Author’s response to reviews

Title: Cardiac Left Ventricular Myocardial Tissue Density, evaluated by Computed Tomography and Autopsy

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Editor Comments:

Please find the reviewer's comments below and attached. In addition, we have the below editorial requests that we would like you to address:

- Please include the email addresses of all authors on the title page.

We have added this to the title page.

- Please clarify whether the ethics committee approved verbal consent from next of kin. If so, please clarify this in the manuscript (declaration section, ethics approval and consent to participate).

The ethics committee approved our protocol and approved the verbal and written consents from the next of kin. We have specified this in the Declarations section of the manuscript.

- Author contribution: Please use initials. Also, the corresponding author (Alexandra Gheorghe) is not mentioned in the author contribution section - please correct that.
The contribution of Alexandra G. Gheorghe (AGG) has been added and initials are used.

Best wishes,

Dirk Krüger

BMC Medical Imaging operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

Reviewer reports:

Jonathan Lessick (Reviewer 1): The authors compare postmortem LV mass by CT vs autopsy and calculate myocardial tissue density as a ratio of autopsy mass vs CT volume. They conclude that LVM correlates highly and that tissue density is higher than that reported.

This type of study is appreciated since it is indeed important to verify algorithms based on imaging with "true" values based on actual tissue.

However there are several methodological limitations.

I find it hard to understand why the authors did not compare their density findings with true density calculated as the ratio between LV mass at autopsy and its displaced volume which could have been measured as accepted by water displacement techniques. Since CT measures volumes and not mass, it would be necessary to first show that myocardial volumes are accurately determined.

Answer: We realize that readers may question why volume measurement was not performed by water-displacement techniques, and we do hope that our paper actually addresses this. We have added this to limitations sections, Line 236-240; There are several factors to take into consideration when performing water displacement measurements/techniques on cadaver hearts. While water displacement works accurately with solid objects, biological tissue is by its nature permeable and may be compressed or distended, and it may be fixed or unfixed. For this study, given that we wanted to investigate CT-derived volume measures, as this is what is used clinically, we hence chose to base our volumes of this method.

Results of CT thresholding techniques are highly dependent on the threshold used. It is unclear how thresholds and window width were chosen nor whether different values were compared. It is essential to examine how these factors may affect results. In my opinion this is the probable
reason for the density results obtained. Optimal thresholds may also differ for the endocardial and epicardial borders.

Naturally partial volumes effects may be important. What slice thickness was used when marking the myocardial borders?

Answer: We are aware that the CT evaluations depend on the thresholds and window used.

Threshold: The myocardium is known to have a mean HU of 50 HU (We did not test other thresholds. Whereas it may be hard to distinguish myocardium from blood pooling in CT scans of living individuals, this is possible in dead individuals where the blood has clotted and the HU values for blood pool are somewhat higher. In our CT scans the measured HU in the bloodpool had a mean of 68±13, whereas the measured HU in the myocardium had a mean of 47±7 HU. However, some degree of overlap and misinterpretation can of course not be ruled out, but we also think the effects may work in both directions. Thus, we have added the sentence to the limitations section, Line 247-249: “Due to the relatively close HU values of the blood pool and the myocardium, the myocardium may have been overestimated in some cases and underestimated in other cases”.

We agree that the optimal threshold may differ for the epicardial and endocardial borders - We have now added this to the limitations section, Line 249-251:

” We used a HU threshold for myocardial tissue of HU 50±10, nevertheless different values may apply for epicardial and endocardial borders”.

Window: We used level=200 and width=1000, which is the normal window settings for chamber evaluations in the commercial software programme, Vitrea (Vital Images Inc). We did not try to compare different values. We have now added this to the methods section, Line 115.: 

"We used normal cardiac window settings with a level=200 HU and width=1000."

Naturally partial volumes effects may be important. What slice thickness was used when marking the myocardial borders?

Answer: We agree. Partial volumes may play a role here. We used 1mm slice thickness for the CT-evaluations. We have now added this to the limitations-section, Line 249.250.

Also, in the absence of contrast medium, it is difficult to reliably and consistently visualize the boundary between muscle and blood. In Figure 1, for example, I would definitely have marked the blood pool further towards the apex.

Answer: The authors agree with the reviewer about Figure 1, in that sense that it is confusing and the reader/reviewer may believe it is images of the same heart. This is not the case in Figure 1, as
it is two different heart images, one showing the differentiation between myocardial tissue and the blood pool and the other one is simply to illustrate the borders. We apologize for any confusion and have now changed Figure 1 to display the same heart slice.