HISTORICAL VIGNETTES AND A CURRENT PERSPECTIVE ON WOMEN'S CONTRIBUTIONS TO BRACHYTHERAPY

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***Abstract*—** Beyond Marie Curie, the historical account of the development of brachytherapy by men is well documented and recognized. Yet there have been tremendous contributions by women since the inception of brachytherapy, from both clinical and technical perspectives. This report provides vignettes of select women and captures the historical context for their contributions to the field.

***Keywords*—** Brachytherapy, Women, Development, History.

1. INTRODUCTION

With the accidental discovery of radioactivity in 1896 by Henri Becquerel at the École Polytechnique in Paris, and the subsequent deep investigation of naturally occurring radioactive substances and minerals (later identified and labeled as radium and polonium) in 1898 by Pierre Curie and Maria Skłodowska-Curie at the École Municipale de Physique et de Chimie Industrielles (also in Paris), all three were awarded the Nobel Prize in Physics in 1903 [1]. Based on self-experimentation and before Becquerel's passing in 1908 (for unknown causes, possibly due to radiation poisoning) and Pierre Curie (being killed by a heavy horse-drawn cart) in 1906, they posited that the radioactive emanations could be used in medicine [2]. Pierre Curie suggested to a Parisian physician (Henri-Alexandre Danlos) that their radiochemical reductions could possibly provide therapeutic benefit [3]. Application of radionuclides for radiation therapy spread globally [4,5], in large part due to the continued investigations of Maria Skłodowska-Curie and her efforts to share these sources, expand production, and develop source calibration standards. As documented by Skowronek [6], she was the first woman in Europe to receive a natural science doctorate, the first female laboratory head, lecturer, and professor at the Sorbonne University in Paris, and the first person to be twice awarded the Nobel Prize (the 2nd was for Chemistry in 1911). All the while raising two daughters alone. Only then was she slowly recognized on the international stage of scientific leaders (Fig. 1). These are amazing accomplishments, especially considering the culture at the time when women were not accepted or taken seriously in scientific circles.

Following Marie Curie's extraordinary accomplishments and the birth of brachytherapy, this report focuses on a select group of women who have made substantial contributions early to the field of brachytherapy. Not all female contributors to the advancement of brachytherapy are included in this article, and those involved with conventional clinical or technical aspects are excluded. As a means of not excluding any contemporary individuals, only women who have passed are described in detail. Please also note that the authors are not professional historians who have obtained original materials for providing these historical vignettes. The original aspect to this report is the historical focus and modern perspective on women innovators in brachytherapy.

A

B

Fig. 1. (A) Marie Curie sits in concentration with fellow Parisian Henri Poincaré during the extended photographic exposure at the invitation-only Solvay Conference on Physics in 1911. Ernest Solvay (seated 3rd from left) was not in attendance, but was photoshopped into the official print. (B) Having attended every Conference since its inception, Curie is joined at the 7th Solvay Conference on Physics in 1933 for the first time with other women (seated in the first row), including her eldest daughter (Irène Joliot-Curie, a future Nobel Laureate) and Lise Meitner. The 8th Solvay Conference on Physics was held in 1948, after World War II and long after Curie died in 1934 due to radiation poisoning. Images taken from the public domain.

2. WOMAN INNOVATORS IN BRACHYTHERAPY

Margaret Cleaves grew up in rural Iowa and shadowed her physician father up until his death when she was 13 [7]. She earned a medical degree at age 25 in 1873 from the State University of Iowa. Cleaves' first position was at the Iowa State Hospital for the Insane. Here she spearheaded and spread awareness about the imperativeness of female physicians for female patients in order to offer care and correctly recognize and treat gynecological pathology. She later set up private practice where her mission was to promote regular pelvic exams to catch disease early since male physicians were reluctant to do this. The current culture was misguided and associated women's insanity with remotely presenting disease such as in the pelvis. Continuing her championing of women's healthcare, she brought attention to a neurological disorder (neurasthenia), which at the time was being diagnosed in overworked men (c.f., chronic fatigue syndrome) [8]. Cleaves recognized the prominence of overworking in women too and called attention for women to also be possibly diagnosed with neurasthenia. She traveled to New York and Paris to learn more about electrotherapy, and Aronowitz and colleagues posit that she sought familiarity with the new application of electricity to medically treat insane patients [8]. This application of electricity was termed *Franklinization* after Benjamin Franklin. In 1903 she learned of radium and acquired sources on loan from the University of North Carolina. The ^{226}Ra was contained inside a glass vial, which did not substantially attenuate the beta and low-energy radiation. Her first patient was a man with a painful sarcoma of the inner cheek that failed to respond to x-ray exposures. After two treatments with radium, the pain subsided and the therapy was considered a success. Her second patient was a woman with advanced squamous cell carcinoma of the cervix who failed prior treatment with UV light and internally-applied x-rays. Again, two treatments were given on subsequent days and the therapy was also considered a success. She then traveled to Atlantic City to present her findings at the American Electro-Therapeutic Association annual conference [9]. Cleaves appears to be the first globally to have used the newly created ^{226}Ra sources for intracavitary gynecologic brachytherapy, which remains the most frequently used application of brachytherapy [7].

