Introduction

My name is Gayle Woloschak. I am a Professor of Radiation Oncology and also Radiology at Northwestern University where I have worked for 15 years. Prior to that I was employed at Argonne National Laboratory (a DOE facility) for 13 years. At the time I left I was a Senior Scientist in the Biosciences Division. I am a radiation biologist and molecular biologist and active in a number of radiation societies, national and international radiation advisory agencies, and a member of other radiation-related teams.

I'm going to let some questions shape my discussion.

What is low dose radiation?

Before I describe what low dose (vs high dose) radiation means, I would like to remind everyone that ionizing radiation surrounds us daily. It is part of the natural background from sunlight and the earth's crust, and radioactive chemical elements are present in what we eat, drink and breathe. All of this constitutes natural background radiation. Doses of radiation categorized as low dose radiation are higher than natural background. Most often low dose radiation exposures occur when we are close to nuclear clean-up sites, or they might result from occupational or accidental exposures or exposure to medical low-dose diagnostic procedures such as CT scans. Any of these low dose exposures are thousands of times lower than the radiation therapy doses used to treat cancer patients. These therapy doses belong to the category of medium and high doses of radiation.

What don't we know? Why don't we understand low dose radiation?

The most significant known risk from exposure to low dose radiation is considered to be cancer. If I ask a room of radiation biologists what the risk is for cancer formation from low doses of radiation, I get every answer possible: from "a little radiation is good for you, you should go sit in a radioactive spa to boost your immune system" to "radiation risk for cancer decreases as the dose decreases" to "risk from low doses is worse per unit dose than risk at high doses". So – we do not know the precise relationship between low dose radiation exposure and cancer induction. Why is there so much disagreement on this question? Because we have contradictory data.

One source of this problem is that many of the low dose studies done in the past were performed with cells in a test tube. A direct leap from cells to humans is never done in medicine because it is not accurate. Before clinical trials of any sort (drugs, radiation, etc.), for example, numerous animal studies are routinely done.

In addition to the question of cancer risk, some of the recent low dose studies in the EU, UK, Japan and China suggest that we may need to explore additional issues. We may need to study low dose effects on the unborn and newborns in greater detail than we have before. We may need to study effects on the central nervous system and cardiovascular system. Until we have more research, questions will remain.

Why is closing this gap in understanding of paramount importance in the US?

Contradictory data (such as those on low dose induced cancer) make for contradictory assumptions. Our radiation protection policies deal with low doses of radiation because that is precisely the level of environmental and occupational exposures that can and should be regulated. Radiation protection is designed for a healthy population with the view of preserving health. With regard to low dose radiation these policies are based on the assumptions we make about low dose radiation effects. So, a small change in our knowledge can make for drastic changes in recommended policy with respect to acceptable levels of radiation for clean-up sites, radiation in water, and others. What this means is that closing the knowledge gap will allow us to balance spending money in cleaning up waste with optimal protection of the exposed public and workers. It is a matter of course that citizens must be protected from dangers associated with radiation exposure, but over-protection may be wastefully expensive and deplete funds that could be used for other strategic goals for the nation.

What needs to be done in the research community to solve this issue? What was DOE's role in funding discoveries in the field?

Work resulting from the DOE Low Dose program led to many significant findings. For example, some unique biological responses to low dose radiation were found that are not evident at high doses. This means that a simple extrapolation from high dose effects to low doses effects would not be correct. Much of this work was in the discovery phase and thus was done with cells in culture and never made its way to be tested in whole animals. This limits our ability to apply this work to human beings, which is our end goal.

Since the time when the DOE low dose program was terminated, biomedical science has continued to progress. New technologies have been developed and new discoveries have been made. Incorporating sensitive new techniques in low dose radiation research on animals would be essential as would modeling with new computational approaches. Fine-tuned models could be developed to set the stage for fine-tuned decisions and evidence based protection policies.

Before the DOE Low Dose Program, DOE was the leader in the radiation research science world-wide. Large-scale studies in animals were done ranging from low dose occupational-type exposure to high dose nuclear disaster type exposures. I am in awe when I look at the volume, planning, design and structure of these experiments done with animals for the entire duration of their lives. For reasons unknown to me, DOE terminated these studies without really completing a full analysis of the data (we are talking about data from 50,000 mice, 30,000 rats, 25,000 dogs). I was not involved in the studies at the time they were done, although I had a small project to evaluate some of the tissues from those projects immediately after DOE terminated the program.

