

combined state of exhilaration in appreciation of the beauty of the work and of disgust at his inability to arrive at this interpretation despite his years of contemplation on the subject.

In investigations by Edwin M. McMillan^{1.6} at Berkeley and others elsewhere, one of the radioactivities produced in the neutron bombardment of uranium was found to behave differently than the others. This beta radioactivity with a half-life of about two days did not separate by recoil from thin layers of uranium, as did the energetic fission products, when uranium was bombarded with slow neutrons. Segrè, thinking that this was an indication that it might not be a fission product, performed a chemical separation to see if it was a transuranium element *produced* as the daughter of the previously well-known β -particle-emitting ^{239}U . He was unsuccessful and published a Letter to the Editor^{1.7} entitled “An Unsuccessful Search for Transuranic Elements,” identifying the two-day radioactivity as being due to a rare earth element because of his lack of chemical expertise.

1.2. Early Days at the Berkeley Radiation Laboratory

The invention of the cyclotron at Berkeley by Ernest O. Lawrence and M. Stanley Livingston in 1931^{1.8} started a new era in physics by making a giant leap possible with a relatively simple device. Up to this time progress in the production and study of artificial radioactivities was very slow, because although α -emitting sources prepared from natural ores were used initially in the discovery of artificial radioactivity by the Joliot-Curies, the intensities that could be achieved in this manner were very small. The nonresonant accelerators that soon became available provided much current but could not attain sufficiently high energies to do very much in the way of interesting chemistry or physics. The cyclotron, on the other hand, was a relatively simple device and could be constructed inexpensively by physicists anywhere in the world with only modest help from the Berkeley “cyclotroneers.”

Lawrence was an amazing person with a tremendous amount of drive. He immediately recognized that his invention would be a boon for research and he soon became a “promoter” and learned how to popularize his creation. This he did by offering the help of his laboratory and its people to other laboratories so that they too could take advantage of this revolutionary new tool. He also became very adept at “scrounging” needed parts from industry at little or no cost to keep the costs down as he continued with his experimentation to build ever-larger cyclotrons. His laboratory started out with a tiny demonstration “proton merry-go-round” that could be held in one hand (without the magnet) and gave an energy of 80 keV for molecular hydrogen ions. After this success new cyclotrons were built with increasingly large diameters of the magnetic pole faces to enable the experimenters to learn more about the details of how the device worked.

The next step was 1.22 MeV and they progressed soon to the 27-inch machine that could make large amounts of radioactivity with 10–15 mA of 6 MeV deuterons. In August 1937 it was converted into the 37-Inch Cyclotron to get several times that current at 8 MeV. As a result of the broad interests of Ernest and his brother John, who was a medical doctor, the scope of investigations in the Radiation Laboratory extended beyond basic research. They included the practical interdisciplinary applications of these new tools of investigation with special emphasis on applications to medicine. Thus one of the chief driving forces to inspire higher currents and higher energies was the need to make large quantities of radiosodium for patient treatment. Later, when Robert Wilson discovered that 90% or more of the beam was lost before extraction, he and Martin Kamen devised probes covered with ferrous phosphide that would skim off this internal wasted beam to make ^{32}P and ^{59}Fe for the biologists; in this way they could meet the needs of biologists and physicists at the same time. In one fell swoop they had multiplied the usefulness of the 37-Inch Cyclotron by an order of magnitude in 1938.

Glenn Seaborg was in the right place at this time to begin his basic contributions to the Laboratory. In an address in 1970 to the

Society of Nuclear Medicine while Chairman of the U.S. Atomic Energy Commission, he told the story of how he became involved with cyclotron research:

“My collaborator in most of this work was a young nuclear physicist, John J. Livingood. Our association extended over a period of about five years (1936–1941) even though he left Berkeley to accept a position at Harvard University near the end of 1938. The transmutation reactions which led to the production of these radioisotopes were effected first with the 27-Inch Cyclotron, which later became the 37-Inch Cyclotron, in the old Radiation Laboratory, and finally with the 60-Inch Cyclotron in the Crocker Laboratory. The old Radiation Laboratory was a picturesque place, crowded almost beyond belief with its large complement of cages full of mice, for use in the experiments by the biomedical pioneers, and apparatus used by the other experimentalists and the cyclotron builders.



