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HISTORICAL REVIEW OF CALIFORNIUM-252 DISCOVERY AND DEVELOPMENT

by

Dean H. Stoddard

E. I. du Pont de Nemours & Co.
Savannah River Laboratory
Aiken, SC 29808

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International Workshop on Neutron Therapy
Brachy vs. Beam Therapy

University of Kentucky
April 21, 1985

Historical Review of Californium-252 Discovery and Development

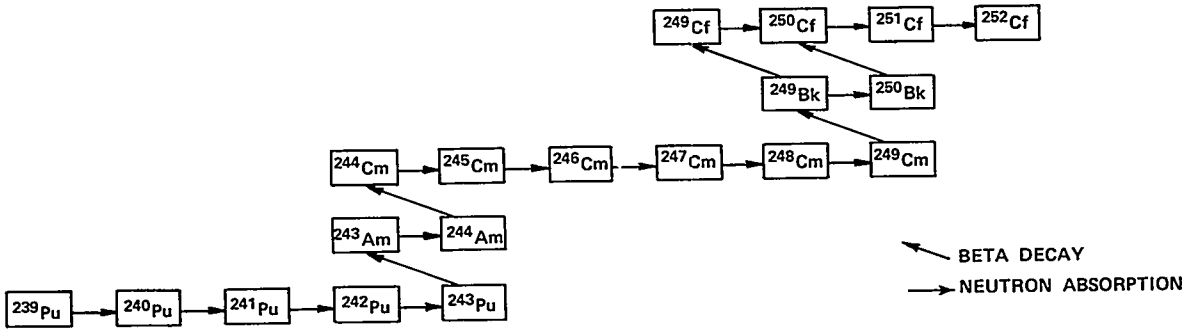
An Introductory Talk by Dean H. Stoddard, Staff Engineer
E. I. Du Pont De Nemours & Co.
Savannah River Laboratory
Aiken, South Carolina, 29808

The first isotope of californium (^{245}Cf) was produced in 1950 by S. G. Thompson, K. Street, Jr., A. Ghiorso, and G. T. Seaborg at the Radiation Laboratory of the University of California at Berkeley. They used the Berkeley 60-inch cyclotron to bombard curium-242 targets with helium ions having energies of 35 million electron volts. Only a very small amount of the isotope was produced.

The isotope californium-252 was first identified along with isotopes of curium and berkelium in the debris from a thermonuclear test explosion in 1952. During the explosion, uranium was subjected to an intense, although short, neutron irradiation so that the uranium atoms absorbed many neutrons before decaying by beta emission to form these isotopes of higher atomic number.

Larger quantities of californium-252 can be synthesized by irradiating plutonium-239 or its transmutation products (^{242}Pu, ^{243}Am, and ^{244}Cm) with neutrons in a nuclear reactor. Elements of higher atomic number are built up by successive neutron captures interspersed with beta decays. Thirteen successive neutrons must be added to each nucleus of ^{239}Pu to convert it to ^{252}Cf (Figure 1).

The first macroscopic amounts of ^{252}Cf were produced by long-term irradiations in the Materials Testing Reactor at the National Reactor Testing Station in Idaho (Figure 2). B. B. Cunningham and S. G. Thompson at Berkeley succeeded in isolating this product in 1958.


