RADON RESEARCH IN MULTI DISCIPLINES: A REVIEW

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COURSE OUTLINE

I. Fundamentals of radon physics: review
II. Radon research in geology
III. Radon research in radiation biology
IV. Radon research in medicine
V. Radon research in health physics
Earth & Planetary Science
Radon research in multi disciplines - summary
Student Presentations
Radioactivity Laboratory demonstration

DETAILED COURSE WORK

The course work involves the following:

1. **January 17, 18, 19, 22, 25 1-3 PM**
   5 sessions each of 2 hours - 25%
2. **Study Assignments - 4 - 20%**
3. **Project**
   Literature Survey – Writing a report - 30%
4. **Project Presentation - 25%**

Required percentage to pass this course is 95%
Grading: P/F

Session 4
Radon Research In Medicine

Objective 1 of 3

1. Introduction

2. Human cancer from ionizing radiation:

2.1 The epidemiological evidence

2.2 Population studies: External radiation exposure and ionization by internal radiation

3. Some examples of radon research studies in medicine

3.1 Leukemia:

- **Radon dose and ionizing effects to red bone marrow**

Objective 2 of 3

3. Some examples of radon research studies in medicine (continued):

3.2 Water solubility of radon

- **3.2.A Radon, fluoride and multi-element analysis of ground water**
- **3.2.B Radon concentrations in open and bore well water**
- **3.2.C Water radon contamination in the human body**
- **3.2.D Bio-kinetics of radon from drinking water**

3.3 Internal alpha radiation and nephropathy

- **Internal alpha radiation effects on kidney & dysplastic changes of internal alpha radiation injury**

Objective 3 of 3

3.4 Other radon research studies in medicine:

3.4.A Biomarkers for kidney injury by alpha radiation

3.4.B Exposure of radon and its progeny to human teeth

3.4.C Clinical effects of exposure to radon in controlled environment.

3.4.D Primary care physicians - Environmental history - Public health effects: An Italian survey

1. INTRODUCTION

Radon an internal alpha radiation source

Radon, a naturally occurring radioactive gas is a source of alpha radiation.

Exposure dependent human health risks attributable to inhalation of radon and its progeny are studied extensively in places like

- dwellings,
- schools,
- underground tunnels,
- mines
- spas

Radon an internal alpha radiation source …

- **Radon in the environment contributes to about half of total background exposure of a person amounting to about**

  1.5 - 2 mSv per year.

- 1Sv = 100 Rem
- 1mSv = 0.1 Rem
- 1 Rem = 1 Rad x 1QF x 1DF

1 Rad = 1R = 100 ergs absorbed per gram of any substance

QF = Quality Factor, similar to RBE is a factor expressing relative effectiveness of radiations with differing linear energy transfer

DF = Dose Distribution Factor accounts biological effect due to non uniform distribution of internally deposited radionuclides

What is known

- 50% of the primary health care physicians seem to be aware of the etiology of lung cancer from the radiation effects of bronchial epithelial cells due to the inhalation of radon and its progeny.

- Radon, dissolved in body fluids, becomes a source of internal alpha radiation causing nano-injury at the cellular level.

What is not known ...

- Medical research investigates the role of environmental radon as a source of

  internal alpha injury causing

  onset of malignant or

  dysplastic changes

  of the organ structure as a

  response to the cellular injury.

- dysplastic changes mean other than cancerous changes, for example fibrosis in kidney, fibrosis in liver, morphology of the organ attacked by alpha particles.

