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The hazy dawn of brachytherapy

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Abstract

The discovery of radium by Pierre and Marie Curie in December 1898 opened a new era in science and within a few years provided medicine with a new means of tumor treatment. Their personal contribution to the start and early development of clinical applications should not be overlooked. The Curies did not limit their support to providing radium sources to medical pioneers but took a deep interest in the horizons of radiumtherapy. Pierre was one of the first to search for and demonstrate a biological effect of radium radiation. He investigated the radioactivity of the waters of hydrotherapeutic resorts. Marie took care of the measurement of the medical sources personally, convinced that the result of the treatment depends on the precise knowledge of the amount of radium applied. Her perseverance resulted in the establishment of the Institut du Radium (1909) in which, besides the physico-chemical laboratory, a biological department was set up. The latter became the Fondation Curie (1920), a leading medical center of treatment and training, with an integrated team of physicists, radiobiologists and clinicians led by Regaud. One hundred years after the discovery of radium, patients benefit today from the extensive clinical experience that has been collected over the years and from sophisticated developments in application techniques, dosimetry and quality assurance; the professional risk has been precisely assessed and the improvements in material and procedure have enabled the medical personnel to work in hazard-free conditions. This outcome results from the continuous progress that the pioneers gave impulse to. This paper intends to recall their efforts and achievements, as well as the difficulties and the problems they encountered during the first 2 decades when the sturdy foundations of brachytherapy were built.

Keywords: Radium; Brachytherapy; X-Ray

1. Introduction

The biological effects of X-rays were almost immediately observed and their application to therapeutic use was initiated within 6 months of the discovery. Interest in roentgentherapy spread frantically throughout the world and stimulated rapid technical and clinical developments.

It took several years for the therapeutic use of radioactivity to appear on the scene and the initial steps were slow and uneven. Two decades of incoherent efforts were necessary before brachytherapy was to emerge as a promising tool in the treatment of cancer. Numerous technical, scientific, clinical and psychological reasons contributed to the delay.

The discovery of radioactivity by Henri Becquerel in March 1896 was a monumental event opening a new scientific era. However, the minimal activity of uranium restricted scientific studies and prevented prospects for practical application. The discovery of radium by Pierre and Marie Curie in December 1898 gave a tremendous impetus to the interest in radioactivity. Free rein was given to imagining technical applications for inexhaustible powerful sources of energy. In fact, industrial prospects were to remain confined to the production of luminous dials and therapeutic use was to become the main application of radium. However, medical prospects had to wait for evidence of some action on living tissues which was delayed on account of the scarcity of suitable sources.

2. First studies on the biological effects of radium radiation

In October 1900, Walkhoff [94] mentioned a skin reaction following a deliberate application of a radium source. His report was very concise, i.e. five lines in a three-page general review in a journal of amateur photography. Nevertheless, it created a great stir. The autoexperiment was repeated by Giesel [53] and P. Curie [12] (Fig. 1). Becquerel experienced fortuitous irradiation by carrying a sealed glass tube containing several decigrams of radium chloride for 6 h in his vest pocket. He recorded [12] in detail the evolution of the skin reaction, from erythema to pigmentation, ulceration and healing with lasting depigmentation and telangiectasiae [11].

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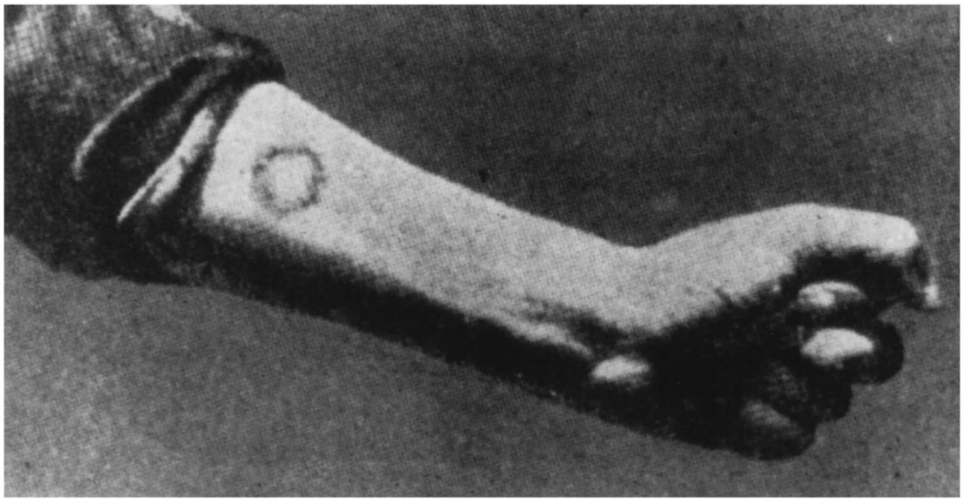

Fig. 1. Pierre Curie's self-inflicted severe skin reaction after a deliberate application of a radium source on the forearm [12] (courtesy of Museum Marii Sklodowskief-Curie, Warsaw). Zimmern mentioned (in Ref. [72] p. 362) having previously tried this kind of experiment by carrying a radium source on his arm for 20 days but failed to observe any reaction because of the low activity of the source.

