Mutat Res Fund Mol Mech Mutagen 806 (2017) 81–87

Contents lists available at ScienceDirect

Mutat Res Fund Mol Mech Mutagen

journal homepage: www.elsevier.com/locate/mut

Short communication

The legacy of William Morgan: The PNNL years

Antone L. Brooks*

Washington State University, 6802 West 13th Kennewick, WA 99338, United States

ARTICLE INFO

Article history:
Received 6 December 2016
Accepted 6 March 2017
Available online 18 March 2017

Keywords:
Molecular biology
Internal emitters
Research management

1. Commentary

1.1. Early years

My friendship with William F. (Bill) Morgan started in the late 1970s. I was working as a technical representative at the Atomic Energy Commission in Washington D.C. and was involved in a review of Sheldon Wolff's laboratory at University of California, San Francisco. Bill had just joined the Wolff group as a post-doctoral fellow; he was working on radiation-induced chromosome aberrations in humans. Our review team gave the laboratory very good marks, but when the funding decisions were announced, it was marked for closure – the mysterious workings of the government. In later years, Bill was always quick to remind me that I had helped to shut down his research program! However, Bill was a very productive scientist right from the start and his research moved him quickly along the path to success.

1.2. Scientific direction

Bill and I continued to have close interactions. When the DOE Low Dose Research Program was formed, we served together on a committee providing input into the Biological and Environmental Research Advisory Committee (BERAC) Report Program plan for Biological Effects of Low Dose and Dose Rate Radiation. Leading radiation biology scientists were chosen to form a subcommittee of the BERAC charged with developing a set of recommendations for the new DOE Low Dose Radiation Research Program. The members of the subcommittee were:

- Robert Ullrich, Chair, Department of Radiation Oncology, University of Texas Medical Branch, Galveston, TX (Chair);
- Antone L. Brooks, Washington State University-Tri-Cities, Richland, WA;
- David Brenner, Columbia University, Center for Radiological Research, New York, NY;
- Richard J. Bull, Pacific Northwest National Laboratory, Richland, WA;
- Eric J. Hall, Radiation Oncology Center for Radiological Research, Columbia University, New York, NY;
- William F. Morgan, Professor of Radiation Oncology, University of California, San Francisco, San Francisco, CA;
- Julian Preston, Chemical Industry Institute of Toxicology, Research Triangle Park, NC;
- James Flynn, Decision Research, Eugene, OR;
- Henry N. Wagner, Jr. Director, Division of Radiation Health Science, Johns Hopkins Medical School, Baltimore, MD;
- Susan S. Wallace, Chair, Department of Microbiology and Molecular Genetics Director, Markey Center for Molecular Genetics, University of Vermont, Burlington, VT;
- Dr. Gayle E. Woloschak, Center for Mechanistic Biology and Biotechnology, Argonne National Laboratory, Argonne, IL.

The subcommittee prepared a report for the Office of Biological and Environmental Research, providing background information that DOE used to write the first call for proposals and indicating the directions which the program should take. This exercise was critical in providing a good start to this important program. Bill was a key

* Tel.: +1 509 727 4451.
E-mail address: tbrooks@tricity.wsu.edu

http://dx.doi.org/10.1016/j.mrfmmm.2017.03.002

member of this subcommittee and his colleagues regarded him as one of the giants in the field.

Bill served on many review panels to evaluate proposals for research funding, for DOE, Environmental Protection Agency (EPA), National Institute of Environmental Health Sciences (NIEHS), National Aeronautics and Space Administration (NASA), and other agencies. Bill had important influence on funding decisions; when he talked, everyone listened, and opinions about the value of a proposal often changed – for the better or the worse.

Bill and I were the co-chairs of a National Commission on Radiation Protection (NCRP) committee, funded by NASA, to evaluate radiation effects on astronauts. The title of the resulting report was "Potential Impact of Individual Genetic Susceptibility and Previous Radiation Exposure on Radiation Risk for Astronauts". This committee tackled a question of great significance to the manned space program. If an astronaut had previous radiation exposure from any source (*e.g.*, medicine, high elevation aviation, environmental exposure) and could expect to receive additional exposure on a space mission which would put them above the regulatory limit, they could not go on the mission.

One case, in particular, brought this issue to NASA's attention. An astronaut had received cancer radiation therapy; this dose plus the anticipated space-flight dose would put him over the allowed limit. NASA was considering removing this astronaut from the planned mission – after he had invested years of his life in preparation. This case prompted many interesting discussions by the committee. An ethics specialist on the committee was resolved that the astronaut should not fly; an astronaut member of the committee was equally firm that the astronaut in question should be allowed to make his own decision and to fly the mission if he so wished. The debate was intense. Ultimately, the ethicist resigned from the committee and was replaced. Bill played a key role in resolving the dispute and the report was finally written [1].

