is asthma? Asthma is a serious chronic illness that causes inflammation of the airways and increased production of mucus in them. In addition to wheezing, symptoms include coughing and tightness in the chest.

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A Message from our Director

As I write this note, farmers in Iowa and North Carolina are struggling to rebound from major natural disasters in 2008. Many Agricultural Health Study participants have been impacted by unprecedented flooding in Iowa and severe drought in North Carolina.

On behalf of the entire AHS team, I would like to express our sincere concern for the welfare of the agricultural communities in both states. The economic loss and psychological impact of these events are undoubtedly great. Our thoughts and prayers are with you and your family as recovery is underway.

You are central to the success of our research. Without you, we would not be able to make new discoveries that may help to improve the health of future generations of farm families. Even if you are no longer farming, we appreciate your continued help.

We have now completed nearly 30,000 interviews to update information on health status and farming practices. Be assured that your confidentiality is always protected.

This newsletter will give you a glimpse of recent findings. For more information, please visit **www.aghealth.org** or call us at **1-800-217-1954**.

My sincere best wishes to you and your family,

Michael C.R. Alavanja, Dr PH
Principal Investigator
Agricultural Health Study
National Institutes of Health

A radon decay product retrospective detector has been recently calibrated with NCI for use in epidemiologic studies

- Glass-based radon progeny measurement
- Measures contemporary radon gas concentration
- Measures contemporary radon progeny deposition
- Measures retrospective deposition

  of radon decay products in glass

  surfaces via implanted ^{210}Po

Nationwide assessment of work place exposures warranted

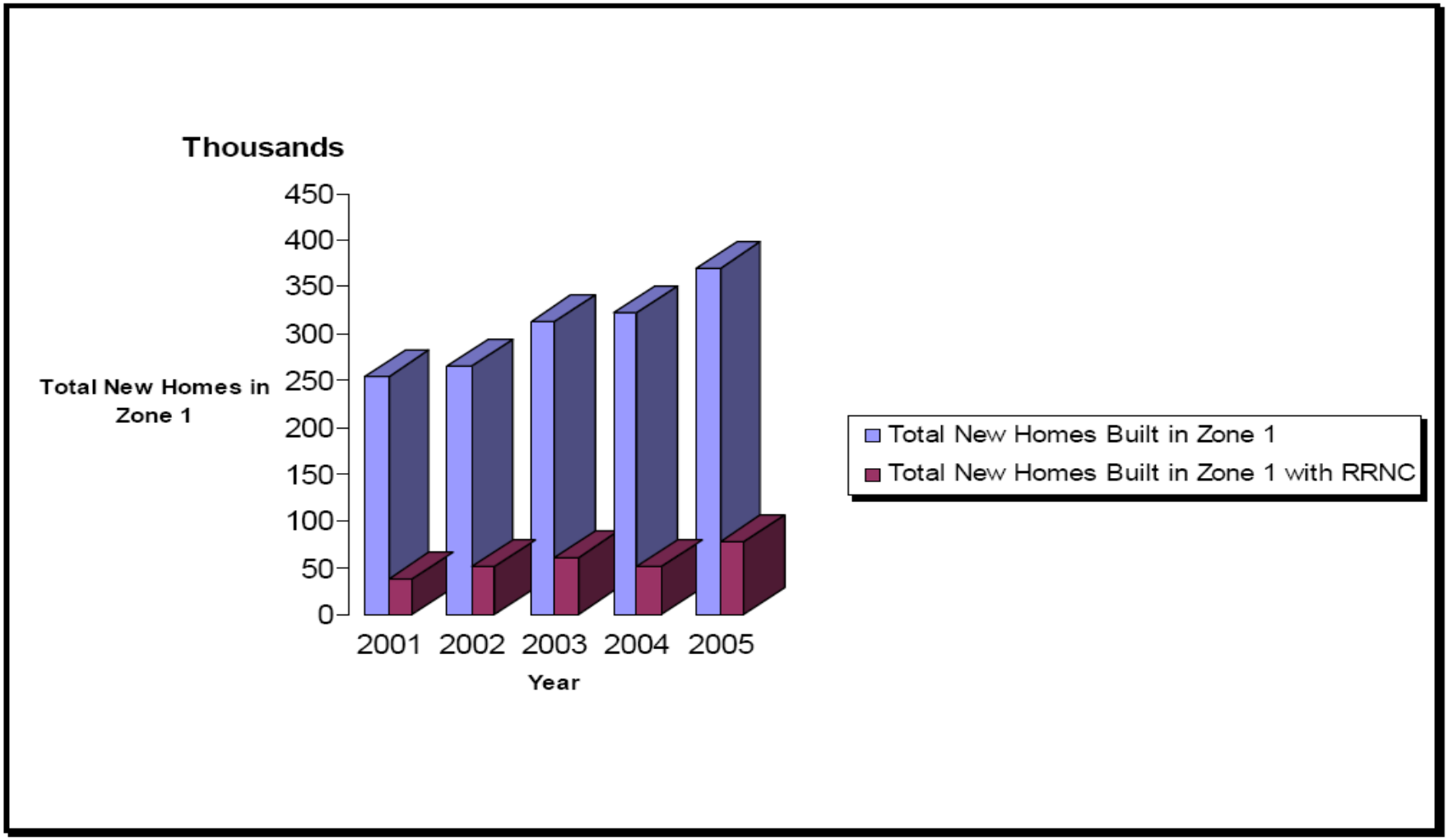
- Mine workers, including uranium, hard rock, and vanadium
- Workers remediating radioactive contaminated sites, including uranium mill sites and mill tailings
- Workers at underground nuclear waste repositories
- Radon mitigation contractors and testers
- Employees of natural caves
- Phosphate fertilizer plant workers
- Oil refinery workers
- Utility tunnel workers

