

## Effect of Gadolinium Deposition on $^{18}\text{F}$ -FDG PET/CT of Dentate Nucleus and Globus Pallidus

**TO THE EDITOR:** I read with great interest the recent article in *Journal of Nuclear Medicine Technology* by Bauer et al. entitled, "Do Gadolinium-Based Contrast Agents Affect  $^{18}\text{F}$ -FDG PET/CT Uptake in the Dentate Nucleus and the Globus Pallidus? A Pilot Study" (1). The authors' initial idea of visualizing the functional effect of gadolinium deposition in the brain by  $^{18}\text{F}$ -FDG PET is quite smart. However, this issue is delicate, and the impact of the results of this study on the medical community is large. Therefore, even in a pilot study, a careful study design is needed to support the conclusions. In this kind of case-controlled retrospective study, it is essential to control confounding factors so that they are as equal as possible between the two groups.

I have three important concerns about this study. First, the authors performed whole-body PET on the subject group but dedicated brain PET on the control group. The high-resolution dedicated brain protocol might have contributed to the higher SUVs in the control group. SUV differences of up to 40% have been found between high-resolution images (7 mm) and low-resolution images (10 mm) for smaller lesions measuring less than 2 cm<sup>3</sup> (2). Second, the median age of the subject group (54 y) was higher than that of the control group (36 y). Increased age might have contributed to the lower SUVs in the subject group. Third, the disease status of the patients was not clearly indicated. The need for multiple contrast-enhanced MR examinations in the subject group might have been due to the presence of diseases that affect the SUVs of the dentate nucleus and globus pallidus. Dividing the patients into two groups with multiple confounding factors that cannot be ignored might have had a significant effect on the results. The authors could have combined the patient data into a single pool and performed multivariate analysis to produce reliable results for this important issue.

### REFERENCES

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**Shinji Naganawa**

*Nagoya University Graduate School of Medicine  
65 Tsurumai-cho, Showa-ku  
Nagoya 466-8550, Japan  
E-mail: naganawa@med.nagoya-u.ac.jp*

Published online Mar. 9, 2017.  
DOI: 10.2967/jnmt.116.187591

**REPLY:** We thank Dr. Naganawa for his interest in our article, in which we present the findings from our pilot study investigating  $^{18}\text{F}$ -FDG uptake in the brain after repeated gadolinium-based

contrast agent administration (1). In our retrospective analysis, patients who had previously undergone 3–6 contrast-enhanced MRI studies demonstrated significantly decreased uptake in the dentate nucleus and globus pallidus on  $^{18}\text{F}$ -FDG PET/CT (measured as decreased median SUV<sub>max</sub>) compared with patients with no history of gadolinium-based contrast agent administration. Given the strong emerging interest in the focus of this study and the potential impact of our early findings, we read Dr. Naganawa's comments with great interest.

In principle, we agree with the three points Dr. Naganawa raised. Patients in the subject group underwent whole-body PET/CT as part of an oncologic workup, whereas those in the control group received a dedicated brain PET/CT study as part of a traumatic brain injury protocol. We agree that this difference in imaging protocol could have been a confounding factor in the evaluation of  $^{18}\text{F}$ -FDG uptake and SUV<sub>max</sub> calculation; however, since this pilot study was retrospective, we were restricted to using those available patients whose clinical and imaging histories met our criteria. The study design was also the main cause for the difference in age between the two groups (36 vs. 54 y). This too could have been a source of confounding, although we did perform an additional analysis to determine whether an interaction effect from age was present and found no effect in our small sample sizes. Finally, we agree that the differences in patient disease status could have been an issue. The patients in the control group had clinical histories for which at least one unenhanced brain MRI study was indicated, whereas those in the subject group had indications for multiple contrast-enhanced MRI studies, of which at least two were brain studies. Although these patients may have had a variety of issues that warranted their MRI studies, we did exclude any patients with known brain lesions or prior brain irradiation that may have affected  $^{18}\text{F}$ -FDG distribution and uptake patterns.

Although the initial findings from our pilot study were exciting, we agree that more research is needed for validation. In an ideal situation, a prospective study design would be used that would account for many of these issues that were raised. Participants with no history of gadolinium-based contrast agent administration would receive a baseline PET/CT study, followed by one or more contrast-enhanced MRI studies, and finally a follow-up PET/CT study for comparison. Rather than having separate groups that were controlled for demographics and clinical status, each participant would be self-matched and therefore serve as his or her own control. The time and resources needed to conduct such a study would be greater, but it would provide a more rigorous validation of our findings.

### REFERENCE

1. Bauer K, Lathrum A, Raslan O, et al. Do gadolinium-based contrast agents affect  $^{18}\text{F}$ -FDG PET/CT uptake in the dentate nucleus and the globus pallidus? A pilot study. *J Nucl Med Technol.* 2017;45:302–305.

**Medhat Osman**  
**Austin Turner**

*Saint Louis University  
3615 Vista Ave.  
St. Louis, MO 63110  
E-mail: mosman@slu.edu*

Published online Mar. 9, 2017.  
DOI: 10.2967/jnmt.117.191577

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