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Radon Exposure and Human Health: What Happens in Volcanic Environments?

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Abstract

Volcanic activity can cause hazardous effects to the environment and the health of the exposed persons such as an increased risk for the development of several cancers. In geothermal areas, volcanic gases such as radon are continuously vented from the main crater, from fumarolic fields or diffused through soil. The continued long-term exposure to radon can enhance the risk of lung cancer being considered the leading cause of lung cancer following tobacco smoking. The chronic exposure to volcanogenic radon requires the development of biomonitoring methods that will assist in the evaluation of the effects of exposure to this genotoxic element. The Human Biomonitoring with the use of exfoliated buccal cells is minimally invasive, and the endpoints of the buccal micronucleus cytome (BMCyt) assay are the biomarkers of effect most recently used to measure genetic damage for the exposure to genotoxic and cytotoxic xenobiotics. The BMCyt assay has been used in a number of occupational studies, and positive results were detected as a consequence of exposure to pesticides, metals, and industrial chemicals that are suspected to cause cancer. Regarding the chronic exposure to volcanic environments, many studies revealed a rise in the numbers of MN in buccal exfoliated cells, indicating an increased risk for cancer. This chapter aims to cover the main health hazards and biomonitoring methods for populations chronically exposed to volcanic environments, allowing an estimate of health risks and to implement risk management measures regarding the exposure to certain compounds.

Keywords: radon, volcanic environments, biomonitoring, BMCyt assay

1. Radon

1.1. Definition, physical and chemical properties

Radon was discovered by Fredrich Ernst Dorn in 1898. The name is derived from radium, as it was first detected as an emission from radium during radioactive decay. It is a naturally occurring radioactive gas of the noble gas family, is odorless and tasteless and, is produced by the decay of radium in the uranium decay chain. Radon is measured in terms of its activity (curies or becquerels), and these measurements provide information regarding how much a radioactive material decays every second ($1 \text{ Ci} = 37 \text{ billion Bq} = 37 \text{ billion decays per second}$).

Radon also undergoes to radioactive decay, being divided in two parts (one part is called radiation, and the other part is called a daughter or progeny). In the air, the radioactive daughters (isotopes of polonium, bismuth, and lead) tend to attach to surfaces and to aerosol particles such as dust and cigarette smoke [1, 2, 3].

1.2. Sources in the environment

Radon is a radioactive compound, which rarely occurs naturally in the environment, being mostly derived from human activities; some of the potential sources of anthropogenic radiation include x-rays and other types of radiation used in medicine, radioactive waste generated by nuclear power stations and scientific research centers, and even electromagnetic radiation from television sets and microwave ovens.

On the other hand, radon isotopes are formed naturally through the radioactive decay of uranium or thorium, being present in rocks and soil. The decay products of ^{222}Rn , such as ^{218}Po and ^{214}Pb , can attach to particles in the air and be transported this way in the atmosphere being deposited on land or water by settling or by rain [4]. The human exposure to radon can occur by uranium mining activities (since uranium minerals emit radon gas), the occurrence of granitic bedrocks located underneath buildings [5], the use of building materials that contain variable uranium and radium concentrations, and exposure to volcanic activity.

1.3. Volcanic environments

During and after eruptions, volcanoes release hazardous gases such as sulfur dioxide (SO_2), sulfuric acid (H_2SO_4), hydrogen sulfide (H_2S), hydrogen chloride (HCl), hydrogen fluoride (HF), carbon dioxide (CO_2), and radon (Rn) [6]. These gases have both acute and chronic health effects: carbon dioxide and sulfur gases are the main gases responsible for acute mortality due to their asphyxiating and/or toxic properties; radon, due to its radioactivity, has important chronic effects, and thus, even at low doses, a long-term exposure may also pose a significant health risk.

