High residential radon health effects in Saxony (Schneeberg Study)

"Analysis of the likelihood of female inhabitants
of Schneeberg and Schlema (Saxony)
contracting lung cancer as a result of radon exposure
in dwellings arising from mining and geologically-induced factors, and studies concerning the reconstruction of exposure".

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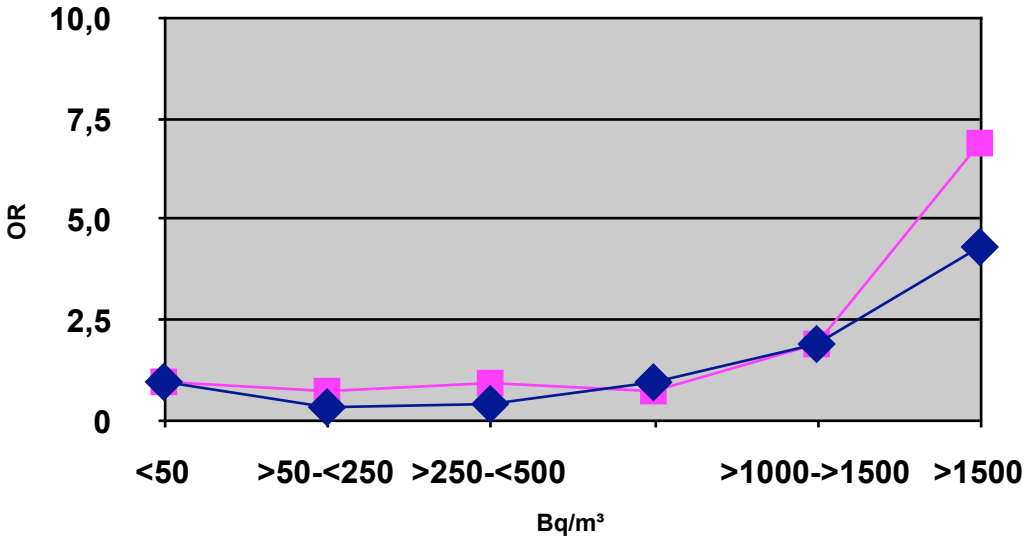
Content

Executive Summary

The available data from indoor radon studies were considered by BEIR VI to be not yet sufficient to develop a general risk-assessment model or to estimate precisely the magnitude of risk posed by radon in houses. In its conclusions, BEIR VI recommends that the power of an indoor radon study to detect an excess risk could be enhanced by targeting special populations, such a population with high exposures, a broad range of exposures, and low residential mobility. The preferential use of non-smokers was not recommended. Otherwise the Schneeberg study completely complies with BEIR VI recommendations regarding its conditions.
An increased and significant OR could be established with the Schneeberg study by two forms of analysis in the higher exposure-categories only. Below a radon-concentration of $48 * 10^6$ (Bqh/m^3) accordingly 1000 Bq/m³ and a residential duration of 20 years the OR is not elevated. Significantly elevated OR after both forms of the analysis are detectable at the exposition level of > 1500 Bq/m³ (figure below).
The risk estimation of the Schneeberg study for lung cancer from indoor radon is not in accordance with the results from miners and population studies, which state an excess risk for 10%/100 Bq/m³ radon exposure. If such risk estimates are true, in the highly

Dose response relations for the lung cancer risk by cumulative radon exposure at two levels of data analysis with raw data and stratified data

exposed population of Schneeberg such lung cancer risks must have been easily established.



That is not the case. From the risk estimate of the Schneeberg study even a safe threshold value was found and a significantly elevated risk appeared at >1.500 Bq/m³ only. Great efforts were taken to explain such discrepancies in comparison to the results from other studies. One reason could be the favourable study conditions of the Schneeberg study (highly exposed population, mainly non-smoking women, exposed fraction very high and a relatively high power etc.). The other reasons are related to characteristics of the other studies especially with the low

exposure to indoor radon and a high exposure to tobacco smoke and a low power. The results from the Schneeberg study are on the other hand enough founded to make further research in that key population a top priority and hesitate to introduce prematurely legal limits for indoor radon.

1. Introduction

Background

In 1537, the famous physician Paracelsus, first described the high incidence of a lung disease among silver miners in the Schneeberg region of Saxony in Germany (PARACELSUS). The unspecified lung disease, called mountain sickness, became later known in medical history as the Schneeberg lung disease. It was 1879 identified by the local physicians Härting and Hesse as lung cancer (SCHÜTTMANN 1988) and definitely related to the extremely high radon levels in these mines by ROSTOWSKI et al. 1926.

The pathologist RISEL already recommended in 1929 epidemiologic research in the general population of this area because he assumed elevated lung cancer rates due to indoor radon in non-miners (STAATSARCHIV). In 1935 LANGE, chief surgeon of the hospital in Aue, closely located to Schneeberg, conducted an ecologic study with 266 cases of lung cancer. From regional maps with different levels of radium in the ground, he assumed respective indoor radon levels in houses. The regions with the highest radium levels in the ground showed a threefold incidence of lung cancer than regions with low levels of radium in the ground. Further research about the biological effects of indoor radon in this region before Word War II was conducted by TELEKY 1937 and BRAND 1938. Both authors related the elevated lung cancer risk in houses to ionising radiation from the ground.

The uranium rich Ore Mountains (Erzgebirge) became at the begin of this century a research centre for the biophysical properties of radium located in Schlema (SCHÜTTMANN 1988) and a branch of the Kaiser Wilhelm Institut für Biophysik, Frankfurt am Main, was founded there.

After World War II the Soviet Union initiated one of the worlds greatest uranium mining activities (WISMUT) to produce between 1945 to 1990 about 220.000 tons of uranium for nuclear armament. The mining activities started in total disregard of the until than accumulated knowledge of the detrimental health effects for the miners and the general population. After 1960, measures for the protection of health and safety standards were introduced. Possible side effects

of the mining activities on the population by radon were denied over the period of uranium mining until 1990, when Germany became reunited.

Research in the detrimental health effects of uranium mining for the miners and the general population in the region of the Ore Mountains (Erzgebirge) started only in 1990, when the Federal Ministry of the Environment funded an epidemiologic study. The study was conducted by HEINEMANN, MARTIN, CONRADY et al. 1992 as an ecologic study based on linkable data from hospital records, cancer registry, death certificates, population registers by age and sex as well as communities and indoor radon levels. Besides the comprehensive data linkage, the study was the first ecologic study not based on county data but on community data to relate more closely exposure and the population. For the miners up to about 12.000 lung diseases were estimated, about 9.000 from hitherto secret files by the WISMUT company for occupational induced lung cancers, and 3.000 from the cancer registry for East Germany. The population risk for lung cancer, besides for communities with a high proportion of miners, was not generally as elevated as expected. In Schneeberg and Schlema, only elevated lung cancer risks for women could be established. These findings were cautiously interpreted as possibly radon related due to the high indoor radon exposure and the absence of smoking in the female population. Further research was recommended with an analytic approach. This approach became realised only in 1995 when the Schneeberg study was accepted by the European Commission for funding within its 4th Framework Programme.

Study area

The **core study area** are the two closely located towns Schneeberg and Schlema in Saxony with about 20.000 and 3.000 inhabitants respectively. These two towns are situated in the former county of Aue, nowadays the county Aue-Schwarzenberg with about 180.000 inhabitants at 1980. The **extended core study area** comprises the district Aue-Schwarzenberg for the inclusion of cases of lung cancer collected from the cancer registry for communities other than Schneeberg and Schlema (diagnosis controls).
For reasons of comparability **Dresden South**, a part of the capital of Saxony with relatively high indoor exposure to radon, is included in this study with lung cancer cases and controls.

The core study area and its study population have some characteristics that distinguish them from other study areas and their populations and ensure despite its small size a high enough power of the study:

- Highly exposed to indoor radon with a wide range of exposure from 50 Bq/m³ to >3.000 Bq/m³.
- The exposed fraction of the population is very high.
- The majority of the study population of women are non-smokers.
- The population has a very low residential mobility.
- The study region is included in a cancer registry since 1952 to the present day.

Exposure level to radon

The high exposure level in the core study area is caused by mining and geologically induced factors. The towns of Schneeberg and Schlema are partially undermined by medieval mining activities mostly for silver and after WW II by present day mining activities for uranium. The recent mining activities beneath the two towns started in 1945 and ended in Schneeberg and Schlema earlier than 1960. After this in the shafts and galleries a natural ventilation existed keeping the radon levels in the average of the year, despite seasonal fluctuations, quite stable. This resulted in equally stable indoor radon levels in houses, especially those affected by former mining activities. To measure the possible influence of mining activities on current radon measurements, studies concerning the reconstruction of exposure are introduced into the study, limited to special areas of Schneeberg and Schlema, where such influences were suspected.

The median exposure level for cases at 209 Bq/m³, register controls at 160 and hospital controls at 104 Bq/m³ for indoor radon in Schneeberg has the potential to make the study population a new key population in radiation research besides the Japanese A-bomb survivors and nuclear industry workers.

The lung cancer risk from radon: ongoing discussion

There is no debate about radon being a carcinogen in humans. The World Health Organisation (WHO) and the U.S. Department of Health and Human Services, as well as the U.S. Environmental Protection Agency (EPA), have classified radon as a "Class A" human carcinogen. What is questioned is whether low radon levels such as those found in most residences may increase the lung cancer risk.
The scientific community continues therefore to debate the size of the lung cancer risk of radon and the shape of the dose-response relationship curve. Most scientists belief that the risk associated with radon increases in direct proportion with the radon concentration - according to the linear no-threshold theory (LNT) of radiation. Others believe that there could be a safe threshold value.

The reason for the prevailing uncertainties about radon health risks are that all of the residential studies have been too small and the exposure levels and the proportions of population under exposure too low to provide - due to lack of power - conclusive information.

The most recent and comprehensive presentation of miners and population studies estimating the health effects of exposure to radon has been compiled in BEIR VI 1999. The available results from miners and population studies were critically evaluated and the uncertainties for the risk estimates were considered. The overall magnitude of ERR/exposure varied substantially among the 11 miner cohorts discussed in BEIR VI, ranging from 0,16 (China) to 5,06 (Radium Hill). Only 5 from the 11 miner studies could present data on smoking. The exposures of the underground miners have been estimated on the basis of incomplete information, and ad hoc

procedures have been used to complete gaps in the measurement data. Despite these limitations BEIR VI has taken the results from miner studies only as the basis for developing risk estimates for both occupational and residential exposure to radon.

The available data from indoor-radon studies were considered by BEIR VI not yet sufficient to develop a general risk-assessment model or to estimate precisely the magnitude of risk posed by radon in houses. In its conclusions BEIR VI recommends that the power of an indoor-radon study to detect an excess risk could be enhanced by targeting special populations, such a population with high exposures, a broad range of exposures, and low residential mobility. The preferential use of non-smokers was not recommended. Otherwise the Schneeberg study would fully comply with BEIR VI recommendations, regarding its study conditions.

BEIR VI concedes despite its general adherence to LNT, that the assumption of linearity down to the lowest exposures was based on mechanistic considerations that could not be validated against observational data. Alternative exposure-risk relations, including relations with a threshold, may be operative at the lowest exposures.

The estimated number of lung cancer deaths for the U.S. for 1995 attributable to indoor residential radon progeny exposure varies - depending on the risk model applied by BEIR VI - between 15.400 to 21.800 total cases. These figures are based on an average indoor exposure of 46,25 Bq/m³ in U.S. homes. The exposure range comprises 0-25 Bq/m³ = 49,9% of all houses to 601+ Bq/m³ = 0,4% of all houses. The exposure level from 0-150 Bq/m³ is found in 94,5% of all U.S. homes (BEIR VI 1999).

Several major case-control studies of lung cancer in relation to long-term measurements of exposure to radon have been conducted (BLOT et al. 1990, SCHOENBERG et al. 1990, RUOSTEENOJA et al. 1991, PERSHAGEN et al. 1992 and 1994, LÈTOURNEAU et al. 1994, ALAVANJA et al. 1994, AUVINEN et al. 1996. These studies were included by LUBIN and BOICE 1997 in a meta-analysis. Of the eight studies, five showed positive associations within some subgroups, but for only three was the principal overall analysis significant in the positive direction. A major limitation of the individual studies, however, is their limited statistical precision and power to detect small risks. The meta-analysis of these studies (LUBIN and BOICE 1997) found a statistically significant positive slope, such that the RR at 150 Bq/m³ was 1,14 (95 percent CI = 1.01 to 1.30) which is almost identical to the corresponding projection from the miner studies (namely, 1.13). The RRs at 150 Bq/m³ in the eight studies differed appreciably ranging from 0.84 (BLOT et al. 1990) to 1.83 (PERSHAGEN et al. 1992), and the heterogeneity in the risk estimates was found to be statistically significant.

Based on the results from BEIR VI, the US Environmental Protection Agency (EPA) is updating its methodology for risk assessment from indoor radon (EPA February, 1999; EPA May, 1999). The method applied for calculating radon risk and risk projections is a mere ecologic approach, that is rejected by EPA for the inherent limitations of the method when results by COHEN 1990 and 1995 are discussed. The estimated fraction of lung cancer deaths in 1995 attributable to radon by EPA (February, 1999) is 12,5% of lung cancer deaths or 19.600 cases. These risk estimates by

EPA should not be regarded as official EPA risk projection. They are presented solely to facilitate the proposed method. The admitted uncertainties in the method are tried to be compensated by several corrections and assumptions, as well as control for the influence of smoking by two categories only for ever and never smokers, and without considering quantitative data of tobacco use. A confounder measured without error can be fully controlled. Nevertheless, a crude measurement or surrogate for a confounder (yes/no) is inadequate to achieve full control and the risk analysis will suffer from confounder misspecification. The exposure level for indoor radon resulting in the projections of lung cancer deaths by EPA is in the average 46,25 Bq/m³.