249Cf
250Cf
251Cf
252Cf
249Bk
250Bk
244Cm
245Cm
246Cm
247Cm
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243Am
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239Pu
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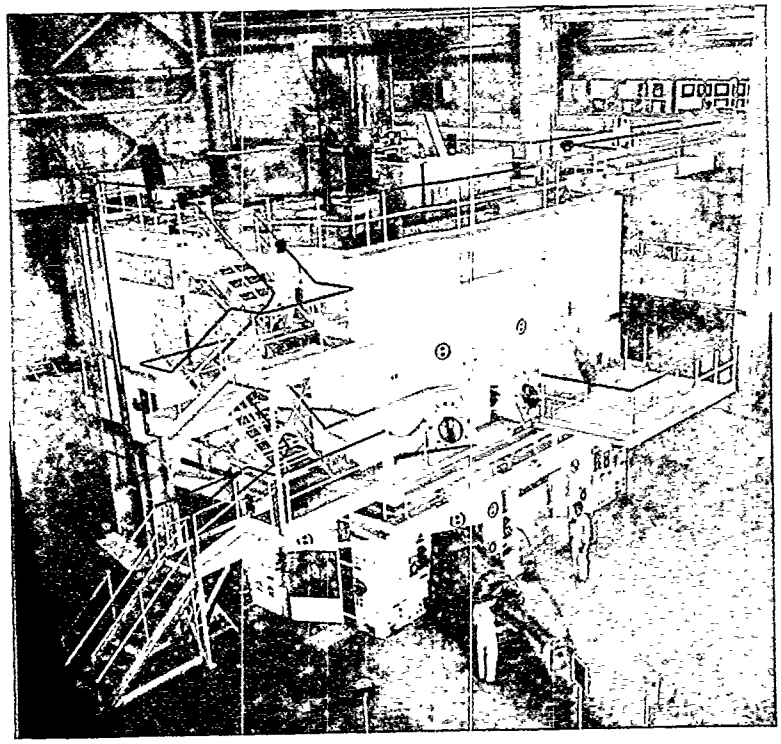
BETA DECAY
NEUTRON ABSORPTION



Twenty-two milligrams of ^{252}Cf were produced through March 1969 by irradiations in the High Flux Isotope Reactor at the Oak Ridge National Laboratory. The product was recovered in the associated Transuranium Processing Plant.

Additional ^{252}Cf was made as a byproduct of ^{244}Cm production at high flux in a Savannah River Plant (SRP) reactor (Figures 3 & 4). This ^{252}Cf and that produced in subsequent high-flux irradiations were used in a market evaluation program.

My involvement with ^{252}Cf began in 1964 at the SRP which is located near Augusta, Georgia. The plant was engaged in a program to produce 3 kilograms of ^{244}Cm for the development and demonstration of power generators. In the chemical processing associated with the manufacture and separation of ^{244}Cm, very small quantities of californium isotopes are collected. During this processing, it was necessary to familiarize ourselves with the properties of the byproduct materials, in particular their radiation properties. Previous chemical separation operations had not required much neutron shielding because the neutron radiation had been far overshadowed by the gamma radiation present. In November of 1964, Dr. Carl S. Schlea (who had an office next door to my office and who was in charge of a group of scientists working on the chemical processing of the ^{244}Cm material) and I (Figure 5) collaborated in the preparation of an article that was published in the June 5th, 1965, issue of Nature magazine. This article was really the start of the whole ^{252}Cf program. The title of the article was "Californium Isotopes Proposed for Intracavity and Interstitial Radiation Therapy". Until that time, the idea of using an isotopic neutron source for radiotherapy probably had not even been considered because the possibility of having a very high intensity radioisotopic neutron source available did not exist. The advantages of neutron radiation were recognized to some degree at that time. During the same month, I also published an Atomic Energy Commission (AEC) Research and Development Report (DP-986) entitled "Radiation Properties of Californium-252." The purpose of that report was to compile the properties of reactor-produced californium which calculated to be about 72% ^{252}Cf. This information was documented for members of the scientific community who later may have been asked to handle ^{252}Cf.