Fig. 1.3. Glenn T. Seaborg, Berkeley Campus, April 1936.

“The start of my partnership with Livingood was the result of an essentially accidental encounter. One day in the spring of 1936 (Fig. 1.3) I ran into Jack somewhere in the area between Gilman Hall (the Chemistry Building) and Le Conte Hall (the neighboring Physics Building). (At that time I was a second-year graduate student in the Department of Chemistry working on my thesis problem, which finally emerged as an investigation of the inelastic scattering of fast neutrons.) He told me that he had a target of the element tin which was being bombarded with 5-MeV deuterons in the 27-Inch Cyclotron at that very moment and asked whether I would like to perform the necessary chemical separations in order to make it possible to identify the transmutation products. The chemical operations would have to be performed immediately after the bombardment was completed within the next hour or so.

“Thus I was literally handed a ‘hot’ target and asked to process it chemically in order to identify the radioisotopes of tin, as well as isotopes of neighboring elements antimony and indium, that might be produced as transmutation products. Naturally I jumped at the chance.

“But the facility he placed at my disposal was hardly luxurious. This turned out to be a corner of a room on the second floor of Le Conte Hall, and the resources consisted of tap water, a sink, a primitive hood, and a small workbench. With some essential materials bootlegged from the Department of Chemistry I performed the chemical separation. Jack’s measurements on these chemical fractions showed the presence of some new radioisotopes of tin, an activity in the indium fraction which we later showed to be due to tin (i.e., the indium had been incompletely separated from tin), and two activities in the antimony fraction. We later proved that one of these latter two activities was due to a well-known radioisotope of copper, produced from copper impurity in the tin target, a possibility that I had not anticipated in this, my first, venture into radioisotope hunting.

“Livingood generously included my name as a coauthor in the ensuing publication, entitled ‘Deuteron-Induced Radioactivity in Tin,’

which thus became my first scientific publication. It cannot be ranked with my better publications because of the errors in the indium and antimony activities, but perhaps these were excusable on account of the unexpected nature of my encounter with Jack and the necessarily makeshift and hasty chemical separations I had to perform.

“The chemical work I performed during my continuing collaboration with Jack while he was still in Berkeley was all done in this little corner of the room in Le Conte Hall. Our teamwork in every instance consisted of Jack’s performing the cyclotron bombardments, after which I dissolved the target material and made the chemical separations. We next mounted my chemical end products on cardboard sheets and covered these with thin cellophane. He then measured their radiation characteristics, using a small Lauritsen quartz fiber electroscope mounted in a sort of cubbyhole room in the basement at the opposite end of Le Conte Hall. Jack constructed and operated the quartz fiber electroscope with consummate skill.

“As our work progressed the measurements all tended to be made on one electroscope which, near the end of 1938, Jack successfully moved to his new home at Belmont, Massachusetts. There he continued measuring the radioactive decay of the many samples he took with him from Berkeley and also measured the decay and absorption properties of additional radioactive samples, which I thereafter mailed to him at Harvard. (The informal process of sending radioactive samples in envelopes by mail was commonly used at that time, a method that has long since been superseded by the much more sophisticated methods required by AEC regulations today.) Jack made the move without missing a single point on our many radioactive decay curves. This indeed became a precious little instrument, critical to our whole research program, simple though it was, and it served this purpose until after the beginning of the war. Then it succumbed when one of his children used it as a plaything. This ended our collaboration, but fortunately most of the key measurements had been made on our samples by this time when the war had called Jack and me to other pursuits.

“My collaboration with Livingood was extracurricular. While it was going on I obtained my Ph.D. degree in May 1937. I then served for two years as the personal research assistant of the great physical chemist and Dean of the College of Chemistry, Gilbert Newton Lewis, and I began, in 1939, my service as a member of the faculty of the University of California, Berkeley. In all instances these occupations were demanding, and had priority on my time and attention.

