

**[<sup>68</sup>Ga]-DOTATATE PET/CT versus MRI: why the comparison of [<sup>68</sup>Ga]-DOTATATE PET/CT to an appropriate MRI protocol is essential**

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We read with interest the article by Janssen and colleagues<sup>1</sup> that analyzed the clinical utility of [<sup>68</sup>Ga]-DOTA0,Tyr3]Octreotate ([<sup>68</sup>Ga]-DOTATATE) positron emission tomography/ computed tomography (PET/CT) in the detection of head and neck paragangliomas (HNPGLs) compared to anatomical imaging with CT/MRI and other functional imaging modalities, including [<sup>18</sup>F]-fluorohydroxyphenylalanine ([<sup>18</sup>F]-FDOPA) PET/CT, [<sup>18</sup>F]-fluoro-2-deoxy-D-glucose ([<sup>18</sup>F]-FDG) PET/CT and [<sup>18</sup>F]-fluorodopamine ([<sup>18</sup>F]-FDA) PET/CT.

In this study, [<sup>68</sup>Ga]-DOTATATE PET/CT was able to detect more lesions (38/38) than all other imaging modalities when only 23 lesions were identified by CT/MRI (p<0.01). Based on those results, the authors concluded that [<sup>68</sup>Ga]-DOTATATE PET/CT may become the preferred functional imaging modality for HNPGLs. Although [<sup>68</sup>Ga]-DOTATATE PET/CT seems a more efficient imaging modality than [<sup>18</sup>F]-FDOPA PET/CT, [<sup>18</sup>F]-FDG PET/CT and [<sup>18</sup>F]-FDA PET/CT, we believe that the comparison with MRI is not valid.

First, the MRI protocol used in Janssen and colleagues' study was suboptimal due to the lack of a contrast-enhanced angio-MRI (CE-MRA) covering the head and neck area. The CE-MRA is known to be the key sequence for the detection of HNPGLs<sup>2-4</sup> and is now broadly used in radiologic departments. Paragangliomas are highly vascularized tumors and the arterial enhancement of HNPGLs highlighted by the CE-MRA, in combination with the localization of the lesion, make MRI a very specific imaging modality unlike what the authors state, with specificity exceeding 94%.<sup>2-4</sup> Furthermore, detection rates of MRI in the study are not consistent with the current literature as sensibility and specificity reach 90% and more with a proper MRI protocol.<sup>2-4</sup>

Secondly, CT and MRI were evaluated together as a single imaging modality even though 3 patients didn't receive a head and neck MRI. This may have biased the results by underestimating the detection rates of CT/MRI as MRI has been known for a long time to be superior to CT for the detection of HNPGLs.<sup>5</sup>

The authors also state that [<sup>68</sup>Ga]-DOTATATE PET/CT provides the advantage of a whole-body imaging unlike MRI. Yet, whole-body MRI is feasible and is currently recommended by the Endocrine Society and by the European Society of Endocrinology for the follow-up of genetically predisposed patients.<sup>6-8</sup>

To our knowledge only one study showed a higher detection rate of [<sup>68</sup>Ga]-DOTATATE PET/CT when compared to a proper MRI protocol that included a CE-MRA.<sup>9</sup>

We acknowledge that [<sup>68</sup>Ga]-DOTATATE PET/CT is a very promising imaging modality for the detection of HNPGLs. However, we believe that the superiority of [<sup>68</sup>Ga]-DOTATATE PET/CT over MRI cannot be asserted by this study and should be confirmed by further studies comparing [<sup>68</sup>Ga]-DOTATATE PET/CT to an appropriate MRI protocol including a CE-MRA.

## References

1. Janssen I, Chen CC, Taieb D, et al. 68Ga-DOTATATE PET/CT in the Localization of Head and Neck Paragangliomas Compared with Other Functional Imaging Modalities and CT/MRI. *J Nucl Med Off Publ Soc Nucl Med*. 2016;57(2):186-191. doi:10.2967/jnumed.115.161018.
2. Neves F, Huwart L, Jourdan G, et al. Head and neck paragangliomas: value of contrast-enhanced 3D MR angiography. *AJNR Am J Neuroradiol*. 2008;29(5):883-889. doi:10.3174/ajnr.A0948.
3. Gimenez-Roqueplo A-P, Caumont-Prim A, Houzard C, et al. Imaging work-up for screening of paraganglioma and pheochromocytoma in SDHx mutation carriers: a multicenter prospective study from the PGL.EVA Investigators. *J Clin Endocrinol Metab*. 2013;98(1):E162-E173. doi:10.1210/jc.2012-2975.
4. Gravel G, Niccoli P, Rohmer V, et al. The value of a rapid contrast-enhanced angio-MRI protocol in the detection of head and neck paragangliomas in SDHx mutations carriers: a retrospective study on behalf of the PGL.EVA investigators. *Eur Radiol*. 2016;26(6):1696-1704. doi:10.1007/s00330-015-4024-5.
5. Vogl T, Brüning R, Schedel H, et al. Paragangliomas of the jugular bulb and carotid body: MR imaging with short sequences and Gd-DTPA enhancement. *AJR Am J Roentgenol*. 1989;153(3):583-587. doi:10.2214/ajr.153.3.583.
6. Lenders JWM, Duh Q-Y, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942. doi:10.1210/jc.2014-1498.
7. Plouin PF, Amar L, Dekkers OM, et al. European Society of Endocrinology Clinical Practice Guideline for long-term follow-up of patients operated on for a phaeochromocytoma or a paraganglioma. *Eur J Endocrinol*. 2016;174(5):G1-G10. doi:10.1530/EJE-16-0033.
8. Favier J, Amar L, Gimenez-Roqueplo A-P. Paraganglioma and phaeochromocytoma: from genetics to personalized medicine. *Nat Rev Endocrinol*. 2015;11(2):101-111. doi:10.1038/nrendo.2014.188.
9. Archier A, Varoquaux A, Garrigue P, et al. Prospective comparison of (68)Ga-DOTATATE and (18)F-FDOPA PET/CT in patients with various pheochromocytomas and paragangliomas with emphasis on sporadic cases. *Eur J Nucl Med Mol Imaging*. 2016;43(7):1248-1257. doi:10.1007/s00259-015-3268-2.