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Letter to the Editor: "The role of imaging in the management of progressive glioblastoma. A systematic review and evidence-based clinical practice guideline" [J Neurooncol 2014; 118:435-60]

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To the Editor,

We have read with interest the review by Ryken et al. [1] about the role of imaging in the management of progressive glioblastoma. In general, we agree with this review but we cannot support the opinion that the routine use of Positron-Emission-Tomography (PET) to identify progression of glioblastoma is not recommendable.

The authors have considered PET using the amino acid tracer ^{11}C-methyl-L-methionine (MET), but the use of MET is limited to PET centers with an on-site cyclotron due the short half-life of ^{11}C (20.4 min). In recent years, the clinical application of ^{18}F-labeled amino acids such as O-(2-^{18}F-fluoroethyl)-L-tyrosine (FET) or 3,4-dihydroxy-6-[^{18}F]fluoro-L-phenylalanine (FDOPA) has spread considerably due to the logistical advantages of the ^{18}F label (half-life, 109.8 min) [2]. FET can be produced with high yields similar to the widely used FDG and distributed in a satellite concept. In Europe, MET PET has been replaced in many centers by the more convenient PET tracer FET, which is now established as a routine tool for brain tumor imaging in more than 30 neurooncological centers in Germany, Austria and Switzerland. In these countries, the clinical acceptance is high and we estimate that more than 10.000 PET scans using FET have been performed in brain tumor patients during the last 5 years.

The diagnostic accuracy of FET PET in the differentiation of tumor progression orrecurrence from radiation-induced changes is convincing. A sensitivity and specificity of FET PET for the detection of tumor progression or recurrence of 100% and 93%, respectively, has been reported, compared with 93% and 50% for MRI alone [3, 4]. The additional use of dynamic FET PET allows a differentiation of high-grade and low-grade recurrences with a sensitivity and specificity of > 90% [5]. Similar results have also been reported for the differentiation of

recurrent brain metastases from radiation-induced changes with an accuracy of 93% [6]. Furthermore, a prospective study evaluated the prognostic value of early changes of FET uptake after postoperative radiochemotherapy in patients with glioblastoma [7, 8]. PET responders with a decrease of the tumor/brain ratio of more than 10% had a significantly longer disease-free survival and overall survival than patients with stable or increasing tracer uptake after RCx. Additionally, a reliable treatment monitoring was also demonstrated in various experimental approaches (e.g., radioimmunotherapy, convection enhanced delivery of paclitaxel) and for antiangiogenic treatment with bevacizumab and irinotecan [7-12].

Using FDOPA PET, a recent study including 110 patients reported an accuracy of 82% to detect recurrent glioblastoma and FDOPA uptake was a significant predictor of progression-free survival [13]. Excellent results with FDOPA PET were also reported regarding the monitoring of antiangiogenic treatement [14] and for the differentiation of recurrent brain metastases from radiation-induced changes [15].

Moreover, we would like to point out that the excellent results of SPECT with respect to differentiation of tumor recurrence mentioned in the review of Ryken et al. is based on the use of the amino acid tracer IMT [16], which delivers similar results as FET PET but at lower spatial resolution [17].

In summary, we consider PET using ^{18}F-labelled amino acids such as FET or FDOPA as one of the most promising imaging methods in the management of progressive glioblastoma. In the review by Ryken and colleagues, this recent development has not been adequately addressed.

