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100 Years of Radiation Research in the Footsteps of Failla

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Gioacchino Failla was initially appointed to operate the radon plant at Memorial Hospital in 1916. What to most people would have been a part-time temporary position was to him a career. He was not satisfied to simply fabricate radon seeds, he wanted to understand the physics and biology of the radiation emitted by the progeny of radium. His was not the first medical physics group in the United States, though it was one of the earliest, but it was the first to put such emphasis on the biological effects. After more than 28 years at Memorial Hospital, Failla moved his research group to Columbia University Medical Center and his pioneering work, blending physics and biology, has continued to date at Columbia by those that he trained or inspired, under three directors that followed him.

The story of radiation research at the Biophysics Laboratory, that became the Radiological Research Laboratory, that became the Center for Radiological Research, begins with Dr. Henry Janeway (Fig. 1A). He was a founding member of the American Radium Society, and gave his name to the eponymous lecture of that society. Dr. Janeway graduated with an M.D. from the College of Physicians and Surgeons at Columbia University in 1898. He practiced as a surgeon in several posts until in 1915 he was appointed Chief of the Radium Department at Memorial Hospital in New York City. This was a new appointment to exploit the sizeable amount of Radium that had been given to the hospital by a consortium of benefactors. The amount of radium given to the hospital had reached 3.75 grams, an extraordinary supply for the time (*1*)

Janeway suffered from a rare bone tumor, an adamantinoma of the mandible. He underwent several unsuccessful surgical attempts to remove the tumor, and in the course of time received a radium implant. The radium needles of the day were typically 5 cm long and 4 mm in diameter; they were pushed through the tumor, spaced about 1 cm apart and left in place for 7–10 days. Figure 1B shows a radiograph of a typical radium implant of the floor of the mouth to give an impression of what it must have been like. Janeway found it to be extremely painful and uncomfortable and he was led to exclaim ''*There has to be a better way!*''.

The better way turned out to be radon seeds. Radon emanation is a radioactive gas given off by radium as it decays, and if trapped in a thin glass tube it, in turn, decays and results in a radioactive seed a few millimeters in length with a half-life of about four days (*2*). These small seeds turned out to be much more comfortable than radium needles, but they had to be fabricated for each patient and could not be reused. Janeway hired Gino Failla, a young graduate student in the physics department at Columbia University, to operate the radon plant (Fig. 2), which was a replica of the one built at Harvard by William Duane (*3*). Many years later, Dr. Juan Del Regato, one of the founding members of the American Society of Therapeutic Radiology and Oncology, in writing about the pioneers in the field of Radiation Research said of Failla. . . .''*What would have been just a job to someone else, Failla turned into the initiation of a remarkable career. He learned to operate the plant, but he also learned everything known about radioactivity and its medical uses*.'' (*4*). He was not content to simply fabricate radon seeds, he wanted to understand both the physics and the biology of the radiation emitted.

As the United States entered the First World War, Failla was assigned to the Scientific Attaché of the United States embassy in Rome. After his service there (1918–1919), he returned home via Paris, where he met Marie Curie, who had just resumed her research work. She was so interested in his work that she encouraged him to return and qualify for a doctorate from the University of Paris. This he did several years later, spending a sabbatical in Paris in 1923 to complete his doctorate with Marie Curie as the Chair of the committee that reviewed his thesis (*5*).

Failla was at Memorial from 1915 to 1942, developing the medical physics and biophysics department. It was not the first medical physics department in the United States, but it was probably the first to focus attention on the

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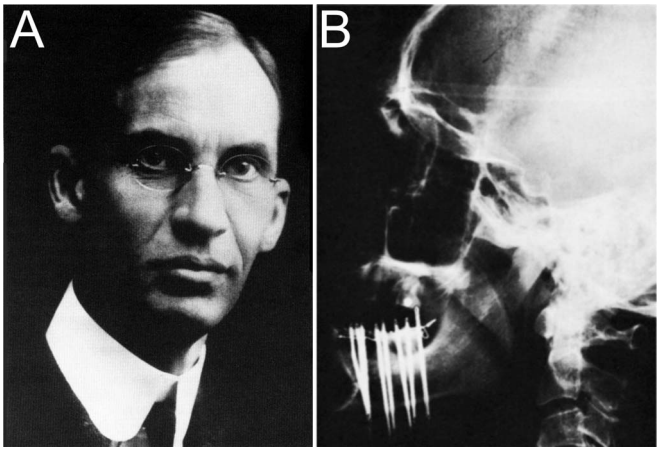

FIG. 1. Panel A: Henry Janeway, M.D., Chief of the Radium Department at Memorial Hospital. Panel B: Typical radium needle implant to treat a cancer of the floor of the mouth.