Bill replaced me on the NCRP as the Chairman of Committee One, responsible for writing reports related to the setting of radiation standards. NCRP wanted another report on the effects of low doses of radiation (BEIR VIII). I was in favor of it; Bill was not. Bill won.

1.3. Pacific Northwest National Laboratory (PNNL) cell and molecular biology

Bill was a full Professor at Johns Hopkins University, where he had developed a strong research team. He left that post to become Director of Radiation Biology and Biophysics in the Biological Science Division at the Pacific Northwest National Laboratory (PNNL) in Richland WA. We had many discussions about the differences between working in academia and in the National Laboratory system, but he took the government position anyway. This was a challenging transition for Bill, but with the support of his wife Marianne Sowa and his new charge Leyla Resat, a talented young pre-teen, he was up to the task. Bill adjusted to the fact that he was no longer completely in charge of his life as a scientist. He needed to get permission for whatever he wanted to do – attending a meeting, getting editorial help, or bringing in an outside scientist for a seminar. Bill was willing to jump through these hoops, but sometimes he would forget, and this would lead to an animated discussion with management.

Bill assembled a strong research team: Tom Weber (transcriptional regulation), Colette Sacksteder (protein cellular localization and interactions), David Stenoien (molecular biology, phosphoproteomics, and epigenetics), Susan Varnum (protein microarray), Marianne Sowa (cell signaling and imaging), Dave Springer (secretory regulation and epigenetics), Qibin Zhang (metabolomics), John Miller (bioinformatics and microdosimetry), Katrina Waters (data integration and biostatistics) Harish Shankaran (model development), and many graduate students. This team had an excellent tool-kit but most of the members had little background in radiation biology. Nevertheless, Bill was able to convince them to leave their own projects and focus on an integrated, systems-based radiation biology program (Fig. 1). This was one of Bill's greatest achievements at PNNL. The figure shows that the team had a wide variety of high-throughput technologies and the program was designed to develop and test hypotheses, using modern molecular and cellular biology methods. From these hypotheses, it would be possible to develop predictive models and to test them at all levels of biological organization.

Bill had a talent for working with others to get the basic science done. Fig. 2 illustrates the significance of the research and how it could feed biological data from one level of biological organization to the next. There are both damaging and protective processes at all levels of biological organization. Mechanistic data help to define these processes and, consequently, the research has impact on setting radiation standards.

1.4. Communications

As the chief scientist, I was responsible for the DOE Low Dose Research Program web site. When I retired, DOE transferred the web site from Washington State University to PNNL, with Bill in charge. It was more work than he expected. Working with Bill, I developed a deep admiration of his scientific ability and formed a strong friendship. I appreciated how much Bill did for the scientific community. Bill set up debates for me at Radiation Research Society and Health Physics Society meetings. Bill was the moderator on both occasions. At Radiation Research, I debated Mike Atkinson (Fig. 3) on the question, "Should the Dose Dose-rate Effectiveness Factor (DDREF) be set at 1?" It was great fun, because if the DDREF is set at 1, then everything is linear. I like curves; so I said that all you have to do to set the DDREF at 1 is to ignore more than 70 years of research! At the Health Physics Society meeting, I debated with Jerry Puskin (EPA) and the issue was "Is there a level of radiation that is not dangerous?".

1.5. Internally deposited radioactive material

Bill had not been very active in the Health Physics Society, but after moving to PNNL, we had many discussions about it. The Society held a meeting in Spokane in 2005 and Bill attended. He was very impressed with the fact that this society worked hard to make science and regulations match and he jumped into the society's activities with vigor. He also discovered the paucity of good data on risk from internally deposited radionuclides. This resulted in a close association with the U.S. Trans-Uranium Registry (USTUR) and an interest in related research. The USTUR has been following up the health status of nuclear industry workers who may have had contamination with transuranic elements, including Pu. Bill met at the USTUR weekly and he funded a student, Chris Nielsen, to bring modern molecular and cellular biology approaches to research on the deposition, distribution, and effects of internally deposited radioactive material (IDRM). Chris and Bill combined the experimental beagle dog data with the human data to make it more applicable to standard setting. He was especially interested in determining the responses associated with molecules, cells and tissues in range of the alpha particles. This interaction resulted in two important manuscripts [2,31]. It was possible to relate the pathology and molecular biology in the dog with the changes observed in the human subjects.

