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Epidemiologic Studies Cannot Reveal the True Shape of the Dose–Response Relationship for Radon-Induced Lung Cancer

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Abstract

A long-standing controversy is the correct shape of the dose-response relationship for lung cancer induction by inhaled radon (eg, residential radon) at low levels. A probabilistic approach is used in this commentary to show that cohort and case-control epidemiologic studies cannot reveal the true shape of the dose-response relationship for radon-induced lung cancer. Using the indicated approach, it is found that while the dose response for radon-induced lung cancer is expected to be threshold-increasing, the dose-response curve for the cancer incidence when cancers caused by smoking and other carcinogens are included is expected to be threshold-decreasing (ie, threshold-hormetic), as low-level radon can protect from cancer induction by other carcinogens via stimulating the body's natural defenses against cancer. These defenses include DNA damage repair, removal of aberrant cells via apoptosis, suppression of cancer promoting inflammation, and anticancer immunity.

Keywords

lung cancer, radon, dose response, hormesis, LNT

Introduction

A current debate relates to whether epidemiologic studies of cancer risk (if any) from low-dose-radiation exposure can be reliable and accurate.[1] This relates in part to *claimed adjustments for competing risk factors to reduce ucertainty*.[1,2] The adjustments supposedly eliminate the different influences of the different risk factors considered other than the radiation source of interest. Of special interest is whether the shape of the radiation-dose-response relationship can be revealed for the low-dose region even when such adjustments are attempted since data used are usually quite noisy and there can be unknown interactions between different carcinogenic risk factors. A potential important contribution to data noise relates to exposure misclassification.

Many epidemiologic studies have been carried out with forced application of the linear no-threshold (LNT) model which assigns risk of harm from even very small radiation doses, including from low-level residential radon. In doing so, noise in the data used and multiple risk factors influences and interactions among different risk factors have been *inadequately addressed*.

A *probabilistic approach* is used in this *commentary* to show why cohort studies of lung cancer (or cancer mortality) risk from low-level radon exposure (via inhalation) cannot be trusted to reliably yield the correct dose-response curve shape. First, a simplified hypothetical scenario that relates to an epidemiologic study of the possibility of lung cancer being caused by chronic low-level radon inhalation exposure is presented. *All references to radon exposure should be understood to apply to radon radioactive progeny*.

Only 2 risk factors (both carcinogenic) are involved for the simplified radon exposure scenario considered in the following section, namely, radon (and related inhalation exposure level) and smoking. *All references to smoking should be understood*

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to apply to smoking-related carcinogens. For the indicated scenario, the focus is on white male heavy smokers (age 60 years or older) with an elevated lung cancer risk from smoking since the age of 20 (years) that are also chronically exposed via inhalation over years to low-level residential radon. The risk assessment approach used for 2 carcinogenic risk factors is then modified to allow for additional carcinogenic risk factors and risk modifiers (eg, gender, age). Because cancer data used in epidemiologic studies are quite noisy, the impact of the noise on trying to resolve dose-response curve shape is addressed.

Probabilistic Model 1: 2 Risk Factors

In the hypothetical scenario addressed here, radon and smoking (heavy smokers) are the only risk factors for lung cancer among the population of interest (*adult white males, age 60 years or older, smoking since age 20*). For the heavy smokers, lung cancer risk as a function of smoking level Y (a categorical variable) is elevated and given by the function G(Y) whose mathematical structure is unspecified (not necessary here). The risk function G(Y) relates only to smoking and not to radon. For chronic radon exposure (via inhalation), at level X (average concentration evaluated over an extended period), and for *never smokers*, the risk of radon-induced lung cancer is given by the function F(X), whose mathematical structure is also unspecified (not necessary here). The risk function F(X) therefore relates specifically to *radon-caused lung cancer* and is unrelated to smoking (adjustment for smoking is made to get F(X) when based on data for smokers). For combined exposure to radon and cigarette smoke, H(X, Y) accounts for *interactions* (statistical) between radon exposure and inhaled cigarette smoke.

