nent. As we all strive to reduce the overall radiation exposure to our patients, we must continue to balance both the radiation dose (risk) and the clinical benefit.

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Role of SPECT/CT, Versus Traditional Practices, in Individualizing Treatment of Thyroid Carcinoma

Individualizing patient management has been a major development in the field of oncology and has been conceptualized in recent management protocols for differentiated thyroid carcinoma. Dr. Avram, in a lucid review (*1*), has nicely portrayed the advantages of SPECT/CT over conventional planar imaging. We thank the author for her excellent deliberation and would like to share traditional teachings about planar radioiodine imaging and our own experience with dose decisions and risk stratification in patients with multifocal radioiodine uptake in the neck or upper mediastinum.

At the time of our residency (in a center considered to be the busiest in thyroid cancer management in India), a common teaching was that multifocal uptake in the neck (especially outside the thyroid bed) on preablation scintigraphy would argue for a higher ablative dose of radioiodine than when uptake is confined to a solitary area, as the former likely suggests diseased nodes. This scenario corresponds to cases 2 (Fig. 2) and 3 (Fig. 3) of the review by Dr. Avram. If the foci on radioiodine scintigraphy corresponded to a clinically obvious neck node on palpation or was adjudged sufficiently large by ultrasonography (as mentioned in case 3), the preference would be for surgery before radioiodine therapy, whereas foci that represented a subcentimeter-sized nonpalpable node would be considered for radioiodine ablation upfront. Another common teaching was that after radioiodine ablative therapy, if an abnormal focus was seen in the neck on the 6-mo follow-up ^{131}I scan, its location and pattern required comparison with findings on the preablation and posttherapy scans obtained at the postthyroidectomy visit. If they matched, that would suggest persistent residual neck tissue, whereas if they did not, that would be indicative of a diseased lymph node. This was particularly the case when uptake in the thyroid neck residue merged with uptake in an adjacent node, as corresponds to case 4 (Fig. 4). If this group of patients is treated with a lower ablative dose of ^{131}I, the follow-up scan at 6 mo might demonstrate uptake only in the lymph node, as the residual normal thyroid (being the first filter of administered iodine) would have been ablated by that time. Surgeons commonly prefer not to perform surgery again if the node is subcentimeter-sized on ultrasonography or not clinically palpable and suggest that the referring physician consider radioiodine therapy. As mentioned by Dr. Avram, the prescribed dose for patients in whom unsuspected regional nodal metastases are discovered is 5.5 GBq, compared with 1.1 GBq for patients who have only neck residue.

The scenarios represented by cases 2–4 are common in practice and often are the cause for recurrence or persistence of disease in patients with differentiated thyroid carcinoma. The better lesion delineation and clarification offered by SPECT/CT thus lead to a change in the prescribed radioactivity to higher than the commonly used ablative dose. Many of us now have become quite attuned to interpreting and deciding on these intricacies in planar imaging, but beyond doubt, the better-quality images of SPECT/CT would obviate assumptions and be particularly useful to beginners. We strongly believe that risk stratification in thyroid carcinoma should not be restricted to clinical and histopathologic characteristics alone and that scan patterns (particularly multifocal uptake in a preablation study or an iodine-avid node on a follow-up scan) also should play an important role in clinical decision making, a pertinent fact highlighted by the author. Although well recognized by practitioners, this issue has been given relatively less emphasis in the current guidelines and needs to be addressed.

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REPLY: I thank Drs. Basu and Abhyankar for their letter and excellent comments on the use of preablation radioiodine scintigraphy for the management of thyroid cancer patients. As outlined in their letter, a classic teaching in nuclear medicine was that preablation radioiodine planar scans provide important information that may influence ^{131}I therapeutic decisions. The findings on preablation scans defined the target of radioiodine therapy (remnant ablation, nodal metastases, or distant metastases), directly affecting the selection of prescribed ^{131}I activity for ablative or tumoricidal treatment. Despite these advantages, over the years—as the controversy over stunning developed—the field evolved toward fixed-dose ^{131}I ablation of residual thyroid tissue after thyroidectomy, because posttherapy ^{131}I scans with better count density appeared to provide more diagnostic information than preablation scans. In this process, the contribution of preablation scans to therapeutic decisions was minimized, and staging, risk stratification, and management decisions became increasingly