One year later in June, 1966, A. R. Boulogne of the Savannah River Laboratory (SRL) manufactured the first ^{252}Cf needle for medical uses. The needle was designed after the radium needles which had been in use for some time. He made the needle in a laboratory glove box and hood (Figure 6) using paraffin blocks as movable shielding around his equipment. Boulogne's early needles were prepared by electrodepositing

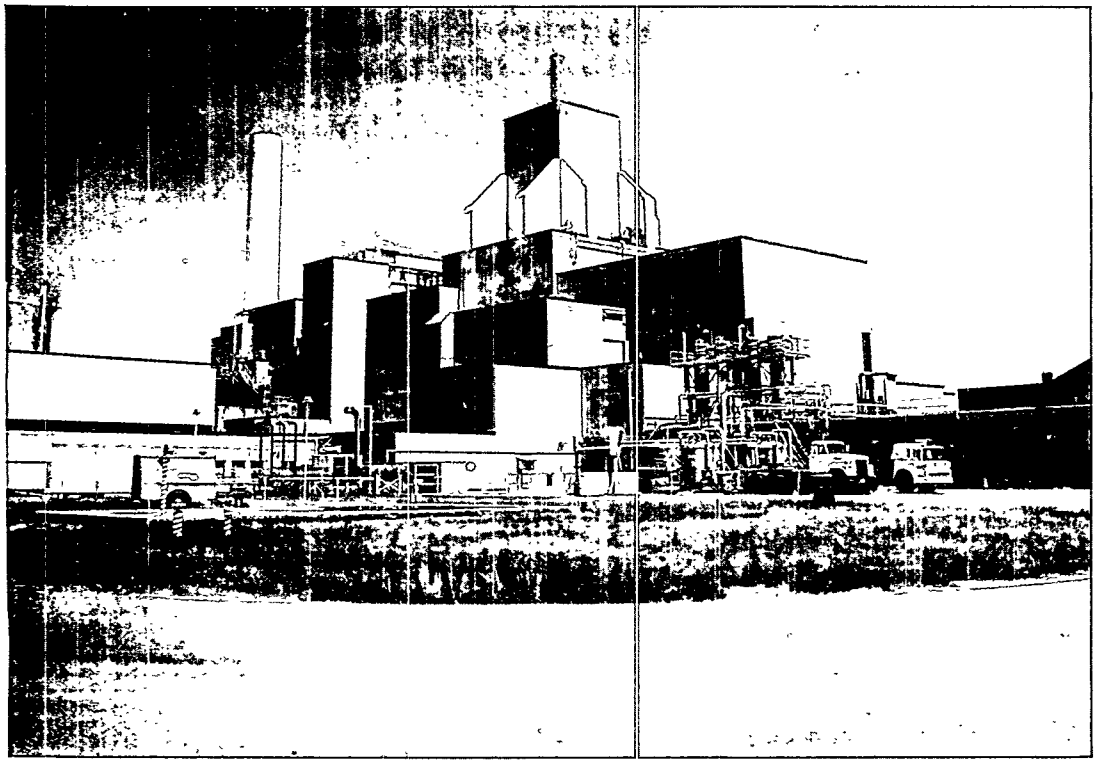


Figure 3. A Savannah River Plant Reactor Building

Figure 4. Reactor Assemblies After Irradiation

Figure 5. Carl S. Schlea and Dean H. Stoddard (1965)

