The application of Radioactive substances and X-Ray irradiation in the therapy of Pilonidal Sinus Disease – a historical sidestep

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ORIGINAL ARTICLE

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ABSTRACT

Introduction: In the early 20th century, high recurrence rates of Pilonidal Sinus Disease (PSD) after surgical therapy led to exploration of new approaches. The discovery of X-rays by Röntgen and the Curies' work on radioactive elements marked pivotal moments, and lead to new experimental therapeutic approaches to PSD with ionizing radiation during this period.

Methods: Historical review of all publications in PubMed and beyond, combining PSD and Roentgen irradiation and treatment with radioactive substances.

Results: A number of methods using either Röntgen beam therapy of doses between 250 and 600 rad or radioactive Thorium / Radium containing ointments and solutions to be injected could be identified and are described in detail. PSD, with its seemingly unchangeably high risk of recurrence, was treated with radioactivity and Roentgen applications however these interventions faded from practice, ultimately ceasing by the mid-1960s due to safety concerns.

Conclusion: Although highly likely, we were unable to prove a definitive causative link between the application of radioactivity in the treatment of PSD and the subsequent emergence of enduring complications, such as carcinomas.

Keywords: Radioactivity, Radium, Thorium, Roentgen therapy, irradiation, XRT, Pilonidal Sinus Disease

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INTRODUCTION

Pilonidal sinus disease (PSD), also known as pilonidal cyst, is a chronic inflammatory condition of skin and subcutaneous tissue caused by sharp hair fragments [4,5] from the occiput. [6] Initially thought to originate from embryonic remnants [7-9], PSD has now been recognized as an acquired ailment.[10,11] According to the currently acknowledged theory, sharp hair fragments caught in the upper third of the intergluteal fold penetrate the skin barrier when drilled into by rolling friction due to gluteal muscle movements. If scale orientation is “advantageous” (open side of scales pointing outwards), movement into deeper tissue layers is to be expected.[12,13] While tract or nest formation occurs, either acute or chronic infection may follow and necessitate further treatment. At the beginning of the 20th century, 67 years following the first publication of PSD by Herbert Mayo [14], recurrence rate following surgical therapy was high, exceeding 30% 10 year after surgery.

Despite a plethora of therapy options explored, which included wide excisions and months long open wound therapy, wound closure with tension sutures[15], metal wires[16-18] and gauze pressure drapes to avoid in-wound-cavities[19,20], primary wound healing was scarce and recurrences all too common occurred in these mostly young men and women aged 15-30 years. The unsatisfying rate of therapeutic success during the beginning of the 20th century led physicians to venture further. This era was influenced by early advancements in the research of ionizing radiation and radioactivity, and it is the subject of this review to explore where these two fields intersect.

Although sub-gamma high energy electromagnetic radiation has been generated unknowingly as early as 1785 by William Morgan[21], Wilhelm Conrad Röntgen was the first to coin the term “X-Ray“ in 1895. He employed an electrode array placed within a partially evacuated glass tube, known as Hittorf’s tube, to accelerate free ions present inside the tube. Upon striking the glass wall or anode, the kinetic energy of ions was dissipated in the form of “a new kind of Rays“ which would light up a fluorescent screen of barium platino-cyanide placed across the room.[22]

After his initial observation, Röntgen investigated the potential of X-Rays to penetrate various materials, including sheets of paper, pine boards, aluminium blocks and his wife’s hand.[22] Latter resulted in the first medical radiograph. For his work he was awarded the Nobel prize in 1901.

When Röntgen´s discoveries were presented in the following year at the Paris academy of science, the French physicist Henri Becquerel was among the captivated audience. Inspired by the results, Becquerel conducted multiple experiments in an attempt to explain X-Rays as a passive phenomenon associated with fluorescence.[23] However he soon learned that radiation was an active property of uranium salts, which continued for months, even when the material was kept in complete darkness.[24] Despite all his

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efforts to explain the origin of the energy contained in the uranium with respect to modern thermodynamics, he would not succeed and adjourn his work on X-Rays for the time being.
In the year 1897 Marie and Pierre Curie where the first to quantify the radiation emitted by uranium using an ionizing chamber. Marie would also investigate various other materials, which she borrowed from fellow researchers. Among them was a sample of thorium, which showed similar ray emitting properties as uranium.[25,26] In their pertaining publication "Sur une nouvelle substance fortement radio-active contenue dans la pechblende" from the year 1898, the term "radioactive" was used for the first time in history.[27]

Pechblende or Uraninite, as it is known today, is a naturally occurring mixture of uranium, thorium and various other radioactive substances. It was first discovered in the 15th century in St. Joachimsthal (todays Jáchymov) located in the ore mountain range delineating modern Saxony from Bohemia.[28] Long before its radioactive properties where observed by Marie and Pierre Curie, Uraninite was discarded as a by-product of silver mining, or even ground up and used as pigment.[29] Upon measuring the radioactivity of Pitchblende, Marie made an unexpected discovery: The measured activity of the sample was significantly exceeding the activities accounted for by the decay of uranium and thorium alone. Marie deduced, that at least one additional radioactive substance must be present in the sample.

She fractioned the sample and investigated each fraction for the presence of radioactivity, which lead to the analytical proof of the two previously unknown elements 84 and 88. The former should be known as Polonium, to honour Marie's home country, and the latter as Radium.[27] For their discoveries, Henri Becquerel as well as Marie and Pierre Curie won the Physics Nobel prize in 1903.

