Author's response to reviews

Title: Iodine concentration calculated by dual-energy computed tomography (DECT) as a future parameter to evaluate thyroid metabolism in patients with hyperthyroidism

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Author’s response to reviews:

Jianping Dai (Reviewer 1):

There are some errors in the manuscript. Please see the attached file.

#0 First page (abstract):

This page is automatically generated on the web site. So, we can’t control font styles, like superscript. Please see our abstract in next page.

#1 Please rewrite the BACKGROUND part.

The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

We completely revised the BACKGROUND section in the abstract.

#2 We can get rid of comma in this sentence.

We deleted it.

#3 Style of citation numbers: superscript

Please note that BMC Medical Imaging uses square brackets instead of the superscript style for the in-text reference citations.
#4 plural, correlations is better than correlation.
We revised the word “correlation” to “correlations.”

Ronnie Sebro (Reviewer 2):

#1 First, the authors compare the uptake values of each lobe of the thyroid gland separately and compare that to the CT attenuation of each gland - as stated in my earlier review this results in increased correlation because of within-individual correlation.

We do not agree with this comment.
In a clinical situation, CT images are affected by artificial noise or X-ray beam artifacts because of surrounding bones, clavicles, shoulders, and vertebrae. Therefore, we could not achieve better correlation between CT attenuation and iodine concentration. For example, we often encountered the beam hardening artifact. Hard materials follow high attenuation lines like a long tail. The X-ray beam is irradiated from various angles from the X-ray tube in a CT scanner; therefore, the right and left lobes exhibit different effects from the surrounding hard structures. Therefore, most physicians and technologists experience difficulty in measuring CT attenuations in the thyroid gland. If we use the average CT attenuation from both lobes, the R value would be improved and become similar to theoretical expected data. Since we want to emphasize the discrepancy between the actual measured data and the expected data, your recommendation can be applied to improve our data. However, since CT values in right and left lobe were varied, we describe them (26 ROIs) honestly.

#2 The authors can assess the veracity of this statement by measuring the superior, middle and inferior lobes of each thyroid gland separately and compare those to the CT attenuation of the superior, middle and inferior lobes of the thyroid gland - naturally this correlation will be greater in magnitude (and more significant) than that assessing each lobe separately and naturally, greater in magnitude than that assessing each patient separately.

Theoretically, yes.
We have to reduce the effect of the beam hardening effect from the surrounding bones, particularly the cervical vertebrae. As mentioned in the Materials and Methods section, we chose a slice that would be affected by these types of artifacts. We have already investigated the effect of bones on iodine concentration in the thyroid gland, although this has not been published. However, this is not the main issue in the present study. Therefore, we did not discuss this point extensively and have simply described the way to select a slice in the Materials and Methods section.

#3 The graphs should have the estimated correlation R as well as the p-values. I suspect that figure 5d should be more significant than the authors believe. This graph looks more clustered than Figure 5b.
The most important thing is that there are correlations between the iodine concentration calculated by DECT and the uptake ratios of thyroid scintigraphy. The comparison with Figures 5d and 5b is not so important. We just want to show the correlation between iodine concentration calculated by DECT and the results of thyroid scintigraphy. Here we showed R and P values for four graphs in Figure 5: a) R = −0.493, p = 0.087, b) R = −0.680, p < 0.05, c) R = −0.420, p = 0.1532, and d) R = −0.507, p = 0.073. However, we defined p > 0.05 as not significant. We believe that because the p values are not statistically significance, R values need not be included in these figures.

#4 Figure 4 should be repeated by individual rather than by lobe analysis.

This is the same issue as #1. If we use average data in 13 individual patients, the p value was 0.2448 (R = 0.1207) and was therefore not significant. This represents positive data for this research study because the phantom study and preliminary study showed extremely high linear correlation between CT attenuation and iodine concentration by DECT. This is the difficulty in applying CT images to evaluate thyroid function. Therefore, so far, this report is the first research study to show thyroid function using CT images.

#5 The discussion seems to conflict with the introduction. In the introduction, the authors expect a low CT attenuation density and use reference 5 for this assertion. Then in the discussion, the authors talk about edema and vascularity as lowering the CT density.

In page 20 (Discussion section),

“However, in our study, only a moderate linear correlation was observed between 123I uptake at 3 h and CT values of the thyroid gland in vivo, while the iodine concentration, as evaluated by DECT, showed a better correlation with 123I uptake. Although the reasons for these results are not entirely clear, there are some possible explanations.”

Reference 5 describes thyroid function: under iodine restricted diets, iodine storage in the thyroid gland will be reduced. Therefore, the CT value of the thyroid gland will also decrease. In the sentences shown above, we discuss the reason why we could not achieve high linear correlations in human data, similar to phantom data.

#6 The authors also loosely use Graves disease and hyperthyroidism interchangeably. The results may have been different if the patient had solitary adenoma, pituitary disease contributing to hyperthyroidism, multinodular goiter etc. Graves accounts for the majority of hyperthyroidism cases, but not all.

We have described our definition of the patients included in this study with the following sentence on page 8 (Materials and Methods, Patients):

“Thirteen consecutive female patients (mean age, 53.7 ± 13.2 years) underwent both iodine scintigraphy and DECT before radioactive iodine (131I) ablation therapy”
In clinical situations, we do not perform RAI for patients with solitary adenomas or pituitary adenomas. And our inclusion criteria noted “Grave’s disease or hyperthyroid patients with a strong suspicion of Grave’s disease.”

#7 The authors also talk about a single CT measurement - they are in fact referencing the CT attenuation /attenuation density. This paper needs to be written clearer.

We did not acquire CT (DECT) images after RAI therapy, as mentioned in the manuscript.

#8 In the Methods, it seems temporally that the DECT followed the RAI study. The time between both studies was not noted. Why was the DECT even ordered? Thyroid gland volumetry was performed, but not reported etc.

On page 8 (Materials and Methods, Patients).

“Thirteen consecutive female patients (mean age, 53.7 ± 13.2 years) underwent both iodine scintigraphy and DECT before radioactive iodine (131I) ablation therapy”

We have mentioned that DECT was performed before RAI to measure the thyroid volume and optimize the radioactive iodine dose. To prevent the readers from misunderstanding the order between RAI and DECT, we have added the following sentence to the image acquisition protocol.

“Before radioactive iodine ablation therapy, basal thyroid gland volumetry was performed with dual energy technique with a dual source CT scanner (SOMATOM Definition flash; Siemens Healthcare, Forchheim, Germany).”