For West Germany the number of radon induced lung cancer deaths has been estimated by STEINDORF et al. 1995 at 2.000 annually (400 in females and 1.600 in males) resulting in a portion of 7% of all lung cancer deaths attributable to radon with an arithmetic mean for indoor radon of 49 Bq/m³ and 8% of the homes are above the 100 Bq/m³ level. Adjusting for the intermediate relationship for smoking and radon, STEINDORF et al. 1995 found an attributable risk to be about 4-7% for smokers and 14-22% for non-smokers.

In order to solve some of the controversies in the radiation research community about LNT and collective dose, the Director of NRPB and Chairman of ICRP, Roger Clarke, presented a proposal the concept of "Controllable Dose" (CLARKE, August 1998). "Controllable Dose" is the dose, or sum of the doses to an individual from a particular source, that can reasonably be controlled. The principle is, if the risk to the most exposed individual is trivial, then the total risk is trivial, irrespective of how many people are exposed. The issue is, whether the LNT-Dose-Response relationship is appropriate for regulating low-dose radiation.

Most recent publications of epidemiologic studies on the risk from indoor radon (WICHMANN et al. 1997, 1998a and 1998b, DARBY et al. 1998, PERSHAGEN et al. 1994, LUBIN 1998) will be discussed in chapter 5.

2. Objectives

2.1 Main and secondary null hypotheses

The concept for analysis and the methods of analysis applied to this "Schneeberg Study" concentrate on testing of the following main and secondary null hypotheses:

Main null hypotheses:

- The relative risk of women (in Schneeberg and Schlema) to develop lung cancer is not elevated due to the radon exposure at the residence or working place if confounders are controlled for.

- Likewise, the relative risk of women (in Schneeberg and Schlema) to develop lung cancer is not elevated to the various levels of exposure with radon in the residence or workplace, if confounders are controlled.

- In the past in Schlema and in some houses in Schneeberg, no higher radon concentrations appeared than presently.

Secondary null hypothesis:

- A radon exposure in childhood leads not to an elevated lung cancer risk.

The following objectives of the study have been achieved:

- Estimation of the relative lung-cancer-risk (OR) by exposure to radon in dwellings with main emphasis on non-smoking women.
- Dose-Response-Analysis under consideration of differently accumulated expositions over time and cancer-histology.
- Establishment of uniform dosimetric foundations for the linkage of the study-results with other case-control studies as prerequisite for a joint-analysis over the range from low to very high levels of radon exposures.
- Possible methods for the reconstruction of past exposures.
- Examination of the dose-response curve and the slope of the linear component of dose.
- Recommendations for Public Health measures in radon-prone areas

2.2 Definition of cases and controls

Cases

All female lung cancer cases of the core study area Schneeberg and Schlema between January 1, 1952 and December 31, 1989 which are registered in the local cancer registry. All documented, by a death certificate, female lung cancer cases between January 1, 1990 and December 31, 1997 in Schneeberg and Schlema.

- The inclusion criteria for cases are:

Female lung cancer diagnosed between January 1, l952 and December 31, l997,
registered in the local cancer registry in Aue (until September 15, l990) or death certificates in the public health department in the rural districts of the study areas until December 31, l997, living at least 25 years of the last 35 living years in the Aue district.
All reported and valid cases with the diagnosis of lung cancer which fulfils the Criterion of Reliability of the Oxford Classification are taken into account in the study.

- Comparative group of diseased

Female patients with lung cancer from other communities than Schneeberg and Schlema in the district of Aue-Schwarzenberg which have at the average a lower radon exposure than the cases in Schneeberg and Schlema. This group will be used to answer the question of whether or not there are differences in the risk factors between women diseased in Schneeberg and Schlema, in comparison to women diseased in other communities than Schneeberg and Schlema in the district of Aue-Schwarzenberg.

Inclusion criteria for the comparative group of diseased:
Female lung cancer diagnosed between October 1, l952 and December 31, l990,
same vital statistics as cases

Controls

Under consideration, mainly a retrospective study is conducted, depending on the hypotheses to be examined, different control groups have been formed.

- Population controls (cancer registry)**.**
  Population controls have been selected from the cancer register journal of Schneeberg or Schlema in the relevant regions where the respective cases live. Four population controls have been selected for each lung cancer case.

Inclusion criteria for population controls:

Female cancer illness with no known radon or smoking effect, which is different from lung cancer and free from metastases in the lung, diagnosed between January 1, l952 and December 31, l990, (the exclusion of other cancer localisation's with a possible radon causation will be completed in agreement with the protocol of the „Ardennes Eifel Study“ before commencement of the data analysis).
Population controls have to meet the matching criteria of 5 year age groups at date of diagnosis, same vital statistics as cases,
living at least 25 years of the last 35 living years in the Aue district (for the analysis a separate group with lifelong residence in Schneeberg or Schlema will be formulated)
comparable request for cases based on death certificates from January 1, l991 to December 31, l997.

- Population controls (Hospital controls)
  Hospital controls who were enlisted in the hospital journals have been selected from Schneeberg or Schlema in the relevant regions where the respective cases live. Two hospital controls have been selected for each lung cancer case.

Inclusion criteria for hospital controls:

Female cancer illness with no known radon or smoking effect, which is different from lung cancer and free from metastases in the lung, diagnosed since January 1, l996,
list of ineligible diseases for hospital controls is in the study-protocol of the “Ardennes-Eifel-Study.”
Hospital controls meeting the matching criteria of 5 year age groups at date of diagnosis
living at least 25 years of the last 35 living years in the Aue district (For the analysis a separate group with lifelong residence in Schneeberg or Schlema will be formulated).

Comparable request for cases based on death certificates from January 1, l991 to December 31, l997.

For the recruiting phase of cases and controls there has been no exclusion for occupation, but for no exposure status, no residential address, no diagnosis, less than 25 years residence in the Aue district.

2.3 Necessary sample size

When sample size requirements are discussed to secure a sufficient power of population studies than large sample sizes are requested to compensate for low exposure levels and confounding factors. This results in unrealistic sample size requirements that cannot be met, or the low power of recent population studies is not revealed by its authors.

However, even with a large sample size a clear picture of lung-cancer risk posed by residential radon exposure may not result from studies conducted in low exposure areas, and almost all cases are smokers. The part of controls that are smokers is not in proportion to the smoking status of the general population. Therefore, it is advisable to conduct studies with small sample sizes in key populations highly exposed to radon over a wide range in the absence of main confounders such as smoking.

The following assumptions require determination: Type I Error (α), Type II error (β): power (1 - β) and proportion of exposed in the population in order to determine the sample size necessary to address the main and secondary hypotheses.

Usually a Type I error of 0,05 and power in the area of 0,8 - 0,95 will be pre-set. From examinations of the exposure distribution in the population of Schneeberg before commencement of the study, it was known that one third of the population is exposed to radon (Po = 0,3). In the following table, estimations of the necessary sample sizes are presented which are necessary to detect a pre-set relative risk with different statistical power.

Table 1 clearly shows that very few cases are needed under the presupposing conditions for Schneeberg/Schlema, in order to achieve a relative risk of 2,5 with a likelihood of 80%, if 4 controls per case are chosen (n = 43). With an increasing expected relative risk of 3,5 and 4,5 the necessary number of cases decreases to 23 and 17 respectively.

Tab. 1: Minimal numbers of cases required to detect different levels of relative risk, α =0,05 two sided, share of the exposed 0,3, β = 0,80 and β = 95 (SCHLESSELMAN 1982).

Number of controls	Relative Risk

per case	2,0	2,5	3,0	3,5	4,0	4,5
Po = 0,3, α = 5 %, β = 0,80						
1	140	79	55	42	34	29
2	90	52	37	29	24	20
4	74	**43**	30	**23**	19	**17**
10	65	37	26	20	17	14
Po = 0,3, α = 5 %, β = 0,95						
1	210	114	79	60	49	42
2	152	86	59	46	37	32
4	126	72	49	38	31	26
10	111	63	43	33	27	23

3. Progress and results

3.1 Case and control data (WP1)

Data pool

The most effective way to proceed in the analysis of a case-control study is from the simple to the complex (SCHLESSELMAN 1983). The analysis of the Schneeberg study has been performed in two stages from a descriptive analysis to the risk analysis. The available pool of data files for each way of analysis can be seen in table 2.

Tab. 2: Data pool for female cases and controls by study area and method of analysis

Type of analysis **Study area**	**Cases**	**Controls**
Descriptive analysis		
District Aue-Schwarzenberg	154	-
Dresden South	196	55
Total for descriptive analysis	**350**	**55**
Risk analysis		
Schneeberg-Schlema: Cancer registry Death certificates Hospital	 73 12 -	 378 - 181
Total core study area	**85**	**559**

Cancer registry

The data collection for cases and register controls for the Schneeberg study is based on the local registry of the National Cancer Registry for East Germany. In the former German Democratic Republic (GDR) the National Cancer Registry was founded in 1953. It was mandatory for each doctor to notify the local cancer registry by standardised forms. The completeness of collected incident cases was 95%. The quality of the cancer registry has been confirmed after reunification of Germany by ENDERLEIN et al. 1995. Nowadays the cancer registry continues on the Federal States level based on a new Federal Law for Cancer Registry dated 1. January 1995. The Federal States from the former GDR created the Common Cancer Registry for the New Federal States to keep the data collected from 1952 to 1990. Cases and register controls for the Schneeberg study were collected according to the inclusion criteria cited under 2.2.

Death certificates

After unification of Germany, a legislative gap regarding cancer registration and completeness of incident cases existed for several years. The drop in completeness of data collection was dramatic from 95% before to 20% after 1990. Therefore, the Schneeberg and Schlema cases from 1990 to 1997 were collected from local death certificates. In the meantime, Saxony introduced again the doctor's obligation to notify the newly founded Tumour Centres by standardised forms to secure a high completeness of data collection. For the years 1995 to 1997, Saxony had already achieved a completeness of 78% (GIESEN 1999), and aims at 95% for the near future.

Questionnaires for cases, controls and next of kin

For the hospital controls, the necessary data were obtained by personal interviews with patients eligible in the study, in the Miners Hospital in Schneeberg and the District Hospital in Aue. The next of kin from cases and register controls were personally interviewed based on the same questionnaire form. For this study, a questionnaire was developed and validated in an earlier study (CONRADY et al. 1995).

The following main items have been asked:
Name,
Date of birth,
Residential addresses since birth,
Addresses of work places and duration of jobs (working history**),**
Smoking behaviour (actively, passively),
Exposure at work places (other than radon).

Socio-economic status

Characteristic of the socio-economic status is that its association with disease and death is maintained independently of the specific pathways by which the association is maintained. A key variable in this cumulative process is occupation. Occupation is regarded as the means by which

a person's principal resource (education) is converted into the principal reward (income). The exercise of occupation links two sets of advantages: the resources that are needed to achieve a specific occupational position and the rewards that accrue to those who have attained this position.
The ERICSON-GOLDTHORPE 1992 scheme is used to classify women from the Schneeberg study into occupational classes. From this five socio-economic classes were derived:

1 Administrators and professionals,
2 Routine non-manual workers,
3 Self-employed individuals,
4 Skilled manual workers,
5 Unskilled manual workers.

For data analysis the five classes were reduced to three, because the classes 1 and 3 included too few participants. Class 1 was thus included into class 2, and class 3 into class 4. In the end remained three occupational classes, considering the frequency of the occurrence of the different classes, depending on the special socio-economic composition of the female population in Schneeberg and Schlema:

Routine non-manual workers,
Skilled manual workers,
Unskilled manual workers.

Other sources

Other sources especially for diseased cases and controls were:
- District authority for documents (birth certificates),
- Local office for the registration of residents,
- Housing departments,
- Patient department for lung diseases and tuberculosis (PALT).

The main items collected from these sources are presented in table 3.

Overview of data sources

Due to its mainly retrospective approach of the case-control study data collection could be based on different data sources presented in table 3.

Tab. 3: Data sources for female cases and controls by important variables for data files

Sources	Cases	Controls
Cancer registry 1960-1990		
Name	X	X
Address	X	X
Date of birth	X	X

Date of diagnosis	X	X
Date of death	X	X
Diagnosis	X	X
Histology	X	X
Autopsy	X	X
Smoking behaviour	X	X
Occupation	X	X
Death certificates 1990-1997		
Currant name	X	
Name at birth	X	
Address	X	
Date of death	X	
Diagnosis	X	
Histology	X	
Next of kin	X	
Hospitals (interviews)		
Name		X
Residential addresses		X
Date of birth		X
Smoking behaviour		X
Working history		X
Next of kin (interviews)		
Name	X	X
Residential addresses	X	X
Date of birth	X	X
Smoking behaviour	X	X
Working history	X	X
District authority for documents (birth certificates)		
Name at time of birth	X	X
Residential address	X	X
Local office for registration of residents		
Name	X	X
Name at birth	X	X
Residential addresses	X	X
Occupation	X	X
Next of kin	X	X
Housing departments		
Identification of case dwellings	X	
Next tenants	X	
PALT		

Smoking behaviour	X	X
Occupation	X	X
Residential address	X	X

Several items could be collected from different overlapping sources, so the relevant data could be compared and checked for validity. That applies in particular to data for the smoking status from cancer registry forms for cases and register controls and questionnaires for next of kin as well as files for population based screening examinations for lung diseases (PALT = Out Patient Department for Lung Diseases and Tuberculosis).

Assessment of data quality

To ensure the reliability of case and control data, additional efforts have been made to validate case and register control data extracted from the local cancer registry. By interviewing next of kin from lung cancer cases, their information at the time of diagnosis about their smoking behaviour was cross-checked for 35 cases. With 31 cases (88,6%) the information were in agreement. With register controls from 106 interviews, 95 information regarding smoking habits at the time of diagnosis have been confirmed (89,6%).

Data protection

The legal foundation for the protection of data privacy is the German Federal Law of Data Protection (Bundesdatenschutzgesetz, BDSG). Data collection and processing for cases and controls has considered additionally the Data Protection Law by the Saxony state. Data collection by questionnaires for hospital controls and next of kin was based on informed consent and that was established in writing. The processing of data was conducted in anonymous form only and publications of results from the study will be done in a way that personal data are not revealed.

