Environmental Radon Gas and Degenerative Conditions – An Overview

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Abstract

Radon, a naturally occurring radioactive gas, has variable distribution in the environment as a decay product of uranium occurring in a wide range of rocks, soils and building materials. Although radon dissipates rapidly in outdoor air, it concentrates in the built environment, and inhalation of ^{222}Rn and its progeny ^{218}Po and ^{214}Po is believed to provide the majority of the radioactive dose to the respiratory system. While the connection between radon and lung cancer has long been recognised and investigated, recent studies have highlighted potential links between radon and other conditions, among them Multiple Sclerosis, Alzheimer's and Parkinson's Diseases, and Paget's Disease of Bone. A strong case exists for clarifying the relationship between radon and these other conditions, not least since radon remediation to reduce lung cancer may conceivably have additional benefits hitherto unrecognised. The present status of the postulated links between environmental radon gas and degenerative conditions is reviewed, and recommendations for further research into leveraging current anti-radon campaigns are made.

1 Environmental Radon Gas

1.1 Occurrence

Radon is a naturally occurring radioactive noble gas, having variable distribution in the geological environment as a decay product of uranium [1], commonly occurring in a wide range of rocks and soils, and in building materials incorporating or manufactured from these. The incidence is governed by geochemical affinities, with primary concentrations of uranium generally lowest in basaltic igneous and carbonate sedimentary rocks, medium values occurring in the bulk of sandstones, with felsic igneous rocks, with their hydrothermally mineralised auroles, exhibiting the highest concentrations [2]. Within these broad classifications, secondary geological processes may significantly modify this simplistic classification, with the result that unexpectedly high radon concentrations may occur in otherwise innocuous areas, and the converse. There are three naturally occurring isotopes, ^{222}Rn, a direct product of ^{226}Ra in the ^{238}U decay-series with a half-life of 3.8 days, ^{220}Rn, a decay product of ^{232}Th, with a half-life of 55.6 s, and ^{219}Rn, a decay product of ^{235}U, with a half-life of 3.6 s. Of the three isotopes, ^{222}Rn is the most significant, its relatively long half-life and high mobility enabling it to move out of the bedrock, particularly if this is well-faulted, into the soil overburden, where it ultimately forms part of the soil gas.

The distribution of environmental radon is geographically dependent, exhibiting significant variations across relatively small distances, generally in response to

local geological conditions. This is particularly true in the British Isles, which possess a complex geology extending virtually continuously from the Pre-Cambrian to the Holocene.

Figure 1 shows the geographical distribution of radon across the United Kingdom [3] and the Republic of Ireland [4]. Although the highest levels are found in the granite areas of the South-West peninsular (Devon and Cornwall), elevated levels are found elsewhere in the country, with localised regions of high concentration found in Northamptonshire in the English Midlands and in Derbyshire in the Peak District. Similar mapping is under way, or completed, for much of Europe.

