Low radiation dose to treat pneumonia and other inflammations

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Abstract

Infection, the invasion of pathogenic microorganisms and viruses, causes reactive inflammation mediated by endogenous signals, with influx of leucocytes with distinct properties and capable of mounting a cellular or antibody response. Different forms of inflammation may also occur in response to tumours, in allergy and autoimmune disorders. Pneumonia, respiratory tract infection and septic shock for instance can arise as serious complications of the Covid-19 virus. While radiotherapy has been most widely used to control malignant tumours, it has also been used for treatment of non-malignant diseases, including acute and chronic inflammation in situations where anti-inflammatory drugs may be ineffective or contraindicated. The present review examines the history and prospects for low dose anti-inflammatory radiation treatments, the present interest largely being motivated by the increased incidence of pulmonary disease associated Covid-19 infections. Evidence in support of the suggested efficacy are covered, together with an appraisal of one of a number of potential convenient sources that could complement external beam arrangements.

Keywords: radiotherapy, X-rays, low X-rays dose, pneumonia, lungs, infection.

Introduction:

The spread of Covid-19 coronavirus (SARS-CoV-2) and with it the widespread advent of homeostasis breakdown, has led to greater appreciation worldwide of frailties in the pulmonary system, especially in those suffering pre-existing health issues. Acknowledging the major efforts being made towards seeking effective treatment, particularly in respect of patients requiring breathing assistance, a notable increase in interest has been noted in low dose radiotherapy treatments to inhibit the inflammatory phase of the illness which appears to be the main cause of death.

In this review, the focus is upon low dose radiation treatments for asthma, pneumonia and other lung diseases, accompanied by possible response mechanisms, and studies to-date. The work will also look at potential treatment options (e.g. external beam, radioactive aerosols, gases, e.g. ^{222}Rn, also ^{133}Xe and ^{85m}Kr) and dose regimes. Also worthy of consideration is the potential link to radiation hormesis, noting that in 1896, the year that followed that of the discovery X-rays, hormesis was first used to treat inflammation and cancer, as recorded by Shrader (1, 2).

While the physiologic response to ionising radiation is typically understood to be directly proportional to the logarithm of dose (3, 4), at the lower dose end at values approaching annual exposure levels observed in areas of higher background, hormesis has been suggested to be a useful adaptive phenomenon. In particular, it is considered to stimulate the immune system, improving physiological performance and increasing mean lifespan (4), the opposite effect arising at large doses (5). This simulation of the immune system has been the subject of a good many studies (6, 7). Radiation is not usually the first treatment option for non-malignant diseases, because of the risk of radiation tissue damage (with higher doses) and malignant induction as a late sequela, but for many decades radiotherapy has been used to ameliorate acute and chronic inflammation. The situation has been reviewed by others, several quite recently (8), others offering primary data extending back to the early decades of the 20th century (e.g. Rousseau et al., 1942, the particular group offering patient data from their use of 120 kVp x-rays delivering doses of some 1.75 Gy air dose at a dose rate of ~ 0.15 Gy min^{-1}) (9).

Anti-inflammatory drugs vs low dose X-ray in treating covid-19

The present resurgence in interest in low dose treatments is clearly linked to efforts to find effective and safe treatments for Covid-19, a viral disease with an associated high morbidity rate, especially for those expressing immune-supressed responses. Pneumonia and other assorted lung diseases have been noted to be serious complications of Covid-19, accompanied

by cytokine release syndrome. This syndrome can lead to death from respiratory failure. The pathology of Covid-19 can be divided into three stages; the first stage directly arising from the virus, with the patient being seen to benefit from the use of anti-inflammatory drugs. The second stage is caused by the host immunological response to a viral pneumonia. Depending on the degree of resulting hypoxia, the patient may need assisted or mechanical ventilation as well as drugs such as sulphonamides or potent glucocorticoid steroids, obviously to be used with caution. The latter class of drugs do reduce lymphocyte numbers and their functional role is noted in providing cell mediated immunity. While the majority of patients do not evolve into this third stage, the disease can at this stage develop into a syndrome of extra-pulmonary systemic hyper-inflammation and release of pro-inflammatory cytokines.

