PATIENTS
FOR SAFER NUCLEAR MEDICINE

August 1, 2025

Dear Editor of the Journal of Nuclear Medicine –

We represent Patients for Safer Nuclear Medicine (PSNM), a coalition of over 30 patient advocacy organizations dedicated to promoting transparency when significant amounts of radiopharmaceuticals are inadvertently extravasated during medical procedures.

PSNM is supported by several corporations in the nuclear medicine space, and a patient safety hospital grading organization, The Leapfrog Group. Some of the most esteemed nuclear medicine physicians, physicists, technologists, vascular access experts, and radiologists — who are also members of the Society of Nuclear Medicine and Molecular Imaging, the Health Physics Society, and the American College of Radiology — generously give their time to answer our questions.

Coalition members were pleased to see the article *"Extravasation Frequency of [177Lu]Lu-DOTATATE: Insights and Implications Derived from 1,314 Cycles of Treated Patients—A Single-Site Analysis"* by Kayal et al[1]. We were glad to see that this center monitors and characterizes extravasations of a radiotherapeutic. However, we have several concerns and questions.

From our understanding it appears the authors imaged patients three to four hours after administration of the radiopharmaceutical.

1. *Why wait hours to identify the extravasation?*
2. *If clinicians know earlier that a patient is being extravasated, could they stop the administration and minimize the extravasated activity?*
3. *Later in the article, the authors discuss mitigation techniques to reduce radiation exposure, but shouldn't these techniques be applied at the time of extravasation rather than hours later?*
4. *When the authors quantified the activity near the injection site at time of imaging, hasn't the patient's lymphatic system already cleared much of the extravasation? Did the authors underestimate the amount of radiation exposure that patients experienced?*
5. *Why does this center inject patients in areas of flexion and not the forearm, where vascular access experts recommend gaining access?*

[1] https://jnm.snmjournals.org/content/early/2025/06/26/jnumed.124.269411

We have consulted with our Medical Internal Radiation Dose experts and are curious why this center would calculate the dosimetry using a region of interest that is established three to four hours post administration, rather than a standard volume such as 15 cc around a voxel of the highest SUV? Interestingly, the authors mention the use of a standard volume for a region of interest in the control group to "ensure consistency and robust comparisons," but they don't do this for the extravasated patients. Doesn't the center's approach underestimate the absorbed dose, given that using a larger tissue volume lowers the calculated dose and that reporting without a standardized volume lacks consistency?

The authors state that no adverse events, including cutaneous tissue damage or deterministic radiogenic skin injuries, were observed immediately or in the following days or weeks. Our understanding of this isotope is that the energy does not travel far (~1-2mm) when the isotopes decay. It is also our understanding from attending a webinar with Dr. Boerma, a radiation biologist, that tissue damage from ionizing radiation can take months to years to develop.

1. *Why would the authors expect to see skin damage?*
2. *Why do the authors not mention this fact? What technology do they use to assess effects on healthy tissue under the skin?*

In the *Discussion* section, the authors conclude that steps can be taken to reduce a center's extravasation rate. This conclusion is significant, since we have participated in many public comment sessions where the community has repeatedly stated that extravasations were nearly impossible to avoid, which we know is not true.

We are concerned that the authors' delayed measurements, imprecise activity assessments, and overly large regions of interest may underestimate the absorbed tissue dose, potentially giving other clinicians a false and unwarranted sense of security.

The authors' conclusion of a median absorbed dose of ~ 0.5 Gy seems extraordinarily low for an extravasation of a therapeutic radiopharmaceutical and is certainly the result of their approach to dosimetry. Furthermore, the authors suggest that extravasations will pose minimal tissue risk.

We are further dismayed by the section *Discussion: Implications of Results*. The authors appear to use their flawed dosimetry approach and focus on skin effects rather than underlying tissue effects to conclude that these extravasations do not have any patient clinical implications and there is no need to really continue follow-up imaging. They go on to conclude that they have "substantial evidence that extravasation is a rare complication of [^{177}Lu] Lu-DOTATATE administrations and if necessary safeguards—such as careful verification of vein patency—are observed, it is of little clinical significance." Isn't it fair to say that their conclusion may be the case for these technologists, but it is not transferable to other centers or technologists?

While we were initially pleased to see that a center had taken the time to study this issue, we became increasingly dismayed as we read how the study was conducted. In the end, our concerns were realized when we noticed that the authors recognized Pat Zanzonico for his "crucial contributions to conceptual framework of this work." PSNM is familiar with Mr. Zanzonico, a vocal advocate against the reporting of extravasations to the NRC.

Our big takeaway from this study is that efforts can be made to monitor extravasations and characterize them, but the NRC must step in with objective, not subjective, dosimetry approaches that will help clinicians robustly compare the severity of extravasations.

We are alarmed that a center may be using flawed dosimetry to downplay patient risk—a message seemingly intended for other treatment centers, which is deeply discouraging to patients.

Thank you,

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Member of the Patients for Safer Nuclear Medicine Coalition

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