According to Gasparini and Mantovani [7], the radon release, in volcanic systems, occurs mainly due to (a) the radon presence in rocks, minerals, pore fluids, and groundwater; (b) the release of magma fluids ascent to the surface, heating the nesting rocks; and (c) the increase in temperature that causes removal of the radon present in interstitial fluids and even into

groundwater. Radon is considered a useful tracer of volcanic activity due to the ability to be transported from depth (by carrier gases such as CO_2) without being chemically altered [8]. However, volcanic environments are complex, and the nature of the driving force can change during gas ascent, depending on the physical-geological conditions in the environment that the gas encounters. Variations in temperature, pressure, mechanical stresses, chemical reactions, and mineral precipitation can change the gas-bearing properties of geological formations [9].

In a study developed in all regions of the Former Yugoslav Republic of Macedonia, it was shown that indoor radon concentration measurements in dwellings were significantly different between seasons, being the highest values observed in the winter and autumn [10]. Also, in the Vulsini Volcanic district in Northern Latium (Central Italy), Cinelli et al. [11] performed a series of soil gas radon measurements to estimate the radon radiation risk; the authors observed that soil gas radon concentration ranged between 7 and 176 kBq/m^3 , revealing a large degree of variability particularly related to the different lithologies of the studied sites.

Considering that, in volcanically active environments, radon can be continuously vented from the volcano main crater, from fumarolic fields, or diffusely emitted through soil [12]; these environments present continuous health risks to the populations living in their vicinity, as it happens in the volcanic islands of the Azores archipelago.

The Azores archipelago is located in the North Atlantic Ocean, in the triple junction of the North American, African, and Eurasian plates [13], and is formed by nine islands of volcanic origin that represent the emerged part of the Azores Plateau. As a result of the Azores archipelago location on an active plate boundary, the islands are subjected to frequent seismic and volcanic activity, including eruptions and degassing processes. The São Miguel Island, located in the eastern group of the archipelago, has one of the most active and dangerous volcanoes of the archipelago, the Furnas volcano. Its activity is marked by the presence of fumarolic fields [14] and extensive soil diffuse degassing areas [15, 16] that surge the radon concentration increase [17]. In 2014, Silva et al. [18] surveyed the indoor radon concentration in some buildings from the villages of Furnas and Ribeira Quente (located in degassing areas in the vicinity of Furnas volcano); the annual radon concentration ranges between 23 and 6403 Bq/m^3 . The level of indoor radon exceeds the limit defined by the regional legislation (150 Bq/m^3) (D.L.R No. 16/2009/A Art. 51) in 33% of the Furnas village buildings and in 21% of the ones of Ribeira Quente. Further up, Silva et al. [19] applied a series of regression models demonstrating that barometric pressure, soil water content, soil temperature, soil CO_2 flux, air temperature, relative air humidity, and wind speed are the statistical meaningful variables explaining between 15.8 and 73.6% of ^{222}Rn variations in Furnas volcano vicinity.

2. Human exposure to radon

Human exposure to natural ionizing radiation is largely due to radon. It is estimated that the worldwide radon contribution constitutes as much as 50% of the overall radiation dose, reaching values of about 1.15 mSv/year per capita [20].

Although the atmospheric concentration of radon is usually low, this gas tends to accumulate within confined environments with reduced or no air exchange, such as buildings, dwellings, tunnels, caves, and mines. During the radon decay process, alpha, beta, and gamma radioactive particles are released and can be inhaled and deposited on the bronchial epithelium of exposed individuals; considering that the alpha particle can disrupt the DNA structure within cells of the lining epithelia, and especially lung cells, exposure to this irradiation can contribute to an increased risk of lung cancer [17].

The effects of radon exposure in human health have been known since the sixteenth century, although radon was only discovered at the turn of the twentieth century. Still, it was only in the 1940s that a causal link between lung cancer in miners and radon exposure was established [21]. Taking in consideration that the studies on underground miners consistently demonstrated an increased risk of lung cancer caused by radon and its progeny, International Agency for Research on Cancer (IARC) classified radon as a human carcinogen in 1988 [22]. Later on in the 1970s, indoor radon accumulation in domestic buildings was first observed being considered to play a role in the epidemiology of lung cancer [23]. Considering that the awareness of the potential for hazardous exposure, due to accumulation of radon in indoor environments, has increased during the times, several programs were established to carefully monitor and control radon concentration in closed spaces, such as households located in areas where geogenic radon is highly likely to occur.

