Radionuclide Therapies in Molecular Imaging and Precision Medicine

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KEYWORDS

• PET/CT • SPECT/CT • ^{131}I MIBG • ^{131}I therapy • ^{90}Y microspheres
• Peptide radionuclide receptor therapy

KEY POINTS

- Individualized treatment, also known as precision medicine, aims to target tumor cells to the maximum extent while minimizing the toxicity to the organs at risk.
- Determination of radionuclide therapy doses according to patient-specific data, such as age, weight, height, kidney function, and other generic information, is not sufficient to provide precision medicine.
- For each patient, an individualized dosimetry workup should be determined not only using patient-specific data demographics but also according to the patient-specific radionuclide distribution.
- Recent introduction of single-photon emission computed tomography (SPECT)-based and PET-based dosimetry in routine clinical use has improved applications of precision medicine in radionuclide therapy.

INTRODUCTION

With recent advances in molecular imaging and cancer therapy, a rapid growth in radionuclide therapy as part of precision medicine is expected. Dual-purpose therapeutic and diagnostic ("theragnostic") radiopharmaceuticals permit low-dose imaging with one radionuclide to assess biodistribution kinetics for tumor dosimetry, as well as radionuclide therapy at high doses using a different radionuclide but the same uptake pattern. Recent developments in the imaging modalities, including PET/computed tomography (CT), PET/MR imaging and SPECT/CT contribute to the more precise localization of radiopharmaceuticals and thus dosimetry calculations. The ability to predict precisely the radiation dose before delivery of the therapy is an important component of personalized medicine. In this article, we focused on use of ^{131}MIBG, ^{131}NaI therapy, peptide radionuclide receptor therapy, and targeted delivery of radionuclides with embolizing ^{90}Y microspheres.

METAIODOBENZYLGUANIDINE

Metaiodobenzylguanidine (MIBG) is an analog of guanethidine that shares structural features of norepinephrine, developed in 1979 as a diagnostic agent for imaging of the adrenal medulla.[1] Cellular MIBG uptake occurs by 2 different pathways. The

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dominant means of uptake is mediated by the noradrenaline (NA) transporter as an active ATPase-dependent, saturable system.[1–3] The second pathway is nonspecific, low-level diffusion. As most tumors of neural crest origin have high levels of NA transporter, radiolabeled MIBG has been used successfully for imaging of a variety of neuroendocrine tumors (NETs), with higher sensitivities for pheochromocytoma (PHEO), paraganglioma (PGL), and neuroblastoma (NB) than other NETs.[4]

Demonstration of adequate targeting by using either ^{131}I MIBG or ^{123}I MIBG is a prerequisite for successful ^{131}I MIBG treatment. ^{131}I-labeled MIBG decays by beta radiation, releasing energy to tumor cells. Beta particles are responsible for most cell damage and deposit their energy within a localized tissue region of a few millimeters from the decay origin.[4]

A variety of drugs may interfere with MIBG uptake by tumor cells; hence, they should be discontinued before therapy. A full list of interfering agents and suggested cessation times has been published.[2–5] Patients using antihypertensive medications can be prescribed phenoxybenzamine (alpha blockade), atenolol, or nifedipine.[4] Patient selection criteria include adequate bone marrow reserve (hemoglobin $\geq$9 g/dL, white blood cell count $\geq 3.0 \times 10^9$/L, platelets $\geq 100 \times 10^9$/L) and renal function (glomerular filtration rate $\geq$30 mL/min). Therapy is contraindicated for patients who are pregnant or breastfeeding. Female patients of reproductive age must agree to birth control for 6 months after therapy. Patients should be able to follow radiation safety instructions. Acute spinal cord compression and hemodynamic/neurologic instability are also contraindications. Patients should have a reasonable performance status (Karnofsky >60) and a life expectancy of at least 3 months.[2–5]

Free radioactive iodine in the administered dose may accumulate in the thyroid gland and may result in hypothyroidism.[2–5] To prevent this side effect, administration of agents that block the radioactive iodine uptake in the thyroid gland are necessary. These agents include potassium iodine (KI), saturated solution of potassium iodine (SSKI), or Lugol solution.[4,5] The recommendation is to start thyroid blockade 24 to 48 hours before therapy and continue for 10 to 15 days after therapy.

Although diagnostic MIBG is approved by the Food and Drug Administration (FDA), ^{131}I MIBG treatment in the United States is not FDA approved. ^{131}I MIBG treatment is performed either under the practice of medicine or with an investigational new drug grant[4] (**Figs. 1** and **2**).

Data regarding use of ^{131}I MIBG in PHEO and PGL are limited to a few prospective studies. There is currently no consensus on an optimal

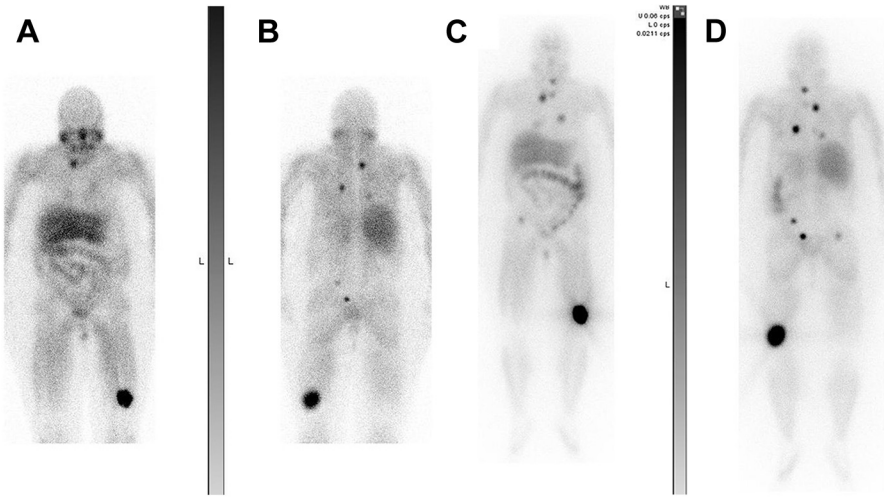

Fig. 1. A58-year-old woman presenting with intractable hypertension 5 years ago. Patient underwent abdomen MR imaging and ^{123}I MIBG studies. There was a large left adrenal mass with local invasion, which was avid in the MIBG study. Patient underwent left adrenalectomy and left nephrectomy. Pathology was PHEO. Patient presented with distal femoral fracture after 3 years. Fracture was fixed with intramedullary rod placement. Pathology result of the femoral fracture was positive for metastatic PHEO. Patient underwent whole body ^{123}I MIBG study. (*A*) Anterior and (*B*) Posterior show multiple foci of radiotracer uptake in the chest, abdomen/pelvis, and distal left femoral region, corresponding to bone and intrathoracic metastasis from PHEO. Patient underwent 419 mCi of ^{131}I MIBG therapy. Posttherapy imaging (*C, D*) showed foci of radiotracer uptake with more conspicuous uptake compared with before therapy.

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