These observations of a biological effect of radium radiation stimulated laboratory and clinical studies.

Experiments were carried out on the growth and the lethality of simple organisms, namely mushrooms [33], bacteria [5,75,89], amoebae and trypanosomes, on eggs and batrachian embryos [17], on plants [87] and seeds [10], on the skin and other tissues of mammals [14,30]. The biologists collected significant data in 2 years. They observed the radiosensitivity of growing tissues, the effect on cell division [74] and the teratogenic effect on embryos [17] and related the cellular effect to the action on nuclear chromatin [17]. They studied the effect on the nervous tissue [18] and demonstrated that it was not due to a direct action on the nervous cell [30]. They achieved the disappearance of grafted tumors in mice [4,83]. Physicians undertook various clinical studies on the effects on the skin, the nervous system, the eye, etc.

However, the methodology was awkward. The description of the experimental conditions was vague; in some experiments the source is passed over the irradiated area or floating on the culture solution. The specification of the source was too concise or neglected.

In fact, measurement of the source strength was very difficult due to the inhomogeneity and inconstant proportion of the radiation components and to geometrical factors related to the size, shape and position of the source. The technical means already available for assessing the quantity and quality of the X-ray beam were of no use to the radioactive source. The strength of the source was measured by an ionization method initiated by Becquerel a few days after his discovery of radioactivity and developed by the Curies and Rutherford. Danne [29] designed for practitioners an electroscope easier to handle than the sophisticated laboratory electrometers. The source strength was expressed by the mass of uranium producing the same ionization. The quantity defined was ambiguous. It should refer to the radium salt used. As pure radium bromide has a strength of 2 000 000, i.e. it produces an ionization 2 000 000 times that of an equal weight of uranium, the statement that the source has a strength 200 000 means that the salt it is made of contains 10% of pure radium salt. Thus, the specification of a source requires the mention of the mass of salt (and mass per unit area). However, the role played in the measurement of a source by its shape and filtration is not clearly considered. The quality was specified by the relative contribution of the radiation components assessed by a series of filters.

However, the concept of dose was dawning. Béclère [9] had a clear conception that radiation 'acts only where it is absorbed and in proportion to its absorption'. He realized the role of geometry and wrote that for a point source the radiation intensity decreases as the inverse square of the distance but he added that 'if the source has some extent one can assume that the radiation consists of parallel rays', a statement showing that the computation of a geometrical factor was still remote. This early endeavor in assessing a quantity sensibly related to the biological effect is fascinating. However, it was short-lived and for a long time the specification of an irradiation will be confined to mg·h (Appendix A).

The lack of appropriate measurement was probably the cause of some conflicting findings on the magnitude of biological reactions and on the relative sensitivity of different tissues. Many conclusions of the preliminary experiments now appear very doubtful. Bouchard et al. [19] ascribed to radon inhalation the death in 1 or a few hours of guinea pigs kept in a closed box containing radium and Danysz [30] reported that implanting a radium tube on the brain of a rabbit causes a hemiplegia within 2 days. These very rapid effects seem more likely related to asphyxia and trauma than to the irradiation.

