PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Evaluation of clinicians' knowledge and practices regarding medical radiological exposure: findings from a mixed methods investigation (survey and qualitative study)
AUTHORS	Lumbreras, Blanca; Vilar, Jose; Gonzalez-Alvarez, Isabel; Gilabert, Mercedes; Parker, Lucy; Pastor-Valero, María; Domingo, María Luisa; Lorente, María Fermina; Hernandez-Aguado, Ildefonso

VERSION 1 - REVIEW

REVIEWER	Lawrence T. Dauer Memorial Sloan Kettering Cancer Center Departments of Medical Physics and Radiology United States of America
REVIEW RETURNED	05-May-2016

GENERAL COMMENTS	Manuscript details the results of a quantitative and qualitative survey of 515 physicians to assess knowledge and practices associated with diagnostic imaging. While there are limitations associated with such studies, these are delineated well by the authors, including difficulties with generalization of results. The methods are cogent and logically presented. Several general statements are made that may not be specifically supported by the results and additional clarifications need to be made in a revised manuscript. 1. Abstract - Page 4, line7, and General Comment - the paper frequently uses the term 'radiation safety' as a general statement. This should be defined more specifically in terms of diagnostic medical imaging, perhaps refer to relevant ICRP, IAEA, or other EU documents/guidance. 2. Abstract - Page 4, line 22, a 'sample of clinicians' was sought for the study. While the methods section later gives a bit more information on the sampling methodology and rationale, more should be included to describe. Also include an expanded discussion of the limitations this sampling induces. 3. Abstract - Page 4, line 33, and General Comment - the manuscript often refers to the 'best approach to inform patients about benefits and risks' but the methodology never includes asking patients themselves. (For example see Thornton et al, Radiology 2015 http://pubs.rsna.org/doi/abs/10.1148/radiol.15132905). Please be sure to change this wording throughout to clarify that it is what the clinicians who were surveyed thought to be most appropriate for communicating. 4. Abstract, Page 4, line 42, and General Comment - in several places the manuscript refers to the 'risk associated with' diagnostic

	imaging tests, but the specific assumptions behind this risk assessment are never provided. This is a significant problem for the manuscript as the evaluations of clinician perspectives includes 'risk'. Several sections need to be significantly reworded. 5. Article Summary, Page 5, lines 23-48 - see previous comments and revise as necessary. 6. Introduction, Page 6, lines 31-37 - it is identified that physicians need a 'clear understanding of the effective dose received by each test' in order to have an effective communication on risk and benefit. Authors should have perhaps included an assessment of the knowledge of the benefits. Is there evidence-based literature on quantification of the benefits of such imaging? (For example, see Zanzonico 2016 http://www.ncbi.nlm.nih.gov/pubmed/26808890). 7. Introduction - Page 6, line 54-56 - this sentence should be reworded because references 4-6 appear to have already evaluated clinician awareness (or lack of awareness). What is the purpose then specifically for this study? To evaluate awareness in two hospitals in Spain? Be much more specific. 8. Materials and Methods - Although the number of physicians 'sampled' is given, the fraction of sampled physicians to the total number of physicians is not provided. It is very difficult, if not impossible, to evaluate the representativeness of the sampling. 9. Materials and Methods, page 9, lines 26-30 - expand this sentence to give specific details on how the comparisons were completed and what the basis of comparability. Was this considered a validation test? Were statistics applied/used? 10. Survey design, page 9, line 55 - 'The survey was piloted by a number of medical staff prior to use...' This statement is extremely general. Be very specific about how pre-testing, modification, and re-testing was performed. 11. Focus group guides, page 11, lines 44-55 - the authors often refer to the 'cancer risk' or 'true cancer risk' (e.g., in the tables/figures) associated with these tests. Note that this is an area of much debate. The current high-quality epidemiological studies have only suggested statistically significant increased risks above 100-150 mGy (see UNSCEAR, ICRP, NCRP and others). In addition, the International Organization of Medical Physics has highlighted the substantial imprecision in estimating population cancer risks from imaging and noting the dangers of extrapolating risk estimates for radiation doses < 100 mSv (Hendee, W. R. Policy statement of the international organization for medical physics. Radiology 267, 326–327, 2013). The establishment and use of risk coefficients to estimate public health determinants from individual or population exposures must be considered in the context of uncertainties in the estimates. Uncertainties have been suggested as being up to a factor of 3 lower or 3 higher than the value itself (UNSCEAR. Report of the United Nations Scientific Committee on the effects of atomic radiation. Fifty-ninth session. General Assembly Official Records Sixtyseventh session, supplemental No. 46. A/67/46. United Nations Scientific Committee on the Effects of Atomic Radiation (2012).). Indeed, the American Association of Physics in Medicine has stated that 'risks of medical imaging at effective doses below 50 mSv for single procedures or 100 mSv for

