Author's response to reviews

Title: Vibration Response Imaging: evaluation of rater agreement in healthy subjects and subjects with pneumonia

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Author's response to reviews: see over
To: The Editor, *BMC Medical Imaging*

August 15th, 2009

Dear Editor,

Please find enclosed our revised manuscript entitled “*Vibration Response Imaging: evaluation of rater agreement in healthy subjects and subjects with pneumonia*” by K. Bartziokas et al. The manuscript was revised in light of reviewers’ comments.

Please find below a point by point response to all issues raised by reviewers.

**Answer to Reviewer 1**

Dear Madam/Sir,

Thank you so much for your valuable comments that helped us to improve by far our manuscript: “*Vibration Response Imaging: evaluation of rater agreement in healthy subjects and subjects with pneumonia*” by K. Bartziokas et al. Please find a point-by-point response to your comments.

On behalf of the authors, I would like to ask you to review this manuscript and to consider the possibility of acceptance for publication in the *BMC Medical Imaging*.

**Comments to the Author (in capitals)**

Response of the authors (lowercase in blue)
THE AUTHORS INVESTIGATED AGREEMENT BETWEEN DIFFERENT PHYSICIANS IN EVALUATING IMAGES DERIVED FROM LUNG SOUND RECORDINGS UTILIZING A NEW, NON-INVASIVE TECHNOLOGY. FOR EACH NEW TECHNOLOGY, IT IS ESSENTIAL THAT THE RESULTS ARE RELIABLE AND THAT THEY CLEARLY DIFFERENTIATE BETWEEN NORMAL FINDINGS AND FINDINGS FROM PATIENTS WITH PATHOLOGIES. IN THIS STUDY, BARTZIOKAS AND CO-AUTHORS DESCRIBED AGREEMENT AMONG RATERS WHO EVALUATED THE DIFFERENT ASPECTS OF VRI IMAGES THAT WERE USED TO DETERMINE HEALTHY LUNG PATTERNS FROM ABNORMAL DISTRIBUTION OF LUNG SOUND INTENSITY IN AREAS CORRESPONDING WITH CONSOLIDATION ON CHEST RADIOGRAPHS.

Thank you for your useful and constructive comments.

THE RESULTS ARE CONVINCING; HOWEVER, THE STUDY DESIGN IS LACKING A SYSTEMATIC STUDY OF THE INTER- AND INTRA-OBSERVER AGREEMENT IN INTERPRETATION OF THE IMAGES. IF THE AUTHORS CAN ELABORATE ON THE ANALYSIS, IN A MANNER SIMILAR TO MAHER ET AL (AS REFERENCED IN THE CURRENT STUDY), THEN THIS STUDY WOULD FURTHER VALIDATE THIS TECHNOLOGY AS AN APPLICABLE TOOL WITH MINIMAL TRAINING AND VALIDATE THE DEVICE’S ROLE IN DISEASE STATES. THERE ARE SOME CRUCIAL ELEMENTS OF THE STATISTICAL ANALYSIS THAT SHOULD BE CLARIFIED IN ORDER TO STRENGTHEN THE STUDY DESIGN AND THE FINDINGS. IN GENERAL, THE AUTHORS SHOULD REVIEW THE STATISTICAL DESIGN OF MAHER ET AL AND CONSIDER UTILIZING THE STATISTICAL TESTS IN THAT PUBLISHED WORK (I.E. INTRA-CLASS
CORRELATION).

We certainly agree that our statistical analysis could be improved. Maher’s paper you have mentioned is based on equations which give the inter-rater agreement taking into account different variables and provides ICC. In light of your constructive comment we performed analysis based on Maher’s methodology by assessing intra-rater reliability and inter-rater agreement (Statistical Methods, page 9 and 10). Results were presented accordingly (Results, Qualitative Interpretation of VRI images, page 11)

1. THE AUTHORS DIDN’T STATE THE FINDINGS FOR INTRA-OBSERVER AGREEMENT ANALYSIS THAT WAS DESCRIBED IN THE METHODOLOGY.

We agree that we should provide results for intra-observer agreement. These results are now presented based on Maher’s methodology in page 11 (paragraph: Intra-rater reliability).

2. NEED TO DESCRIBE THE METHODOLOGY FOR COMPARING AGREEMENT AMONG THE 6 DIFFERENT REVIEWERS VERSUS THE GOLD STANDARD PHYSICIAN DIAGNOSIS (BASED ON PHYSICAL EXAMINATION, MEDICAL HISTORY AND CHEST X-RAY). STATE SPECIFICALLY THAT CHEST X-RAYS WERE PERFORMED ON HEALTHY CONTROLS, IF THIS WAS THE CASE.

By using the methodology you recommended we evaluated agreement for several VRI features between reviewers including agreement as whether abnormalities on VRI-MEF corresponds to the areas of pulmonary consolidation on chest radiography. Methodology is described in Methods (page 8, last 5 lines).