During the first two decades of the 20th century, the ore deposits of Jáchymov, Czechia would continue to serve as the main source of uranium, thorium, polonium and radium. The purification and refinement process of these elements was tedious and costly. In a multistep process uraninite was roasted, washed, boiled and dissolved. A metric ton of uraninite yielded merely 100 mg of radium chloride.[30] In the beginning, the Curies and their team where performing most purification steps manually in a shed on the premises of *Ecole Municipale de Physique et de Chimie Industrielles* in Paris. However, when demand started to pick up, the process was industrialized, increasing the availability of radioactive substances and in turn augmenting its popularity.

The discovery of ionizing radiation, radioactivity and its seemingly miraculous properties where perceived with great excitement among scientists and the general public alike. Despite first reports of the inherent health risks, an almost dithyrambic application overwhelmed its´ influence in medicine, cosmetics, industry and politics for the decades to come. Radiation spas opened, radioactive water and chocolate were sold, as radiation craze went wild.[31] No scientific study assessing the effects and dangers of radiation has been published so far.

X-RAYS AND PSD

Following the discovery of X-Rays, their bench-to-bedside transition in medicine happened quickly, enabled by lenient or absent regulatory authorities and a great need for the expansion of diagnostic and therapeutical capabilities. Several events coincided on the 29th of January 1896, 60 days after Röntgen published his discoveries. These would provide the groundwork for what is known today as radiotherapy. Emil Hermann Grubbé was the first to anecdotally notice the biological effects of X-Rays and started using them therapeutically in a patient with breast cancer on this day.[32] Grubbé, a Chicago-based manufacturer of vacuum tubes and a second-year medical student, observed inflammatory changes and depilation on the dorsum of his hand after exposing it to X-Rays generated by one of the tubes he had previously assembled. His initial observation was later complemented by further reporting from other specialists and confirmed by experiments on the rodent model conducted by Kienböck.[33]

On the same day Glover Lyon, a physician working in London, hypothesized in a letter to the Lancet that X-Rays possess antimicrobial effects.[34] His claim sparked the interest of many doctors, as his discovery was hoped to put an end to the pre-antibiotic area where bacterial infections often lead to severe or lethal disease.

The use of X-Rays for the treatment of PSD started slowly. Large variability is seen in indication, time course, dose and voltage peak among authors reflecting the experimental fashion in which the therapy was applied (Table 1). The main strategies were:

1. Preoperative irradiation to achieve depilation of the area
2. Preoperative irradiation to reduce the number of pathogens in the wound
3. Post-surgical irradiation to promote radiogenic inflammation, thus “augmenting” host immune response

Smith was the first to suggest adjuvant irradiation for the treatment of PSD in 1937. In his trial 6 patients where irradiated after primary closure with the intent of wound sterilization and depilation. The results were inconclusive, and no improved outcome - as compared to controls - could be observed.[35]
Shortly after, Turell presents 4 patients which underwent post-surgical irradiation of recurrent PSD. All patients presented with failure of primary wound closure with or without continuous purulent discharge. The sacrococcygeal area was irradiated with total doses between 675 and 825 Roentgen (5.92 - 7.24 Gy) over the course of 6-8 weeks with a peak voltage of 125 kV. In all patients cicatrization of the wound was observed and wound closure was achieved within 2 months without infection or recurrence.[36]

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In the year 1944 Sher claimed that the adjuvant irradiation of the area with X-Rays accelerates recovery and decreases the recurrence rate. This should be especially true in patients with small draining sinuses and minimal discomfort or those with acutely draining or ruptured abscess. Furthermore, he observed that in patients with recurring infection X-irradiation following radical surgery could lead to definitive remission in selected cases. Sher employed a treatment regimen consisting of 80 Roentgen (approximately 0.70 Gy) administered every 3 - 4 days for a total of 8 sessions. The peak voltage of the accelerator was set to 140 kV, producing considerably hard X-Rays.[37]

Despite an ongoing discussion about the etiology of PSD during the early 20th century, the presence of hair in the sinus tract and on the skin has been strongly associated with prolonged and complicated healing. Thus Goldmann stated in 1952 that the preoperative use of depilating roentgen irradiation lead to higher success rates of surgical excision. He consecutively concluded „that the combined therapy of roentgen epilation of the operative field preceding surgical excision with primary closure has a definitive place in the treatment of pilonidal disease.“ In his case series with n = 26 patients all received a roentgen dose between 250 and 600 Roentgen (approx. 2.19 - 5.26 Gy) at a peak 80 - 100 kV about 4 days prior to surgical excision. Before the irradiation, the area was shaved and washed with soap and 70% ethanol solution. After 7 days of bed rest all 26 Patients had no clinical signs of wound infection and within a 1 - 8 year follow up, all patients remained without late complications.[38]

Swinton and co-workers opted - in contrast to Goldman - for post-surgical depilatory irradiation. In their case series n=15 patients with draining sinuses in the anogenital region (10 of which diagnosed with PSD) were irradiated with an epilating dose of 350 - 450 Roentgens (3.1 – 4.0 Gy) on average 10 days following primary midline wound closure. Epilation lasted for 8 - 10 weeks, before hair density returned to the pre-radiation baseline. Well aware of the dangers associated with radiation injury to pelvic organs, Swinton recommended to explore different cosmetic agents of depilation, which however would be “so well known to women and so little known to us [men]“.[39]

The introduction of X-Ray application in treating Pilonidal Sinus Disease illustrates the experimental nature of novel medical interventions during that era. The evolving approaches proposed by various physicians, ranging from adjuvant irradiation after surgery to preoperative depilating irradiation showcased the evolving understanding of radiation's potential in wound healing and infection control. These diverse approaches were often based in empirical observations, and exemplify the spirit of medical discovery that characterized the early 20th century.

