

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Whole body counter assessment of internal radio-contamination in end-stage renal disease patients living in areas affected by the Fukushima Daiichi nuclear power plant disaster: a retrospective observational study
AUTHORS	Shimmura, Hiroaki; Tsubokura, Masaharu; Kato, Shigeaki; Akiyama, Junichi; Nomura, Shuheji; Mori, Jinichi; Tanimoto, Tetsuya; Abe, Koichiro; Sakai, Shuji; Kawaguchi, Hiroshi; Tokiwa, Michio

VERSION 1 - REVIEW

REVIEWER	Noboru Takamura Nagasaki University
REVIEW RETURNED	28-Aug-2015

GENERAL COMMENTS	<p>Shimmura et al. assessed the internal radiation exposure in patients with end-stage renal disease (ESRD) around Fukushima Dai-ichi Nuclear Power Plant (FDNPP) and found that radio-contamination level with Cs-137 were limited among them.</p> <p>Major points:</p> <ol style="list-style-type: none"> 1. Authors should describe how to recruit the control group. They should also describe inclusion and exclusion criteria of the group in Methods section. They also should indicate the clinical information of the control group (average age, sex ratio, body mass index) which affected the body burdens of Cs-137. 2. Lines 128-133: Authors described that "hemodialysis requires large amounts of tap water that could be contaminated with radionuclides that were reported to have been released from the crippled nuclear power plant", but water was contaminated by radioiodine (I-131), not radiocesium (Cs-137 and Cs-134). The different mechanism of water contamination by radioiodine and radiocesium should be clearly described. 3. Lines 273-277: As mentioned above, authors should separately describe about the relationship between the contamination of tap water and radioiodine and radiocesium. <p>Minor points:</p> <ol style="list-style-type: none"> 1. Lines 222-226: This paragraph should be replaced in "Discussion". 2. Line 228: "radionucleides" should change to "radiocesium".
-------------------------	--

REVIEWER	Bruce A. Napier Pacific Northwest National Laboratory USA
-----------------	---

REVIEW RETURNED	23-Sep-2015
-----------------	-------------

GENERAL COMMENTS	This article is a clear description of cesium-137 radiation measurements in ESRD patients and a control group in the vicinity of Fukushima, Japan. The results will be useful for researchers and regulators concerned with the fate of environmentally-distributed radionuclides in the event of nuclear accidents. In this case, they should also be welcomed by local citizens as evidence that post-Fukushima radiation doses are low to the general public. The measurements imply that the food supply is and has been kept at levels safe for public consumption - the measurements, if assumed to be at equilibrium, imply that daily intakes are less than 2 Bq/day for the measured population which means that food supplies are being maintained at levels far below the Japanese standard of 100 Bq/kg. It would be helpful if Figure 1 also contained the information from the non-ESRD control group for comparison.
------------------	---

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Noboru Takamura

Institution and Country: Nagasaki University, Japan.

Please leave your comments for the authors below

Shimmura et al. assessed the internal radiation exposure in patients with end-stage renal disease (ESRD) around Fukushima Dai-ichi Nuclear Power Plant (FDNPP) and found that radio-contamination level with Cs-137 were limited among them.

Major points:

1. Authors should describe how to recruit the control group. They should also describe inclusion and exclusion criteria of the group in Methods section. They also should indicate the clinical information of the control group (average age, sex ratio, body mass index) which affected the body burdens of Cs-137.

Thank you for raising a critical issue. In the revised text, we now include more detailed information for non-ESRD patients. This screening project allowed anyone, including voluntary hospital visitors and patients, who wanted an assessment of their internal radio-contamination levels free of charge, to undergo testing at the Jyoban hospital. In the previous version, all of the assessed non-ESRD visitors and patients were included in the non-ESRD group.

However, based on your comments, and after an analysis of the non-ESRD control group, we realized that most of the control subjects were schoolchildren, and as such the age-matching comparisons were not appropriate. Since the rates of Cs metabolism in the body and renal Cs excretion are known to be age-dependent, as per your suggestion we formed sub-groups of the original subject pool that had the same age range as the ESRD patients (25-83). The newly collected group subjects (238 subjects) mentioned in the revised manuscript had a median age of 53.5 years, 45.0% females. We believe that these values are comparable to the ESRD group.