2. HUMAN CANCER FROM IONIZING RADIATION

- 2.1 The epidemiological evidence
- 2.2 Population studies:
  External radiation exposure and
  ionization by internal radiation

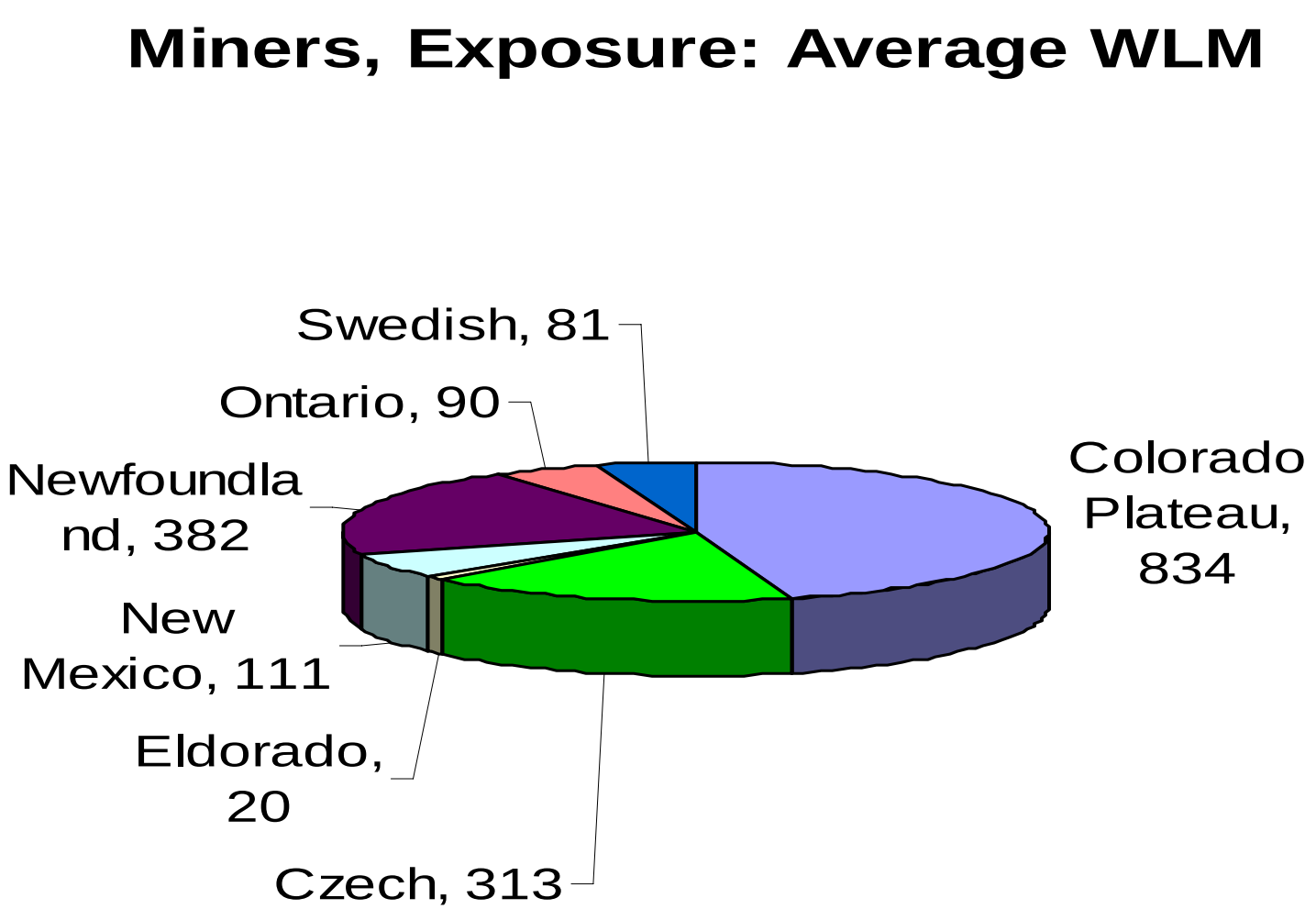
2.1 The epidemiological evidence

Some, early, major epidemiological studies conducted on underground miners:

- Ontario Uranium Miners
- Swedish Iron Miners (Malmberget)
- Colorado Plateau Uranium Miners
- Czech Uranium Miners
- Eldorado (Beaverlodge) Uranium Miners
- Newfoundland Fluorospar Miners
- New Mexico Uranium Miners