“Our motivation in searching for new radioisotopes was simply the fascination of exploring an exciting new frontier of science. Usually we gave little thought to the possibility that one of the objects of our search would have practical value. But we were in for some surprises. For one thing, medical researchers on two occasions expressed the hope that radioisotopes of specific elements with desirable half-lives would be found — and we were fortunate enough to hit the jackpot. In addition, as the years passed, we have witnessed the appearance of many a delayed jackpot. At the time of their discovery we would have scoffed at the idea that many radioisotopes would ever have any practical value. Yet some of those that would have been most scorned have turned out to be among the most valuable. And I think there is a lesson here, a lesson that we know well and that everyone should understand: we cannot very often predict the practical applications of basic science, but we can predict that those applications will occur, to the enduring benefit of man.

“Our first immediately practical jackpot came early in the collaboration between me and Jack Livingood. We had learned that Prof. George H. Whipple of the University of Rochester was hoping to have a reasonably long-lived radioisotope of iron for use in his studies of hemoglobin in human blood. A visiting chemist from England, Fred Fairbrother, had begun to collaborate with Livingood in the spring of 1937 on this problem but his visit ended before completion of the work. Livingood turned to me, and this was our second team effort.

“With some advance warning, I was able to plan the chemical separation more carefully, to guard against the mixed results from

the hasty work with tin. Jack bombarded iron with 5.5-MeV deuterons in the 27-Inch Cyclotron. When the target came off the cyclotron, around dinnertime as I remember, my chemical setups were ready.

“In my determination to make an extremely clean chemical separation into fractions containing iron and the expected transmutation products cobalt and manganese, I worked all night making precipitations and repeated reprecipitations. When Jack came to work early in the morning just as the sun was rising, I handed him the three fractions and he began his measurements using his electroscope. The iron fraction was found to contain the radioactive isotope iron-59. When the first production run was made with the cyclotron, the resulting iron-59 was sent by E.O. Lawrence to Dr. Whipple, who performed the first tracer experiments on the blood, and these experiments opened up a new era in our understanding of iron metabolism and blood formation.

“Almost at the same time Dr. John H. Lawrence and his colleagues at Berkeley began studies of the blood, using iron-59, which have continued since at Donner Laboratory at rising levels of sophistication. This work and research by other investigators elsewhere has revolutionized our knowledge of blood formation and dynamics and the management of blood diseases. With the possible exception of iodine, the biological behavior of no other element has been studied so thoroughly. Iron-59 also plays a prominent role today in the diagnosis of various blood dyscrasias.

“Prof. Whipple worked in a group of scientists whose impact on what was then an infant field is still felt. One member of the group was Dr. P.F. Hahn, now deceased, who made significant contributions. Another was Dr. William F. Bale, who is still at the University of Rochester and with whom I still have occasional contact, since he is a member of the AEC’s Advisory Committee on Biology and Medicine. Although my current interests no longer bring me in touch with Prof. Whipple, I am told that he still comes to work every day at the University of Rochester — at the age of 92!

“In the course of our investigation we also bombarded cobalt with neutrons and found a very long-lived radioactive isotope of cobalt,

confirming the indications of others that such an isotope existed, and our later work identified this as the now well-known cobalt-60. Jack and I continued this line of investigation by bombarding pure cobalt samples, some with neutrons and some with deuterons furnished by the 27-Inch Cyclotron, followed by very careful chemical separation experiments. These bombardments and chemical separations took place in the summer of 1937, and by the spring of 1938 our decay and radiation absorption measurements had pretty well established the radioactive properties of cobalt-60 for which we eventually measured a half-life of 5.3 years. Today cobalt-60 is estimated to be used annually for over 4,000,000 therapeutic irradiations in the United States alone.

“In the course of subsequent work, and on the basis of our bombardments of iron with deuterons in the 37-Inch Cyclotron, we also discovered and measured the radioactive decay properties of iron-55, eventually shown to have a half-life of about 2.6 years, and cobalt-57, which we later characterized as having a half-life of about 270 days. These latter investigations were not completed until after Livingood left Berkeley in late 1938 to take up his position in the Cyclotron Laboratory at Harvard University. Both of these radioisotopes found their place in the stable of radioisotopes useful in medicine. The soft X-rays emitted by iron-55 have curtailed its clinical applicability. However, it is used in investigative studies with iron-59 when double labeling is necessary. Cobalt-57 is used in the Schilling test, which evaluates the absorption of vitamin B₁₂ from the intestine, particularly in patients suffering from pernicious anemia.

“Perhaps the most interesting of all of my collaborations with Jack Livingood, and one having special personal meaning to me, was the discovery (while he was still in Berkeley) of what is now the work-horse of medical radioisotopes, namely iodine-131.