To date, there has been no standardized treatment for such a hyper-inflammatory state. The only treatment options are those aimed at the side effects caused by the virus, such as inflammation and pulmonary acute respiratory distress syndrome (ARDS). Inhibition of this process is the aim of inflammation treatments, as in the case of using corticosteroids. Indeed, the WHO in a report of October 2020 have put on record that to-date corticosteroid dexamethasone has been the only drug found to be effective for therapy of patients with severe disease (WHO Director General briefing on Covid-19 of 16 October 2020) (10), although similar steroids, such as prednisolone, have been recommended along with high dose antibiotics in severe pneumonias due to pneumocystis infection. While low dose radiotherapy is known to have an anti-inflammatory effect, it must also be mentioned that high dose radiation can lead to inflammation via the production of pro-inflammatory cytokines (11), as well as the known mutagenic risk, which can lead to cancer induction. As such, it is to be anticipated that low dose treatment would only be considered for those displaying the effect of ARDS. Here it is to be mentioned that pneumonia, infection and inflammation of the lungs, caused by bacterial, viral or fungal infection, results in the alveoli filling with fluids making breathing more difficult, resulting in low oxygen levels in the blood stream and consequent deleterious effects, death included.

During the first half of the 20th century low doses of X-rays (of some 50 mGy to 1.5 Gy, as couched herein in SI dosimetric terms) were used to treat the three forms of pneumonia; lobar, bronchopneumonia, and atypical pneumonia. Data have been shown to support the claim that the treatments were effective, this form of treatment proving to have similar competency to that of serum therapy and sulphonamides (9). Besides treating pneumonia with X-rays, other inflammatory diseases such as furuncles and carbuncles (caused by staphylococcal infection)

were also treated with a single dose of X-rays, of 0.75-2 Gy (12). Carried out during the first half of the 20th century, they were reported to be effective, resulting in rapid decrease in acute pain and accelerated healing process. The general perspective was that X-ray treatment at these doses induced reduction of inflammation, with promotion of healing via a combination of immune alterations, such as enhanced phagocytosis and anti-localization effect on the pathogenic organism leading to death (12).

The anti-inflammatory effect of low doses of X-rays were observed in a number of other pioneer studies (9, 13). The investigations of Heidenhain and Fried on panaritium and paronychia (caused by bacteria, virus or candida) were based on the use of single doses of 1.0 – 1.5 Gy, work cited in associated literature of the time (13). Subsequently Pape and Seyss (1949) (14) recommended the use of even smaller doses, viz 0.05 Gy, a value not differing greatly from some of the more elevated dose diagnostic x-ray procedures. In the latter cases, the particular applications was not of pulmonary treatments but of skin, with skin and nail inflammations reviewed by Fröhlich et al., 2008 (15), Table 1 being presented together with other evidence for cure and improvement rates that were suggestive to be of a compelling nature. Concerning the foregoing review of historical low dose treatments of pneumonia and other inflammation, the authors have sought to provide the best possible representation of the existing literature, no substantive report being knowingly excluded from the review. Similar comments can be made in regard to the sections below, reference being made to a number of modern approaches, all remaining at the clinical trials stage.

Table 1: Results of radiotherapy for panaritium and paronychia.

Authors	No. of patients	Cured		Improved		Total (%)
	N	N	%	N	%	
Heidenhain & Fried (1924) (13)	6	2	33	3	50	83
Kingreen (1926) (16)	6	2	33			33
Pape & Seyss (1949) (14)	76	71	93			93
Holeczke (1962) (17)	91	38	41	27	30	71
Böhringer & Nitz (1973) (18)	202	159	79			79
Hassenstein (1976) (19)	24	15	63	7	29	92
Drescher et al. (1979) (20)	51	37	62	7	14	86
Fröhlich et al. (2001) (21)	252	89	36	114	45	81

From: Inflammatory Disorders: Furunculitis, Hidradenitis, Panaritium and Paronychia, Dietmar Fröhlich, Dieter Baaske, Michael Glatzel, pp 523-536. In: Radiotherapy for Non-Malignant Disorders (Ed: Michael Heinrich Seegenschmiedt, Hans-Bruno Makoski, Klaus-Rüdiger Trott, Luther W. Brady). Pub: Springer. (2008) (15).

