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REVIEW

Radium - from discovery to the present day – narrative review

Angelika Edyta Charkiewicz[1] · Ivana Djuricic[2] · Vanja Todorovic[2] · Jacek Nikliński[1] · Jaime Conceição[3,4,5] · Brizita Djordjevic[2]

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Abstract

Following its discovery, radium was initially promoted as a therapeutic agent for a wide range of conditions, including skin disorders, allergies, visual problems, joint pain, and as a general health-enhancing remedy. However, subsequent research demonstrated its significant radiological toxicity and harmful effects on human health. Despite these risks, more than a century after its discovery, certain radium isotopes continue to have limited medical applications, particularly in the treatment of specific cancers. Following ingestion, radium is absorbed into the body and behaves similarly to calcium, resulting in its deposition in bone tissue. A proportion of absorbed radium is eliminated through feces and urine, while the remaining fraction may persist in the skeleton and contribute to long-term internal radiation exposure. The severity and onset of adverse health effects are closely related to the absorbed dose and duration of exposure. Chronic exposure to elevated radium levels has been associated with hematological abnormalities, cataracts, dental and jaw damage, bone cancer, and increased mortality. Advances in radiobiology, radiation protection, and personalized medicine continue to improve the safety and effectiveness of radiation-based treatments. Modern radiotherapy, including selected applications involving targeted radionuclide therapy, requires a detailed understanding of radiation dose distribution, biological responses, and patient-specific factors. The optimization of re-irradiation strategies remains an important clinical challenge that requires careful assessment of previous radiation exposure, tissue tolerance, and potential risks. Because radium exposure can occur through ingestion, inhalation, or dermal contact, continued monitoring, appropriate regulatory frameworks, and access to specialized analytical methods remain essential components of public health protection. International cooperation and strengthened surveillance programs are needed to ensure the safe management of radium-containing materials and minimize potential health risks.

Keywords Radium · Toxicity · Sources · Radiotherapy · Public health · Preventive medicine

✉ Angelika Edyta Charkiewicz
angelika.charkiewicz@umb.edu.pl

Ivana Djuricic
ivana.djuricic@pharmacy.bg.ac.rs

Vanja Todorovic
vanja.todorovic@pharmacy.bg.ac.rs

Jacek Nikliński
jacek.niklinski@umb.edu.pl

Jaime Conceição
jmconceicao@ualg.pt

Brizita Djordjevic
brizita.djordjevic@pharmacy.bg.ac.rs

[1] Department of Clinical Molecular Biology, Medical University of Bialystok, Waszyngtona Street 13, Bialystok 15-269, Poland

[2] Department of Bromatology, Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, Belgrade 11221, Serbia

[3] Faculty of Sciences and Technology, Universidade do Algarve, Faro 8005-139, Portugal

[4] Algarve Biomedical Centre Research Institute (ABC-Ri), Universidade do Algarve, Faro 8005-139, Portugal

[5] Centre for Interdisciplinary Studies (CEIS20), Universidade de Coimbra, Coimbra 3000-186, Portugal

Introduction

Radium was discovered in 1898 by Marie Skłodowska-Curie and Pierre Curie in Paris while investigating the radioactivity of uranium-containing minerals. After many attempts, Marie Skłodowska-Curie isolated 1 dg of almost pure radium chloride. She determined the atomic weight of radium to be 225 and presented her findings in her doctoral thesis on June 25, 1903. Marie Skłodowska-Curie awarded the Nobel Prize in Physics in 1903 jointly with Pierre Curie and Henri Becquerel and the Nobel Prize in Chemistry followed in 1911 (Fig. 1). The Nobel Committee took into account her in-depth investigation of this element, including the isolation of radium and the study of its nature and compounds [2, 71,77]. In his analysis, Salerno demonstrated, based on archival letters from Maria Skłodowska-Curie, how occupational exposure negatively affected her health [78]. This highly distinguished and talented scientist experienced, among other things, dermatitis, radiodermatitis, tinnitus, cataracts, miscarriage, tuberculosis, and aplastic anemia, which later led to her death, following her many years of research and observation. This difficult period in science, due to the world war and the prevailing male patriarchy meant that she herself was often the victim of mobbing [2, 78]. However, later scientists repeatedly emphasized that her laboratory had become an important signpost for radium research.

Radium and radon are different elements, with radon being a radioactive noble gas formed by the decay of radium [2]. Radium (alkaline earth metal) and radon (a radioactive noble gas) differ significantly in terms of their physicochemical properties, biokinetics, exposure routes, and health significance [2, 16]. Radon is an inert (noble) gas found in nature either as a gas or dissolved, mainly in water [69]. Radium-223 used in nuclear medicine is a synthetically produced radionuclide, manufactured under highly controlled conditions and administered within a strictly regulated therapeutic framework [2, 16, 65, 75].

Radium (Ra, atomic number 88) is a silvery-white, shiny, and soft metal. It reacts slowly with oxygen to form radium oxide and more vigorously with water to form $Ra(OH)_2$ [16, 65, 75]. It reacts easily with nitrogen in the air to form radium nitride [71]. In this radioactive chemical element (IIa), 34 radium isotopes (mass numbers ranging from 201 to 234) have been identified, which retain their highly harmful activity for several weeks, except radium-227 ($t_{1/2} = 42.2$ min), radium-230 ($t_{1/2}$ = 93 min), radium-224 ($t_{1/2}$ = 3.66 days), radium-223 ($t_{1/2}$ = 11,4 days), radium-225 ($t_{1/2}$ = 14.9 days), radium-226 ($t_{1/2}$ = 1600 years), and radium-228 ($t_{1/2}$ = 5.75 years) [2, 64, 92].

Radium-226 and radium-228, the two most extensively studied naturally occurring radium isotopes, should be considered separately because they originate from different natural radioactive decay series, which influences their environmental distribution and exposure pathways:

- Radium-226 is a member of the uranium-238 (U-238) decay series. Owing to its long half-life (1,600 years), it is widely distributed in the Earth's crust and groundwater and serves as the primary precursor of radon-222, a major contributor to indoor radiation exposure;

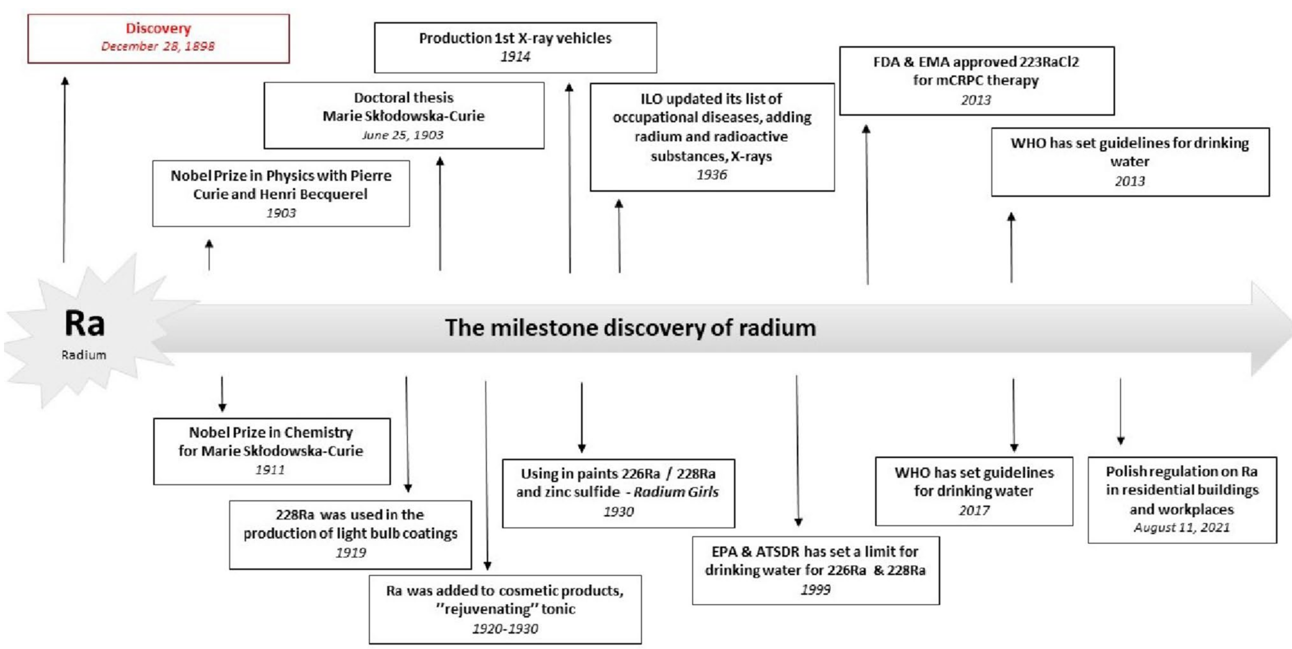

Fig. 1 The history of radium and its uses

- Radium-228 belongs to the thorium-232 (Th-232) decay series. Its considerably shorter half-life (5.75 years) results in a different environmental distribution, with elevated concentrations typically occurring in thorium-rich geological formations, such as monazite-bearing sands and certain granitic rocks.