Nevertheless, a biological action was demonstrated and

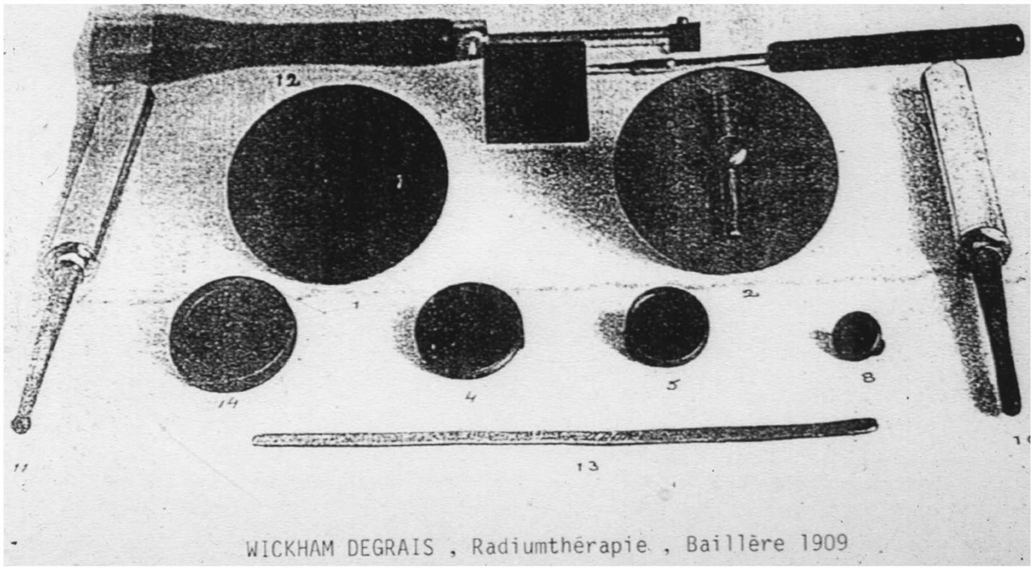

Fig. 2. Surface applicators and endocavitary tubes coated with radioactive varnish [97].

gave rise to great hopes in the potential therapeutic value of radium.

Bactericidal properties aroused great interest in the clinical community. A high sensitivity was claimed for gonorrhea, rabies, trachoma and syphilis, which were thought to benefit from local treatment by radioactive ointment or general treatment by ingestion or injection of radioactive solution. Other biochemical effects were contemplated, i.e. stimulation of physiological mechanisms [42,93] and of drug effectiveness[58] and attenuation of poisons including snake bite [76].

Pharmacological preparations were either radioactive (containing radium) or radioactivated (by placing them in a closed vessel containing radium powder in order to incorporate radon). Radon inhalation, suggested by Soddy [85] for treatment of tuberculosis, could also be of interest in many other cases (Le Radium 1904;1:23–61). For this purpose individual inhalators were manufactured and collective treatment rooms were built in hospitals. The absorption of radon by the human body was studied [45].

Another broad field of clinical exploration was related to neurological effects. Darier [31] reported analgesic and neurosthenic effects on various cases of neuralgia, anesthesia and paresis. Raymond and Zimmern [79] observed that tabetic pains vanish like magic after a short exposure. The neurological effects ascribed to radium led to applications for syringomyely, post-surgical neuritis and paralysis [8,91] and for the treatment of mental diseases. It was observed that a strong radium source placed close to the eye might cause a sensation of light. This retinal stimulation raised the prospect of using it to restore vision in some cases of blindness [63] or, more modestly, as a test of functional integrity of the retina [60].

One may wonder why so many upright and experienced physicians trained in careful observation deluded themselves with doubtful clinical findings. The placebo effect on patients enjoying the privilege of a marvelous new treatment may have contributed to convincing them of astonishing effects. The belief of the clinicians in the alleged therapeutic qualities of radium was to last several decades. It had an impact on the public and unfortunate consequences in medicine.

It encouraged the public misconception of the magic of radioactivity in the cure of pathological disorders, alleviation of pain, regulation of physiological functions and stimulation of good health.

The radioactive content of mineral waters was emphasized as an index of their quality as a drink or for bathing to insure against innumerable diseases [43,68] or for general health purposes. People were offered radioactive ointments and dressings for pain relief and for the cure of ulcers and burns, radioactive powder for digestive problems, bathtubs with radioactive sides, radioactive bed sheets, radioactive soap and beauty cream to prevent aging of the skin. This mercantilism was fortunately not too hazardous to the customers since the radioactivity of the products was minimal, if any.

These insubstantial ideas about the potential therapeutic virtues of radium aroused greater interest among the medical pioneers than more sensible prospects based on objective effects on cells and tissues. They blurred the initial efforts towards rational therapeutic utilization and had a lasting influence on its development. Groundless assertions that radium had a selective action on pathological cells and could normalize cancer cells [39], that the cellular effect of radium could spread at a distance throughout pathologic tissues, that it differed from the effect of X rays (for a long time roentgentherapy and radiumtherapy will be considered as basically distinct disciplines; their association raised overrated problems and the question of adding the doses

Fig. 3. A nurse is holding the radium surface applicator on the patient's skin. In short treatment sittings the irradiation was presumably achieved by β-rays emitted by a lightly filtered applicator. However, the back of the applicator did not provide any great protection against the γ. The occupational hazards of radiumtherapy were emphasized in 1914 [55,70].

will only be solved when the roles of the fraction size, the dose rate and the overall treatment time are understood and assessed) and that radium radiation could help heal X-ray burns would only be fully eradicated 50 years later by scientific radiobiology.

Nevertheless, rational utilization emerged from this confusing background. The technical development of suitable sources was a major requirement for the development of clinical applications.

3. The initial material

Radionuclides of low specific activity, uranium and thorium, had been used in plaster for dermatological diseases and then abandoned (Rehns commenting on the method in Le Radium 1904;1:207 asks skeptically 'how many months or years of exposure to get an erythema?'). Radium was obviously more suitable for therapeutic use which would hence be called radiumtherapy. However, other radionuclides (radon, mesothorium) were used and the less restrictive denomination of curietherapy was suggested by Degrais at the 1913 London International Congress. The present term of brachytherapy would appear 2 decades later (1931).