3.2 Dosimetry (WP2)

Radon gas measurements

For indoor radon measurements in a region highly exposed to radon dosimeters from ALTRAC were used, due to its high measurement capacity and measurement precision. The ALTRAC dosimeters are based on CR 39 detector material. The dosimeter box is completely made of a special type of permeable and conductive plastics without use of any additional filter material to hold the daughter products of radon. That means the whole dosimeter box is the filter. The diffusion time of radon inside is about eight minutes so that thoron cannot contribute to the measuring result.
The ALTRAC dosimeters have been successfully tested at seven official intercalibration exercises or blind tests respectively (NRPB, BfS, EML, PSI). The uncertainty of the measured radon-222-concentration was in each case less than 20%. The detectable range of radon comprises 15 - 40.000 Bq/m³ (time of exposure 90 d).

The next table shows the maximum exposure times for several types of dosimeters to demonstrate the special suitability of ALTRAC dosimeters for long term measurements in an environment with especially high levels of indoor radon.

Tab. 4: Maximum exposure times of different dosimeters*

Type of Dosimeter	250 Bq/m³	1.000 Bq/m³	15.000 Bq/m³
ALTRAC (CR 39)	20.000 d	5.000 d	350 d
MAKROFOL	500 d	125 d	10 d
KODAK	3.350 d	850 d	55 d

*According to DIN 2570-1

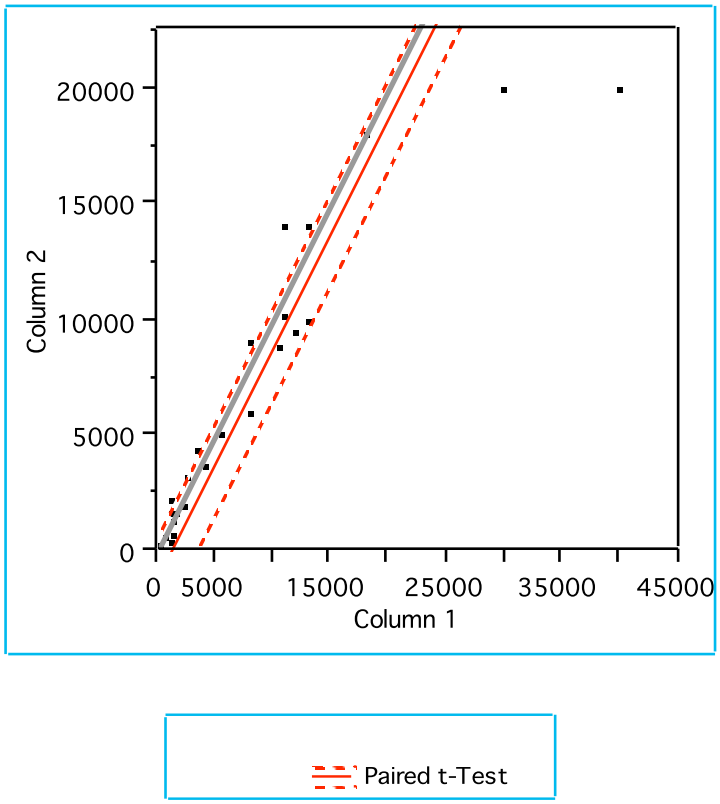
Due to seasonal changes in indoor radon concentration and possibly influences on the indoor radon levels by former mining activities especially in a small part of the old city centre of Schneeberg the validity of current one year indoor radon measurements to describe the past indoor radon exposure for relevant cases and controls was tested besides the application of the retro measurement technique. The test objects were one house in the "Georgengasse" and a group of 24 houses in the old city centre of Schneeberg.
For the house in the "Georgengasse" (no number due to data protection) indoor radon values from repeated one year measurements are available over a period from 1990-1995. This house was suspected to be influenced in its indoor radon levels by mining induced factors.

Tab. 5: Results from repeated one year radon measurements (Bq/m³) 1990-1995 in a house in the "Georgengasse" Schneeberg

Monthly period	1990 - 1991	1994	1995
October - December	429	-	-
January - March	1703	-	-
April - June	1743	-	-
July - December	865	-	-
Annual mean	**1294**	**1280**	**1705**

The mean for the time period 1990-1995 is 1461 Bq/m³ with a standard deviation of 219 Bq/m³ only confirming a quite stable exposure level to indoor radon. Additionally a glass sample of 60 years from the house was used for a retro measurement. The cumulative radon exposure estimate from that glass sample is with 1.300 Bq/m³ in a good accordance with the annual mean of the current measurements (Tab. 5). For the group of 24 houses in the old city centre of Schneeberg one year indoor radon concentrations were measured before and after subsoil modifications deriving from present attempts, to reduce radon levels in the houses by a change in the ventilation regime down the mine.

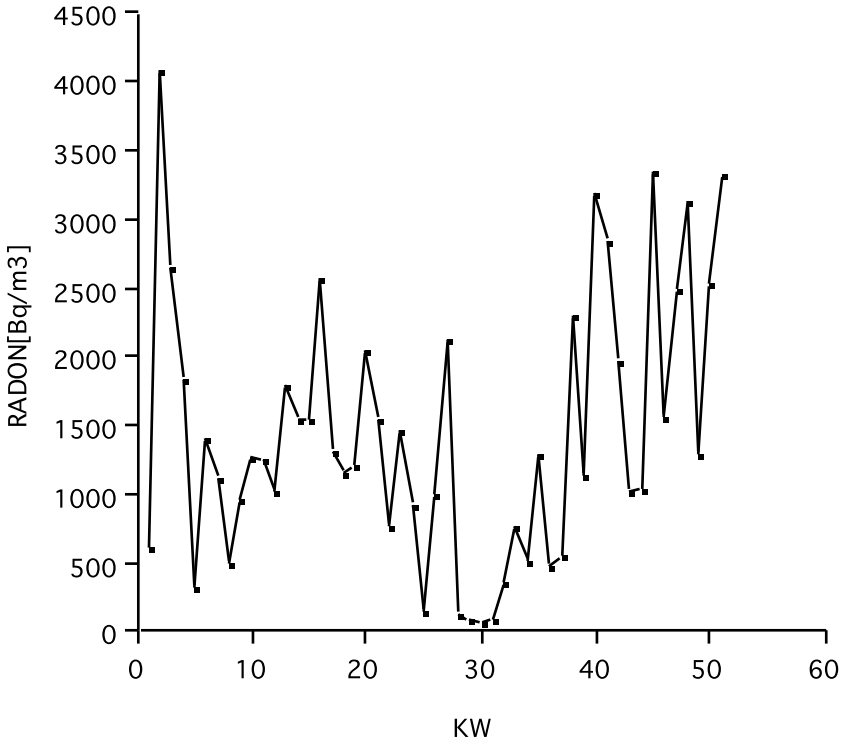
Fig. 1: Comparison of the indoor radon concentration in 24 Schneeberg houses (cellar) before (Column 1) and after subsoil modification (Column 2) 1997-1998



Only in two of the 24 houses (otliers in the right corner above) about 50% reduction in indoor radon concentration could be measured. This change is within the range of natural variations in indoor radon levels, typical for that area. The influence of a changed ventilation regime in the mines beneath the 24 houses is negligible if measurable at all.
As a result from the investigations in the house "Georgengasse" and especially the 24 houses in the centre of Schneeberg can be concluded, that the exposure conditions for indoor radon must have bee stable for the investigation period of the Schneeberg study, when even rigorous attempts by technical means where futile to change the natural ventilation regime in the mine beneath the old centre of Schneeberg being in existence from about 1960, when mining activities ended there.

As an example for the special seasonal slope over a one year period of the curve for indoor radon levels in houses influenced by mining factors one house in the old centre of Schneeberg was chosen for a continuous one year measurement by an alpha-guard system (Figure 2). The year is divided by calendar weeks (KW). From the slope of the curve you can see the seasonal influence of the indoor radon level - very high in the winter, very low in the summer and increasing again in the autumn up to winter levels. From this figure can bee seen, that only one year measurements can give the right indoor radon value, short time values taken in the summer period are wholly misleading. But despite the seasonal changes in the indoor radon level, one year measurements repeated at various years yield quiet constant values as already discussed (Tab. 5).

Fig. 2: Weekly and seasonal changes in the indoor radon level over one year in a Schneeberg house



KW = calendar week

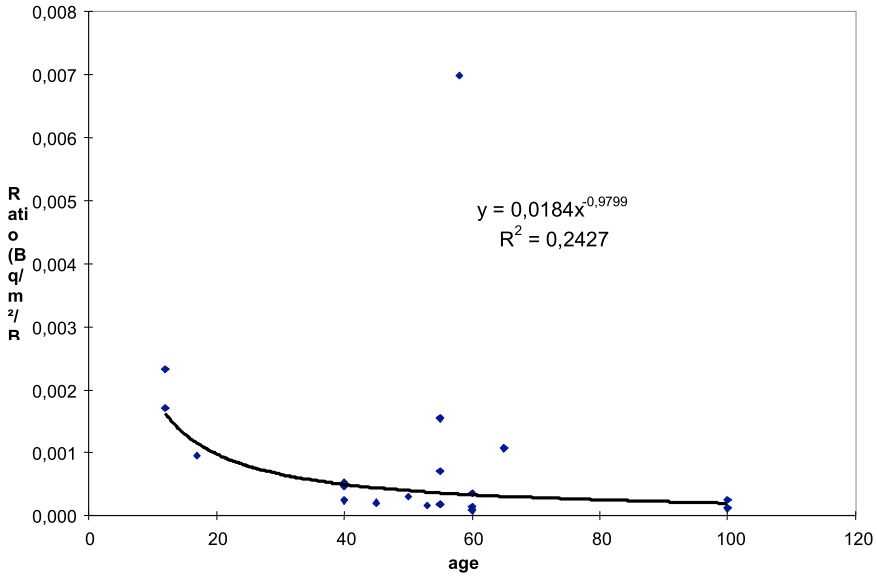
Retro measurements

In epidemiological studies about the risk of indoor radon, accurate assessment of past exposures is a first order problem. In order to validate to what extent the results of current one year radon measurements in the Schneeberg-Schlema area are representative for past situations, the reconstruction technique based upon the determination of trapped Po-210 activity in glass objects was used systematically. The surface activity of glass sheets was measured using Po-210 detectors by RUG. These detectors were fixed on indoor glass surfaces for three months. For each Po-210 measurement a radon concentration measurement was done for one year using ALTRAC dosimeters. A ratio was defined as being the implanted activity (Bq/m^2) divided by the radon exposure of the glass sheets ($kBq * year/m^3$).

The first field test of this new method was done in the preparative phase of the Schneeberg study. Past and current radon measurements were done side by side in some 20 houses. The results showed clearly that the ratio of glass implanted Po-210 activity over cumulated exposure wasn't constant over time (Tab. 6) and did give the first indications of the existence of some loss mechanism. This was confirmed in later experiments. The nature of this mechanism is not yet

fully understood, although there are indications that corrosion may effect the implanted activity in the course of time.

Tab. 6: Results from a first comparison exercise of current and past measurements in 20 houses in Schneeberg 1995



The results from this pre-test were promising enough to include this method in the Schneeberg study. The outliers (great differences between current and past radon measurements, for example ratio 0,007 in Tab. 6 and the low R^2 of 0,24 caused some changes in the method, laid down in guidelines for measuring Po-210 on glass. The outlier for example at ratio 0,007 was not caused by measurement errors but can be explained by changes in the ventilation beneath the measured house in Schlema. The current measurement was about 100 Bq/m³ but the past indoor radon level before changes in underground ventilation yielded about 6000-7000 Bq/m³.

The main changes in the selection of glass samples were:

- Exclusion of window glass exposed to sunlight, instead mirror glass, glass covering pictures/painting, photos, cabinet glass, glass in internal doors, glass from wall clocks was chosen.
- Introduction of a special questionnaire to document mitigation measures to have a chance to explain outliers.

The special study concerning the reconstruction of exposure included in the Schneeberg study comprised 78 houses. In these houses, situated mainly in the old centre of Schneeberg, one year indoor radon measurements were accompanied by Po-210 measurements on eligible glass samples. The results are presented in two figures, demonstrating the linear fit of the curve - past radon versus present radon - in two versions: firstly, outliers are included without correction for mitigation and secondly, outliers are corrected for mitigation. The procedure for the correction

process and choice of the valid value measured (past or current measurement) is described in the following chapter " Categories of indoor radon measurements".

Fig. 3: Po-210 glass measurements (past radon) versus one year radon gas measurements in Bq/m³ (present radon) in 78 houses in Schneeberg-Schlema

Without correction for mitigation

The figure "Without correction for mitigation" resulted in a linear fit with $R^2 = 0,57$ only. When corrections for mitigation are included, see figure "With mitigation included", the linear fit improves considerably and R^2 increases to 0,85. When from the sample in the figure "With mitigation included" mitigated dwellings and not lived in at the time of measurement (constantly closed windows increase radon level) were excluded, the best fit with $R^2 = 0,96$ is found as presented in figure 5.

Currently this method is applied systematically, besides in the Schneeberg study, in the ongoing epidemiological studies in Sweden and Italy and much attention will be given to this technique in the next Radon Epidemiology project under the 5th Framework Programme of the E.U.

Fig. 4: Po-210 glass measurements (past radon) versus one year radon gas measurements in Bq/m³ (present radon) in 78 houses in Schneeberg-Schlema

With correction for mitigation

Fig. 5: Po-210 glass measurements (past radon) versus one year radon gas measurements in Bq/m³ (present radon) in 78 houses in Schneeberg-Schlema

With correction for mitigation minus houses not lived in at the time of measurement

This technique was especially thoroughly investigated under the E.U. contract FI4P-CT95-0025 and did proof its reliability and practicality in several quality control exercises organised over the last years as part of the E.U. contract FI4P- CT96-0065.

Selection of appropriate objects and detailed information on the exposure conditions permit to obtain a good estimate of the radon level of the past. Additionally these measurements have not given any hints, that current measurements are not representative for past exposure, if subsequent

controls for changes in the construction of the houses in the past are taken into account (mitigation measures etc.).