Although the two isotopes are determined and reported separately in radiological analyses, both present similar health concerns in drinking water. As alkaline earth elements, they behave chemically like calcium, are incorporated into bone tissue following ingestion, and contribute to internal radiation exposure, thereby increasing the risk of bone-related adverse health effects [9].

This review aimed to examine the available literature on radium, with particular emphasis on its environmental origins and associated health effects, and to highlight its considerable toxicity across multiple biological systems. A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science to identify relevant peer-reviewed publications. The search included combinations of the keywords “radium”, “toxicity”, “sources”, “environmental exposure”, “radiotherapy”, and “public health”. To complement the scientific literature, authoritative reports and guidelines published by the United States Environmental Protection Agency, European Commission, the International Atomic Energy Agency, International Commission on Radiological Protection and the World Health Organization were also reviewed. The retrieved literature was critically evaluated, and the most relevant and up-to-date evidence was selected to provide a comprehensive overview of radium occurrence, biological effects, and public health implications.

Background radiochemistry of radium: Sources in Food, Cosmetic, and Medical Products

A groundbreaking discovery in the 19th century led to the introduction of products with alleged low levels of radioactivity onto the market. These were mostly medicines, food products, and cosmetics. The supposedly subtle radiation was supposed to strengthen the body, boost vitality, support the overall healing process, and, more importantly for women, improve beauty through rejuvenation [24, 35].

Radium was most commonly found in cosmetic products used mainly in the 1930s, giving the skin a luminescent quality. At that time, cosmetic companies used radioactive materials and falsified data to promote a completely new quality of their products, giving the skin a radiant beauty. Radium was most often added to moisturizing or anti-aging creams [22]. In the 1920s, radium was also added to bottled water [2 µg/60 mL / 2 µCi (74 kBq)] and promoted as a “rejuvenating” tonic (Radithor) or a cure for ticklishness or sexual impotence [30, 57, 95]. It was added to candy, chocolate, and radonators (water siphons). Games and toys for children were also produced, including radon-containing golf balls [65].

Brazil nuts are rich in selenium but also have a high, but variable, radon content. A literature review by scientists [52] presents interesting information on Brazil nuts (21 brands of Bolivian origin) purchased from the largest supermarket and pharmacy chains in Germany in November and December 2022. The analyses were carried out in an accredited laboratory. The authors highlight gaps in the available literature on the content of radium-226 (^{226}Ra) and radium-228 (^{228}Ra), except for studies conducted in Germany, where the level of ^{226}Ra was 49 mBq/g (range: 17–205), and that of ^{228}Ra was as high as 67 mBq/g (range: 12–235). The other countries analyzed (the United States, selected European countries, Brazil, Singapore, Japan, and Guyana) showed lower levels of ^{226}Ra and ^{228}Ra. There is a lack of complete data on the levels and harmfulness of these elements in Brazil nuts, which could unequivocally confirm the same levels worldwide. These researchers conclude that thorough human intervention studies could contribute to a better understanding of the long-term health effects of these nuts. Therefore, the Federal Office for Radiation Protection in Germany recommends that people with special needs (e.g., nursing mothers, pregnant women, children, and adolescents) avoid consuming Brazil nuts [52].

Selected food samples and beverages from local Egyptian markets, collected in 2022 and 2023, were analyzed for ^{226}Ra activity concentration and showed lower levels of this radionuclide in pasta. Gamma-ray spectrometry analysis showed the highest levels of this radionuclide in bread samples, a staple of the Egyptian diet [1].

Nevertheless, exposure to high levels of natural radium may result from consuming drinking water sourced from, for example, a deep well or near a radioactive waste disposal site. The updated Environmental Protection Agency [25] guidelines from 1999 set a drinking water limit of 5 picocuries per liter (5 pCi/L) for radium-226 and radium-228 (combined), and a soil concentration limit for ^{226}Ra in uranium tailings and thorium mill tailings of 5 pCi/g in the top 15 cm of soil and 15 pCi/g in deeper soil layers [9, 56, 72].

The World Health Organization (WHO) guidelines stipulate that harmless exposure in drinking water should be 100 µSv/year, without causing any detectable adverse health effects [106]. According to the Agency for Toxic Substances and Disease Registry (ATSDR), the acceptable upper level of ^{226}Ra and ^{228}Ra in drinking water in the United States is 185 mBq/L (5 pCi/L). The safe levels in drinking water, according to the WHO, are 500 mBq/L for gross alpha activity and 1,000 mBq/L for gross beta activity [5, 56].

Unconventional medical treatment using radium

Radium-based treatments

After its discovery and the awarding of the Nobel Prize in 1903, radium entered its golden age. It was recognized as an important element in improving health. At that time, radium clinics with a wide range of activities began to develop, including radioactive dressings, pills, chocolates, and the treatment of early stages of cancer. Radium was also added to ointments, creams, toothpastes, medical pillows, etc. [77, 78, 79, 94]. Nowadays, this toxic element is not permitted in any product, including foods, cosmetics, or pharmaceuticals. Its controlled use in medicine is based only on the recommendations of a doctor.

Radon-based spa therapies

Natural hot springs (including thermal baths) can be a significant source of exposure to radioactivity, posing a serious threat through frequent use [2, 3, 52]. Interestingly, radon spas are still in operation, providing paramedical treatments. The Radium Palace in Jáchymov, Czech Republic (opened in 1912) and other similar spas or radon-rich springs still exist in Austria, Germany, Romania, Bulgaria, Poland, Russia, Italy, France, Greece, Serbia, Chile, and Japan. Radioactive bath concentrations vary by region and location; e.g., Bad Gastein Spa in Austria reported < 1,000 Bq/L, and Jáchymov reported approximately 2,500 Bq/L [2, 18, 110].

In thermal baths and spas in Dehloran (Iran), concentrations of ^{226}Ra and ^{228}Ra were measured in water samples, where higher concentrations were found in soil samples irrigated with hot spring water, while in bathtubs and spa galleries, they significantly exceeded the recommended values (1,880–2,450 Bq/m³ and 790 ± 135 Bq/m³ to 1,050 ± 120 Bq/m³, respectively) [3]. Similar studies were also conducted in other rooms in thermal spas and therapy rooms, in soil, rock, and therapeutic mud, including in Lądek-Zdrój, Poland [67], the Rudas and Hévíz thermal spas in Hungary [48, 88], and Serbia [66], etc. Adelikhah et al., [3].

In the United States, this treatment in a spa has not yet been approved by the American Medical Association and is not covered by insurance; treatment is at the patient's discretion. One suggestion is a 10-day course of treatment and 32 h in the mine without supervision, staff, government health agency inspection, or patient documentation [2, 27]. Another method practiced is placing joints affected by rheumatic disease in radioactive sands during a "beneficial vacation" in Safaga, Egypt [2].

Exposure pathways

This late-19th-century discovery was recommended in 1898 as a remedy for many ailments, including skin diseases, allergies, vision problems, joint pain, and the most serious diseases, as well as for improving well-being and general condition [2, 58]. Today, therapy (in warm water and steam baths) is used to treat painful degenerative or inflammatory joint diseases, e.g., of the spine (Bechterew's disease). This therapy is most often administered via skin application, by inhaling radon gas/vapor, or by drinking water containing radon [2]. Exposure to radium may occur via skin absorption, inhalation, ingestion, or injection, each leading to systemic incorporation and subsequent radiological effects. Once ingested, nearly 80% of the substance is excreted in feces almost immediately, while the remaining residue is slowly excreted in urine and feces over the days following exposure. Prolonged exposure to high levels of radiation can cause anemia, cataracts, broken teeth, jaw fractures, cancer (mainly bone cancer), and death. However, the relationship between the amount of radium to which the human body is exposed and the time required for these adverse health effects to develop is still unknown. Exposure is measured using urine or exhaled-air tests, employing specialized equipment [52, 72, 95]. Summary of radium toxicity in individual parts of the human body was described in Table 1. Figure 2 presents a conceptual framework distinguishing between location of negative impact, exposure, radium compounds, radiation therapy.

Environmental exposure to radium occurs primarily via inhalation, skin contact, or ingestion of contaminated substances. Such exposure may arise from proximity to radioactive materials at varying concentrations in hazardous sites, mines, or industrial accidents. The severity of resulting health effects depends on individual factors, including age, sex, nutritional and health status, genetics, and lifestyle, as well as on exposure characteristics such as dose rate, total absorbed dose, and the volume of irradiated normal tissue [24, 69, 72, 79].

Pathological effects in the digestive system

Acute reactions are caused by high doses of radiation used in external radiotherapy and include anorexia, esophagitis, and nausea. It can also lead to inflammation of the salivary glands, xerostomia, mouth ulcers, fistulas, intestinal strictures, and diarrhea [49, 86, 104].