3. PG. 7: VRI ITEM #3 THAT WAS EVALUATED: PRESENCE OF ARTEFACTS (YES/NO) – SHOULD ALSO REPORT THE NUMBER OF ARTEFACTS, SINCE A THRESHOLD OF <3 OR >3 WAS USED FOR LATER ANALYSIS.
We used a threshold of 3 that represented the number of raters (50% of them) who unidentified artefacts in VRI image. We acknowledge that the way we have initially presented this information could be improved. We therefore present results regarding artefacts in Results (page 11, lines 2-4) and Figure 3 and we modified a relevant comment in discussion (page 15, second paragraph, last three lines).

4. PG. 7: HOW WERE THE FINDINGS FROM ITEMS #4-6 COMBINED IN ORDER TO REPORT ON LOCALIZATION OF ABNORMALITY AGREEMENT IN TABLE 2? In table 2 we have used the average of agreement for all items evaluating localization of abnormalities to give an average of agreement regarding localization. This is not presented in our revised manuscript. In light of your comments regarding our methods, we have used a different aproach based on Maher’s methodology. We omitted table 1 and we present agreement regarding VRI features in Figure 3.

5. PG. 7, WERE ALL THE IMAGES THAT WERE USED FOR THE BLINDED ANALYSIS OF THE 6 PHYSICIANS ALSO USED FOR INTRA-OBSERVER EVALUATION? WERE THE IMAGES PRESENTED TWICE? All images were presented twice for intra-observer evaluation in a random order. This issue is now clarified in Methods (page 9, lines 1 and 2)

6. IF THE IMAGES WERE PRESENTED TWICE FOR THE INTRA-OBSERVER EVALUATION, THEN WHICH RESULTS WERE USED FOR ASSESSING INTER-RATER AGREEMENT AFTERWARDS ONCE INTRA-OBSERVER AGREEMENT WAS ESTABLISHED (THE 1ST OR 2ND ASSESSMENT)? You are right that this issue should be clarified. We used results obtained from first evaluation to assess inter-rater agreement. This information is given now in Methods (page 8, last two lines).
7. PG. 9, WHICH TEST WAS USED TO ESTABLISH A P VALUE OF 0.2 FOR TESTING SIGNIFICANCE BETWEEN VRI RECORDING TIME IN PATIENTS AND CONTROLS?

A T-test was used and this information is given in the text now.

8. PG. 9: ADD “AMONG THE PATIENTS WITH PNEUMONIA”...20 CASES HAD COPD, 8 CASES ARTERIAL HYPERTENSION...

Done as recommended.

9. TABLE 1: ARE THE NUMBERS REVERSED FOR GENDER IN THE CONTROL GROUP (I.E. DISTRIBUTION OF F/M IS DIFFERENT THAN FOR PATIENTS)?

You are right. This type error was corrected.

10. TABLE 2: SINCE THERE IS GOOD AGREEMENT BETWEEN RATER ASSESSMENTS AND CHEST X-RAY FINDINGS, REPORTED IN TABLE 2, ONE CAN ASSUME THAT THERE WAS GOOD AGREEMENT BETWEEN THE RATERS; HOWEVER, THE AUTHORS SHOULD STATE THE RANGE OF VARIABILITY AMONG THE RATERS.

Details for inter-rater agreement including range of variation between raters is now given in Results –‘Inter-rater agreement’ (page 11, 3rd paragraph).

11. TABLE 2: DON’T NEED TO INCLUDE YES/NO CATEGORIZATION FOR THE PRESENCE OF ARTEFACTS.

In light of your major comment to use an analysis based on Maher’s paper, table 2 is not presented now and details regarding artefacts and agreement on their presence is now given in the text (page 11, lines 2-4) and in Figure 3.
12. TABLE 2: ABNORMALLY DECREASED SIGNAL –LEFT LOWER ZONE: THE VALUE OF 0.58 FOR OVERALL AGREEMENT SEEMS LOW, SINCE AGREEMENT FOR CONTROLS IS “1”...PERHAPS THIS IS A TYPO?

You are right that there was an error in the table regarding this variable.


In light of your comment we tried to improve this part of discussion could be improved; we now present details for in ICC for inter-rater rater reliability and inter-rater agreement and we provide Maher’s values so a comparison between the two studies could be done. In addition, we underline that Maher’s paper assessed intra and inter rater agreement more extensively. (Page 12, last paragraph, and page 13, first paragraph)

14. DISCUSSION: WERE THE RESULTS OF TOTAL LEFT DISTRIBUTION VERSUS TOTAL RIGHT INVESTIGATED? THE RESULTS FOR LEFT LOWER LOBE MIGHT HAVE BEEN DIFFERENT THAN RIGHT LUNG DUE TO THE DIFFERENT NUMBER OF LOBES IN EACH LUNG.

We acknowledge that we have performed a qualitative evaluation and we have not evaluated results of total left versus total right distribution. In light of your comment, a relevant
comment was added in discussion underlying this limitation (page 15, 1st paragraph, lines 2-6)

15. DISCUSSION: CAN ADD TO THE DISCUSSION THAT IN GENERAL, KAPPA UNDERESTIMATES THE STRENGTH OF AGREEMENT, SO IT IS POSSIBLE THAT THE RESULTS COULD EVEN BE MORE ROBUST THAN REPORTED.
You are right, results obtained by methodology you advised are more robust. In our revised manuscript we used these results and thus we have not commented kappa values.

