Author’s response to reviews

Title: Detection of cervical lymph node metastasis in head and neck cancer patients with clinically N0 neck—a meta-analysis comparing different imaging modalities

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To Reviewer Professor Jens E. E. Meyer

Thanks for reviewing our manuscript. We have modified our manuscript as following:

1. **RE: “write some sentences in the discussion on the alignment of the results of the preoperative imaging and the histologic specimen after neck dissection.”**

   We have added one paragraph (p. 13, paragraph 2) and marked in red color.

   The alignment of the results between preoperative imaging and histologic specimen after neck dissection should be taken into consideration. According to previous reported literatures[11, 12], the rate of regional recurrence in pN0 patients varying from 3% to 10%. Applying only the histopathological results as reference standard, one could underestimate the real occult metastasis rate. Therefore, we included studies using either pathological examinations, or clinical follow-up results, or both as references. Besides, the criteria for positive results in pre-operative diagnostic imaging were not uniform in different institutions, and may be operator-dependent. These variations all leaded to heterogeneity in this meta-analysis, and this was the reason to adapt a random effect model for data pooling.

2. **RE: “the common reader of this paper has difficulties in understanding the value of the negative and positive pre- and post-examination nodal metastasis probability in the manuscript”** We gave modified the paragraph (p11, paragraph 1) and marked in red color. In 1994, Weiss et al.[3] recommended with decision analysis that when the probability of occult cervical metastases is
more than 20% (with a positive predictive rate above 20%), the neck should be
electively treated. Based on Bayesian theory, the predictive probability of neck
nodal metastasis given that a test is negative or positive depends on the pre-test
probability (baseline possibility), and the sensitivity and specificity of the test.

According to our results, if the pretest prevalence (baseline possibility) of clinical
occult neck metastases was set at 30%, the post-test negative predictive rate with
negative CT, MRI, PET, and US results increased to 82%, 84%, 86% and 84%,
respectively (with a positive neck lymph node metastasis rate below 20%),
meaning a “watchful waiting policy” is possibly justified in these cases.

Besides, we modified the Table 3 and Figure 3. We use “positive predictive
value*” instead of “Posterior positive possibility (%)” and “negative predictive
value&” instead of “Posterior negative possibility (%)” and remarked as *:

Possibility of neck nodal metastasis following a “positive” imaging result; &:

Possibility of “absent” neck nodal metastasis following a “negative” imaging
result. In Figure 3, we modify the y-axis title as “positive predictive value”
instead of “posterior probability” and x-axis title as “baseline possibility” instead
of “prior probability. And we modified the figure legend as “the positive
predictive value generated based on Bayesian theory and the collected data”

Sincerely yours.