Table 1 Summary of Ra toxicity in individual parts of the human body

Location of Negative Impact	Effects of Radium Poisoning and a Brief Summary
Digestive system	- Ra can be absorbed through the digestive tract and skin - Acute reactions to radiation include anorexia, esophagitis, and nausea - Long-term exposure to ^{226}Ra causes sialitis, xerostomia, mouth ulcers, fistulas, intestinal strictures, and diarrhea - When ingested, it accumulates mainly in the stomach, small intestine, colon, and bones - After the first 4 h after injection, ^{223}Ra migrates from the blood and liver and accumulates in the colon and bones - Body burden of Ra falls below 10% after 30 days [24, 49, 37, 58, 86]
Respiratory system	- External radiation therapy can cause lung cancer, pulmonary fibrosis, and radiation pneumonitis - Absorbed into the lungs, it remains there for months - Location of Ra within the lungs depends on its chemical form [2, 10, 24, 86, 109]
Reproductive system	- Internal exposure results in a decrease in pregnancies and live births - Prolonged exposure to radiation may result in reproductive system disorders, e.g., cystitis, sexual dysfunction, infertility, or early menopause [14, 24, 61, 78, 79, 80]
Development and potential disorders	- Exposure to radium at a young age results in fractured teeth, reduced bone growth, vision problems, and breast tumors - Treatment with radium during childhood may result in the development of certain cancers in adulthood [76, 83, 108]
Immune system	- Exposure manifests in immunotoxic effects, autoimmune dysfunctions, and various types of inflammation - Excessive and acute radiation in tissues can cause strain on soft tissues, e.g., the pelvis, including strain and thickening - Workplace radiation exposure can lead to leukemia, a complete lack of granular leukocytes, leukoblastic groups, and lymphoid tissue in the bone marrow [8, 34, 79, 80,95]
Neurvous system	- Time-dose analysis considering dementia, Alzheimer's disease, Parkinson's disease, etc. - Acute complications of radiotherapy cause discomfort and pain - Long-term exposure leads to myelopathy, brain changes, encephalopathy, hearing loss, middle ear inflammation, and other neurological diseases - Untreated radiation-induced ulcers cause infections, reduced quality of life, mental suffering, and mortality due to overwhelming infection [24, 47, 58]
Circulatory system	- Long-term exposure to radiation can contribute to cardiovascular disease (CVD), such as atherosclerosis, pericardial fibrosis, and cardiomyopathy - High doses of radiation damage blood vessels, leading to oxidative stress, endothelial dysfunction, and inflammation - Microvascular damage in irradiated tissue reduces blood flow, leading to ischemia, fibrosis, necrosis, or tissue loss - Likely development of hypertension in individuals treated at a young age with radiotherapy or anthracycline chemotherapy [6, 24, 62, 68, 103]
Metabolic and other diseases	- ^{224}Radium-224 injected intravenously, preferentially accumulates in the bone tissue - Parenteral administration of ^{224}Ra accumulates in the liver, resulting in a number of harmful side effects - High doses of radiation can also lead to kidney damage or kidney cancer [32,62,69,85]
Skeletal system	- Prolonged irradiation results in necrosis and bone fractures, bone cancer, cancer of the jaw or skull - Alpha particles penetrating the bone cause damage to nearby cells, cell death, mainly osteoblasts [2,24,38]
Skin	- Early side effects of radiotherapy include erythema, hyperpigmentation, dry skin softening, and hair loss - Late side effects include dryness, fibrosis, ulcers, telangiectasia, ischemia, dyschromia, dyspigmentation, and even skin atrophy - Radiation adversely affects skin wound healing [24, 34, 39, 86]

Table 1 (continued)

Location of Negative Impact	Effects of Radium Poisoning and a Brief Summary
Cancer	- Radium decay may cause bone, lung, mammary gland, and sinus cancer as a result of inhalation - Ingested form causes bone cancer, multiple myeloma, breast cancer, and leukemia, among others - Radiotherapy is used to treat skin cancer, retinal cancer, central nervous system cancer, oral and laryngeal cancer, esophageal cancer, cervical cancer, vaginal cancer, prostate cancer, and lymphoma - When used as a complementary treatment with other therapies, it is used to treat lung, breast, uterine, bladder, rectal, testicular (seminoma), and certain soft tissue cancers - In pain relief and skeletal preservation after bone metastases, reduction of headaches and vomiting; it may alleviate obstruction due to compression of the bronchi, esophagus, ureter, or lymphatics [2, 3, 15, 20, 50, 54, 70, 90, 102]
Molecular aspects	- Radiation and biological radiology can cause DNA damage (genetic mutations, chromosomal aberrations, cell death, neoplastic transformations, disturbances in the cell cycle and cell proliferation, effects on normal tissues, teratogenesis, cataractogenesis, and carcinogenesis) - Radiotherapy damages DNA by causing single and double-strand breaks, damages proteins and membranes [11, 24, 39, 108, 111]

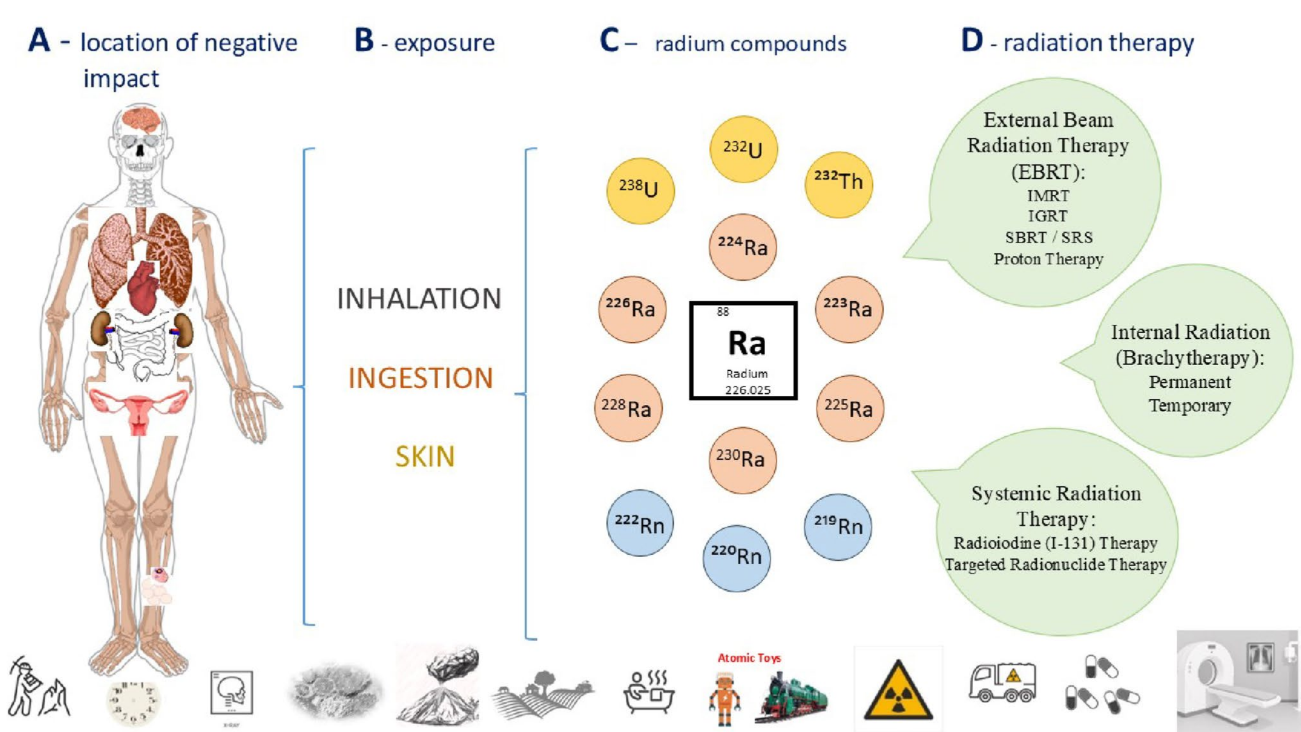

Fig. 2 Conceptual frameworks distinguishing between location of negative impact, exposure, radium compounds, and radiation therapy

After ingestion, ^{226}Ra passes through the stomach and is then excreted in feces and urine. Peak total activity is reached within 17 h of ingestion, with varying retention in the small intestine, colon, and bones [2, 37,58].

The large intestine is also exposed to 1 Bq ^{226}Ra retention after consuming plant products within 1 h (e.g., 8.32 µSv for adult men). Plants absorb radionuclides from the soil as they grow, and therefore, large amounts are found in plant and animal-based foods. However, the concentration of radionuclides in consumables varies depending on local geology, climate, and agricultural practices [1].

Promoted methods for removing radium from contaminated patients include calcium administration or the use of sodium alginate, a seaweed derivative [2, 29].

Pathological Effects in the Respiratory System

Environmental exposure in the form of external radiation therapy can lead to many serious diseases, including lung cancer, pulmonary fibrosis, and radiation pneumonitis, which is most commonly associated with tobacco smokers [24, 46, 58]. Absorption into the lungs results in it remaining there for many months, gradually being released into the bloodstream and other parts of the body, including the bones [72].

