J of Nuclear Medicine Technology, first published online March 9, 2017 as doi:10.2967/jnmt.117.191577

Letter to the Editor Response

REPLY: We thank Dr. Naganawa for his interest in our article in which we present the findings from our pilot study investigating ^{18}F-FDG uptake in the brain after repeated gadolinium-based contrast agent (GBCA) administrations (*1*). In our retrospective analysis, patients who had previously undergone 3 to 6 contrast-enhanced MRI studies demonstrated significantly lower uptake in the dentate nucleus and globus pallidus at FDG PET/CT (measured as decreased median SUV_{max}) compared to patients with no history of GBCA administrations. 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 while 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 FDG uptake and SUV_{max} calculation; however, since this pilot study was retrospective in nature, 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 years). This too could have been a source of confounding, although we did perform additional analysis to determine if 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. Patients included in the Control group had clinical histories for which at least one unenhanced brain MRI study was indicated, while those in the Subject group had indications for multiple contrast-enhanced MRI studies, of which at least 2 were brain studies. While 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 FDG distribution and uptake patterns.

While 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 GBCA 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 their 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.

REFERENCES

1. Bauer K, Lathrum A, Raslan O, et al. Do gadolinium-based contrast agents affect the 18F-FDG PET/CT uptake in the dentate nucleus and the globus pallidus? A pilot study. *J Nucl Med Technol.* 2016.

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