Categories of indoor radon measurements

Results from long-term indoor radon measurements together with retro measurements will be categorised as follows:

Category	Criteria and steps to be taken
1	Long-time measurement with ALTRAC dosimeters for 12 months. Places of measurement: living room, sleeping room Results from UG retro measurement not more than the two-fold value of the long-term radon measurements at the same places of measurements or at least at one place. Result: Actual radon measurement is validated.
2	Long time measurements with ALTRAC dosimeters for 12 months. Places of measurements: living room, sleeping room Results from UG retro measurement more than the two-fold value of the long-term radon measurements at the same places of measurements. *Explanation:* Mining influences by time? Clarification by time window for retro result. Construction changes by time? Clarification by time window for retro result. Result: Retro measurement is valid for the respective time window *No explanation:* Analysis at the spot of measurement. Consider repeat of retro Measurement. Result. Depending on result of analysis or repeated measurement.
3	**3.1**: In case of great discrepancies between the results from long-time measurements of indoor radon and radon in the cellar, look for construction changes and make retro measurements. Result: Apply corrections to the long-time measurement. **3.2:** In case of loss of one dosimeter for long-time measurements in the living room or sleeping room, the average ratio from Schneeberg between radon measurement results from the living and the sleeping room will be applied to replace the value from the lost dosimeter. Result: Complete data for both places of measurements. **3.3:** In case of missed long-term indoor measurements for houses torn down or measurements refused, the replacement of data can be considered by measurement results in neighbouring houses, expert rating or the average indoor radon value by Gauß-Krüger-Koordinates from Schneeberg. Result: Replacement of missed indoor values.

Establishing an individual exposure

The radon-exposition of the probationers was determined by average from the measured radon-concentrations in the living- and sleeping-room. The cumulative exposition was calculated with a stay-time of 6.000h/a and under application of a equilibrium-factor of 0,4. This cumulative exposition of one year was multiplied with the years of the total-residential-duration in each

measured apartment. If it was the last lived in apartment, 5 years of the total-residential-duration were subtracted. If several apartments were measured, the total-exposition of the probationers resulted from the addition of the individual exposition-phases.

Assessment of exposure data quality

Due to the availability of exposure measurements that were measured before possible mitigations and the validation of current measurements by past measurements, the exposition-estimations could take place completely with measurements of the present radon-concentration. That means, no current measurement was substituted by past radon values.

The method of the retrospective radon-measurement was used to judge the present exposition-situation regarding its stability in the past. The research question was, whether in comparison to the past (to the lifetime of cases) other exposition-situations prevailed as today. To this, retrospective measurements were done in areas of Schneeberg and Schlema, that were under the suspicion, that over the observation time of the study unstable exposition situations occurred from mining and geologically-induced factors. Such possible influences could be excluded by the retrospective measurement technique.

3.3 Data analysis (WP3)

Descriptive analysis

In the following table 7 the derivation of matched sets for the core study area Schneeberg/ Schlema starting from the available data pool for cases and controls (table 2).

The data were checked for meeting the quality criterion laid down in the study protocol. From the data pool of 85 cases 13 had to be excluded, this are 15,3%. From the reasons for exclusion you can see, what criterion could not be fulfilled (histologic type of cancer not in accordance with the study protocol, occupation as an uranium miner, duration of stay too short, no radon dose could be established).
With the register controls from the data pool of 378 controls, 96 controls had to be excluded, this are 25,4%. The share of refusals is with 23 controls, 24% from the total exclusion, the highest proportion. The register controls include probationers from 1960 on, so to gather enough information about these category of controls is especially complicated due to the time elapsed.

From the data pool of 181 hospital controls, only 18 had to be excluded, this are 9,9%.
When comparing the row "Eligible probationers" and "Probationers used", it can bee seen, that a surplus of controls exists, even when a proportion 1:4 is applied. This made is possible to choose the most suitable controls for matching with cases.

Tab. 7: Derivation of matched sets for the core study area Schneeberg/Schlema

	Cases	Register controls	Hospital controls	Total
Base line data	**85**	**378**	**181**	**644**
Reasons for exclusion:				
Refusal	-	23	-	23
Histology	3	-	-	3
Miners	2	-	-	2
Duration of stay	3	57	9	69
No radon exposure	5	16	9	30
Exclusion total	**13**	**96**	**18**	**127**
Rate of exclusion	15,3%	25,4%	9,9%	19,7%
Eligible probationers	72	282	163	517
Probationers used	**72**	**226**	**62**	**360**
Change hospital controls		+14	-14	
Matched sets (1:4):				
Cancer registry/ Register controls	60	240		1/4
Death certificates/ Hospital controls	12		48	1/4
Matched sets total	**72**	**240**	**48**	**1/4**

To secure the proportion 1:4 for cases from the cancer registry with controls, 14 controls from the hospital controls had to be added to the 226 register controls, to achieve that end. Finally 72 matched sets with 4 controls could be established for data analysis: 60 cases from the cancer registry with 240 register controls (14 hospital controls included) and 12 cases based on death certificates with 48 hospital controls.

The distribution of the smoking status among cases and controls used for data analysis can be seen from table 8. From the cases with information about the smoking status available 78% are non-smokers. The rate for non-smokers among register controls and hospital controls is with 94% even higher. Information about the smoking status are not available for 9 cases and 42 register controls, that is 13% and 19% respectively.

The distribution of the occupational status among cases and controls used for data analysis can bee seen from table 9. The proportion of unskilled manual workers is with 64% the highest among cases, followed by register controls with 58% and hospital controls with 35%. The group of the skilled manual workers is with about 7-10% quite evenly distributed among cases and controls. The proportion of skilled non-manual workers is with 25% the lowest among cases, followed by register controls with 32% and hospital controls with 58%.

Tab. 8: Description of the matched cases and controls used from the core study area by smoking

Group	Non-smoker*	Smoker*	Not available**	Total
Cases	49	14	9	**72**
	77,8%	22,2%	12,5%	
Register controls	173	11	42	**226**
	94,0%	6,0%	18,6%	
Hospital controls	58	4		**62**
	93,5%	6,5%		

*Percent from total minus not available **Percent from total

Tab. 9: Description of the matched cases and controls used from the core study area by occupational status

Group	Skilled non-manual worker*	Skilled manual worker*	Unskilled manual worker*	Not available**	Total
Cases	15	6	38	13	**72**
	25,4%	10,2%	64,4%	18,1%	
Register controls	50	15	91	70	**226**
	32,1%	9,6%	58,3%	31,0%	
Hospital controls	35	4	21	2	**62**
	58,3%	6,7%	35,0%	3,2%	

Percent from total minus not available **Percent from total

The distribution of the age at diagnosis and the histologic type of lung cancer among cases from Schneeberg/Schlema, the district Aue-Schwarzenberg and Dresden-South can bee seen from table 10 cases from Schneeberg/Schlema diseased earlier in comparison to cases from other regions and the proportion of the histologic type of the small cell carcinoma is distinctly elevated.

Tab. 10: Mean age and distribution of lung cancer cases by histology with cases from Schneeberg in comparison to cases from the district Aue and Dresden-South

		Histologic type				Diagnostic
Region (cases)	mean age	small cell	squamous	adeno	others	confirmed
Schneeberg (72)	65	23	15	7	8	53
		43,40%	28,30%	13,20%	15,10%	72,60%
District Aue (154)	65,1	29	20	14	26	89
		32,60%	22,50%	15,70%	29,20%	58,79%
Dresden-South (196)	67,4	22	13		33*	68
		32,35%	19,11%		48,53%	34,69%
East Germany	67,4					

*Adenocarcinoma included

The distribution of the register controls and hospital control by diagnostic groups (ICD 9) can bee seen from table 11 and table 12.

Tab. 11: Distribution of register controls by diagnostic group for cancer (ICD 9)

Diagnostic groups	ICD 9	N	%
Digestive system	150-159	104	46,0
Bones, connective tissues, skin, breast	170-175	53	23,5
Urinary tract, genital organs	179-189	52	23,0
Lips	140-149	2	0,9
Other sites	190-199	14	6,2
Leukaemia	200-208	1	0,4
Larynx	160-165	0	0
Total	140-239	226	100

The register-controls come with a share of 92,5% mainly from the diagnosis-groups ICD 9, 150-189, with the cancer sites: digestive system, bones, connective tissues, skin, breast, urinary tract and genital organs).

The hospital controls originate with 72,6% from the first three diagnostic groups: circulatory system, immune system and digestive system.

The decisive factors for the dose from indoor radon exposition of the probationers are the radon-concentration and the residential-duration. The corresponding parameters are summarised for the individual probationers in table 13. The median residential-duration is longer than 30 years with exception of the comparative group of diseased for cases and controls from Dresden-South. From this description by residential-duration can be seen the low residential mobility of the Schneeberg cases and controls. The comparative group of diseased from Dresden-South is clearly more mobile from what a median residential-duration of only about 21 years with the cases and 23 years with the controls results.

Tab. 12: Distribution of hospital controls by diagnostic groups other than cancer (ICD 9)

Diagnostic groups	ICD 9	N	%
Circulatory system	390-395	30	48,4
Immune system	240-279	8	12,9
Digestive system	520-579	7	11,3
Muscle-skeleton system	710-739	6	9,7
Infections	001-139	3	4,8
Respiratory system	460-519	2	3,2

Urinary and genital system	580-629	1	1,6
Symptoms	780-799	3	4,8
Accidents	800-999	1	1,6
Other		1	1,6
Total	140-239	62	100

Regarding the median radon-concentrations and cumulative expositions distinct differences exist with a generally higher exposition level for cases and controls from Schneeberg. Further is noteworthy, that in comparison to the register-controls the later born hospital-controls have much lower indoor exposition levels. However, the average radon-exposition-values of the controls from Schneeberg are clearly higher than controls and cases from Dresden-South.

Tab. 13: Comparison of the radon-concentration and cumulative radon-exposition between the probationers from Schneeberg and female lung cancer cases and controls from Dresden-South

	years of	exposition * (5% - 95% value)			
Group	residential	median radon Bq/m³		total radon	
	duration	cellar	(lr+sr)/2*	Bqh/m³ * 10^6	WLM
Schneeberg					
cases	31,5	730	209	15,9	25,6
		(90-17000)	(45-4010)	(0,72-265)	(1,1-424)
register controls	30	540	160	10,3	16,5
		(90-6400)	(40-875)	(0,65-57)	(1-91)
hospital controls	33	290	104	6,7	10,8
		(80-13000)	(40-675)	(0,7-51)	(1,1-57)
Dresden-South					
cases	25,6	100	92,5		
controls	30,6	67,5	65		

A more elaborate analysis of the radon-exposition was done by histologic types in comparison to its matched controls. The results are presented in table 14.

As expected, always higher radon-concentration-values exist in the dwellings of the lung-cancer-cases in comparison to their controls from what normally higher cumulative expositions resulted. Merely with the small cell carcinoma cases, no higher cumulative radon-expositions are found in the comparison to their controls. However, the variation-width of the cumulative radon-exposition is essentially greater in comparison to the controls in direction of higher expositions. A possible explanation for this result could be a longer residential-duration of the controls and the higher share of smokers in comparison to the cases.

The most distinct differences in the cumulative exposition between cases and controls exist in the group of other histologic categories and with adenocarcinoma. However, the case-numbers are relatively low here, too.

Tab. 14: Comparison of the measured and cumulative radon-exposition with lung-cancer-cases and controls by histologic type [(5%-95% values)]

Histologic type	Radon Bq/m³		Total radon		
	Cellar	*(lr + sr)/2	Bqh/m³ *10⁶	WLM	Number
Small cell cases	770	180	10	16	23
	(20-17000)	(80-2267)	(1-177)	(1,7-283)	
controls	495	142,5	10,3	16,6	92
	(110-5500)	(40-860)	(0,6-58)	1-93)	
Squamous cases	870	300	24	38	15
	(240-29000)	(50-7100)	(0,2-545)	(0,4-872)	
controls	520	187,5	10	16	60
	(60-3200)	(38-315)	(1-51)	(1,6-82)	
Adeno cases	1160	206	149	23,8	7
	(180-8600)	(85-3606)	(6-556)	(10-891)	
controls	385	132,5	7,1	11,4	28
	(140-3900)	(45-1600)	(0,9-51)	(1,4-81)	
Others cases	4140	501	36,3	58,2	8
	(130-11000)	(65-3858)	(0,6-100)	(1-160)	
controls	430	135	6,9	11	32
	(60-4300)	(15-695)	(0,2-43)	(0,34-69)	
missings cases	470	185	14,5	23,2	19
	(50-19000)	(20-5350)	(0,72-154)	(1,2-247)	
controls	460	132	8,5	13,6	76
	(70-12000)	(35-900)	(0,4-59)	(0,6-94)	

* lr = living room, sl = sleeping room

Risk analysis by logistical regression

The risk-analysis of the data was conducted by conditional logistic regression under application of the STATA™-Software. The analysis was done in different steps:

- raw data
- adjusted for confounders, smoker-status, year of birth, occupation,
- stratified for non-smokers without consideration of the histology
- stratified for non-smokers with histologic confirmation of the diagnosis as the highest qualitative level of the analysis

Table 15 shows the sample sizes available in the individual steps of analysis.

Tab. 15: Number of available cases and controls by steps of analysis

Level of analysis	Cases	Controls	Total
Raw	72	288	360
Adjusted for			
Smoking	63	246	309
Occupation	59	189	248
Stratified for			
Non-smokers	49	231	280
Histology	38	172	210

As the most essential confounder of the probationers the smoking-behaviour and the year of birth were identified for their lung-cancer-risk. These variables were examined in the analyses for trend and dose response relation. The analyses took place with the currently measured and the cumulative radon-exposition of the probationers.

Between the different steps of analysis, mostly identical effects are found. Subsequently, only the results of the raw analysis and of the stratified analysis are compared. The stratified analysis includes only non-smokers an and histologic confirmed lung-cancers in reference to the cumulative radon-exposition. This approach of analysis provides the best possible quality of results.