	multiple procedures over short time periods are too low to be detectable and may be non-existent' (AAPM. AAPM position statement on radiation risks from medical imaging procedures. PP 25-A. American Association of Physicists in Medicine, 2012). The authors need to expand and clarify the discussion of 'risk' significantly. Alternatively, the authors could remove the 'risk' results and only (perhaps much more appropriately) refer to the typical doses from imaging tests. 12. Qualitative Study, page 16, lines 48-50 - it is unclear what the authors mean by 'radiation exposure accumulates through an individual life.' We all receive daily background exposures? Dose damage accumulates? Risk increases with accumulated medical imaging tests? What is the basis for this statement? What references support this statement that is supposedly evaluated in the focus group participants? 13. Page 22, line 25-28. 'There are many situations where the quantitative analysis does not cover the entire reality, lacking some relevant information.' Expand this discussion specifically for this study. What areas are difficult to interpret in these results? 14. Figure 1 - on what basis is the 'cancer risk associated with different medical imaging' being evaluated? Also, blue box indicates 'true cancer risk' - given the huge uncertainties at these very low doses, truth is difficult (and likely impossible) to ascertain even in large populations, let alone for an individual. 15. Annex II, page 42 - table - table heading indicates %, but the values appear to be given as fractions? 16. Supplementary Figure 1 - is this assuming a chest x-ray 'unit' of risk? or dose? Dose is the more appropriate comparison.

REVIEWER	Atul Padole Massachusetts General Hospital, Boston, MA, US
REVIEW RETURNED	29-May-2016

GENERAL COMMENTS	The study is very well designed and written. Introduction and material and method sections are very good. Some part of results section can be moved in discuss section.

REVIEWER	John D Mathews University of Melbourne Australia I am studying cancer risks following CT scans in childhood; this gives me some insights, but I do not believe it constitutes a real conflict of interest.
REVIEW RETURNED	12-Jul-2016

GENERAL COMMENTS	This is an interesting study, apparently triggered by the European recommendations on Radiation Protection and Safety. The results show, not unexpectedly, that even radiologists have a limited understanding of the regulations and risks from radiation.

	The references do not include any of the more recent reports on the ACTUAL cancer risks following CT scans (eg Pearce et al 2012; Mathews et al 2013), which emphasize the apparently greater risk of cancer following exposure in childhood. The 2016 update of the EC guidelines was accessed by the authors, but would have been too late to have influenced the study. As of now, the context of the study, and some of the the risk estimates used in the questionnaires can be seen as somewhat out of date. One might also quibble with the (EC) metrics used to quantify cancer risk (eg in Fig. 1), which are difficult to interpret and ignore the strong age-dependency of risk. Nevertheless the study provides a valuable summary of how difficult it is for well educated professionals (including EC regulators) to learn about radiation risks and to modify their practice accordingly. A case can be made for publication, if only because the results should be useful in devising better educational and regulatory strategies for use in future years.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

1. Abstract - Page 4, line7, and General Comment - the paper frequently uses the term 'radiation safety' as a general statement. This should be defined more specifically in terms of diagnostic medical imaging, perhaps refer to relevant ICRP, IAEA, or other EU documents/guidance.
In agreement with the reviewer, we have changed the term ‘radiation safety’ to ‘medical radiological exposure’. This term is defined in the Directive 2013/59/Euratom.

2. Abstract - Page 4, line 22, a 'sample of clinicians' was sought for the study. While the methods section later gives a bit more information on the sampling methodology and rationale, more should be included to describe. Also include an expanded discussion of the limitations this sampling induces.
We have now included a more detailed description of the sampling methodology and the main limitations associated with the sampling process in the abstract (page 4, lines 18-24).

3. Abstract - Page 4, line 33, and General Comment - the manuscript often refers to the 'best approach to inform patients about benefits and risks' but the methodology never includes asking patients themselves. (For example see Thornton et al, Radiology 2015 http://pubs.rsna.org/doi/abs/10.1148/radiol.15132905). Please be sure to change this wording throughout to clarify that it is what the clinicians who were surveyed thought to be most appropriate for communicating.

We have changed the term to clarify this point in the abstract (page 5, lines 2-3) and in the manuscript (page 9, lines 22-23; page 10, lines 6-7; page 21, lines 22-23; page 23, lines 18-19).

4. Abstract, Page 4, line 42, and General Comment - in several places the manuscript refers to the 'risk associated with' diagnostic imaging tests, but the specific assumptions behind this risk assessment are never provided. This is a significant problem for the manuscript as the evaluations of clinician perspectives includes 'risk'. Several sections need to be significantly reworded.