When inhaled, radon enters the bloodstream from the lungs, where it quickly spreads throughout the body. Once absorbed into the pulmonary blood, it is carried by the arterial blood to the tissues and then from the tissues into the venous blood [69].

Radium deposition in the lungs depends on its chemical form, the size distribution of inhaled particles, and the alpha- and beta-emitting radionuclides that induce ionization of nearby biological molecules. Thus, the distribution of radionuclides near lining cells and distal airways in the lungs is responsible for the development of various types of cancer [2].

Dobrzyński et al. [23] using Bayesian statistical analysis, confirmed the hypothesis resulting from a meta-analysis of 34 studies, showing that the relative risk of lung cancer is independent of radon concentrations below 838 Bq/m^3. However, during occupational exposure an analysis of Mallinckrodt Chemical Works (MCW) employees (1942–1966) found no association between radiation, dust exposure, or dose and lung cancer [62]. Meanwhile, an increased risk of lung cancer has been reported among uranium workers [109] exposed to underground radon concentrations or among atomic bomb survivors [10].

It is worth noting that external beam radiotherapy can cause pulmonary fibrosis and radiation pneumonitis, but there is no evidence that exposure to radium can cause these conditions.

Pathological effects in the reproductive system

Initial observations of 603 women employed in the radium industry before 1930 showed that radium and internal occupational exposure to alpha particle radiation resulted in a significant decrease in pregnancies and live births [80]. The frequently cited and described cases of Radium Girls revealed difficulties in becoming pregnant or infertility [78, 79, 80]. It has also been shown that long-term radiation exposure can result in other types of reproductive system disorders, such as cystitis, sexual dysfunction, infertility, vaginal stenosis, nephropathy, dyspareunia, and early menopause [14, 24, 61].

Currently, controlled modern therapeutic, pelvic radiation and long-term androgen deprivation therapy (ADT) are the standard treatments, resulting in irreversible infertility, obstruction of the ejaculatory duct, testicular damage and hypogonadism, suppression of spermatogenesis, reduced semen volume, reduced sperm motility, and sperm DNA damage. This treatment model, especially in people of reproductive age, can result in later fertility problems, encouraging men to store sperm in banks and consult a fertility specialist before undergoing prostate cancer therapy. Psychosexual disorders are also a very significant consequence of treatment. There is an urgent need for thorough cohort and epidemiological studies focused on fertility and the survival of children after pregnancy, their condition, and the quality of health [4, 14, 96].

Pathological effects on development and potential disorders

There is a known case of a 4.5-year-old girl who developed cataracts after being injected with ^{226}Ra at 15.6 µCi/kg (577 kBq/kg) [12, 95]. Previous studies suggest that exposure to radium during childhood or adolescence can result in serious health effects, such as fractured teeth, reduced bone growth, and breast tumors. Injected ^{224}Ra has been shown to significantly reduce growth in young children by damaging the growth plate in long bones [95] and fracturing teeth [83].

A retrospective cohort study of 3,440 exposed individuals who were treated as children (between 1945 and 1981) for ear, nose, and throat conditions in clinics in the Netherlands observed 23 benign tumors of the head and neck [76]. A follow-up study conducted in Washington County (Maryland, USA) between 1943 and 1960 in 904 individuals treated with nasopharyngeal radiation for craniopharyngioma showed possible radiation damage to the pituitary gland due to decreased pituitary hormone production. It was also likely that changes in sexual or hormonal development occurred in early life. However, the authors suggest further and more detailed studies to test this hypothesis [108].

The authors of the following studies describe the relationship between radiation dose, exposure type, and underlying biological mechanisms, highlighting how therapeutic radiation exposure in children may lead to various adverse health effects.

Pathological effects in the immune system

Even short exposure to Ra, as used in modern, controlled therapeutic radiotherapy, can cause serious health consequences, including immunotoxic effects, autoimmune dysfunction, and various forms of inflammation, which can induce further pathological changes [94].

Such acute radiation exposure can induce the release of inflammatory mediators, including transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ), and interleukins (IL-1 and IL-α). These mediators contribute to inflammatory responses in affected tissues, causing soft tissues, such as those in the pelvis, to become swollen, thickened, and inflamed [8, 34].

Occupational exposure was reported in the case of a chemist who developed leukemia after 14 years of working with radium. An autopsy of this patient revealed a virtually complete absence of granular leukocytes, leukoblastic groups, and lymphoid tissue in the bone marrow [95]. Similar results were obtained in the aforementioned Radium Girls [59 ,95].

Pathological effects in the nervous system

Martinez et al., presented a possible link with the intake of ^{226}Ra, ^{228}Ra, and related photon environmental exposures. Time- and dose-dependent response analyses estimate the lifetime risk for specific causes of death, with particular emphasis on dementia, Alzheimer's disease, Parkinson's disease, and other motor neurons [58].

Acute complications of even controlled radiotherapy most often cause malaise and pain, while long-term exposure leads to myelopathy, brain changes, encephalopathy, hearing loss, and otitis media [24, 47].

Pathological effects in the circulatory system

Some studies support the effects of long-term external radiation exposure on cardiovascular disease, including atherosclerosis, pericardial fibrosis, and cardiomyopathy. In irradiated tissues, microvascular damage may reduce blood flow, resulting in ischemia and contributing to the development of fibrosis and tissue necrosis [6, 24].

Earlier cases in the history of radium use in the workplace point to the occurrence of anaemia amongst female radium painters in the early 1930s [59, 95].

High doses of even controlled radiation damage blood vessels, also leading to oxidative stress, endothelial dysfunction, and inflammation. This entire mechanism can raise blood pressure. The damaged vascular structure results from impaired nitric oxide (NO) production and activation of the renin–angiotensin–aldosterone system. The most frequently mentioned potential risk factors increasing heart damage include dose exceeding 30–35 Gy, young age, large volume of irradiated heart, exposure time, use of chemotherapy and hormone therapy, occurrence of additional lifestyle diseases (e.g., diabetes, dyslipidemia, hypertension, smoking, obesity), and occupational or environmental exposure. Hypertension is likely to develop in people treated with radiotherapy at a young age, which may emerge over time and with significant radiation exposure. There is also no hard evidence linking hypertension to drugs used in chemotherapy (e.g., anthracycline chemotherapy at a dose $\geq$ 100 mg/m^2). Timely intervention, broadly understood prevention, and regular monitoring of blood pressure are recommended to effectively reduce the potential risk of cardiovascular disease in people exposed to radiation [68, 103].

Long-term observation of employees at MCW, in occupational exposure, showed a positive dose-response between radiation and CVD. However, the authors note that this association may be confounded by smoking, which was not assessed in the study [62].

The probable effect of radiation on blood pressure may have a genetic basis. However, this has been confirmed only in Wistar Kyoto rats so far [89]. The extent to which diagnostic and therapeutic radiotherapy increases the risk factors for cardiovascular disease, including hypertension, requires further epidemiological research.

Pathological effects in the metabolic system and other diseases

Since radon is soluble in water, high concentrations in drinking water can be a significant route of environmental exposure. In such cases, radon is easily absorbed from the digestive tract (e.g., the stomach and small intestine) into the bloodstream [69].

Meanwhile, controlled therapeutic radiotherapy, in a 20-year follow-up of a group of patients who had received an injection of ^{224}Ra into the bone, showed that in 20 people treated for tuberculosis (out of 682 adults and 218 young people) developed liver cirrhosis, liver tumors, liver cell cancer, and bile duct cancer [85].

Observational analyses of workers at MCW indicated an association between radiation exposure and kidney cancer, although this relationship was observed only in a small number of cases involving higher radiation doses [62]. A similar finding was reported by Golden and others [32]. Respiratory exposure and environmental radon levels were measured in both cohorts. This long-term, multicentre study, considering factors such as lifestyle, socio-economic status, occupation, occupation history, year of birth, genetic and family history, and radiation dose, indicated an increased risk of kidney cancer with increasing exposure to both environmental and occupational radiation [62].

Pathological effects in the skeletal system

Additional concerning effects of this toxic element include its association with bone cancer [80, 94]. Prolonged occupational exposure results in necrosis and bone fractures [24, 38].

The chemical structure of ^{226}Ra (an isotope of radium), as used in modern, controlled therapeutic radiotherapy, is similar to that of calcium, which is why it targets bone, releasing mainly alpha particles and damaging nearby cells. When ingested, it primarily causes cancer of the jaw or skull. Alpha therapy is currently recognized as an effective treatment for bone metastases, and targeted therapy is used for bone metastases [2].

McKay et al., demonstrated that in patients (at the Dana–Farber Cancer Institute and Massachusetts General Hospital, Boston, USA) with advanced renal cell carcinoma (aRCC) and bone metastases, treatment with ^{223}Ra and VEGF in first-line or subsequent-line therapy is safe. This therapy is primarily feasible and biologically active. The skeleton is one of the metabolically active organs that undergoes constant remodeling. This dynamic process of resorption and formation is driven by osteoclasts and osteoblasts [60].

