Author's response to reviews

Title: Aluminum concentrations in central and peripheral areas of malignant breast lesions do not differ from those in normal breast tissues

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Author's response to reviews: see over
Campinas, November 28, 2012

Christina Chap  
Executive Editor – BMC Cancer

Dear Ms. Chap,

We are pleased to resubmit our manuscript for further publication consideration in BMC Cancer; this is the second revision of the text. The issues raised by the referees – either mandatory or discretionary revisions - were addressed carefully. Please find, in the next pages, a detailed response to the referees’ concerns.

We hope the manuscript can now meet the quality requirements of BMC Cancer and can be deemed acceptable for publication.

We are looking forward to receiving your response.

Yours truthfully,

Luis Sarian
Comment 1: “The authors have made significant efforts to improve their manuscript. The following are suggested Discretionary Revisions.

I would like to have seen matched-pairs statistical analyses comparing the aluminium content of tumour tissue (all) with 'normal' breast tissue. At the moment these comparisons seem to be between two types of tumour tissue and non-tumour tissue? When this is done for unfatted tissue, as is the case in this research, it would be important to try to compare like with like in the terms of the fat content as tissues with higher fat content give both higher 'dry' weights and our previous research suggested that aluminium was less likely to accumulate in breast fat (oil) compared to the non-fatty tissue. One way of matching like with like would be to compare % water loss during drying. Non-fatty tissue tends to lose about 80% of its wet weight while fatty tissue may lose only 10-20% of its wet weight.”

Response 1: Firstly, thank you very much for your second round of revision. We expanded Table 2 in order to encompass your suggestion of comparing normal X tumor tissues. Your suggestion of adjusting the calculations to the % water loss of each sample is fantastic. However, since we performed aluminum measurements only in defatted and dried tissues, we believe there is no need for further concentration corrections.

Comment 2: “The authors should be aware that Krewski et al is also a non-peer reviewed publication funded by the aluminium industry! Again, i would prefer it if such types of publication were not cited.”

Response 2: Thank you again. This reference was replaced by the old and seemingly reliable “Ganrot PO (1986). Metabolism and possible health effects of aluminum. Environ Health Perspect 65:363-441.”
Reviewer: Philippa Darbre

Reviewer's report:

Comment 1: “The revised version of the manuscript has addressed some of the comments made in my original review. However, some have not been addressed. The main outstanding comment which has not been addressed is as to why the data have been analysed solely on the basis of three linear groupings. In the revised manuscript, the methods section under statistical analysis now states that "Log-transformed () values were used, since the raw data showed marked skewness". If this is so, why then are the data still grouped into three linear groupings for analysis? The data need analysing on the basis of a log distribution and not a linear distribution and would be better analysed using original raw data, not an artificial set of three linear groupings.

Response 1: We have now included the mean aluminum concentrations with respective standard deviations in tables 3-5. The categorical grouping, in three levels, was performed using the three-tiered percentile distribution of the data. We kept both the means and the categorical distributions, because one of the reviewers asked us to evaluate if there was a trend in Al concentration from normal tissue to the central areas of the tumors, and that was better accomplished using chi-squares for trends (only applicable to categorical data). In tables 3-5, the first p values apply to the differences in means (using log transformation to validate the calculations, as explained in the statistics section – quoting Douglas Altman, it is possible to “…perform the calculations on the log data and transform the answers back to the original scale”), and the second are related to the trend analysis. All tables are accompanied by a footnote detailing these procedures. The log-transformed values of the Al concentration are not shown, since they are meaningless to the reader and were only used to allow the computations.

Table 2 was expanded in order to encompass the Reviewer #2 suggestion of comparing the mean Al concentrations in diseased vs. normal tissues. All calculations follow the same steps described in the original version of the manuscript and were not modified.

Thank you very much for reviewing our manuscript again and for the useful suggestions.
Reviewer: Ferdinando Mannello

Reviewer's report:

Comment 1: “No further requests.”

Response 1: Thank you very much for your help during the review process.