Local injections of radium and radon solutions continued. However, curietherapy would essentially be carried out with solid sources.

The earliest applications began with crude devices consisting of small rubber bags, small celluloid capsules or aluminum cases containing some loose radioactive powder, which were placed on or passed over the skin. The sources were soon more precisely designed and attention was paid to a uniform and stable radium distribution. In the first decade the most common tools in France [49,61] were metal sheets (Fig. 2) on which the radium salt, usually baryum and radium sulphate, was glued by a varnish which could withstand boiling water and chemical cleansers. However, the varnish could not withstand the irradiation with the course of time. More lasting surface applicators were later designed with radium embedded in a thin layer of enamel or placed in a flat case with a very thin metal wall.

They were disk-shaped or more often quadrangular to allow their juxtaposition. Their area varied from one to tens of square centimeters and their radium load amounted to milligrams or centigrams. For short applications they were mounted on a stem, possibly tiltable, which was hand-held by the operator (Fig. 3), the patient or the mother for a child. Some plates were bent for a better fitting to curved areas. The contribution of the different radiation components at the applicator surface depended on the preparation and on the sheet of mica or aluminum which might line the surface; it varied from 0% to 80% for the alphas, from 20% to 90% for the betas and from 1% to 10% for the gammas. Wickham [96] insisted on the necessity of hardening the radiation as a function of the thickness to be treated by means of additional filters (0.01–2 mm of aluminum, or 0.5–3 mm of lead).

Another kind of flat applicator was provided by pieces of canvas impregnated with a flexible radioactive varnish which were convenient for irregular surfaces and allowed covering of broad areas.

Metallic spheres or tubes (Fig. 2) coated with or containing radium salt powder or rolled pieces of radioactive canvas were designed for endocavitary applications in the rectum or the vagina; the thinner ones could be placed in the ear channel, in the urethra, or in the uterine cervix. Wickham designed a gynecological applicator assembling a uterine tube and a cervical cupel, both pieces with radium coating. Dominici designed a corkscrew-shaped instrument (Figs. 4 and 5) holding the radium tube along its axis, easily placed in the vagina or the rectum and providing a spacing of the mucosa.

Intratumoral implantations started in 1904 in several places [1,40,66,90] using small glass tubes, in a thin filter wall of silver or gold, with an overall size of a few millimeters in diameter and 1–3 cm in length. The tube was implanted after an incision or by means of a trocar (Wick-

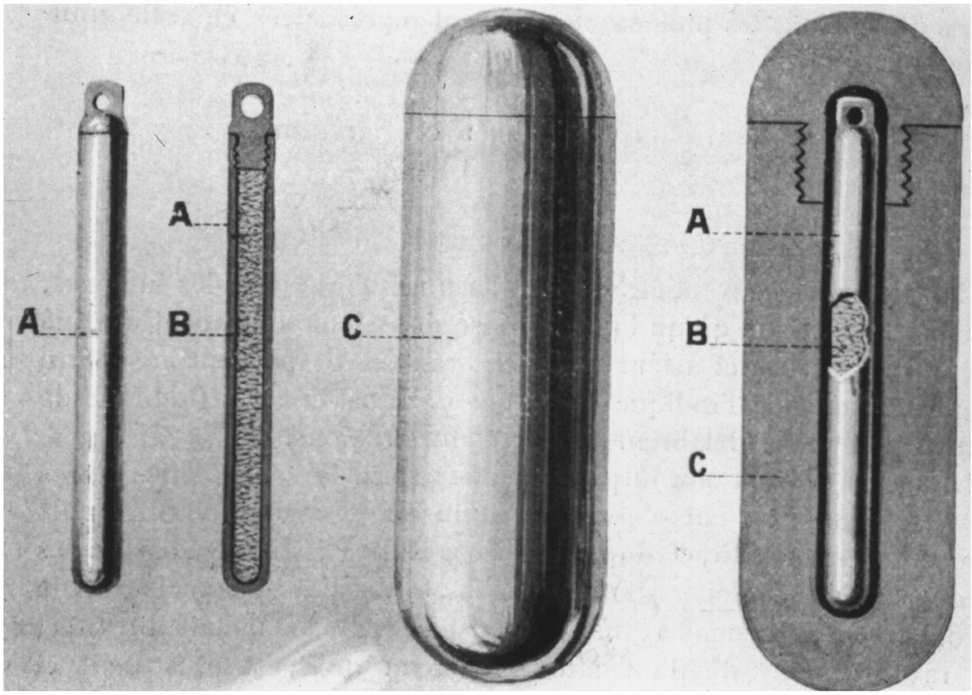

Fig. 4. Dominici tubes with heavy filtration used for endocavitary applications and intratumoral implantations [49]. The radium salt is squeezed in the tube by the tube end which is tightly screwed and brazed. The thick case C of silver or lead is a protective wall for the transport of the tube.

ham and Degrais [97] used sharpened goose quills) to realize a primitive manual afterloading technique. The pioneers usually inserted a single tube and repeated the implantation at different sites. This technique caused severe necroses.