Future prospects

The serious pulmonary complications of Covid-19 occur via mechanisms that have yet to be fully elucidated, albeit resulting in massive release of proinflammatory cytokines (the so-called cytokine storm), in turn causing the syndrome of acute respiratory distress (ARDS). The first known death from Covid-19 was recorded in Wuhan in January 2020, and by the end of May 2020 was the leading cause of death in the world, exceeding breast cancer and malaria. Although radiotherapy is not usually the first treatment option in challenging acute and chronic inflammation, there is nevertheless a history of such use as previously discussed.

Presciently, Calabrese and Dhawan (2013) reviewed the use of low-dose radiotherapy (LD-RT) for the treatment of pneumonia from the 20th century, reporting good response rates, reducing pneumonia mortality from approximately 30% to 10% on average, and resolution of symptoms (22). The mechanism of X-ray LD-RT good response is due to the induction of an anti-inflammatory phenotype that brings about the reduction of inflammation and pain, promoting tissue recovery, leading to a rapid reversal of clinical symptoms, resulting in the resolution of the disease. The authors concluded a single dose in the range of 0.3-1 Gy could induce anti-inflammatory response (23). Conversely, for Covid-19 patients in the acute phase of the disease, in the event of moderate or severe “cytokine storm” (hyper-inflammatory state), Dhawan et al. have proposed a total dose of 0.3-0.5 Gy in the thoracic region of patients to decrease the intensity and severity of Covid-19 pneumonia (24).

In current trials, as for example at Emory University (25), low dose (0.5 to 1.5 Gy) radiotherapy is now being investigated in treatment of the Covid-19 ARDS situation, Hess at al. reporting a pilot study in a single institution. The group have reported evaluation of the safety and efficacy of a single-fraction, low-dose whole-lung radiation for five elderly hospitalised subjects (out of nine screened). Of median age 90 years (range, 64-94 years) these were Covid-19 pneumonia patients that were oxygen dependent (four out of the five were nursing home residents with multiple comorbidities), with a follow-up for a minimum of seven days. Both lungs of the patients were irradiated with a single dose of 1.5 Gy, delivered over a course of 10-15 minutes. Four (80%) of the treated Covid-19 elderly patients showed rapid improvements in breathing, and recovered to allow the breathing of room air within a mean of 35 hours (range, 3-96 hours)

and suffered no acute toxicity or cytopenia. It was concluded that low-dose whole-lung is safe and shows early promise of efficacy (25).

Further to the above, Algara et al. (2020) reported a multicentric prospective clinical trial to evaluate the efficacy of bilateral lung low-dose radiotherapy for interstitial pneumonia in Covid-19 patients, the step being undertaken to improve respiratory function (11). Ten patients were enrolled for the exploratory phase to assess the feasibility and efficacy of LD-RT lung irradiation, with the aim of an increase in efficiency of 20% PaO_2/FiO_2 ratio [partial pressure of oxygen (PaO_2) and percentage of fraction of inspired oxygen (FiO_2)] with respect to the pre-irradiation value for continuation of study. Phase 2 refers to a non-randomized comparative phase in two groups. For this, a total of 96 patients have been enrolled, divided in accord with a 1:2 ratio (32 and 64, forming the control and experimental groups respectively). The control group will only receive pharmacological treatment, while the experimental group will receive pharmacological treatment and LD-RT. The objectives are an increase in PaO_2/FiO_2 in covid-19 patients with pneumonia, the safety of bilateral lung LD-RT, and an improvement in the radiology image. The primary completion date is estimated at May 4 2021, with a study completion date of July 1 2021 (11).

Given the outlook for successful outcome from low dose radiotherapy, one issue worthy of exploration is the potential use/utility of various potential candidate radioactive gases as alternatives to external beam arrangements, some being currently applied in lung imaging studies, as for example ^{133}Xe and ^{85m}Kr. Moreover, it is known that in some countries current use is being made of radon gases for therapy. Indeed, in Japan radon is being applied for adjuvant therapy for various types of cancer (26-28), also as part of an investigation of the treatment of asthma. In the latter case Mitsunobu et el. (2003) investigated the treatment of bronchial asthma, with nine asthmatics involved in a pilot study in a hot springs room of high humidity within which the radon levels were 2.080 kBq m^{-3} (29). Nasal inhalation, understood to be the most efficient means of uptake, was performed for 40 minutes each day, on day 1, 7, 14, 21, and 28 from the onset of therapy. Measurements were made of the activities of superoxide dismutase (SOD) and catalase (CAT), component parts of an endogenous enzymatic and non-enzymatic antioxidants defence grid, also their suppressive effect upon lipid peroxidation. Also measured following maximal inspiration was the forced exhalation volume of air exhaled in the first one second (FEV_1). Among adults, an FEV_1 of less than 1 L indicates significant lung disease. At 28 days, the $\%FEV_1$ was observed to be significantly increased in association with increased CAT activity and decreased lipid peroxide level (29).

