Reviewer's report

Title: The effects of low dose X-irradiation on osteoblastic MC3T3-E1 Cells in Vitro

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Reviewer: Lexie Holliday

Reviewer's report:

I am still not entirely clear on the rationale for the manuscript. There seems to be a suggestion that low dose radiation might be tested to promote fracture healing in the clinic. I want to be clear that the data from this article does not in any way support such studies. A great deal of animal work would be required to justify thinking about such studies, and safety data regarding possible deleterous effects of low dose radiation would have to be developed, weighing benefits with risks.

With that caveat, the authors have worked to improve the manuscript by providing quantitative alkaline phosphatase data and quantitative real time PCR as requested. However, while these results are statistically significant, they might easily be a cell culture artifact generated by slightly altered proliferation rates.

The real question, it seems to me, is why low dose radiation is having the effects; including the increases in gene expression detected. Is the hypothesis must be some type of response to minor radiation damage, and consequently would likely be associated with slightly increased risks of radiation-associated pathologies. I think the authors need to address this question. I emphasize that the positive changes reported are quite small, but statistically-significant.

If the take home message of the article is low dose radiation probably does not have significant increased safety risk (ie no obvious reason to worry about normal CT scans or fluoroscopy) then I am much more comfortable with the manuscript; but the conclusion seems to hint at the need for clinical studies to examine using low dose radiation to enhance fracture healing. In my view this is very, very, very premature. Current radiation use practices are probably acceptable, but not (in my mind) testing specific use for enhancing fracture healing.

I may have misinterpreted the authors' suggestions about future research plans. Perhaps this issue could be clarified.

The English remains unacceptably rough in places despite the comments of the previous review. Since BMC Muscular Disorders does not professionally edit, this really must be corrected by the authors.

Finally, I question whether there are scientific advances in this article. While BMC Muscular Disorders aims to put less emphasis on interest level, it is still not clear
that the current article makes a useful contribution to the field. If it is setting the stage for low dose radiation to be tested for fracture healing in the clinic, then I can not support it unless there are plans for many intermediate studies in tissue culture and in animals. If it isn't, then the authors must be clear on what they consider to be the significance of the manuscript.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No Competing interest.