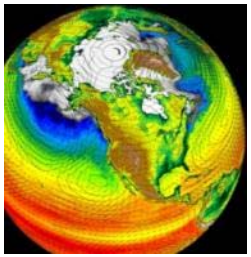
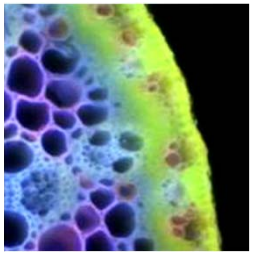
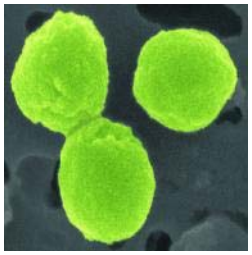


Office of Biological and Environmental Research
Low Dose Radiation Research

Report of the Low Dose Radiation Subcommittee to BERAC Charge

October 28, 2016

Judy D. Wall

DOE BER Role in Low Dose Radiation

DOE only U.S. federal program whose mission is basic research in low dose radiobiology relevant to risk assessment.

BER was the DOE office responsible

Low Dose Radiation program was initiated in 1998

Conclusive evidence for or against increased cancer risk at low dose has not been obtained

BEIR VII Phase 2, 2006, National Academies

Charge to BERAC

Patricia Dehmer, Acting Director, Office of Science

10-08-2015

"…to establish a subcommittee to provide advice that will inform the Office of Science's response to the… recommendation regarding defining a research program that would lead to conclusive results on whether low dose radiation (<0.1Gy) causes cancer in humans."

Genesis of Charge

Low Dose Ionizing Radiation:

Gamma rays and X-rays

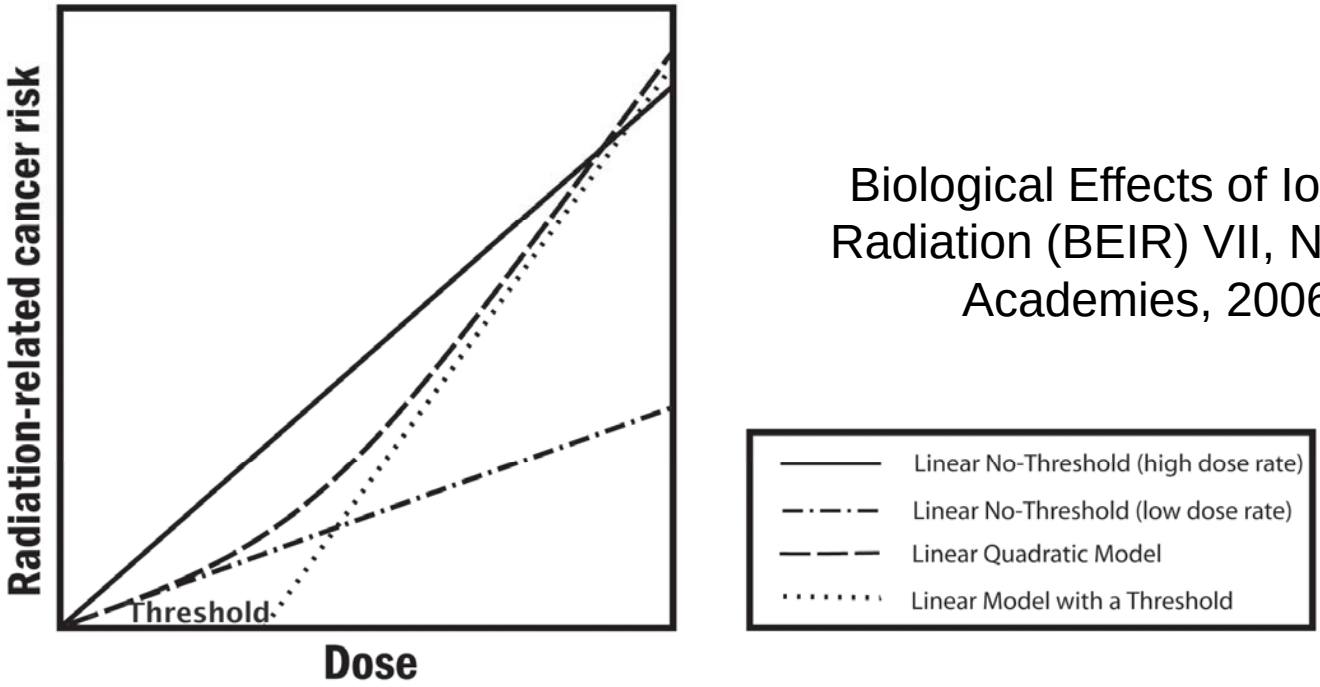
Low dose, <100 mGy and low rate, <5 mGy/h

Controversy:

Is there a threshold to the dose-response curve?