To-date, the various low dose therapies applied to tackling ARDS have made exclusive use of penetrating photon beams. While these provide an intense external source, as a means of electron dose deposition they are relatively inefficient, with x-ray transmission typically dominating over absorption. The use of a gaseous source might well improve upon the dose deposition efficiency, providing a close-up treatment also delivering dose where it is needed. However, in respect of gaseous sources, among the various questions that would need to be answered would be whether it is possible to produce the radioactivity in sufficient specific activity in order to deliver the low-dose therapeutic effect that is being sought, also taking into account other considerations such as practicality and safety? In the case of the use of ^{133}Xe in lung insufficiency studies, unless specifically protected by exhaust systems and rooms with negative pressure, delivery is typically in a closed system involving respirators and spirometers, with leakproof tubing to mitigate radionuclide loss into the working environment. A similar arrangement would be expected of radon therapy, with exhaled gas controlled in compliance with the appropriate regulations attached to the use of radionuclides.

Among other questions of viability are whether candidate nuclides could realistically represent the needs of theranostic agents, x- and gamma emissions providing for source distribution/localisation and particulate emissions the dose deposition. In the following we look in some detail at the case for radon therapy, a predominant alpha emitter, deferring discussions of the viability of other radioactive gases, the ^{99m}Tc-based technegas included (formed of ^{99m}Tc –labeled solid graphite particles of submicron diameter, approximately 100 nM (0.005-0.2 μm) in argon carrier gas), to future opportunity.

Deposition-flux of ^{222}Rn towards delivering lung dose

Notwithstanding, the controversial aspects of radon as a therapeutic agent, adopted for many years in treating various diseases, including low back pain, high blood pressure, and cancer, it is nevertheless the case that direct α-particle hits and reactive oxygen species (ROS) damage biomolecules. In the case of ROS, these are predominantly hydroxyl radicals and hydrogen peroxide. Damaged cells also send signals to adaptive biological protection systems that function against the effects of radiogenic and nonradiogenic toxins and also pathogens. This is suggested to stimulate many of the natural protection systems of the body that normally cope with endogenous oxidative stress and the effects of toxins, injuries, diseases, etc (5, 30). If low-dose γ-radiation occurs in the hormetic dose and dose-rate range, these are suggested to function much more intensely (4, 12, 22, 26-28, 30-34). Here, the complexity associated with the production of dedicated short-lived radionuclides for targeted α-emitting therapies can be

compared against the relative ease of fabricating radon gas sources from the ubiquitous supply of naturally occurring ^{226}Ra. Accordingly, the possibility of using radon inhalation therapy in confronting ARDS may offer both radiobiological as well as practical appeal. Subsequent to therapeutic intake, the gas will disappear quite rapidly (^{222}Rn has a physical 3.8-day half-life), with no anticipation of long-term tissue accumulation (28).