Ref: National Academy of Sciences, BEIR Reports

2.1 The epidemiological evidence …



Note: Maximum average WLM is taken for Ontario

Ref: EPA 1993

2.1 The epidemiological evidence ...

Biological effects of Ionizing Radiation - BEIR Reports

- **2006 BEIR VII:**
  Health Risks from exposure to low levels of ionizing radiation, BEIR VII Phase 2,
- **1999 BEIR VI:**
  Health effects of exposure to radon, BEIR VI,
- **1990 BEIR V:**
  Health effects of exposure to low levels of ionizing radiation, BEIR V,
- **1988 BEIR IV:**
  Health risks of radon and other internally deposited alpha-emitters
- **1980 BEIR III:**
  The effects on populations of exposure to low levels of ionizing radiation. Final Report
- **1979 BEIR II:**
  Considerations of health benefit-cost analysis for activities involving ionizing radiation exposure and alternatives : a report
- **1972 BEIR I.**
  The effects on populations of exposure to low levels of ionizing radiation.

2.2 External radiation exposure and ionization by internal radiation

- Uranium and thorium are sources of environmental radon and thoron.

  They are present in the environments like rocks, soils, indoor and outdoor air and water and building materials.
- Radon daughters are predominantly attached to aerosols.

2.2 External radiation exposure and ionization by internal radiation …

Radon daughters can be inhaled from indoor air

- radon rich rocks or
- radon emanating from building materials,
- basement fills,
- bed rocks under house
- radon rich water

2.2 Population Studies

- Several population based studies have shown health risk of radon in relation to lung cancer
- Inhalation of radon and thoron daughters leads to deposition and irradiation in the human respiratory tract and onset of lung cancer .
- A clear association of lung cancer and radon rich environment is established by studies on population at risk.

2.2 Population Studies

References:

- **A combined analysis of North American case-control studies of residential radon and lung cancer,**
  D. Krewski et al,
  Journal of Toxicology and Environmental Health Part A, 69:533-597, 2006
- **Health Risks from exposure to low levels of ionizing radiation, BEIR VII Phase 2,**
  R. Jostes, National Academy Press 2006
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- **Lifetime risk of lung cancer due to radon exposure projected to Japanese and Swedish populations**
  Doi, M. Nakamura, Y.Sakashita, T.; Ogiu, N.Lagarde, F. Falk, R
  Health Physics, v 80, n 6, 552-62, June 2001.

3. Some Examples of Radon Research Studies in Medicine

- 3.1 Leukemia
- 3.2 Water solubility of radon and health effects
- 3.3 Internal alpha radiation and nephropathy
- 3.4 Other studies

3.1 Leukemia:

- **Radon dose and ionizing effects to red bone marrow**

3.1 Leukemia

- Human cancer from ionizing radiation from naturally occurring radioactive materials like radon is well studied.
- Indoor air quality is getting effected – one cause being, the radon concentration in indoor air is usually higher compared to outdoor air.
- In recent times, human health risks in the form of leukemia have been evaluated due to inhalation of radon and radon progeny in indoor air.

3.1 Leukemia …

- When internally transported in the body radon and radon progeny may cause various types of leukemia and liver cancer.

Radon research in medicine include such studies as

- Childhood leukemias from internal delivery of radon and thoron
- Internal alpha radiation and nephritis.

3.1 Leukemia …

Currently, leukemia is associated more and more with ionizing radiation effects of radon daughter products.

Epidemiological studies indicate that increased radon levels at home are associated with significant increase in incidence of leukemias in both children and adults.

25% risk of leukemias at any age group may arise from radon levels of 50Bq/m^3.

3.1 Leukemia …

- **positive correlation** with Incidence of all leukemia combined and chronic lymphocytic leukemia alone associated with cumulative radon exposure.
- **positive correlation** with radon exposure in the home, and incidence of myeloid leukemia, cancer of the kidney, melanoma, and certain childhood cancers, globally.
- incidence of myeloid leukemia, 6-12% and as high as 23-43% of incidence may be attributed to radon.
- 13-25% (world average) of myeloid leukemia at all ages may be caused by radon at 50 Bq/m^3,

3.1.A Radon exposure to bone marrow – UK study

The dose due to the inhalation of short-lived radon daughters was estimated. Measurements were conducted on blood and marrow.