MINOR COMMENTS:

Donne as advised.

2. IN ADDITION THERE ARE SPELLING AND GRAMMATICAL ERRORS THAT SHOULD BE CORRECTED.
The revised manuscript was revised for grammar and spelling errors (K.Pappa – aknowledgement).

Thank you for the thorough and helpful reviewing you made. We hope that we have adequately responded to your excellent comments.

D. Makris
Dear Madam/Sir,

Thank you so much for your valuable comments that helped us to improve by far our manuscript: “Vibration Response Imaging: evaluation of rater agreement in healthy subjects and subjects with pneumonia” by K. Bartziokas et al. Please find a point-by-point response to your comments.

On behalf of the authors, I would like to ask you to review this manuscript and to consider the possibility of acceptance for publication in the *BMC Medical Imaging*.

**COMMENTS TO THE AUTHOR (IN CAPITALS)**

Response of the authors (lowercase in blue)

THE MANUSCRIPT IS DEVOTED TO EVALUATION OF AN INTERESTING NEW DIAGNOSTIC TECHNIQUE THAT HAS TWO POTENTIAL ADVANTAGES: NO RADIATION AND BEDSIDE AVAILABILITY.

I WOULD LIKE TO PROVIDE SOME COMMENTS:

1. THE QUESTION POSED BY THE AUTHORS IS WELL DEFINED, THE MANUSCRIPT IS DEALING WITH EVALUATION OF QUALITY AND INTERPRETABILITY OF THE NEW TECHNIQUE (VRI)

2. THE METHODS FOR THE EVALUATION ARE APPROPRIATE AND WELL DESCRIBED IN DETAILS ALTHOUGH LACK OF A RADIOLOGIST INCLUDED IN THE INTERPRETATION OF THE STUDY POSES A PROBLEM IN THE RELAIBILITY OF THE REFERENCE (CHEST RADIOGRAPH/CT) FOR THE FINAL
DIAGNOSIS OF PNEUMONIA.

You are right. In light of your comments a relevant comment was added in discussion.(page 15, last four lines)

3. THE DATA SEEMS TO BE SOLID.

4. DOES THE MANUSCRIPT ADHERE TO THE RELEVANT STANDARDS FOR REPORTING AND DATA DEPOSITION ? - YES

5. THE DISCUSSION AND CONCLUSION ARE VERY LOGICAL AND BASED ON THE DATA WITH RELEVANT REFERENCES PROVIDED IN DISCUSSION

6. ARE LIMITATIONS OF THE WORK CLEARLY STATED?

THERE SOME POINTS THAT I THINK NEED TO BE ADRESSED:

A. THE TECHNIQUE IN NOVEL AND REALLY INTERESTING, BUT EVALUATION OF 20 HEALTHY AND 23 SICK (PNEUMONIA) PATIENTS IS NOT SUFFICIENT JUST BASED ON THE NUMBER OF CASES AND A LARGER COHORT OF PATIENTS NEED TO BE EVALUATED ON A PROSPECTIVE BASIS.

In light of your comment we underline this issue in discussion (page 17, last three lines)

B. IT IS NOT CLEAR FOR ME IF THERE IS ANY WAY TO DISTINGUISH BETWEEN PNEUMONIA, ATELECTASIS, ASPIRATION OR HEMORRHAGE BASED ON THIS TECHNIQUE. ALTHOUGH THIS DIFFERENTIATION IS NOT ALWAYS POSSIBLE ON THE BASIS OF CONVENTIONAL RADIOGRAPHY, IT STILL CAN BE DONE IN MANY CASES. C. FURTHER VALIDATION OF THIS TECHNIQUE MIGHT BE BASED ON COMPARISON WITH COMPUTER TOMOGRAPHY TO EVALUATE THE SPECIFICITY OF THE TECHNIQUE RAHTER THAN SENSITIVITY.
You are right that separation of cases for pneumonia, atelectasis, aspiration or hemorrhage could give further useful information for this method. However, patients have not performed systematically diagnostic tests that could answer this question adequately. In light of your advice relevant comments were added in discussion to underline this limitation (page 16, last paragraph, page 17 first paragraph).

7. DO THE AUTHORS CLEARLY ACKNOWLEDGE ANY WORK UPON WHICH THEY ARE BUILDING, BOTH PUBLISHED AND UNPUBLISHED? YES, AS I STATED, THE PRIOR WORK IS NICELY DEPICTED IN THE REFERENCES

8. DO THE TITLE AND ABSTRACT ACCURATELY CONVEY WHAT HAS BEEN FOUND? YES

9. IS THE WRITING ACCEPTABLE? THE PAPER IS NICELY WRITTEN

Thank you for the thorough and helpful reviewing you made. We hope that we have adequately responded to your excellent comments.

Sincerely,

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