

### Misinterpretation of $^{18}\text{F}$ -FDG Studies in Oncology

**TO THE EDITOR:** The survey finding by Karantanis et al. (1) of perceived greater “overinterpretation” than “underinterpretation” of  $^{18}\text{F}$ -FDG PET/CT studies in oncology on the part of referring physicians is supported by data from a prior report in *The Journal of Nuclear Medicine* by Biggi et al. (2). This work showed a better failure-free survival (FFS) rate in patients with Hodgkin disease and positive interim PET scans interpreted locally than in patients judged to have positive scans by a central reading group. The FFS rates for patients with negative scans were identical between local and central interpreters. Therefore, the discrepancy in the FFS rates in patients with positive interim scans can be accounted for only by overinterpretation, that is, false-positive interpretations, on the part of the local interpreters.

In fairness to local interpreters, there is more pressure on them clinically than on central interpreters whose opinions are not used in caring for the patients. There is arguably more pressure when it is known that a result will be used to guide further decisions on treatment.

My own impression of this is that because of the relative consequences, many interpreting physicians are more worried about missing a cancer than having a false-positive result. A missed cancer can progress to the detriment of the patient and with liability risk to the interpreting physician, whereas overcalls are often never discovered because therapy goes forward with apparent success and everyone is happy. From this standpoint, the data from Biggi et al. are unique and eye-opening because outcomes were tracked over time, revealing the impact of overinterpretation, which does not come without medical and financial costs. If we are to use the results of PET/CT in oncology to guide risk-adapted therapy, the interpretations must be accurate.

In the context of international telemedicine, we have seen a similar phenomenon with pathology interpretations. In one case of a lesion falsely diagnosed as cancer, we asked the originating pathologist about his interpretation. He was quite candid and said the patient was a VIP. He was not sure of the diagnosis and had no local expert to consult. He reasoned that if he called the lesion benign, and it turned out to be cancer, his position would be in jeopardy. On the other hand, if he called the lesion cancer, the treatment was certain to be successful and all parties would be satisfied with the outcome.

Equally interesting is the observation of Hicks (3) in the accompanying perspective. Hicks notes that he has seen cases in which he has made a positive finding only to be overruled by a negative biopsy result but with disease becoming manifest later in the same area. He posits the likelihood of pathologic sampling errors but with the surgeon left thinking the PET scan was a false-positive.

An article by Haseebuddin (4) in the same issue of *JNM* as Biggi’s report sheds important light on Hick’s observation. Haseebuddin’s work provides data on FFS in patients with prostate cancer studied with  $^{11}\text{C}$ -acetate for lymph node staging. Patients with “false-positive” PET scans demonstrated higher rates

of failure than those judged to have had true-negative scans. Again, having outcome data is pivotal in considering the possible explanations. It is most likely that the discrepancy in FFS rates between true-negative and false-positive PET scans is due to surgical or pathology sampling errors—disease was present but missed on biopsy. However, another intriguing possibility is that PET scans with various agents might actually become positive before histopathologic criteria for cancer are met. Since we have always taken histopathology as the gold standard, this possibility has not been substantively considered or studied.

Perhaps it is time to challenge the gold standard.

### REFERENCES

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### The Impact of Image Reconstruction Bias on PET/CT $^{90}\text{Y}$ Dosimetry After Radioembolization

**TO THE EDITOR:** We read with great interest the paper entitled “The Impact of Image Reconstruction Bias on PET/CT  $^{90}\text{Y}$  Dosimetry After Radioembolization” (1). In this paper, Tapp et al. showed that commercial software that truncates the negative pixels (resulting from random-coincidence correction) can display a significant positive bias in  $^{90}\text{Y}$  PET imaging. We would like to bring some additional information to the attention of readers and PET system manufacturers.

We were also confronted by this problem while developing a correction method for the spurious-coincidence contamination occurring in  $^{86}\text{Y}$  PET imaging (2): directly subtracting the estimated spurious-coincidence sinogram from the 511–511 keV true-coincidence sinogram (i.e., prompt minus delayed coincidences) resulted in numerous negative pixel values due to the high fraction of spurious coincidences generated by the multiple  $\gamma$  cascades present in  $^{86}\text{Y}$  decay (3). Afterward, truncating these negative pixels before ordered-subsets expectation maximization reconstruction ended up in significant bias. Additional smoothing of the spurious-coincidence sinogram only partially improved the reconstruction.