With the two forms of analysis a significant trend was established between lung-cancer-risk and radon-exposition. The year of birth seems to exert a preventive effect on the lung-cancer-risk, because younger probationers in Schneeberg had a greater chance to live in the modern district of the town with lower indoor radon levels in modern buildings than for older age groups who lived preferably in the old town centre of Schneeberg with higher radon levels.

Tab. 16: Results of the trend-analyses between lung-cancer-risk and radon-exposition at the example of all probationers and with non-smokers with histologic confirmed diagnosis (adjusted)

Level of analysis	Odds - Ratios	95% CI
Raw	**1,508**	**1,25 - 1,82**
Radon	**1,457**	**1,15 - 1,84**

(smoking)	**5,615**	**2,19 - 14,4**
(year of birth)	**0,937**	**0,90 - 0,98**
Non-smokers, Histology	**1,485**	**1,15 - 1,91**
(year of birth)	**0,982**	**0,96 - 1,00**

The analysis of a possible dose-response-relation was conducted after the cumulative radon-expositions of the probationers were divided in to five exposition-categories. The analysis was done with reference to the group total radon, in accordance with exposition category 0 = OR 1, with < 2,4 * 10^6 Bqh/m^3 or an exposition with at most 50 Bqm^{-3} for 20 years.

The distribution of the probationers on the individual exposition-categories and the estimated Odds-Ratios are presented in the tables 17 and 18 for the raw analysis as well as stratified by non-smokers and histology. The analyses was done adjusted for the year of birth.

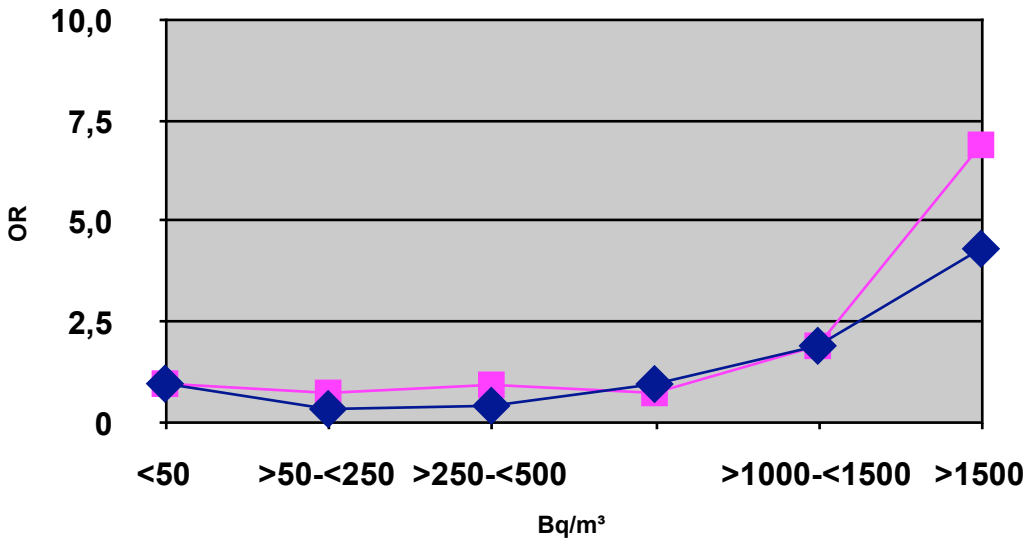
Tab. 17: Distribution of the probationers by exposition-categories and OR Raw data (smokers, all types of histology and cases without confirmed histology included)

Bqh/m³ *10^6	category	Bq/m³	controls	cases	total	OR	95% CI
< 2,4	0	<50	47	14	61	**1**	
>2,4 - 12,0	1	>50-<250	134	17	151	**0,37**	0,16-0,86
>12,0 - 24	2	>250-<500	54	10	64	**0,45**	0,17 - 1,20
>24 - 48	3	>500-<1000	31	10	41	**0,99**	0,36 - 2,78
>48 - 72	4	>1000 - <1500	13	6	19	**1,94**	0,59 - 6,33
>72	5	>1500	9	15	24	**4,35**	1,47 - 12,90
			288	72	360		
Trend							
Radon						**1,43**	1,19 - 1,72
Year of birth						**0,98**	0,91 - 0,98

Tab. 18: Distribution of the probationers by exposition-categories and OR Stratified data only for non-smokers and lung cancer histologic confirmed

Bqh/m³ * 10⁶	category	Bq/m³	controls	cases	total	OR	95% CI
<2,4	0	<50	25	5	30	**1**	
>2,4 - 12,0	1	>50-<250	89	12	101	**0,77**	0,23 - 2,64
>12,0 - 24	2	>250-<500	26	6	32	**0,97**	0,22 - 4,37
>24 - 48	3	>500-<1000	22	3	25	**0,77**	0,14 - 4,11
>48 - 72	4	>1000 - <1500	4	2	6	**1,94**	0,28 - 13,61
>72	5	>1500	6	10	16	**6,93**	1,29 - 37,05
			172	38	210		
Trend							
Radon						**1,45**	1,10 - 1,91
Year of birth						**0,97**	0,92 - 1,01

Fig. 6: Dose response relations for the lung cancer risk by cumulative radon exposure at two levels of data analysis with raw data and stratified data



An increased and significant OR can be established by the two forms of analysis in the higher exposition-categories only. Below a radon-concentration of 48 * 10^6 (Bqh/m³) accordingly 1000 Bq/m³ and a residential duration of 20 years the OR is not elevated. Significantly elevated OR after both forms of the analysis are detectable at the exposition level of > 1500 Bq/m³. The identified OR are relatively stable.

That becomes clear, too, if the distribution of the probationers is analysed by percentiles of the cumulative radon-exposure, to exclude a possible influence on the Odds-Ratios from the differently wide exposition-categories and with it the strongly fluctuated case-numbers of probationers (table 17 and 18). Table 19 shows this new distribution for cases and controls and adjusted for occupational status. Like the analyses in table 17 and 18 a clear dose-response-trend is determined for the radon-exposure, with only the highest exposition-category shows a significantly elevated Odds-Ratio. Due to the smaller numbers with probationers in the individual

exposition-categories, the variability of the estimated Odds-Ratios is however clearly greater in comparison to the types of analyses in table 17 and 18.

Tab.: 19 Distribution of the probationers by percentiles of the cumulative radon exposure and OR (CI 95%)

Bqh/m³ * 10^6	percentile	controls	cases	total	OR	CI 95%
0,084-1,08	<10	21	4	25	1	
1,08-2,7	10-20	22	6	28	1,01	0,22-4,79
2,70-4,56	20-30	31	3	34	0,51	0,09-2,92
4,56-7,05	30-40	25	2	27	0,34	0,05-2,31
7,05-9,50	40-50	25	8	33	1,59	0,36-7,10
9,50-12,88	50-60	24	3	27	0,74	0,13-4,13
12,88-18,19	60-70	17	6	23	1,71	0,34-8,59
18,19-28,98	70-80	22	3	25	0,74	0,12-4,55
28,98-54,72	80-90	18	6	24	2,44	0,46-13,03
54,72-83,32	90-95	8	6	12	2,19	0,35-13,74
83,32-557,85	95-100	3	12	15	**36,8**	**3,15-386,09**
		216	59	275		
trend radon					1,23	1,09-1,38
trend occupation					1,69	0,79-1,61

As already demonstrated in table 14, between the different histologic types of lung cancer and their controls, clear exposition-differences exist. However the case-numbers at disposal are partially very low so that a careful interpretation is recommended regarding a possible relation between histologic type and causation by radon.

In table 20 the results of the trend-tests composed by histologic type are presented.
All types of lung carcinomas show a significant as well as with other types a border-significant trend with radon exposure, if an data analysis with raw data is performed (smokers and all types of histology included).

If the influence of smoking is eliminated, in that only non-smokers are analysed (Tab. 21), it is only the small cell carcinomas, that show a border-significant trend. All other carcinomas lose meaning under these more stringent conditions of analysis, what especially stresses attention of the Squamous epithelium-carcinoma, the typical smoker-carcinoma.
Merely with the small cell carcinomas, a dose-effect-relationship is found, that corresponds to the one when all carcinomas are included. Only in the highest exposure-category (>1500 Bq/m³), a statistically significantly elevated Odds-Ratio can be determined. The same tendency, but without statistical significance, exists with the Squamous epithelium-carcinomas. Adenocarcinoma and the other histologic types are not to analyse due to the low case-numbers.

Tab. 20: Trend analysis with conditional logistic regression by tumour histology (*smokers included*), (non-smokers only)

Histology	Odds-Ratios	CI 95%	Cases	Controls

Small cell Carcinoma	*1,39* **1,26**	*1,03-1,89* **0,90-1,76**	*23* **18**	*92* **76**
Squamous Carcinoma	*2,04* **0,82**	*1,14-3,65* **0,04-17,31**	*15* **10**	*60* **44**
Adeno-carcinoma	*2,60* **2,49**	*1,03-6,63* **0,69-8,94**	*7* **5**	*28* **22**
Other types	*1,69* **1,57**	*0,99-2,85* **0,78-3,23**	*8* **5**	*32* **30**

Tab. 21: Trend analysis with conditional logistic regression by tumour histology for non-smokers only and total radon exposure (CI 95%)

Bqh/m³ * 10⁶	**Category**	**Small cell**	**Squamous**	**Adeno**	**Others**
<2,4	0	1,00	1,00	Not calculable	Not calculable
2,4-12,0	1	1,26 (0,27-5,97)	0,64 (0,06-7,34)		
12,0-24	2	0,59 0,08-4,26)	1,85 (0,15-22,29)		
24-48	3	1,37 (0,19-9,77)	2,82 (0,17-45,94)		
48-72	4	1,80 (0,26-12,63)	10,67 (0,22-508,60)		
>72	5	**7,68 (1,26-46,87)**	**17,17 (0,58-551,56)**		

3.4 Data pooling

The study protocol for the Schneeberg study was discussed in detail with the partners IPSN and RUG to enable data pooling with the European Radon Study "Studies of lung cancer risk and radon exposure in dwellings" (FI4P-CT95-0033). The data pooling especially with the case-control studies from the Ardennes-Eifel Region (RUG) and the Bretagne (IPSN) will be discussed with the partners.

4. Main achievements

4.1 Tests of the null hypotheses

The conditional logistical regression-analysis led regularly to a significant proof of an existing trend to a higher risk for lung-cancer. The first null hypothesis, after which the relative risk for lung-cancer with women is not elevated due to the exposure with radon, is not upheld and is rejected.

The second null hypothesis to be tested supposed no relation between exposition-level and risk for lung cancer. The corresponding analyses resulted in a clear dependence on the exposition-level. The second null hypothesis is rejected too.

The third null hypothesis supposed that present and past radon-concentrations don't differ in the apartments. The application of the retro measurement technique confirmed this hypothesis.

The examination of the secondary null hypothesis, that a radon exposure in the childhood leads to an elevated lung cancer risk, cannot be tested presently due to not yet available measurements in the apartments of the childhood.

4.2 Study power

In a first step the power calculation was conducted for the total of 72 eligible cases and 288 eligible controls considering distribution parameters only without including confounders of different kinds. The power calculation was based on results from LUBIN et al. 1988, who stated, that important exposures are frequently continuous and dichotomization may result in a "not exposed" category that has little practical meaning. In addition, if risks vary monotonically with exposure, then dichotomization will obscure risk effects and require a greater number of subjects to detect differences in the exposure distributions among cases and controls. This applies to the Schneeberg study, too, were the median value of the exposure level to indoor radon is 209 Bq/m³ for cases and 160 Bq/m³ for register controls. The special study question is, how many cases and controls are necessary, with a pre-determined power and significance, to distinguish of each other two distributions, characterised by the expected value and variance. For this purpose the example by LUBIN et al. 1988 is used.

To apply the LUBIN formulae (9) p. 366, under (i) the possibility exists, to determine μ_0, σ_0, μ_1 and σ_1 and to introduce the following numbers from p. 368:

Variable	Cases	Controls
Expected value μ	24,75	17,98
Variance σ^2	2468,88	629,64

These values emerge with different prerequisites to the expected risk and an assumed distribution with an expectation-value of 18 and variance 648 in the population. In the article by LUBIN, rounded values became used, i.e. 18 and 648 for intrinsic value and variance after 60 years.

We calculated the power for 72 cases, 288 controls. With a significance-level of 5% (two sided) and the expected values and variances from above we concluded a power of 69.4%.

For the two approaches of risk analysis presented in table 17 and table 18 the following power with the OR for exposition category 5 (corresponds to WLM >72 and >1500 Bq/m³) results:

Tab. 22: Power for the two approaches of analysis according to table 17 and table 18

Approach of analysis	Exposure category	Exposed cases %	Exposed controls %	% power
Raw data	5	20,83	3,125	98,32
Stratified data	5	26,31	3,49	99,76

An improved estimation of the study power is achieved by the inclusion of the residential-duration. The median values of the total-residential-duration are 31,5 years with the cases and 30 years with the controls. The median values are 32,8 years with cases and 31,9 years with controls. Median values for the age are 65 years with the cases and 66 years with the controls. As a consequence, the radon-exposition is defined virtually over 50% of the years of life. After the procedure of LUBIN et al. 1988 under utilization of the data of the Schneeberg study, 72 cases and 288 controls, a power resulted of 54%, in the case of two single apartments in 60 years.

4.3 Suitability of retro-measurement technique in radon-epidemiology

The combination of indoor radon concentration measurements and retrospective control became a useful procedure to validate current exposure measurements in epidemiologic studies. As a result from the Schneeberg study a high degree of agreement from current and historic measurement can be achieved, when dwellings with altered indoor radon concentrations in the past can be identified, qualified assessments are made about the possible causes and time for such changes and the valid radon value for a time period of about up to 30 years can be established for radon risk estimation. The measurement of correspondence between current and past measurement can achieve more than 90% (R^2) when the method is applied correctly. For future studies in radon epidemiology the reconstruction of past exposure should become standard use.

The project result from RUG for the retro-measurement technique of past indoor radon will become part of the Technology Implementation Plan, category A.