Author	Year	N	Indication	Total Dose (Gy)	Schedule	pkV (kV)	Filter	Outcome
Smith, R	1937	6	Postoperative primary, depilation					Inconclusive
Turell, R	1940	1	Postoperative secondary	5,92	56 d	125	None	No recurrence after 5 months follow-up
	1940	1	Postoperative secondary	5,7	42 d			No recurrence
	1940	1	Postoperative	7,24	56 d			No recurrence
	1940	1	Postoperative	6,14	56 d			No recurrence
Sher, JJ	1944		Conservative	5,6	24 - 32 d (8 sessions, 3-4 d apart)	140	3 mm AL	enhance healing, make surgery unnecessary
	1944		Postoperative primary	5,6	24 - 32 d (8 sessions, 3-4 d apart)	140	3 mm AL	enhance healing
	1944		Postoperative secondary	5,6	24 - 32 d (8 sessions, 3-4 d apart)	140	3 mm AL	enhance healing
	1944		preoperatively	5,6	24 - 32 d (8 sessions, 3-4 d apart)	140	3 mm AL	enhance healing
Turell, R Gladstone, A	1951							„Irradiation therapy hardly has any usefulness in the treatment of primary lesions, but is effective in the treatment of recurrences
Goldmann, B	1952	26	Preoperative depilation	Ø3,86 (2,19 - 5,26)	Single session 1 - 13 d (ø 4 d) ante interventum	80 - 100	None, 0,5 mm and 1,0 mm AL	Primary closure in all cases, 10 d hospitalization. No recurrence after 1 - 8 year follow up.
Swinton, MW	1955	10	Postoperative primary, depilation	3,07 - 3,95	Single session 10 d post interventum	90	9 none, 1 filter	Hair growth at baseline after 8 - 10 weeks.

Table 1: Overview of historical X-Ray treatment indications for Pilonidal Sinus Disease, applied irradiation intensity and outcome.

DISCOVERY AND USE OF RADIOACTIVE ISOTOPES

The astonishing discovery of Radium by Marie Curie in 1898 sparked a fervor of exploration, as scientists sought to unravel the properties of these new radioactive elements and harness their potential benefits for medical applications. With the backdrop of rapidly advancing scientific understanding, the early 20th century witnessed the first instances of radium's utilization in the realm of medicine. While it remains unclear who was the first physician to utilize radioactive elements in therapy, names like Tracy, Bickel and Lazarus [40] are certainly among them.

Unlike the electromagnetic radiation produced by an X-Ray cathode, radioactive substances are Elements that emit radiation as a result of their unstable nuclear structure. Whenever the atomic nucleus undergoes a decay, the original element is transformed into a different element or isotope. During this process the nucleus loses energy which is emitted in the form of radiation. This radiation may be corpuscular, such as α and β particles, or in the form of electromagnetic waves, as seen in ɣ rays. This process repeats until the nucleus reaches a stable state. The sequence of decays and intermediates is predictable for each element, constituting a so called “decay chain“ with the sum of decay products making up the

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“emanation“ (decay products), which are emitted. Three of these decay chains held notable historical significance and are relevant in this discussion:

- The Thorium series, beginning with the naturally occurring ^{232}Thorium and reaching its stable state with ^{208}Pb. (Table 2)
- The Actinium series, beginning with the naturally occurring ^{236}U and reaching its stable state with ^{208}Pb. (Figure 5b)
- The Uranium series, beginning with the naturally occurring ^{238}U and reaching its stable state with ^{206}Pb. (Figure 5a)

In contrast to X-Rays, the energy of a radioactive element is dissipated as long as the element is present in the organism. It is important to know that the speed of radioactive decay cannot be changed.

As radioactive preparations can be injected, ingested, inhaled or applied on skin and mucosa, the novelty of radium's applications in medicine was accompanied by new challenges. Early researchers faced issues related to dosimetry, safety, and ethical considerations, as there was no tool to measure radioactivity easily and reliably. Furthermore, thorough understanding of the biological interaction with the living cell was not achieved yet, and late radiation effects were unknown. These limitations in the understanding of radiation's effects posed a risk to both patients and medical professionals not yet known in full.

At the beginning, there was only euphoria.

In early experiments it was thought that micro doses of radium have a “revitalizing“ effect on organisms: Crops would grow stronger and yield more fruits, and in humans radium could prevent hair from greying, erythropoiesis was promoted, blood pressure was lowered, intestinal peristalsis was stimulated and the excretion of toxins was believed to be enhanced (e.g. uric acid) [41-43]. Together with aggressive marketing and lobbying campaigns [31] this lead to a very heterogenous group of indications for the use of radioactive preparations in private and in medicine, including the application in soft tissue rheumatism, ulcus cruris, rickets, gastrointestinal conditions such as chronic inflammatory bowel disease, atherosclerosis and many more.[44] Radioactive pastes where externally used for malignancies of the skin, to induce hair loss, to prevent hair loss and to treat soft tissue infections.[45]

These initial forays into medical applications of radioactivity set the stage for the intricate relationship between radiation and medicine in the decades to come.