Bill reviewed the data developed in the beagle by the Atomic Energy Commission as a result of concern over nuclear testing fallout and exposure of the general public. This was a well-integrated and coordinated effort by national and specialty laboratories. These studies used the dog as the experimental animal, examining differ-

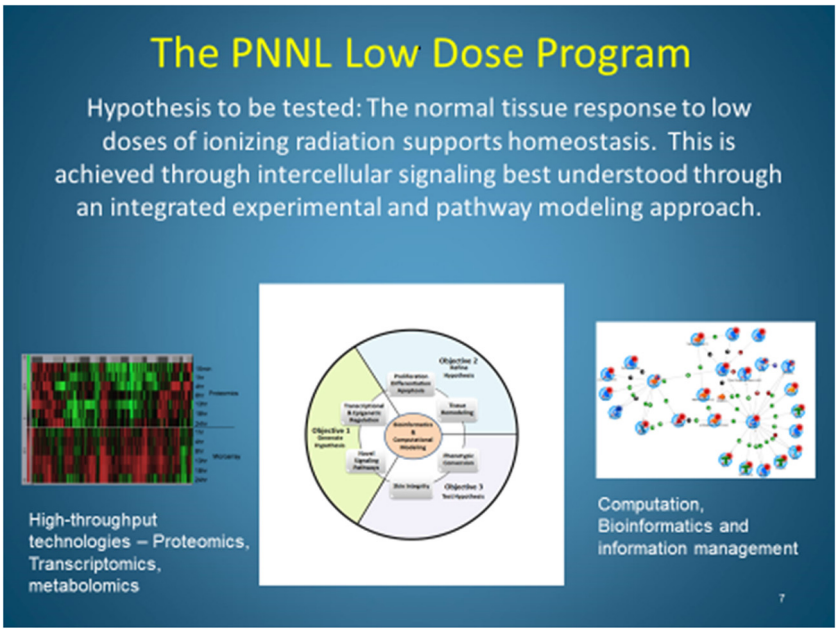


Fig. 1. Outline of the Low Dose Radiation research program at the Pacific Northwest National laboratory with the methods, objectives and Hypothesis tested.

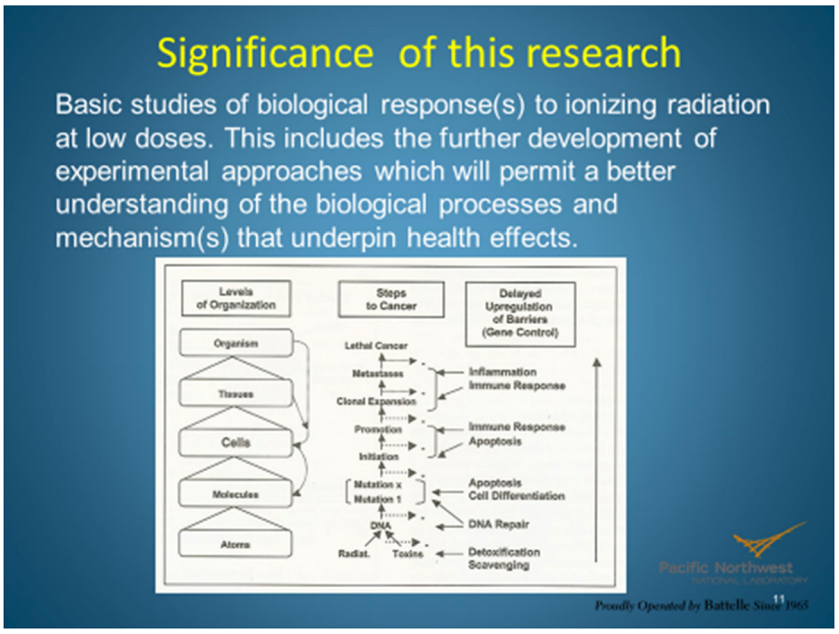


Fig. 2. This figure outlines the significance of the research being conducted and suggests ways to extrapolate and connect different levels of biological organization in a systems approach to risk evaluation.

ent radionuclides and routes of intake. Bill even plowed through the reviews of early results from these studies [3] and the experimental design and animal numbers are carefully covered [4]. Since dogs are longed lived and larger than rodents, it is possible to derive much data on initial deposition and distribution, without serial sacrifice. The beagle is also a good model for radiation-induced cancer. The incidence of spontaneous cancers in dogs increases with age with a pattern similar to that observed in humans. Radiation-induced cancer frequency and types are also similar to those in humans. Each animal can receive repeated radiological and physiological measurements and the dose and biological response can be related to time after exposure.