Edith Quimby was born in 1891 and graduated from high school in Boise, Idaho. After completing a master's degree from the University of California, she moved to New York in 1919 to work as a medical physicist at Memorial Hospital with Gioacchino Failla, the medical physicist director. Having a woman work in this field was exceedingly rare, but they worked together for over forty years [10]. In 1941 she was appointed as assistant professor at Cornell University, was promoted to full professor in 1954, and retired in 1960. Quimby was awarded the Janeway Award by the American Radium Society in 1940, received the Gold Medal from the Radiological Society of North America in 1941, was elected president of the American Radium Society in 1954, received an honorary doctorate from Rutgers University in 1956, was awarded the Gold Medal from the American College of Radiology in 1963, received the William D. Coolidge Gold Medal from the American Association of Physicists in Medicine (AAPM) in 1977, and became the first female Gold Medalist from the American Society of Radiation Oncology (ASTRO) in 1978, one year after the award was established. Quimby died in 1982. In 1996, the AAPM transformed their Achievement in Medical Physics Award to the Edith H. Quimby Lifetime Achievement Award. Quimby made numerous contributions to the field of radiological physics, but is most known today for developing a simple algorithm for permitting accurate yet quick brachytherapy dose calculations that accounted for the patient-specific geometry of the implant. The method became known as the Memorial System, which provided uniform loading of source strength to produce inhomogeneous dose distributions [11, 12]. It contrasted with the method developed by Paterson and Parker at the Holt Radium Institute in Manchester which provided non-uniform loading of source strength to produce homogeneous dose distributions [13]. Her approach revolutionized and simplified the approach to brachytherapy dose calculations in the pre-computer era and harmonized clinical practice in the U.S. and beyond.

For further perspective on women's contributions in the prior century, the University of Chicago documents the tribulations and accomplishments of Anna Hamann as their first full-time radiation oncologist [14]. She studied under Wilhelm Röntgen despite his documented intolerance for female medical students, yet she successfully completed training and subsequently pursued research with Otto Hahn during his discovery of radioelements and subsequent awarding of the Nobel Prize in Chemistry (1944, denying recognition and contributions from Jewish physicist Lise Meitner) [15].

Frédéric Joliot, Curie's son-in-law, established a Betatron at the Institut Gustave Roussy (IGR) in 1953 to treat patients. A medical physicist was needed to calculate the patient dose distributions. Andrée Dutreix (neé Sigonneau) fearlessly took on this role as one of the first medical physicists in Paris using the FORTRAN code, also to calculate brachytherapy dose distributions in the 1960s [16]. She later married Jean Dutreix, a storied radiation oncologist who even sought training with Louis de Broglie (Nobel Prize in Physics 1929).

Rosalyn Sussman Yalow grew up with modest means and was inspired to pursue science upon reading a biography on Marie Curie and attending a colloquium by Enrico Fermi. While pursuing a Ph.D. at the University of Illinois at Champaign-Urbana, she was the only woman of the 400 faculty members. After earning a doctorate in nuclear physics, she moved back to New York in 1945 and volunteered to work with Quimby at Memorial Hospital to improve her laboratory skills. There, the medical physicist director Gioacchino Failla recruited her to the Bronx Veterans Administration Hospital to set up a radioisotope service. At the VA she became pregnant. Their extant policy was that women had to leave once they were five months pregnant – she ignored it [17]. She is quoted as saying, "The only difference between men and women in science is that the women have the babies. This makes it more difficult for women in science, but… it is merely another challenge to be overcome." At the VA her research acumen blossomed where she furthered the development of the radioimmunoassay technique. She applied this technique to insulin (her husband was a diabetic), demonstrating that Type II diabetes was not due to insulin production, but due to an antibody rejecting it. For this work and generalizing the technique [18], Yalow shared the 1977 Nobel Prize in Physiology or Medicine and is considered the mother of endocrinology. She is also quoted [17] as saying, "The world cannot afford the loss of the talents of half of its people if we are to solve the many problems which beset us."