“One day in the spring of 1938 the late Dr. Joseph G. Hamilton, one of the outstanding nuclear medical pioneers, ran into me on the steps of Le Conte Hall and mentioned the limitations on his studies of thyroid metabolism imposed by the short lifetime of the radioac-

tive iodine that was then available to him. He was working with iodine-128, which has a half-life of only 25 minutes. When he inquired about the possibility of finding an iodine isotope with a longer half-life, I asked him what value would be best for his work. He replied, "Oh, about a week." By this time my partnership with Livingood was in full swing; Jack prepared tellurium targets which we bombarded in the 37-Inch Cyclotron, some with 8 MeV deuterons and some with neutrons, and I put them through chemical separation and identification procedures working in my Le Conte Hall quarters. I recall that we wore gas masks and obstetrical gloves in order to avoid acquiring the dreaded "tellurium breath." We escaped this curse but I don't know whether these precautions were actually necessary.

"We were soon able to identify iodine-131, and luckily enough, its half-life turned out to be eight days. This isotope is now used some two million times a year for the diagnosis and treatment of thyroid disease and in a large number of other applications, including the diagnosis of kidney and liver disorders and function tests of these organs, to screen for pulmonary emboli by lung scans, to locate brain tumors and melanosarcomas and to determine blood or plasma volumes and cardiac output. Furthermore, over 99% of all *in vivo* nuclear medicine procedures utilize this isotope. I have the added satisfaction that my mother had her own life extended by many years as a result of treatment with iodine-131.

"A similar pattern developed in our work on zinc-65, also carried out in 1938 while Livingood was still in Berkeley. Here we followed up on the work of others who had observed a radioisotope of zinc with a half-life of about seven months produced by the deuteron bombardment as well as the proton bombardment of copper. Livingood prepared and bombarded a zinc target with 8 MeV deuterons in the 37-Inch Cyclotron and I performed the chemical separations which made it possible for us during 1938 to assign this radioactivity to zinc-65, characterize its half-life as 250 ± 5 days, and to determine the energy of the radiations, with the help of Jack's measurements with his electroscope. This radioisotope found limited

use in the scanning of the prostate gland and in the study of insulin uptake in the pancreas, but other methods have proved to be more successful.

“My roles in the discovery of technetium-99m and cesium-137 involved collaboration with other colleagues and in these instances we had no premonition concerning their ultimate beneficial applications to medicine when the work was performed. My collaboration with Emilio Segrè began in the summer of 1938 soon after his move, a number of months before his family, from Palermo, Italy, to the United States. On the basis of his familiarity with my publications with Livingood describing our work on new radioactive isotopes, he sought me out as a collaborator. He had participated at Palermo with his colleague C. Perrier in the discovery of the first synthetic element, technetium, with the atomic number 43.

“Segrè was anxious to pursue his investigations of this intriguing new element, and within a few days after our first encounter we had arranged for the bombardment of molybdenum with 8-MeV deuterons in the 37-Inch Cyclotron. In this case we collaborated on the chemical separations, using the techniques worked out by Segrè and his coworkers at Palermo, and we isolated a fraction designed to contain any isotopes of the element with the atomic number 43. We performed our chemical separations in a rather well-equipped little chemistry laboratory situated in the newly occupied Crocker Laboratory. We measured the radioactive decay and the radiation absorption properties through the use of an ionization chamber connected to a vacuum tube electrometer system — a rather more sophisticated detection apparatus than that which Livingood and I had been employing. To our delight, we discovered an isotope of great scientific interest, because it decayed by means of an isomeric transition with emission of a line spectrum of electrons coming from an almost completely internally converted gamma ray transition.

“This concept was so new to the experts in the Radiation Laboratory, including J.R. Oppenheimer and E.O. Lawrence, that we were asked to delay our publication until additional measurements and interpretations could be evolved. In the meantime, Segrè’s former

Italian colleague, Bruno Pontecorvo, then working in Paris, observed and published a description of a similar isomeric transition which he had observed in an isotope of rhodium. This was a form of radioactive decay which had never been observed before this time.