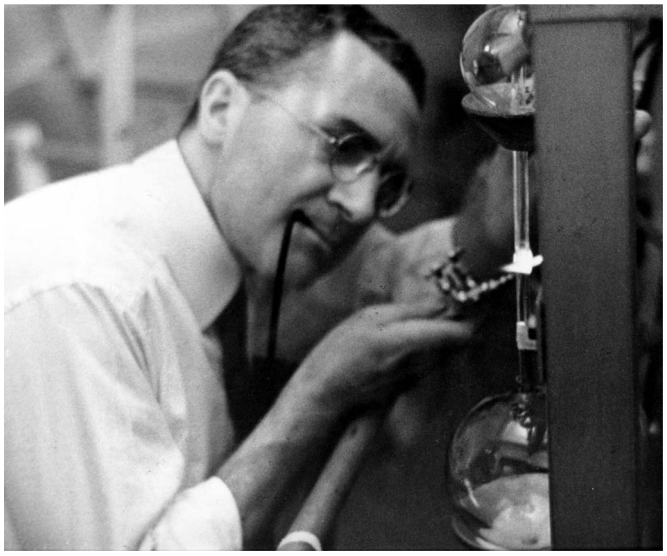

FIG. 2. Gioacchino Failla operating the radon plant at Memorial Hospital.

FIG. 3. Panel A: Edith Quimby was hired as an assistant to Failla in 1919. She planned for it to be a temporary appointment while her husband was in graduate school, but she stayed for 60 years. Image reproduced, with permission, from (*10*). Panel B: Edith Quimby, still working at the RRL at 85 years of age. Panel C: Titus Evans had been a graduate student of Failla and became the first editor of the journal *Radiation Research*. Image reproduced, with permission, from (*10*). Panel D: Pat was a graduate student of Failla, but had to find a new supervisor when romance blossomed and she became Failla's second wife.

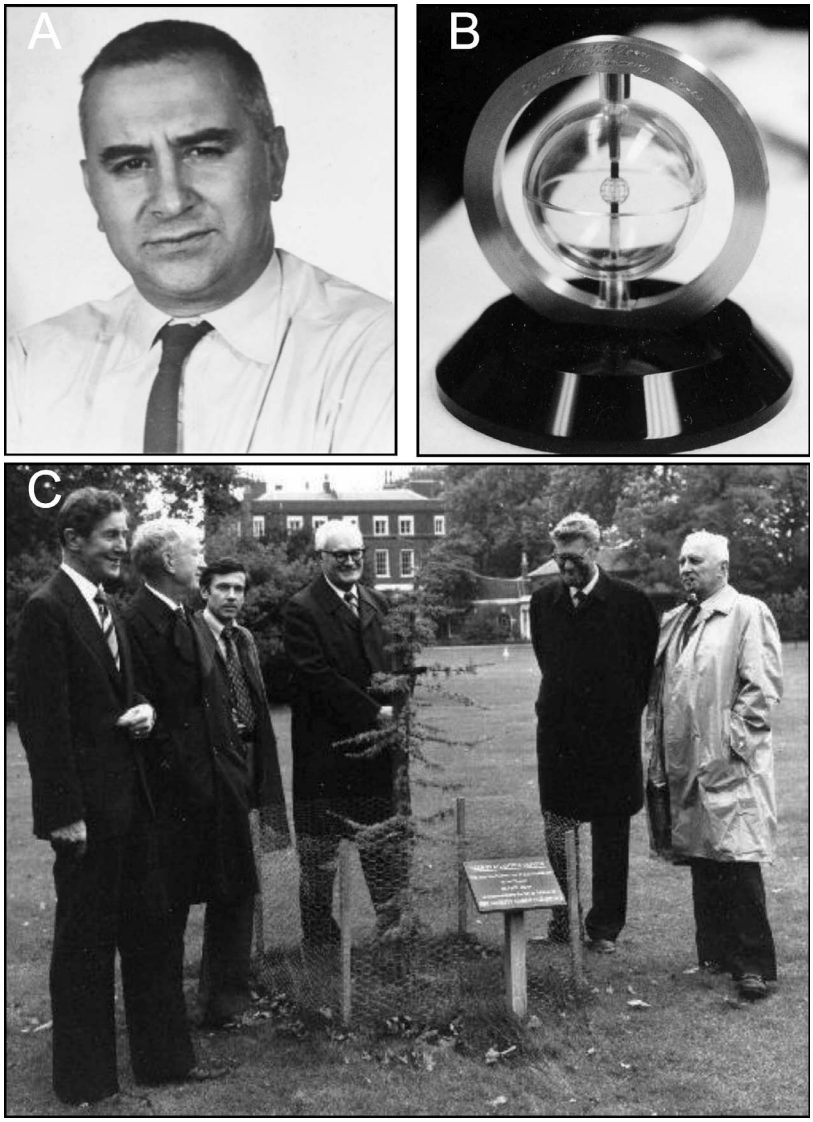

FIG. 4. Panel A: Harald Rossi was a great admirer of Failla, and was a logical choice as Director of RRL when Failla retired. Panel B: Gas Proportional Counters, known the world over as ''Rossi Counters'' were in use in physics laboratories on both sides of the Atlantic. Panel C: Harald Rossi was a member of many committees but was most proud of his long service on the International Commission of Quantities and Units (ICRU). The main commission met at the National Physical Laboratory in England in 1978. Pictured from left to right: Alan Jennings; Kurt Liden; Albrecht Kellerer; Harold Wyckoff; André Allissy; Harald Rossi.

biological effects of radiation, hence the title ''Biophysics Laboratory.''

During World War II Failla was seconded to the Manhattan Project to organize the neutron dosimetry involved in the development of the A-bomb. In 1942 he moved his entire research group from Memorial Hospital to The College of Physicians and Surgeons of Columbia University; relieved of most routine medical physics duties, he was able to concentrate all his efforts on research funded by a contract from the Atomic Energy Commission.

Dr. Failla's accomplishments were many. He was the first to recognize the need to measure absorbed dose, and devised and built dosimeters to accomplish the task (*6*). He was first to realize that the same physical dose of different radiations (gamma rays from radium and 140 kV X rays were all he had available at the time) produce different levels of biological effect (*7*). This led ultimately to the concept of Relative Biological Effectiveness, i.e., RBE.

In 1919 Failla hired Edith Quimby as an assistant physicist. She took the job on a temporary basis while her husband was in graduate school, and ended up staying for 60 years, becoming arguably the most famous woman medical physicist in the country. She is best remembered for devising a system of rules for radium implants that were widely used in the United States; the well-known ''Quimby Rules''. In the time before computers, a system of dosimetry that included rules for the placement of needles, rules for the distribution of the radioactive material, and nomograms to

FIG. 5. Panel A: Ruth Hill was on the staff of RRL in the 1950s and 1960s. She is best known for her work isolating radiosensitive mutants of *E. coli*. Image reproduced, with permission, from (*10*). Panel B: Roberts Rugh was on the staff of RRL in the 1950s and 1960s. He was well known for his work on radiation-induced anomalies in the developing embryo and fetus. He was advised not to travel to Egypt and the Middle East because of his resemblance to Moshe Dayan! Panel C: Albrecht Kellerer was recruited from Munich in 1968 and stayed at the RRL for 10 years. He helped to put Rossi's Theory of Dual Radiation Action on a sound mathematical basis. He also collaborated closely with the biologists on data analysis. Image reproduced, with permission, from (*10*).

easily assess how long the implant should be in place to achieve the required radiation dose, represented a major contribution to the practice of radiation oncology. She was also a great educator and co-authored ''*Physical Foundations of Radiology*'', the first physics textbook for radiologists (*8*). Edith Quimby gave the Gold Medal Janeway lecture in 1940 (*9*), and she became so prominent in that society that the rules were changed to allow her, with a Sc.D., to become president of the society in 1954 (Fig. 3A). She remained active until her mid-eighties (Fig. 3B), commuting to Columbia-Presbyterian by subway from her home in Greenwich Village. The stature of both Failla and Quimby in the field of radiology and radiation research is illustrated by the fact that both have prestigious awards named after them; the Failla Award of the Radiation Research Society and the Edith H. Quimby Lifetime Achievement Award of the American Association of Physics in Medicine.

Failla was one of the founding members of the Radiation Research Society, and indeed the Society was largely his initiative. Titus Evans (Fig. 3C) had been a graduate student of Failla and was appointed as the first editor of the Society's journal *Radiation Research*. It was not all work and science at the Radiological Research Laboratory (RRL), since romance flourished too. Patricia McClement was also a graduate student of Failla, but had to find a different supervisor when she became Failla's wife in 1949 (Fig. 3D).

In 1960 Failla retired from Columbia and moved to a post-retirement position at the Argonne National Laboratory. Tragically, he was killed shortly afterwards in an automobile accident. Harald Rossi was appointed Director of the RRL; the first passing of the torch.

Harald Rossi (Fig. 4A) was born in Vienna, but in 1939 moved with his family, first to England and then to the United States, in order to escape the Nazi threat. He completed his Ph.D. at Johns Hopkins, but quickly found himself in the United States Army when conscription was introduced after Pearl Harbor. Failla had to use his considerable influence with the Atomic Energy Commission to get Rossi released from the army, to be his assistant on the Manhattan project, and to join him on the faculty of Columbia University. Rossi was a great admirer of Failla and they worked closely together for about 16 years. As a consequence, he was a logical successor to Failla as Director of the RRL. Harald Rossi is best known for his development of the concept of microdosimetry, simulating a volume comparable to the nucleus of a mammalian cell by using a tissue equivalent gas at low pressure (*11*). Microdosimetry required the design and construction of elaborate measuring devices, the so-called Rossi Counters (Fig. 4B), which were used in many laboratories around the world. Harald Rossi served on many committees, but was most proud of his long service to the International Commission on Radiological Units (Fig. 4C).

During the 1950s and 1960s there were also several well-known biologists on the staff of the RRL. Ruth Hill (Fig. 5A) is best known for first isolating radiosensitive mutants of *E. coli*. Roberts Rugh (Fig. 5B) was responsible for much of the early work that elucidated the effects of radiation on the developing embryo and fetus.

The year of 1968 saw the recruitment of two new faculty members. The first was Albrecht Kellerer from Munich, Germany (Fig. 5C). He worked closely with Harald Rossi on the development of the Theory of Dual Radiation Action, the aim of which was to explain the biological effects of different types of radiation in terms of physical events that could be measured in gas proportional counters. Rossi had already designed and built the counters, but it was the genius of Kellerer to develop the theory on a sound mathematical basis (*12*).