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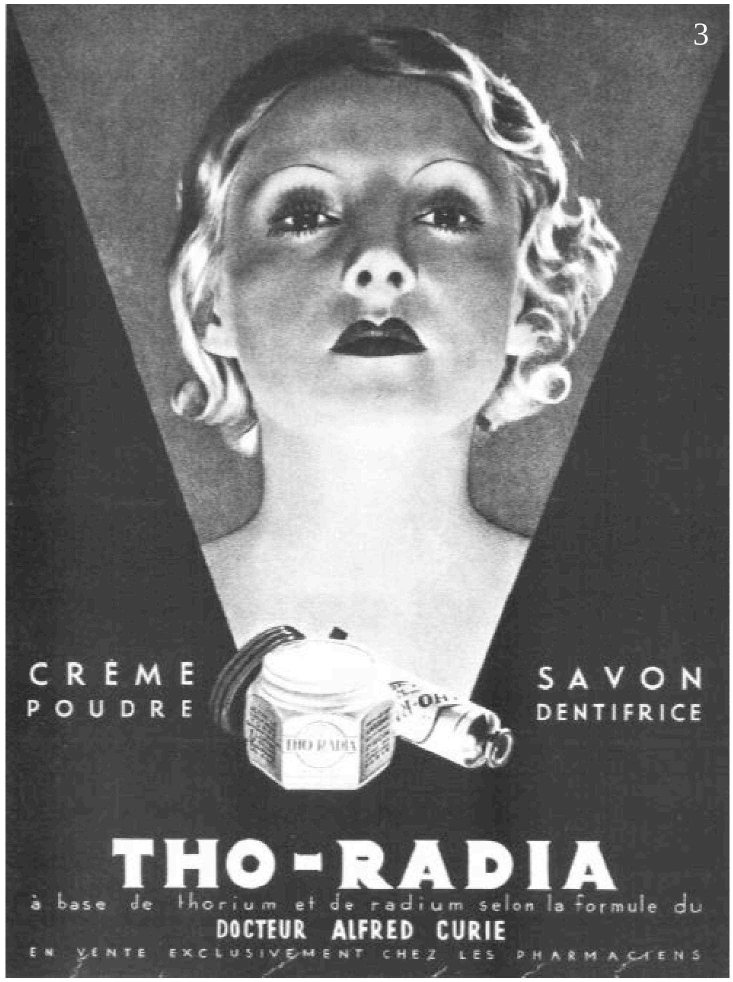


Fig 1 (left upper): Radium Suppositories, Labelling: *"15 days Course Vita Radium Suppositories. Guaranteed to contain [r]eal [r]efined Radium and to be perfectly harmless."* Image reproduced with courtesy and permission of Oak Ridge Associated *Universities* (*ORAU)*.[1]
Fig 2 (left lower): Radioactive toothpaste produced by Auergesellschaft, Berlin. Image reproduced with courtesy and permission of ORAU.[2]
Fig 3 (right): Advertisement for THO-RADIA cosmetic skin cream. Cinema advertisement 1935; Image reproduced with courtesy and permission of Oak Ridge Associated *Universities* (*ORAU)*.[3]

THE URANIUM SERIES

Uranium (U) is a radioactive element that belongs to the actinides. With a nucleus containing 92 protons, it is the heaviest element found in nature. The isotope ^{238}U is most abundant, accounting for over 99% of naturally sourced uranium and constituting the starting point for the Uranium series. With a half-life of 4.47 billion years, ^{238}U is the most enduring element in this series. Although Uranium was first isolated from Pitchblende by the German chemist Martin Klaproth in 1789, it was Becquerel who described its ray emitting properties. Through a sequence of decays, Uranium emits mostly α and β particles before it converts into the gaseous ^{226}Ra (alpha particles are helium particles, and beta equals electron emission).

Radium (Ra) is a radioactive chemical element, that belongs to the group of alkaline earth metals. It contains 88 protons in its nucleus, making it the heaviest element of its group. With a half-life of 1601 years, ^{226}Ra constitutes the second and final long-lived isotope before the rest of the series progresses via a row of less stable intermediates to stable lead. As previously referenced, Marie and Pierre Curie where the first to extract Radium chloride from Uranite in 1898. [46] In its emanation, we find α emitters such as ^{222}Rn, ^{218}Po and ^{218}At, as well as β emitters, such as ^{214}Pb, ^{210}Ti and ^{206}Hg.

Radium was administered per os, via inhalation, as ointment or injection. For many purposes, mineral water or saline were infused with a metered dose of Radium Emanation (mainly ^{222}Ra), using a so-called Emanation Activator or Emanator. One such device was invented by Dr. Saubermann and produced by the Radium LTD, London. The handling was relatively inexpensive and effortless, as a rod of insoluble radium salts was left to soak in the vessel for 24 hours, giving off radium gas, which dissolved in the water.[42] The volumetric activity was measured in “Maché Units ״or “Maché Einheiten“ (1 ME = 13.45 Bq/L). Depending on indication, Bickel suggests to administer three doses of radioactive water per day.[44] His Emanator could enrich up to 200 mL with a concentration of 1000 ME daily.

To our best knowledge there is one patient in the literature where radium was used to treat his Pilonidal Sinus Disease. In 1934 Thomason describes the medical history of a 34-year-old seamstress who presented with chronic issues in the sacrococcygeal region. Her symptoms included a foul draining sinus posterior to the anus, buttock swelling, fever, and constipation. The patient's problems began at the age of six. Over the years, she underwent multiple surgeries due to recurrent sinus disease with secretion. At age 25, a large tissue mass containing hair was removed. Despite this, the patient continued to experience symptoms.