3. Biomonitoring

Traditionally, the term biomonitoring can be simply defined as a way to provide information about exposures to chemicals in living organisms. Exposure is commonly assessed by a spectrum of questionnaire data and ecological, environmental, or biological measurements. Biological measures of exposure allow the assessment of internal dose, by measuring the parent chemical or its metabolite or reaction product in the human blood, urine, milk, saliva, and adipose or other tissues [24]. Nowadays, and ever since Wild [25] proposed an environmental complement to the genome in determining risk of disease, termed the exposome (totality of exposures throughout the lifespan), researchers started to include in biomonitoring studies the cumulative measure of exposures to both chemical and nonchemical agents, such as diet, stress, and socio-behavioral factors. The exposomic approaches go a step beyond traditional biomonitoring, aiming to capture all exposures that potentially affect health and disease.

3.1. Human biomonitoring

When individuals or populations are exposed to a chemical, it may be absorbed and distributed among the bodily tissues, metabolized, and/or excreted (i.e., absorption, distribution, metabolism, and excretion (ADME)). For the assessment of the human exposure to a given xenobiotic, biologic measurements of the chemical can be made after the absorption step or during each of the subsequent steps of ADME [26]. This is called human biomonitoring (HBM), which is an approach for assessing human exposures to natural and synthetic compounds from

the environment, occupation, and lifestyle; this scientifically developed methodology allows an evaluation of factors, such as cumulative exposure or genetic susceptibility, to a certain chemical compound allowing the extrapolation for adverse risks and health effects, such as cancer.

The data obtained in HBM studies integrate exposure from all routes (oral, inhalation, dermal, transplacental) and allow (1) establishing population reference ranges, (2) identifying unusual exposures for subpopulations, (3) evaluating temporal variability and trends within a population, (4) validating questions designed to estimate individual exposure, and (5) examining associations with health outcomes in epidemiologic studies. Therefore, HBM has tremendous utility, providing an efficient and cost-effective means of measuring human exposure to chemical substances, handing unequivocal evidence that both exposure and uptake have been taken place [27, 28].

3.2. Biomarkers

Biomarkers are commonly used as “agents” to measure the concentrations of chemical substances, their metabolites, or reaction products in human tissues or specimens, representing an integrative measurement of exposure to a given agent (i.e., the internal dose), that result from complex pathways of human exposure and also incorporate toxicokinetic information and individual characteristics such as a genetically based susceptibility [29].

In 1993, the WHO [30] provided three classifications of biomarkers—exposure, effect, and susceptibility—but with the rise of genomics and other advances in molecular biology, the biomarker classification has suffered some changes through time. In 2001, the Biomarker working group defined five classifications: (1) antecedent biomarkers, to identify the risk of developing an illness; (2) screening biomarkers, to screen for subclinical disease; (3) diagnostic biomarkers, to recognize overt disease; (4) staging biomarkers, to categorize disease severity; and (5) prognostic biomarkers, to predict future disease course. In this paradigm, biomarkers are viewed on a continuum between markers of exposure and markers of effect, with markers of susceptibility spanning the continuum.

The markers of effect are applied in the comparison of case and control, target and nontarget tissues, or dose and time to response, where a correlation between the biomarker and biological effect can be demonstrated; the markers of susceptibility are defined as the genetic factors that influence the body’s sensitivity to a chemical but can also include biological factors, such as age, nutritional status, and lifestyle.

The continuous progress in molecular and analytical methods to measure biomarkers for linking exposure with health outcomes and new approaches in exposome research will enable a more comprehensive and integrated analysis across the biomarker continuum [31].

3.3. Micronucleus

Micronucleus (MN) is defined by Schmid [32] as a microscopically visible, round, or oval cytoplasmic chromatin mass next to the nucleus that is formed from acentric chromosomes, chromatid fragments, whole chromosomes, or chromatids. Micronucleus formation results

from two basic phenomena in mitotic cells, which are chromosome breakage and the dysfunction of the mitotic apparatus.