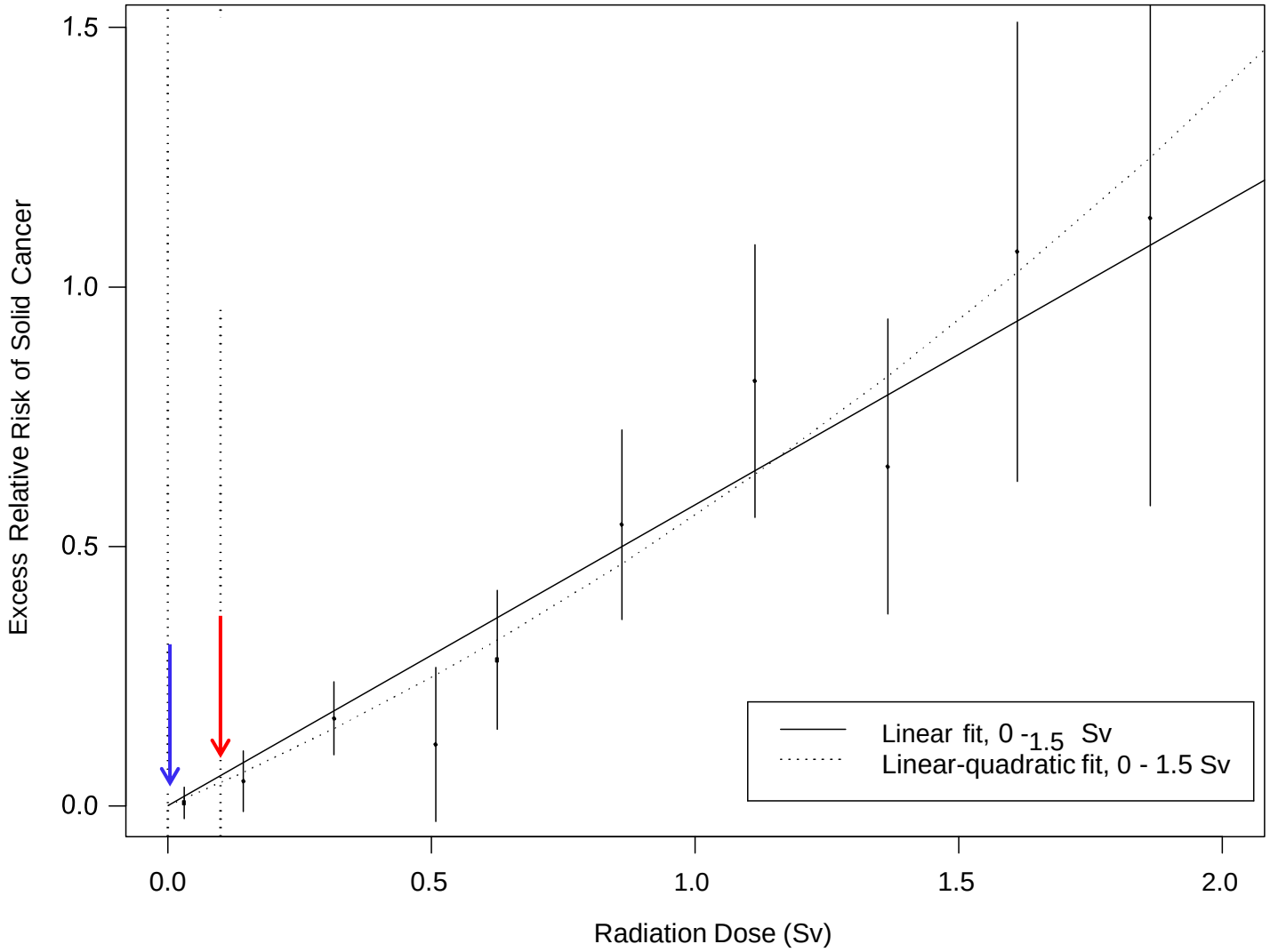
The Linear No-Threshold (LNT) model implies no dose is safe.

Molecular studies provide substantial evidence for repair of radiation damage.



Biological Effects of Ionizing Radiation (BEIR) VII, National Academies, 2006

Solid Cancers, Japanese Atomic Bomb Survivors
Life Span Study (LSS)



BEIR VII Phase 2, 2006, National Academies

Limitation to Linear No Threshold Model

Epidemiological data with numerous cohorts are consistent with LNT but statistics are not strong and confounding effect numerous.