The lung cancer incidence (probability of cancer) is given here by R(X, Y), which is evaluated, for R(X, Y) << 1, as follows:

$$R(X,\ Y) = F(X) + G(Y) + H(X,\ Y). \tag{1}$$

Here G(Y) is significantly greater than 0 due to heavy smoking but much less than 1. The interaction H(X, Y) can be negative (eg, when there is a hormetic[3] effect of irradiation, or when F(X) = G(Y) = 1 but excluded here) or positive (enhanced harm due to deleterious interactions) depending on values for X and Y. Also, R(X, Y) > 0 does not necessarily mean harm from radon at level X, as it may relate to smoking level Y only, especially for a low radon level.

R(X, Y) might be 1 of 4 different types of functions of X (for low levels) for a given level of Y: (1) no-threshold-increasing; (2) no-threshold-decreasing (ie, no-threshold-hormetic); (3) threshold-increasing; and (4) threshold-decreasing (ie, threshold-hormetic). These are reasonable assumptions and not more than 1 can be true. If true, then specific conclusions can be drawn. However, only plausibility or implausibility is addressed in this article. For no-threshold-increasing, a very small radiation dose would have to cause lung cancer by itself or interact with cigarette smoke to lead to a lung cancer that would not otherwise have occurred. The smallest radiation dose is from a single ionization event, which by itself cannot cause cancer and interacting with smoking is implausible. Indeed, Katz and Waligorski[4] pointed out that radiobiological data obtained with different ionizing radiation types demonstrate that *millions of ionizations may be required for cancer induction*. They then concluded that if the no-threshold-increasing risk model were valid, the number of needed ionizations would have to be reduced to the highly implausible value of 1. The contradiction renders the no-threshold-increasing risk model highly implausible. Included in this risk model category is the LNT model.

For no-threshold-decreasing risk, a single ionization event would have to prevent a smoking-related cancer (hormetic effect) for someone and this is not plausible. Should a single ionization event be sufficient for preventing cancer, then no cancers would be expected from any cause as many harmless natural ionization events take place in our bodies daily throughout life. Thus, a single-radiation-hit-related hormetic response for lung cancer is highly implausible. For threshold-increasing risk, only radiation doses above the threshold (many ionizations) for harm would cause cancer in someone and this is plausible.[4] For threshold-decreasing risk, only radiation doses above the threshold for a hormetic response (lung cancer prevention) would prevent smoking-related cancer and this is plausible. Thus, there are but 2 plausible possibilities for R(X, Y) for low levels of X: threshold-increasing and threshold-decreasing (ie, threshold hormetic response as is supported by existing data from cohort[2] and case-control studies[5,6]). Again, LNT is not plausible.[4] This is, therefore, also the case for relative risk RR(X, Y), which is given as a function of R(X, Y) by the following:

$$RR(X,\ Y) = R(X,\ Y)/G(Y). \tag{2}$$

An estimator r(X, Y) of R(X, Y) based on noisy epidemiologic data with associated noise $\epsilon\{r(X, Y)\}$ (stochastic quantity with both positive and negative values) for each combination of X and Y of interest is given by the following:

$$r(X,\ Y) = R(X,\ Y) + \epsilon\{r(X,\ Y)\}. \tag{3}$$

Because of the stochastic noise $\epsilon\{r(X, Y)\}$, r(X, Y) can take on many different values, some greater and others less than the true risk R(X, Y). An estimator of RR(X, Y) is rr(X, Y), with associated noise $\epsilon\{rr(X, Y)\}$. Because of noisy data, rr(X, Y) can be as large as 2.0 and as low as 0.5 in the absence of any radiation exposure effect.[1] Since the focus is on heavy smokers and radon, R(X, Y) although unknown is significantly greater than 0 due to smoking and may be larger than $\epsilon\{r(X, Y)\}$.

An estimator g(Y) of G(Y) based on noisy epidemiologic data for heavy smokers with associated noise $\epsilon\{g(Y)\}$ for each value of Y of interest is given by the following:

$$g(Y) = G(Y) + \epsilon\{g(Y)\}. \tag{4}$$

Although G(Y) is unknown for heavy smokers, it is significantly greater than 0 and may be larger than $\epsilon\{g(Y)\}$.