This aberration is induced by genotoxic stress caused by a clastogen or an aneugen xenobiotic; the clastogen involves the induction of either chromosome fragments that lag behind the separating chromosomes or a chromatin bridge between chromosomes at the anaphase of mitosis; the aneugen causes a daughter cell to have an abnormal number of chromosomes by disrupting the whole chromosomes bound to the mitotic spindle at anaphase; by disrupting the spindle checkpoint, the chromatin is separated from the newly forming nucleus and forms an independent nucleus-like structure, the micronucleus [33].

Since this chromosomal aberration is a frequent and significant response to exposure to mutagenic agents, it has been extensively used to identify potential genotoxic exposures and also chromosomal instability [34].

3.4. Buccal micronucleus cytome (BMCyt) assay

The continuous chromosomal damage in fully differentiated cells (as in the buccal epithelial cells) implies that damage occurred in the basal cell layer during earlier nuclear divisions. Considering that buccal epithelial cells are in direct contact with inhaled and ingested substances and/or elements and more than 90% of all human cancers are of epithelial origin, it can be argued that buccal epithelial cells represent a preferred target site for early genotoxic events induced by carcinogenic agents [35]. Therefore, the MN assay using exfoliated buccal cells can be considered the most suitable biomonitoring approach for the detection of increased cancer risk in humans, when the exposure to genotoxic agents occurs via inhalation or ingestion.

The buccal micronucleus cytome (BMCyt) assay is a useful and minimally invasive method that allows screening for both genomic damage and cytotoxicity events [36]. This technique is minimally invasive [37] and is frequently used in biomonitoring studies of occupational and environmental exposure to carcinogenic substances [38–40].

This assay involves the collection of exfoliated buccal epithelial cells from inside the cheeks by scraping the oral mucosa, smearing onto glass slides, and staining by the Feulgen method; this methodology allows the examination of cells to determine the frequency of MN and other genomic damage markers such as karyorrhexis (nuclear disintegration associated with the loss of nuclear membrane integrity), karyolysis (nuclei completely depleted of DNA and therefore appear as Feulgen-negative ghost-like), and pyknosis (small shrunken, intensively stained nucleus); these anomalies are associated with both cytotoxicity (necrosis and keratinization) and genotoxicity (apoptosis) being considered as effective biomarkers for populations exposed to mutagenic and carcinogenic agents [41].

Factors such as the minimal invasiveness of cell collection, high reliability, and low cost of BMCyt have contributed to the worldwide success for epidemiological studies enabling the early detection of carcinogenic effects in the cell exposed to various carcinogenic agents [42].

4. Case studies

It has been demonstrated that exposure to radon can induce lung tumors and other cancers in experimental animals [43]. Also, a radon dose-related carcinogenicity has been shown through epidemiologic studies of miners and case-control studies in the general population [44–47].

In Europe, Darby et al. [48] in a collaborative study that included 13 case-control studies in 9 European countries, each of which registered over 150 people with lung cancer and 150 or more controls and which included data about radon levels over 15 years, found that the risk of lung cancer (after stratification for study, age, gender, region of residence, and smoking) increased by 8% per 100 Bq/m³ increase in radon concentration. In the United States, Krewski et al. [49] evaluated the risk associated with prolonged residential radon exposure, combining data from seven large-scale case-control studies (4081 cases and 5281 controls), and these authors also found that the risk of lung cancer due to exposure to residential radon was increased by 10% per 100 Bq/m³.

For the biomonitoring of the human populations, the application of easy and noninvasive techniques is necessary; for the last 10–15 years, there has been an increase in the use of cytogenetic monitoring techniques, such as the buccal micronucleus cytome (BM-Cyt) over the use of MN in lymphocytes. Nevertheless, there are only a few studies, developed in the Azores, that apply this assay for the risk assessment of the chronic exposure to radon of volcanic origin.

