

## Saul Hertz and the Birth of Radionuclide Therapy

Frederic H. Fahey DSc and Frederick D. Grant MD

Boston Children's Hospital  
Harvard Medical School

Thanks to James Thrall, MD  
and Barbara Hertz



frederic.fahey@childrens.harvard.edu

Fahey FH, Grant FD, Thrall JH.  
EJNMMI Phys. 2017;4:15.



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### Case 1

Elizabeth D. is referred with hyperthyroidism  
No ophthalmopathy  
Basal Metabolic Rate (BMR) +30

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### Case 1

Elizabeth D. is referred with hyperthyroidism  
No ophthalmopathy  
Basal Metabolic Rate (BMR) +30

3/31/1941 – Dr. Saul Hertz performs the first  
human radioiodine therapy  
on this patient

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## Elizabeth D. – First Radioiodine Therapy

	Basal Metabolic Rate	Radioiodine Administered Activity	Urinary Excretion in 72 h
Pre-Therapy	+30		
March 31, 1946		2.1 mCi	20%
April 16, 1946		1.3 mCi	28%
Post-Therapy	- 7		

Thyroidectomy:

34 g thyroid, histology demonstrates involution

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## Prerequisites to radioiodine therapy

1. Understand role of iodine in thyroid function
2. Discover radioactivity
3. Develop the tracer principle
4. Treat thyroid disease with radiation
5. Produce artificial radioactive isotopes
6. Ask the question

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## Iodine and the Thyroid

- Iodine, meaning “violet colored,” was discovered in 1811 by French chemist Bernard Courtois.
- Eugen Baumann (Berlin)
  - 1895 demonstrates that thyroid full of “thyroidine” which is 10-15% iodine
  - Thyroidine administration reverses myxedema
- Adolf Oswald 1899
  - 1899 - isolates thyroglobulin
- Edward C. Kendall (Mayo Clinic)
  - 1919 - isolates crystalline thyroxine



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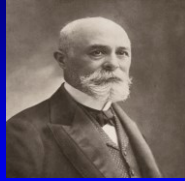
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Röntgen and Bequerel:  
"Chance favors the prepared mind."

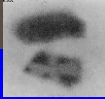
Louis Pasteur



Wilhelm Röntgen  
(1845-1923)  
November 1895  
Nobel Prize 1901



Henri Bequerel  
(1852-1908)  
March 1896  
Nobel Prize 1903  
(shared with Marie & Pierre Curie)



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Pierre and Marie Curie and Family



Pierre Curie  
(1859-1906)



Marie with daughters  
Ève and Irène



Marie Skłodowska Curie  
(1867-1934)

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Hevesy demonstrates the tracer principle



Nobel Prize in 1943 for  
development of the tracer  
principle

1913: Demonstrated that radium D is  
a radioisotope of lead (Pb-210)  
1923: Discovered the element  
hafnium with Dirk Coster

LIII. THE ABSORPTION AND TRANSLOCATION  
OF LEAD BY PLANTS.

A CONTRIBUTION TO THE APPLICATION OF THE  
METHOD OF RADIOACTIVE INDICATORS IN THE  
INVESTIGATION OF THE CHANGE OF SUBSTANCE  
IN PLANTS.

By GEORGE HEVESY.

From the Institute of Plant Physiology of the Agricultural High School,  
and Institute of Theoretical Physics of the University, Copenhagen.

(Received May 6th, 1923.)

Biochem J XVII: 439-445 (1923)

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## Treatment of Thyroid Disease by Ionizing Radiation

Archives of Internal Medicine

VOL. 31 MARCH, 1923 No. 3

FURTHER OBSERVATIONS ON THE ROENTGEN-RAY TREATMENT OF TOXIC GOITER\*

J. H. MEANS, M.D., AND G. W. HOLMES, M.D.  
BOSTON

Means JH and Holmes GW, Arch Intern Med. 1923;31(3):303-341

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## The Curie tradition continues



Irène Curie and Frederic Joliot  
1934: Association Curie-Joliot Curie ACJC

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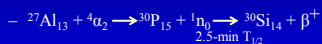
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## Artificial Radioactivity

- Jan 1934: Frederic and Irène irradiate aluminum with alpha particles (from  $^{209}\text{Po}$ )

- Neutron emission - immediate (alpha-n reaction)
- Positron emission - not immediate but decays with time




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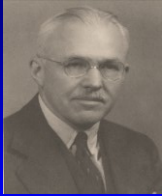
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## Who was at the luncheon?



J. Howard Means, MD  
Chief of Medicine, MGH  
Founder of Thyroid Unit



Saul Hertz, MD  
Chief, Thyroid Unit, MGH

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## The question: Can iodine be made radioactive?



