Radon impact in patients with broncho-pulmonary cancer in centre areas of Transylvania

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Abstract: - Lung cancer is the most frequent cause of mortality caused by malignancies in the world. Radon, the second recognized carcinogenic agent involved in the development of lung cancer, after smoking, is a noble gas with a high mobility. By being continuously generated by soil sources of radium or from construction materials, it becomes omnipresent in our lives. Our objectives are: developing a regional radon laboratory; the establishment of local maps linked to radon exposure, the epidemiological investigation of patients with lung cancer in the centre counties of Transylvania, in correlation with the level of exposure to radon and cigarette smoke; tracking histopathological type of lung cancer in relation to radon exposure; studies on laboratory animals regarding the influence of radon dose and dose rate in the development of lung cancer. Once identify the elevated concentrations of radon in homes, it will be possible to installate a barrier at the ground floor of buildings that will prevent radon passage. Any effort to support the reduction of radon concentration in dwellings, as well as smoking cessation will increase health in population affected by these agents and will reduce the number of deaths due to lung cancer.

Key-Words: - lung cancer, radon, smoking, morpho-pathological type of the lung cancer, prevention, smoking cessation

1 Introduction

Lung cancer (LC) represents the most frequent cause of mortality caused by malignancies in the world. The annual number of new cases since 1990 was of 1.04 million (12.8% of all new malignancies cases), and it increases by a 3% rate a year [15]. Out of these cases 58% were diagnosed in developed countries. All over the world lung cancer is by far the most common type of cancer in males. Within the European Union, it is responsible for 21% of all cancers encountered in males; it has a high mortality rate as it is responsible of 29% of the deaths caused by malignancies. The epidemiological data corresponding to females within the European Union are considerably lower, 5% less in what the incidence is concerned and 9% less deaths caused by lung cancer [2].

Another carcinogen agent that is known to be involved in the development of lung cancer is radon, an inert chemical gas (with a 3.8-day halving time), is a natural pollution agent for the atmosphere.

The radon concentrations from the exterior are low but on the inside the radon is found in higher concentrations especially in houses and small buildings, and in most countries radon is the most important source of exposure to natural radiations [17].

The 3.8-day halving time allows it to disperse in the air and soil before it degrades, through the emission of alpha particles, in a series of radioactive short life span products. Two of these, polonium 218 and polonium 214, also degrade through the emission of alpha particles [14].

If inhaled, the radon is most times quickly exhaled, but its degradation components with short action time, which are solid, tend to deposit on the bronchial epithelium, exposing the bronchial cells to alpha radiations.

The radio-biological evidence suggests that these cells, exposed even if to a single alpha particle, can be severely damaged.

Therefore, the risk of lung cancer in the case of radon in small doses is directly proportional with the number of exposed cells, which suggests that the relation dosage-response is a linear one [10,11].

Submission of particles in certain areas of the respiratory tract varies with particle size, respiration rate, the ratio between nasal cavity and mouth inhaled air, size and shape of various parts of the
respiratory tract. There are several mechanisms of particle deposition depending on their diameter: Brownian motion - is the main mechanism for particles deposition with a diameter of up to several hundred nm, Gravitational deposition - becomes significant for particles larger than 0.2μm in the peripheral respiratory airways and pulmonary alveolus and Inertial impact - occurs at the respiratory tract in those places where air flow changes direction (nose, oropharynx), this process being important for particles with a diameter greater than 2μm and causing preferential accumulation of particles at bifurcations [3].

For most people the dose of radiation that reaches the bronchial level is determined by the concentration of radon in the house.

In the studies regarding radon and lung cancer the risk is quantified in terms such as radon concentration more frequently than radiation dose, because the concentration can be directly measured.

The atmospheric pollution with radon is ubiquitous, but the highest radon concentration to which the population was ever exposed was encountered in mines, especially in uranium ones.

The studies carried out among miners with known exposure showed a clear association between radon and lung cancer [10,11].

Through the data analysis from 13 case control studies regarding the relative risk of lung cancer due to radon exposure (quantified through the radon concentration measured in Becquerel/m3), carried out in 9 European countries, which included 7148 patients with lung cancer and 14208 witnesses, the following were observed:

- the average radon concentration in the witness’ homes was 97 Becquerel/m3 (Bq/m3), with 11%>200 Bq/m3 and 4%>400Bq/m3.
- 4 cases of lung cancer developed at a medium concentration of 104Bq/m3
- the risk of lung cancer increases by 8,4 % (confidence interval 95%, 3% until 15,8%) on a radon increase of 100Bq/m3
- the relation dose-response seems to be linear
- in the absence of other death causes, the absolute risk of developing lung cancer at the age of 75 and through exposure to radon concentrations of 0, 100, 400 Bq/m3 was estimated at 0,4%, 0,5%, 0,7% for temporary smokers, and 25 time higher (10%, 12 % and 16 %) for cigarette smokers.