Radon gas decays via a series of solid short-lived radionuclides (Table 2), the progeny freely attaching with the aerosols in air, depending in great part upon the size of aerosols. The free fraction, when inhaled along with air, is mostly removed in the upper part of the respiratory tract; conversely, the aerosol-attached fraction adheres to the mucosa of the trachea and lung surface. Some are taken up by alveolar epithelial cells and transferred into the bloodstream together with oxygen. The progeny decaying in the lungs will dissipate their energy in the lung cells, the basal cells being accordingly affected/damaged (Table 2). The probability of lung tissue damage depends upon the amount of energy dissipated per unit mass, i.e. dose received by different regions of the lung. Nearly the entire lung dose arises from inhalation of the radon progeny aerosol and not from the parent radon gas itself. As radon is inert, when inhaled, the short-lived radon progenies are assumed to be attached to particles of an activity median aerodynamic diameter of 200 nm. A large proportion of the inhaled radon progeny deposits in the respiratory tract of the lung, while almost all of the gas that is inhaled is subsequently exhaled. Notwithstanding the short half-lives of the radon progeny (<30 min), dose is delivered to the lung tissues well in advance of major clearance occurring, either by absorption into the blood or by particle transport to the alimentary tract. Dose to lung is defined as the energy absorbed per unit mass of the lung tissue. Doses from inhaled radon are determined largely by the deposition of its alpha particle-emitting decay products on the lining epithelium of the respiratory tract. Two of the short-lived radon progenies (^{218}Po and ^{214}Pb) decay by alpha emission and dominate dose to lung tissues. As a consequence, the lung dose contributes more than 95% of the effective dose, a highly efficient process when compared against the situation for external beam photon sources.

Table 2: Physical characteristics of ^{222}Rn and its progeny. Data were retrieved from the ENSDF library via the NuDat-2.8 interface (http://www.nndc.bnl.gov/nudat2/). Low intensity (< 4%) γ-lines are omitted.

Radionuclides	**Half-life**	**Decay mode**	**Decay energy (keV) and Intensity (%)**			**Mean dose (MeV/Bq-s)**	**Tissue range (μm)** (Lea, 1955) (35)
			Eα (Iα)	$E_{(\beta^-)mean}$ $(I_{(\beta^-)total})$	**Eγ (Iγ)**		
^{222}Rn	3.8222 d	α (100)	5489.48 (99.920)	-	-	5.4851	41
^{218}Po	3.098 m	α (99.98); β^- (0.02)	6002.35 (99.9789)	-	-	6.00108	47
^{214}Pb	26.8 m	β^- (100)	-	223 (100.9)		0.225	
					241.9950 (7.251)	0.01755	
					295.2228 (18.42)	0.05438	
					351.9321 (35.60)	0.12529	
^{214}Bi	19.9 m	α (0.021); β^- (99.979)	-	642 (99.7)		0.640	
					609.320 (45.49)	0.2772	
					1120.294 (14.92)	0.1671	
					1764.491 (15.30)	0.2700	
^{214}Po	163.6 μS	α (100)	7686.82 (99.9895)	-	-	7.68601	71
^{210}Pb	22.20 y	β^- (100)		6.1 (100)		0.0061	
					46.539 (4.25)	0.001978	
^{210}Bi	5.012 d	β^- (100)		389 (100)		0.389	
^{210}Po	138.376 d	α (100)	5304.33 (100)			5.30433	39
^{206}Pb	Stable						

The absorbed dose (in Gy) from a treatment involves complex calculation, made more challenging still given the mechanisms by which the different radiations produce health effects. The concentration of radon progeny is usually expressed through the quantity called potential alpha energy concentration (PAEC) defined as total energy of alpha particles emitted by the radon progeny in a unit volume of air and calculated from the following formula:

$$\text{PAEC} = \sum_{i=1}^{4} C_i E_i \quad (1)$$

with C_i the number of atoms of the ith radon progeny in 1 m^3 of air and E_i the corresponding potential alpha energy in units of joule (J).

The exposure to radon progeny X (expressed in J s m^{-3}) is the product of the average PAEC and duration of exposure:

$$X = \text{PAEC} \times t \quad (2)$$

The exposure can be quantified in terms of the time integral of the activity concentration of radon gas (h Bq/m^3). This is related via the equilibrium factor, F, which is a measure of the degree of disequilibrium between radon gas and its progeny. The fraction of the intake deposited in the respiratory tract mainly depends on physiological parameters such as breathing rate.

Herein, we express the dose received as simply the radon concentration and duration of each treatment, recognizing each patient will inhale air at a different rate. Taking into account the above-mentioned factors, a method for calculation of dose received by human lung has been developed by the ICRP (1966) (36). Here the detailed procedure by which dose has been calculated has been assigned to an Appendix to this work.

