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Historical Vignette

Dr. Saul Hertz Discovers the Medical Uses of Radioiodine (RAI)

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Primary sources document Dr. Saul Hertz (1905 - 1950) as conceiving and developing radioiodine (RAI) as a diagnostic tool and as a therapy for thyroid diseases. Dr. Hertz was the first and foremost person to develop the experimental data on RAI and apply it to the clinical setting.

Saul Hertz was born on April 20,1905 to Jewish parents who had immigrated to Cleveland, Ohio. He received his A.B. from the University of Michigan in 1925 with Phi Beta Kappa honors. After graduating from Harvard Medical School in 1929, at a time of quotas for outsiders, he fulfilled his internship and residency at Cleveland's Mt. Sinai Hospital.

In 1931, he came back to Boston to join the newly formed Thyroid Unit at The Massachusetts General Hospital serving as the Chief from 1931 - 1943.

On November 12, 1936 Dr. Karl Compton, president of the Massachusetts Institute of Technology, spoke at a luncheon lecture at Harvard Medical School. His topic was *What Physics can do for Biology and Medicine*. Dr. Hertz spontaneously and solely asked Dr. Compton, "Could iodine be made radioactive artificially?" Dr. Compton responded in writing on December 15, 1936, "To my chagrin I have come across the memorandum I made on your question about radioactive iodine. Iodine can be made artificially radioactive."

MGH's Chief of Medicine and founder of The MGH Thyroid Unit, confirms that Dr. Hertz solely and spontaneously asked MIT President Compton the pivotal question, in his letter to the Markle Foundation that funded the building of the MIT Cyclotron. Dr. Means stated, "Our primary interest was in iodine metabolism and when it became apparent that there might be a radioactive isotope of iodine, it at once occurred to Hertz that we might make use of them to solve a problem we were already working on."

A collaboration was established between MGH's Dr. Hertz and MIT physicist, Dr. Arthur Roberts. In late 1937, animal studies involving 48 rabbits demonstrated that the normal thyroid gland concentrated Iodine 128, and the hyperplastic thyroid gland took up even more radioactive Iodine. Physicist Arthur Roberts created non cyclotron I-128 based on Enrico Fermi's work. When the paper reporting their results was ready for publication, MIT's lab director, Robley Evans, insisted his name be added an author as it was a condition of Arthur Roberts's employment. Hertz and Roberts had designed and executed the animal studies, analyzed the data and wrote the paper. Robley Evans had not participated. Evans' dictated a letter to the publisher that Hertz had to sign, so Robley Evans name was added to this benchmark paper having taken no part in the actual research.

In early 1941, Dr. Hertz administer the first therapeutic treatment of MIT Markle

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Cyclotron produced RAI to Elizabeth D, at The Massachusetts General Hospital in Boston. Hertz developed the first series of clinical trials of twenty-nine patients with hyperthyroidism. This proved to be a success.

At the outset of the experiments in 1937, Dr. Hertz thought there might be equally promising therapeutic possibilities in the treatment of carcinoma of the thyroid. Hertz reported to The Markle Foundation his 1942 clinical trials of patients treated with RAI for thyroid cancer. In 1943, Dr. Hertz was commissioned to serve in the Navy during World War II. Upon his return from serving his country Hertz found that Dr Earl Chapman who had carried on Hertz's work had teamed up with MIT's Robley Evans. Chapman and Evans submitted a paper to The Journal of The American Medical Association (JAMA) claiming propriety over the discovery of the medical uses of RAI to treat hyperthyroidism. MGH's Dr James Thrall in his presentation in April, 2016 at The MGH Museum stated, "Chapman and Evans had basically stolen his (Hertz's) work…the most flagrant, unethical, academically reprehensible behavior…worst yet, Saul Hertz died in 1950 and these two gentlemen spent a great deal of time and effort rewriting history." Two articles, Hertz and Roberts as well as Chapman and Evans appeared side by side in JAMA's May 11, 1946 issue demonstrating the effective use of RAI in treating Graves ' disease.

After the war, on March 12, 1946, Dr. Hertz wrote, "…it is a coincidence that my new research project is in Cancer of the Thyroid, which I believe holds the key to the larger problem of cancer in general." In 1946, Dr. Saul Hertz established the Radioactive Isotope Research Institute, with a major focus on the use of fission products for the treatment of thyroid cancer, goiter, and other malignant tumors. He joined the Beth Israel Hospital staff in Boston, where he led his colleagues in the refinement of treating thyroid cancer. RAI is the first and Gold Standard of targeted cancer therapies. In 1949, Dr. Hertz established the first Nuclear Medicine Department at The Massachusetts Women's Hospital where he expanded his research to other forms of cancer. He passed from a sudden death heart attack in 1950. Saul Hertz is the father of theranostics. Today's boom in radiophamceuticals is modeled after RAI to diagnose and treat cancer and other diseases.

Dr. Hertz's use of radioactive iodine as a tracer in the diagnostic process, as a treatment for Graves' disease and in the treatment of cancer revolutionized the treatment of thyroid diseases. He overcame the racism of his time, institutional politics, unethical publishing practices and a world war interrupting his clinical trials to bring his work to fruition. Dr. Hertz left a profound and enduring legacy by prolonging the lives of countless generations of patients, integrating the sciences in the quest to conquer cancer and providing the foundation of precision medicine. Hertz's breakthrough research changed the paradigm with the establishment of collaborative teams. Let us be thankful to Saul Hertz and for all those who have carried his dream forward.