In a recently published study by ALAVANJA et al. 1999 with Missouri women another approach in the application of past exposure measurements was applied. For the risk estimation results from mean indoor CR-39 surface monitor readings were used only, that measured systematically higher indoor radon values than the one year measurements from indoor radon detectors. The results suggest for the authors of the study, that current air measurements may be understating the actual risk associated with residential radon exposure. This unexplained assumption can be discussed in comparison to the results from the Schneeberg study, when the publication by MAHAFFEY et al. (in press) about the measuring method of past radon history, applied in the Missouri study, is available.

4.4 Evidence for the necessity of non-smoking probationers

As BEIR VI 1999 stated, the lung cancer risk from smoking amounts to 10-20 and that from indoor radon to 0,2-0,3 only. Due to the overwhelming risk level for lung cancer from smoking, the contribution of each single factor has to be determined, when radon studies are conducted with mostly smokers among cases and controls. A confounder as smoking can be fully controlled in individual studies without error when correctly measured. But that is the point. The smoking behaviour is measured in epidemiologic studies mostly based on retrospective statements of the probationers. The forgetfulness of the probationers as well as the suppression of the smoking behaviour in their mind with cases just diagnosed for lung cancer influence the validity of self-reported data on smoking behaviour considerably. The results from the Schneeberg study demonstrate, that the self-reported smoking behaviour of lung cancer cases that are made at time of diagnosis are biased due to an obvious tendency to repress and minimise their smoking habit.

Even with a precision in the self-reported smoking history of one cigarette per day, the relative error enclosed in an example discussed in chapter 5.1 with the estimation of the risk comprises 13%. In other words, under-reporting of one cigarette per day results in a 13% error in radon risk estimation.

The sensitivity with the estimation of risk when smokers are included, could be demonstrated by the Schneeberg study comparing the results from two approaches represented in table 17 and table 18. With only 22% of smokers among cases and 6% among controls the statistical significant OR at an cumulative exposure level corresponding to >1500 Bq/m³ results in an OR of 4,35 (raw data - smokers, all types of histology included) and 6,68 (stratified data - non-smokers only and lung cancer history confirmed).

The dominant influence of smoking on the lung cancer risk in comparison to the weak influence from indoor radon and the problems to control the confounder smoking, results in the necessity do conduct epidemiologic studies in the lung cancer risk from indoor radon with non-smokers only.

4.4 Contribution to the discussion of LNT?

It was not the purpose of this study to test the LNT model. However, the evidence of the Schneeberg study strongly indicates that its results are not in accordance with the LNT assumption. The risk estimations for lung cancer due to indoor radon exposure are derived by direct observation in a key population for such research. The Schneeberg study is considered by its authors as a contribution to the growing body of scientific evidence that the LNT model might not be valid in the low dose range. Further research is needed to validate the results from the Schneeberg study and comparing them to other studies with non-smoking women not yet published (for instance FIELD and PERSHAGEN).

5. Discussion

.1 The risk estimation

The risk estimation of the Schneeberg study for lung cancer from indoor radon is not in accordance with the results from miners and population studies, which state an excess risk for 10%/100 Bq/m³ radon exposure and became by an important part of the scientific community, despite prevailing uncertainties, regarded as valid. If such risk estimates are true, in the highly exposed population of Schneeberg such lung cancer risks must have been easily established. That is not the case. From the risk estimate of the Schneeberg study even a safe threshold value was found and an significantly elevated risk appeared at >1.500 Bq/m³ only. Great efforts were taken to explain such discrepancies in comparison to other studies. One reason could be the favourable study conditions of the Schneeberg study (highly exposed population, mainly non-smoking women, exposed fraction very high and a relatively high power etc.). The other reasons are related to characteristics of the other studies especially with the low exposure to indoor radon and high exposure to tobacco smoke and a low power. Despite these explanations, the results from the Schneeberg study are only cautiously interpreted as not in accordance with the LNT model, because one single study cannot be used for a change in the paradigm of radiation protection. The results from the Schneeberg study are on the other hand enough founded to make further research in that key population a top priority and hesitate to introduce prematurely legal limits for indoor radon.

5.2 The influence of smoking on risk estimation

An analysis by LUBIN 1990 resulted in different factors in population-based case-control studies for not achieving the study-power in comparison to the originally planned one. The available case-numbers are mostly not sufficient according to the analysis by LUBIN 1990 to be able to uncover the suspected health effect at all. Such factors are for example a high mobility of the study population, confounders as cigarette smoking, a too low range of the exposition-spectrum, errors in the exposition-measurements and a lower value of the risk-coefficient than previously assumed. With a risk-coefficient of 0,5% WLM already 9.947 cases and 19.894 controls are necessary if the average residential-duration amounts to 20 years and the study includes smokers. The then attainable study-power amounts to 60% only.

The risk-coefficient of 0,5%/WLM corresponds to the result of a Meta-Analysis of 11 miner-studies (LUBIN et al.1995), which also includes the study of XUAN et al. 1993, that has determined a value for the excess-risk of 0.16% /WLM. Therefore the assumption is justifiable that the risk-coefficient for the radon-induced lung-cancer-risk for the population might exist in the wide range from 0,50-0,16%/WLM.

The effects of these assumptions to the risk-coefficient in considering smoking behaviour are presented in table 4. This table shows in its parts A and B the attainable study-power with a pre-determined number of cases in dependence on the number of the exposed in the control-population and the share of the exposed (p0). Furthermore, the table contains the necessary case-numbers in parts C and D to achieve a study-power of 90% under different assumptions about the risk-coefficient (ERR) obtained from newer results of miner-studies and the proportion of smokers. The average indoor radon exposure is determined at 80 Bq/m³, about the two-fold value

of the average in Germany.
The study-power of a case-control-study for the lung-cancer-risk of the population by indoor radon decreases dramatically with the diminution of the risk-coefficient even if 6.000 cases and 6.000 controls are included. The considered variation of the risk-coefficient in table 4, column 1, between 1,5-0,49 corresponds to that in miner-studies and the smaller coefficients between 0,2-0,16 is derived from the hitherto for confounders most extensively controlled miner-study (XUAN et al. 1993).

If the influence of smoking is taken into account, the necessary number climbs for cases and controls with an assumed proportion of smokers in the control-population from 50% and a risk factor of 0.49% /WLM up to 32.405. With a case to control relationship of 1:1 64.800 probationers have to be included into the examination. If the risk factor of XUAN et al. 1993 is applied, this number increases to 174.956 cases and controls i.e., 350.000 probationers would have to be included in the study.
With these calculations, the influences from mobility, mistakes in the exposure measurement and other factors, from which each one increases the necessary case-numbers further, isn't considered. The presentation in table 4 should demonstrate that the disclosure of a radon-induced lung-cancer-risk is rather unlikely taking the usual study conditions into account regarding case-numbers, exposure level, share of the exposed and inferior width of the exposure range. If radon health effects were nevertheless stated, the probability that a bias might have been at work should be considered. In that case the radon exposure attributed lung-cancer-risk is possibly attributable to another risk factor associated with lung-cancer (confounder).

Primarily the smoking behaviour of the probationers has to be considered more comprehensive as the possible confounder distorting risk estimations in population based radon studies. As BEIR VI 1999 stated, the lung cancer risk from smoking amounts to 10-20 and that from indoor radon to 0,2-0,3 only. FIELD 1998 stated as a result from the IOWA Radon Lung Cancer Study in a region with the highest exposure level to radon in the US, obviously, the risk we found from radon exposure pales in comparison to the lung cancer risk posed by smoking.
Due to the overwhelming risk level for lung cancer from smoking the contribution of each single risk factor has to be determined, when radon studies are conducted with mostly smokers among cases and controls. The smoking behaviour is controlled in the population-studies mostly based on retrospective statements of the probationers. These statements are subject to a recall-bias, that depends on the quality of the memory and the memory-willingness of the probationers and remains despite all efforts uncontrollable in its true size as will be demonstrated later. Resulting from this, risk-estimations from radon studies with smokers are prone to additional uncertainties that makes an interpretation of alleged health effects of exposure to radon more or less impossible. By misclassifications of the smokers, considerable falsifications can appear when the influence from smoking has to be evaluated (SUADICANI et al. 1997). This problem is discussed extensively also in a Science article (TAUBES 1995).

The forgetfulness of the probationers as well as the suppression of the smoking behaviour with cases of lung cancer can influence the validity of self-reported data on smoking considerably. ROSKOE et al 1994 already reported, that 13% of the cases of supposedly non-smoking miners

had declared in former examinations cigarette-consumption and 11% otherwise tobacco use. Own examinations by the authors of this report with 111 lung-cancer-patients from an ongoing WISMUT miners study (CONRADY et al. 1999) confirm this effect. In a comparison of self-reports by miners with lung cancer with former self-reports in health examinations when not diseased, apparent discrepancies can be observed.

Tab. 23: Influence of the exposition-rate (po), risk-coefficient (ERR) [% WLM-1] and share of smokers on the study-power (1 - β) and necessary number of cases of a case-control study with a constant radon-exposure, median 80 Bqm-3, cases: controls 1:1, error 1. type (α=5%)

A	**Power calculation**	**4.000 cases**		
	p_0 1%	**P_0 4%**	**p_0 6%**	**P_0 10%**
ERR				
1,500	0,988	1,000	1,000	1,000
0,490	0,356	0,877	0,965	0,997
0,200	0,101	0,269	0,370	0,536
0,120	0,061	0,172	0,167	0,240
B	**Power calculation**	**6.000 cases**		
	p_0 1%	**P_0 4%**	**p_0 6%**	**P_0 10%**
ERR				
1,500	0,999	1,000	1,000	1,000
0,490	0,496	0,969	0,996	1,000
0,200	0,313	0,377	0,513	0,709
0,120	0,074	0,170	0,229	0,335
C	**Sample size calculation**	**Power 90% Share of smokers 0%**		
	p_0 1%	**P_0 4%**	**p_0 6%**	**P_0 10%**
ERR				
1,500	2380	630	436	283
0,490	16579	43197	2961	1881
0,200	89688	23228	15863	10001
0,120	241261	62464	42607	26800
D	**Sample size calculation**	**Power 90% Share of smokers 50%**		
	p_0 1%	**P_0 4%**	**p_0 6%**	**P_0 10%**
ERR				

1,500	4672	1237	857	556
0,490	32405	8442	5787	3677
0,200	174956	45311	30944	19509
0,120	471011	121771	83062	52246

From supposedly 16 non-smoking miners with lung cancer 6 (38%) were smokers. From 33 lung-cancer-patients, who have reported a daily consumption of less than 10 cigarettes at the time of diagnosis, 8 (24%) smoked according to their own reporting in health examinations before their illness approximately the double quantity. These results clearly demonstrate that the self-reported smoking behaviours, that are made at time of the diagnosis of lung cancer, have to be taken very cautiously since an obvious tendency exists with lung cancer patients to repress and minimise their smoking behaviour. Similar results are reported by MARK et al. 1998 and DIETZ et al.1998.

Effects of this recall-bias were appraised by LEMBCKE 1997. The smoking of cigarettes is regarded as the most important cause for lung-cancer. Let's look at a common risk through smoking and radon now. Then, it seems logical that big uncertainties with faulty self-reported statements of the probationers about the smoker-past arise in the calculation of the lung-cancer-risks attributable to the comparatively low radon-exposition. In the end that can lead to the effect, that the complete lung-cancer-risk in studies with a high share of smokers can be explained as a consequence of smoking and the radon attributable risk is dominated by the uncertainties with the smoker-statements.

For the treatment of uncertainties and errors in the statements of the probationers about the smoking history, there are different accesses. In BEIRVI p. 168f, a stochastic access is chosen, which demands however some prerequisites for the distribution-function of the chance-variable „smoking “. A purely analytic method would be the following: the „joint effect “from radon and smoking has to be modelled. Generally one assumes that too few data about the smoking behaviour are available, to model in adequate quality this „joint effect “ (BEIR VI p. 152, „Adjustment for Smoking Status“). A multiplicative-additive model is therefore recommended (BEIRVI p. 154: „... This analysis indicates that the effects of ever-smoking and radon progeny exposure are not incorporated multiplicatively, but as a sub-multiplicative mixture.“)

Be ß the relative risk-coefficient for radon, than is the relative risk R(W) by radon

$$R(W) = 1 + \beta W$$

From LUBIN et al. 1990 we have

$$R(W,S) = (R(W)R(S))^{\theta}(R(W) + R(S) - 1)^{(1-\theta)}$$

though R(W) is defined as above and for the relative risk R(S) by smoking also a linear dependence is presupposed:

$$R(S) = 1 + \gamma S$$

With it marks γ the relative risk-coefficient for smoking and S the number of the cigarettes, which the relevant person consumed during the period as a smoker. Clearly, that for θ = 0 an additive and for θ = 1 a multiplicative connection exists. For θ∉[0,1] a discussion of the model becomes questionable. If θ is sufficiently small the relative risk R(W,S) tends to zero. For analysing the spread of error in R(W) and R(S) the following derivation is determined

$$\frac{\partial R(W,S)}{\partial R(W)} = \frac{(R(W)+\theta(R(S-1))(R(W)R(S)^{\theta}}{R(W)(R(W)+R(S)-1)^{\theta}}$$

$$\frac{\partial R(W,S)}{\partial R(W)} \xrightarrow[R(W)\to\infty]{} R(S)^{\theta}$$

and with it

This derivation is growing monotone for R(W)>0 and consequently is

$$\frac{\partial R(W,S)}{\partial R(W)} < R(S)^{\theta} \xrightarrow[R(S)\to\infty]{} R(S)\theta - \theta + 1.$$

and analogous

as a bound for errors ΔR(W,S) for R(W,S) regarding errors ΔR(W) respectively ΔR(S) in the

$$\frac{\partial R(W,S)}{\partial R(S)} < R(W)^{\theta}$$

relative risks R(W) respectively R(S) emerges

$$\Delta R(W,S) \le \Delta R(W)R(S)^{\theta} + \Delta R(S)R(W)^{\theta}$$

By an example we want to demonstrate how dramatically errors from a faulty self-reported smoking history is reflected in the total-mistake. So be θ=0.5 and the relative risk R(W) by radon R(W)=2 ± 0.2 and consequently ΔR(W)=0.1. Further be R(S)=1+γS, that concludes that S describes the amount of the daily smoked cigarettes as a smoker and γ the risk coefficient. With S the statements may swing between 5 and 15 cigarettes per day, resulting in S=10±5 and consequently

$$R(S) = (1+10\gamma) \pm 5\gamma$$

For γ≈1 be valid ΔR(S)≈5 and the relative risk for smoking R(S) results in R(S)=11±5 and

$$\Delta R(W,S) \le 0.2 \times 11^2 + 5 \times 2^2 = 7.4$$

for the common risk we found R(W,S) = 16.25 and the relative error amounts to about 46%. Under the consideration, that the model itself cannot be justified adequately and additionally statements about the smoking status are missing completely, it is easily conceivable that relative errors clearly higher than 75% occur. Even with a precision in the self-reported smoking history of one cigarette per day, the relative error enclosed in the above example with the estimation of the risk comprises 13%.