2. Lines 128-133: Authors described that "hemodialysis requires large amounts of tap water that could be contaminated with radionuclides that were reported to have been released from the crippled nuclear power plant", but water was contaminated by radioiodine (I-131), not radiocesium (Cs-137 and Cs-134). The different mechanism of water contamination by radioiodine and radiocesium should

be clearly described.

We appreciate your concern and have mentioned the details in the revised manuscript by adding the following sentences (lines 130-141 in the final version):

"In this regard, end-stage renal disease (ESRD) patients undergoing hemodialysis (HD) could represent a patient population among affected residents, since Cs tends to be eliminated via urine, and urine production may be compromised in ESRD patients due to severely impaired kidney function. In addition, HD requires large amounts of tap water that could have been contaminated with radionuclides dispersed from the crippled nuclear plant, including radioiodine (I-131) as well as Cs. However, this possibility seems unlikely except for the period immediately after the disaster, since the I-131 half-life is short (8 days) and Cs is presumably trapped during common water purification processes (e.g., coagulation-flocculation-sedimentation) used for drinking water in Japan."

3. Lines 273-277: As mentioned above, authors should separately describe about the relationship between the contamination of tap water and radioiodine and radiocesium.

Thank you for your helpful comment regarding the relationship between tap water contamination and radioiodine and radiocesium. We have changed the sentence as follows:

"Even immediately after the disaster, Cs appeared to be effectively trapped within muds in river beds and areas affected by the tsunami, and indeed was generally undetectable in drinking water in the affected areas. However, monitoring of potential I-131 contamination of tap water immediately after the disaster was likely far more important than internal radiocontamination measurements in HD patients since I-131 cannot be removed by coagulation-flocculation-sedimentation purification processes, but instead must be removed by special purification measures, including activated charcoal treatment and separation with reverse osmosis membranes."

Minor points:

1. Lines 222-226: This paragraph should be replaced in "Discussion".

We have moved the sentence into the Discussion section on lines 252-256 in the final version.

2. Line 228: "radionuclides" should change to "radiocesium".

We have accordingly replaced the word.

Reviewer: 2

Reviewer Name: Bruce A. Napier

Institution and Country: Pacific Northwest National Laboratory, USA.

Please leave your comments for the authors below

This article is a clear description of cesium-137 radiation measurements in ESRD patients and a control group in the vicinity of Fukushima, Japan. The results will be useful for researchers and regulators concerned with the fate of environmentally-distributed radionuclides in the event of nuclear accidents. In this case, they should also be welcomed by local citizens as evidence that post-Fukushima radiation doses are low to the general public. The measurements imply that the food supply is and has been kept at levels safe for public consumption - the measurements, if assumed to be at equilibrium, imply that daily intakes are less than 2 Bq/day for the measured population which means that food supplies are being maintained at levels far below the Japanese standard of 100 Bq/kg. It would be helpful if Figure 1 also contained the information from the non-ESRD control group

for comparison.

We appreciate your kind comments about our work. In the revised text, we now include more detailed information for non-ESRD patients. This screening project allowed anyone, including voluntary hospital visitors and patients, who wanted an assessment of their internal radio-contamination levels free of charge, to undergo testing at the Jyoban hospital. In the original version, all of the assessed non-ESRD visitors and patients were included in the non-ESRD group.

However, based on your comments, and after an analysis of the non-ESRD control group, we realized that the most of the control subjects were schoolchildren, and as such the age-matching comparisons were not appropriate. Since the rates of Cs metabolism in the body and renal Cs excretion are known to be age-dependent, as per your suggestion we formed sub-groups of the original subject pool that had the same age range as the ESRD patients (25-83). The newly collected group subjects (238 subjects) mentioned in the revised manuscript had a median age of 53.5 years, 45.0% females. We believe that these values are comparable to the ESRD group.

The information for the non-ESRD control group is now included in the Figure 1.

VERSION 2 – REVIEW

REVIEWER	Noboru Takamura Nagasaki University, Japan
REVIEW RETURNED	26-Oct-2015

GENERAL COMMENTS	Authors adequately revised according to the suggestion of this reviewer. I think that now this manuscript should be accepted.
-------------------------	---

REVIEWER	Bruce A. Napier Pacific Northwest National Laboratory, USA
REVIEW RETURNED	22-Oct-2015

GENERAL COMMENTS	The responses to the editorial and reviewer comments are adequate and appropriate. The paper now reads more smoothly than the initial draft. The re-definition of the control group is beneficial.
-------------------------	--