The conclusion was that radon exposure is responsible of 2% of deaths of cancer in Europe [4].

Smoking, the major risk factor in development of lung cancer, is considered nowadays a large scale epidemic, and its stopping represents a main objective of the World Health Organization, because it is estimated that 8 million people a year will die until 2030, and approximately 1 billion will die during the XXI century because of tobacco. The tobacco intake is a risk factor for 6 of the 8 main mortality causes [18].

The relative risk of lung cancer development in smokers in comparison with non-smokers is of 15:1 and of 25:1 in heavy smokers. The following are also important:

- duration of smoking period – the number of years is considered the most accurate predictor of lung cancer
  - the period in which smoking started
  - the number of cigarettes packs per year – variables with the highest accuracy in establishing the relation between active smoking and lung cancer [1,9].

Numerous studies document the reduction of the relative risk of developing lung cancer in ex-smokers in comparison with those who continue to smoke. In these studies, ex-smokers have a 10-80% higher risk of developing lung cancer in comparison with the persons who have never smoked, but in comparison with current smokers, their risk is 20-90% [10].

There are sample studies, carried out in the United Kingdom, USA and Japan, which show a decrease of the mortality risk through lung cancer by 80-90% in ex-smokers who haven't been smoking for the past 15 year [6].

2 Problem Formulation

Studies on radon have been first carried out in the United States and Canada and during the last 15-20 years they have become an important field of research in the countries of the European Union [14, 15]. Nowadays, exposure to radon is considered to be the second hazard for bronchus-pulmonary cancer, the first one remaining smoking. Recent studies estimate that radon exposure has a 55% share to the natural irradiation burden of population. Moreover, in areas where the natural exposure is 5-6 times higher than the worldwide average (2.2 mSv/year) this share can increase up to 90% [13].

2.1 Developing a regional radon laboratory

The World Health Organization (WHO) have classified radon as a "Class A" known human carcinogen, because of the wealth of biological and epidemiological evidence and data showing the connection between exposure to radon and lung cancer in humans. This requires making a regional radon laboratory, which can be a support and a reference point for other laboratories existing in The
Hygiene and Public Health Institutes.

The laboratory will measure the radon concentration in air, water, soil and construction materials in different locations in the two districts. The radon measures in air will be taken indoors and outdoors and the stressed areas will be the ones of patients diagnosed with lung cancer.

The proposal is based on the national and international experience of over 20 years of the team in Cluj (The Faculty of Environmental Science from „Babes Bolyai” University (UBB) - Prof. C. Cosma and „Iuliu Hateganu” University of Medicine and Pharmacy - Conf. Doina Todea). The team started in 1996 in a pilot study called Ardeni-Eifel, financed by EC and which followed the correlation between radon exposure and lung cancer.

2.2 The establishment of local maps linked to radon exposure

A second objective is to design maps for radon exposure. The section of the radon exposure measurement, for the cases included in the study and the control group, monitor over 800 houses with double measurements (living room and bedroom) in two different seasons, for a three year period, consisting of more than 3000 measurements in counties of Transilvania.

The analysis will be done in the UBB laboratory, using controlled development and automatic installation in reading the detectors. Also, within this group, we’ll consider the development (increment) of a performant radon room (the control of quality), which allows verification on the precision of the measurements performed.

2.3 Epidemiological study of patients with lung cancer in the centre counties of Transylvania in correlation with the level of radon exposure and cigarette smoke.

The complexity of the study consists in measurements which will be performed with integrated detectors during long periods of times in two seasons to increase the confidence regarding the exposure assessment and that the project will include a case-control study.

This study is a nested case-control study that will investigate the possible etiological factors associated with lung cancer morbidity (especially radon and smoking).

A sample of adults ages 30 –79 years with histological confirmation of lung cancer diagnosed in medical services from this territories and adults age 30 –79 years without lung cancer, from this area who will be asked to participate in the case-control study.

A detailed interview using a questionnaire on environmental and occupational exposure to radon, building materials of dwellings and other potential exposure to ionizing radiations (medical history of radiology procedures for diagnosis and medical history of radiotherapy), will be conducted both with cases and controls. It will also pursue the non-smoking, smoking and ex-smoking status and among the last two categories will assess nicotine dependence by filling Fagerstrom questionnaire.

Data management and data analysis will be performed in STATA Software version 5.0. For data analysis, the logistic regression model will be used in order to estimate the risks (“odds ratios”) and to test the statistic significance of the causal associations.

2.4 Tracking the histopathological type of lung cancer in relation to radon exposure

Among the proposed objectives we also follow the histopathological type of lung cancer.