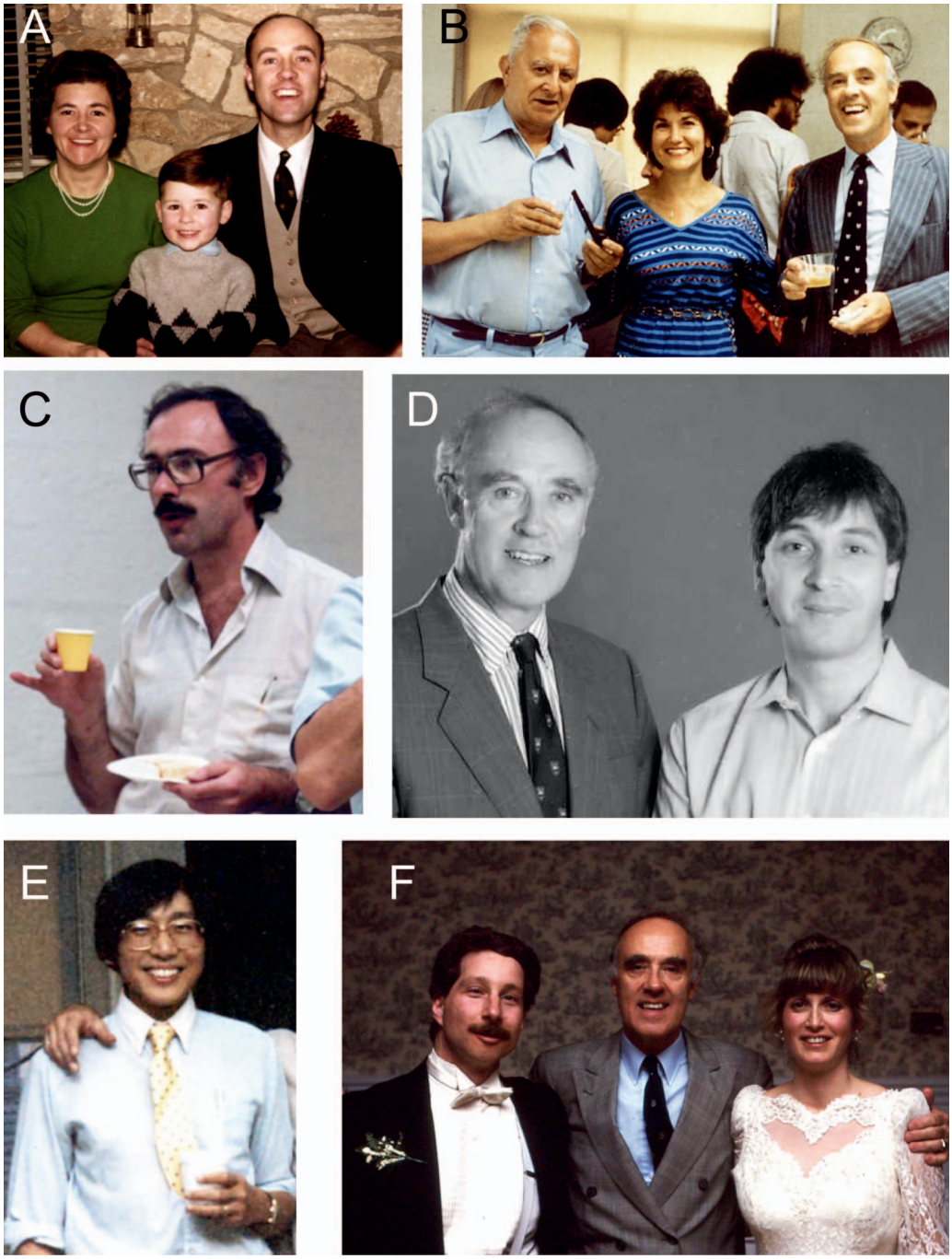

FIG. 6. Panel A: Eric Hall was recruited from Oxford in 1968 to bring mammalian cell culture to RRL. The little boy, Simon, is now a Professor of Urology in New York City. Panel B: The first person that Eric Hall hired was Carmia Borek, pictured here with Harald Rossi to the left and Eric Hall to the right. At the Weitzman Institute in Israel she had developed the system of *in vitro* oncogenic transformation assay based on hamster embryo fibroblasts. Panel C: Charles Geard was hired from the Australian National University in 1974 to bring expertise in cytogenetics to RRL. Panel D: David Brenner (right) was recruited to RRL in 1980 and quickly formed a close friendship and collaboration with Eric Hall (left) and the biology group, analyzing data. Panel E: Tom Hei was recruited in 1983 to set up the mutagenic assay system developed by Charles Waldren. Panel F; From left to right: Howard Lieberman; Eric Hall; Jaime Rubin. Jaime was the first molecular biologist hired at RRL, followed closely by Howard. They were married several years later.

The other new arrival was Eric Hall, whose function was to add mammalian cell culture techniques to the RRL (Fig. 6A). The first person he hired was Carmia Borek (Fig. 6B), who had developed the technique of recognizing oncogenic transformation in hamster embryo cells while at the Weitzman Institute in Israel. This assay became one of the trademarks of RRL in the 1970s and 1980s.