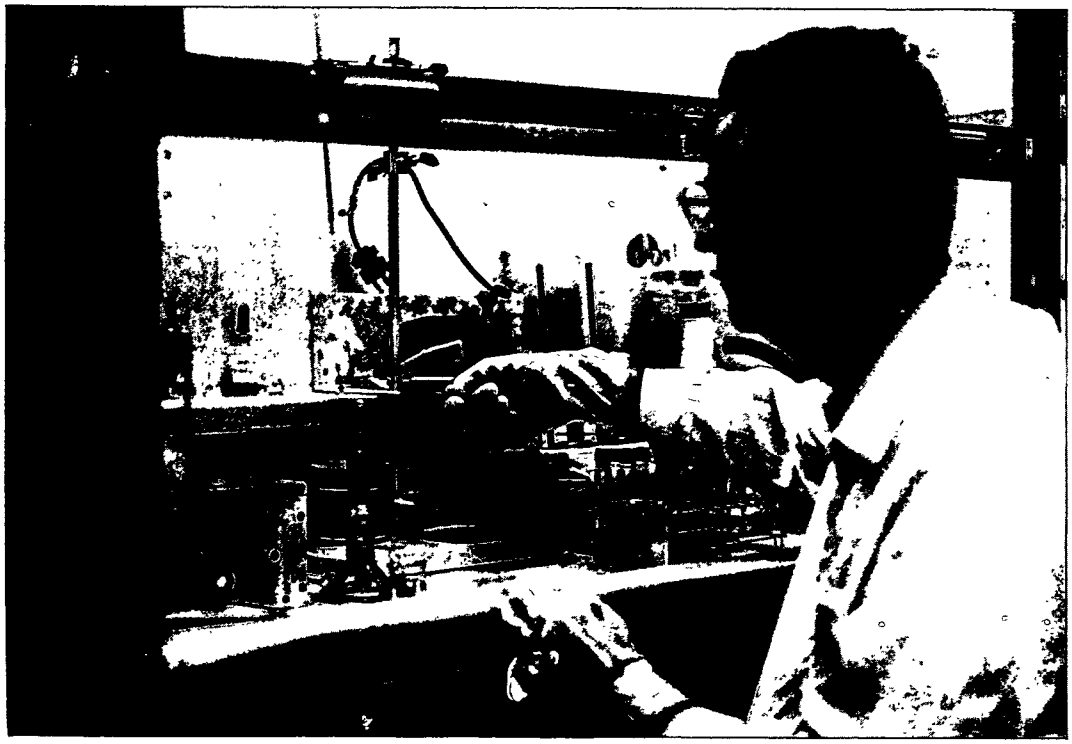


Figure 6. A. R. Boulogne Working With a Needle (1966)

californium on a platinum-irridium wire, and then doubly encapsulating the wire in platinum-irridium.

The californium for the first needle was purified by H. P. Holcomb of SRL (Figure 7) in August, 1965, from 0.82 microgram produced during one of the irradiations to obtain ^{244}Cm. Later, in October, 1966, Holcomb extracted and purified 14 micrograms of ^{252}Cf (including 6 grams of high purity material for medical work). This material was extracted from some glove box High Efficiency Air Filters that the SRL had obtained from Lawrence Radiation Laboratory in Berkeley, California.

In July 1966, dosimetry studies were started at SRL by C. N. Wright, A. R. Boulogne, W. C. Reinig, and A. G. Evans. This work was published in "Radiology" in August 1967.

In September 1966, the medical program was outlined for the Atomic Energy Commission's Division of Biology and Medicine. This division was brought into the picture at the request of Frank P. Baranowski who was Director of the Division of Production for the AEC at the time (Figure 8). Frank Baranowski was a prime mover in the californium program while he held that position.

To ensure that production capability would be compatible with the long-term demand for ^{252}Cf, the AEC's Division of Production began a market evaluation program. This program involved the lending of test quantities of encapsulated californium sources to potential users, and seeking their advice on the amount of californium that might be required over the long haul. The market evaluation program was under the direction of a group of people at SRL who published the findings of these studies in reports called "Californium-252 Progress." Twenty-two reports were issued beginning with number 1, dated October 1969, and continuing to number 22, dated May 1978. The cover of the original report had a graphic design representing tracks of fission fragments from the spontaneous fission of ^{252}Cf (Figure 9). Neutrons accompany the fission fragments, but are not visible. The tracks were made by depositing a particle of $^{252}Cf_2O_3$ on a glass microscope slide, allowing the fission fragments to strike the glass, and subsequently developing the tracks by etching the glass in hydrofluoric acid. Members of the market evaluation group who were major contributors over the years included Du Pont employees W. C. Reinig, P. H. Permar, and W. R. Cornman, and AEC employees E. S. Goldberg and W. B. Wilson.