It was of interest to look at the major target organs from IDRM. The radionuclide deposits in the body according to its chemical nature. ^{137}Cs is uniformly distributed, ^{131}I deposits in the thyroid, ^{90}Sr in bone, ^{144}Ce–^{144}Pr in liver and bone. For each of these radionuclides, it was possible to determine the dose and dose rate to the target organ for each dog and to combine this information with the diseases produced, allowing a direct measurement of the resulting cancer risk. The physical state of the radionuclide also determines its fate. For example, following inhalation of radionuclides in fused-clay particles, activity stays in the lungs and associated lymph nodes. In these studies, the physical half-life was combined with the biological half-life to determine the effective half-life of the material in the lung as primary target organ.

Fig. 3. Photograph of the members of the debate at the Radiation Research Society. Question: Should the Dose Dose-Rate Effectiveness Factor be one?.

Research was conducted to study the role of dose distribution, total dose and dose rate on the induction of cancer in the lung by inhalation of beta-gamma emitting radionuclides. This research used radionuclides with a range of physical half-lives: ^{90}Sr, ^{144}Ce, ^{91}Y or ^{90}Y. The effective half-lives, which combine biological clearance with physical half-life, range from 2.5 days (^{90}Y) to 5.6 years (^{90}Sr). Each radionuclide was delivered in a fused-clay matrix and inhaled as small particles. Large lung doses delivered over a wide range of changing dose rates resulted, with little dose delivered to the remainder of the body [5]. After exposure, the animals are evaluated over their lifetime for the development of disease. This results in dose–response and dose–rate response relationships to be used in risk assessment. Such information is not available for human subjects. Bill carefully reviewed the literature on these studies. From such studies, biological effects can be related to radiation exposure, dose rate, *etc.* [6]. Bill recognized the value of these data and through his efforts was able to get all the data from these studies collected and transferred to Gayle Woloschk at Northwestern University. This initiative preserved valuable data that might otherwise have been lost.

2. Whole-body exposure to ^{137}Cs

Bill's interest in IDRM was also a response to the Fukushima nuclear accident. ^{137}Cs was the major radionuclide of concern at Fukushima. Bill convinced Erika June Peterson to do her M.Sc. research at WSU on "Dose-rate effects of ^{137}Cs on survival time in the beagle dog". Two very interesting observations came out of this thesis. First, animals exposed to low levels of ^{137}Cs had better survival times than controls. This was related to the fact that, in the controls, there was a relatively high frequency of kidney disease, not present in the animals that had inhaled low levels of ^{137}Cs. Did low doses of radiation alter disease patterns? Small sample size and selection of animals seemed to be a problem but the question is still a valid one. Second, the lifetime survival was not different between the low dose groups and the control.

2.1. Lung

Extensive research has been conducted on the health effects of inhaled radioactive materials [3,4], including radionuclides both beta-gamma and alpha emitting radionuclides. To evaluate the effects of dose rate, research was conducted using beta gamma emitting radionuclides with a range of physical half-lives: ^{90}Sr, ^{144}Ce, ^{91}Y or ^{90}Y. Dose rate changes rapidly with time for the short-half-life materials; thus, using a single dose rate to describe the biological response is difficult [5]. Fig. 4 shows the results for dogs

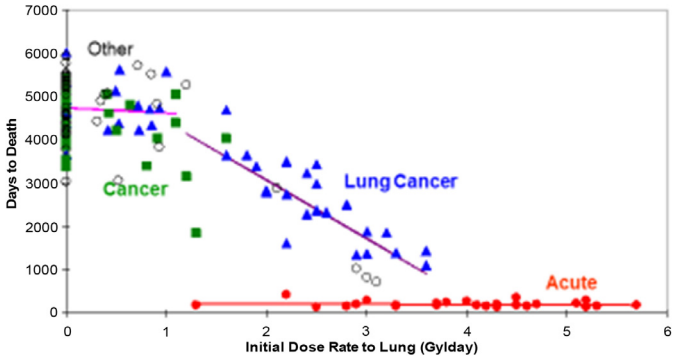
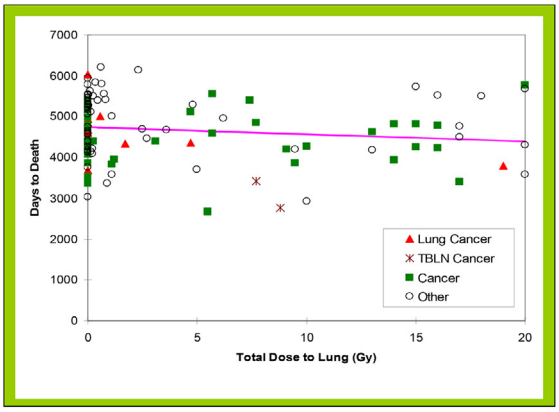