Dominici [37] advocated thick filtration to select the ultra penetrating radiation. He designed tubes (Fig. 4) with a wall of silver or gold (0.5–1.5 mm thick) in which the radium salt (sulphate) was squeezed and sealed by screwing and brazing the tube end. The tubes were 2–4 cm long with a radium load of 10 mg per cm of active length. The Dominici tubes were to become the standard material for endocavitary applications in France [81] and were widely adopted abroad [77]. The heavy filtration could alleviate the complications of endocavitary applications. However, the problem of the intratumoral implantations called for a more uniform irradiation that Stevenson [86] achieved with the needle puncture in 1914. While Stevenson used regular perfusion steel needles containing capillary glass tubes filled with radon, the Dominici principle of heavy filtration was applied to the

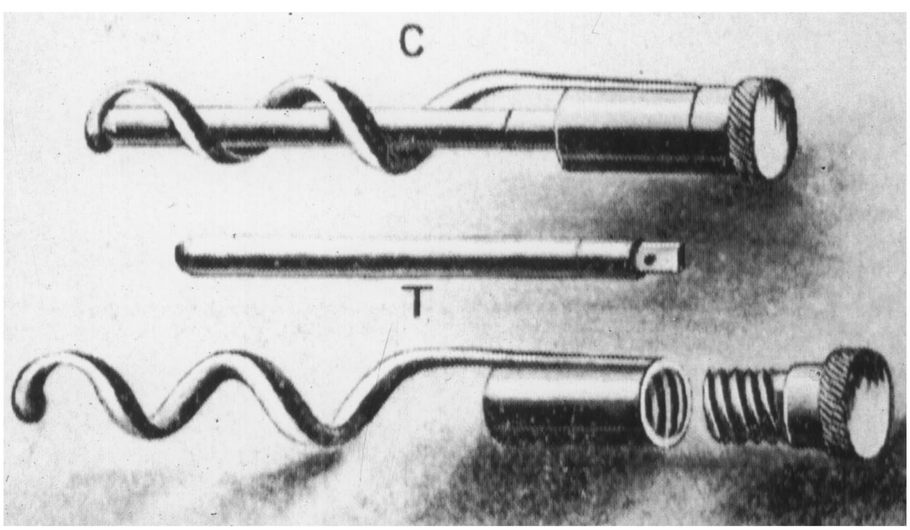

Fig. 5. Dominici applicator for endocavitary treatment [49]. The radium tube is held on the axis of the corkscrew-shaped spacer.

platinum radium needles which were designed at the Fondation Curie in the 1920s [80].

4. Early clinical development (1901–1920)

The first publication on treatment by radium was made in 1901 by Danlos [26], a dermatologist at the Hopital Saint-Louis in Paris. He treated some cases of lupus with a material loaned to him by P. Curie consisting of some small rubber bags or celluloid capsules a few millimeters thick containing radium and baryum chloride with an activity of 1000–5000 (approximately 0.5–2.5 mg radium) which were maintained on the skin for 24–48 h. The irradiation caused a blister from the 6th to the 20th day and then an ulceration which healed in 6 weeks to 3 months.

The following year, Danlos [27] discussed the posology, compared the results of radium and conventional treatments of that time (abrasion, caustics, UV) and predicted a great future for radium in dermatology [28]. The same year Blandamour [15] and Hallopeau [57] presented additional cases and radium treatment of skin disease had started in Germany [90] and probably other countries (Austria and England) [16]. Its development was rapid [82,88,90,95]. Wickham and Degrais [96] explored actively the therapeutic possibilities on many skin diseases, i.e. lichen, eczema, psoriasis, hairy pigmented and vascular naevi, prurit, neurodermatitis, leucoplasia and cheloids. Their instruments, which were limited in number at the beginning, were considerably increased by the founding in 1906 of the Laboratoire Biologique du Radium (chaired by Dominici, with Danne as a physicist) under the auspices of Armet de Lisle, director of a radium factory. One must point out that clinical development was hindered by the low availability of suitable

Table 1
Radium treatment of skin cancer (1902–1908)[a]

Year		No. of cases
1902	Danlos (France)	2
1903	Mackensie Davidson (UK)	3
1904	Williams (USA), Lassar (Germany)	23
1905	R. Abbe (USA)	2
	Rehns and Salmon (France)	2
	Exner (Germany)	1
	Boikoff (Russia)	1
	Darier (France)	1 (eyelid)
	Mouby (UK)	3
	Heynantse (Russia)	13
	Abbe (USA)	3
1906	Blaschko (Germany), Schiff (Germany), Wickham (France)	13
1907	Wickham, Degrais (France)	41
	Abbe (USA)	77
	Morton (USA)	6
1908	Wickham, Degrais (France)	80

[a] From Dominici and Barcat [40].