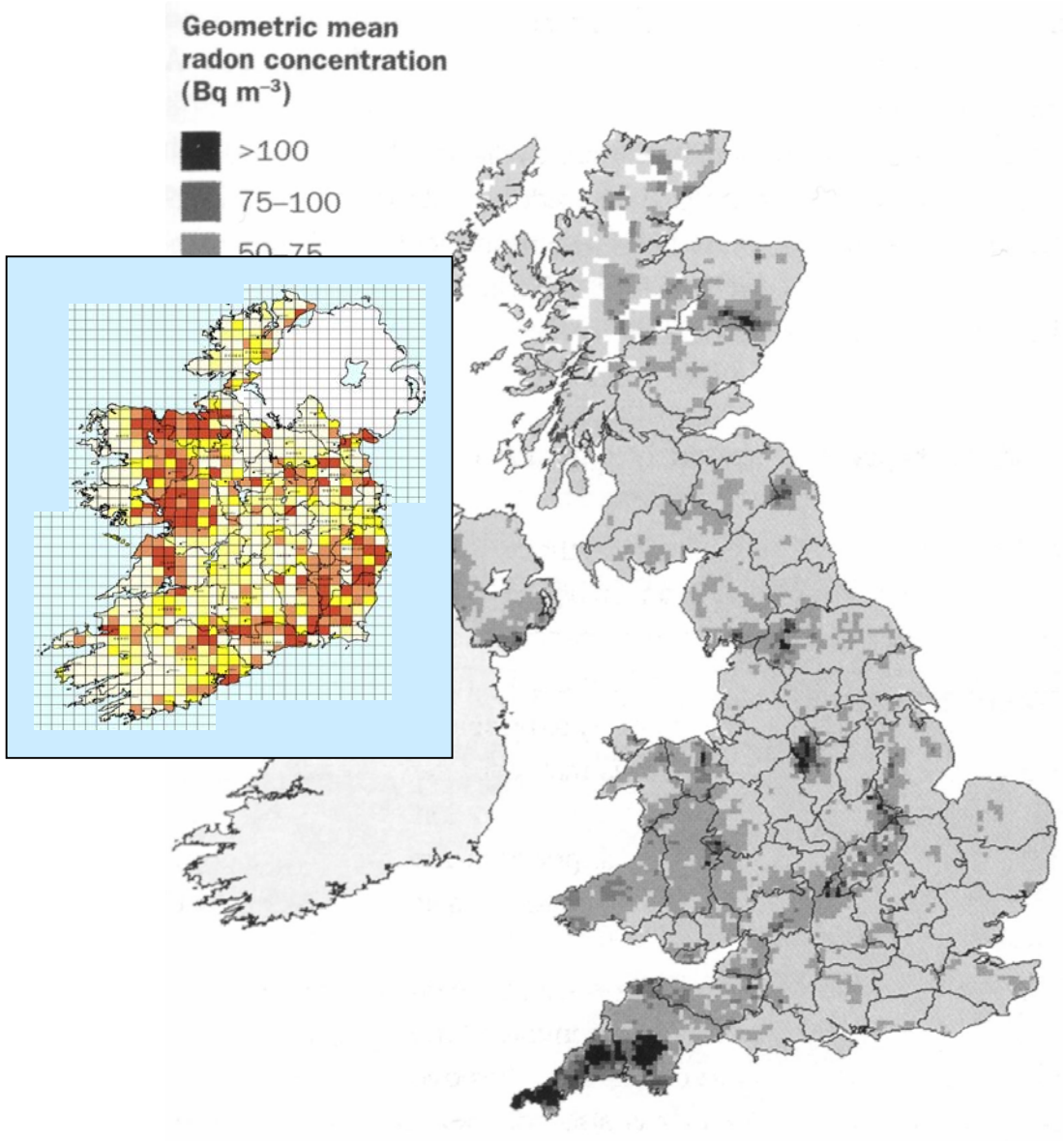

Figure 1: Geographical distribution of radon across the United Kingdom [3] and (inset) the Republic of Ireland [4]

Although radon dissipates rapidly once in outdoor air, it concentrates in the built environment, typical ingress routes being cracks in walls and floors, drains and loose-fitting pipes. For UK dwellings, the mean radon concentration is around 20 Bq·m^{-3}, compared to 4 Bq·m^{-3} in outside air [5], but concentrations up to

17,000 Bq·m^{-3} have been found in homes in Cornwall, England [6], and even higher concentrations in Co. Kerry, Ireland [7].

1.2 Physiology

The most significant isotope, ^{222}Rn, decays by ¤-emission (half-life 3.8 days) to ^{218}Po and thence to ^{214}Po, both ¤-emitters, the final decay product being the stable lead isotope ^{206}Pb. These heavy-metal daughter-products are highly toxic and are readily adsorbed onto atmospheric particles, posing a significant health hazard. Inhalation of ^{222}Rn, and its ¤-emitting progeny ^{218}Po and ^{214}Po, is believed [8] to provide the majority of the radiation dose received by the respiratory system. This radioactivity damages the sensitive inner lining of the lung, increasing the risk of lung cancer, and a direct consequence of the trapping of radon and its decay products in the lung has been the association between enhanced levels of environmental radon and increased risk of lung-cancer [9, 10, 11], and the recognition of radon as a multiplicative factor in the incidence of lung-cancer among smokers. It is estimated [10] that the annual mortality from exposure to radon in buildings represents 9% of all deaths from lung cancer in Europe, suggesting that around 3000 deaths annually are caused by exposure to radon and its progeny in the Europe.

Radon is known to form clathrate structures with water and alcohols, both of which are abundant in animal tissue. Radon is lipid-soluble, nearly two orders of magnitude more soluble in hydrocarbons with some polar functions as compared with water [12], and does not distribute evenly throughout the body [13]. Although most inhaled radon is immediately exhaled, some becomes trapped in the lungs and migrates to the blood-stream, from whence it accumulates in lipid tissue throughout the body, with the highest concentrations occurring in the brain, bone-marrow and nervous system. Although radon gas dissolves readily in lipids, with solubility increasing with increasing number of carbon atoms per molecule [12], moving freely around the body, including into and out of the brain despite the blood-brain barrier, its highly neurotrophic and neurotoxic heavy-metal decay products are lipid-insoluble, remaining trapped at the location where they are generated. They consequently provide localised sources of both radioactivity and heavy-metal toxicity, leading to radiation damage and chemical injury to the body cells.

1.3 Radon and Degenerative Conditions

In addition to lung-cancer, radon and its progeny have recently become associated with an increasing number of degenerative conditions [14, 15, 16]. Recent study of the occurrence of heavy-metal radon progeny ^{210}Po (¤-emitter) and ^{210}Bi (¤-emitter) in human brain tissue demonstrated that radon can irreversibly infest the human brain with toxic radioactive heavy metals, with 10-fold increase in radioactivity relative to control subjects [14]. Taking into account the integrated environmental radon exposure experienced by the brain during the course of a typical human 70 year life-span, and the number and size of cells in a 1.5 kg human brain, it has been estimated that this exposure is responsible for the generation of sufficient high-energy ¤-particles to hit and destroy every cell of the brain more than once in a lifetime [17]. These particles induce deleterious biological effects along their pathway in direct proportion to their initial energies. These effects include the generation of free radicals, which are postulated to enhance further the

trapping of heavy-metal radon decay products, with consequent further brain damage.

Extensive studies over the past two decades in the UK and elsewhere have resulted in the identification of substantial geographical variability in radon concentrations in the domestic environment, with significant correlation demonstrated between mean annual radon concentrations and underlying geology, while an increasing number of pilot studies of the influence of such geographic variability on the incidence of degenerative conditions has recently been reported.

The convergent conclusions of these apparently diverse studies suggest that detailed consideration of the overall relationship between environment radon gas and degenerative conditions is now appropriate. We present here an overview of the status and principal conclusions to date of a number of such investigations, together with some suggestions as to future study.

2 Multiple Sclerosis and Radon

2.1 Aetiology and Prevalence

Multiple Sclerosis (MS) is a disorder of the central nervous system, manifesting as acute focal inflammatory demyelination and axonal loss with limited remyelination, culminating in the chronic multifocal sclerotic plaques from which the disease gets its name [18]. MS is the most common cause of serious neural disability in young adults in the UK, with exposure to some environmental agent before the age of 15 years being postulated [19] as a factor in its later development in genetically susceptible individuals. Early studies of MS in the UK were supportive of an increasing latitudinal gradient between the south of England and the north of Scotland [20]. Although a more recent study challenged this concept [21], its findings are suggested to have underestimated absolute numbers, and re-analysis of earlier results suggests that evidence for a latitudinal gradient within England is less convincing [22] although increased prevalence in Scotland compared with England and Wales remains [23]. On a broad global scale, prevalence generally increases with latitude [24], although broad areas of Africa and Asia are relatively unaffected.