In the present example of radon gas treatment, clearly to be appreciated is the much greater linear energy transfer (LET) of alpha particle radiation, with for instance Sedlak (2019) (37) concluding that for radon progeny the oncogenic effect is comparable to that of alpha particles with an LET of 75 keV μm^{-1}. For x- and gamma-ray irradiations the LET is more typically encompassed within the range 0.2 to 3 keV μm^{-1}, a fact pointing to the much greater radiobiological effectiveness (RBE) of the radon gas progeny, with an expectation that lower doses provide for the same effect as that obtained with much greater photon irradiation doses, clearly linked to the much-reduced range of high LET radiation in tissues. Balanced against these positives are a number of patient-based realities, lung lesions tending to be peripheral

(extending deep within the bronchial tree), with a consequent need for simulation of dose distribution towards controlling dose delivery. As part of the need for optimum radon concentration, account needs to be included of ventilation/perfusion, the upper lobes being the better ventilated, and of a patient being prone or supine for some fraction of the time, factors that can foreseeably affect radiation dose distribution. Additionally, given that the gelatinous lung and the bronchial lumen inflammation may themselves oppose gaseous diffusion, this might be expected to give rise to greater dose in the upper bronchial tree relative to its lower and most affected regions. These are issues in which Monte Carlo simulations might be expected to play a major role in obtaining elaboration.

Conclusion

While the use of low dose X-ray treatment of lung diseases has a history of in excess of 80 years, empirical evidence for the verity of treatment remains limited. Associated with the limitation is the reality that since the 1940s the side effects of pulmonary disease have been overwhelmingly managed by anti-inflammatory drugs, accordingly with low dose treatments retaining little interest. However, the situation is changing with the advent of Covid-19 pandemic and the acute respiratory distress syndrome (ARDS). To-date this has accounted for the loss of many lives, particularly so among the elderly among whom there is found to be a reduced ability to fight off the infection and inflammation, even in the presence of the use of anti-inflammatory drugs such as corticosteroids. Low dose therapy may well represent a promising tool in suppressing severe inflammation, albeit with a body of evidence that remains sparse, a matter that deserves to be revisited and addressed. Moreover, it also should not be assumed that external beam penetrating photon radiation offers the best radiobiological solution for those who are triaged to receive such treatment. There would seem for instance to be a good case for investigating gaseous sources, delivering dose where needed. Given that, steroid medications can be contraindicated in some patients, or have to be discontinued, so there may be subclasses of patients where radon or other gaseous sources may be a good alternative. Issues of practicality and safety notwithstanding, including to medical carers in the vicinity of sick patients, the relative risks from mutagenic response would seem small when there are those who are confronted by manifest ARDS. The need for more in-depth research is greatly apparent, with this also examining the question of optimum dose and the radioprotection of hospital staff.

Appendix 1

A factor has been chosen for the conversion of Equilibrium Equivalent Concentration (EEC) of radon into effective dose equivalent rate. Both ICRP (1981) (38) and OECD (1983) (39) have given the functions derived from the dosimetric models relating the effective dose equivalent to PAEC in terms of aerosol activity median diameter (AMD) and free atom fraction of potential alpha energy (f_p). The typically adopted AMD = 0.2-0.3 and $f_p \leq 0.05$. The effective dose equivalent (H_E) can be obtained by using the radiation weighting factor W_R=20 for alpha particles and tissue weighting factor W_T = 0.06 for the respiratory tract of lung. A simplified formula can be used to calculate the effective dose equivalent per unit of potential energy exposure (i.e., dose coefficient), as follows:

$$H_E = W_R \times W_T \times B_R \times f_p \quad (3)$$

UNSCEAR (1988) (40) have reported a simplified breathing rate coefficient (B_R) of 0.8 m^3/h for the male general population by considering both indoor and outdoor residence, while Marsh (2000) (41) reported a breathing rate of 0.78 m^3/h for an average weighted physical activity of an adult Caucasian male. The average breathing rate for a reference adult male at home is 0.78 m^3 /h (ICRP, 1994) (42). (ICRP, 1993) (43) recommended the dose coefficient of 4 mSv per WLM (working level month) for members of the public. Using the conversion 1 WLM = (6.37E+5/F) h Bq/m^3 where F (= 0.4) is the equilibrium factor (Harrison and Marsh, 2011), the dose coefficient for radon progeny for a general population becomes 2.51 nSv.m^3/hBq. ICRP (2010) (44) again reviewed and analysed more recent epidemiological data on lung cancer risks from radon, and provided a revised detriment-adjusted nominal risk coefficient of 5×10^{-4} per WLM. Using this risk coefficient and the revised detriment values published in ICRP (2007) (45), the dose conversion convention gives values of 9 mSv per WLM for members of the public (5.65 nSv.m^3/hBq) (Marsh et al., 2010) (41). The range of effective dose equivalent per unit of potential energy exposure obtained from the OECD, UNSCEAR and ICRP are as in Table 3.