The reviewer is right. Although there is evidence showing that even low doses of ionizing radiation may increase lifetime risk of cancer, there is also evidence supporting that these risks are small for adults (Tubiana M et al, Radiology 2009; http://pubs.rsna.org/doi/pdf/10.1148/radiol.2511080671).
In order to clarify the manuscript, we have changed the expression 'risk associated with diagnostic imaging tests’ to ‘long-term potential risks of ionizing radiation from medical imaging’.

5. Article Summary, Page 5, lines 23-48 - see previous comments and revise as necessary.
According to previous comments, we have changed the article summary (page 6).

6. Introduction, Page 6, lines 31-37 - it is identified that physicians need a 'clear understanding of the effective dose received by each test' in order to have an effective communication on risk and benefit. Authors should have perhaps included an assessment of the knowledge of the benefits. Is there evidence-based literature on quantification of the benefits of such imaging? (For example, see Zanzonico 2016 http://www.ncbi.nlm.nih.gov/pubmed/26808890).

The reviewer is right, we could have included an assessment of the physicians' knowledge of the benefits. In this sense, we have included a sentence in the discussion section including this aspect as a limitation. We also refer to the paper of Zanzonico and to an additional reference related with the topic (page 26, lines 21-25).

7. Introduction - Page 6, line 54-56 - this sentence should be reworded because references 4-6 appear to have already evaluated clinician awareness (or lack of awareness). What is the purpose then specifically for this study? To evaluate awareness in two hospitals in Spain? Be much more specific.
The aim of the study is to assess the impact of the initiatives carried out to increase clinician awareness of medical radiation exposure; explore the challenges they face when addressing the potential risk to the health of their patients and to learn what clinicians think to be most appropriate for communicating medical radiological exposure to patients. These data will help the design of strategies to improve compliance with the Basic Safety Standards Directive (EU 2013). We have reworded the sentence to clarify this point (page 9, lines 1-2), and rewritten the aim of the study in the abstract (page 4) and in the introduction accordingly (page 10).

8. Materials and Methods - Although the number of physicians 'sampled' is given, the fraction of sampled physicians to the total number of physicians is not provided. It is very difficult, if not impossible, to evaluate the representativeness of the sampling.
We have included the total number of physicians and the percentage to assess the response rate and representativeness of the sampling (pages 11-12).

9. Materials and Methods, page 9, lines 26-30 - expand this sentence to give specific details on how the comparisons were completed and what the basis of comparability. Was this considered a validation test? Were statistics applied/used?
We compared the clinical and demographic variables and the different items included in the survey between those physicians who answered the questionnaire electronically with those who completed it in person. We have included a more detailed description in pages 12-13.

10. Survey design, page 9, line 55 - 'The survey was piloted by a number of medical staff prior to use...' This statement is extremely general. Be very specific about how pre-testing, modification, and re-testing was performed.
According to the reviewer, we have detailed this point in page 13, lines 17-25.

11. Focus group guides, page 11, lines 44-55 - the authors often refer to the 'cancer risk' or 'true cancer risk' (e.g., in the tables/figures) associated with these tests. Note that this is an area of much debate. The current high-quality epidemiological studies have only suggested statistically significant increased risks above 100-150 mGy (see UNSCEAR, ICRP, NCRP and others). In addition, the International Organization of Medical Physics has highlighted the substantial imprecision in estimating population cancer risks from imaging and noting the dangers of extrapolating risk estimates for

radiation doses < 100 mSv (Hendee, W. R. Policy statement of the international organization for medical physics. Radiology 267, 326–327, 2013). The establishment and use of risk coefficients to estimate public health determinants from individual or population exposures must be considered in the context of uncertainties in the estimates. Uncertainties have been suggested as being up to a factor of 3 lower or 3 higher than the value itself (UNSCEAR. Report of the United Nations Scientific Committee on the effects of atomic radiation. Fifty-ninth session. General Assembly Official Records Sixtyseventh session, supplemental No. 46. A/67/46. United Nations Scientific Committee on the Effects of Atomic Radiation (2012).). Indeed, the American Association of Physics in Medicine has stated that 'risks of medical imaging at effective doses below 50 mSv for single procedures or 100 mSv for multiple procedures over short time periods are too low to be detectable and may be non-existent' (AAPM. AAPM position statement on radiation risks from medical imaging procedures. PP 25-A. American Association of Physicists in Medicine, 2012). The authors need to expand and clarify the discussion of 'risk' significantly. Alternatively, the authors could remove the 'risk' results and only (perhaps much more appropriately) refer to the typical doses from imaging tests.