Double-strand DNA breaks induced by alpha particles of ^{223}Ra, as used in another controlled therapeutic radiotherapy, can lead to cell death in many areas, including those with increased osteoblastic activity [36, 39]. In this case, researchers from Massachusetts did not observe an association between mutations in DNA repair genes and clinical benefits from therapy; however, the interpretation of these findings is limited by the small sample size. This pathological process leads to the destruction of cancer cells and adjacent bone lesions, while also contributing to stabilization of the tumor microenvironment [60]. ^{223}Ra, an alpha-emitting radionuclide, is a calcium mimetic preferentially taken up by osteoblastic bone metastases [39].

Observations have shown that the injection of ^{224}Ra significantly slows the growth of long bones [95] and increases tooth fragility [83]. Prolonged exposure to high levels of radiation during radiation therapy can cause fractured teeth, jaw fractures, cancer (mainly bone cancer), and death [72, 95].

Pathological effects in the skin

Radium is absorbed through the gastrointestinal tract and skin, even from external sources [33, 94, 111]. Haubner et al., emphasize in their review paper that proper wound healing involves appropriate cell interactions [34]. Biological mechanisms at the cellular level that are important for this process include the interaction of keratinocytes, skin fibroblasts, and endothelial cells. Proper wound healing requires a tightly regulated sequence of cellular interactions. However, radiation-induced tissue damage disrupts this process and promotes recurrent inflammatory reactions, even during therapeutic treatment [24].

Nitric oxide promotes wound healing by regulating collagen deposition and tissue remodeling. Molecular and biological alterations induced by radiation have been observed in keratinocytes during controlled treatment, compared with non-irradiated skin. In irradiated tissue, fibroblasts exhibit altered activity, resulting in the disorganized deposition of collagen bundles [34].

TGF-β plays an important role in nearly all phases of wound healing, with TGF-β1 levels remaining elevated in fibroblasts and endothelial cells long after modern, controlled radiotherapy [39].

Early side effects of radiotherapy, including erythema, hyperpigmentation, dryness, and hair loss, should also be considered. Late side effects involve dryness, fibrosis, and ulcers, telangiectasia, ischemia, dyschromia, dyspigmentation, and even skin atrophy [24, 34, 86].

Unfortunately, radiation-induced tissue damage may continue to progress for many years after the completion of modern radiotherapy. The plastic surgery literature has consistently documented the detrimental effects of radiation on skin wound healing, with numerous studies proposing various approaches to enhance skin regeneration [24, 34]. Meanwhile, occupational exposure, particularly among people who painted shields in the past, often resulted in chronic radiation exposure of the skin and mucous membranes, especially in the lips and tongue [95].

Occupational exposure, such as even a bath and elevated water/steam temperatures, tends to promote radon penetration into the skin by increasing blood circulation [2].

Carcinogenic effect of radium

It is well established that the products of radium decay are associated with an increased risk of cancers of bone, lung, mammary gland, and paranasal sinus cancers, most commonly as a result of inhalation exposure. In contrast, ingestion of radium has been linked to bone cancer, multiple myeloma, breast cancer, and leukemia, among other malignancies [2, 3, 102].

The benefits of ratiotherapy

Radiotherapy plays an important role in prolonging life in the treatment of not only advanced prostate cancer but also selected types of cancer [11, 74]. From the early 1900s, radium was increasingly used to treat various localized cancers including uterus, cervix and rectum, particularly in "radium institutes," established in France and Poland, where Marie Skłodowska-Curie played a significant role in the development of radium research and its medical applications [2]. Radiotherapy has been used for over 120 years in the treatment of a wide range of malignancies including skin, retinal, central nervous system, oral and laryngeal, esophageal, cervical, vaginal, and prostate cancers, as well as lymphoma. It is also used as a complementary treatment in combination with other therapies (surgery, chemotherapy) for lung, breast, uterine, bladder, rectal, testicular (seminoma), and soft tissue cancers. Radiotherapy can also serve an important palliative role in oncology. In some patients, it is used to relieve pain or preserve skeletal integrity in the presence of bone metastases. In cases of central nervous system metastases, radiotherapy may alleviate symptoms such as headache and vomiting associated with increased intracranial pressure. It can also relieve obstruction caused by compression of the bronchi, esophagus, ureter, or lymphatic vessels. The effects of radiation therapy, which may be permanent or progressive, are classified as acute (occurring within 10–14 days after the initiation of treatment) and late or long-term (developing more than 3 months after the completion of therapy). The effects of accidental ingestion, inhalation, or absorption of radium differ significantly from those of therapeutic administration. For example, vaginal stenosis is a side effect of cervical cancer treatment during brachytherapy (temporary implantation of radium sources into the vagina and cervix) [24, 73].

It should be emphasized that the Institut Curie, located in Paris, Saint-Cloud, and Orsay, is considered one of the birthplaces of modern radiotherapy, originating from the pioneering discoveries of Marie Skłodowska-Curie. The institute possesses one of the most comprehensive technical platforms for radiotherapy in Europe. The type of radiotherapy (Table 2) is selected according to the location of the radiation, with two main categories distinguished: external and internal radiotherapy. Currently, ultra-precise proton therapy is used mainly in pediatric patients and adults mainly for the treatment of certain tumors, e.g., ocular tumors. Clinical trials conducted at the Institute include patients with prostate, bladder, breast, lung, and brain tumors, etc. [73].

^{223}Ra became the first radioactive isotope approved for the treatment of castration-resistant prostate cancer (CRPC), often with symptomatic bone metastases without visceral metastatic disease. Researchers are often trying to safely incorporate it into the treatment regimens of currently used therapies (e.g., chemotherapy, immunotherapy, and hormone therapy) to make the overall treatment more effective. However, some combination therapies and their effects are still not available (e.g., radiosensitizing chemotherapy) [15, 70]. Numerous clinical trials are underway to evaluate the efficacy of ^{223}Ra in combination with multiple treatment methods [13, 15, 74].

As emphasized by Conte et al., further research is necessary to understand the highly complex mechanisms underlying prostate tumors and the impact of other biomarkers [15]. Meanwhile, multicenter studies conducted in Italy [20] were also of significant interest in predicting the survival-prolonging effect of chlorochloride ^{223}Ra ($^{223}RaCl_2$) for patients with metastatic castration-resistant prostate cancer (mCRPC). As many as 581 patients with symptomatic bone metastases were retrospectively analyzed over more than 10 years. Patients received a minimum of one cycle of $^{223}RaCl_2$ therapy via intravenous injection of 55 KBq/kg body weight (every 28 days in planned cycles). It was demonstrated that $^{223}RaCl_2$ is a beneficial option in symptomatic mCRPC. Researchers emphasize that the analyzed therapeutic component has high therapeutic efficacy [20, 90]. It prolongs survival in younger and older patients [28]. $^{223}RaCl_2$ was approved by the Food and Drug Administration in 2013 as a therapeutic option for mCRPC, including for patients with symptomatic bone metastases and no evidence of visceral involvement [19]. In 2018, the Committee for Risk Assessment and Safety, as part of EMA Pharmacovigilance, decided that $^{223}RaCl_2$ could be used as a third-line therapy only [51, 82]. ^{223}Radium was approved in Europe in November 2013, and the European label was updated in 2018 by the European Committee for Risk Assessment, which recommended risk minimization procedures to the European Medicines Agency (EMA) [82]. The effect of collateral radiation may be the therapeutic efficacy of new radiopharmaceuticals, in particular $^{223}RaCl_2$, which have the potential for systemic radiation treatment of metastatic breast and prostate cancer [11, 81, 93].

Not all anal tumors respond similarly to chemoradiotherapy. As described by Bobel and McGee in their review, studies from multiple centers have examined the effect of radiation surgical interval (RSI) on specific tumor subgroups. Unfortunately, many observational studies confirm that increased RSI is uncertain and may introduce confounding factors, affecting perioperative and oncological outcomes. The authors conclude that mildly prolonging RSI may improve pathological complete response (pCR) for rectal cancer patients undergoing proctectomy, showing even a slight improvement in long-term oncological outcomes. The presented conclusions suggest that, to achieve optimal benefits in patients requiring proctectomy after long-term radiotherapy, the procedure should be performed between 8 and 12 weeks after radiotherapy [8].

Table 2 Types of radiation therapy [73]

External radiotherapy	Curietherapy	Vectorized internal radiation therapy
- Most commonly used,	- A radioactive source inserted into the body,	-Is developing in the fields of nuclear medicine and metabolic radiotherapy,
- Radiation beams directed at the tumor,	- Direct contact with the tumor,	- Radioactive source administered directly into the mouth or via intravenous infusion.
- Passes through the skin,	- Mainly used for gynecological and prostate cancers.	
−2 types of radiation: photons or protons (proton therapy),		
- Contact therapy used for skin tumors.		

Currently, therapeutic strategies allow us to determine the tumor-specific tolerance dose, improve the timing of the regimen, and identify the sources of radiation. However, this progress does not yet completely protect healthy tissues [24, 34, 54, 74, 105]. Therefore, further research in this area seems necessary.

