Author's response to reviews

Title: Unfiltered signal averaged P wave analysis - further validation of the method

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Author's response to reviews: see over
Dear Editors,

Thank you for considering our manuscript ‘Signal-averaged P wave analysis for delineation of interatrial conduction – further validation of the method’, for publication in BMC Cardiovascular Disorders. It is now our strong belief that the manuscript is suitable for publication.

Point-by-point answers (written in bold) to the questions raised by the reviewers are supplied below.

Regarding the references supporting the methodology, an unfortunate typing error was included in the previously submitted manuscript. The web-link for reference 10 has now been changed, making it easily available. Finally, it is important to underscore that the thesis referred to in ref 10 is based on four peer-reviewed papers, and has been publically defended.

The manuscript has been improved using professional copyediting assistance as suggested.

Sincerely,
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REFEREE 1.
Reviewer's report:
General
This manuscript was improved after the revision. However, some points still need attention.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

No major points.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) I think that the most important limitation in present version is the definition of ‘total reproducibility’. Although, in Figure 4, data analysis showed non-significant different errors between groups, indicating that data from all groups probably came from the same parental population, in a strictly statistical sense, a complete numerical match may not be the case. The term ‘total’
should not be used in a common sense. Consider, for instance, that the amount of elements in each tested group from L1 to L6 to be increased 10 fold, or 100 fold, would this lack of statistical significance still hold? Or would a significant difference be unveiled, regarding, for instance, groups L2 and L4? Would, therefore, last so-considered hypothetical findings invalidate present conclusions, since statistical tools and confidence limits were chosen to base study analyses upon? I understand that a first approach to overcome this issue would be to provide a post-hoc power sampling analysis, answering the question: 'What would be the number of elements in groups L2 and L4 to provide a projected statistical significance?' Another and perhaps simpler way to solve this issue would be to provide a strict definition of 'total reproducibility' under Statistical Analysis heading (page 6) to be employed in present article. For instance, 'Total reproducibility is defined as...'.

As stated in the previous response the term ‘total reproducibility’ only refers the automated algorithm. It is our firm belief that any automated procedure will always be totally reproducible. This is not the same as perfect performance, i.e. the performance of the automated procedure may be variable, but the results will always be reproducible.
A sentence has been added in the Definitions section, indicating the above statement.

2) In page 2, paragraph 3, line one, ‘...most commonly used...’ I disagree. It needs to be substantiated with data. Clinical studies frequently employ 12-lead surface ECG to derived P-wave length from lead D2, directly. This sentence should be revised.

We fully agree! The sentence was the result of a narrow “signal-averaged” perspective. The sentence has been rephrased.

3) In page 5, paragraph 3, line 3, ‘... they were discharged’. What does it mean? Did it have neither maximum nor minimum? Was the whole ECG discharged or only that particular beat? Please, explain further.

What is meant is that maxima and minima with amplitudes less than one fifth of the total P wave amplitude were considered to be too small to be counted as maxima and minima. Therefore that particular maximum or minimum was discarded, i.e. not considered by the automated algorithm.
This has been clarified in the revised manuscript.

4) In page 6, paragraph 3, line 3, inform which set of ECG was used to assess P wave morphology.

This was the ‘evaluation set’. This has been clarified in the revised manuscript.

5) In figures 3 and 4, please, correct SE to SD.
In fact, standard error is used in figures 3 and 4, and consequently, this has not been changed.

Discretionary Revisions (which the author can choose to ignore)
1) In page 7, paragraph 3, line 3 and 7 ‘Taken together’ was written twice, as well as ‘observed’.
This has been changed.

REFEREE 2
Reviewer's report:
General
The text has benefited greatly from the changes. All my queries have been answered to my satisfaction.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
None

Discretionary Revisions (which the author can choose to ignore)
None

REFEREE 3
Reviewer's report:
In my opinion the authors did not answer sufficiently to my criticisms. In particular they based the validation method on references which are not reviewed papers and this does not allow a proper evaluation of averaging method.

By an unfortunate mistake the "dots" in the provided web-link for reference 10 were not printed out in the submitted pdf. This has now been changed.
The web-link provides easy access to the thesis, which in detail describes the used method. Hence, the reference in publicly available.
The thesis is based on four published papers, which all have been peer-reviewed and accepted in renown medical journals. The thesis has been peer-reviewed and publically defended.

REFEREE 4
Reviewer's report:

General

General Comments: The ms. by Holmqvist et al deals with Signal-averaged P wave analysis for delineation of intraatrial conduction—further validation of the method. The authors studied 131 healthy subjects and another set of patients with heart disease were used as training set; however the results in these patients were not presented separately. Not surprisingly, the authors find that the duration of the P wave is dependant on methodology (i.e. magnification, baseline filtering, band-pass filtering, duration of signal averaging and obviously the noise level. The findings are not at all surprising and indeed, expected. The authors use confusing terminology in particular intraatrial block rather than intraatrial conduction delay.

We agree that the term inter-atrial block is not uncontroversial. However, the use of inter-atrial block or delay are used interchangeably throughout the literature. For example references 6, 8, 9 and 19 use intratrial block for describing a P wave duration exceeding 120 ms, while reference 1 use the term conduction disturbance.

Changes have been made according to the suggestions below.

Specific Comments:
Under Background:
Ph 2, line 3: ‘in’ should be deleted.

This has been done.

Pg 2, line 5: ‘used’ should be deleted.

This has been done.

Pg 2, line 7: Prolongation of the P wave doesn’t reflect inter-atrial block but rather intra-atrial conduction delay.

Changes have been made accordingly.

Pg 7, under Discussion, line 6: again the authors refer to intraatrial block.

Changes have been made accordingly.

Pg 7, under Discussion, line 16: the authors use a value of 120 msec to designate intra-atrial block. This reviewer disagrees with the use of such terminology. Indeed, the number 120 msec. may reflect abnormal value i.e. prolongation of intraatrial conduction but in no way reflects block.
Changes have been made accordingly.

The ms. needs considerable editing and is cumbersome to read.

The manuscript has been edited by a professional copy editor.