WE DO NOT DISPENSE TO THE LAITY DIRECT.

The Saubermann Radium Emanation Activator

For the Preparation of Radio-Active Water

(i.e.: Water containing Radium Emanation).

This apparatus is designed especially for the "sipping treatment," as recommended by Prof. PAUL LAZARUS and Dr. SAUBERMANN; also for use in Dentistry, and for the preparation of Radio-Active Baths.

It is the only apparatus for Emanation Therapy in which the Radium is visible in the dark.

FIG. 1

REGISTERED TRADE MARK

Activator No..........................

Dosage........*Maché Units per Diem.*

Hire Rate from .... *to* .... *One month*............. *Three months*.......... *Six months*.............

Purchase Price.......................

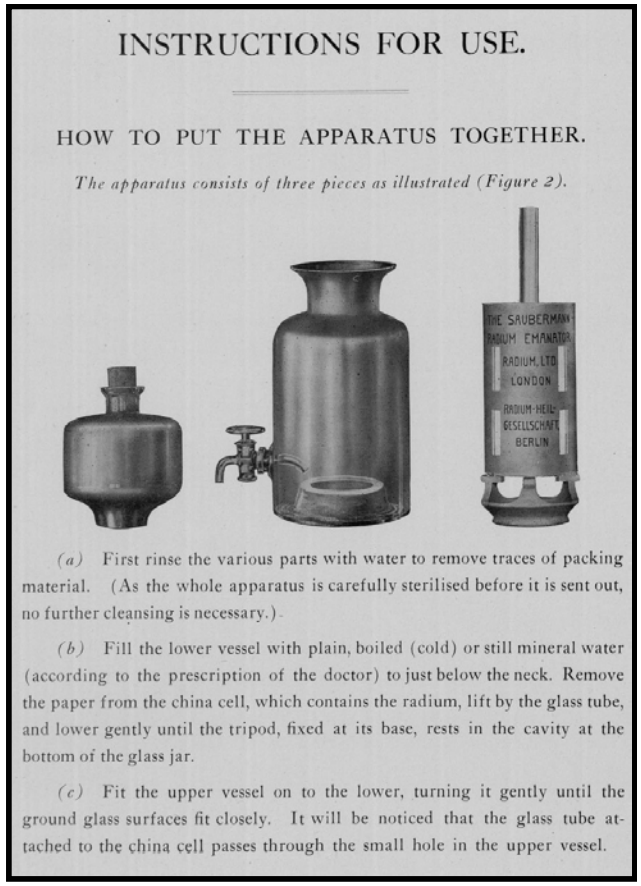
Prescribed by.......................

For.......................

NOTE.

When returning the apparatus it is essential that it should be packed exactly as received; our case and packing material must be used. Each part of the apparatus must be separately packed in the compartment provided for it, and nothing must be placed inside the glass bottle. If any breakage occurs through neglect of these instructions, a charge of 10 dollars per glass bottle and 20 dollars per porcelain cell will be made to cover the replacing of the broken part. All the broken parts, including the contents of the cell, must be returned to us in case of accident.

FRANK HARTMAN
RADIUM PRODUCTS
1921 WALNUT ST.
Philadelphia, Pa.


INSTRUCTIONS FOR USE.

HOW TO PUT THE APPARATUS TOGETHER.

The apparatus consists of three pieces as illustrated (Figure 2).

(*a*) First rinse the various parts with water to remove traces of packing material. (As the whole apparatus is carefully sterilised before it is sent out, no further cleansing is necessary.)

(*b*) Fill the lower vessel with plain, boiled (cold) or still mineral water (according to the prescription of the doctor) to just below the neck. Remove the paper from the china cell, which contains the radium, lift by the glass tube, and lower gently until the tripod, fixed at its base, rests in the cavity at the bottom of the glass jar.

(*c*) Fit the upper vessel on to the lower, turning it gently until the ground glass surfaces fit closely. It will be noticed that the glass tube attached to the china cell passes through the small hole in the upper vessel.

Fig 4: Instructions for the use of the Saubermann Radium Emanation Activator. (Radium Limited Corp., around 1900)[47]

Upon examination, a draining sinus was found, and X-rays were performed. During surgery in August 1929, the coccyx and lower three-fourths of the sacrum were removed, and sinuses were partially dissected. However, the symptoms persisted. In November 1929, two cysts were dissected from the rectum, and a dose of radium was introduced into the wound during the surgery. Symptoms still persisted, leading to a final surgery in February 1930. The rectum was cleaned, and the sinus tract was dissected out, resolving the patient's long-standing issues.[48] The role of radium in this patient´s recovery appears inconclusive in this case. Despite its application during the November 1929 surgery, her symptoms persisted. The subsequent successful resolution of her condition in February 1930 suggests that radium may not have played a significant role in her ultimate recovery.

