From the Field to the Laboratory and Back: The “What ifs”, “Wows” and “Who Cares” of Radiation Biology

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Dr. Antone L. Brooks
Thanks

• Thanks to NCRP for selecting me to give this presentation, especially Drs. Tenforde and Morgan who have supported me at NCRP.

• Thanks to Dr. Roger O. McClellan for the introduction and helping me get a good start in science.

• Thanks to the scientists I have worked and published with over the years.

• Thanks to the funding agencies that have funded my research.
Nuclear weapons were part of my early life
Fallout from over 100 A-bombs above ground.
Above Ground Nuclear Tests

1. Sedan  July 6  104 KT
2. Little Feller II  July 7  22 T
3. Jonnie Boy  July 11  500 T
4. Small Boy  July 14  1.65 KT
5. Little Feller I  July 17  18 T
Human Body Burdens $^{137}\text{Cs}$ Following Fallout Utah (1962)

- Female 8
- Female 26
- Female 54
- Male 19
- Male 37
- ALB

Bq Total Body Burden

- Aug-62
- Dec-62
- Apr-63
Wow!!

It was on everything and in everything!

My research demonstrated lots of radioactive material in our bodies. We need to be sure we have not underestimated risk!!
What can I do to help understand the effects of internally deposited radioactive materials?
What if...

• I get cancer?
• My children are not OK?
• Fallout causes a cancer epidemic?

My First Scientific Meeting

• How much is a pCi?
• How much is a Bq?
Who Cares?

Everyone!

1963

The limited nuclear test-ban treaty was signed.
To Cornell for PhD!

WHAT IF...

The radiation we have all been exposed to causes genetic damage?
Use of Chromosome aberrations as a measure of biological change induced by radiation

• Made measurements *in vivo*, Chinese hamsters

• Made measurements in both somatic and genetic tissue (Risk thought to be similar at this time)

• Made measurements as a function of both dose and time after exposure


CHROMATID ABERRATIONS

Acute dose of 1.0 Gy

BREAKS/CELL

TIME POST-IRRADIATION (hr)

BREAKS = CHROMATID + ISOCHROMATID
DELETIONS + (2) (EXCHANGES)

TESTES

• BONE MARROW (Brooks)

• BONE MARROW (Bender & Gpoch)

Cornell
But people breathe and eat fallout...

What if...

internally deposited radioactive materials are more hazardous than external radiation?
Internal Emitters

• Most research at this time was following single acute exposure

• Very little information on the biological changes induced by internally deposited radioactive material was available
What if…

injected or inhaled $^{90}$Sr-$^{90}$Y was much more hazardous than acute radiation?
$^{90}\text{Sr}-^{90}\text{Y}$

- Long physical and biological half-life
- Deposits and stays in the bone and lung
- Large dose to the bone or lung at a low dose-rate
- Potential for leukemia as well as lung and bone cancer
• Samples from the environment were measured in pCi/liter or pCi/kg range

• Chinese Hamsters were injected with $\mu$Ci $^{90}$Sr/g body weight (5-9 orders of magnitude higher than the environment) to study chromosome aberrations and cancer.
## Low-LET Studies

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<td>1966 $^{91}$Y (soluble)</td>
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OCCURRENCE OF DEATHS FROM BONE CANCER FOR BEAGLES FED $^{90}\text{Sr}$ AT DAVIS

TIME AFTER BIRTH & AVERAGE BETA DOSE RATE TO SKELETON (LOG SCALES)

O. RAABE
Dose Response for Life Shortening Following Inhalation of 90-Strontium Fused Clay Particles

Days to Death vs. Cumulative Dose (Gy)

- Cancer
- Heart Cancer
- Other
- Lung Cancer
- TBLN Cancer
- Acute
Wow!!

It takes a lot of radioactive material to produce biological changes!

It takes a lot of disintegrations to make a Sv!!!

Low dose-rate from $^{90}$Sr $^{90}$Y was less effective than high dose-rate in producing lung and bone damage.
Heightened concern about Plutonium produced by fallout and nuclear power

- Plutonium is retained in the lung, bone and liver with long physical and biological half-lives.
- Plutonium produces a large dose to the target organs.
- Cells “hit” by a single alpha particle result in a large cellular dose.
What if…

$^{239}\text{Pu}$ is the most hazardous substance known to man?
Dose Response for Radiation-Induced Chromosome Aberrations

Wow!! Plutonium is no more hazardous than any other alpha emitter, more hazardous than beta-gamma emitters.
What if…
a single $^{239}\text{PuO}_2$ particle deposited in the lung can cause cancer?

