Author’s response to reviews

Title: Computed tomography scan based prediction of the vulnerable carotid plaque

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Version: 1 Date: 24 Aug 2017

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BMIM-D-17-00127

Computed tomography scan based prediction of the vulnerable carotid plaque

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BMC Medical Imaging

Dear Editors,

Thanks for the relatively positive comments regarding the manuscript "Computed tomography scan based prediction of the vulnerable carotid plaque" (BMIM-D-17-00127).

We have addressed each point raised, however, a few were difficult to handle and need further explanation from the reviewer.

Below is a specified point-by-point response letter describing what amendments have been made to the manuscript and where these can be found, and the changes are tracked.
Best wishes,

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Reviewer reports:

Jianping Dai (Reviewer 1): In this study, it found that CTA-software cannot be used in risk assessment of patients, due to poor specificity and NPV. The correlation between in vivo CTA and ex vivo NCCT was strong, proposing it to be used in both scientifically and clinical settings. However, there are many errors in this manuscript which should be addressed.

Page 6 line 9, missing the full spelling of IPH.

AU: Thanks. However, it is introduced before, so it is now full spelt on page 5, line 4.

Page 8 line 6 there was missing space between p and <, also between < and 0.05

AU: Missing spaces have been removed – including some other places than these ones
Page 8 line 53, figure or figured?
AU: Thanks. This typo error has been changed to figure – including some other places than these ones

Page 11 line 3 and line 17 generel or general?
AU: Thanks. These spelling errors has been changed to general

Page 14, line 33, We thank study nurse Susanne Petersen?
AU: We can’t see anything wrong in that,- her name is Susanne Petersen, and she kindly assisted in obtaining informed consents.

Page 15, line 47, 321 p. p.?
AU: Yes, where did that come from? It has been deleted. Thanks.

Page 16, the title of table 1 is too brief to understand the content of it.
AU: Yes, it is quite short. It has been changed to: ”Table 1: Baseline characteristics of included patients stratified by presence of intraplaque haemorrhage in the removed stenotic carotid plaque”

Figure 2, Figure 3 and Figure 4 was obscured. Figure 3 so small, typesetting is too crowed to watch.
AU: We have no idea why it is so,- they seemed ok for us. However, reviewer2 also complains about the quality, so we have tried to increase the solution. Hope they work better now.

Mahsa Ghaffari (Reviewer 2): 1. Adding ROC diagram is necessary. Further analysis such as area under the curve should be calculated to quantify the accuracy of your tests.
AU: This needs further explanation from the reviewer to fulfil. The validation of this study is based upon a dichotome variable: +/-IPH.
ROC curve analysis needs a measurement – a numerical scale- performed by one of the two methods.

From our point of view, it is possible to perform. The quantity of the accuracy is fully described by sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

2. The study need better representation of statistical analysis.

AU: This needs too further explanation from the reviewer to fulfil. What is missing? We have only used standard statistics and all tools are mentioned? Normally trivial statistical procedures are not described in details? The interpretation of Kappa values is inserted in the discussion.

3. Page 11, low case study (only 16 patients) should be added to limitation of this study. In the abstract 53 patient case is written while many retrospective cases were not acceptable for this study!

AU: We fully agree, however, at page 11, it already says: ”…but measurements form only sixteen patients were obtained. A much larger sample size is needed to confirm the correlation and provide and equation for transformation of quantities between CTA and NCCT”. Isn’t that sufficient?? Nevertheless, we have added “This is a major limitation” in between the two sentences.

4. Figure 4 are not readable and are not at the level of scientific paper. The reviewer suggest to increase the quality of Figure 4 and add more explanation for Bland-Altman plot.

AU: We have increased the quality of the figures in general according to reviewer 1. We have included some additional text telling what is shows according to point 5.

Figure 4 captions, change from (A) Strong positive correlation between NCCT CALS and CTA CALSs. (B) Bland-Altman plot between NCCT CALS and CTA CALSs to:

“(A) Graph indicating strong positive linear correlation in measuring CALS between CTA and NCCT. (B) Bland-Altman plot. X-axis shows the mean calcification score of the two methods. Y-axis shows the difference of the calcification score measured by the two methods. The red line indicates mean difference, black lines indicate the 95% confidence levels of the mean. Circle dots indicates mean values for CALS between CTA and NCCT. If no association between the difference of the measurements existed, the dots should be placed on the redline, but here a clear tendency of increased disagreement with increasing calcification is observed”.
5. The reviewers are concerned that all figure captions contained only brief descriptions, failing to illustrate the need or impact of the graph. Could the authors please include text in the figure captions which direct the reader towards the notable features of each graph?

AU: We believe that further explanation for figure 1 is not needed, and if so, would become very extensive. Figure 2 captions, is changed from, Appearances of a vulnerable plaque using semi-automated software on CTA. (A) Sagittal section of carotid artery showing the severity of CS and the distribution of the histological components. (B) Transverse section showing the reduced lumen of the vessel, and the distribution of the histological components to:

“Appearances of a vulnerable plaque using semi-automated software on CTA. (A) Sagittal section of carotid artery showing the severity of CS. (B) Transverse section showing the reduced lumen of the vessel. The colours illustrate the distribution of various histological components of the CS based on different HU values, which is automatically calculated by the software”.

Figure 3 captions, change from Histograms comparing histological calcifications and CTA CALS with the IPH containing group and with the non IPH-containing group to:

“ The severity of macrocalcifications, microcalcifications and CTA CALS was compared between the IPH containing group and the non IPH-containing group. Significant difference was only observed for microcalcifications (P=0.034).”

Figure 4 captions, change from (A) Strong positive correlation between NCCT CALS and CTA CALSs. (B) Bland-Altman plot between NCCT CALS and CTA CALSs to:

“(A) Graph indicating strong positive linear correlation in measuring CALS between CTA and NCCT. (B) Bland-Altman plot. X-axis shows the mean calcification score of the two methods. Y-axis shows the difference of the calcification score measured by the two methods. The red line indicates the mean difference, black lines indicate the 95% confidence levels of the mean. Circle dots indicate mean values for CALS between CTA and NCCT. If no association between the difference of the measurements existed, the dots should be placed on the red line, but here a clear tendency of increased disagreement with increasing calcification is observed”.

Yudong Zhang (Reviewer 3): In this paper, the semi-automated CTA software had a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 89.1% (95% CI, 73.6% - 96.4%), 31.3% (95% CI, 12.1% - 58.5%), 75% (95% CI, 59.3% - 86.2%) and 55.6% (95% CI, 22.6% - 84.6%).

This is a good paper, but several related literature are missing, see


Synthetic Minority Oversampling Technique and Fractal Dimension for Identifying Multiple Sclerosis. Fractals. 2017, 25(4), Article ID: 1740010

AU: Thanks for the compliment. We have looked at the references, and find them hard to see the relevance of. It may due to complementary expertise of the reviewer, but we simply don’t get the point, and are thus not capable to include them in a proper them.

Editorial Policies

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Declarations

- Ethics approval and consent to participate (AU: See page 13)
- Consent to publish (AU: See Page 13)
- Availability of data and materials (AU: See Page 13)
- Competing interests (AU: See Page 13)
- Funding (AU: Page 14)
- Authors' Contributions (AU: Page 14)
- Acknowledgements (AU: Page 14)