Table 1. Body's Natural Defenses Against Cancer That are Stimulated by Low Radiation Doses Such as are Associated With Low-Level Radon (based on Scott).[3]

Defense Against Cancer	Health Benefit
Epigenetically regulated DNA damage repair and antioxidant production	Prevents persistent genomic instability
P-53-independent selective apoptosis of aberrant cells	Removes neoplastically transformed cells
Suppression of inflammation	Reduces cancer risk
Anticancer immunity and diminution of growth signals	Destroys cancer cells and inhibits tumor growth

An estimator f(X) of F(X) (risk for radon-induced lung cancer) with associated noise $\epsilon\{f(X)\}$ derived from epidemiologic study data for *never smokers* is given by the following:

$$f(X) = R(X,0) + \epsilon\{r(X,0)\} = F(X) + \epsilon\{f(X)\}. \quad (5)$$

Here, F(X) = R(X,0) and $\epsilon\{f(X)\} = \epsilon\{r(X,0)\}$. The assignment of Y = 0 indicates that smoking effects do not apply. For low-level radon exposure, F(X) is either 0 or close to 0. Thus, *ϵ{f(X)} is the predominant term rendering it impossible to uncover F(X)* as a function of X in an epidemiologic study of lung cancer risk from radon exposure.

For F(X) to be a no-threshold-increasing risk function, a single ionization event would have to induce lung cancer in someone and this is implausible.[4] Thus, *there is but one plausible possibility for F(X) (in this hypothetical scenario) for low-level radon exposure: threshold-increasing.* Both hormetic and LNT responses are implausible, although a hormetic response has been demonstrated for lung cancer incidence (or related RR) when there are multiple risk factors (including carcinogenic factors) including radon and smoking.[2,3,5,6] In this case, R(X, Y) applies rather than F(X). Thus, *R(X, Y) can be hormetic but for F(X) this is implausible!* The indicated conclusions apply to both cancer incidence and cancer mortality. Related to hormetic responses, it is now recognized that low-dose radiation can stimulate a hierarchy of natural anticancer defenses in the body referred to as hallmarks of cancer suppression.[3] The currently known natural defenses that operate at the molecular, cellular, tissue/organ, and whole-body levels are summarized in Table 1.

For smokers, a more complex relationship for the estimator f(X) applies because adjustments are needed for both smoking and for interactions between radon and smoking, as reflected by the following probabilistic relationship:

$$F(X) = R(X,\ Y) - G(Y) - H(X,\ Y). \quad (6)$$

Thus, addressing the adjustments (removal of smoking influences via subtraction) leads to the following estimator f(X) of F(X):

$$\begin{aligned} f(X) &= r(X,\ Y) - g(Y) - h(X,\ Y) \\ &= R(X,\ Y) + \epsilon\{r(X,\ Y)\} - [G(Y) + \epsilon\{g(Y)\} \\ &\quad + H(X,\ Y) + \epsilon\{h(X,\ Y)\}]. \end{aligned} \quad (7)$$

The term h(X, Y) is an estimator of H(X, Y), but cannot be obtain directly from data. Noise associated with h(X, Y) is given by $\epsilon\{h(X, Y)\}$. An assumed mathematical relationship can be assigned for h(X, Y), but cannot be considered reliable with the exception of when based on a validated mechanistic model. No such validated model exists. Thus, h(X, Y) is unknown and so is $\epsilon\{h(X, Y)\}$. In addition, $\epsilon\{r(X, Y)\}$, $\epsilon\{g(Y)\}$, and $\epsilon\{h(X, Y)\}$ are stochastic (noise). This makes it essentially impossible to reliably uncover F(X) from an epidemiologic study involving smokers for low-level radon exposure.

A very interesting observation is that because F(X) has to be 0 for no radiation exposure, RR for radon-caused lung cancer cannot be evaluated because division by 0 is not possible. This is also the case for threshold deterministic effects, such as lethal damage to the bone marrow. Relative risk can, however, be evaluated for lung cancer incidence R(X, Y) since G(Y) > 0. Thus, reports of the risk estimate f(0) > 0 and RR = 1 for the unexposed group in an epidemiologic study implies that risk being assigned is due in part to noisy data rather than radon and/or adjustment for the other carcinogenic risk factor influence was deficient.

The indicated findings are based on the hypothetical scenario with but 2 carcinogenic risk factors (radon and smoking) for the same race (white) and gender (male). In the next section, the same approach is used to address what would be expected when additional carcinogenic risk factors and different risk modifiers (e.g, race and gender) are involved.