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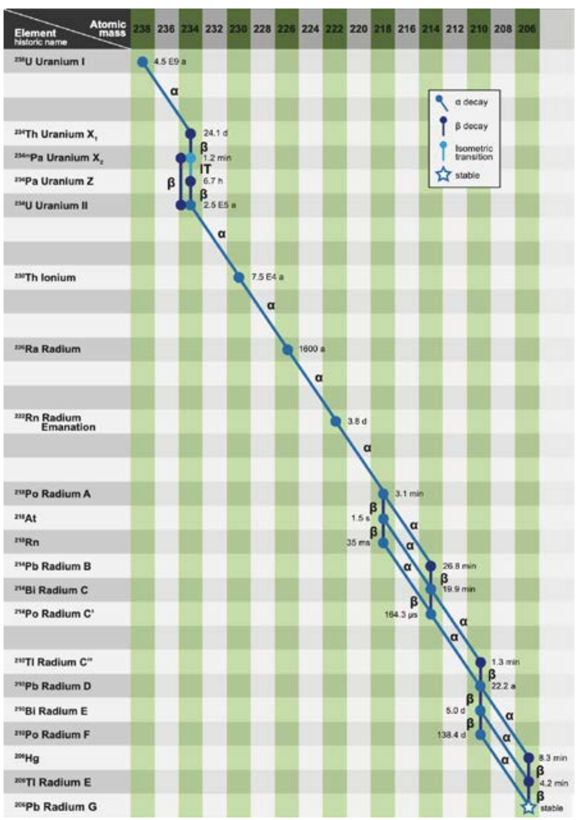
THE THORIUM SERIES

Thorium (Th) is a metallic chemical element with an atomic number of 90, exhibiting weak radioactive properties.[49] Shaded by the discovery of Uranium and its decay products, Thorium has received less attention for the decades following its initial discovery. Among the first authors to suggest the medical relevance of thorium was the American physician Samuel G. Tracey. In his 1904 publication called “Thorium : A Radio-Active Substance With Therapeutical Possibilities” he recommended thorium inhalation for the treatment of respiratory tuberculosis.[50] However, Thorium was expensive and its radioactive yield low. It was only when Otto Hahn successfully isolated the significantly more radioactive “Mesothorium" and “Radiothorium“ in 1907, that the Thorium series gained more access to clinical utilization. Mesothorium, identified as Radium-228 and Actinium-228, emits β radiation. Unlike the α radiation emanating from radium decay, β emissions may penetrate several centimeters into the deeper layers of the skin. Their decay with resulting isotopes is shown in Figure 5a for ^{238}Uranium and 5b for ^{236}Uranium and ^{232}Thorium.



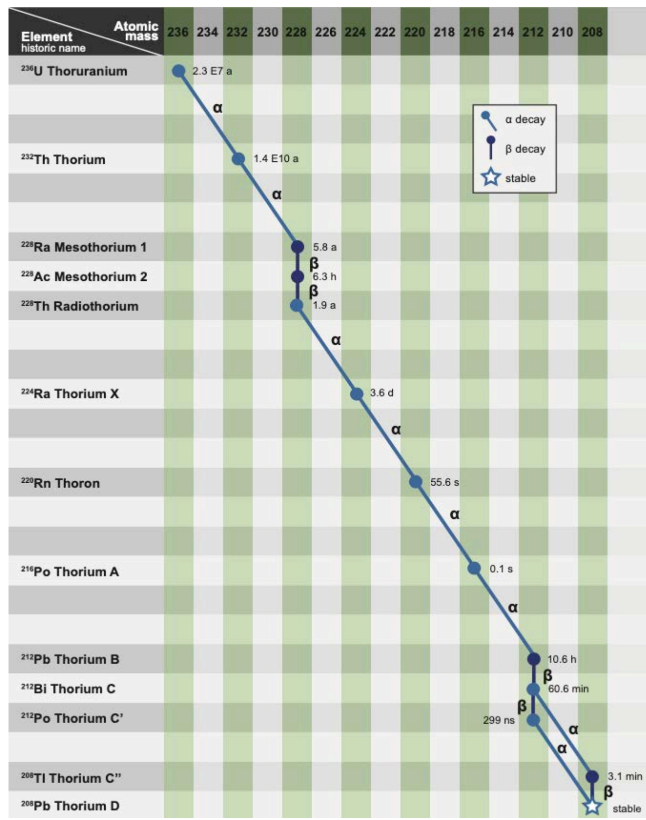


Fig 5a (left): ^{238}Uranium decay and isotopes
Fig 5b (left): ^{236}Uranium and ^{228}Actinium decay and isotopes

Thorium X was an intermediate of the Thorium series, that gained traction in Europe during the early 20th century due to its cost effectiveness and higher potency compared with Radium emanation. After its discovery by Lord Rutherford in 1900, it took more than 35 years until Thorium X would become commercially available in the United States. [51] Thorium X was largely composed of ^{224}Ra which undergoes a series of mostly α decays to ultimately form stable ^{208}Pb (Table 2). The activity of Thorium X and its products is climaxing after approximately 2 days and 90% of its total energy is dissipated within 10 days. Thorium X was deemed a secure treatment modality owing to its shallow depth of penetration in tissues and its short half-life.[52,53] In contrast to radium, Thorium X is well soluble in water as well as in alcohol, allowing the preparation of creams, ointments and ethanol-based solutions. Most of the commercially available thorium X was provided by the "Deutsche Gasglühlicht-Auergesellschaft" in Berlin, as it was a by-product of gas-bulb-production.[53] Once delivered, the product had to be used up within 48 hours. Storage and handling were relatively easy, as weak α-particles can be blocked by a mere sheath of paper. Cotton-tipped applicators where used for application.[54]

Table 2: Decay chain of ^{232}Thorium. Please note that ^{212}Bi undergoes both β- and α-decay (approx. 64% β- and 36% α-decay).[55]