Strong evidence from radiobiological experiments for repair of DNA damage, transcriptional changes and adaptive responses that might provide a threshold effect.

Lack of a mechanistic understanding of low dose radiation effects at molecular level limits a comprehensive integration.

Radiobiological Studies

Prevailing view is that lab studies can be carefully controlled.

-- How does low dose rate in lab studies compare with a 30 year career of occupational exposure?

-- Do results from animal model studies extrapolate to results in humans?

-- Do results from cell culture experiments extrapolate to cells in tissues or animal models?

-- How is the function of the immune system tested in the laboratory models responding to radiation?

Subcommittee Members

- **Michael B. Bellamy,** Nuclear Engineer, Center for Radiation Protection Knowledge, ORNL
- **Amy Berrington de González**, Branch Chief and Senior Investigator, NCI

- **David G. Hoel,** Director, Division of Environmental Risk Assessment, NIH National Institute of Environmental Health Sciences (retired)

- **Arthur M. Katz,** Program Manager at DOE for numerous topics including low dose radiation health effects (retired)

- **Jerome S. Puskin,** Director, Center of Science and Technology, Radiation Protection Division, EPA (retired)

- **Zhi-Min Yuan,** Director, John B. Little Center for Radiation Science, Harvard T.H. Chan School of Public Health
- **Judy D. Wall,** Curators' Distinguished Professor, Univ. of Missouri (Chairperson)

Invited Discussants

- **Sally A. Amundson,** Assoc. Prof. Radiation Oncology, Columbia University Medical Center
- **Mary Helen Barcellos-Hoff**, Prof. & Vice Chair of Research, Department of Radiation Oncology, UCSF

BER Observers

- **Sharlene Weatherwax,** Associate Director
- **Todd Anderson,** Director, Biological Systems Science Division
- **Tristram West**, Senior Technical Advisor

Charge to BERAC

Patricia Dehmer, Acting Director, Office of Science

10-08-2015

Questions to address:

1. The appropriate research goals for such a [research] program that would lead to conclusive results;

2. DOE and BER mission-relevant goals for such a program;

3. The appropriate scope of a "small, sustained, high quality research program;"

4. Whether conclusive results could be obtained on the cancer risk in humans posed by low dose radiation; and

5. Additional federal agencies or funding bodies with equities in such a research program.

Responses to Charge: Question 1

1. **Research goals that would lead to conclusive results on whether low dose radiation causes cancer in humans.**

   a) Unequivocal results are a low probability outcome.

   b) Realistic goal is to provide data that decrease the uncertainty in risk estimates.

Responses to Charge: Question 2

2. DOE and BER mission-relevant goals for such a program

Further the understanding of DNA metabolism, chromosome stability and epigenetic inheritance.

Identify chemicals or proteins that could protect microbes from mutagenesis from a range of radiation doses.

Responses to Charge: Question 3

3. Scope of a "small, sustained, high quality research program;"

One or more workshops should be convened that engages a larger group of key scientists from systems biology and epidemiology to formulate a research path forward.

Responses to Charge: Question 4

4. Whether conclusive results could be obtained on the cancer risk in humans posed by low dose radiation.

a) With unlimited resources, there is a probability that this question could be answered.

b) With a "small, sustained, high quality research program" progress would likely be made in reducing the uncertainty in risk estimates.

Responses to Charge: Question 4

5. Additional federal agencies or funding bodies with equities in such a research program.

NRC, NIH, EPA, DHS, DOD and NASA would have an interest in the outcome of pursuing the health effects of low dose radiation. The goals below might be pertinent.

- **Understand the disparity between epidemiological data and radiobiology data for the outcomes of low dose/dose rate radiation.**
- **Improve confidence in the shape of the dose response curve.**
- **Apply a systems biology approach to obtain differential molecular features that can be used to monitor responses to low dose radiation.**
- **Use genome resequencing to follow progression of DNA changes occurring following ionizing radiation exposure.**

In Summary

- **Epidemiological improvements:**
  - **Confounders identified and many avoided**
  - **Dosimetry more exact**
  - **Registries for cancer facilitate data collection**
  - **Numbers increased sufficiently to reach statistical significance**
- **Laboratory research improvements:**
  - **New tools (mutant construction, sequencing, etc.)**
  - **3D models introduced and animal models better**
  - **Roles of immune system and tissue responses**
  - **Understanding of the mechanism of cancer development more mature**
- **If a research program for low dose is maintained, the radiobiology community should be engaged to plan future research efforts to decrease the uncertainty in risk.**

Thank you!