- the component of dose due to pure radon is dependent on the fat content of the marrow,
- the solubility of radon in fat is about 16 times that in tissue.
- modification factor has to be applied for higher deposition of daughter products in children,
- age-dependent dose from long-lived radon daughters was estimated based on uranium miners and natural exposure data.
- for the average UK indoor exposure to radon gas of 20 Bq/m^3 dose estimates were made.

Ref: Richardson et al 1991.

3.1.A Radon exposure to bone marrow – UK study …

The radon and thoron derived annual dose to the active bone marrow	
New born	30 and 40 microSv/yr
10 year old child	70 and 40 microSv/yr
40 year old adult	90 and 30 microSv/yr
Wide range limits exist due to uncertainties in the accumulation of ^{210}Pb in bone, and ^{210}Po in marrow. Ref: Richardson et al 1991.	

3.1.A Radon exposure to bone marrow – UK study …

Conclusions:

- The alpha radiation dose due to radon and thoron inhalation is significantly higher than the dietary component.
- However, for infants, the dose due to component of thoron daughters seems to be dominant.
- This work shows that there is significant dose to red bone marrow from radon and thoron.
- The possibility of leukemia induced by these radiation sources warrants further investigation.

3.1.B Ionizing radiation effects on bone marrow - France review

- Review of available data on the average equivalent dose from natural and some therapeutic and diagnostic exposures to the red bone marrow
- Age dependency on exposure levels is examined for available data.

Ref: Rommens et al , 2001.

3.1.B Ionizing radiation effects on bone marrow – France review …

The sources of exposure to ionizing radiation studied are :

- **medical examinations involving x-rays (diagnostic radiology),**
- **inhalation of radon and thoron,**
- **cosmic irradiation,**
- **terrestrial irradiation**
- **intakes of natural radionuclides.**

3.1.B Ionizing radiation effects on bone marrow – France review …

The total equivalent dose to the red bone marrow is estimated at	
adults > or =18 years old	2.4 mSv / year
children 3-17 years old	2.7 mSv / year
infants 0-1 year old	5.4 mSv / year

Ref: Rommens et al , 2001.