More recently, there are many others who have made substantial contributions to the field of brachytherapy. Marilyn Stovall developed computerized brachytherapy treatment planning methods [19, 20] with fellow medical physicist Bob Shalek at the MD Anderson Cancer Center, and is mostly recognized for studying radiation epidemiology to associate radiation dose with clinical outcomes such as radiation toxicities and tumor control [21].

Monique Pernot instigated several long-term brachytherapy-oriented clinical trials of hundreds of patients in Nancy, France for a variety of disease sites [22] and developed plastic molds for brachytherapy applicators, 30 years ahead of the current push in brachytherapy for patient-specific 3D-printed applicators.

Judith Stitt's passion was orchids and social justice as well as developing the Madison System for cervical brachytherapy to addresses HDR brachytherapy capabilities such as dose optimization and differing applicator geometries [23, 24] with Bruce Thomadsen and her senior radiation oncologist Dee Buchler, who was a strong women's advocate and board-certified in gynecology surgery, medical oncology, and radiation oncology [25, 26]. Equally important, Stitt was the first female radiation oncologist to serve on the U.S. Nuclear Regulatory Commission's Advisory Committee on the Medical Uses of Isotopes towards setting national regulatory and safety standards [27].

Jean St. Germain was a medical physicist at Memorial Sloan Kettering Cancer Center who examined the benefits of radiotherapy for pediatric patients like Pernot and evaluated radiation safety for an assortment of therapy and imaging modalities including brachytherapy [28, 29]. St. Germain was inspired by Curie and was fortunate to have spent time with her daughter [30]. Her further passions included opera where she was a Juilliard-trained soprano soloist who frequently gave recitals in New York City.

Christine Haie-Meder's career blossomed over 30 years ago at the IGR where she built upon the deep experience of the French radiation oncologists in treating most any cancer with brachytherapy in a scientific manner. She has developed numerous clinical trials and led European efforts to compare brachytherapy with external-beam radiotherapy for improved outcomes. Through these efforts, she helped transition IGR from using low-dose rate (LDR) sources to high-dose rate (HDR) remote afterloading with dose optimization with improved dose conformity and has coordinated Groupe Européen de Curiethérapie activities to set common standards for gynecological brachytherapy and with magnetic resonance imaging(MRI)-guidance [31, 32].

Patricia Eifel is a Stanford-trained radiation oncologist who served as faculty on the Harvard Medical School and has been at the MD Anderson Cancer Center in Texas, U.S. for over 30 years. She was the first woman to be awarded the Henschke Award by the American Brachytherapy Society (ABS) in 2010, served as President of the ABS and ASTRO, and was awarded the ASTRO Gold Medal in 2018 [33]. Eifel sought brachytherapy training at IGR, developed several gynecological practice standards with the U.S. National Comprehensive Cancer Network [34], discovered the utility of concurrent chemotherapy in combination with brachytherapy for the treatment of cervical cancer [35], and developed a shielded applicator for cervical brachytherapy that is compatible with CT imaging [36], paving the way for conformal brachytherapy with shielding and deviations from the AAPM TG-43 dose calculation formalism where the patient and applicators are assumed to be water equivalent [37-40].