During the time frame between the 1st of October 1992 - 31st of December 1997 the "Iowa Radon Lung Cancer" study was carried out, an epidemiological witness case study which intended to show the relation between the state as smoker, the exposure to radon inside inhabited spaces and lung cancer encountered in Iowa female patients and a component of this study was observing the morpho-pathological type of the lung cancer encountered in the female patients included in the study.

In order to assess the exposure to radon in this study, WLM15-19 (Working Level Month) was used as measuring unit in this study. The odds ratio to develop lung cancer adjusted according to age, education, active smoking for 5 previously selected categories of exposure to radon: 0-4.23; 4.24-8.47; 8.48-12.7; 12.71-16.94; >16.95 WLM15-19 was of 1.00; 1.34; 1.73; 1.62; 1.79.

The specimens for histopathological examination were obtained through the resection of the tumor, through biopsy (trans-bronchial or fine needle aspiration biopsy), cytological examination (sputum, bronchial brushing, and bronchial lavage).

It was seen that adenocarcinoma is predominant among the histopathological types of lung cancer, followed by the squamous carcinoma, the small cell carcinoma, the giant cell carcinoma and the adenosquamous carcinomma.

A comparison between the encountered types of lung cancer was carried out:
- among the 397 re-assessed female patients of the “Iowa Radon Lung Cancer” study and
- 2593 female patients, aged 40-84, diagnosed with lung cancer and recorded in the Iowa Surveillance, Epidemiology, and End Results Registry between the 1st of May 1993 and the 30th of October 1996 without recording a statistically significant difference [7, 8].

2.5 Lab animal study (rats) to obtain a deeper insight upon the influence of the Radon exposure doses and flow in the triggering of lung cancer

Development of special experimental facilities in order to create controlled radon enriched environments in the laboratory in order to study the incidence of bronchus-pulmonary tumours on animals as well as to obtain a detailed insight in physiological morph-pathological changes of the respiratory tract with the purpose of obtaining the necessary knowledge for prevention.

In the case of lab animals two lots will be monitored: a control group and an experimental one (radon exposed). Animals from both groups will be monitored during the study and the haematological and respiratory modifications will be noted. On the basis of the radiological and morph pathological exams, complementary data will be obtained with the purpose of establishing an accurate diagnose of radon induced bronchus-pulmonary tumour. The experimental reproduction of bronchus-pulmonary tumours on lab animals gives us the possibility of establishing an average radon dose able to start the pathological process.

3 Problem Solution

Since smoking and radon are two carcinogenic agents whose role in developing lung cancer was highlighted in countless studies, any effort that helps quitting smoking, as well as reducing the radon concentration in people’s homes, will lead to an improved health state and a lower number of deaths due to lung cancer for the population affected by these agents.

In areas with high radon concentrations the local authorities as well as the population will be informed about the risks in order for measures to be taken for preventing the migration of radon from soils inside the already existing buildings.

New buildings shall respect legal directives when architectural planning is made in order for radon levels to be reduced.

This aspect concerns also cheap isolation and ventilation plans as well as the choice of building materials as some can enhance the radon concentration through emanation.

Also, in order to avoid the exposure to high radon concentrations in homes, there are affordable solutions: a barrier can be installed on the ground floor of new buildings to prevent the passing though of radon, and in other buildings with high radon concentration the basement ventilation can be intensified [10].

The first step in the world fight against the smoking epidemic consisted in the signing of the WHO Framework Convention for Tobacco Control in Geneva, May 2003. Romania signed this convention on the 25th of June 2004 and ratified it on the 27th of January 2006. The signing and ratification of this convention by Romania is a extremely important fact, because the prevalence of teenage smokers in our country (13-15 years, 22,2% of the males and 14,8% of the females) is distressing. In order to fulfil the objectives of the Framework Convention for Tobacco Control, WHO created the MPOWER package, containing 6 steps to counter fight the smoking epidemics and reduce the mortality rate due to tobacco:

M – Monitor tobacco use and prevention policies
P – Protect people from tobacco smoke
O – Offer help to quit tobacco use
W – Warn about the dangers of tobacco
E – Enforce bans on tobacco advertising, promotion and sponsorship
R – Raise taxes on tobacco [18]

4 Conclusion

Epidemiological studies (“Radon- Lung cancer risk” studies) on humans as well as experiment on animals have been carried out and are still in progress in Europe and worldwide. The results of these studies are used as basis for the development of legal directives for different countries as well as for the general information of public regarding radon exposure risk.

Based on data collected in this epidemiological study regarding the radon exposure among patients with lung cancer (first in our country) and by monitoring radon exposure in the subjects and witnesses from this study areas, will be determined the risk maps and will be facilitated rapid implementation of preventive measures.

Thus, the project is an opportunity to stimulate scientific activity in the high performance peak areas of medicine and environmental science, with direct applicability in increasing the population health and reduce the number of deaths due to lung cancer. It also represents a real basis for policy makers in
developing a regional plan for reducing radon exposure.

References: