Reviewer’s report

Title: Efficacy of 99mTc-DTPA SPECT/CT in Diagnosing Orbitopathy in Graves' Disease

Version: 0 Date: 25 Oct 2018

Reviewer: Laszlo Galuska

Reviewer’s report:

The topic of article is actual, the Grave's orbitopathy (GO) is a persistent diagnostic problem in endocrine practice. The data about the diagnostic effectivity of 99mTc-DTPA SPECT/CT hybrid system in GO compared with other methods are new informations.

The content of manuscript is well structured, the printing mistakes are rare. At page 10, 17 line instead of „out” the „our” is correct.

The abstract is a correct mirror of manuscript, the conclusion of it is well established.

The background is a substantial summary of pathophysiological basics of GO and the methods used in different medical specialities dealing with the diagnosis of it. The description of nuclear medicine method including the uptake mechanism of 99mTc-DTPA at inflammatory site is clear. At the 29 line the „99mTc-DTPA radiotracer” expression is first used. To exclude the mistake with labelling radionuclide it would be useful to insert there a bracket with „radiopharmaceutical” expression, meaning the „tracer” is a synonym of „radiopharmaceutical” in later text.

In materials and methods chapter the number of patients is sufficient for statistical analysis. The details of compared methods are clear. At SPECT CT method the explanation of increased radiopharmaceutical accumulation at inflammatory sites is OK but the craniofacial muscle as reference region is not usual. (The brain is most frequently used.) The interpretation of high activity is subjective, visual. It isn't known the threshold count number or quotient which could separate the active and inactive cases. To compare the diagnostic effectivity of three different methods isn't easy, so I think the author's interpretation of SPECT-CT results in this manner is useful for statistical analysis.

Result chapter. In the lack of "gold standard" method the author's assumption for better positive or negative classification is tolerable. The statistical tables and results of analysis are correct. On the basis of statistical analysis I also agree that the SPECT/CT has the highest accuracy in the correct diagnosis of active orbithopathy compared with MRI and CAS, respectively. The anatomic informations (severity of exophthalmos and muscle thickness) could be independent from the biological activity of orbithopathy. It is another possible cause wherefore the measurement differences were not statistically significant.

The discussion chapter include the former publications in the topic of GO and SPECT. The idea of authors about the biological activity („we mean the detection of the presence or absence of the
active form of GO") is incomplete. The biological activity mean a quantitative scale, (numerical grading) of 99mTc-DTPA uptake in the whole orbital cavity from the normal value to extremely high level. This activity uptake (AU) is parallel with (molecular) biological activity of illness which is the goal of different anti-inflammatory therapies. The disadvantage of AU calculation is the necessity of pre-calibration of SPECT system and the use of a small software package for final calculation. The spatial resolution of any SPECT system is enough for correct data acquisition and AU calculation. (The cold area of eye globe is a stable reference point.) The goal of authors was comparison of more methods and they don't use it. (But I think in their later endocrine SPECT-CT routine it will be included.).

I agree with authors that the SPECT-CT gives much more precise localisation of inflammatory sites especially in case of maxillary sinus inflammation.

The possible cause of contradict between the active and non-active forms of GO and the thickness of the oculomotor muscles discussed at page 10 is the pathologic rebouliding of muscles when the active inflammation „burn out" but the thick muscle remain.

The radiation protection data are valuable part of manuscript.

The conclusion is correct I agree with it.

References.

It would be useful to expand the references with papers published after 2015.

Figure legend

It would be useful to add a last sentence: „The physiological 99mTc-DTPA uptake of nasal mucosa is visible at both cases"

Reviewer conclusion:

After above mentioned small corrections I recommend the publication of manuscript.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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