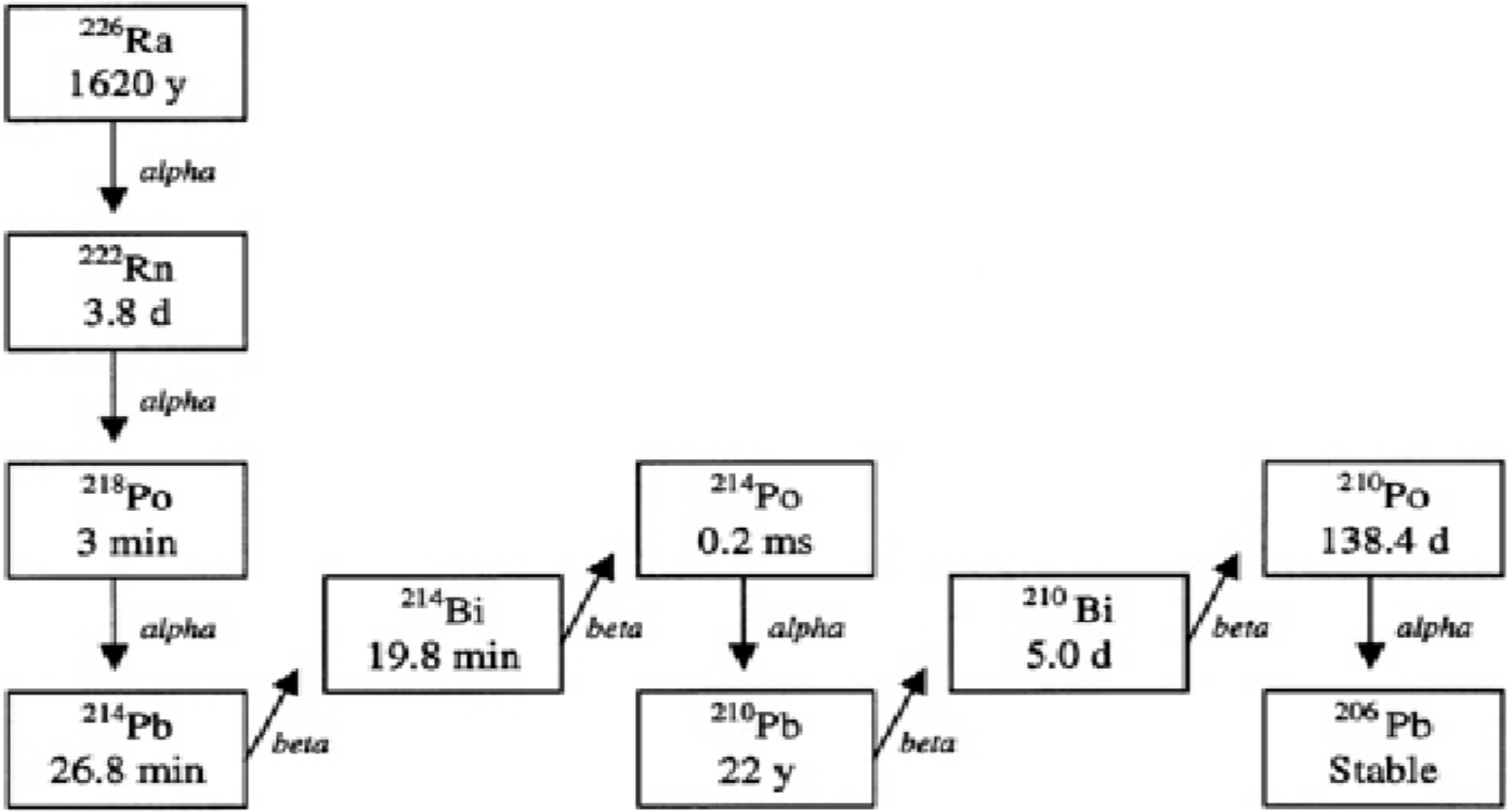
Summary of data from UK and France

The **radon and thoron,** estimated annual dose to the active bone marrow - UK	
New born	30 and 40 microSv/yr
10 year old child	70 and 40 microSv/yr
40 year old adult	90 and 30 microSv/yr

The **total equivalent dose** to the red bone marrow is estimated - France	
infants 0-1 year old	5.4 mSv / year
children 3-17 years old	2.7 mSv / year
adults ➢or =18 years old	2.4 mSv / year

- **The high level of exposure for infants is by contribution of ^{210}Po.**

Radon Decay


226Ra
1620 y
alpha
222Rn
3.8 d
alpha
218Po
3 min
alpha
214Pb
26.8 min
beta
214Bi
19.8 min
beta
214Po
0.2 ms
alpha
210Pb
22 y
beta
210Bi
5.0 d
beta
210Po
138.4 d
alpha
206Pb
Stable

3.1.B Ionizing radiation effects on bone marrow ...

Conclusion:

- The studies of radiation ionization due to medical exposure and exposure by natural radionuclides, emphasize the importance of obtaining more information about these sources of exposure.

3.2 Water solubility of radon

- 3.2.A Radon, fluoride and multi-element analysis of ground water
- 3.2.B Radon concentrations in open and bore well waters
- 3.2.C Water radon contamination in the human body – model study
- 3.2.D Bio-kinetics of radon from drinking water

3.2.A Radon, Fluoride and other multi-element analysis of ground water

- Radon and fluoride contents in hard rock groundwater samples of private drinking water wells in Oslo and Bergen were analyzed, 62 elements were additionally determined by inductively coupled plasma mass spectrometry (ICP-MS).
- There is strong correlation between characteristics of host rock and the corresponding Oslo-Bergen data. Range of variation of concentrations is in 2-6 orders of magnitude.