Considering the geologic context of the archipelago, some studies have been developed to biomonitor the health effects of the chronic exposure the compounds released by the volcanic activity. In the study of Amaral et al. [50], it was observed that the population living in the vicinity (inside the crater) of Furnas volcano presented higher rates of cancer of the lip, oral cavity, and pharynx, in both sexes, and of female breast cancer. The relative risk analysis revealed a higher risk for lip, oral cavity, pharynx, and breast cancer in this population compared to a population inhabiting an island without historical records of volcanic activity. According to these authors, these higher cancer rates could be partially explained by the chronic exposure to environmental factors resulting from volcanic activity. More recently, Rodrigues et al. [51] in a study carried with inhabitants of Furnas volcano demonstrated that the chronic exposure to a volcanically active environment results in genotoxic and cytotoxic effects in human oral epithelial cells; this research group used the buccal micronucleus assay and observed that the frequencies of micronucleus and other nuclear anomalies were significantly higher in the Furnas inhabitants when compared to the inhabitants of an area without volcanic activity. Also, the inhabitants of Furnas village presented a 2.4-fold higher risk of having a higher frequency of micronucleated cells.

More recently, Linhares et al. [52] took a step forward in this investigation and evaluated the DNA damage in the buccal epithelial cells of individuals chronically exposed to indoor radon in Ribeira Quente inhabitants, a village within 7 km (in the south flank) of the Furnas volcano. The authors shown that indoor radon concentration correlated positively with the frequency

of micronucleated cells and that the exposure to indoor radon is a risk factor for the occurrence of micronucleated cells in the inhabitants of the hydrothermal area.

The results obtained in these studies demonstrate a significant association between chronic exposure to indoor and the occurrence of DNA damage evidencing the usefulness of biological surveillance to assess mutations involved in pre-carcinogenesis, reinforcing the need for further studies with human populations. Likewise, these studies set the basis for the use of the BMCyt assay in volcanic areas worldwide to assess the effects of the chronic exposure to genotoxic substances and/or elements.

5. Risk management

It has been reported that more than 60% of the ionizing radiation a person receives every year can be caused by natural sources of radiation and more than 50% of this radiation can be due to radon and the products of its disintegration. Hence, maintaining radon safety is a critical challenge, and this has been actively discussed throughout the last few decades [53]. To assure a public health risk assessment, factors such as the source, the pathway, and the receptor must be considered.

The indoor radon concentration is associated with factors such as the building structure (such as construction material, pavement, ventilation, and the presence of basements or air boxes), as well as the ventilation measures taken. These factors are particularly relevant in households built on volcanic hydrothermal areas, where soil diffuse degassing can be very intense. As for the consequences of human exposure to indoor radon, these will depend of factors such as the concentration of radon indoors, the duration of exposure, the general health status of the individual, and the synergistic effect with smoking.

In order to manage the risk, primary strategies such as education and prevention activities must be established to prevent/diminish the entrance of radon into the buildings [54]. However, this may not be easily achieved, since the indoor radon varies considerably by region and locality and is greatly affected by the household structure as well as soil and atmospheric conditions. Consequently, often the development of secondary strategies to remediate the effects of indoor radon is required, such as taking measures in the construction of the household by selecting an adequate foundation type, location, building materials used, entry points for soil gas, and building ventilation systems.

At an individual level, it is necessary to ensure an adequate past medical history or family medical history, since individuals who have chronic respiratory diseases such as asthma, emphysema, and fibrosis may be more susceptible to the respiratory effects of radon and radon progeny. Due to the reduced expiration efficiency and the increased residual air volume of these individuals, radon and its progeny would be resident in the lungs for longer periods of time, increasing the risk of damage to the lung tissue.

The above-discussed epidemiologic studies clearly evidence the carcinogenicity of radon in volcanically active environments. However, radon control efforts appear to be held up, and

the cost-effectiveness of current strategies and interventions is questionable; therefore, the continuous biomonitoring of the populations exposed to radon in volcanic areas is necessary to further implement risk management measures.