2.2 Possible Mechanism for Radon

The oligodendrocyte, a principal target of immune attack in MS, synthesises and maintains the myelin sheath of up to 40 neighbouring nerve axons in the central nervous system. Compact myelin consists of a condensed membrane, spiralled around axons to form the insulating segmented sheath needed for saltatory axonal conduction. In MS, the lipoproteins of the myelin sheaths around the axon of the nerve cell are lost in a degenerative process of demyelination, severely affecting salutatory conduction. Lykken and Momčilović [25] proposed a mechanism in which the myelin sheath lipids take up inhaled lipid-soluble environmental radon. In this delicate and sensitive environment, subsequent □- and □-particle emission damages the myelin cell nuclei irreversibly and punctures the myelin sheaths beyond the point of repair, causing permanent nerve impulse propagation failure. As noted above, one outcome of this radioactive decay process is free-radical generation, leading to potential peroxidative damage to the myelin lipid portion [26].

2.3 Ecological Studies

Recent studies in Ireland [27], Norway [15], Sweden [28], and the USA [16] have suggested a connection between environmental radon and Multiple Sclerosis (MS), with a higher incidence of MS being identified in regions with higher mean domestic radon concentrations.

Gilmore and Grennan [27] noted that MS prevalence rates in the north-west of Ireland are among the highest in the island, and that this area, particularly Donegal, is one of the highest radon-emitting areas, with extensive high-uranium granite bedrock geology. On a county-by-county basis, good correlation was observed between mean radon level and membership of the MS Society in Ireland, with the lowest prevalence across central Ireland (Kerry to Meath). A questionnaire survey showed that MS sufferers in the north-west were more likely to be living in their childhood home or its locality, and more likely to live in homes with private (well) water supplies. Both of these factors imply the potential for higher lifetime exposure to environmental radon gas. McGuigan et al. [29] confirmed the presence of a statistically-significant MS prevalence difference between the north-west and the south-east, but took no account of environmental considerations, attributing the difference to differing population genetics deriving from the 13th century Norman occupation of the south-east and the 17th century Scottish settlement of the north.

Using spatially-moving bivariate correlation analysis, Bølviken et al. [15] studied MS mortality in 73 rural municipality aggregates in Norway, and demonstrated significant positive correlation for rates of MS with indoor air radon content, coupled with significant negative correlation for MS rates versus fallout of magnesium (Mg) and precipitation. Under their proposed hypothesis that the content of radon and radon progeny in inhaled air is a risk factor for MS, the development of harmful radon levels in the air is influenced by atmospheric fall-out of magnesium and other elements of marine origin through their ion-exchange with the radon precursor, radium, and by the annual precipitation, through its effect on soil moisture and outwash of radium and related constituents in the soil. Some of the epidemiological characteristics of MS were shown to be not incompatible with observed environmental conditions, with plausible explanations of the role of environmental radon being offered. These include:

- *Altitude and Latitude gradient*
- *Gender response*
- *Temporally-increasing incidence in northern Europe*
- *Risk in migrants aged <15 reflects place of birth rather than ultimate residence.*

Although not explicitly reflecting the influence of radon gas and its progeny, Axelson et al. [28] studied exposure to ionising radiation, confirming correlation between both occupational and diagnostic exposure to X-rays and MS among patients from two areas of southern Sweden. In support, cases were noted where X-ray examination of MS patients accelerated the demyelination process, leading to the suggestions, firstly that bombardment by ionising radiation might actually trigger demyelination in susceptible individuals [30], and secondly, that radiation-induced free radical generation and oxidative damage are of importance in the pathogenesis of MS [26].