Ref: Reimann et al, 1996.

3.2.B Radon in open and bore well waters

^{222}Rn concentrations in ground water of open well and bore well samples from various locations of coastal Karnataka and Kaiga, India have been investigated by emanometry method.

3.2.A Radon, Fluoride and multi-element analysis of ground water …

- Concentrations of several elements (e.g. Ba, F, Fe, Mn, Na, Rn) exceed current drinking water action levels in a significant number of cases.
- High concentrations of Be, Mo, Th and U were observed; these may effect public health.
- There will be economic and toxicological impacts of these findings, hence need immediate assessment.

3.2.B Radon in open and bore well waters …

	The effective dose
Open well water 0.14-25.4 Bq/ L median value of 3.74 Bq/ L	0.09 microSv/ year -204.2 microSv/year
Bore well water 0.22-197.0 Bq /L median value of 5.75 Bq/ L.	0.2 microSv/year - 1586.9 microSv/year Ref: Mahesh et al, 2001

3.2.C Water radon contamination in the human body - model

- Simulation of a multicompartmental model of the radon contamination in the human body

- Assumption :
  - 100% of the ingested radon will be in the stomach;
  - blood stream carries radon to different organs of the body;
  - **r**adon is absorbed and released differently by different organs;
  - **r**adon is retained bythe fat retains for the longest time.

3.2.C Water radon contamination in the human body – model …

- The radiation doses in the different organs and tissues were estimated.
- Observation showed that the stomach experienced maximum dose, in agreement with the prediction.
- For the present study, the highest stomach dose was evaluated as 115 mSv per y(.

Ref: Sharma et al, 1997

3.2.D Bio-kinetics of radon from drinking water

- Stomach is the predominant organ for the dose from ingested radon. This is well established by studies.
- Rate of radon loss from the stomach is the important parameter in dosimetric modeling.
- In the present Maine study, two subjects ingested radon-rich water. The radiation in stomach was measured using a NaI(Tl) detector.

3.2.D Bio-kinetics of radon from drinking water …

- The activities of ^{214}Pb and ^{214}Bi peak regions were plotted as a function of time after ingestion.
- The model was fitted to the experimental data by changing bio-kinetic parameters such as the rate of radon loss from the stomach.
- The present study suggested that a part of radon stayed longer than 20 min in the stomach than expected in the previous models. (Ref: Ishikawa et al 2003)

3.3 Internal Alpha Radiation and Nephropathy

- **Internal alpha radiation effects on kidneys**

  &

  dysplastic changes due to internal alpha radiation injury

3.3 Internal alpha radiation and nephropathy

Internal irradiation of kidneys happens as a consequence of

- Radio-immunotherapy
  (note: therapy means the radioactive substance will reach the tumor and not the normal tissue)
- radiation accidents,
- nuclear terrorism.

This can result in radiation nephropathy.

3.3 Internal alpha radiation and nephropathy …

The observed histopathologic changes of lessened kidney functions are

- **glomerular, (means injury to glomerulus which is a network of capillaries)**
- **tubular, (means injury to renal tube, which is a long tube of permeable wall consisting of proximal and distal tubules and a loop)**
- **endothelial cell nuclear pleomorphism,**
  (pleomorphism means the occurrence of various distinct forms by a single organism or within a species, similar to polymorphism)
- **focal tubular cell injury,**
- **lysis: (means injury by means of breaking down, like in electrolysis)**
- **karyorrhexis (means injury by break down of nucleus of the cell)**

3.3 Internal alpha radiation and nephropathy …

The observed histopathologic changes (continued):

- tubulolysis (injures the cortex by gradual thinning)
- collapsed tubules,
- glomerular crowding,
- glomerular cell count decrease,
- juxtaglomerular cell count increase

  They are specialized cells which secrete renin, blood vessel consrictor
- interstitial inflammation

3.3 Internal alpha radiation and nephropathy …

The observed histopathologic changes (continued):

- **tubular atrophy**
- **mild interstitial fibrosis**
- **increased degranulation**
- **increased blood urea nitrogen with time-dependent reduction in renal functions**

3.3 Internal alpha radiation and nephropathy …

Conclusions:

- **Internally alpha-particle irradiation causes**
  triggers a chain of histopathologic changes
  resulting in progressive
  renal parenchymal damage
  along with loss of kidney functions.