Probabilistic Model 2: Multiple Risk Factors

Here R(X, Y) is replaced by R[X, **Z**], where **Z** is a vector of all carcinogenic risk factors and risk modifiers and their levels (or indicators, for variables such as gender and race) other than radon which is still represented by level X. F(X) is replaced by F[X], which applies to the same population as for R[X, **Z**]. G(Y) is replaced by G[**Z**] and H(X, Y) is replaced by H[X, **Z**]. It follows that lung cancer risk (or lung cancer mortality risk) for the population of interest and given **Z** is as follows:

$$R[X, \mathbf{Z}] = F[X] + G[\mathbf{Z}] + H[X, \mathbf{Z}]. \quad (8)$$

R[X, **Z**] is expected to be threshold-increasing or threshold-hormetic for radon exposure and for a given **Z** for reasons already indicated for probabilistic model 1. The same is true for RR[ ] which is given by the following:

$$RR[X, \mathbf{Z}] = R[X, \mathbf{Z}]/(G[\mathbf{Z}] + H[0, \mathbf{Z}]), \quad (9)$$

where H[0, **Z**] accounts for all interactions excluding with radon (X = 0 is used for radon exclusion). Where a hormetic dose-response curve is implicated (as in some previous

studies[2,5-7]) and observations are significant, the decreasing portion of the hormetic response for low-level radon exposure likely involves lung cancers caused by carcinogenic risk factors other than radon and elimination or prevention of the cancers via radon stimulation of the body's anticancer defenses (ie, a radon exposure health benefit that can be characterized by a benefit function[7]). Using r[X, **Z**] as an estimator of R[X, **Z**] based on noisy epidemiologic data with noise $\epsilon\{r[X, \mathbf{Z}]\}$ and using g[**Z**] as an estimator of G[**Z**] with noise $\epsilon\{g[\mathbf{Z}]\}$, and using h[X, **Z**] as an estimator of H[X, **Z**] with noise $\epsilon\{h[X, \mathbf{Z}]\}$, leads to the following adjusted lung cancer risk estimator f[X] for lung cancer risk F[X] for radon-caused lung cancer (or lung cancer mortality):

$$f[X] = R[X, \mathbf{Z}] + \epsilon\{r[X, \mathbf{Z}]\} - (G[\mathbf{Z}] + \epsilon\{g[\mathbf{Z}]\} + H[X, \mathbf{Z}] + \epsilon\{h[X, \mathbf{Z}]\}). \quad (10)$$

Because of the stochastic noise terms ($\epsilon\{\dots\}$) and their expected predominance for low-level X and because of the unobtainable interaction term estimate,

$$h[X, \mathbf{Z}] = H[X, \mathbf{Z}] + \epsilon\{h[X, \mathbf{Z}]\}, \quad (11)$$

there is no way to reliably uncover F[X] for low-level radon exposure, as was the case with only 2 risk factors (radon and smoking). Indeed, *the noisy data situation is much worse for multiple carcinogenic risk factors* since $\epsilon\{g[\mathbf{Z}]\}$ has to be much more noisy than $\epsilon\{g(Y)\}$, which applies when smoking is the only other carcinogenic risk factor besides radon, and H[X, **Z**] has to be much more complex than H(X, Y), which also applies when smoking is the only carcinogenic risk factor besides radon.

The Impact of Deficient Adjustments

Cohort study researchers of radon exposure-related lung cancer have reported an RR of 1 for the assigned unexposed group, even after supposedly adjusting for influences of other risk factors. This means that adjustments were likely deficient, because *with complete and efficient adjustment there should be no remaining risk*; in which case, RR cannot be evaluated because the denominator for the RR calculation would be 0. To account for deficient adjustments, **Z** in equations used for RR evaluation can be replaced with $\mathbf{Z}_d$, where d indicates deficient adjustment (ie, some risk factor influences for carcinogenic factors other than radon still remain). The next section relates to RR evaluation under circumstances of deficient adjustments and addresses what is called here the *vanishing noise trick*.