In December 1966, Dr. Harold L. Atkins of Brookhaven National Laboratory, one of the first investigators in the medical application business visited SRL. Dr. Atkins did a lot of preliminary work on dosimetry, relative biological effectiveness, and skin tolerance. Pigs were used in the

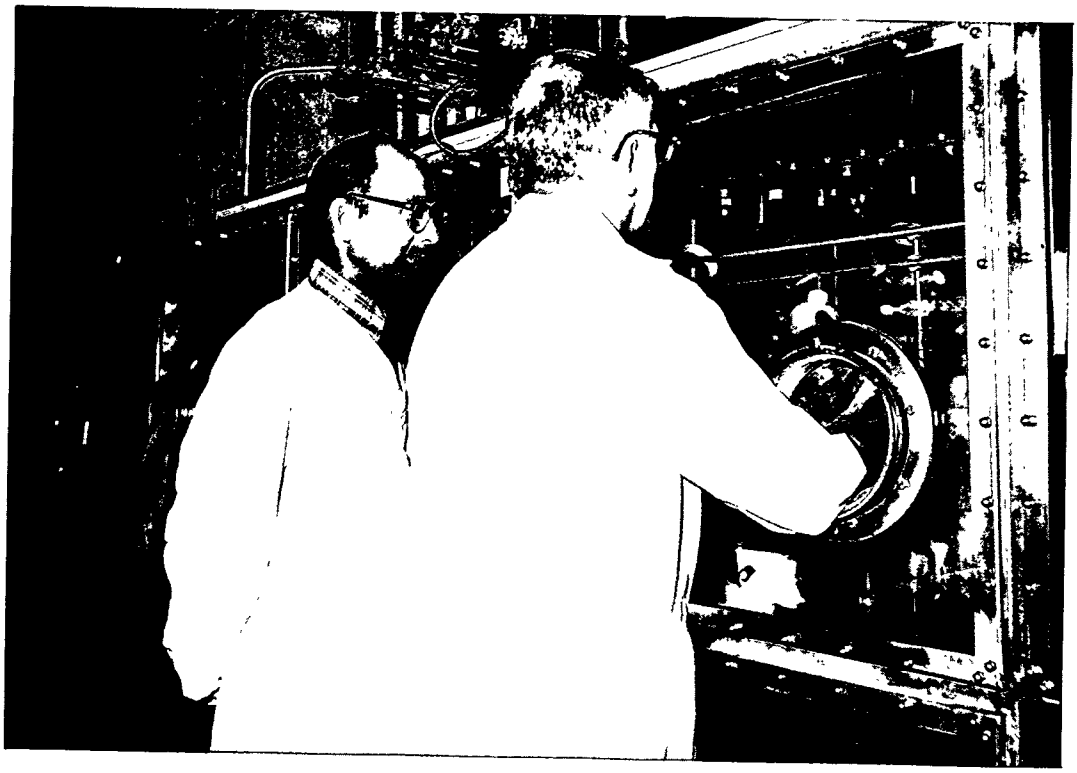


Figure 7. H. P. Holcomb (1984)

Figure 8. F. P. Baranowski (1985)

initial studies for the skin tolerance determinations (Figure 10).

A list of the medical source evaluators and the year they began their investigations is shown in Figure 11. The list is discussed briefly below:

Brookhaven National Laboratory received their first ^{252}Cf needle in June 1967. This lab was the first laboratory to evaluate such a needle.

In March 1968, the M. D. Anderson Hospital, Houston, Texas began studies and became the second medical source evaluator. Dr. James Brennan from the University of Pennsylvania, and Dr. Roger Berry, from the Radiological Laboratory, Oxford, England, collaborated in some Oxygen Enhancement Studies at the M.D. Anderson Hospital. Also, Dr. Stewart Bushong, Baylor University College of Medicine, began using ^{252}Cf applicator tubes on hamster ovary cells at M. D. Anderson.

In 1969, a more formal procedure was set up for the biomedical studies. This procedure used the expertise of a Biomedical Advisory Panel and the AEC Division of Biology and Medicine. The possibilities for ^{252}Cf studies included cancer therapy, production of short-lived radiopharmaceuticals, medical activation analysis, and neutron radiography. The primary goal however was to direct the studies involving surface, interstitial, and intracavitary therapy. The AEC Division of Biology and Medicine coordinators for the program were J. Goldstein, C. R. Richmond, E. T. Still, and W. W. H. Weyzen.