“Segrè and I were able to show that this radioactive isotope of the element with the atomic number 43 (later given the name ‘technetium’ by Perrier and Segrè) decayed with a half-life of 6.6 h and that it was the daughter of a 67-h molybdenum parent radioactivity. This chain of decay was later shown to have the mass number 99, and after the convention of designating isomeric states of measurable half-life with the symbol ‘m,’ meaning ‘metastable,’ was established, the 6.6-h activity acquired the designation ‘technetium-99m.’

“Its radiation quality, short half-life and pharmacologic versatility make technetium-99m ideally suited for medical use. The physical characteristics allow the physician to administer high doses at a substantially lower irradiation exposure to the patient and, because of the higher count rates, greater sensitivity in sequential imaging. There are now molybdenum-99 generators of technetium-99m in hospitals all over the United States and in many other parts of the world. This radioisotope is used in more than 2,000 diagnostic procedures daily in the United States alone involving the diagnosis of thyroid, liver, brain and kidney disorders. (*Note: Today, 1998, technetium-99m is the workhorse of nuclear medicine, used in some 10,000,000 diagnostic procedures per year.*)

“My involvement with the discovery of cesium-137 presents an entirely different story. After the discovery of fission by Hahn and Strassmann in December 1938 many radioactive fission products were characterized in laboratories all around the world, but the evidence concerning radioactive isotopes of rubidium and cesium was scanty or lacking. Therefore, in the late fall of 1940 I asked an undergraduate student, Margaret Melhase (now Mrs. Robert Fuchs), to take some uranium which had been bombarded with neutrons furnished by the 60-Inch Cyclotron and make chemical separations designed to look for hitherto unknown radioactive fission products such as cesium. She performed her chemical separations on the top

floor of the old 'Rat House,' which even at that time was an ancient ramshackle wooden building dating from the earliest days of the Department of Chemistry at Berkeley. Her measurements of the radioactive decay and radiation absorption properties were performed through the use of a Lauritsen quartz fiber electroscop situated in the cavernous auditorium of the abandoned East Hall. This was an ancient building which had been moved from its original site at the present location of Le Conte Hall to a spot just to the south of Faculty Glade at about the present location of Morrison Hall on the Berkeley campus. (These, by the way, were the quarters in which, working the graveyard shift during the winter of 1936–37, I had performed my Ph.D. thesis experiments on the inelastic scattering of fast neutrons.)

“Miss Melhase also used a Lauritsen electroscop situated on the third floor of Gilman Hall in the latter stages of her research after she had graduated to this higher status. She continued her work until the summer of 1941, by which time she had established the presence of a very long-lived radioactive fission product in the cesium fraction which on the basis of subsequent work we can now identify as being due to the 30 year cesium-137. This isotope has found substantial applications as a gamma ray source in medical therapy similar in its use to that of cobalt-60.

“This, then, has been a brief account of the manner in which our early work at Berkeley led to a number of practical, and largely unanticipated, benefits to mankind.

“In closing, let me say that, despite your remarkable achievements in the last three decades, I am confident that you are only at the beginning of the application of radioisotopes for human welfare. No one could have imagined, back in the 1930s, that you could have accomplished as much as you have. Nor can we visualize the uses of radioisotopes by the close of this century. That these tools will be of immeasurable benefit in the prevention and alleviation of human suffering, and in ways we cannot now imagine, seems assured.”

But Lawrence was not content. As far as he was concerned more energy was the name of the game — and his next jump was to a

cyclotron with a pole tip of 60 inches! When asked why it was so big he replied, “Because we can get the money for it!” But the problems do not increase linearly with the diameter of the pole tips, they increase as some much higher power, and although Lawrence had raised the money to build it he also needed first class engineering help. He was fortunate, in that William Brobeck turned up to work for nothing. This was the man who took over the complicated tasks of building Lawrence’s dreams, the 60-Inch and the 184-Inch Cyclotrons. In February 1939 beam hunting began in earnest, but it was not until September that operation of the 60-Inch Cyclotron could be called “routine” when a system of crews was set up so that the most efficient use of the time could be made. Figure 1.4 shows Lawrence and some of his people in front of the very large magnet before the vacuum chamber was installed. It was Brobeck who organized the builders of the 184-Inch Cyclotron on an industrial, almost military scale, setting up a “directing committee” as supervisors; even safety, especially electrical, was given a prominent place. The bureaucracy was needed to get the jobs done on time; prior to this time cyclotrons had been constructed in a somewhat haphazard way. This was the