Especially sensitively however, the model doesn't react to possible fluctuations in θ. In the linear case (θ= 0) is the relative error with 42.5% somewhat low and in the multiplicative case with 50.5% of course somewhat higher than in the mixed approach.
The question is unconsidered, whether the lung cancer risk from smoking actually depends linearly on the number of the cigarettes daily smoked.

An elevated lung-cancer-risk for instance RR 1,6-1,9 (WICHMANN et al. 1993 and 1998) presumably induced by indoor radon in studies with more than 90% smokers among its cases, can therefor easily be explained by faulty self-reports of the smoking behaviour by the participants in the radon study.

Tab. 24: Comparison of the self-reported smoking behaviour from lung cancer patients prior to diagnosis and at time of diagnosis

Smoker-status	Time at diagnosis	Time prior to diagnosis	Deviation N	%
Non-smoker	16	10	6	38
<10 cigarettes/d	33	25	8	25
10-19 cigarettes/d	62	58	4	6

SCHÜTTMANN 1999 argues: before the commencement of cigarette smoking, lung cancer was an extreme seldom disease, despite the legitimate assumption, that the size of the indoor concentration of radon might have had a similar level than nowadays.
In the absence of cigarette smoking and given about the same indoor radon concentration, epidemiologic studies might have found at least similar results of the lung cancer risk attributable to indoor radon as claimed for today. Instead of epidemiologic studies SCHÜTTMANN 1999 reviewed the statistic for autopsies from the pathologic institute of the town hospital in Dresden (Saxony) from 1852 until the presence. During the period 1852 - 1876 from 8.716 autopsies only 0,06% were a primary lung cancers. From 1877-1884 from 4.172 autopsies 0,21% and from 1885 - 1894 from 7.228 autopsies 0,43% primary lung cancers were diagnosed. These figures are several orders of magnitude away from recent risk estimations for the lung cancer risk from indoor radon, even if doubts in the suitability of the statistics of historic autopsies for such a judgement are considered.

Summarising can be stated, that the lung-cancer risk from indoor radon-exposure has not been clearly proven in its true value until now. The case-numbers necessary taking the usual study-conditions into account to achieve a sufficient study-power were never reached even if a meta-analysis of these studies has been conducted. The risk-estimations for indoor radon presented in population and miners studies are subject to uncontrollable distortions, that are not rectifiable even with a meta-analysis, for of the high proportion of smokers alone. The dominant influence of the smoking behaviour on the lung-cancer-risk in comparison to the weak influence from indoor radon by the low radon levels in most population studies and the problems to control the confounding factor, results in the necessity to conduct preferably studies with non-smokers.

5.3 The possible influence of smoking on the slope of the dose-response curve

The BEIR VI report emphasised the need, that any risk assessment for indoor radon has to address the effect of radon on never-smokers and ever-smokers of tobacco, due to differing patterns of effect observed with radon exposed miners. STEINDORF et al. 1995 and LEENHOUTS 1999 for example discuss the different effects of radon on non-smokers and smokers, too. Another reason to examine the influence of smoking and radon on indoor radon risk calculation might be a biologically one. It is now well-known that the dose-response curves for certain radiogenic cancers are non-linear in the low dose range, that DNA damage can be repaired, and that cellular DNA is in a dynamic state in which damage is constantly occurring and being repaired. This repair capacity might have been weakened in smokers due to the constant exposure to the cancerous tobacco smoke, resulting in a linear dose-response curve when mainly radon exposed smokers are examined for their radon induced lung cancer risk. If such a biological modifying effect on the repair capacity exists, it could be seen in population studies for the health effects of exposure to radon with non-smokers only. Than the slope of a non-linear component in the dose-response curve for the low dose region of exposure to radon could be revealed.

5.4 Explanations for differences with the results from other studies

In communicating risks, there is a need to clearly distinguish between risk estimates derived from direct epidemiological observations and risks estimated for lower levels of exposure on extrapolation. The latter method was applied with the BEIR VI Report.
Available data on lung cancer risk and residential radon exposure from eight indoor radon case-control studies (LUBIN and BOICE 1997) were too limited to model effects directly. The BEIR VI committee rejected them because of their low statistical power but did not hesitate to use them as supportive evidence for the LNT model at low levels of radon.
The estimation of lung cancer risk from residential radon therefore relied on extrapolations of results from studies of underground radon-exposed miners, who where generally more highly exposed. Several assumptions were required to extrapolate miner results to the residential setting (LUBIN 1998). The assumptions for developing a miner-based risk model and extrapolating lung cancer risks from miners to the general population suffer from several serious shortcomings that call into question the validity of the risk estimations. Some of these shortcomings were discussed

in chapter one, "The lung cancer risk from radon: ongoing discussion" and the distorting influence of smoking on radon risk estimations under 5.1 and 5.2.

The main explanation for the differences in results from the Schneeberg study in comparison to results from most of the miner as well as population studies might be, that the Schneeberg study is less prone to the shortcomings discussed above.

- The study power is with at least 54% higher than the study power from all other population studies, even if these studies comprise more cases than the Schneeberg study, because of the influences from confounding factors as smoking, the low level of exposure to radon and the low fraction of the exposed population. The study power of the Schneeberg study is acceptable, when the study conditions for such epidemiologic studies are taken into account. The study power can be regarded as preliminary, because it can be increased by the inclusion of additional cases from the region and by data pooling.

- The exposure level for cases and controls is higher than in other population studies with a wide range of exposure from 50 Bq/m³ to more than 3.000 Bq/m³ resulting in median values for cases with 209 B/m³ and for register controls with 160 and hospital controls with 104 Bq/m³. The exposure level for controls in the Schneeberg study is in the average higher than the exposure level of cases in other population studies.

- The majority of the study population are non-smoking women, so the risk from radon can be observed directly without confounding influences from active smoking. In combination with the high level of indoor radon the radon effect on the lung cancer risk can be determined more precisely than in studies with very low exposure levels and mainly smokers as cases and controls.
- Special efforts were undertaken to determine the radon dose for at least 25 years for cases and controls. This effort was supported by the very low residential mobility of the study population in comparison to other studies.
- Radon measurements from dwellings, suspected for changed exposure levels in the past, were validated with the reconstruction of past exposure, so some of the current radon measurements could be corrected for remedial influences or for mining induced factors.

All these factors might explain the differences with most of the other population studies. The possibility, that the results of the Schneeberg study are biased by one or several unknown confounding factors has to be taken into consideration. From the authors point of view such modifiers of the risk calculation are not feasible. Especially when the study power is taken into account. The final assessment of the validity of the results from the Schneeberg study will come from the scientific community, to which the study will be presented for discussion.

5.5 Recommendations for radon-epidemiology, radiation research and Public Health

Radon epidemiology

The results from the Schneeberg study give support to the assumption, that radon epidemiology, estimating the lung cancer risk from indoor radon, has not yet come to a conclusion. The prevailing uncertainties in risk estimates in miners and population studies, especially the dominant influence from smoking, make it imperative to proceed in the research in non-smoking key populations only. Therefore the authors of the Schneeberg study propose to proceed with the research to determine more precisely the possible threshold level and the slope of the dose response curve (linear, quadratic). Significant results for the OR between indoor radon and lung cancer can be achieved in the low dose range - lower than 1.500 Bq/m³ - with a cohort approach only. Within the 5th Frame Work Programme a subsequent proposal will be submitted.

Radiation research

The special properties of the study area in the Schneeberg region and its study population make it a key population in radiation research to test the LNT model and the probability of causation analyses due to high level of the etiologic fraction of lung cancers by epidemiological means. This should be done preferably with a cohort study and the partners from the Schneeberg study.

The search for specific changes of the human genome due to the high burden with alpha-radiation, to develop and test new methods in biological dosimetry, has more favourable chances for success under the study-conditions in Schneeberg as in areas with low levels of radon exposure. In the framework of a planned co-operation with the Leiden University Medical Centre a common proposal to DG XII is in preparation

Introduction of limits for indoor radon

A Commission recommendation on the protection of the public against indoor exposure to radon was adopted in 1990 (90/143/Euratom). The recommendation establishes a reference level for remedial action in existing dwellings and a design level for the purpose of establishing construction codes for new buildings. These levels were set in terms of annual effective dose, 20 mSv respectively 10 mSv, as well as in terms of radon gas concentration with 400 Bq/m³ in existing dwellings and 200 Bq/m³ in new ones. Risk analyses from recent population studies seem to support these already existing recommendations. A recommendation has no legally binding character. The economic consequences to introduce uncertain results from miners and population studies into law codes are demonstrated in the following table 22. The costs for remedial actions for existing dwellings are an estimation with about 2.500 ECU on average per dwelling. If all dwellings in OECD countries above the action level of 400 Bq/m³ have to be remediated about 11 Billion ECU have to be spend. With an action level of about 1.000 Bq/m³ this will cost less than 1 Billion ECU, a difference of 10 Billion ECU.

Table. 25: Buildings in OECD countries above given radon levels and possible costs for remediation (ECU)

Radon Bq/m³	Homes	Million ECU
100	30000000	-

200	10000000	-
	Homes above action level	
400	2500000	6250
600	1000000	2500
800	450000	1125
1000	250000	625
1500	90000	225
Total	**4290000**	**10725**

Own calculation based on CLARKE 1998

To quantify by direct observation the unbiased relationship between indoor radon exposure and lung cancer is crucial before limits for indoor radon levels could be introduced. As long as Public Health effects are dubious, no new regulations should be imposed on the public causing billions of ECU without a certain Public Health effect.

If remedial actions are intended for existing or new dwellings, for this purpose only building codes for radon protection are advisable.

The recommendation from this study regarding limits for indoor radon is, not to introduce premature limits based on epidemiologic studies with too much uncertainties regarding the validity of their risk estimates for lung cancer. The amount would be spend more effectively in the health care systems of the OECD countries for smoking related diseases or more specific for the prevention of smoking. Until more reliable results from epidemiologic studies can be presented, reference levels only should be applied as an interim guidance for the public.

5. Publication

Over the whole period of the contract the following publications were done:

1. Cauwels P., Poffijn A., *The use of an Empirical Correlation between Surface Activity and Integrated Radon Exposure in a Retrospective Radon Measurement.* IRPA regional Symposium on Radiation Protection in neighbouring Countries of Central Europe 1997.

2. Poffijn A., Cauwels P., *The Challenge of Radon Assessment.* Proceedings of the European Conference on Protection against Radon at Home and at Work June 2-6, 1997, Praha, Czech Republic.

3. Poffijn A., Conrady J., Cauwels P., Martin K., *A Preliminary Study for the Application of Retrospective Radon Measurements for Epidemiological Studies in the Schneeberg Area.* IRPA regional Symposium on Radiation Protection in neighbouring Countries of Central Europe 1997

4. Cauwels P., *De studie van de geimplanteerde laag van radondochters in glas: fysische en chemische benadering.* Scriptie voorgedragen tot het behalen van de graad van Licentiaat in de Wetenschappen groep Natuurkunde.

5. Conrady J, Martin K, Nagel M, *Weniger Modelle - spezifischere analytische Studien zum Radonrisiko in Wohnungen sind notwendig*. Bundesgesundheitsblatt 39, März 1996/3. Ed. Robert Koch Institut Berlin

6. Conrady J, Nagel M, Martin K, *Vergleichende Analyse der räumlichen und zeitlichen Verteilung von Krebserkrankungsfällen in Gebieten mit hoher natürlicher Strahlenbelastung im Vergleich zur Umgebung des Zentralinstituts für Kernforschung (ZfK) Rossendorf.* Ed. Sächsisches Staatsministerium für Soziales, Gesundheit und Familie und Sächsisches Staatsministerium für Umwelt und Landesentwicklung, Dresden, März 1997

7. Martin K, Conrady J, *Thesen - Der Beitrag der Epidemiologie zur integrierten Bewertung radiologischer und chemisch-toxischer Kontaminanten*. Materialien zu Strahlenschutz/Umweltradioaktivität 3/1997, Ed. Staatsministerium für Umwelt und Landesentwicklung, Dresden, November 1997

8. Conrady J, Martin K, *Linearität vs. Realität - Beispiel Lungenkrebs und Radonexposition*. Materialien zu Strahlenschutz/Umweltradioaktivität 3/1997, Ed. Staatsministerium für Umwelt und Landesentwicklung, Dresden, November 1997

9. The Final report will be presented on the PreCura home page (www.precura.de)

10. The following publications in the American Journal of Epidemiology are intended based on the Final report, agreed upon between the partners of the study (titles are not yet finalised):

    Method and results from the retro measurements in Schneeberg. RUG
    The true size of the lung cancer risk from indoor radon: hidden behind a smoke screen? PreCura, RUG, IPSN

The Final report will be presented additionally on the PreCura homepage (www.precura.de).