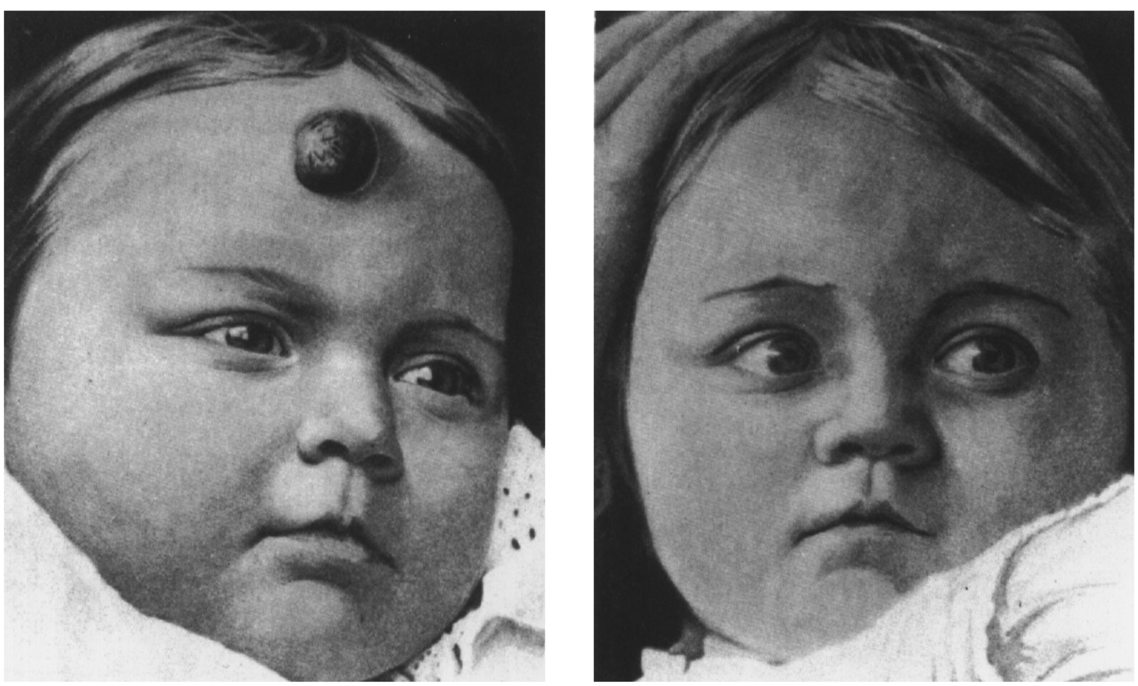

Fig. 6. Treatment of hemangioma by radium surface applicator (in Ref. [98]: Planche III). Applicators were disks of 1.1 cm in diameter coated with radium varnish (2.5 mg radium). The radiation components were $\beta = 90\%$, $\gamma = 10\%$. Two applicators were applied at opposite places of the lateral surface of the tumor (2 cm in diameter) and then at two places in the perpendicular direction; then one applicator was applied on the top of the tumor. The authors coined the term crossed fires for this technique. Each application time was 15 min and the total duration of a sitting was approximately 45 min (the authors state that at a depth the total exposure time is 1 h and 15 min!). The treatment consisted of 22 sittings in 3 months. A regression of the tumor was observed 2 months after the start of the treatment and full disappearance was observed at 6 months.

sources. Industrial radium extraction from the uranium ore was only done in France and Germany until 1913 when a radium factory was started in the USA to process the ore of the Colorado Plateau which rapidly increased the world radium supply (estimated to 30 g). In 1908, Wickham had 17 applicators at his disposal and claimed more than 8000 applications. These treatments had been mainly applied to non-malignant skin diseases. For most of them, radium would be supplanted by X-rays, which were particularly more suitable to extended lesions. However, radium will remain the treatment of choice for hemangioma (Fig. 6) for a long time due to the belief in its specific action on the vascular endothelium and to the enthusiastic results reported by Wickham and Degrais [98] and for cheloids due to the belief in its specific property for scar lysing [8,62].