Fig. 4. The influence of inhalation of ^{91}Y on life span in the Beagle Dog. The causes of death are illustrated in the figure with acute lung deaths as red circles, lung cancer (blue diamonds), other cancers (green squares) and non-cancer deaths as open circles. High dose cause acute death, next lower doses high incidence of lung cancer and lower doses no significant changes from controls.

that inhaled ^{91}Y, with the initial dose-rate plotted against survival time and the causes of death shown as different symbols: acute lung deaths, red circles; lung cancer, blue diamonds; other cancers, green squares; non-cancer deaths, open circles. Similar patterns were seen for each of the inhaled radionuclides. With high initial dose-rates (1.5–3 Gy/day), a large dose was delivered within a single cell cycle (the average cell cycle time in lung epithelial cells is about 30 days). Such high dose rates would be calculated to deliver large doses (45–90 Gy/cell cycle), causing extensive cell death; almost all of the animals died within one year of the inhalation, from acute lung damage, including radiation pneumonitis and fibrosis [5]. As the dose rates decreased to 1–3 Gy/day, survival time increased and the frequency of lung cancer was very high. Perhaps the chronic inflammatory disease, cell death, cellular and tissue disorganization were critical in the formation of lung cancer. However, when initial dose rate was further decreased (0.2–1.0 Gy/day or 6.0–30 Gy/cell cycle) the acute cell killing was reduced, cell replacement was possible and most of the dogs did not die early from acute lung damage.

In dogs whose lungs were exposed to high doses and high dose rates, high levels of reactive oxygen species (ROS) would be expected [32]; chronic inflammatory disease was present [7] as well as tissue disorganization [8] and modification of the immune system [9]. All of these factors play major roles in cancer development. If this dose was delivered as an acute lung exposure, all the dogs would quickly die. As the dose rate further decreased, protective processes may have been initiated, such as protective adaptation [10] and selective apoptosis of transformed cells [11].



	Lung Cancer	Total Cancer
Control	8/54= 15%	26/54= 48%
Exposed	4/64= 6%	29/64= 45%

Fig. 5. The biological responses summarized for of all the inhaled beta-gamma radionuclides that resulted in a total integrated dose to the lung of less than 20 Gy. There was no significant difference between this exposed group and the controls.

This illustrates that dose rate and dose distribution are both important, especially when the total dose is high. The major point of this graph is to demonstrate a marked dose rate effectiveness factor (10–30) when measuring acute deaths from radiation, depending on the radionuclide. Exposure to ^{90}Y is more similar to acute exposure, since each cell receives almost all of the dose in a single cell cycle. As the effective half-life increases, the dose per cell cycle is reduced, repair and repopulation are possible, and survival increases. However, when the dose rate is lowered to a level where the animals do not develop chronic inflammatory disease, the lifespan and lung cancer frequency are not significantly different from the controls. This effect was seen even though the lung dose was as high as 20 Gy. Using the information that 0.1 Gy results in 100 "hits/cell", an acute exposure to 20 Gy would result in 20,000 hits in each cell. If the turnover time of cells in the lung epithelium is about 30 days and it takes ^{91}Y 180 days to deliver 90% of the dose (20 Gy), then on the average, each cell would receive an estimated 3300 "hits/cell/cell cycle". Fig. 5 shows that even with these large numbers of hits, there was neither life shortening nor increase in cancer frequency in the lungs. This illustrate the ability of the lung to repair damage and further supports the presence of a large dose-rate effectiveness factor, which would be infinity if no cancers were induced in the exposed group [5].