“Hot Particle Hypothesis”
Non-Uniform Dose Distribution from Plutonium Inhalation
Non-Uniform Distribution of $^{239}$Pu in the Liver of Chinese Hamsters following injection with citrate or oxide particles.
The Influence of $^{239}$Pu Dose-Distribution on Chromosome Aberration Frequency

Brooks et al
Cumulative Liver Tumor Incidence After $^{239}$PuO$_2$ or $^{239}$Pu Citrate Exposure

Brooks et al.
Results of Research

• The “hot particle hypothesis” is not supported by the data.

• To get cancer, it is necessary to expose as many cells to alpha particles as possible.

• How do we resolve such observations with the “hit theory”?
Wow!!

The tissue is responding as a unit, not as single cells.
Health Risks of Radon

• Radon is responsible for more than half of the background radiation

• Uranium miners were developing a high frequency of lung cancer

Move to PNNL
What if...

Radon is killing us in our homes?
Radon Mitigation and Lung Cancer Risks

STOP SMOKING 120,470

BIER VI
Table 3-10

Mitigation Smoker Homes

Mitigation Non-Smoker Homes
Wow!!

Radon alone is not the second (or third!) cause of lung cancer
Who Cares?

EPA and Congress passed laws to make testing of homes mandatory and mitigation in high level homes. BEIR VI calculated risk from collective dose. Most of the dose is from homes with levels below the EPA action level.
What if…

health risks from environmental contamination from other energy sources was greater than the health risk from nuclear power?
Toxicology of Energy Production

- Each national laboratory was assigned an energy source.
- Our techniques were applied to evaluate the risks associated with the energy source.
- Cell killing, mutations, SCE’s chromosome aberrations, lung damage, cancer were end points.
- ITRI was given “Diesel Exhaust” and “Fluidized Bed Coal Combustion”.
WOW!!
Radiation is a good cell killer
Compared to chemicals
radiation is a poor mutagen
and Carcinogen
Who Cares??
Nuclear Waste Cleanup

• Is expensive $$$$!

• Senator Peter Domenici

• Washington State University

• Are our low dose regulations based on real science?
New Technologies

• The Human Genome was sequenced.

• New technologies, such as microbeams, were now available to test health risks in the low dose region, where it couldn’t be measured before.

Can health risks in the low dose region now be understood?
What if...

the LNTH overestimates risk??"
Chief Scientist for
DOE Low Dose Radiation Research Program

- Are the mechanisms of action the same for low and high doses of radiation?
- Do we need to change current paradigms in radiation biology?
- Is the LNTH an accurate scientific description for the dose-response relationship for cancer in the low dose region?
Biological Responses Induced by Low Doses of Radiation

- Adaptive Response
- Genomic Instability
- Bystander Effects
Extensive research on biological effects of low dose radiation resulted in many new observations making paradigm shifts in radiation biology essential.

- Hit theory vs Bystander and tissue effects
- Linear dose-responses vs Protective adaptation
- Mutation theory vs Genomic instability

The mechanisms of action of these phenomena are being carefully documented and understood.

Low-dose responses are non-linear at all levels of biological organization (Molecular, Cellular, Tissue, Organism, Humans?) and suggest that LNT overestimates risk.
Are the mechanisms the same at low vs. high doses?

Three lines of evidence point to a transition in transcript expression profiles in the range of 10-25 cGy.

In collaboration with D. Nelson, K. Krishnan

(Wyrobek, et al., LLNL)
Fetal Radiation Exposure and Coat Color Change in Male Avy Mice

Bernell and Jirtle 2011
Network reconstruction using Integrated data are more comprehensive and accurate (Systems Biology)
What if...

mechanisms of action are different at high and low doses of radiation?
Mechanisms of Action

- At low doses genomics, proteomics, microRNAome, metabolomics, etc. show different responses at low doses and high doses.
- Many low dose responses are known to be involved in reducing damage
- Altered post-transcriptional protein modification
- Epigenetic changes
- Impact of oxidative status of the cell
- Radiation-induced changes in selective apoptosis
- Cell/cell, cell/matrix interactions
Wow!!

World-wide low dose research has defined many mechanisms involved in new low dose biological phenomena.

(US-DOE, European Union, Japan, Korea)
Who Cares?

Regulators and Scientists

Meeting with the regulators from federal agencies and the DOE Low Dose Research Program.