Also in 1969, the Hospital of the University of Pennsylvania began evaluating ^{252}Cf as a neutron source for clinical use in the treatment of surface and interstitial lesions.

In 1970 The committee for Radiation Therapy Studies, an advisory group to the National Cancer Institute, established a californium-252 subcommittee. This subcommittee was to review experimental results reported by the evaluators and to plan anticipated cancer therapy work with ^{252}Cf. This committee was composed of

J. T. Brennan, MD - Hospital of the University of Pennsylvania
H. L. Atkins, MD - Brookhaven National Laboratory
J. R. Castro, MD - M. D. Anderson Hospital and Tumor Institute
H. G. Seydel, MD - American Oncologic Hospital
R. Million, MD - University of Florida
G. D. Oliver, PhD - M. D. Anderson Hospital and Tumor Institute

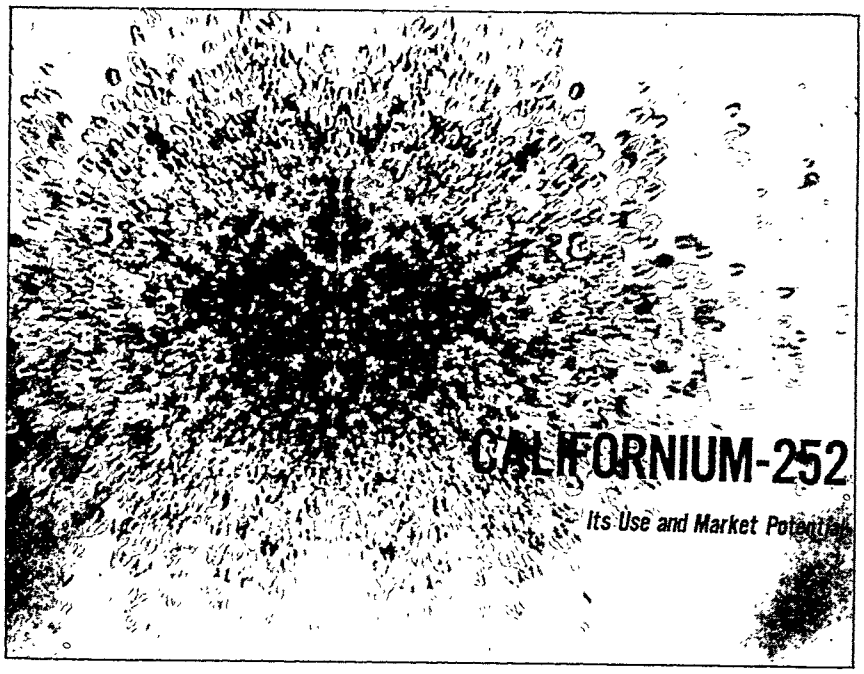


Figure 9. Tracks of Fission Fragments from ^{252}Cf

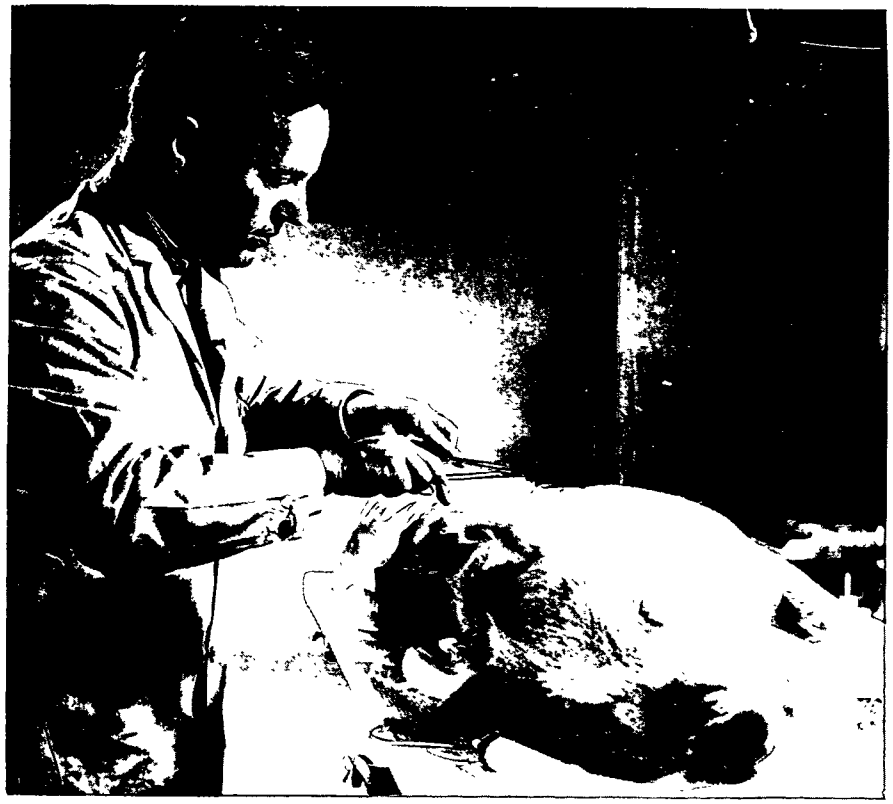


Figure 10. H. L. Atkins Irradiating Skin of Pig with ^{252}Cf

Institution	Investigator	Year
Brookhaven Nat'l Lab.	H. L. Atkins	1967
	L. J. Goodman	
M. D. Anderson Hosp.	W. H. Grant	1968
	J. R. Castro	
	G. D. Oliver	
Hosp. Univ. of Pennsylvania	L. W. Davis	1969
	P. Littman	
Univ. of Cincinnati	J. G. Kereiakes	1970
Sloan-Kettering Institute	J. S. Laughlin	1970
	G. D'Angio	
	L. L. Anderson	
	B. S. Hilaris	
	A. Vallejo	
Christie Hospital, England	D. Green	1971
Churchill Hospital, England	R. J. Berry	1971
Univ. of California	T. L. Phillips	1971
Pacific Northwest Lab.	M. F. Sullivan	1971