We agree with the reviewer, calculating risks for small doses of radiation is an area of much debate. UNSCEAR considers, in its 2012 report, that it is unlikely that risks are dramatically different above and below the level at which statistical significance has already been established. It also acknowledges that statistical significance below the current levels may not be achieved for a long time, because the power of epidemiological studies decreases too much as we approach levels of dose similar to the background.
The scope of this article cannot reach this level of detail. So following the reviewer's advice, we have removed the risk results in both the quantitative study (clinicians' knowledge of regarding the cancer risk associated with different medical imaging tests, figure 1) and the qualitative evaluation (in the adapted radiation equivalence table we have deleted the column showing the long-term cancer risk associated with each test, annex 2).

12. Qualitative Study, page 16, lines 48-50 - it is unclear what the authors mean by 'radiation exposure accumulates through an individual life.' We all receive daily background exposures? Dose damage accumulates? Risk increases with accumulated medical imaging tests? What is the basis for this statement? What references support this statement that is supposedly evaluated in the focus group participants?
The current paradigm of radiation protection states that stochastic effects follow a Linear Non-Threshold model, with all radiation received above the background level adding a small, linear probability to those effects happening through an individual's lifetime (ICRP 103).
The concern we detected is directly related to this: if all radiation "matters" but some clinicians are unaware of this and require imaging tests for their patients without discussing benefits and risks. Those clinicians that are aware will have to explain not only the tests that they prescribe, but also the ones that were never explained to the patients.
We have modified the expression to clarify this point and we have added a reference (page 22, lines 2-4 and reference 17).

13. Page 22, line 25-28. 'There are many situations where the quantitative analysis does not cover the entire reality, lacking some relevant information.' Expand this discussion specifically for this study. What areas are difficult to interpret in these results?
The analysis of the discussion clinicians-patients may be limited if we only apply quantitative methods such a survey. Qualitative methods can give us an overview of clinicians' point of view when ordering medical imaging examinations involving ionizing radiation. We have expanded this topic in the discussion section.
14. Figure 1 - on what basis is the 'cancer risk associated with different medical imaging' being

evaluated? Also, blue box indicates 'true cancer risk' - given the huge uncertainties at these very low doses, truth is difficult (and likely impossible) to ascertain even in large populations, let alone for an individual.
According to reviewer's advice and as we commented previously, we have deleted 'risk' results in both quantitative and qualitative evaluation. Thus, we have not incorporated this figure in this paper (page 26, lines 2-5).
15. Annex II, page 42 - table - table heading indicates %, but the values appear to be given as fractions?
The values are percentages.
16. Supplementary Figure 1 - is this assuming a chest x-ray 'unit' of risk? or dose? Dose is the more appropriate comparison.
This is a mistake. The unit is dose and we have changed it.

Reviewer: 2

The study is very well designed and written. Introduction and material and method sections are very good. Some part of results section can be moved in discuss section.
We thank the reviewer for his comments. In accordance with suggestions made by one of the other reviewers, we have removed the results on long-term potential risk of ionizing radiation from medical imaging. We feel both the results and discussion section have improved.

Reviewer: 3
This is an interesting study, apparently triggered by the European recommendations on Radiation Protection and Safety. The results show, not unexpectedly, that even radiologists have a limited understanding of the regulations and risks from radiation.

The references do not include any of the more recent reports on the ACTUAL cancer risks following CT scans (eg Pearce et al 2012; Mathews et al 2013), which emphasize the apparently greater risk of cancer following exposure in childhood. The 2016 update of the EC guidelines was accessed by the authors, but would have been too late to have influenced the study. As of now, the context of the study, and some of the risk estimates used in the questionnaires can be seen as somewhat out of date. One might also quibble with the (EC) metrics used to quantify cancer risk (eg in Fig. 1), which are difficult to interpret and ignore the strong age-dependency of risk.
Following the reviewer's advice, we have explained the significant associations between the estimated radiation doses provided by CT scans to red bone marrow and brain and subsequent incidence of leukaemia and brain tumours in children and young adults. (Discussion page 25, lines 9-11). Moreover, we have introduced a reference on this issue.
We agree with the reviewer that fig 1 is difficult to interpret without taking into account the age-dependency of risk. I accordance with this comment, and the suggestion made by one of the other reviewers, we have removed this figure to avoid confusion.

Nevertheless the study provides a valuable summary of how difficult it is for well educated professionals (including EC regulators) to learn about radiation risks and to modify their practice accordingly. A case can be made for publication, if only because the results should be useful in devising better educational and regulatory strategies for use in future years.