Saul Hertz, MD  
(1905 – 1950)

1925: A.B. Michigan  
1929: M.D. Harvard  
1929-31: Mt. Sinai, Cleveland  
1931-43: MGH Thyroid Unit  
- Chief, Thyroid Clinic

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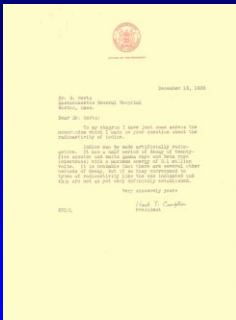
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December 15, 1936

Dr. S. Hertz  
Massachusetts General Hospital  
Boston, Mass.

Dear Dr. Hertz:

To my chagrin I have just come across the memorandum which I made on your question about the radioactivity of Iodine.

Iodine can be made artificially radioactive. It has a half period of decay of twenty-five minutes and emits gamma rays and beta rays (electrons) with a maximum energy of 2.1 million volts. It is probable that there are several other periods of decay, but if so they correspond to types of radioactivity like the one indicated and they are not as yet very definitely established.

Very sincerely yours

Paul T. Compton  
President

HTC/L

Follow-up letter from  
Dr. Compton to Dr. Hertz  
December 15, 1936

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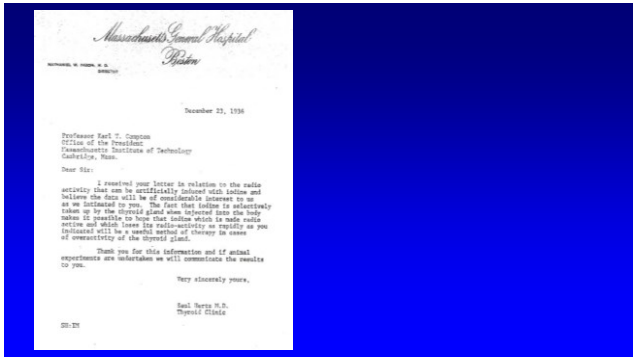
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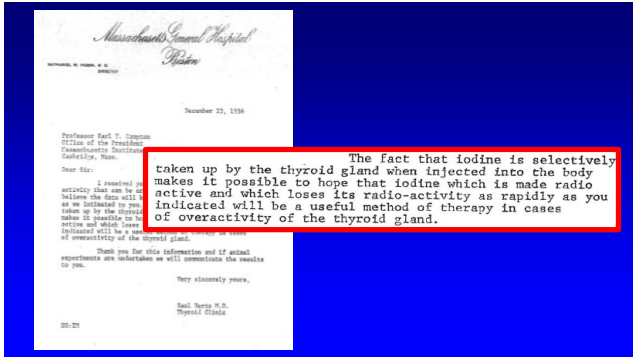
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## MGH/MIT Collaboration

<p>J. Howard Means, MD Chief of Medicine, MGH Founder of Thyroid Unit</p> 	<p>Saul Hertz, MD Chief, Thyroid Unit MGH</p> 
<p>Robley Evans, PhD Asst. Professor Physics MIT</p> 	<p>Arthur Roberts, PhD MIT</p> 

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## Isotopes of Iodine

Isotope	Half-life	Decay	Energy	Production
$^{123}\text{I}$	13.2 h	EC	159 keV (83%)	$^{123}\text{I-NaI}$
$^{124}\text{I}$	4.2 d	$\beta^-$ $\gamma$	1550+ keV 511 keV	$^{124}\text{I-NaI}$
$^{125}\text{I}$	57.4 d	EC	35 keV (100%)	$^{124}\text{Xe}(n,\gamma)^{125}\text{I}$
$^{127}\text{I}$			STABLE	
$^{128}\text{I}$	25 min	$\beta^-$	440-1400 keV	
$^{130}\text{I}$	12.4 h	$\beta^-$ $\gamma$	620-1000 keV	$^{130}\text{I-NaI}$
$^{131}\text{I}$	8.1 d	$\beta^-$ $\gamma$	250-810 keV 364 keV (81%)	$^{130}\text{Te}(n,\gamma)^{131}\text{I}$ $^{235}\text{U}$ fission

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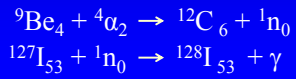
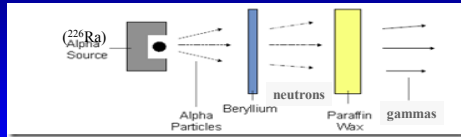
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## Production of $^{128}\text{I}$ (25-min $T_{1/2}$ )

Use of a Ra-Be neutron source




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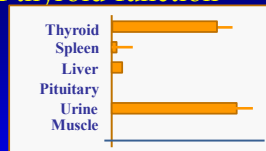
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## Hertz and Roberts (1937) : *In vivo* $^{128}\text{I}$ tracer studies of thyroid function



**Proceedings**  
 of the  
**Society**  
 for  
**Experimental Biology and Medicine**  
 Vol. 26, MAY, 1938, No. 4  
 995 P.  
**Radioactive Iodine as an Indicator in the Study of Thyroid Physiology.\***  
 S. HERTZ, A. ROBERTS AND ROSELY D. FRANK (Introduced by Henry Jackson.)