The first mention of tumor treatment is an application made in 1902 in Vienna to a cancer involving the palate and the pharynx [65]. Skin cancer presented a more promising outlook. Its treatment by radium was initiated in 1903 by Goldberg and London [54] in St. Petersburg. The clinical study (Table 1) was actively developed in Austria, England [64], France [32,82], Germany [56] and the USA [2,20,24,67,100]. It was demonstrated that lasting cures could be obtained for tumors of small thickness and extent. In 1907, Wickham reported 61 cures in 67 patients with a follow-up exceeding 10 months. He related his results to lining the applicator with adequate filters (Table 2). Similar results were reported [40] by Williams (23 cases) and Abbe (77 cases). These results were significant in that they proved the possibility of sterilizing malignant tumors, which was still doubted [78]. However, they were very modest and Béclère [9] and Balthazard [6] warned that the technique should be restricted to superficial tumors of less than 3–4 cm in diameter. Some results were presented for small tumors of the eyelid [32] and the cutaneo-mucosal edge of the lip.

The treatment of epitheliomas of the mucous membrane of the mouth, tongue, floor of the mouth and soft palate was disappointing. Dominici and Chèron [41] considered that surface applications could only achieve a tumor regression, a slowing down of the growth, an alleviation of the pain and an improvement in nutrition. They advocated the implant of tubes in tumors of the tongue and floor of the mouth but late results were not reported. As a general assertion Chevrier in 1910 stated positively that no permanent cure had been observed for mucous membrane epitheliomas [23]. Treatment of carcinoma of the breast by surface applicators or tube implant was tried in 1904 [1] but was not actively continued.

Endocavitary treatments opened a broad field of applications. They allowed the placing of the radiation source close to deep located diseases that external X-ray beams could only reach with some efficiency by causing severe radiodermatitis.

Gynecological treatments were undertaken in 1904 by Foveau de Courmelles [52] on fibromas and by Wickham mainly on infectious diseases. The radium-coated devices they used provided only a shallow irradiation. The ultra hard radiation of Dominici tubes enabled more penetrating irradiation. The results on fibromas were greeted with unanimous enthusiasm. Chèron and Bouchacourt [21] reported that in 120 fibromas which did not exceed three to four finger's breadth above the pubis they obtained 117 permanent hemostasiae and 108 regressions; results were more modest (20%) for large tumors.

The treatment of cancer of the cervix was initially much less successful [71]. The results improved when Dominici filtered tubes became the standard material from 1907 onwards [22,38]. However, reports of permanent cure were exceptional until 1910. The general trend was to leave the priority to surgery when the tumor was really operable, i.e. limited to the cervix, radium being possibly associated as post-operative adjunction to prevent recurrence, or prior to facilitate surgery in limit cases [47]. Considering the heavy post-operative mortality of enlarged surgery (30%), many surgeons advocated restricted vaginal hysterectomy completed by radium. The indications left for straight radium treatment, inoperable tumor and recurrence, were of course not very gratifying. However, the results (with mesothorium) reported by Krönig, Bumm and Döder-

Table 2
Treatment protocols with a surface applicator[a]

	Additional filter (mm)[b]	Session time	Session number/ overall time (days)[c]
Eczema and neurodermatitis	0	1–3 min	3/3
Lichenification	0.04–0.08 Al	3–6 min	5/5
Pigmented naevus and cheloids	0.04–0.08 Al	1 h or 3 h continuous[d]	4/4 or 1
Superficial skin cancer	0.5 Pb	1 h	3/3
Skin cancer	1 Pb	3 h or 12–72 h continuous[d]	6/6 or 1
Breast cancer	2 Pb	10–12 h	7/14
	3 Pb	10–12 h	15/30

[a] Disk, 6 cm; 0.20 g radium salt; radiation distribution (without filter): $\alpha = 10\%$, $\beta = 87\%$, $\gamma = 3\%$ (from Wickham and Degrais [97]).
[b] Plus five to 10 paper sheets or rubber-coated canvas.
[c] Series possibly resumed at 1 or 2 week intervals.
[d] Continuous irradiations were less usual than fractionated irradiations.

lein at the 1913 International Gynecological Congress [34,48] gave an impetus to further clinical studies and the results improved steadily [59].

Endocavitary treatment was also applied to less accessible tumors.

In 1904, Exner [46] and Einhorn [44] started treating tumors of the esophagus by forcing a catheter holding the source through the obstructed channel and achieved an improvement in swallowing. Guisez reported a semblance of cure in three out of 12 patients. Cancers of the stomach were treated by esophageal catheter or through a fistula.

Endocavitary treatment of cancer of the rectum was undertaken by Foveau de Courmelles [51] using a radium-coated tube (15 daily applications of 15 min) and by Dominici with a silver tube containing 5–10 cg of radium applied 12–24 h per month. They achieved the regression of bulky tumors and Dominici and Chèron [41] added, in the case of thick infiltration of the rectum wall, an implant (5 cg tube for 24 h, repeated every month). The extended duration of these treatments does not now suggest any hope of cure.

Tumors of the prostate, adenoma [36] and cancer [73] were treated by rectal or urethral catheters by transvesical or transperineal placement of the source on the tumor.