Thorium series	Historical name	Primary mode of decay	Half-life
^{232}Thorium	Thorium	α	1.4 x 10^{10} years
^{228}Radium	Mesothorium 1	β^-	5.75 years
^{228}Actinium	Mesothorium 2	β^-	6.15 hours
^{228}Thorium	Radiothorium	α	1.91 years
^{224}Radium	Thorium X	α	3.66 days
^{220}Radon	Thoron	α	55.6 seconds
^{216}Polonium	Thorium A	α	0.15 seconds
^{212}Lead	Thorium B	β^-	10.6 hours
^{212}Bismuth	Thorium Ca	β^- and α	60.6 minutes
^{212}Polonium	Thorium Cb	α	0.3 x 10^{-6} seconds
^{208}Thallium	Thorium Cc	β^-	3.05 minutes
^{208}Lead	Thorium D	Stable, no decay	Σ 42.6 MeV

The German dermatologist Josef Jadassohn laid the foundation for the external application of Thorium X in the treatment of dermatological and soft tissue diseases. Following his appointment as the head of the University Hospital of Dermatology in Bern, he published a series of pioneering papers that documented initial achievements in the utilization of Thorium X for various dermatoses.[56,57] In addition, various authors could prove the bactericidal effects of α radiation in a series of ex vivo experiments.[58] Building upon these early therapeutic successes, the application of Thorium X extended to the treatment of other medical conditions, including psoriasis, lichen simplex, atopic dermatitis and naevus flammaeus.

Thorium X in the treatment of PSD

In 1925 Albert Simons used unshielded rods of Thorium X, produced for this purpose by the Auergesellschaft to treat various soft tissue fistulas. For this purpose, the rod is inserted into the fistula and locked in place by a wound dressing. Over the course of 4 - 7 days, a total dose of 1 - 2 millicurie (27 - 74 MBq) was emitted.[59]

In 1960 Feit et al. conducted a clinical trial with two patient groups.[60] The first patient group (n = 30) consisted of patients with an acutely draining sinus, that was primarily treated with Thorium X. The sinus was opened and the abscess drained. The wound was debrided and the floor of the abscess exposed; then subsequently Thorium X was instilled. "Excellent results" were achieved after 6 - 17 months of follow up. In patient group 2 (n = 10) Patients with persistent PSD where treated adjuvantly with Thorium X. Seven of which had a small persisting sinus tract and cysts, 2 others had a sinus only. Patients "responded favorably" to the treatment. In total 7 patients made a complete recovery after 12 - 14 months (four of these underwent a second Thorium X instillation). Alcohol, lacquer and ointment were available as vehicles to deliver Thorium X with a typical dose of 100 - 300 µCi [3.7 - 11.1 TBq] of total radioactivity, using 2 applications per week continued for 6 - 10 weeks.

If post abscess wounds or lay open wounds were present, these were cleaned with acetone and thorium X applied with a cotton swab. The wound was packed with thorium X soaked gauzes and covered with nitrocellulose, cotton and an external dressing. At the evening or morning before the next visit, the dressing should be removed and a dry cover reapplied after a "sitz bath". Treated in this way, 28 of 30 patients healed well, and no recurrences were seen between 6 and 17 months of follow up. Observed adverse events include temporary erythema, marginal excoriation and hyperpigmentation. Follow up visits revealed decreased hair growth and the development of cirrhotic tissue at skin level.

The author notes an upcoming awareness about the dangers of radioactivity, but feels that safety of external use of Thorium X could be proven by an event-free 50-year track record.

A short half-life of 6.7 days and a short tissue penetration of several millimeters up to one centimeter enabled easy handling by doctor and patient. Accordingly, Feit concluded in 1960 the use of Thorium X in PSD therapy is claimed to be more cost effective than surgery, may save the patient from a surgery risks and is easier to implement. Although promising an even larger study, Feit never published one. The public started sensing an increased risk associated with the indiscriminate use of radioactive isotopes…

THE DANGERS OF IONIZING RADIATION

The knowledge of adverse effects of ionizing radiation are as old as the technology itself. It is a common misconception that the awareness of the dangers of ionizing radiation didn't arise until decades after its discovery. Instead, the hazards´ knowledge was rather disregarded or accepted for the sake of technological progress. It was already Röntgen, who noticed macroscopic changes, including erythema and ulcerations on his hands after working around his newly discovered X-Rays. In a letter from 1897 to a colleague he describes his observations. Other pioneers of the field would meet more terrible fates: Clarence Dally, who was an employee of Thomas Alva Edison, would assist Edison with a number of experiments with X-Ray cathodes, during which he was exposed to a cumulative dose most probably larger than 3000 rad in years before.[61] In the year 1904 Dally died from metastatic cancer at the age of 39, making him the first victim of X-Rays.

The work of researchers like Pappenheim, Plesch, Politzer and Pauli [62,63] - to only name a few - is exemplary for a growing body of evidence, that suggested a causal association between irradiation, the new elements and profound tissue changes, giving rise to malignancy. Arthur Pappenheim, best known for the homonymous staining method, 1912 administered deleterious doses (3 - 10 ME) of Thorium X to rabbits, either intravenously or per os. It could be seen that Thorium-X administration severely damages the bone marrow within days, manifesting as a marked leukopenia, accompanied by parenchymal injury to hepatic and renal tissues.[62] Local adverse effects after external use of Thorium X were described by Svend Lomholt in 1923.[64] In 1937 a case report on a deadly Thorium-X-intoxication was published of a 26 year old female treated at the Charité in Berlin, who ingested Thorium in large amounts in (successful) suicidal intention.[65] In the 1950s Fishman and Witten described cellular atypia after cutaneous application of Thorium X to rabbit and human skin respectively.[66,67]

Later the use of topical Thorium X for vascular malformations has been linked to the development of basal cell carcinomas with decades of latency.[68-70] New knowledge about chronic tissue changes, tissue destruction and neoplasia occurring decades after exposure to irradiation emerged. While publications on Radium therapy of tissues other than cancer were common between 1940 and 1970, these steeply dropped off in the seventies (Figure 5). Finally, with the emergence of the Therac-25 radiation overdose incidents *during the 1980s, the prevailing public sentiment demanded more prudence in the handling of radioactivity. From then on, no more accounts of the irradiation and therapeutic use of ionizing radiation for Pilonidal Sinus Disease could be found after this time.