• First Day Scientists talked, Regulators slept
• Second Day Regulators talked, Scientist slept
• Third day DOE talked and everyone else slept
Who Cares?

News reporters, media editors and scientists

• Much of the scientific data suggested that the risk was not as high as LNTH

• After the scientific presentations the News reporters suggested, “Very interesting but I cannot get such information by my Editor.”

• What would the response be if the risk was much higher than LNTH?
The Dinosaur of LNTH remains useful for regulations but is scientifically dead for low-dose risk assessment.

All these cell and molecular responses are radio-protective !!!!
Back to the Field- Fukushima

• Appreciate all the information at this meeting.

• Interesting to compare to
Mean Monthly Concentrations of $^{137}$Cs in deer muscle and vegetation (Colorado)

Wicker et al. 1965
Correlation of $^{137}\text{Cs}$ radioactivity between peripheral blood and organs

\[ Y = 21.3X \]
\[ R^2 = 0.759 \]

\[ Y = 11.8X \]
\[ R^2 = 0.837 \]

\[ Y = 9.84X \]
\[ R^2 = 0.853 \]

\[ Y = 5.23X \]
\[ R^2 = 0.808 \]

\[ Y = 7.78X \]
\[ R^2 = 0.717 \]

\[ Y = 4.50X \]
\[ R^2 = 0.257 \]

Figure 1

Manabu Fukumoto
2012
**137Cs Environmental and Effects Levels**

- **100,000,000 Bq**
  - Marked Life Shortening in Dogs
  - 138,000,000 Bq/kg

- **10,000,000 Bq**
  - No Cancer Increase in Dogs
  - 38,000,000 Bq/kg

- **1,000,000 Bq**
  - No Life Shortening in Dogs
  - 55,000,000 Bq/kg

- **100,000 Bq**
  - Highest Soil Concentration in Finland
  - 78,000 Bq/m³

- **1,000 Bq**
  - Action level for 137Cs
  - 1,200 Bq/kg

- **100 Bq**
  - Highest level of 137Cs in Cattle Fukushima

- **10 Bq**
  - Lowest Chernobyl Reindeer Meat 2008
  - 142 Bq/Liter

- **1 Bq**
  - Highest Peak in Milk, Utah
  - 11 Bq/Liter

- **0.1 Bq**
  - Bq/liter milk Seattle WA Chernobyl

**Notes**

- **Global Fallout Reindeer Meat 1968**
  - 2,760 Bq/kg

- **Total 137Cs Deposited from NTS (Nevada)**
  - Total 137Cs Deposited from Global Fallout (Eastern US)
  - > 3,000 Bq/m³

- **Highest Human, Utah**
  - 725 Bq/kg

- **Highest Concentration in Women, Chernobyl 1987**
  - 6,930 Bq (Whole Body Burden)

- **General Consumption Limit for Adults**
  - 1,000 Bq/kg

- **General Consumption Limit for Infants**
  - 100 Bq/kg
Nevada Fallout

Figure 7. Cesium-137 deposition density resulting from the cumulative effect of the Nevada tests generally decreases with distance from the test site in the direction of the prevailing wind across North America, although isolated locations received significant deposition as a result of rainfall.

Simon et al. 2006
World wide fallout in the United States

Figure 3.18. Cesium-137 deposition density (Bq/m²) due to global fallout.
What Causes Cancer?

- Cigarette smoke
- Diet & nutrition
- Chronic infection
- Occupational exposure
- Genetic
- Alcohol drinking
- Environmental factors including radiation

WHO
My answers to major “What ifs..?” of Radiation Biology

• What if fallout has produced a cancer epidemic in Utah? (It has Not)

• What if internal emitters are more hazardous than acute external exposure? (NO)

• What if Plutonium is the most hazardous substance known to man and a single particle can cause lung cancer? (NO)

• What if Radon is a major cause of lung cancer? (NO not without Cigarette smoke)
My answers to major “What ifs..?” of Radiation Biology

• What if nuclear power presents a greater health impact than other sources of power production? (NO)
• What if the mechanisms of action following high doses is the same as that following low doses? (NO)
• What if LNT overestimates cancer risk in the low dose region (I think it does)
Summary

• I have enjoyed my career as a radiation biologist. Radiation science has been such a wonderful experience for me, I even named my dog “Sievert” since it is worth 100 of those rems.
Summary

• There have been many “What ifs..”, “Wows!” and “Who Cares?” during my journey.

• What the future holds I cannot predict, but I wish I had another 30+ years to see it play out.

• Thanks to all of you and to my family.