Journal of Nuclear Medicine, published on May 8, 2025 as doi:10.2967/jnumed.125.269865

Business Model Beats Science and Logic: Dosimetry and Paucity of Its Use

TO THE EDITOR: Theranostics began with NaI-131 for diagnosis and treatment of hyperthyroidism and thyroid cancer. For a time after this, ^{89}Sr-chloride and ^{153}Sm-ethylenediaminetetramethylene phosphonate were used for the treatment of bone metastases and ^{90}Y-ibritumomab tiuxetan and ^{131}I-tositumomab were used for follicular B-cell lymphoma; all have since been discontinued, which is beyond the current discussion. Recently, ligands attached to somatostatin receptors (i.e., Lutathera; Novartis) and prostate-specific membrane antigen (i.e., Pluvicto; Novartis) have dramatically changed the theranostic landscape.

Both Lutathera and Pluvicto use a 200-mCi fixed dose per cycle (over 4 and 6 cycles, respectively) and thus do not use radiation dosimetry. They are also both outpatient treatments for which reimbursement has been overall positive and case numbers continue to increase. By contrast, ^{131}I-metaiodobenzylguanidine (Azedra; Lantheus), which was approved by the Food and Drug Administration for metastatic pheochromocytoma, was less successful. It allowed up to 500 mCi per session but required dosimetry calculations. Given the high dosage, the Nuclear Regulatory Commission guidelines required the patient to be admitted, the treatment room to be shielded, and the nursing and floor staff to be specially trained. Despite this, the reimbursement under its diagnosis-related group (DRG) was unable to cover the radiopharmaceutical cost; the treatment never became popular, and the vendor has since removed it from the market.

The effectiveness of radioiodine therapy is dependent on intact NaI symporters and successful organification in target cells. Similarly, Lutathera and Pluvicto require the presence of somatostatin receptors or prostate-specific membrane antigen, respectively, to function. Given that they require the functional integrity of the target cell, common wisdom recommended treating "hard and fast" the first time. Subsequent treatment then involves "diminishing returns". Unlike external-beam radiation therapy, with which interspersed normal tissue is spared via fractionation of the total dose, unsealed radionuclide therapy is aimed at giving the largest dose possible at the first treatment session. Treatment dosage then becomes a balance between therapeutic levels to the target and low levels to critical and vital organs. To complicate things further, the target organ of therapy may not necessarily also be the critical organ. For example, we treat patients with amino acid infusions to decrease radiation toxicity to the kidneys during Lutathera treatment.

Even heterogeneous malignancies, such as the neuroendocrine tumors, are nonetheless given a standard dose (200 mCi in the case of Lutathera). Despite its availability, we neither use dosimetry nor adjust the dose; we instead act as if "one size fits all."

Not only do we fractionate the therapy dose but we also give the same dose every time. However, using 200 mCi does not require hospitalization by Nuclear Regulatory Commission criteria. It avoids all the issues with hospitalizing a radioactive patient and does not get stimmed by the DRG.

So, the lesson we have learned is that dosimetry and appropriate dose will only be successful if the dose assessment is less than 200 mCi and treatment is done in an outpatient setting. If the calculated dose increases to more than 2,000 mCi, there is a decreased chance that it will be performed—just like what happened to ^{131}I-metaiodobenzylguanidine.

Although there may be ways of performing low-cost or free dosimetry and there may be data supporting dosimetry-adjusted dosage, clinical practice will not change unless the DRG for radionuclide therapy allows us to bill the radiopharmaceuticals separately and nuclear medicine staff are prepared to organize inpatient therapy. As such, future developments must keep not only science and evidence in mind but also regulatory, reimbursement, and business issues.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

Michael D.F. Goldenberg*
Taranjit S. Gill
Jitesh Dhingra
**Imaging Institute, Allegheny Health Network*
Pittsburgh, Pennsylvania
E-mail: michael.goldenberg@ahn.org

Published online May 8, 2025.
DOI: 10.2967/jnumed.125.269865