When I moved from Argonne National Laboratory to Northwestern University in 2002, I asked for permission from Argonne to move the tissues to Northwestern since no one was using them at Argonne; I was denied permission. A year later, a colleague called to tell me that the tissues were

in the trash bin (literally). At that time, I called DOE to ask them intervene with the Argonne National Laboratory Biology Division to allow me to rescue the tissues for scientific studies. With DOE's help these materials were moved to Northwestern.

When DOE reinvigorated its interest in radiation with the Low Dose Program, I was able to obtain funding for two projects over 8y: Both were done jointly with Univ. Chicago, the latter also included Univ. California Davis. These projects included analyses of archival tissues and some new animals exposed to very low doses and low dose-rates of radiation.

However, by this time other institutions (Pacific Northwest National Laboratory near Richland, WA; Inhalation Toxicology Research Institute—now Lovelace—in Albuquerque, NM), similar to Argonne's Biology division, were closing their massive radiation research studies. As investigators who planned these studies were retiring, they contacted me as a means of securing that their work would be preserved. Their desire was to merge their materials with those from Argonne which we now curated. Part of our commitment to DOE was to make the tissues available to investigators around the world and the datasets available on a website that can be accessed by anyone. DOE agreed to fund the cost of the transport of the tissues, my University covered the costs so as not to lose the material, but the Low Dose program terminated and we never received reimbursement for the costs.

Ultimately, this entire archive came to my laboratory at Northwestern, and it is the University that has supported it since the termination of the DOE Low Dose Program.

What was the result of termination of the DOE Low Dose Program?

For my own group, the termination of the DOE Low Dose program means a constant struggle to preserve materials and data from DOE irradiated animal archive. There is great value in both the tissues and the datasets. As noted before, new techniques and new knowledge available to use today have allowed scientists to examine old tissues in new ways. Because of the continuing world-wide interest, we have made both the tissues and the datasets available to all interested investigators as much as possible. Nevertheless, the continued lack of funding from DOE has put the archive and the data in jeopardy, and much of the data we obtained particularly on the dogs and rats has not been made available online. When one thinks of the costs of doing life-long experiments with 50,000 mice, 30,000 rats and 25,000 dogs today (and the fact that animal husbandry at such a scale is not really possible in today's world), the fact that these data are sitting in a box in a storage facility feels horrible to me as a scientist. Thankfully, recently we obtained an NIH-NCI grant that may permit at least some additional curating of the data.

For the US radiation community, the loss of the DOE low dose program had devastating effects:
-The radiation community for low dose has been decimated. Low dose radiation biologists participate in recommendations for radiation protection, for designing approaches to deal with radiation accidents, for dealing with population exposures. In the US today these committees are occupied predominantly by retired scientists. Very few new radiation biologists are coming

through the ranks who will be able to replace them. We are not able to train the next generation of radiation protection scientists in the US and will be dependent on foreign support.
-NASA has a need for low-dose work with radiation types unique to space exposure; complementary work must be done with earth-type radiation exposures. NASA reported to the NASA Space Radiation Discipline working group (which I chaired) that they were looking for collaborators in Europe to facilitate their work. In the past DOE was their partner.
-We have lost much of the infrastructure to do low dose work in the US. Many facilities in the US are antiquated and have not been updated in over 10y; some have even been decommissioned. In many cases, the capacity to perform this type of research would take time to re-build.
-The US is currently using low dose exposure effects data from science done in Europe, China and Japan to support our regulatory policies. This is of concern because: (1) other countries often have agendas in their research programs that are not consistent with our agendas; this is not to say that the research results are not correct, merely that the research design is set up to examine particular questions that may not be of equal priority in the US; (2) we do not have the capacity to reproduce any of those findings in the US to verify that they are accurate; and (3) in effect we are permitting other countries to set the radiation agenda for the world.

I would like to end this by summarizing with three key points:

1. Health effects of low dose radiation exposures remain ambiguous.
2. Policies regulating radiation exposures rely on models developed for high dose exposures; this may not be accurate
3. New technologies are changing science continually; their impact on our understanding of low dose radiation has great potential.