Two major institutions (the European Society for Radiotherapy and Oncology (ESTRO) and the European Organisation for Research and Treatment of Cancer (EORTC) have jointly developed a comprehensive consensus on re-irradiation practices, standardising definitions, reporting and clinical decision-making. This consensus emphasizes the importance of interdisciplinary collaboration in evaluating patients for re-irradiation. Key considerations include patient performance status, estimated life expectancy, and response to the initial course of radiotherapy, all of which are critical for determining eligibility for re-irradiation. The recommendations advocate a patient-centred approach, with clear communication regarding treatment goals, expected benefits, and potential risks.Lee and Hoskin, [54].

Pathological Effects in the Molecular Aspects

Unfortunately, radiation and biological radiology can affect many areas, including DNA damage, genetic mutations, chromosomal aberrations, cell death, neoplastic transformations, disturbances in the cell cycle and cell proliferation, effects on normal tissues, teratogenesis, cataractogenesis, and carcinogenesis [108, 111].

Free radicals damage DNA very quickly, within 1 s to several hours after radiation exposure [108]. In modern, controlled therapeutic radiotherapy damages DNA by causing single- and double-strand breaks and by transferring DNA strands. This situation can repair damaged DNA in the cell or, conversely, lead to apoptosis. Radiation also damages proteins and membranes, causing breaks in surrounding cells, including nearby cancer cells [11, 24, 39]. DNA damage from mutations leads to cancerous changes in various areas of the lungs, depending on the distribution of radionuclides [2].

The alpha particles produced involve high linear energy transfer (LET) radiation with dense ionizing tracks, causing complex DNA damage. Unfortunately, alpha particles also induce cytotoxicity in non-irradiated neighboring cells through specific radiation-induced side effects. Understanding the effects of $^{223}RaCl_2$ and other alpha-particle emitters has significant therapeutic potential due to the short range of the emitted alpha particles. The decay of ^{223}Ra affects the production of daughter radionuclides by emitting alpha particles, beta particles, and gamma rays. Low absorbed doses of ^{223}Ra particles (< 0.0073 and < 0.079 Gy) suggest that $^{223}RaCl_2$ may provide additional clinical benefits by inducing biological effects in cancer cells [11]. Alpha ^{223}Rais the first radionuclide to prolong overall survival in patients with mCRPC, reduce pain associated with bone metastases, and have limited toxicity, confirming its efficacy and usefulness [74].

Redmont et al., suggested that during modern, controlled therapeutic radiotherapy with ^{223}Ra, DNA damage in circulating lymphocytes should be monitored, together with hematological parameters such as RBC count and hemoglobin levels. These measures may serve as potential biomarkers for predicting an individual patient's response and sensitivity to therapy. The authors further reported that the level of DNA damage observed in patients treated with higher activities of ^{223}Ra was not significantly associated with metastatic burden or treatment-related toxicity. They hypothesized that interindividual variability in treatment response may instead be related to differences in gene expression profiles, particularly involving genes associated with DNA damage recognition and repair pathways [74]. Therefore, even modern low-dose radiation therapy requires careful long-term monitoring and extended patient follow-up to detect and manage potential late adverse effects.

Environmentally degrading effects of radium

Naturally, radium is found in uranium ores [2, 71]. This silvery-white metal forms from the decay of uranium and thorium in the environment. Low levels have been observed in soil, water, rocks, plants, coal, and food, with no change in their content over time [2, 56, 72] . Radon exposure depends on the occupational source (e.g., uranium mining, caves, mines) or environmental source (e.g., home, offices). Indoor radon levels are influenced by local geology, building materials, and household lifestyle factors [2, 69, 69]. In a study conducted in Iran at a spa (in Dehloran), the maximum doses of radiation from radon inhalation for tourists and staff were 0.13 and 5.5 mSv/yr^{-1}, respectively, exceeding the limit in that country (5 mSv/yr^{-1}). The average exposure duration was 15 h/year for visitors and 1468 h/year for employees [3].

It should be emphasized that artificial radionuclides in soil are mainly the result of atmospheric nuclear weapons testing (1945–1963) and a series of nuclear accidents, including those in Windscale (1957), Kyshtym (1957), Chernobyl (1986), and Fukushima (2011). It is also linked to natural disasters, where it can be transferred from the soil to vegetables and, consequently, through grass consumed by cows to their milk [79]. During the normal operation of nuclear reactors, nuclear fuel production facilities, and spent nuclear fuel reprocessing plants, small quantities of radionuclides may be released into the environment under strictly controlled and regulated conditions [98].

In addition to these anthropogenic sources, naturally occurring radionuclides of terrestrial and cosmogenic origin are continuously present in the environment and circulate through air, water, soil, rocks, and the food chain. Human exposure to radionuclides occurs through both internal and external pathways. Internal exposure results primarily from the ingestion of contaminated food and drinking water and the inhalation of airborne radionuclides, whereas external exposure arises from cosmic radiation and terrestrial radionuclides present in soil, rocks, and building materials [26, 56].

Uwatse et al., emphasize the importance of monitoring food composition to ensure its safety and suitability for human consumption. Toxic substances, particularly radionuclides, may originate from multiple sources, including environmental contamination, especially when food products are sourced from regions with elevated natural radioactivity, as well as from inadequate production practices or food adulteration [99].

The first uranium mining and extraction took place in the former Czechoslovakia and Germany, in Eastern and Central Europe, isolating over 300,000 tons of uranium ore from the end of World War II to the late 1990s [2, 63].

Radon content has been reported in many products, including:

- Light bulbs,
- Watch or aircraft dials, dial paints, adhesives, luminescent dyes,
- Electromagnetic switches in telephones,
- Cosmetics (e.g., moisturizers, lipsticks, nail polish, toothpaste, vermilion, medical pillows),
- Medicines,
- Food products (e.g., butter, chocolate, "rejuvenating" tonic),
- Bathing water, thermal water, drinking water,
- Uranium mining [2, 3, 22, 30, 31, 35, 56, 58, 78].

Unfortunately, its harmful effects were discovered relatively late in watch factories, where ^{226}Ra or ^{228}Ra and zinc sulfide were used in paint in the 1930s. At that time, the so-called Radium Girls, while precisely painting the numbers on the dials, touched their lips with brushes coated with toxic paint, giving them a conical shape and consuming almost 2 g/day of paint (approx. 43 µg of radioactive material). In addition, the dust was inhaled and settled on their hair, skin, and clothes. The adverse health effects of radon exposure included jaw necrosis and tooth loss, non-healing ulcers, bone fractures, anemia, cancer, ultimately leading to a violent and very painful death. Class action lawsuits stemming from such harsh and harmful working conditions prompted decision-makers at the time to develop new, safe labor policies. It is worth noting that young women working in large companies were unaware of the risks associated with exposure and its adverse effects. It has even been suggested that information was deliberately concealed [2, 24, 33, 58, 71, 78]. ^{228}Ra was also used around 1919 in the production of light-bulb coatings, which exhibited greater brightness than its derivative, ^{226}Ra [58].

When discussing exposure to radium through food, attention should be paid to the quantitative distinction between radionuclides and naturally occurring potassium (^{40}K), which is often the main contributor to natural radioactivity in food. The mere presence of radium without quantitative context or comparative radiological significance can be misleading to consumers and researchers alike, and consequently to scientists [9].

The three main radon isotopes - ^{222}Rn, ^{220}Rn, and ^{219}Rn - are found as daughter radionuclides of the radium isotopes (^{226}Ra, ^{224}Ra, and ^{223}Ra). They are members of three natural radioactive decay chains, originating from ^{238}U, ^{232}Th, and ^{235}U. Accordingly, the isotopes ^{222}Rn, ^{220}Rn, and ^{219}Rn are reffered as radon, thoron, and actinon. Only two isotopes (^{222}Rn and ^{220}Rn) are the primary sources of radon exposure relevant to radiation protection [69].

The distribution of average radiation levels in Ireland is as follows: Radon (59.2%), Medical (10.4%), Cosmic (8.9%), Thoron (8.4%), Food (7.1%), Gamma radiation on the ground (5.8%), Occupational (0.3%) [9].