- Subway tunnel workers
- Construction excavators
- Power plant workers, including geothermal power and coal
- Employees of radon health mines
- Employees of radon balneotherapy spas (waterborne radon source)
- Water plant operators (waterborne radon source)
- Fish hatchery attendants (waterborne radon source)
- Employees who come in contact with technologically enhanced sources of naturally occurring radioactive materials
- Incidental exposure in almost any occupation from local geologic radon sources
- Agricultural exposures

POLICY

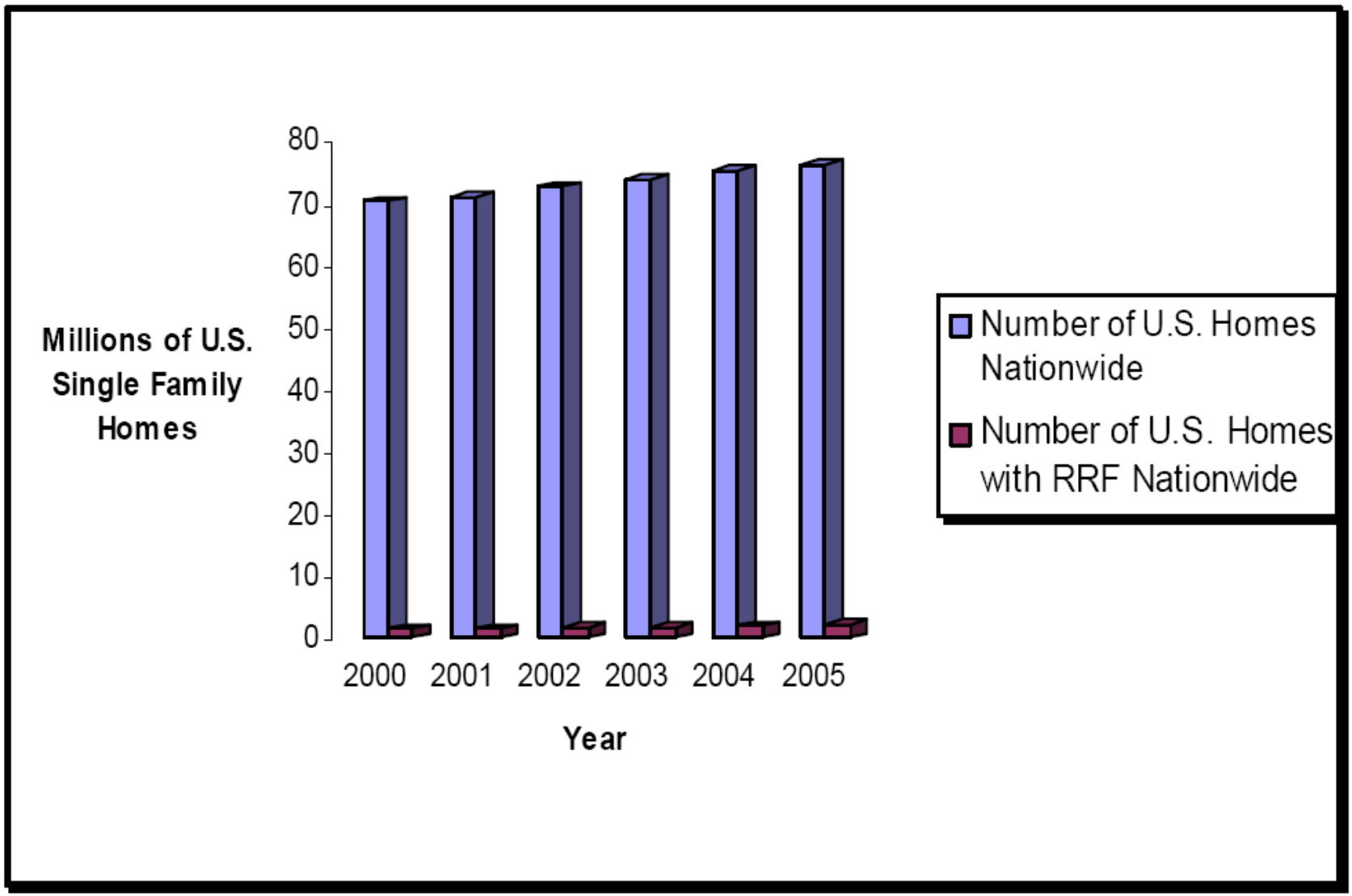
- The U.S. EPA deserves significant credit for their tremendous leadership over the past 20 years to reduce radon exposure on many fronts.
- Nonetheless, we are loosing the battle against reducing an individual's exposure to radon.
- The adverse health effects from radon will increase as more people are exposed, with the aging of our population, and with increased medically-related radiation exposure.

From 2008 Office of Inspector General Report – total of number of homes built in high radon areas compared to number of homes constructed with radon resistant features