predicated by clinical–pathologic criteria (i.e., age of patient and results of surgical pathology) as reflected in several guidelines (*1–4*). Advancing imaging technology with SPECT/CT facilitates accurate interpretation of classic planar scintigraphy, validating the classic teaching that the decision to use or omit radioiodine therapy should not be based solely on clinical and histopathologic criteria but should include specific thyroid cancer imaging to evaluate for the presence of regional and distant metastases. The contribution of fusion radioiodine SPECT/CT for characterization of focal central neck and distant activity in patients with thyroid cancer has been increasingly recognized, as summarized in 2 recent review articles (*5,6*), bringing into focus the use of preablation SPECT/CT for completion of staging and risk stratification before ^{131}I therapy. The current SNMMI Practice Guideline for Therapy of Thyroid Disease with ^{131}I support the view that routine preablation scintigraphy can be useful in guiding ^{131}I therapy and discusses the selection of prescribed ^{131}I activity for treatment (*7*). This recently updated guideline reflects the evolution toward a treatment approach that integrates the elements of clinical and histopathologic risk stratification with imaging information for arriving at an individualized therapeutic decision. And this precisely addresses the excellent points made by Drs. Basu and Abhyankar in their letter to the editor, which I very much welcomed.

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Not-So-Random Errors: Randomized Controlled Trials Are Not the Only Evidence of the Value of PET

TO THE EDITOR: We noted with interest the recent publication of "Randomized Controlled Trials on PET: A Systematic Review of Topics, Design, and Quality" (*1*) in *The Journal of Nuclear Medicine*. We are sure that this article will be confrontational to members of the nuclear medicine community as it again highlights the wide gulf that exists between our profession's assessment of the patient benefits of PET and the conclusions reached by a highly influential international health technology assessment agency. This continues a theme addressed by us in a recent review in *The Journal of Nuclear Medicine* (*2*). Unfortunately, we believe that Scheibler et al. offer a rather simplistic analysis that is based on a superficial review of original data and lacks appropriate clinical perspective. Further, our critical evaluation suggests several methodologic, factual, and conceptual limitations that render the authors' conclusions untenable.

Even the primary motivation for the review is flawed. The authors opine that randomized controlled trials (RCTs) are a critical component of evidence-based medicine (EBM) and are therefore required to evaluate the benefits of any new technology. It is, however, quite wrong to state that the principles of EBM require RCT evidence before valid conclusions can be drawn about the benefits of new diagnostic tests. A seminal article defining the values of EBM states that "Evidence-based medicine is not restricted to randomized trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions. To find out about the accuracy of a diagnostic test, we need to find proper cross-sectional studies of patients clinically suspected of harboring the relevant disorder, not a randomized trial" (*3*).

RCTs are most useful when the mechanism of action of treatments is not fully understood or when there is uncertainty about the benefits versus risks. Unlike drug trials, in which 2 different therapies cannot be administered to a single patient to assess differential response or outcome, it is possible to perform more than one diagnostic test in an individual patient and ascertain which is superior. There is already abundant evidence that the diagnostic accuracy of PET/CT is superior to conventional staging approaches in many cancers (*4*), thus decreasing the need for RCTs and potentially making them unethical (*5*). Moreover, many of the RCTs identified by the authors, especially RCTs under way involving lymphoma, are primarily randomized trials of new risk-adapted therapeutic approaches rather than studies of PET per se. These involve a so-called enrichment design, in which the results of PET are used to enrich the sample before randomization. As such, almost all assume, on the basis of previously published studies (*6*), that PET provides superior prognostic stratification compared with conventional imaging. Even superficial analysis of the titles or the summary protocols of most of these trials makes it patently clear that they are not an evaluation of PET but rather are testing whether alternative treatment strategies can improve outcomes in patients stratified by PET. This is no different from almost any RCT in oncology, which uses imaging for determining patient eligibility or for stratification and as an integral component of response assessment—often a key study endpoint. It would be as nonsensical to consider such studies as being evaluations of conventional imaging as it is to consider many of the cited studies as being trials of PET.

In a more general context, if the authors used their methodology to ascertain the utility of a vast array of investigations or therapeutics such as chest radiography in patients with shortness of breath, defibrillation in cardiac arrest, or use of antibiotics in sepsis, the findings would similarly suggest a lack of clinical utility since randomized trials are lacking for these medical procedures. As