Edward Hines Jr. V.A.Hosp.	S. Stefano	1971
American Oncologic Hosp.	J. J. Young	1971
	H. G. Seydel	
Univ. of Chicago	D. J. Mewissen	1972
	L. H. Lanzl	
Univ. of Kentucky	J. A. Sayeg	1972
	Y. Maruyama	
	J. L. Beach	
Cancer Inst. Hosp.,Tokyo	A. Tsuya	1973
Keio Univ., Japan	S. Hashimoto	1975
	H. Yamashita	
M.I.T.	B. W. Murray	1975
Howard Univ. Hosp.	U. K. Henschke	1976
Wash. Univ. Sch. of Med.	C. A. Perez	1977

Figure 11. Institution, Investigators, and Year Studies Began in the Evaluation Program

Also in 1970, the University of Cincinnati Departments of Radiology and Nuclear Engineering began some work involving dose studies using tissue equivalent phantoms. Sloan-Kettering entered the program this same year.

In 1971 the Christie Hospital and Holt Radium Institute of the University Hospital of South Manchester, the Churchill Hospital of the United Oxford Hospitals, the University of California School of Medicine, the Pacific Northwest Laboratory, the Veterans Administration Edward Hines Jr. Hospital, and the American Oncologic Hospital all entered the program to evaluate ^{252}Cf for radiotherapy.

1972 was the year that the University of Chicago and the University of Kentucky entered the program.

In 1973, the Cancer Institute Hospital in Tokyo, Japan, joined the program and, in 1975, Keio University and the Massachusetts Institute of Technology began evaluations. Also in 1975, a Californium Utilization Meeting was held in San Diego. This meeting devoted some of its time to the discussion of medical applications.

