## Reviewer Recommendation and Comments for Manuscript Number PONE-D-14-25713 Area and volumetric density estimation in processed full-field digital mammograms for risk assessment of breast cancer Original Submission Guo Shicheng (Reviewer 1) Back **Edit Review** Print Submit Review to Editorial Office **Recommendation Major Revision Custom Review Question(s)** Response Comments to the Author Yes 1. Is the manuscript technically sound, and do the data support the conclusions? The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions. Experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The conclusions must be drawn appropriately based on the data presented. 2. Has the statistical analysis been performed appropriately and rigorously? Yes 3. Does the manuscript adhere to the PLOS Data Policy? No Authors must follow the PLOS Data policy, which requires authors to make all data underlying the findings described in their manuscript fully available without restriction. Please refer to the author's Data Availability Statement in the manuscript. All data and related metadata must be deposited in an appropriate public repository, unless already provided as part of the submitted article or supporting information. If there are restrictions on the ability of authors to publicly share data-e.g. privacy or use of data from a third party— these reasons must be specified. 4. Is the manuscript presented in an intelligible fashion and written in standard English? No PLOS ONE does not copyedit accepted manuscripts, so the language in submitted articles must be clear, correct, and unambiguous. Any typographical or grammatical errors should be corrected at revision, so please note any specific errors here. 5 Review Comments to the Author This manuscript provides two automated methods for measuring the area and volume based mammographic density from processed Please use the space provided to explain your answers to the questions above. You images which current is the most common image stored in picture may also include additional comments for the author, including concerns about dual archiving and communication system (PACS). Two evidences from publication, research ethics, or publication ethics. (Please upload your review as an breast cancer risk and association with a prior significant breast attachment if it exceeds 20,000 characters) cancer associated SNPs (rs10995190) suggest the proposed methods were valid. In this article, the study design and research procedure were performed rigorously and comprehensive. However, the following problems should be considered to make the manuscript more rigorous and acceptable. 1, The spelling should be check carefully, hundreds of misprints were full in the manuscript, such as VolparaTM (VolparaTM), and the space between the citation number with the sentence, such as "deletes it[9]", please check the manuscript again to avoid such mistakes. 2, The coefficients of correlation of Figure 1 and Figure S2 were unknown, which should be provided in the result section. Additionally,

2, The coefficients of correlation of Figure 1 and Figure S2 were unknown, which should be provided in the result section. Additionally, the result and conclusion should be provided in detail for each figure and table. (Lines 234-241)

3, The data and the codes should be provided as the supplementary, therefore, it can be repeated by other researchers. R packages would be preferred.

4, As the authors said, CASAM-Vol appeared to mimic well Volpara and CASAM-Vol complement with CASAM-Area in some content. Therefore, why not design a statistic which can integrate both area and volume information simultaneously.

5, the abbreviation "APs" in line 256 was unclear and never be reported in other part of the paper.

in the line of 255, the author should provide the result which is similar with Figure 2b with the adjusted by CASAM-Vol and Volpara-Area.

6, in the line of 256, "After adjusting additionally for Volpara, there remained some evidence of association", this is the result. However, what's the conclusion? More analysis should be conducted to get the reason to interpret this result.

7, The manuscript should be re-arrange, numeric of important results were distributed in the supplementary section which caused the reading was confused, such as Figure S2. they should be merge together with other similar figure and be put in the main body.

 $6.\$ If you would like your identity to be revealed to the authors, please include your name

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