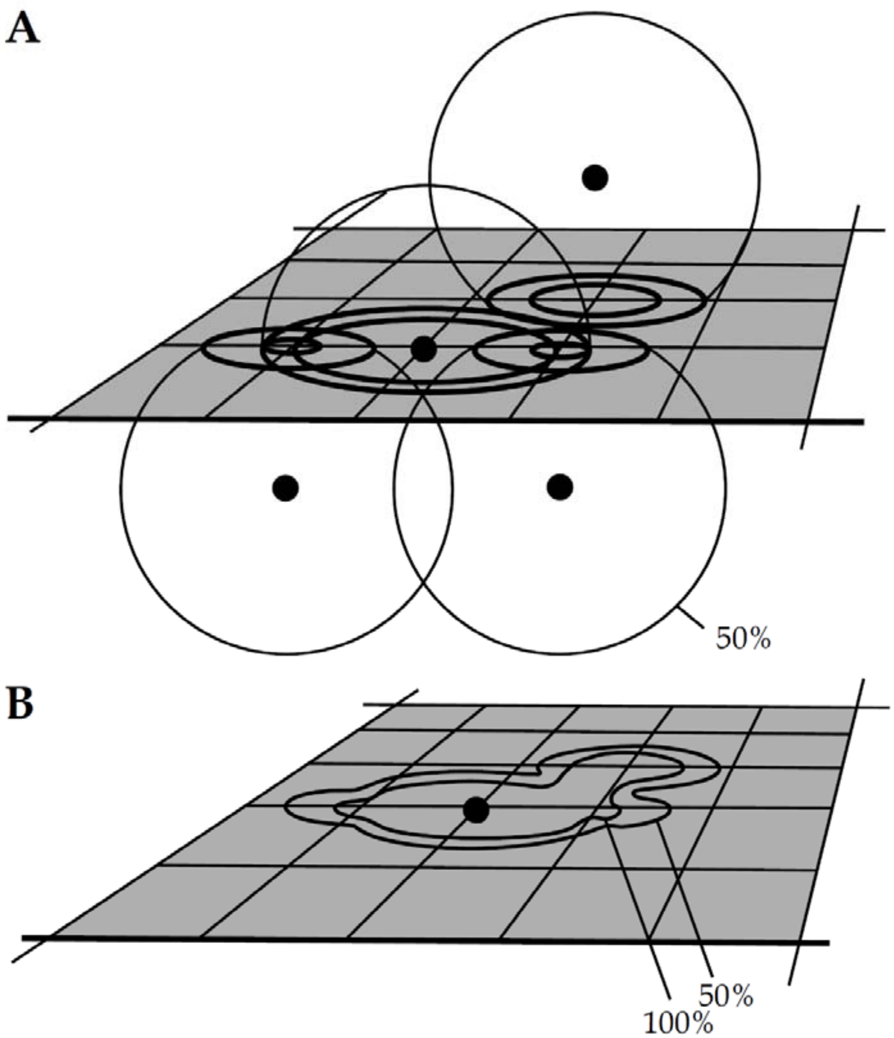

Fig. 2. (A) Assuming spherical dose distributions, doses from four brachytherapy sources are summed onto an arbitrary plane showing the 50% isodose line at the exterior. (B) Removing the 3D perspective, the 100% and 50% isodose lines are depicted. Adapted from Fig. 2 of Aronowitz and Rivard 2014.

3. SOCIAL CONTEXT AND CURRENT ENVIRONMENT

It is hard to appreciate the circumstances many of these women lived in. They must have felt like the outsider in their professional pursuits, often actively being repelled and ill-treated by their male counterparts. These women innovators would recount the few, but rare, allies that supported them and championed their pursuits, though more times than not gender oppression was an unwelcome friction throughout their entire lives [41]. In contrast to the solitude many women endured in the past to be the first in their fields, today more than half of the graduating classes of U.S. medical students are women [42]. This number seems impressive, though a closer look will reveal that the treatment and expectations of women in the classroom and clinic still have a long way to go toward where we should be as a society. As best they could, women have continually challenged the societal pressures against them and have actively pushed the field forward with inclusion, diversity, equity, and accessibility [43].

A prominent challenge for women is to simultaneously manage working while having children. It is often termed "having a family" since the expectations are that she will both create and rear the children as well as maintain the home front. Parenthood brings a whole plethora of unpaid labor that women often take the brunt of, creating an additional barrier to advance in their careers. Across virtually all professions, women are underpaid compared to their male counterparts [44], so adding on the societal pressures that women need to choose between their families and professions (or somehow do the work of two people) makes advancement nearly impossible. When a woman chooses to pursue both work and motherhood with equal vigor, she may be deemed either a *bad mom* or *too work oriented*.

Breaking down these stereotypes and overall misogyny is still a work in progress, though compared to the stone-faced perseverance of the revolutionary women in the past, today there are professional groups that provide a modern networking environment for support and advancement. The International Union for Physical and Engineering Sciences in Medicine has a standing Task Group (Women in Medical Physics and Biomedical Engineering) that strives to increase the visibility and participation of women, supports education and training through focused activities, and gathers data and networks with other groups to push for gender equity [45, 46]. The AAPM formed the Women's Professional Subcommittee in 2017 and has made advances for gender equity in medical physics and promoted women within AAPM leadership positions [47, 48]. Formed in 1997 as a hybrid of three prior organisations, just last year the Institute of Physics and Engineering in Medicine elected its first female president. There is also the Society for Women in Radiation Oncology, who have developed a social media campaign #WeWhoCurie in 2018 that creates a space for women to connect and celebrate women's achievements [49]. While not specific to women, the ABS recently created a Diversity and Inclusion committee as has been common by other societies in the past decade. Organizations such as these and programs recognizing and encouraging women in science are helping to increase gender equity with fewer societal barriers. This approach of course cannot be the sole driver as progressive attitudes and male allies are equally needed to support women in the workplace. Men still hold the majority roles of power and oppression can also come from fellow female counterparts. In light of all the hurdles (past and present), it is inspiring to recount the work of groundbreaking women that moved brachytherapy forward and inspired generations of women scientists.

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