As in Europe, a latitudinal gradient in MS prevalence is found in the United States, ranging from 57 per 10^5 in the south to 150 per 10^5 in the north [31]. Following the 1993 identification of elevated radon concentrations in 92 of the 99 counties in Iowa, Eidbo and Prater confirmed correspondingly high MS prevalence [32], using National Multiple Sclerosis Society (NMSS) membership data. Similar correlations, again using NMSS data, were subsequently identified in Idaho, Minnesota and Washington. In Washington, the highest prevalence (255 per 10^5) was found in Spokane county, which had the highest radon exposure of any county in the state; King county, with the lowest MS prevalence (121 per 10^5), is in the lowest radon exposure region [16].

3 Alzheimer's Disease, Parkinson's Disease and Radon

3.1 Aetiology and Prevalence

Alzheimer's disease (AD) is the most common form of dementia affecting elderly people, with prevalence increasing with age. Known risk factors include age, genetic factors, history of head injury and exposure to toxins and heavy metals, such as zinc and aluminium. Whalley et al. [33] investigated the small-area geographical distribution of AD in Scotland, deriving incidence figures for each of the 898 postcode sectors. The results confirmed non-random geographical distribution of AD in 31 postcode sectors, supporting earlier suggestions by the principal author [34] that both genetic and environmental factors are important.

Parkinson's disease (PD) is a chronic neurodegenerative condition, characterised clinically by resting tremor, rigidity, and postural instability, affecting 1 – 2% of the population over 60 years of age, although seen in younger individuals as well. As with AD, known risk factors include age, genetic and environmental elements, including exposure to toxins and heavy metals such as iron and lead [35]. Geographical variation is significant, with prevalence ranging from 57 per 10^5 in China [36] to 347 per 10^5 in Mississippi, USA [37], while a mortality study in the USA showed strong north-south decreasing rates [38].

3.2 Possible Mechanism for Radon

Lykken et al. showed [39] that inhaled radon does not merely flow quickly in and out of the lungs, but is rapidly absorbed from the lung into the body (via the enhanced lipid solubility noted above) where it accumulates in the cranium. As noted, radon ultimately decays to heavy-metal daughter products which, in addition to being highly neurotrophic and neurotoxic [40], are lipid-insoluble. Hence, they remain in the brain, where they emit additional □- and □-particles and □-radiation over their lifetime, thereby adding chemical injury to the radiation impact on the brain. AD and PD have been the subject of reports showing increased levels of radon progeny in sufferers compared with normal. Momčilović et al. [14] studied the occurrence of environmental radon daughters ^{210}Po and ^{210}Bi in the protein and lipid fractions of cortical grey- and sub-cortical white-matter from the frontal and temporal lobes of patients with AD, PD, smokers and controls. They found 10-fold increase in ^{210}Pb and ^{210}Po (decay product of short-lived ^{210}Bi) radioactivity in the protein fraction from both cortical grey- and sub-cortical white-matter in AD patients and a similar increase in the lipid fraction in PD patients.

Momčilović et al. [14] postulate that the increased trapping of ^{210}Po and ^{210}Bi is due to free-radicals generated during the radon decay process facilitating the formation of highly reactive oxychlorides, with enhanced affinity for heavy metals. These trapped □-emitters damage the brain cells, particularly astrocytes, which are highly radiosensitive, in contrast with the more radio-resistant neurons. In the case of AD, Apolipoprotein E, the major apolipoprotein in the nervous system, is expressed in astrocytes, and its E4 variant may interact abnormally with neuronal cytoskeletal proteins that favour microtubule degradation and the formation of neurofibrillatory tangles, which occur in the brains of AD patients. Thus the amyloid deposits and tangling observed in AD may well reflect the response to injury of the astrocytes. Sufficient radioactivity and free-radicals accompany the presence of radon and its progeny in the brain to act as an apogen to induce such a cascade.

