

REPLY: Thank you for the opportunity to comment on the letter to the editor from Drs. Dahele and Ung. The group from Toronto–Sunnybrook Regional Cancer Center has a longstanding interest and expertise on the subject of PET-planned radiation therapy. We thank them for their continued contributions to the field.

Our objective in publishing our article (1) was to point out that the current methods used to contour ^{18}F -FDG PET for purposes of defining tumor volumes for radiation therapy are problematic. The use of a single threshold for all lung cancers is not appropriate because of the many factors that influence it, including tumor volume and heterogeneity. Currently, PET does not have the spatial resolution or tumor-tracking abilities of 4-dimensional CT. The ongoing RTOG-0515 trial (2) uses CT to contour lung cancer volumes, applying ^{18}F -FDG PET as a guide. The spatial and motion issues are not managed well by PET presently. With the development of gated PET, improvements in the technology are coming.

Drs. Dahele and Ung point out that PET contouring has some advantages, such as improved interobserver consistency and forgiveness when the operator cannot distinguish between normal and abnormal anatomy. These advantages are likely to persist as technology advances. An obvious extension would be the development of automated tumor-contouring tools for treatment planning. Collection of PET-based tumor contours and histopathology specimens, as is being performed in the PET START Trial (3), would be an excellent database on which to develop and test such tools.

We agree that the correlation of PET with tumor pathology is of vital importance. We look forward to the completion of the trial and the reporting of the results.

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Antithyroid Drugs and Radioiodine and the Absence of Evidence

TO THE EDITOR: With interest we read the instructive review on the treatment of thyrotoxicosis by Iagaru and McDougall (1). Therein, the authors stated that the outcome of radioiodine therapy with adjunctive methimazole or carbimazole would be equal to or better than that achieved when no antithyroid medication is admin-

istered. This statement is in compliance with the conclusion of most trials on the subject conducted over the last 60 y, including one of our trials cited in the review (2). Nevertheless, based on recent data the conclusion has to be refuted.

Recent findings from the first systematic review and metaanalysis on antithyroid drugs and radioiodine led us, unexpectedly, to the opposite conclusion (3). Indeed, all adjunctive antithyroid drugs given in the week before or after radioiodine therapy reduced the overall success. On the other hand, we found that concomitant antithyroid drugs reduced the postradioiodine exacerbation of hyperthyroidism and potentially decreased the morbidity and mortality of radioiodine therapy for hyperthyroidism. The major lesson by rebutting most previous studies including one of our own, however, was that even 6 decades of absent evidence still do not mean evidence of absent negative effects of antithyroid drugs on radioiodine treatment.

Every administration of antithyroid drugs in the week before or after radioiodine therapy will alter the overall outcome. Adequately powered trials are warranted to study the effects of longer discontinuation periods.

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3. Walter MA, Briel M, Christ-Crain M, et al. Effects of antithyroid drugs on radioiodine treatment: systematic review and meta-analysis of randomised controlled trials. *BMJ.* 2007;334:514–517.

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REPLY: We thank Professor Walter et al. for their kind remarks about our review on the treatment of thyrotoxicosis (1). Their comments concerning the effect of methimazole on radioiodine therapy are acknowledged. They point out their new data opposing their previously published data showing that methimazole did not increase resistance to ^{131}I (2,3). We are not sure who should receive attribution for the statement that 50% of medical dogma is wrong, the corollary being that if we knew which half we would be in excellent shape.

The ability of antithyroid medications to increase resistance to radiation has been recognized for several decades, but so has the importance of that ability been debated (4). There are those who support that both methimazole and propylthiouracil cause a higher likelihood of failure of ^{131}I and an increased need to retreat the patient. However, at the time of submission and resubmission of our article (October 30, 2006, and January 2, 2007, respectively), the weight of evidence indicated that propylthiouracil and not methimazole was the culprit (5,6). We hope that Walter et al. do not think less of us for failing to include the reference to their metaanalysis. However, their article was published on March 10,

2007 (3). Were we now writing the review, we would most certainly be including their observations. We would also like to reiterate that we recommend stopping methimazole for 5 d rather than 3 d. The paper that we did cite by Walter et al., from 2006, dealt with the shorter stoppage (2). We also believe that administration of 5.92 MBq (160 μ Ci) of 131 I per gram to be retained in the gland is sufficient for a single-dose cure even in patients who were pretreated with antithyroid medications. Physicians using smaller doses might consider an upward adjustment.

We would like to take this opportunity to correct an omission in our review. In discussing the use of lithium as an adjuvant to radioiodine therapy, we quoted the results of a study by Bal et al. but did not include the citation. We are sorry for that oversight and have listed the reference below (7).

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