The Vanishing Noise Trick Used in RR Estimation

Some epidemiologists (eg, Cardis et al,[8] Leuraud et al,[9] and Richardson et al[10]) employ a *vanishing noise trick* when estimating RR for cancer (or cancer mortality) for the assigned unexposed group, although the studies indicated did not address radon exposure (they focus on irradiated nuclear workers). However, the trick also applies to radon exposure. This relates to uncertainty (noise-associated) of the RR estimator rr[X, $\mathbf{Z}_d$] (with noise $\epsilon\{rr[X, \mathbf{Z}_d]\}$) of RR[X, $\mathbf{Z}_d$] in the case of deficient adjustment for competing carcinogenic risk factors, which allows for a RR of 1 for the assigned unexposed group. In the case of radon exposure as addressed here, the vanishing noise trick relates to dividing the baseline risk estimate (reflecting harm from carcinogenic risk factors other than radon) for the assigned unexposed (to radiation) group by itself and getting $rr[0, \mathbf{Z}_d] = 1$, *with 0 uncertainty* (ie, no error is assigned, so data noise is magically vanished). Because the baseline risk estimate r[0, $\mathbf{Z}_d$] for a given $\mathbf{Z}_d$ has uncertainty (here indicated as standard error $SE\{r[0, \mathbf{Z}_d]\}$), an SE needs to be assigned to $rr[0, \mathbf{Z}_d] = 1$. Stated differently, an SE greater than 0 needs to be assigned to a value of RR of 1 for the unexposed group as was pointed out in an earlier publication that addressed serious flaws in several epidemiologic studies.[1] Based on the SE for the ratio of 2 numbers each with associated SEs, this error is $1.4142(SE\{r[0, \mathbf{Z}_d]\}/r[0, \mathbf{Z}_d])$.

For epidemiologic studies, $SE\{r[0, \mathbf{Z}_d]\}$ may be as large as r[0, $\mathbf{Z}_d$] since r[0, $\mathbf{Z}_d$] likely has a wide distribution,[1] in which case the SE for an RR estimate of 1 is 1.4142. For such instances, reported RR estimates for irradiated groups such as 2.0 and 1.5 unlikely indicate harm from radiation exposure, but rather likely reflect working with noisy data and deficient data adjustments for competing carcinogenic risk factors. Also, reported RR estimates such as 0.75 and 0.5 for irradiated groups in such instances unlikely represent a radiation benefit (hormetic response), but rather likely relate to working with noisy data and deficient data adjustments for competing carcinogenic risk factors. These conclusions are consistent with previous findings.[1] An exception would be data showing a significant monotonic trend (increasing or decreasing RR) for a range of exposure levels for low-level exposure. A monotonically decreasing trend was found by Cohen[11] for radon inhalation-associated lung cancer.

Case–Control Studies Unreliability

Case-control studies are less reliable than cohort studies for finding the shape of the RR[X, **Z**] versus dose relationship for low-level radiation exposure since with case-control studies there is no way to directly evaluate the baseline risk and address its uncertainty; rather, RR is indirectly inferred. It follows that the dose–response relationship for RR[X, **Z**] cannot be reliably revealed in cohort or case–control epidemiologic studies of low-level radon exposure. The same is also true for F[X]. *These conclusions also apply to RR evaluation for all cancer types and all radiation types* (eg, alpha, beta, gamma, neutrons, X-rays, combinations of these, etc) because of noisy data and deficient adjustments for influences of competing carcinogenic risk factors.

Where LNT outcomes have been reported in some epidemiologic studies (eg, references[8-10,12]) or assumed in other studies (eg, claimed lung cancer induction in smokers by annual computed tomography [CT] scans[13]), they are based on seriously

flawed and misleading analyses[1] (including employment of the vanishing noise trick[8-10] and forced application of the invalid LNT model[8-10,12,13]). Regarding CT scans, they may actually reduce rather than increase cancer risk.[14] Findings reported here related to residential radon are consistent with previous findings.[7]

Meta-Analyses Studies and Increased Noise

It is important to also comment on meta-analyses studies of lung cancer risk related to radon exposure. Because each data set used in the meta-analysis involves independent noise and unaccounted for interactions between different carcinogenic risk factors specific for each data set, combining the different data may significantly increase rather than decrease uncertainty about cancer risk as is suggested by meta-analysis data used in a recent study.[15]

Conclusions

For low-level radon exposure, the risk for radon-induced lung cancer (or lung cancer mortality) is expected to be a threshold-increasing function of the exposure level. Where the threshold arises will be difficult to resolve because epidemiologic study data are noisy and adjustments for competing risks are deficient.