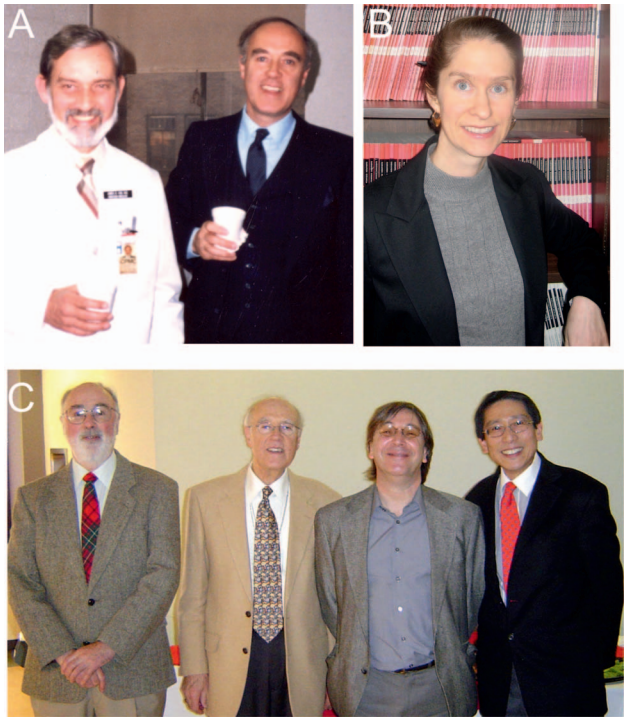

FIG. 7. Panel A: James Cox (left) was appointed Chairman of the newly formed Department of Radiation Oncology in 1984. Eric Hall (right) Director of the newly named Center for Radiological Research, elected to change the academic titles of CRR staff from Radiology to Radiation Oncology. Panel B: Sally Amundson was recruited from NIH in 2003. She was the last academic appointment made by Eric Hall during his 24-year tenure as Director of CRR. Panel C: The Passing of the Torch, December 2007, Eric Hall and Charles Geard, Director and Associate Director of CRR, respectively, are replaced by David Brenner and Tom Hei.

Up to this time the RRL had been funded largely by the Atomic Energy Commission and one of its later incarnations, the Department of Energy. With the expansion of the National Institutes of Health, resulting from the Nixon ''War on Cancer'', the funding of the laboratory became more diversified and this allowed a further expansion of staff. Charles Geard (Fig. 6C) was recruited from the Australia National University in 1974 to add skills in cytogenetics. First Marco Zaider and later David Brenner were recruited from Los Alamos National Laboratory to strengthen the physics expertise of RRL. Eric Hall and David Brenner quickly became close friends and collaborators, with David Brenner providing the mathematical skills to analyze the data produced by the biologists (Fig. 6D). The next recruit was Tom Hei (Fig. 6E), who was given the task of introducing mutation techniques to RRL. It was during the 1980s too that the Radiological Research Accelerator Facility (RARAF) was moved from Brookhaven National Laboratory to the Nevis Campus of Columbia University, but there is a separate account of the history of this facility, so no more will be said of this topic here. (See the article on RARAF by Steve Marino in this issue.)

In 1984, Dr. Rossi stepped down as Director of RRL after 24 years in this position. However, he continued to work for several years as Professor Emeritus with an office at RARAF. Eric Hall was appointed RRL Director with a mandate from the Dean to appoint Assistant Professors; up until this time there had been relatively few tenure track positions at RRL. The first to be appointed was Jaime Rubin aiming to meet the need to move the research agenda in the direction of molecular biology. This was quickly followed by the appointment of Howard Lieberman, with expertise in the molecular biology of S. *Pombe*. These new appointees soon shared interests other than molecular biology and were married several years later (Fig. 6F).

This was a time of considerable change. Up to this time, radiotherapy and RRL had been divisions of radiology under one chairman. Following the tendency in the United States, Columbia University created a new Department of Radiation Oncology with Dr. James Cox (Fig. 7A) as the first chair. RRL was given Center status, becoming the Center for Radiological Research (CRR), with much autonomy and a budget directly from the Dean. The Center was given the choice of retaining academic titles in Radiology or changing to Radiation Oncology, and chose the latter. At the same time, the Dean, Dr. Donald Tapley, gave the title Higgins Professor of Radiation Biophysics to the Director of the new Center.

The last faculty appointment made by Eric Hall was of Sally Amundson (Fig. 7B), who joined the Center in 2003 From the National Institutes of Health, bringing expertise in radiation inducible gene expression. Over the years many Assistant Professors had passed through CRR, but three had risen through the ranks to Full Professor with tenure, namely David Brenner, Tom Hei and Howard Lieberman.

The third ''passing of the torch'' took place at the end of 2007 when Eric Hall stepped down as Director of the CRR, after 24 years in the position, and David Brenner was appointed in his place. Figure 7C shows the former Director and associate Director happily handing over to the new. Under the leadership of David Brenner the Center has expanded with an even wider range of research projects in radiation biology, molecular biology and the establishment of the Center for Minimally Invasive Biodosimetry.

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