Figures 3 and 4 represent indoor Radon Maps in Europe [26] and in the USA [55]

Environmental sources of radium and reviews of the fate and transport of radium in the environment

Analyzing the wide range of human interference, one must consider the impact of oil spills and gas emissions on human health. This problem was observed by Tasker et al., in Pennsylvania, USA In Pennsylvania alone (between 2008 and 2014), the application of O&G wastewater on roads released more than four times as much radium into the environment (320 millicuries) than O&G wastewater treatment plants [91]. The potential and confirmed toxicity of this wastewater is a serious public health concern. Laboratory experiments have shown that nearly all metals in this wastewater are washed off roads after rainfall, potentially reaching groundwater and surface water. The release of known carcinogens (e.g., radium) from roads treated with wastewater is often ignored. The authors analyzed samples of contaminants from 13 U.S. states in O&G wastewater used for road

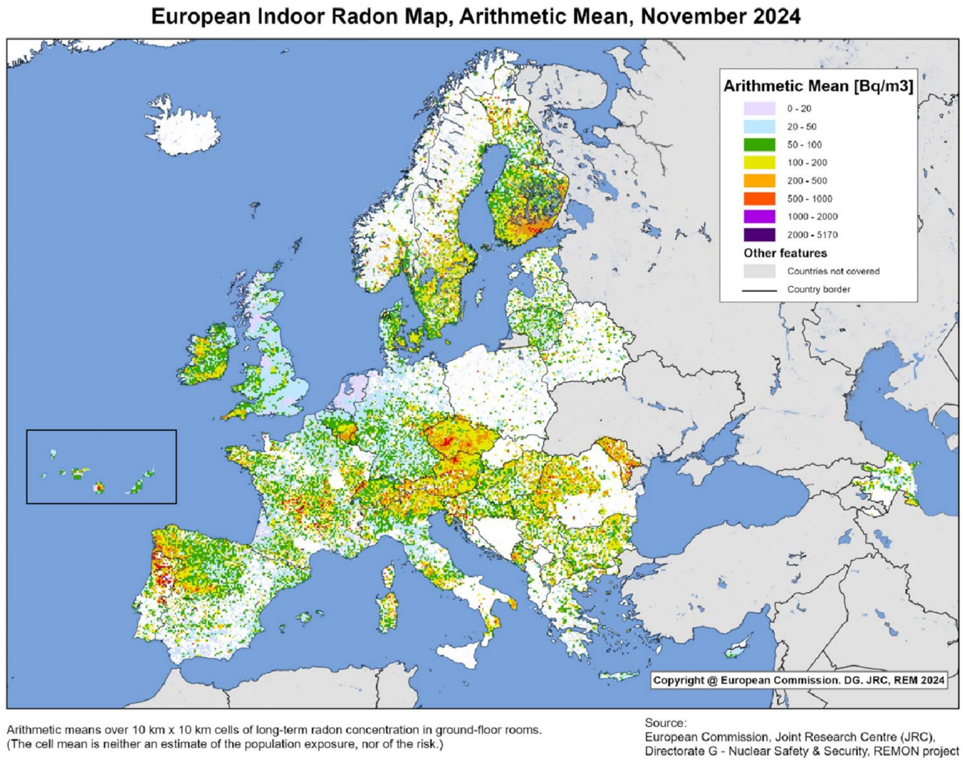

Fig. 3 European Indoor Radon Map (Note: Reproduced from Source European Commission, 2024). Source: European Commission, Joint Research Centre (JRC), REMON Project, © European Union 2024. Reproduced under the Creative Commons Attribution 4.0 International (CC BY 4.0) licence.

construction materials for ^{226}Ra using gamma spectroscopy. The study found that radium was partially retained in road construction materials. Nevertheless, its concentration plateaued after multiple applications of O&G wastewater. Any additional radium used in road construction materials may be transported to surface water or groundwater, but it may also accumulate in local soils. Organic compounds in O&G wastewater also exhibit potential radiotoxicity. Organic compounds in O&G wastewater also exhibit potential toxicity. They may also harm aquatic life and pose a risk to human health [91].

Another analysis conducted by Lauer et al., [53], also in Pennsylvania, this time between 2014 and 2017, was based on detailed analyses ^{228}Ra, ^{226}Ra, and their decay products. Elevated levels of ^{228}Ra and ^{226}Ra were detected in stream sediments near the fallout site (total Ra = 90–25,000 Bq/kg) compared to upstream sediments (20–80 Bq/kg). The results of the study showed that, at all three sites analyzed, elevated levels of Ra were found in stream sediments collected near drainage pipes at waste disposal sites (^{226}Ra = 57–14,949 Bq/kg; n = 26) compared to upstream sediments (^{226}Ra = 9–41 Bq/kg; n = 18) The development of unconventional shale gas in the Appalachian Basin has frequently been associated with various types and mechanisms of water pollution, including the management and disposal of oil and gas wastewater (OGW). The authors suggest that, to prevent the accumulation of radionuclides in the environment, disposal restrictions should be introduced that apply to all types of Ra-rich water, regardless of source. The authors also propose considering the implementation of a policy that differentiates between the treatment and disposal of conventional and unconventional groundwater [53].

It should be pointed out that the increase in natural gas production in the United States over the past decade has been driven by unconventional shale gas and tight sand gas production, which accounted for nearly 30% (0.68 trillion cubic meters). Some energy forecastwers suggest that unconventional production will double by 2035 and account for approximately 50% of total domestic natural gas production. The global estimate of natural gas reserves in unconventional shale formations is approximately 716 trillion cubic meters (2.53×10^{13} Mcf). The global nature of shale gas extraction means that it takes place in countries such as China, Germany, Poland, Australia and New Zealand. There are currently three main potential impacts on water quality arising from shale gas exploration and hydraulic fracturing: contamination of shallow groundwater; potential pathways of flow between deep and shallow formations; and the disposal of production and flowback water. One of the direct and undeniable impacts of shale gas exploration, both in the US and the rest of the world, on water quality is the issue of the management and disposal of wastewater generated by gas extraction. The growing use of hydraulic fracturing technology to boost the productivity and operation of conventional oil and gas wells will lead to an increase in the volume of this type of wastewater in the United States;

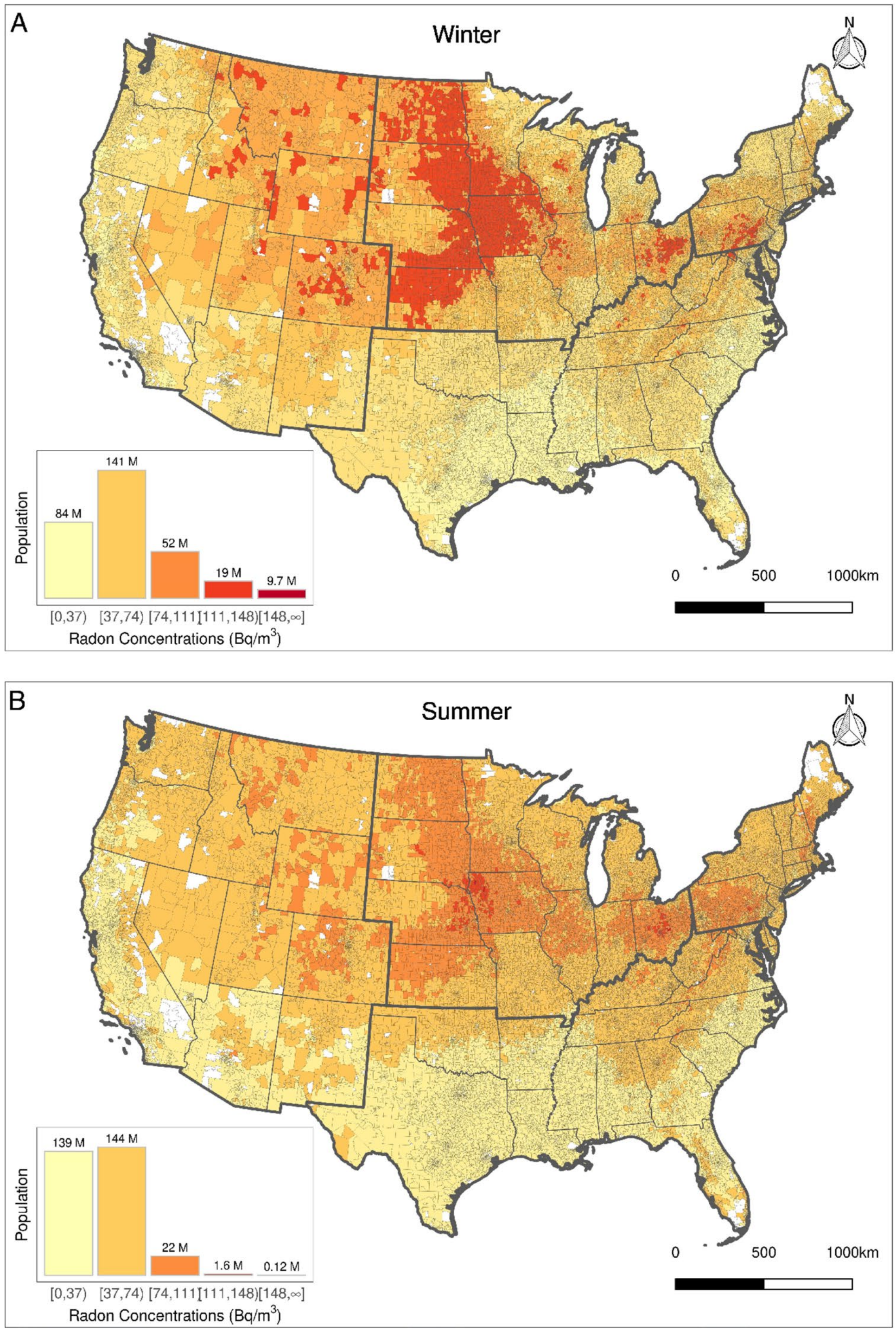

Fig. 4 Clear seasonal variations in monthly radon concentrations in the USA (Note: reprinted with permission from: [55])

consequently, appropriate safety policies are expected to be implemented [100, 101].