Parenchymal damage means damage of the structures of the kidney: for example, glomerulus is for filtering, tubules are for water intake, interstitium is for support.

- **These observations are very different from those seen after gamma or beta irradiation of kidneys.**

3.4 Other radon research studies in medicine

- **3.4.A Biomarkers for kidney injury by alpha radiation**
- **3.4.B Exposure of radon and its progeny to human teeth**
- **3.4.C Clinical effects of exposure to radon in controlled environment.**
- **3.4.D Primary care physicians - Environmental history – Public health effects: An Italian survey**

3.4.A Biomarkers for kidney injury by alpha radiation

Biomarkers specific to densily ionizing high LET radiation

Beta hydroxyguanosine DHGs as evidnce of oxidative stress and iron stores

This is used as a biomarker of DNA damage by alpha damage and the body iron stores.

This can be done by nephrologists because of facility to do Iron profile. This DHGs is also estimated in urine as a marker of kidney injury.

Ref: Prof. P. Neelaprasad (Personal communication – Jan 2007)

3.4.B Exposure of radon and its progeny to human teeth

The objective of this study is to understand the correlation between the ^{210}Pb content in teeth of humans exposed to radon and radon daughter products.

- **The average value of ^{210}Pb is 2 mBq/g in human teeth for populations of various countries exposed to "normal" levels of radon-daughter exposure.**
- **The statistical analytical results are compared to corresponding data published in the literature, relating to the ^{210}Pb content of bones of uranium miners.**

Ref: Clemente et al 1984

3.4.B Exposure of radon and its progeny to human teeth …

^{210}Pb content of human teeth showed positive correlation to

- smoking habits and
- age
- no dependence on gender.

3.4.B Exposure of radon and its progeny to human teeth …

The study indicated the influence of

- exposure rate
- radon-daughter inhalation,
- radon dissolved in body fluids and
- ^{210}Pb metabolism

A comprehensive model is needed that takes into account all these parameters.

3.4.C Clinical effects of exposure to radon in controlled environment.

This study evaluated

the clinical effects of radon and thermal therapy on bronchial asthma in relation to antioxidant enzymes and lipid peroxide.

Ref: Mitsunobu et al, 2003.

3.4.C Clinical effects of exposure to radon in controlled environment …

Nasal inhalation of vapor from a hot spring was conducted once a day under conditions of high humidity.

- The room temperature was 48 degrees C.
- The room radon concentration was 2,080 Bq/m^3.

Note: Read the original article for more details.

3.4.C Clinical effects of exposure to radon in controlled environment …

Observations: (compared to the control)

- Significant increase in the forced expiratory volume in one second (%FEV1)
- Significant decrease in the lipid peroxide level
- Significantly increase in the catalase (CAT) activity
- Significant increase in superoxide dismutase (SOD) activity.

3.4.C Clinical effects of exposure to radon in controlled environment …

Biochemical understanding of the observations:

Ref: Chap. 17 in Review of Physiological chemistry by Harper et al

In simple terms , oxidation is the removal of electron from a substance.

Ex:

Ferrous oxide Fe^{2+} becomes Ferric oxide Fe^{3+}

There will be an acceptor for the electron in an oxidation reaction.

Reduction is gain of electron to a substance.

But the physiological processes of oxidation and reduction involve more reactions and interactions.

3.4.C Clinical effects of exposure to radon in controlled environment …

Enzyme is a protein catalyst. Catalyst accelerates a chemical reaction. Enzymes and coenzymes get involved in oxidation and reduction reactions.