1. Ryken TC, Aygun N, Morris J, Schweizer M, Nair R, Spracklen C, et al. The role of imaging in the management of progressive glioblastoma : A systematic review and evidence-based clinical practice guideline. Journal of neuro-oncology. 2014;118:435-60. doi:10.1007/s11060-013-1330-0.
2. Herholz K, Langen KJ, Schiepers C, Mountz JM. Brain tumors. Seminars in nuclear medicine. 2012;42:356-70. doi:10.1053/j.semnuclmed.2012.06.001.
3. Popperl G, Gotz C, Rachinger W, Gildehaus FJ, Tonn JC, Tatsch K. Value of O-(2-[18F]fluoroethyl)- L-tyrosine PET for the diagnosis of recurrent glioma. European journal of nuclear medicine and molecular imaging. 2004;31:1464-70. doi:10.1007/s00259-004-1590-1.
4. Rachinger W, Goetz C, Popperl G, Gildehaus FJ, Kreth FW, Holtmannspotter M, et al. Positron emission tomography with O-(2-[18F]fluoroethyl)-l-tyrosine versus magnetic resonance imaging in the diagnosis of recurrent gliomas. Neurosurgery. 2005;57:505-11; discussion -11.
5. Popperl G, Kreth FW, Herms J, Koch W, Mehrkens JH, Gildehaus FJ, et al. Analysis of 18F-FET PET for grading of recurrent gliomas: is evaluation of uptake kinetics superior to standard methods? Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2006;47:393-403.
6. Galldiks N, Stoffels G, Filss CP, Piroth MD, Sabel M, Ruge MI, et al. Role of O-(2-18F-Fluoroethyl)-L-Tyrosine PET for Differentiation of Local Recurrent Brain Metastasis from Radiation Necrosis. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2012;53:1367-74.
7. Galldiks N, Langen K, Holy R, Pinkawa M, Stoffels G, Nolte K, et al. Assessment of treatment response in patients with glioblastoma using [18F]Fluoroethyl-L-Tyrosine PET in comparison to MRI. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2012;53:1048-57.
8. Piroth MD, Pinkawa M, Holy R, Klotz J, Nussen S, Stoffels G, et al. Prognostic value of early [18F]fluoroethyltyrosine positron emission tomography after radiochemotherapy in glioblastoma multiforme. International journal of radiation oncology, biology, physics. 2011;80:176-84. doi:10.1016/j.ijrobp.2010.01.055.
9. Galldiks N, Rapp M, Stoffels G, Fink GR, Shah NJ, Coenen HH, et al. Response assessment of bevacizumab in patients with recurrent malignant glioma using [18F]Fluoroethyl-L-tyrosine PET in comparison to MRI. European journal of nuclear medicine and molecular imaging. 2013;40:22-33. doi:10.1007/s00259-012-2251-4.
10. Hutterer M, Nowosielski M, Putzer D, Waitz D, Tinkhauser G, Kostron H, et al. O-(2-18F-fluoroethyl)-L-tyrosine PET predicts failure of antiangiogenic treatment in patients with recurrent high-grade glioma. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2011;52:856-64. doi:10.2967/jnumed.110.086645.
11. Popperl G, Goldbrunner R, Gildehaus FJ, Kreth FW, Tanner P, Holtmannspotter M, et al. O-(2-[18F]fluoroethyl)-L-tyrosine PET for monitoring the effects of convection-enhanced delivery of paclitaxel in patients with recurrent glioblastoma. European journal of nuclear medicine and molecular imaging. 2005;32:1018-25. doi:10.1007/s00259-005-1819-7.
12. Pöpperl G, Götz C, Rachinger W, Schnell O, Gildehaus FJ, Tonn JC, et al. Serial O-(2-[(18)F]fluoroethyl)-L:-tyrosine PET for monitoring the effects of intracavitary radioimmunotherapy in patients with malignant glioma. European journal of nuclear medicine and molecular imaging. 2006;33:792-800.
13. Herrmann K, Czernin J, Cloughesy T, Lai A, Pomykala KL, Benz MR, et al. Comparison of visual and semiquantitative analysis of 18F-FDOPA-PET/CT for recurrence detection in glioblastoma patients. Neuro-oncology. 2014;16:603-9. doi:10.1093/neuonc/not166.

14. Schwarzenberg J, Czernin J, Cloughesy TF, Ellingson BM, Pope WB, Grogan T, et al. Treatment Response Evaluation Using 18F-FDOPA PET in Patients with Recurrent Malignant Glioma on Bevacizumab Therapy. Clinical cancer research : an official journal of the American Association for Cancer Research. 2014;20:3550-9. doi:10.1158/1078-0432.CCR-13-1440.
15. Lizarraga KJ, Allen-Auerbach M, Czernin J, DeSalles AA, Yong WH, Phelps ME, et al. (18)F-FDOPA PET for differentiating recurrent or progressive brain metastatic tumors from late or delayed radiation injury after radiation treatment. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2014;55:30-6. doi:10.2967/jnumed.113.121418.
16. Plotkin M, Eisenacher J, Bruhn H, Wurm R, Michel R, Stockhammer F, et al. 123I-IMT SPECT and 1H MR-spectroscopy at 3.0 T in the differential diagnosis of recurrent or residual gliomas: a comparative study. Journal of neuro-oncology. 2004;70:49-58.
17. Pauleit D, Floeth F, Tellmann L, Hamacher K, Hautzel H, Muller HW, et al. Comparison of O-(2-18F-fluoroethyl)-L-tyrosine PET and 3-123I-iodo-alpha-methyl-L-tyrosine SPECT in brain tumors. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2004;45:374-81.