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References

- [1] Edling C (1985) Radon daughter exposure and lung cancer. *British Journal of Industrial Medicine*, **42**:721-722
- [2] Biermann AH, and Sawyer SR (1995) Attachment of radon progeny to cigarette-smoke aerosols. Lawrence Livermore Natl. Lab., CA (United States). Technical Report UCRL-CR-120647
- [3] Ojo TJ, and Ajayi IR (2014) A review on environmental radon and its potential health risk on humans. *Journal of Environmental Science, Toxicology and Food Technology*, **8**, 1-8
- [4] Agency for Toxic Substances and Disease Registry (ATSDR) (2012) Public Health Statement for Radon. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service
- [5] Denton GRW and Namazi S (2013) Indoor Radon Levels and Lung Cancer Incidence on Guam. *Procedia Environmental Sciences*, **18**:157-166
- [6] Durand M, Florkowski C, George P, Walmsley T, Weinstein P, Cole J (2004) Elevated trace element output in urine following acute volcanic gas exposure. *Journal of Volcanology and Geothermal Research*, **134**:139-48
- [7] Gasparini P and Mantovani MSM (1978) Radon anomalies and volcanic eruptions. *Journal of Volcanology and Geothermal Research*, **3**, 325-341
- [8] Barbosa SM, Donner RV, Steinitz G (2015) Radon applications in geosciences—Progress & Perspectives. *The European Physical Journal Special Topics*, **224**:597-603

- [9] Padilla GD, Hernández P, Padrón E, Barrancos J, Pérez NM, Melián G et al. (2013) Soil gas radon emissions and volcanic activity at El Hierro (Canary Islands): The 2011-2012 submarine eruption. *Geochemistry, Geophysics, Geosystems*, **14**:432-447
- [10] Stojanovska Z, Januseski J, Bossew P, Zunic ZS, Tollefsen T, Ristova M (2011) Seasonal indoor radon concentration in FYR of Macedonia. *Radiation Measurements*, **46**:602-610
- [11] Cinelli G, Tositti L, Capaccioni B, Brattich E, Mostacci D (2015) Soil gas radon assessment and development of a radon risk map in Bolsena, Central Italy. *Environmental Geochemistry and Health*, **37**(2):305-319
- [12] Hansell A, Horwell C, Oppenheimer C (2006) The health hazards of volcanoes and geothermal areas. *Occupational and Environmental Medicine*, **63**:149-156
- [13] Searle R (1980) Tectonic pattern of the Azores spreading centre and triple junction. *Earth and Planetary Science Letters*, **51**:415-434
- [14] Ferreira T, Gaspar JL, Viveiros F, Marcos M, Faria C, Sousa F (2005) Monitoring of fumarole discharge and CO₂ soil degassing in the Azores: contribution to volcanic surveillance and public health risk assessment. *Annals of Geophysics*, **48**:4-5
- [15] Viveiros F, Cardellini C, Ferreira T, Caliro S, Chiodini G, Silva C (2010) Soil CO₂ emissions at Furnas Volcano, São Miguel Island, Azores archipelago: Volcano monitoring perspectives, geomorphologic studies, and land use planning application. *Journal of Geophysical Research*, **115**, B12208, 1-17
- [16] Viveiros F, Cardellini C, Ferreira T, Silva C (2012) Contribution of CO₂ emitted to the atmosphere by diffuse degassing from volcanoes: The Furnas Volcano case study. *International Journal of Global Warming*, **4**(3-4): 287-304
- [17] Appleton JD (2013) Radon in air and water. In: *Essentials of medical geology*. O. Selinus et al. (Eds), Dordrecht, Netherlands, pp. 239-277. Springer Netherlands
- [18] Silva C, Ferreira T, Viveiros F, Allard P (2014) Indoor radon (²²²Rn) monitoring in some buildings at Furnas and Ribeira Quente villages (Furnas Volcano, Azores): public health risk assessment. *Comunicações Geológicas*, **101**, Especial II, 927-931
- [19] Silva C, Ferreira T, Viveiros F, Allard P (2015) Soil radon (²²²Rn) monitoring at Furnas Volcano (São Miguel, Azores): applications and challenges. *The European Physical Journal Special Topics*, **224**(4): 659-686
- [20] UNSCEAR (United Nations Scientific Committee on the effects of Atomic Radiation). (2008). Sources and effects of ionizing radiation. Report to General Assembly, Annex B, United Nations, New York
- [21] Hueper WC (1942) *Occupational Tumors and Allied Diseases*. Springfield, Ill. Charles C Thomas
- [22] International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risks to Humans (IARC) (1988) *Man-Made Mineral Fibres and Radon*. Lyon, France: IARC Press; **43**:33-171