Table 3: The recommendations of the radiation protection agencies for the conversion of potential alpha energy exposure (Bq h m^{-3}) to effective dose equivalent (nSv).

Organization	Dose conversion factor (nSv/h per Bq/m^3)	Breathing rate (m^3/h)	Aerosol activity median diameter (AMD) (µm)	Free atom fraction of potential alpha energy (f_p)
ICRP (42-44, 46-51)	7-17	1.2	0.2-0.3	0.05-0.00
OECD (39)	8-16	0.75	0.1-0.2	0.05-0.02
UNSCEAR (40, 52, 53)	9-17	0.8	0.1-0.2	0.05-0.025

As seen from Table 3, the range recommended by ICRP covers the values recommended by OECD and UNSCEAR. Therefore, the ICRP value of (7-17) nSv per Bq h m^{-3} will be used for conversion of potential alpha energy exposure to dose equivalent. If one wants to use a single value of DCF, the UNSCEAR value of 10 nSv per Bq h m^{-3} is recommended.

It may be noted that all the dosimetric coefficients given above refer to adult members of the public. Correction factors should be applied for infants and children to account for age dependent change in lung mass and breathing rate. The effective dose equivalent for the age group up to ten years might, on the average, be a factor of 1.5-2 greater than for adults.

ICRP develops the aforementioned dose coefficients ((ICRP conversion factor, 1 Bq/m^3 = 7-17 nSv/h) to simplify the calculation of equivalent dose and effective dose for inhaled or ingested radionuclides. In the simplest terms, calculating the dose from inhaling radon involves multiplying the average radon level (e.g. in Bq/m^3) by the time spent, and the right dose coefficient, as follows:

Effective dose (nSv) = Radon level in breathing zone (Bq/m^3) × Time (h) × Equilibrium factor × Dose coefficient (nSv/Bq h m^{-3}) (4)

Here, the radon concentration in indoor air (Bq/m^3), often referred to as Ac (^{222}Rn), appears in relation (4) as the radon gas level in the breathing zone, while F is the equilibrium factor between radon and its progeny indoor air (F = 0.4), time denotes the exposure duration (in h), and D = 2.51 × 10^{-6} mSv (Bq m^{-3} h)$^{-1}$ (ICRP, 1993a) (43) and D = 5.65 × 10^{-6} mSv (Bq m^{-3} h)$^{-1}$ (ICRP, 2010) (44) is the dose conversion factor for the general population.

Assuming the air volume in the lungs to be 3.2×10^{-3} m^3 for 'Reference Man' and assuming further that the short-lived decay products will stay in the lungs, the dose rate due to alpha-radiation can be determined as ICRP (1981) (47, 54):

$$D_{Lung}\left(\frac{nGy}{h}\right) = 0.04 \times A_{Rn\ Air}\left(\frac{Bq}{m^3}\right) \quad (5)$$

In order to calculate the radon concentration needed to deliver 1 Sv/h to a patient, the left-hand side of relation (4) should simply be divided by the radiation weighting factor ($W_R = 20$ for α-particles) and tissue weighting factor ($W_T = 0.12$ for the whole lung, $W_T = 0.06$ for the respiratory tract of the lung). Accordingly, the radon level in the breathing zone is then found to be approximately 2.4×10^9 Bq/m^3 (using $W_T = 0.12$) and 1.2×10^9 Bq/m^3 (using $W_T = 0.06$) for the whole lung and respiratory tract of the lung respectively. In respect of radon generators that can provide for this, at this point we simply cite work on the development and utilization of a safe generator of radon in cell radiation studies, formed from 2.9 GBq of radium salt, providing dose rates from 0.03 to 0.3 Gy h^{-1} (54, 55).

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Conflict of Interest

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