4 Paget's Disease and Radon

4.1 Aetiology and Prevalence

Paget's disease of Bone is a focal disorder of bone remodelling, with onset similar to that of cancers where ionising radiation has been shown to be a causative agent, and consistent with the disease having a localised source, i.e. damage to the osteoclast. It rarely presents before 35 years of age and prevalence increases with age, affecting 2 to 5% of the population aged above 50 years [41]. Of unknown aetiology, evidence favours a viral [42] or bacterial [43] origin, characterised by accelerated disorganised bone remodelling due to a primary abnormality of osteoclasts, together with a genetic element [41,44], although a recent large UK study [45] did not support the role for a virus. Other workers identify unspecified environmental [46][47] and geographical [48][49] influences, the strong time-dependent declining incidence in the UK [50] and elsewhere [51] favouring an environmental contribution to causation [47]. Finally, studies have implicated lead [52], the end-product of the radon decay chain.

4.2 Possible Mechanism for Radon

The hypothesis that radon is responsible for initiating Paget's Disease of Bone stems from the observed similarity of its onset to that of radiation-induced cancers. Although more recent studies [53] dispute the claim, Eatough et al. [54] suggested that leukaemia is linked to radon exposure and proposed a mechanism by which radiation from radon and its daughter products reach the bone marrow [55]. On inhalation, radon gas, ^{222}Rn, is absorbed into the blood and thence into fat, where its solubility is about 16 times that in tissue. Radon decays by □-particle emission, successively to ^{218}Po and thence to ^{214}Po, both also □-particle emitters and both of which are absorbed by bone, the ultimate decay product, as already noted, being ^{210}Pb. Allen et al. [56] calculated that the range of the □-particles emitted by ^{222}Rn, ^{218}Po and ^{214}Po, when present in fat cells in the bone marrow, was sufficient to deliver a significant dose to the embryonic white blood cells, which thereupon transform to leukaemia cells. Independently, the corresponding □-particle ranges in tissues were estimated to be 42.8, 74.2 and 49.5 μm respectively [57]. It is possible, but as yet unproven, that osteoclasts could also be within range of bone-marrow □-emitters. Finally, the observation of elevated cortical bone lead content and reduced trabecular bone lead content in patients suffering from Paget's disease [52] raises the possibility that these re-distributions are the

outcome of additional lead being deposited in the bone system as a direct outcome of the decay of inhaled or ingested radon gas.

5 Conclusions

Although attention has hitherto been focussed on environmental radon gas in the context of its not insignificant determining role in lung cancer, a growing body of experimental evidence suggests that radon may be implicated in the prevalence of other conditions, including Multiple Sclerosis, Alzheimer's and Parkinson's Diseases and Paget's Disease of Bone. Results from recent and ongoing initial studies in these areas have been summarised here. Given the current concern over environmental radon levels generally, a strong case therefore exists for clarification by detailed epidemiological studies of the relationship between radon and these conditions. Campaigns to monitor domestic radon levels, and to encourage remediation where high levels are discovered, have been undertaken in many areas, the prime motivation being the reduction in the overall population risk of lung-cancer. However, the response to these campaigns to date has been, at best, moderate, with positive action being generally greatest among the sections of the population least at risk of lung cancer. Recognition of the linkage between radon and other conditions contributing significantly to the overall health burden has the potential to bring additional, hitherto unrecognised, health benefits, since the associated publicity could increase the likelihood of the public taking action to reduce domestic radon levels, making remediation campaigns potentially more cost-effective.

Although a limited number of ecological studies on Multiple Sclerosis have been reported, no similar investigations appear yet to have been undertaken on Alzheimer's and Parkinson's Diseases or on Paget's Disease of Bone. With radon concentration data for England, Wales, Northern Ireland and much of Scotland now available at resolutions down to postcode sector [58], the opportunity now presents itself to initiate studies of this nature. Note, however, that implementation of a high-resolution study requires availability and access both to high-quality diagnostic data and to detailed exposure history of the individuals concerned.

6 References

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