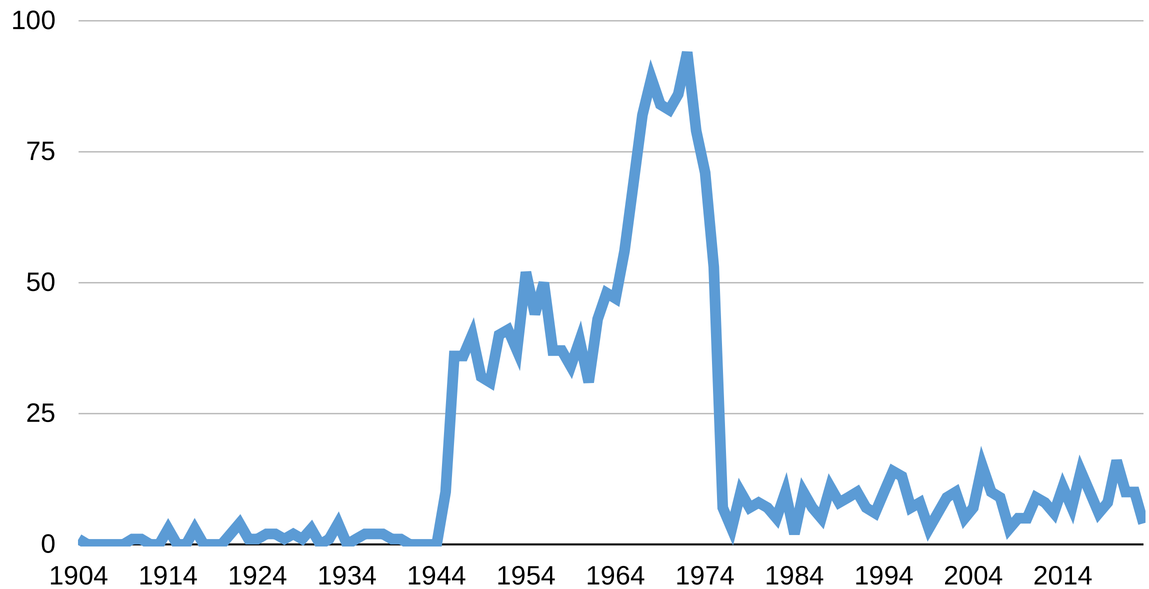


Figure 6: Number of PubMed listed Publications for "Radium AND NOT cancer".[71]

PSD AND PSD-CARCINOMA (PSDCA)

Cases where PSD carcinomas develop after long standing PSD disease are well documented.[72,73] Here carcinogenesis was due to long standing infection. Nevertheless, the task of establishing a causal connection between prior radiotherapy for PSD and the occurrence of malignant disease presents considerable challenges when examined in retrospect. Pilonidal Sinus Carcinoma have been reported between 1883 and now with approximately one case per year published in the literature.[74,75] Safadi et al. have shown that there is severe underreporting by a factor of 2-3 at minimum. PSDCA incidence has been rising[76] within the last 20 years, as PSD incidence has been rising, too.[77,78]

* Therac-25 was a medical linear accelerator (a machine used in radiation therapy for treating cancer) that became infamous for a series of accidents in the 1980s. These accidents resulted in serious injuries and deaths to patients due to overdoses of radiation. These accidents were primarily caused by software and hardware flaws in the machine's control system, which could lead to the machine administering radiation doses thousands of times higher than intended. The Therac-25 incidents served as a stark reminder of the importance of safety in medical devices and led to significant improvements in the design and regulation of medical devices, particularly those involving radiation therapy.

Radiation induced carcinomas can be mostly expected 5-20 years following radiation, thus a rise from pilonidal sinus disease irradiation in the sixties should be expected later in the eighties. This cannot be deduced from the PSDCA data currently available.[79] The number of PSD patients treated with Radioactivity or Radiation is unclear. Tracing these patients 70-100 years following therapy is nearly impossible. Considering that there is a severe underpublishing and underreporting of PSDCA as mentioned above,[75] this could further mask any variations in incidence due to radiation application 70-100 years ago. Due to the inherent risks of radiotherapy, we suspect there could be some cases where neoplasia has developed. Due to the low doses applied as reported, these potentially newly generated neoplasia are possibly few and may not be identified against the powerful epidemiological background noise, and thus can go unnoticed.

DISCUSSION

An era of indiscriminate use of a new technology has come to an end. Fortunately, Radiation therapy and the use of radioactive elements have no more place in the therapy of pilonidal sinus disease. Even well intended before, this reminds us that scientific thinking and systematic investigation is the bedrock of our medical profession, especially when new techniques with promising prospects arise. Keeping this reminder at heart we will be able to protect our patients from indiscriminate use – and further harm, as we have all promised.

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N/A

MULTIMEDIA

N/A

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