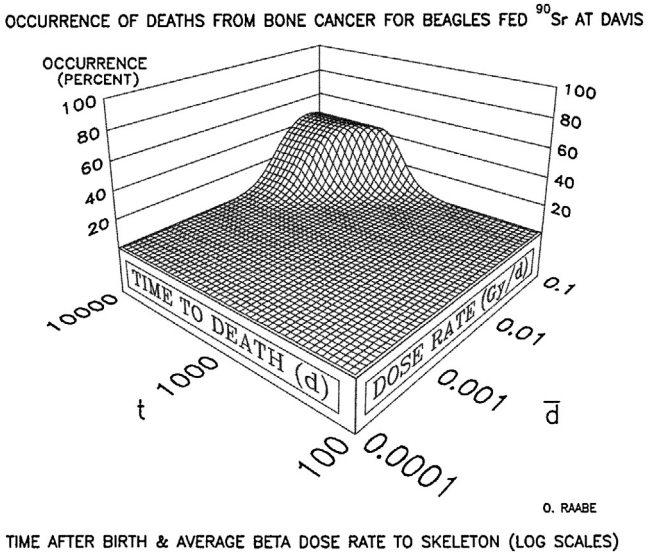


Fig. 6. This figure shows the dose-rate, time and bone cancer incidence plotted in 3-D for animals that ingested ^{90}Sr over their lifetime. The figure illustrates that at early times and after low dose rate exposure there is no increase in bone cancer until the total dose is above about 10 Gy.

2.2. Bone

There have been several very good long-term follow-up studies on the effects of radiation in human bone. The best example is the case of the Ra dial-painters: young women were employed to paint luminescent Ra dials on watches. Ra is an alpha-emitting radionuclide and some of these workers developed bone cancer [29,30]. These data showed that even for alpha emitters there is a marked threshold below which there were no excess bone cancers.

Studies were initiated to evaluate the effect of beta emitters on bone cancer in beagle dogs. Fig. 6 summarizes the data developed at the University of California, Davis. Dogs were fed ^{90}Sr over their entire lifetimes, starting *in utero*. The figure relates radiation dose rate to time of death and bone cancer frequency [12,13]. Since ^{90}Sr concentrates in bone, this was the primary site of cancer development. This figure firmly demonstrates that at low dose rates less than 0.01 Gy/d and at times close to the total lifespan of the dog, there was no increase in the frequency of bone cancer relative to the controls. At higher dose rates (0.01–0.1 Gy/day) and at times longer than 4000 days, there was an increase in bone cancer. This was a late occurring disease after high dose rates which resulted in large doses to the bone (>10 Gy). If this same dose were given in a short time, it would result in 100% lethality.

The non-linear dose response and reduction in the response is related to the low dose rate and the non-uniform distribution of the dose. These types of studies along with human data have led to the development of tissue weighting factors for bone (NCRP 1993), indicating that bone is a very radiation-resistant organ and that doses from radionuclides such as ^{90}Sr are not as hazardous as whole-body doses. For such non-uniform exposures, many of the organs and systems that are important in altering radiation response are not damaged and provide protection against radiation-induced risk. The immune system is an example. Partial body or protracted exposure has the potential to affect the total body immune system [14]. However, when much of the immune system is not exposed to the radiation, there is little effect. It has even been suggested that low-dose-rate exposure may stimulate the immune system and increase lifespan [15]. Acute whole-body radiation exposure, such as used in radiation therapy, can cause

marked suppression of the immune response and an increase in cancer frequency [9]. Under high dose/low dose-rate exposure conditions, tissue disorganization [8], extensive cell signaling [16], chronic inflammatory disease [17], fibrosis [6,7] and changes in ROS status play a major role in subsequent development of cancer. All of these effects are highly dose and dose-rate dependent.

2.3. Liver

Data on radiation-induced liver cancer suggested that the risk was lower in the low dose groups than predicted by linear extrapolation from the high dose groups, suggesting a non-linear dose–response relationship (ICRP 2001). Liver injury plays a major role in induction of liver cancer. The very large doses produced by Thorotrast produce extensive chromosome damage and cell killing [18]. The interaction between liver damage from alcohol consumption and radiation exposure to ^{241}Am causes a marked increase in liver cancer in dogs [19]. Stimulation of cell proliferation by partial hepatectomy following injection with ^{144}Ce–^{144}Pr also increases the frequency of liver cancer [20]. All of these effects indicate that injury, cell proliferation, tissue disorganization and inflammatory disease have a marked influence on cancer induced by low dose-rate radiation exposure, and suggest the need for re-evaluation of the risks from IRDM. In no case was deposition of radioactive material in the body as hazardous as either single-acute or protracted-whole-body radiation exposure. The risks to the lung, bone, and liver from IRDM are probably overestimated; Bill Morgan suggested on many occasions that additional reviews of these data are needed.