The lung cancer risk (or lung cancer mortality risk) for multiple carcinogenic risk factor involvement (with a focus on radon) may be threshold-decreasing (ie, hormetic) as a function of the radon exposure level, but LNT is highly implausible. Thus, extrapolating from high-level radon exposure to low-level exposure using the LNT risk model is unjustifiable.

Where significant hormetic responses for lung cancer risk (or lung cancer mortality risk) are observed for low-level radon exposure, the cancers that are observed are unlikely caused by radon exposure but likely by other carcinogenic risk factors. In addition, the significant decrease in risk is likely due to radon exposure stimulating the body's natural defenses against cancer that include the following: (1) DNA damage repair, (2) apoptosis of aberrant cells, (3) suppression of cancer-facilitating inflammation, and (4) anticancer immunity.

Use of the vanishing noise trick (where no error is assigned to cancer RR = 1 for the unexposed group) in RR estimation should be ended.

Conclusions stated here for lung cancer and low-level radon also apply to all other cancer types and radiation sources for low doses of ionizing radiation.

Authors' Note

The views and conclusions contained herein are those of the author and should not be interpreted as necessarily representing policies or endorsement of his affiliated institution.

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References

1. Scott BR. A critique of recent epidemiologic studies of cancer mortality among nuclear workers. *Dose-Response*. 2018;16(2). doi:10.1177/1559325818778702.
2. Cohen BL. The linear no-threshold theory of radiation carcinogenesis should be rejected. *J Am Physicians Surg*. 2008;13(3): 70-76.
3. Scott BR. Small radiation doses enhance natural barriers to cancer. *J Am Physicians Surg*. 2017;22(4):105-110.
4. Katz R, Waligórski MPR. On the linear extrapolation to low doses. *Radiat Prot Dosimetry*. 1994;52(1-4):197-199.
5. Thompson RE, Nelson DF, Popkin JH, Popkin Z. Case–control study of lung cancer risk from residential radon exposure in Worcester County, Massachusetts. *Health Phys*. 2008;94:228-241. doi:10.1097/01.HP.0000288561.53790.5f.
6. Thompson RE. Epidemiological evidence for possible radiation hormesis from radon exposure: a case–control study in Worcester, MA. *Dose-Response*. 2011;9(1):59-75. doi:10.2203/dose-response.10-026.Thompson.
7. Scott BR. Residential radon appears to prevent lung cancer. *Dose Response*. 2011;9(4):444-464. doi:10.2203/dose-response.11-027.Scott.
8. Cardis E, Vrijheid M, Blettner M, et al. The 15 country collaborative study of cancer risk among radiation workers in the nuclear industry: estimates of radiation-related cancer risks. *Radiat Res*. 2007;167(4):396-416.
9. Leuraud K, Richardson DB, Cardis E, et al. Ionizing radiation and risk of death from leukemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. *Lancet Haematol*. 2015;2(7):e276-e281. doi:10.1016/S2352-3026(15)00094-0.
10. Richardson DB, Cardis E, Daniels RD, et al. Risk of cancer from occupational exposure to ionizing radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). *BMJ*. 2015;351:h5359. doi:10.1136/bmj.h5359.
11. Cohen BL. Test of the linear-no threshold theory of radiation carcinogenesis for inhaled radon decay products. *Health Phys*. 1995;68(2):157-174. doi:10.1097/00004032-199502000-00002.
12. NRC (National Research Council). *Health Risks from Exposure to Low Levels of Ionizing Radiation. Report BEIR-VII. Phase 2*. Washington, DC: The National Academies Press; 2006.
13. Brenner DJ. Radiation risks potentially associated with low-dose CT screening of adult smokers for lung cancer. *Radiology*. 2004; 231:440-445. doi:10.1148/radiol.2312030880.
14. Scott BR. Avoiding diagnostic imaging may be the real health risk, not imaging. *J Am Phys Surg*. 2016;21(3):74-80.
15. Dobrzyński L, Fornalski W, Reszczyńska J. Meta-analysis of thirty-two case–controls and two ecological radon studies of lung cancer. *J Radiat Res*. 2017;59(2):149-163.