In 1976, Howard University joined the program. Also in 1976, an International Symposia was held in Brussels, Belgium. This meeting was sponsored by the European Nuclear Society and the American Nuclear Society and sixty persons from 13 countries attended. The reported information covered medical physics, radiobiology, and medical applications of ^{252}Cf.

In 1977, the Washington University School of Medicine received some sources for evaluation.

I believe it is appropriate that this neutron therapy workshop is being held in Lexington, because as I read the published reports on ^{252}Cf radiotherapy, much of the outstanding and most recent work has come from the University of Kentucky.

In summary, I would like to borrow a figure from a recent publication by Dr. Yosh Maruyama of the University of Kentucky Medical Center, in which he described the evolution of radiotherapy (Figure 12). I have described the involvement of a number of people and institutions from the point of the original suggestion by Dr. Schlea and myself in 1965. I apologize in advance for names of individuals or organizations that I might have inadvertantly left out of this historical review. Everyone at this meeting is interested in the californium story and that's why we are here. Certainly the californium story will be expanded during this meeting. We are all anxiously waiting to hear

more about this promising topic from the distinguished speakers present.

I wish each speaker every success.

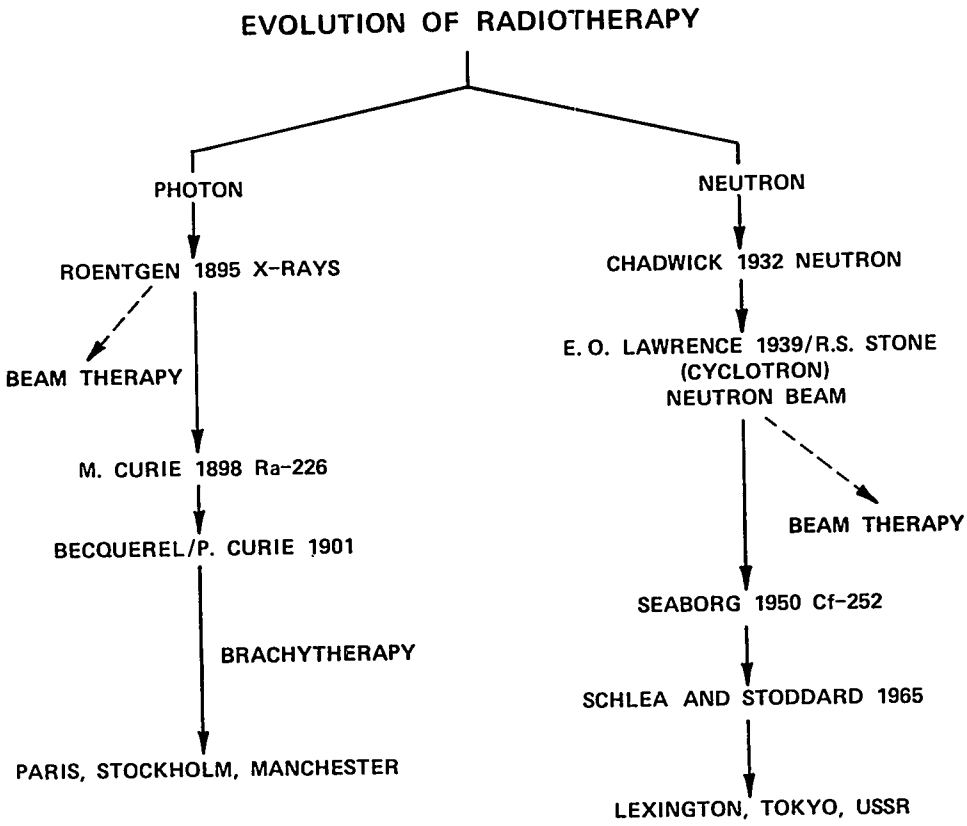


Figure 12. Evolution of Radiotherapy

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