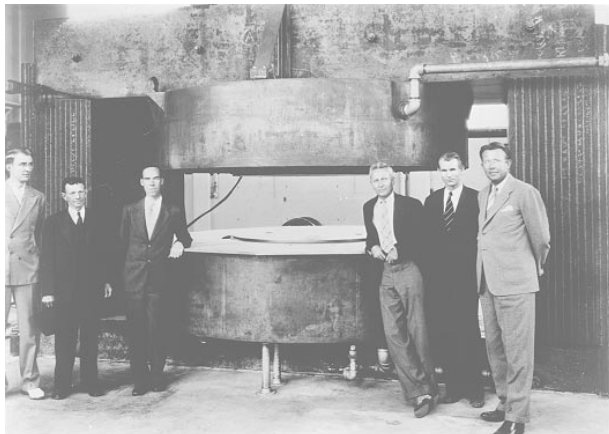


Fig. 1.4. The Crocker Laboratory 60-Inch Cyclotron magnet. *Left to right:* Luis Alvarez, Bob Serber, Bill Brobeck, Donald Cooksey, Edwin McMillan, Ernest O. Lawrence.



Fig. 1.5. Ernest O. Lawrence, Glenn T. Seaborg, and J. Robert Oppenheimer, in early 1946 at the controls to the magnet of the 184-Inch Cyclotron, which was being converted from its wartime use to its original purpose as a cyclotron.

first example of the subordination of the individual to the group; big time science had now arrived and construction of the needed large magnet proceeded based on a scale model made by the young Luis Alvarez. The latest ideas on the large vacuum chamber and the “Dees” were incorporated in the design of the huge machine and work proceeded day and night at a fever pitch. The 184-Inch would be the world’s largest cyclotron for quite some time and its magnet would be extremely important almost immediately for the separation of ^{235}U for the Manhattan atomic energy project (Fig. 1.5).

The 60-Inch Cyclotron was used to make the first two transuranium elements, neptunium (93) and plutonium (94), in 1940 and 1941, and macro amounts of plutonium in 1942 so that Seaborg’s chemists at the Metallurgical Laboratory at the University of Chicago could design and test the chemical process that was to be used at Hanford when the neutron reactors came on-line in 1944 (see Chapter 3). An intense current of deuterons bombarded a beryllium target around the clock, day after day, for months to make the neutrons that were captured in large cans of uranyl nitrate stacked around the cyclotron target. The “hot” material was then sent to the Met Lab, where it was

worked up by a team of chemists. When purified, it resulted in the first plutonium to be seen without the benefit of a microscope. The cyclotron at Washington University in St. Louis also contributed to the early production of microscopic quantities of plutonium.

1.3. Transplutonium Elements

While the Seaborg group was still in Chicago they started their first efforts to make transplutonium elements by sending targets of ^{239}Pu to Berkeley for bombardment with ^4He ions in the 60-Inch Cyclotron. This resulted in the discovery of element 96 in the form of $^{242}\text{96}$, identified in 1944 by a distinctive alpha energy and half-life (see Chapter 4). When the bombardment was repeated months later they were puzzled when they observed a different isotope, $^{240}\text{96}$, with a higher alpha energy and a shorter half-life. The mystery was solved when they found that the cyclotron energy had been increased substantially by another modification in between the two bombardments; they deduced that the excitation functions must be much narrower in width than they had expected. By interposing energy absorbing foils over the target they were able to take advantage of this new tool to fractionate the isotopes and this became a routine procedure in future research. The long distance bombardments continued until the group transferred to Berkeley in 1945–1946.

Now the shorter half-lives became available for investigation, and after the protracted period that it took for the group to set up in its new quarters, elements 97 and 98 were discovered in 1949–1950, as discussed in Chapter 5. The chief reason for the delay was that there were great hazards in dealing safely with the very radioactive americium and curium targets before, during, and after the bombardments and this demanded a lot of special attention. A new one-story laboratory, Bldg. 5, was built for this purpose and there the famed Berkeley glove boxes were developed by Nels Garden and his group. In addition, new methods of detecting α - and X-radiation had to be worked out to detect the meager amount of activity after