Author's response to reviews

Title: A study of 0.5 Tesla dedicated magnetic resonance imaging for the detection of breast cancer in young, high risk women

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Author's response to reviews: see over
Once again, we would like to thank the reviewers for their helpful and constructive comments. Our responses to their points are given below, as well as descriptions of resulting changes in the manuscript. We have also shortened the abstract as required.

Reviewer: Dr. Kimler

Major Compulsory Revisions

1) Use of the BRCAPRO model for cancer risk estimation.

The reviewer is quite correct, BRCAPRO calculates the risk of being a carrier of a germline BRCA1/2 mutation, but, with our extensive knowledge of this high risk population, this can be converted into an absolute breast cancer risk through, as we put it in the previous version of the manuscript “using age-specific penetrance liabilities”. We have expanded on this in the present revision so that the average reader can understand how this was accomplished, and introduced the “CancerGene” program produced by Dr. David Euhus at UT Southwestern at Dallas, which actually performs the calculation. The reviewer is quite right in asking that sufficient explanation be given so that the methodology is clear. We also discuss the limitations of the Gail model at identifying BRCA1/2 carriers and how the CancerGene program, by allowing the conversion of BRCA carrier risk into quantitative cancer risk, allows us to identify potential BRCA1/2 carriers as at high risk for cancer in the same terms as the Gail model. Please note that the BRCA-based model was used to identify 23 of the 30 subjects in our population, suggesting that it is a unique highly “genetic” high risk population. Since BRCAPRO does not actually provide the cancer risk estimations, we have, where appropriate in the text, either referred to the CancerGene program directly or to a “BRCAPRO-based” cancer risk estimation (there are subtleties involved in discussing the Gail and Berry “models”, the Berry model-based BRCAPRO program and the BRCAPRO-based CancerGene program or calculation). Also please note that much of this material was present in early versions of the manuscript (although not as submitted to BMC Women’s Health), but, through review, the manuscript seemed to evolve away from the unique genetic aspects of the study to the unique aspects of the MRI used in the study. We are glad to have the chance to fold in more of this material.

Minor Essential Revisions

1) Figure 2 and clinical description of the patient

Since both reviewers had continuing problems with this Figure, we had our radiologist, Dr. Sumkin, re-evaluate it, and we found it had been constructed incorrectly. We are very grateful to both reviewers for helping us to uncover this problem. The figure has been revised and the benign lesion is now indicated with an arrowhead to distinguish it from the tumor, as requested. We have also added a paragraph to the Results section describing the subject’s MR images and pathologies.
Reviewer: Dr. Causer

Minor essential revisions

1) Figure 2

As mentioned earlier, since both reviewers had ongoing problems with this figure, we had it reviewed by our radiologist and found it to be constructed incorrectly. The revised figure still shows a persistent delayed enhancement pattern, consistent with the clinical report on this patient (Latimer et al., 2005 BMC Med Genet 6:26, reference 43). A paragraph on the MRI and pathological findings on this patient has been added to the Results section, relocating and correcting some of the text from the former legend to this figure.

2) change well-demarcated to "smooth"

The description of this lesion, which is now shown in Figure 2B, has been changed as suggested.

Thank you for the opportunity to receive feedback from the reviewers and to submit our responses. We think the final product has benefited greatly from this interchange.

Wendy Rubinstein