TO THE EDITOR: Recently, PET of the cerebrospinal fluid (CSF) space with $^{68}$GaGa-DOTA has been proposed as a fast and convenient approach for verification of spinal CSF leaks (1). PET-based radioisternography with $^{68}$Ga-ethylidenediaminetetraacetic acid, $^{5}$Co-co-diethyleneriaminepentaaacetic acid (DTPA), and $^{64}$CuCu-DTPA was reported as early as 1982 (2,3). We would like to highlight the existence of another tracer, $^{64}$CuCu-DOTA, for CSF space imaging.

The advantage of $^{68}$Ga-based radiotracers is the wide availability of $^{68}$Ga and a generally convenient and fast production via metal chelation. The disadvantage is the short half-life of 68 min, impairing imaging of slow or intermittent processes. Therefore, the radiopharmaceutical production of $^{64}$CuCu-DOTA, with a half-life of 12.7 h, has been established in our clinic in compliance with standards of good manufacturing practice (4,5).

Since 2018, 5 patients with intracranial hypertension, in whom CT or MRI as well as radionuclide cisternography with $^{111}$InIn-DTPA were inconclusive, underwent PET/CT of the CSF space in the Clinic of Nuclear Medicine, Jena University Hospital, Germany. No immediate or late complications occurred after lumbar intrathecal $^{64}$CuCu-DOTA injection. In 3 cases, a spinal CSF leak was identified.

Because of the shorter positron range of $^{64}$Cu than of $^{68}$Ga, the PET image quality of $^{64}$CuCu-DOTA can be expected to be superior to that of $^{68}$GaGa-DOTA, enabling location and identification of small CSF leaks (6). This high image quality is maintained during delayed imaging performed 20 h after injection and may be particularly helpful to locate cranioencephalic CSF leaks after surgical procedures (case example available in (7)).

Intrathecal injection of CT or MRI contrast agents has been associated with a high probability of adverse events (8,9). Also, $^{111}$InIn-DTPA injections have caused neurologic reactions due to iron sequestration in the CSF caused by excess chelator (10,11). The CSF is a sensible system, exhibiting few proteins and limited buffering capability. Formulations administered into the CSF space should contain ingredients in the smallest possible quantities. The amount of precursor in $^{64}$CuCu-DOTA is lower by a factor of 1,000 than that in CT or MRI contrasts agent, which makes $^{64}$CuCu-DOTA safer for intrathecal injections (5). pH, osmolality, and a low-salt concentration of $^{64}$CuCu-DOTA are optimally adjusted to the CSF fluid. In contrast, the $^{68}$GaGa-DOTA preparation as reported by Evangelou et al. (1) may contain elevated concentrations of NaCl and sodium acetate due to the acidic labeling conditions of $^{68}$Ga (3). Furthermore, $^{64}$CuCu-DOTA production can be performed up to 24 h before administrations, thus granting a longer time frame for application than is possible with $^{68}$GaGa-DOTA.

With regard to the cost and yet limited availability of $^{64}$Cu, PET cisternography with $^{64}$CuCu-DOTA is seen as a reserve, but important, method in difficult cases with intracranial hypertension. Because of the long half-life of the tracer and the high-resolution capabilities of PET/CT, and $^{64}$Cu PET/CT in particular, localization of slow-flow CSF leaks in patients with intracranial hypertension can be enabled. The next research step will be dosimetric evaluation of the new tracer.

REFERENCES

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Published online Mar. 14, 2024.
DOI: 10.2967/jnumed.123.267329