3. Scientific reviews

Bill was very active in writing reviews and summarizing the data published in relatively new fields. Two areas where his reviews had major impact were non-targeted effects and genomic instability. Bill wrote extensive reviews on the bystander effect and on cell/cell and cell/tissue communication, topics which questioned the "hit theory" [21]. Bill, his students, and fellow scientists were among the first to develop systems to measure and monitor genomic instability [22,23]. Bill was also very active on committees and in planning meetings to make sure that the most recent data was available to those who are charged with setting regulatory standards [10,24,25,26]. Indeed, Bill was working in this area at the time of his death.

Bill helped to write a manuscript focused that frames some of the problems that remain in the field of radiation biology [27]. One of Bill's major concerns was to produce information that the general public could use to assess radiation risks [28].

4. Summary

William F. Morgan (Bill) had a significant impact on every field of science that he touched. He was a good science manager and put together a broad-based team of scientists to study the biological effects of low dose and low dose-rate radiation exposures. His publication record and his accomplishments as a science advisor and reviewer were remarkable. While at PNNL, Bill gained a great interest in IRDM; in only a few years, he managed to have an important positive impact on this field. We remember Bill as a happy face, a friendly greeting, a true good friend, and an avid promoter not only of his own interests but ours as well.

Conflict of interest

The author has no financial or other conflict of interest for this manuscript.

Acknowledgments

The author would like to acknowledge the help of Careina Brooks (editing) and Marianne Sowa for providing much valuable information.

References

[1] NCRP Report No. 167, Potential Impact of Individual Genetic Susceptibility and Previous Radiation Exposure on Radiation Risk for Astronauts, Scientific Committee, AL Brooks and WF Morgan, Chairs, 20111–13.
[2] C.E. Nielsen, D.A. Wilson, A.L. Brooks, S.L. McCord, G.E. Dagle, A.C. James, S.Y. Tolmachev, B.D. Thrall, W.F. Morgan, Microdistribution and long-term retention of plutonium-nitrate in the respiratory tracts of an acutely exposed plutonium worker and experimental beagle dogs, Cancer Res. 72 (2012) 5529–5536.
[3] J.N. Stannard, Radioactivity and Health: A History, in: R.W. Baalman (Ed.), DOE/RL/01830-T59 (DE88013791) Distribution Category UC-408, 1988.
[4] R.C. Thompson, Life-span effects of ionizing radiation in the Beagle Dog, in: PNL 6822, UC-408, 1989.
[5] A.L. Brooks, P.E. Eberline, L.A. Couch, B.B. Boecker, The role of dose-rate on risk from internally-deposited radionuclides and the potential need to separate dose-rate effectiveness factor (DREF) from the dose and dose-rate effectiveness factor (DDREF), Health Phys. 97 (2009) 458–469.
[6] F.F. Hahn, B.B. Boecker, R.G. Cuddihy, C.H. Hobbs, R.O. McClellan, M.B. Snipes, Influence of radiation dose patterns on lung tumor incidence in dogs that inhaled beta emitters: a preliminary report, Radiat. Res. 96 (1983) 505–517.
[7] F.F. Hahn, B.A. Muggenburg, M.B. Snipes, B.B. Boecker, The toxicity of insoluble Cerium-144 inhaled by beagle dogs: non-neoplastic effects, Radiat. Res. 155 (2001) 95–112.
[8] M.H. Barcellos-Hoff, It takes a tissue to make a tumor: epigenetics, cancer and the microenvironment, J. Mammary Gland Biol. Neoplasia 6 (2001) 213–221.
[9] P. Kaur, A. Asea, Radiation-induced effects and the immune system in cancer, Front Oncol. 2 (2012) 1–10.
[10] L.T. Dauer, A.L. Brooks, D.G. Hoel, W.F. Morgan, D. Stram, P. Tran, Review and evaluation of updated research on the health effects associated with low-dose ionizing radiation, Radiat. Prot. Dos. 140 (2010) 103–136.
[11] G. Bauer, Low dose radiation and intercellular induction of apoptosis: potential implications for the control of oncogenesis, Int. J. Radiat. Biol. 83 (2007) 873–888.
[12] O.G. Raabe, Three-dimensional dose–response models of competing risks and natural life span, Fundam. Appl. Toxicol. 8 (1987) 465–473.
[13] O.G. Raabe, Concerning the health effects of internally deposited radionuclides, Health Phys. 98 (2010) 515–536.
[14] M. Nagarkatti, P.S. Nagarkatti, A.L. Brooks, Effect of radiation on the immune system: alterations in the cellularity and functions of T cells in lymphoid organs of mouse, J. Toxicol. Environ. Health 47 (1996) 535–552.
[15] Y. Ina, K. Sakai, Further study of prolongation of life span associated with immunological modifications by chronic low-dose-rate irradiation in MRL-lpr/lpr mice: effects of whole-life irradiation, Radiat. Res. 163 (2004) 153–158.
[16] M.H. Barcellos-Hoff, A.L. Brooks, Extracellular signaling through the microenvironment: a hypothesis relating carcinogenesis; bystander effects, and genomic instability, Radiat. Res. 156 (2001) 618–627.
[17] R.C. Pfleger, B.B. Boecker, H.C. Redman, J.A. Pickrell, J.L. Mauderly, R.K. Jones, S.A. Benjamin, R.O. McClellan, Biological alterations resulting from chronic lung irradiation. 1. The pulmonary lipid composition, physiology, and pathology after inhalation by beagle dogs of 144-Ce labeled fused clay aerosols, Radiat. Res. 63 (1975) 275–298.
[18] R.A. Guilmette, N.A. Gillett, A.F. Edison, W.C. Griffith, A.L. Brooks, The influence of non-uniform alpha irradiation of Chinese hamster liver on chromosome damage and the induction of cancer, in: D.M. Taylor, C.H. Mays, G.B. Gerber, R.G. Thomas (Eds.), Risks from Radium and Thorotrast, British Institute of Radiology, London, 1989, pp. 142–148.
[19] G.N. Taylor, R.D. Lloyd, C.W. Mays, Promotion of radiation-induced liver neoplasia by ethanol, Health Phys. 62 (1993) 178–182.
[20] A.L. Brooks, S.A. Benjamin, R.K. Jones, R.O. McClellan, Interaction of ^{144}Ce and partial hepatectomy in the production of liver neoplasms in the Chinese hamster, Radiat. Res. 91 (1982) 573–588.
[21] W.F. Morgan, M.B. Sowa, Non-targeted bystander effects induced by ionizing radiation, Mutat. Res. 616 (2007) 159–164.
[22] W.F. Morgan, J.P. Day, M.I. Kaplan, E.M. McGhee, C.L. Limoli, Genomic instability induced by ionizing radiation, Radiat. Res. 146 (1996) 247–258.
[23] G.J. Kim, G.M. Fiskum, W.F. Morgan, A role for mitochondrial dysfunction in perpetuating radiation-induced genomic instability, Cancer Res. 66 (2006) 10377–10383.