- [23] Axelson, O (1984) Room for a role for radon in lung cancer causation? *Medical Hypotheses*, **13**(1):51-61
- [24] Needham LL, Barr DB, Calafat AM (2005) Characterizing children's exposures: beyond NHANES. *Neurotoxicology*, **26**:547-553
- [25] Wild CP (2005) Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiology, Biomarkers and Prevention*, **14**:1847-1850
- [26] LaKind JS, Sobus JR, Goodman M, Barr DB, Furst P, Albertini RJ, et al. (2014) A proposal for assessing study quality: biomonitoring, environmental epidemiology, and short-lived chemicals (BEES-C) instrument. *Environment International*, **73**:195-207
- [27] Sexton K, Needham L, Pirkle J (2004) Human Biomonitoring of Environmental Chemicals. *American Scientist*, **92**, 38
- [28] Angerer J, Ewers U, Wilhelm M (2007) Human biomonitoring: state of the art. *International Journal of Hygiene and Environmental Health*, **210**(3-4): 201-228
- [29] Ladeira C and Viegas S (2016) Human Biomonitoring – An overview on biomarkers and their application in Occupational and Environmental Health. *Biomonitoring*, **3**:15-24
- [30] World Health Organization (WHO). 1993. Biomarkers - Biomarkers and risk assessment: Concepts and principles, *Environmental Health, Criteria No.155*(93), Geneva
- [31] Dennis KK, Marder ME, Balshaw DM, Cui Y, Lynes MA, Patti GJ, et al. (2017) Biomonitoring in the era of the exposome. *Environmental Health Perspectives*, **125**(4), 502-510
- [32] Schmid W (1975) The micronucleus test. *Mutation Research*, **31**(1):9-15
- [33] Utani K, Kohno Y, Okamoto A, Shimizu N (2010) Emergence of Micronuclei and Their Effects on the Fate of Cells under Replication Stress. *PLoS ONE*, **5**(4): e10089. <https://doi.org/10.1371/journal.pone.0010089>
- [34] Tolbert PE, Shy CM, Allen JW (1992) Micronuclei and other anomalies in buccal smears: method development. *Mutation Research*, **271**:69-77
- [35] Holland N, Bolognesi C, Volders MK, Bonassi S, Zeiger E, Knasmueller S (2008) The micronucleus assay in human buccal cells as a tool for Biomonitoring DNA damage: The HUMN project perspective on current status and knowledge gaps. *Mutation research*, **659**:93-08
- [36] Thomas P, Holland N, Bolognesi C, Kirsch-Volders M, Bonassi E, Zeiger S, et al. (2009) Buccal micronucleus cytome assay. *Nature Protocols*, **4**:825-837
- [37] Bolognesi C, Knasmueller S, Nersesyan P, Thomas P, Fenech M (2013) The HUMNxl scoring criteria for different cell types and nuclear anomalies in the Buccal Micronucleus Cytome Assay: an update and expanded photogallery. *Mutation Research-Reviews in Mutation Research*, **753**(2):100-13

