Author's response to reviews

Title: Tumor volume in subcutaneous mouse xenografts measured by microCT is more accurate and reproducible than determined by 18F-FDG-microPET or external caliper.

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Cover letter to the manuscript: Tumor volume in subcutaneous mouse xenografts measured by microCT is more accurate and reproducible than determined by $^{18}$F-FDG-microPET or external caliper.

Response to Referee 1 (Carla F. M. Molthoff):

1. We agree and have added that it was not unexpected that $^{18}$F-FDG-PET was unsuitable for determination of tumor volume in the discussion, paragraph 7.
2. We agree that inclusion of a therapy related response would have been interesting. However, we chose to focus on volume itself and by which accuracy and reproducibility volume was determined with the used methods.
3. All repetitions have been removed.
4. All repetitions have been removed.
5. A discussion of references 10 and 11 has been added on page 10.
6. What we meant was that SUV values based only on PET images could be encumbered with much error and that it is better to fuse PET and CT images in order to calculate SUV. We agree that it was easily misunderstood and for clarity we have deleted a sentence in paragraph 7.
7. The legends for all figures were scattered in the text, but are now all immediately following the references.

Response to Referee 2 (Rodney Hicks):

- The volume-of-interest was defined by a qualitative assessment. This was unclear but has now been clarified in the text on page 7.
- The small tumors used in our studies did not contain necrotic elements. We agree that this should be stated in the text clearly and we have added this information on page 8.
- A discussion of ultrasound and MRI is now included in the discussion.
Response to Referee 3 (Prof Xiaoyuan Chen):

- We agree that FDG-PET is rarely used for volume measurements and accordingly we have added this in paragraph 7 in the discussion.

- Although straightforward and simple in its idea, we believe this is a very important piece of practical information for cancer researchers working with implanted tumors. It adds especially value to the non-imaging community that at present often relies on caliper measurements with information on how to improve sensitivity in their experiments through collaborating with imaging experts. It is striking how often expensive and advanced cancer studies in mice are performed using only caliper measurements thereby overlooking smaller differences (or needing larger number of animals).

- In contrast to previous studies, we as the first focused on small tumors. It is not trivial that performance known from studies on large tumors can be extrapolated also to smaller tumors.

- Based on our reported data on the methods it is possible for cancer researchers to calculate and compare necessary sample size when planning new experimental studies.

- Taken together, although answering an obvious question by simple means we find our study, which has not previously been undertaken, is of great practical use and importance to cancer researchers.