[a] New homes built with RRNC in Zone 1 is based on EPA's estimate that 60 percent of all homes built with RRNC are in Zone 1.

Number of single family homes and number with radon reduction features



Source: OIG analysis of U.S. Census Bureau data on homes and gross annual radon fan sales data supplied by fan manufacturers to EPA's Indoor Radon Team.

Policy Considerations

- Among other recommendations, the U.S. EPA's Office of Inspector General strongly recommended that the U.S. EPA consider using their authority, including legislation, already provided under the 1988 Indoor Radon Abatement Act (IRAA) to reduce the risk posed by protracted radon exposure.

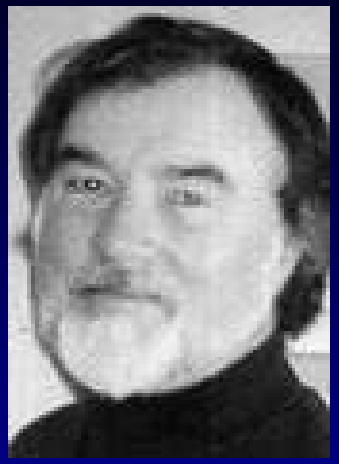
- Numerous cost/benefit analyses have clearly indicated that both mitigation of existing homes and adopting radon resistant new construction features can be justified on a national level (WHO 2008, Steck 2008).

- In order to reduce the number of radon-related lung cancers by half, the current EPA action level for radon may need revisited.

In memory of -

David S. Chase

Manager of the Radon Program for the state of New Hampshire, Department of Environmental Services



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