- Catalase enzyme acts on Hydrogen peroxide and release water molecule and oxygen. Thus increased catalase ennzyme activity decreases peroxide levels.
- Peroxidase enzyme acts on Hydrogen peroxide plus electron acceptor; releasing water molecule and acceptor.
- Dismutase enzyme acts on super oxides converting it into oxygen. Increased Super Oxide Dismutase (SOD) enzyme activity decreases superoxide levels.

3.4.C Clinical effects of exposure to radon in controlled environment …

The peroxide of the lipid gets converted to water by catalase or peroxidase.

Peroxidase enzyme mediates conversion of hydrogen peroxide to water molecules, in this several substances that act as electron acceptors are involved.

$H_2O_2 + AH_2 \Rightarrow 2H_2O + A$ (electron acceptor)

where AH_2 is an enzyme, A is a substrate.

3.4.C Clinical effects of exposure to radon in controlled environment …

Superoxides are formed during reoxidation from molecular O_2.

Superoxide dismutase acts only on superoxide; it is substrate specific.

Super oxides (O_2 -)may be reduced by super oxidase dismutase (SOD). In this process the free oxygen radical gets converted to oxygen.

Oxygen may become potentially toxic by formation of Hydogen peroxide or superoxide.

O_2^- _+ O_2^- + 2H = H_2O_2 + O_2 . So O_2^- becomes positive.

Super oxide dismutase helps in reduction of super oxide.

3.4.C Clinical effects of exposure to radon in controlled environment …

- When oxidation happens reduced substances increase in the body,
- Antioxidants prevent formation of free radicals, prevent release of electrons.
- Antioxidants prevent release of electron, thus preventing reduced substances like superoxide or hydrogen peroxide (the free radicals) and other reactive oxidation species.

3.4.C Clinical effects of exposure to radon in controlled environment …

In the experimental study:

Catalase activity increased.

Catalase enzyme acts on lipid peroxides, converting it to water; releasing electron acceptors. Thus lipid peroxide levels are reduced.

SOD activity increased, which decreases the superoxide levels. When superoxides are decreased, the peroxide levels decrease.

Thus there is overall decrease in free radical levels.

3.4.C Clinical effects of exposure to radon in controlled environment …

Conclusion:

Thus radon and thermal therapy have positive effects on

the pulmonary function by accelerating the reduction

activities of antioxidant enzymes.

However, the long term effects of radon inhalation for therapeutic purposes have to be studied.

Hence currently caution and awareness are required.

Ref: Mitsunobu et al, 2003.

3.4.D Primary care physicians - Environmental history – Public health effects: An Italian survey

Focus of the questionnaire:

- Primary Care Physicians (PCPs) demographics
- practice characteristics,
- knowledge of the major environmental risk factors and related public health effects,
- attitudes about role of environment on public health
- accurate description of environmental exposures history.

3.4.D Primary care physicians …

OBSERVATIONS:

- About 50% of PCPs correctly indicated indoor radon exposure for lung cancer,
- About 28% correctly recognized all health effects related to environmental exposures. respiratory disease.
- Majority of PCPs reported to take a patient history on occupational exposures,
- About a third of PCPs reported to provide education material about environment and public health to their patients.

Ref: Nicotera et al , 2006

3.4.D Primary care physicians

…

PCPs inquiring their patients about environmental exposures were significantly more likely to consider environmental health history taking as an important tool to prevent exposures to environmental hazards.

Radon Research in Medicine

Conclusions:

Radon

- has carcinogenic ‘leukemiogenic’ effects when inhaled or internally delivered.
- has biological effects like reduction of peroxides , increase the action of superoxide dismutase, and enhance the action of catalase to decrease the reactive oxygen species activity in the biological system
- seems to have promising positive therapeutic role in the treatment of bronchial asthma, diabetes and hypertension.

Ref: Prof. P. Neelaprasad, M. D. – Personal communication Jan 2007

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Key words