Reviewer’s report

Title: Environmental radon exposure and breast cancer risk in the Nurses' Health Study II

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Reviewer: Zorana Anderson

Reviewer’s report:

In Article 'Environmental radon exposure and breast cancer risk in the nationwide US Nurses' Health Study II' authors study association between residential radon and breast cancer risk in the Nurses' Health Study II, among 112,639 female nurses (mean age 45 years at baseline), of whom 3,966 developed breast cancer from 1989 until 2013. Radon exposure was estimated at county-level, based on a National Residential Radon Survey (NRRS) in the 1980s. Authors find no association between radon exposure and overall breast cancer risk or, the more common subtype, ER+/PR+ breast cancer, but report suggestive evidence of an association with ER-/PR- breast cancer.

This a first prospective cohort study on radon an breast cancer in a large cohort of American nurses, with well-defined breast cancer via self-reports and medical record review, and well defined information on all major breast cancer risk factors. The study is well designed, statistical analyses appropriate for the data in question, and methods and results are well described, and study rationale well explained. Radon exposure used in this study has been linked to lung cancer in a related study, and seems to be valid proxy of individual exposure to radon. Authors point in the Introduction that some experimental evidence exists on biological plausibility that ionizing radiation from radon could lead to breast cancer development, and make a good argument for a need for the epidemiological study on the topic. Thus, study is important contribution to the evidence base on the health effects related to residential radon exposure.

I propose several minor issues to be addressed before study should be accepted for publication.

Comment 1: Authors adjust for air pollution (PM2.5), although air pollution was not found to be associated to breast cancer in this cohort in a recent study by Hart et al.


Evidence on air pollution and breast cancer currently does not support the causal relationship. And air pollution is not related to radon exposure, so can authors explain a bit more rationale for adjusting for air pollution?

Comment 2: Recent study has linked road-traffic noise to ER- breast cancer subtype, which may in part support the authors statement that ER+ breast cancer are mainly explained by hormonal and reproductive factors, while certain environmental exposures (radon, noise) may explain ER-
breast cancer. Given that authors chose to adjust for air pollution, and not noise (I assume because they have air pollution and lack noise data) some attention should also be given in discussion to road-traffic noise, at least as acknowledgement of the weakness in lack of road-traffic noise data.


Comment 3: Results of significant interaction and association between radon and breast cancer in Western region of US, and even stronger for ER-/PR- in Midwest region, are interesting. Authors state in Introduction, page 3, line 65 that approximately 6% of US homes have radon levels above EPA action level of 400Bq/m³. Are there any data by regions (or states) in what percentage of homes exceeds action levels? Title of Reference 13 seems to suggest that data are available for National and regional level? These would be interesting to look up, as a possible explanation for stronger effects in Western/Midwest regions.

Comment 4: Could authors list which states belong to which region, or even better illustrate regions on a map, along with from which states nurses are recruited from? To a non-US reader this is not obvious, but may help to better understanding of findings related to regional differences in radon-breast cancer association. A Map of radon levels by county/nurses residence may also be very informative.

Comment 5: Could regional differences in association between radon and breast cancer be possibly explained by better assessment of radon exposure in Western/Midwest regions? It is not apparent whether data collected in SRRS and NRSS surveys are representative of entire US, or are there possibly more sampling sites/more data on radon in certain regions? Can authors briefly discuss this.

Comment 6: Radon exposure was estimated based on measurements in 1980's and authors suggest that radon concentrations do not change over time. Are there any publications/reports/data to support this statement?

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