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## The Challenge

### How to producing sufficient quantities of artificial radionuclides

- University of California, Berkeley
  - Ernest O. Lawrence, PhD
  - M. Stanley Livingston
- 1929: Lawrence reads an article describing a linear oscillating accelerator
  - conceives of circular accelerator
  - magnetic resonance accelerator
- Nobel Prize in Physics in 1939




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## MIT Cyclotron

- Means, Compton and Evans go to the Markel Foundation to raise funds for the installation of a cyclotron "primarily for medical purposes"
- They receive a \$30,000 grant from the Markel Foundation for the purchase and installation of the MIT cyclotron
- Installation commenced in fall 1938 and it becomes operational in Nov 1940
- 42" magnet
- Production of therapeutic quantities of radioiodine: I-130 (90%), I-131 (10%)




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SERIAL NO.	CASE NO.	AGE	DATE OF TREATMENT	DOSE OF $^{131}\text{I}$ (mCi)	PRE-TREATMENT THYROID FUNCTION	POST-TREATMENT THYROID FUNCTION	TOTAL TREATMENT PERIOD (WEEKS)	REMARKS	STATUS
1	ELIZABETH D. MGH-173954	30	3-31-41	2.1	hyperthyroid	normal	1	1st treatment	not cured
2	ELIZABETH D. MGH-173954	30	4-16-41	1.3	hyperthyroid	normal	1	2nd treatment	cured

Elizabeth D., First Patient Treated With Radioiodine, March 31, 1941

SERIAL NO.	CASE NO.	AGE	DATE OF TREATMENT	DOSE OF $^{131}\text{I}$ (mCi)	PRE-TREATMENT THYROID FUNCTION	POST-TREATMENT THYROID FUNCTION	TOTAL TREATMENT PERIOD (WEEKS)	REMARKS	STATUS
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2	ELIZABETH D. MGH-173954	30	4-16-41	1.3	hyperthyroid	normal	1	2nd treatment	cured
3	...	...	...	...	...	...	...	...	...
20	...	...	...	...	...	...	...	...	cured

List of Dr. Hertz's patients "Cured" (20)

- ### Hertz and Roberts:
- #### Radioiodine therapy of hyperthyroidism
- Radioiodine therapy with  $^{130}\text{I}/^{131}\text{I}$
  - Chased with cold iodine (per Dr. Means recommendation)
  - Reported initial experience at 1942 ASCI meeting (Hamilton and Lawrence also reported radioiodine treatment of patients in October 1941 at the same meeting)
  - 29 patients treated 1941-1943
  - Follow-up in 1946
    - 9 "not-cured" (in 6 thyroidectomy showed involution)
    - 20 "cured"
  - No strong predictors of clinical response

## 1943: A year of change



Saul Hertz, MD  
Cmdr US Navy



Arthur Roberts, PhD  
Radiation Laboratory, MIT



Earle Chapman, MD  
Thyroid Unit, MGH

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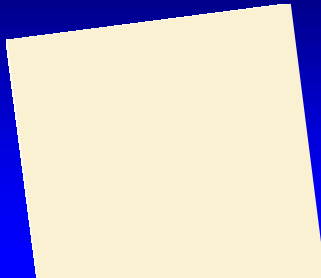
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First radioiodine therapy of thyroid disease: March 31, 1941  
-First reported in 1946:



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## Radioiodine and Thyroid Cancer

- Columbia University
  - 1942: Keston, et al. I-130 uptake in thyroid cancer metastases (one patient)
- Montefiore Hospital
  - 1930: David Marine, Chief of Pathology
  - E.J Baumann iodine chemist
  - Samuel Seidlin, Chief of Endocrinology and founds Medical Physics lab
  - I-131 therapy of thyroid cancer mets in 23 patients



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First radioiodine therapy of thyroid disease: March 31, 1941  
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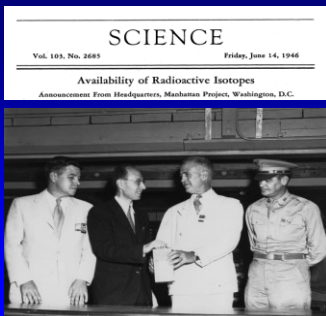
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In honor of Dr. Saul Hertz and all of  
the patients who have been treated  
with radionuclide therapy in the past  
75 years.

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