[24] L.E. Feinendegen, A.L. Brooks, W.F. Morgan, Biological consequences and health risks of low-level exposure to ionizing radiation, Health Phys. 100 (2011) 247–260.
[25] A.L. Brooks, D.G. Hoel, R.J. Preston, The role of dose rate in radiation cancer risk: evaluating the effect of dose rate at the molecular, cellular and tissue levels using key events in critical pathways following exposure to low LET radiation, Int. J. Radiat. Biol. 92 (2016) 405–426.
[26] A.L. Brooks, W.F. Morgan, L.E. Feinendegen, 2015 Health Physics Society Symposium, 13–14 July 2015, Health Risks from low doses and low dose-rates of ionizing radiation, Health Phys. 110 (2016) 241–248.
[27] W.F. Morgan, W.J. Bair, Issues in low doe radiation biology: the controversy continues, Perspective. Radiat Res. 179 (2013) 501–510.
[28] A.E. Waltar, A.L. Brooks, J.M. Cuttler, L.E. Feinendegen, A.J. Gonzalez, W.M. Morgan, 2016. The high price of public fear of low-dose radiation. J. Radiol. Prot. 36, 387.
[29] R.D. Evans, The radium standard for boneseekers – evaluation of the data on radium patients and dial painters, Health Phys. 13 (1987) 267–278.
[30] R.D. Evans, A.J. Finkel, R.J. Hasterlik, A.T. Keane, R.J. Kolenkow, W.R. Neal, M.M. Shanahan, The risk of bone cancer in man from internally deposited radium, Br. J. Radiol. 41 (1968) 391–393.
[31] C.E. Nielsen, X. Wang, R.J. Robinson, A.L. Brooks, J. Lovaglio, K.M. Patton, S.L. McComish, S.Y. Tolmachev, W.F. Morgan, Carcinogenic and inflammatory effects of plutonium nitrate retention in an exposed nuclear worker and beagle dogs, Int. J. Radiat. Biol. 90 (2014) 60–70.
[32] D.R. Spitz, E.I. Azzam, J.J. Li, D. Gius, Metabolic oxidation/reduction reactions and cellular responses to ionizing radiation: a unifying concept in stress response biology, Cancer Metastasis Rev. 23 (2004) 311–322.