Issues in Understanding Exposures to Low Doses of Ionizing Radiation

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Why is studying low dose radiation effects important?
Environmental clean up – Hanford (>$110 Billion to date)
Nuclear Accidents – Fukushima (160,000 evacuated, 20 mGy/yr)
Rad worker exposures
Flight Crews and Astronauts (limits to the Mars mission?)
Potential Terrorist Attacks (dirty bombs, IND) – evacuations?
Security issues (airport backscatter machines)
High natural background exposures – Radon, geographical locations in Karala (India) Yanjing (China)

Medical Diagnostics – >90 million CT scans annually 5-100 mSv each (acute exposure v protracted exposure LDR)

So Why Do We Care About Low Dose Radiation Effects?

Approximately 90 million in the USA this year
CT over exposure to a young patient
Fall from bed and complained of neck pain the following morning
Plain x-rays and then a CT scan of neck ordered by ER
CT table did not index (move) and radiologic technologist manually instituted 151 slices over a period of more than 1 hour
The patient was successfully rescanned by another technician
About 2-3 hours after the first CT attempt he developed a red line around his face at the level of the 151 CT scan slices

Sometimes things do not go as they should!
Hair loss from excessive dose of a CT angiogram
US scientists are warning that radiation from controversial full-body airport scanners has been dangerously underestimated and could lead to an increased risk of skin cancer - particularly in children.


700 million travelers worldwide
Individual dose v collective dose

Remember - We All Have Different Perception of Risk
Questions: How to design a system that limits risk? How do we assign a potential human health risk?

Caveats: This system must take into account:
- The most sensitive organ (breast)?
- The most sensitive individual? *Ethical and legal questions

Where do you draw this line for regulatory purposes?

The dilemma for radiation protection: what is the scientific basis for radiation standards to protect the public from exposures to low levels of ionizing radiation (<0.1 mSv) where there are considerable uncertainties in the epidemiological data.

On one hand: complex biological systems have physiological barriers against damage and disease. Primary damage linear with dose, secondary damage not. Cellular processes block damage propagation to clinical disease.
Everybody knows radiation causes detrimental effects:

When asked "is a low dose of radiation safe?"
will you say "YES"?
or will you say
“There is always the possibility of a detrimental effect but at low doses it’s very very small”

Considerations when integrating molecular, cellular and organismal effects:
Tissues/organs differentially sensitive
Risk varies with
Age
Sex
Socio economic status
Diet and lifestyle
Genetic makeup and race
Dose and dose rate
Radiation quality

So how do we inform the public about potential radiation risks at low doses?
What About in the Low Dose Region?

BEIR VII cited 1386 peer reviewed publications
French Academie des Sciences cited 306 publications
Overlap in publications cited = 68

Radiation Protection Considerations
Science is only one input to risk management
What are the other inputs?
- Tradition
- Not scaring people
- Politics
- Social values
- Economic considerations
- Technological considerations

We have a long legacy of mistrust to deal with!
Plus some widely diverging opinions
- Hormesis - tolerance - acceptance - total denial
Extrapolation from experimental systems:
Cells → tissues → organs → man

What does *in vitro* cell culture tell us about a response in humans?

What *do* *in vivo* models tell us about a response in humans - how do you extrapolate from an animal model to the human population?

Should you?

A predictive, multi-cellular framework is necessary to understand potential effects of exposure to ionizing radiation

This is our multi-scale, systems-level challenge.

Requires understanding the networks and pathways involved
Developing computational modeling approaches to organize complex biological data

A System is a result of interacting parts:

An “interesting” part is one for which the consequences of interaction is non-trivial

The sum of the system is greater than the sum of the parts.

Biological systems are defined by multiple redundant and interdependent signaling networks and metabolic pathways
Context cannot be accurately predicted without multiple sources of data

Well-designed studies with appropriate controls
Gene expression data does not predict protein abundance
Protein abundance data does not predict protein function
Single time points do not provide directionality for correlation to functional outcomes
Network reconstruction requires heterogeneous data for dose-dependent and temporal measurements

My hypothesis is that a predictive, multi-cellular framework is necessary to understand potential effects of exposure to low dose ionizing radiation

- Requires knowing the networks and pathways involved
- Developing the computational modeling approaches to organize complex biological data
- Interactions essential to develop testable hypotheses
- We plan to utilize resources available at PNNL
- Evolving to include new and old model systems
- Expanding the program to include new, young investigators
- PNNL complements other DOE national laboratories, DOE Low Dose and NOTE / DoReMi / MEODI and EpiRadBio investigators, and would like to work with other systems biology programs to increase the power of these investigations

What is the rest of the world doing?

20 year program MELODI Subprogram, e.g., EpiRadBio** CardioRisk Store DoReMi** Members of the EAB

www.hleg.de/

Japan, India and Korea – vibrant new low dose radiation programs

DOE Low Dose Radiation Research Program had a 10 year head start. Now falling behind technically, competitively and in competence.
Comments, questions and suggestions

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Morgan & Bair: Issues in low dose radiation
biology: The controversy continues. A perspective