In a review prepared by [101] the authors suggest several measures related to shale gas development in the U.S. that could alleviate some of the identified problems:

- Enforce a 1-kilometer safety zone between newly installed shale gas wells and existing drinking water wells. This will reduce the risk of flammable gas contamination in drinking water wells in these areas.
- Discussions regarding the presence of natural gas in drinking water focus on whether it occurs naturally or is directly linked to contamination from shale gas well leaks. This issue can be addressed through mandatory baseline monitoring that incorporates modern

geochemical techniques, such as the analysis of major and trace elements.

- Full access to data, including the disclosure of all hydraulic fracturing chemicals, would foster an open, substantive, and scientific discussion that would help mitigate potential legal and social conflicts [100].

One of the interesting studies conducted on 1,270 samples of raw water (prior to treatment) collected from 15 major aquifer systems (PA) used for drinking water in 45 states across all major physiographic provinces in the USA. The samples were analysed for concentrations of the Ra isotopes ^{224}Ra, ^{226}Ra and ^{228}Ra. The results identified seven major aquifers out of the 15 studied in the US within the environmental protection limit of 0.185 Bq/L (5 pCi/L). It was noted that combined Ra (^{226}Ra plus ^{228}Ra) was present in 39 of 971 samples (4.02%) for which both ^{226}Ra and ^{228}Ra were detected. Furthermore, in 40 of 1,266 samples (3.15%) in which at least one of these isotopes [87]. Another study carried out in New Jersey in the USA, where the Kirkwood-Cohansey aquifer is a major source of drinking water and the availability of its resources is limited, has shown that high concentrations of radium are present in some areas [56]. Oil and gas (O&G) exploration, production, and wastewater management represent important anthropogenic sources of naturally occurring radioactive materials (NORM), particularly radium isotopes, which may contaminate soils and water resources. Wastewaters generated during oil and gas extraction frequently contain elevated concentrations of ^{226}Ra and ^{228}Ra, raising concerns regarding their disposal and potential impacts on human health and the environment.

Guidelines of Individual International Organizations

On June 21, 1934, the International Labor Organization (ILO) updated its list of occupational diseases to include conditions associated with exposure to radium, other radioactive substances, and X-rays. The updated list came into force in 1936, and a year later, radiation sickness was included in the occupational disease recognition system in at least five American states. World War II was a key moment in establishing the first exposure limit, set at 0.1 μc [78].

Salerno described in detail the working conditions of Italian migrants, particularly those who arrived in the United States from the early 1900s onward. Even then, extremely harsh and dangerous working conditions contributed to serious illnesses and, not infrequently, deaths. As a result, numerous groups of migrant workers began loud strikes. It was only their sacrifice and many years of struggle in the courts that contributed to the development of societies that endured tough working and living conditions during migration [79]. This high-profile precedent triggered a wave of beneficial changes in the system for introducing workplace controls and safety measures.

The EPA has classified radon as number 18 on the National Priorities List (NPL) out of 1,177. The EPA's assessment of each successive location, the number of locations where radon levels exceed background levels, may change slightly. Radon can have harmful effects on health, and these locations are potential or actual sources of exposure for people [72].

Various international institutions have established limits (μSv/year) for the maximum permissible dose [52]. For the general population, the Bundesamt Für Strahlenschutz [7], the International Commission on Radiological Protection [43], and the United Nations Scientific Committee on the Effects of Atomic Radiation UNSCEAR [84, 97]. Meanwhile, the maximum occupational exposure limit has been set at 2000 μSv/year by the BfS [7], ICRP [43, 44, 45], and UNSCEAR UNSCEAR [84, 97].

The Council of the European Union (December, 2013) developed European Basic Safety Standards (EU BSS), setting a maximum permissible annual average concentration of radon of 300 Bq.m-3 in dwellings and workplaces [93]. Similar guidelines were established by the International Atomic Energy Agency (IAEA) in IAEA Safety Standard Series No. GSR Part 3 [42].

Polish Regulation of the Council of Ministers of August 11, [75], point 4 of the Annex contains conversion factors for radon in residential buildings (1.1 Sv/J h m^{-3}) and in the workplace (1.4 Sv/J h m^{-3}).

Meanwhile, based on epidemiological studies and biokinetic models, the ICRP has also issued a recommendation for radon depending on the location:

- In underground mines (tourist or active), indoors (kindergartens, schools, offices, cafes, etc.) − 3 mSv/mJ h m^{-3},
- Indoors in areas associated with high physical exertion and for employees of tourist routes in caves − 6 mSv/mJ h m^{-3} [69].

In many cases, reference levels or guidelines - or strictly enforced regulations in some countries - apply to new buildings or specific types of workplaces [9, 17, 40, 41, 107]. Table 3 presents guidelines for individual countries and organizations.

Table 3 International exposure limits for radon

Organization	Level by Region	Levels in Workplaces
WHO	100 Bq/m^3 (max 300)	1000 Bq/m^3
EU (General)	≤300 Bq/m^3	300 Bq/m^3
Canada	200 Bq/m^3	200 Bq/m^3 (more than 4 h per day)
USA (EPA)	148 Bq/m^3	100 pCi/L for 40 h per week
UK	200 Bq/m^3	300 Bq/m^3 (annual average)
Ireland	200 Bq/m^3	300 Bq/m^3 (measured over a 3-month period)
Poland	300 Bq/m^3	300 Bq/m^3

Preventive measures focused on the future, intended to reduce the risk of diseases

Since radon and its decay products are recognized carcinogens to which workers in mines or healthcare (e.g., radiologists and pharmacists in radiopharmacy) may be exposed, the development and implementation of detailed occupational safety standards are essential to reduce the risk of disease [2, 46, 56, 102].

Extensive health promotion and preventive measures should be implemented:

- raising awareness of the dangers of radiation, especially among vulnerable populations: pregnant women, young parents, infants, and the elderly;
- implementing training courses for healthcare workers and high-risk workplaces, e.g., mines, radiology, nuclear industry workers, flight crews;
- continuous monitoring of radiation and radon concentrations in the workplace, especially mining cohorts and thermal baths;
- increasing ventilation in exposed areas, from mines to thermal baths;
- improving regular monitoring of factors that interfere with radiation and radon concentration measurements through key non-radiation-related risk factors;
- eliminating radium from all possible residues, e.g., paints, adhesives, old clocks with dyes, radium dial luminizers, relays (electromagnetic switches) for telephones;
- preparing quick, easy, and user-friendly tests to measure all of the above parameters;
- securing hazardous waste sites;
- cost-effective regulatory standards should be developed to support the safe treatment and disposal of O&G wastewater;
- groundwater quality should be routinely monitored, particularly in areas where radium occurs naturally, salinity is increasing, and geochemical conditions promote radium mobilization.

Specific exposure control strategies and occupational exposure limits should be established in accordance with national or regional regulations and should consider key workplace safety measures, including ventilation requirements and permissible radon concentration limits. [3, 9, 21, 78, 79, 91, 95, 102, 84, 97]

Limitation of study

The manuscript provides an overview of fundamental treatment approaches, both contemporary and historical. Individual radiotherapy techniques are not discussed in detail, as this falls outside the scope of the publication. The historical development of radium and its various applications is highlighted, emphasizing regional differences in preventive measures, evidence-based interventions, feasibility, and policy implications. Such differences may arise from multiple factors, including access to medical equipment (e.g., in more or less developed countries), the quality of medical equipment (e.g., age and regular depreciation), and compliance with international or European regulations, which may vary depending on the medical indications, knowledge, and experience of the medical personnel. The section on unconventional medical treatment using radium is also unique for its historical significance and innovation, which was used in practice before the outbreak of World War. The manuscript presents statements on health effects without specifying activity concentrations, absorbed doses, exposure duration, or comparisons with established regulatory limits. The quantitative context of many reported effects cannot be scientifically evaluated, particularly in cases where historical data are incomplete or obscured, such as those associated with the watchmaking industry.

Working Draft No. 3 of the RadoNorm project (WP3, Dosimetry) was developed to estimate potential absorbed doses using updated biokinetic and dosimetric models based on the latest recommendations of the International Commission on Radiological Protection (ICRP). These models describe the time-dependent distribution and retention of radionuclides within the human body, organs, and tissues, enabling retrospective assessment of historical radiation exposure and contributing to improved dose estimation for future generations.

Conclusion

Although radium has well-documented adverse health effects, certain radium isotopes continue to have specific applications, particularly in the treatment of selected cancers. Coordinated international efforts involving scientists, policymakers, and healthcare professionals are essential for developing comprehensive strategies focused on exposure prevention, radiation monitoring, early detection of health effects, and targeted educational initiatives, especially in occupational settings. Furthermore, multidisciplinary research is needed to better characterize the impact of radium exposure on human health and to support the development of evidence-based public health interventions.

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Declarations

Conflict of interest The authors declare no conflict of interest.

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Clinical trial number not applicable.

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