7. Summary of the relevant results

7.1 Introduction

There is no debate about radon being a carcinogen in humans. The World Health Organisation (WHO) and the U.S. Department of Health and Human Services, as well as the U.S. Environmental Protection Agency (EPA), have classified radon as a "Class A" known human carcinogen. A Commission recommendation on the protection of the public against indoor

exposure to radon was adopted in 1990 (90/143/Euratom).What is disputed is whether low radon levels, such as those found in most residences, actually increase the risk of lung cancer.
The scientific community continues therefore to debate the lung cancer risk of residential radon and the dose-response relationship. Currently a majority of scientists believes the risk associated with radon increases proportionally to the radon concentration according to the linear no-threshold theory (LNT) of radiation. Others believe that there could be a safe threshold value.
The reason for the prevailing uncertainties about radon health risks are that all of the residential studies have been too small, and the exposure levels and the proportions of population under exposure too low, to provide - due to lack of power - conclusive information.
The available data from indoor radon studies were considered by BEIR VI to be not yet sufficient to develop a general risk-assessment model or to estimate precisely the magnitude of risk posed by radon in houses. In its conclusions, BEIR VI recommends that the power of an indoor radon study to detect an excess risk could be enhanced by targeting special populations, such a population with high exposures, a broad range of exposures, and low residential mobility. The preferential use of non-smokers was not recommended. Otherwise the Schneeberg study completely complies with BEIR VI recommendations regarding its conditions.
The area and population of the Schneeberg study have some characteristics different from other study areas and populations, and ensure despite the relatively small size a high enough power:

- Highly exposed to indoor radon with a wide range of exposure from 50 Bq/m³ to >3.000 Bq/m³ resulting in median radon values for cases of 209 Bq/m³ and controls of 160 Bq/m³ (register controls) and 104 Bq/m³
  (hospital controls).
- The exposed fraction of the population is very high.
- The majority of the study population of women are non-smokers. For the risk estimation preferably non-smokers and histologic confirmed lung cancers were used.
- The population has a very low residential mobility.
- The study region is included in a cancer registry since 1952 to the present day.

The high average exposure level for indoor radon in the houses in Schneeberg has the potential to provide a new key population in radiation research similar to the Japanese A-bomb survivors and the nuclear industry workers. The favourable study conditions could contribute to clarify some of the prevailing uncertainties in estimating the lung cancer risk due to indoor radon and to radiation protection research and regulatory control.

7.2 Objectives

The following objectives have been achieved:

- Estimation of the relative lung-cancer-risk (OR) by exposure to radon in dwellings with main focus of non-smoking women.
- Dose-Response-Analysis under consideration of differently accumulated expositions over time and cancer histology.
- Examination of the dose-response curve and the slope of the linear component of dose.
- Definition of requirements to test and apply methods for the reconstruction of past exposures.
- Establishment of uniform dosimetric criteria for the linkage of the study-data with other case-control studies for a joint-analysis over the range from low to very high radon levels.

- Recommendations for the planning and introduction of Public Health measures in radon-prone areas

7.3 Results of the research

Risk analysis

The risk-analysis of the data was conducted by conditional logistic regression under application of the STATA™-Software. The analysis was done in different steps:

- Raw data, adjusted for confounders, smoker-status, year of birth, occupation,
- stratified for non-smokers without consideration of the histology,
- stratified for non-smokers with histologic confirmation of the diagnosis as the highest qualitative level of the analysis.

Table 26 shows the sample sizes available in the individual steps of analysis.

Tab. 26: Number of available cases and controls by steps of analysis

Level of analysis	Cases	Controls	Total
Raw	72	288	360
Adjusted for			
Smoking	63	246	309
Occupation	59	189	244
Stratified for			
Non-smokers	49	231	280
Histology	38	172	210

As the most essential confounder of the cases, the smoking behaviour and the year of birth were identified for their lung-cancer-risk. These variables were examined in the analyses for trend and dose response relation. The analyses took place using the currently measured as well as the cumulative radon-exposition of the probationers.
Between the different steps of analysis, mostly identical effects are found. Subsequently, only the results of the raw analysis and of the stratified analysis are compared. The stratified analysis includes only non-smokers and histologically confirmed lung-cancers in relation to the cumulative radon exposure. This approach of analysis provides the best possible quality of results.

With the two forms of analysis, a significant trend was established between lung-cancer-risk and radon-exposition. The year of birth seems to exert a preventive effect on the lung-cancer-risk, because younger probationers in Schneeberg had a greater chance to live in the modern district of the town with lower indoor radon levels than in the old centre.
The estimation of the relative lung-cancer risk (OR) by exposure to indoor radon with females only was conducted and resulted in the two approaches presented below.

The analysis of a possible dose-response relation was conducted after the cumulative radon-expositions of the probationers were divided in to five exposition-categories. The analysis was done with reference to the group total radon, in accordance with exposition category 0 = OR 1, with < 2,4 * 10^6 Bqh/m^3 or an exposition with at most 50 Bqm^{-3} for 20 years (table 27 and 28).

Tab. 27: Distribution of the probationers by exposition-categories and OR Raw data (smokers, all types of histology and cases without histologic confirmation included)

Bqh/m³ * 10^6	category	Bq/m³	controls	cases	total	OR	95% CI
<2,4	0	<50	47	14	61	**1**	
>2,4 - 12,0	1	>50-<250	134	17	151	**0,37**	0,16-0,86
>12,0 - 24	2	>250-<500	54	10	64	**0,45**	0,17 - 1,20
>24 - 48	3	>500-<1000	31	10	41	**0,99**	0,36 - 2,78
>48 - 72	4	>1000 - <1500	13	6	19	**1,94**	0,59 - 6,33
>72	5	>1500	9	15	24	**4,35**	1,47 - 12,90
			288	72	360		
Trend							
Radon						**1,43**	1,19 - 1,72
Year of birth						**0,98**	0,91 - 0,98

The second approach was conducted with stratified data for non-smokers and histologically confirmed lung cancers.

Tab. 28: Distribution of the probationers by exposition-categories and OR Stratified data only for non-smokers and lung cancer histologic confirmed

Bqh/m³ * 10^6	category	Bq/m³	controls	cases	total	OR	95% CI
<2,4	0	<50	25	5	30	**1**	
>2,4 - 12,0	1	>50-<250	89	12	101	**0,77**	0,23 - 2,64
>12,0 - 24	2	>250-<500	26	6	32	**0,97**	0,22 - 4,37
>24 - 48	3	>500-<1000	22	3	25	**0,77**	0,14 - 4,11
>48 - 72	4	>1000 - <1500	4	2	6	**1,94**	0,28 - 13,61
>72	5	>1500	6	10	16	**6,93**	1,29 - 37,05
			172	38	210		
Trend							
Radon						**1,45**	1,10 - 1,91
Year of birth						**0,97**	0,92 - 1,01

The distribution of the probationers on the individual exposition-categories and the estimated Odds-Ratios are presented in the tables 27 and 28 for the raw analysis as well as the stratified one by non-smokers and histology. In figure 7 the slopes of the two approaches of analysis are presented. The analysis was done adjusted for the year of birth.

An increased and significant OR can be established by the two forms of analysis in the higher exposure-categories only. Below a radon-concentration of 48 * 10^6 (Bqh/m^3) accordingly 1000 Bq/m³ and a residential duration of 20 years the OR is not elevated. Significantly elevated OR

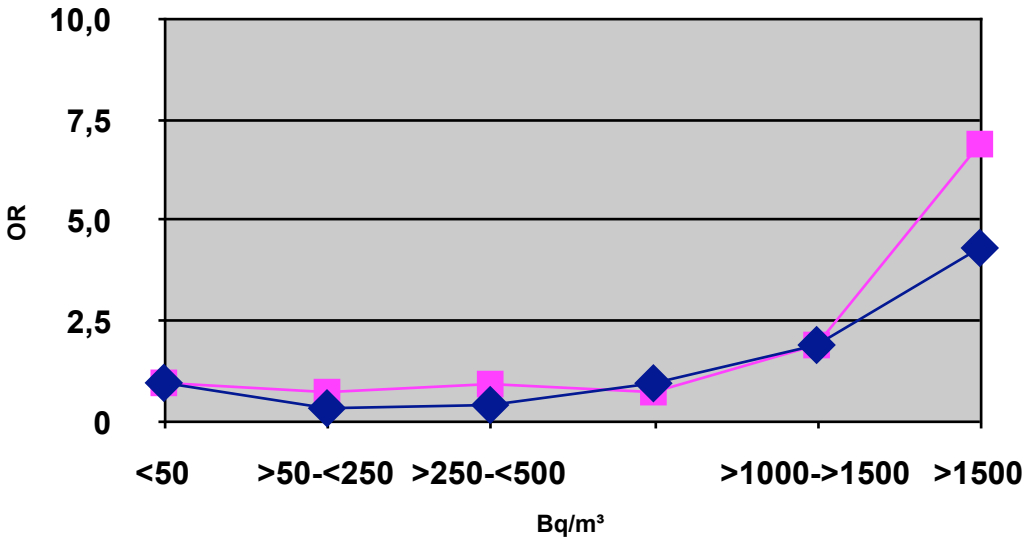
after both forms of the analysis are detectable at the exposition level of > 1500 Bq/m³. The identified ORs are relatively stable.

As a result from a special analysis by OR for tumour types and cumulative radon exposure the Small cell carcinoma might be related to indoor radon.

The risk estimation of the Schneeberg study for lung cancer from indoor radon is not in accordance with the results from miners and population studies, which state an excess risk for 10%/100 Bq/m³ radon exposure and became by an important part of the scientific community, despite prevailing uncertainties, regarded as valid. If such risk estimates are true, in the highly

Fig. 9:Dose response relations for the lung cancer risk by cumulative radon exposure at two levels of data analysis with raw data and stratified data

exposed population of Schneeberg such lung cancer risks must have been easily established.



That is not the case. From the risk estimate of the Schneeberg study even a safe threshold value was found and a significantly elevated risk appeared at >1.500 Bq/m³ only. Great efforts were taken to explain such discrepancies in comparison to the results from other studies. One reason could be the favourable study conditions of the Schneeberg study (highly exposed population, mainly non-smoking women, exposed fraction very high and a relatively high power etc.). The other reasons are related to characteristics of the other studies especially with the low exposure to indoor radon and high exposure to tobacco smoke and a low power. Despite these explanations, the results from the Schneeberg study are only cautiously interpreted as not in accordance with the LNT model, because one single study cannot be used for a change in the paradigm of radiation protection. The results from the Schneeberg study are on the other hand enough founded to make further research in that key population a top priority and hesitate to introduce prematurely legal limits for indoor radon.

The necessity of non-smoking probationers in radon epidemiology

As BEIR VI 1999 stated, the lung cancer risk from smoking amounts to 10-20 and that from indoor radon to 0,2-0,3 only. Due to the overwhelming risk level for lung cancer from smoking, the contribution of each single factor has to be determined, when radon studies are conducted with mostly smokers among cases and controls. A confounder as smoking can be fully controlled in individual studies without error when correctly measured. But that is the point. The smoking behaviour is measured in epidemiologic studies mostly based on retrospective statements of the probationers. The forgetfulness of the probationers as well as the suppression of the smoking behaviour in their mind with cases just diagnosed for lung cancer influence the validity of self-reported data on smoking behaviour considerably. The results from the Schneeberg study demonstrate, that the self-reported smoking behaviour of lung cancer cases that are made at time of diagnosis are biased due to an obvious tendency to repress and minimise their smoking habit. Even with a precision in the self-reported smoking history of one cigarette per day, the relative error with the estimation of the risk comprises 13%. In other words, under-reporting of one cigarette per day results in a 13% error in radon risk estimation.

The suitability of the retro-measurement technique

The combination of indoor radon concentration measurements and retrospective control became a useful procedure to validate current exposure measurements in the Schneeberg study. As a result from the Schneeberg study a high degree of agreement with current and historic measurements has been achieved. Whenever residences with altered indoor radon concentrations in the past can be identified, combined with qualified assessments of the possible causes and time for such changes, the valid radon value for a time period of about up to 30 years or more can be established for radon risk estimation. The measurement of correspondence between current and past measurement can achieve more than 90% (R^2) when the method is applied correctly. For future studies in radon epidemiology the reconstruction of past exposures should become standard use.

Technology Implementation Plan

The project result from RUG for the retro-measurement technique of past indoor radon will become part of the Technology Implementation Plan, category A.

Data pooling with the European Radon Study

The study protocol for the Schneeberg study was discussed in detail with the partners IPSN and RUG to enable data pooling with the European Radon Study "Studies of lung cancer risk and radon exposure in dwellings" (FI4P-CT95-0033). The data pooling especially with the case-control studies from the Ardennes-Eifel Region (RUG) and the Bretagne (IPSN) will be integrated in a new proposal to DG XII within the 5th Framework Programme.

Contribution to the discussion of LNT?

It was not the purpose of this study to test the LNT hypothesis. However, the evidence of the Schneeberg study strongly indicates that its results are not in accordance with the LNT assumption. The risk estimates for lung cancer due to indoor radon exposure are derived by direct observation in a key population for such research. The Schneeberg study is considered by its authors as a contribution to the growing body of scientific evidence that the LNT model might not be valid in the low dose range, and that further research is needed.

7.4 Implications for radiation protection

To quantify by direct observation the unbiased relationship between indoor radon exposure and lung cancer is crucial before regulatory limits for indoor radon levels should be introduced. As long as Public Health effects are highly questionable, no new regulations should be imposed on the public amounting to thousands of millions of ECU in public funds. If remedial actions are intended for existing or new residential buildings, for this purpose only technical building codes for radon protection are advisable. The recommendation from this study regarding limits for indoor radon is not to introduce prematurely limits based on epidemiologic studies with too many uncertainties regarding the validity of their risk estimates for lung cancer. Financial resources should be spend more effectively in the health care systems for smoking related diseases, or even better for the prevention of smoking. Until more reliable results from epidemiologic studies are available, reference levels should be applied only as a tentative interim guidance for the public.

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Annex

The contributions by the partners to this Final report were based on the "Concept for conducting the analysis of the Schneeberg Study" and the described responsibilities therein. The exchange of information took place by phone, e-mail, phone-conference and meetings.