Author's response to reviews

Title: Dose and polymorphic genes xrcc1, xrcc3, gst play a role in the risk of developing erythema in breast cancer patients following single shot partial breast irradiation after conservative surgery

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Author's response to reviews: see over
Dear Dr. Adam Riker,

We are resubmitting a revised version of the above mentioned manuscript. We thank the Editor and the referees for their comments and suggestions. We addressed all the points raised by you and the referees as detailed below. All changes introduced in the manuscript are marked in yellow.

We believe that the present version of the manuscript is acceptable for publication in BMC CANCER.

Looking forward to hearing from you,

Sincerely,

Elisabetta Falvo
Editorial request:

1) Copyediting - Please note that BioMed Central journals are not copyedited prior to publication. We advise you to pay close attention to language during revision of this manuscript. If necessary, please seek the assistance of a fluent English speaking colleague, or have a professional editing service correct your language. For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz (www.edanzediting.com/bmc1). BioMed Central has negotiated a 10% discount to the fee charged to BioMed Central authors by Edanz. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication. For more information, see our FAQ on language editing services at http://www.biomedcentral.com/info/authors/authorfaqs#12.

The present revision of manuscript has been reviewed by an English proof reader in our Institute.

2) Trial Registration Number is present but has to be added in abstract (and removed from title)

This change has been introduced in the present version of the manuscript

3) Ethics - Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/e/policy/b3.htm), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

The approval of this study by our ethics committee of Regina Elena Cancer Institute was introduced in the Materials and Methods section with the specific reference number. (page 6)

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

We modified the manuscript according to the journal style
Reviewer's report

Reviewer 1: Roland Hawkins

Reviewer's report:
Major compulsory revisions: none
Minor essential revisions: none

Discretionary revisions:
1. 1st line of introduction: It is my understanding that the chance of a woman getting breast cancer or carcinoma in situ in a lifetime is about 11%. This is much lower than the percent quoted. Furthermore, I think "incidence" has a definite meaning in epidemiology different from the usage in this sentence. The incidence quoted for the USA is about 124 cases per 100,000 women per year.

The text has been improved according to Referee’s comments. (page 4).

We are very grateful to the referee for his suggestions that allow us to improve the background section of the manuscript.

2. Materials and Methods, section on "end-points". The grading scale for erythema is important and I think should be described explicitly rather than directing the reader to a reference that I found difficult to access.

We have modified this section to help the reader in the interpretation of the text and clarify grading scale for erythema. (page 7).
Reviewer 2: Hua Zhao
Reviewer's report:
Major Compulsory Revisions
This is an interesting study to look at toxicity after radiotherapy for breast cancer patients. The major critique is the sample size. The study population is too small (57 patients). Therefore, no conclusion can be made from this study at all.

The submitted manuscript aims to identify patients at low and high risk of erythema. Due to the particular treatment (a Single dose of radiotherapy), we assumed an erythema rate of 20% and 54% in patient groups at low and high risk, respectively, (groups were identified based on the absence/presence of the above polymorphisms alone or in combination). Thus the minimum sample size was 56 patients with $\alpha=0.05$, 2-tailed test and a power of the study of 80%. This matched with the 38 and 19 patients in low and high risk groups respectively in our study. Thus, these preliminary results can be confirmed from a statistical point of view, despite the limited number of patients.

Further investigation is taking place to confirm our results in a larger cohort.

Also, only three polymorphisms are included in the study.

As reported in the paper, we investigated the following specific polymorphic genes: XRCC1 (Arg399Gln, and Arg194Trp), XRCC3 (5’UTR and Thr241Met), GSTP1 (Ile105Val), GSTA1 and RAD51 (untranslated region). We concluded that three out of seven analyzed polymorphisms showed a statistically significant association with erythema.

Quality of written English: Needs some language corrections before being Published

Language corrections have been made throughout the text. The present revision of manuscript has been reviewed by an English proof reader in our Institute.