- [38] Çelik A, Yildirim S, Ekinçi SY, Taşdelen B (2013) Bio-monitoring for the genotoxic assessment in road construction workers as determined by the buccal micronucleus cytome assay. *Ecotoxicology and Environment Safety*, **92**:265-270
- [39] Hallare AV, Gervasio MK, Gervasio PL, Acacio-Claro PJ (2009) Monitoring genotoxicity among gasoline station attendants and traffic enforcers in the City of Manila using the micronucleus assay with exfoliated epithelial cells. *Environmental Monitoring and Assessment*, **156**:331-341
- [40] Garcia PV, Linhares D, Amaral AFS, Rodrigues AS (2012) Exposure of thermoelectric power-plant workers to volatile organic compounds from fuel oil: Genotoxic and cytotoxic effects in buccal epithelial cells. *Mutation Research*, **747**:197-201
- [41] Fenech M (2007) Cytokinesis-block micronucleus cytome assay. *Nature Protocols*, **2**: 1084-1104
- [42] Bonassi S, Ugolini D, Kirsch-Volders M, Strömberg U, Vermeulen R, et al. (2005) Human population studies with cytogenetic biomarkers: review of the literature and future perspectives. *Environmental and Molecular Mutagenesis*, **45**:258-270
- [43] Monchaux G, Morlier J, Morin M, Chameaud J, Lafuma J, Masse R (1994) Carcinogenic and Cocarcinogenic Effects of Radon and Radon Daughters in Rats. *Environmental Health Perspectives*, **102**(1):64-73
- [44] Schoenberg JB, Klotz JB, Wilcox HB, Nicholls GP, Gil-del-Real MT, Stemhagen A, et al. (1990) Case-control study of residential radon and lung cancer among New Jersey women. *Cancer Research*, **50**(20):6520-6524
- [45] Lubin JH, Boice Jr JD, Edling C, Hornung RW, Howe GR, Kunz E, Kusiak RA, Morrison HI, Radford EP, Samet JM et al. (1995) Lung cancer in radon-exposed miners and estimation of risk from indoor exposure. *Journal of the National Cancer Institute*, **87**(11):817-27
- [46] Duport P (2002) Is the radon risk overestimated? Neglected doses in the estimation of the risk of lung cancer in uranium underground miners. *Radiation Protection Dosimetry*, **98**(3):329-338
- [47] Wichmann HE, Rosario AS, Heid IM, Kreuzer M, Heinrich J, Kreienbrock L (2005) Increased lung cancer risk due to residential radon in a pooled and extended analysis of studies in Germany. *Health Physics*, **88**(1):71-79
- [48] Darby S, Hill D, Auvinen A, Barros-Dios JM, Baysson H, Bochicchio F, et al. (2005) Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. *British Medical Journal*, **330**(7485): 223-226
- [49] Krewski D, Lubin JH, Zielinski JM, Alavanja M, Catalan VS, William Field R, et al. (2006) A combined analysis of North American case-control studies of residential radon and lung cancer. *Journal of Toxicology and Environmental Health, Part A*, **69**(7-8), 533-597
- [50] Amaral A, Rodrigues V, Oliveira J, Pinto C, Carneiro V, Sanbento R, et al. (2006) Chronic exposure to volcanic environments and cancer incidence in the Azores, Portugal. *Science of the Total Environment*, **367**:123-128

- [51] Rodrigues A, Arruda M, Garcia P (2012) Evidence of DNA damage in humans inhabiting a volcanically active environment: A useful tool for biomonitoring. *Environment International*, **49**:51-56
- [52] Linhares D, Garcia P, Silva C, Barrosos J, Kazachkova N, Pereira R, Lima M, Camarinho R, Ferreira T, Rodrigues A (2016) DNA damage in oral epithelial cells of individuals chronically exposed to indoor radon (^{222}Rn) in a hydrothermal area. *Environmental Geochemistry and Health*. DOI: 10.1007/s10653-016-9893-2
- [53] Bissett RJ and McLaughlin JR (2010) Radon. *Chronic Diseases in Canada*, **29**:38-50
- [54] Larsson LS (2014) Risk-Reduction Strategies to Expand Radon Care Planning with Vulnerable Groups. *Public Health Nursing (Boston, Mass.)*, **31**(6), 526-536