The authors of these therapeutic attempts considered as a satisfying outcome tumor regression, slowing down of the evolution, alleviation of pain and functional relief. The long-term results were usually not reported.

Intratumor implants of radium tubes in bulky tumors usually resulted in failure with the exception of the anecdotic cases reported by Abbe (sarcoma of the lower jaw), Morton (sarcoma of the arm) and a few others. Chevrier [23] emphasized 'the challenge of entrusting the radium with the destruction of millions and millions of cells, when a single surviving cell will inevitably cause a recurrence'. He advocated the surgical removal of the bulk of the tumor complemented by radium for destroying microscopic remnants.

Thus, 2 decades after the appearance of radium in the treatment of cancer the overall outcome of the clinical research was mixed. Radium shared with X-rays and surgery easy successes in small cancers of the skin and afforded some interest as adjunct to surgery in gynecology and possibly some other sites accessible to radium placement. In spite of the eagerness and faith of its advocates, its future appeared very doubtful.ndash;

However, radium therapy had reached some maturity. Techniques and clinical indications were described in several textbooks [3,7,13,25,50,69,72,92,99]. Rational curietherapy was clearly separated from fanciful applications (on neurological diseases, infections, etc.) which still had some supporters. The material used for cancer treatment was definitely orientated to pure γ-radiation and there was a trend towards standardization of the shape, size, load and filtration of the tubes and needles. Some basic radiobiological data had been derived from clinical experience on the radiosensitivity of tumor and normal tissues, on the time factor (the action depends on the mode of accumulation of a given dose of energy) [97] and on the optimal duration of the application. World War I greatly hampered research and clinical developments for more than 5 years. However, the knowledge acquired in the first 2 decades provided a stepping stone to the next historical period of 5 decades during which conventional curietherapy steadily improved the techniques, the protocols and the efficacy of endocavitary and interstitial radium treatment and gained prominence for some tumor sites.

Appendix A. Radium, radon, milligram-hour and millicurie destroyed

^{226}Ra is the fifth daughter product of ^{238}U. It decays by α-emission (with a half-time $T = 1620$ years) into ^{222}Rn, chemically inactive gas, which decays by α-emission ($T = 3.825$ days). Subsequent daughter products are short lived up to RaD or ^{210}Pb ($T = 25$ years).

Radiations of interest to brachytherapy are the β-rays (en. up to 3.2 MeV) and γ-rays (en. up to 2.45 MeV, mean 0.8 MeV) from RaB or ^{216}Pb ($T = 26.8$ min) and RaC or ^{214}Bi ($T = 19.7$ min). They are thus the same for radium and radon.

When a source of radium is sealed, radon and subsequent daughter products (up to RaD) reach radioactive equilibrium within a few weeks and the emission remains constant during a few decades of utilization. Radon can be pumped from a vessel containing a solution of radium salt; when sealed in a glass tube or gold seed, its daughter products reach radioactive equilibrium within a few hours and the emission decreases with the radon half-time (3.825 days).

Radon has attractive features for brachytherapy. As it is continuously produced in the radium container it is possible to draw some gas at reasonable intervals to make numerous sources. It allows some flexibility in the load and size of the sources. Its half-time is convenient for permanent implant and a leak of a radon source is less hazardous than that of a radium source. The interest in radon was emphasized at the 1910 Brussels Congress of Radiology. Sophisticated facilities were set up in treatment centers to prepare the sources. Their measurement had to be made on the spot and physicists were recruited for this task, initiating the profession of hospital physicists. However, due to the constraints of their preparation radon sources were abandoned (in the 1920s in Europe and later in the USA) when reliable metal radium needles became standard material.

The millicurie destroyed (mcd) was a unit used to quantify radon treatment [35]. It was derived from the curie unit first proposed at the 1910 Congress of Radiology as the quantity of radon in equilibrium with 1 g of radium. The mcd quantifies the amount of radiation emitted by 1 millicurie of radon up to full decay. It is the same as that emitted by a constant activity of 1 millicurie maintained during a time equal to the mean life of radon, i.e. half-life/log2 = 132 h. As the radiation of interest from a sealed radium source is emitted by daughter products of radon, the mcd is also the quantity of radiation emitted by 1 mg of radium for 132 h. For the sake of unification of the units the radium applications could also be expressed in mcd, with the equivalence 1 mcd = 132 mgh. The two units, mgh and mcd, relate to the total amount of radium used in an application times its duration. Their significance is restricted to comparing treatments with identical distribution of identical sources. However, they remained the usual quantification in brachytherapy for a long time and hindered the development of dosimetry which was initiated by Sievert in 1921 [84], put in practical use in the 1930s by Paterson-Parker and Quimby and had to wait 4 decades more to be universally adopted.

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