PET/CT an Integral Tool for Cancer Diagnosis and Staging

Cancer doesn't have to be a death sentence. Just as screening mammograms have been linked to lower mortality rates for breast cancer,[1] the hope is that low-dose CT lung cancer screening will enable identification of the disease at an earlier stage before it spreads to other tissues or organs.

"Lung cancer is a devastating disease with very poor survival rates because patients often present in a late stage—3 or 4," says Brandon Howard, MD, PhD, Department of Radiology, Nuclear Medicine Division, Duke University Health System. "The National Lung Screening Trial trial demonstrated a mortality benefit when certain high-risk patients were screened with low-dose CT."

Dr. Howard explains that within the ACR's Lung-RADS™, the most concerning nodules are classified as 4A or 4B, depending on the size of the nodule. The goal he says is to properly triage these small pulmonary nodules. ACR's

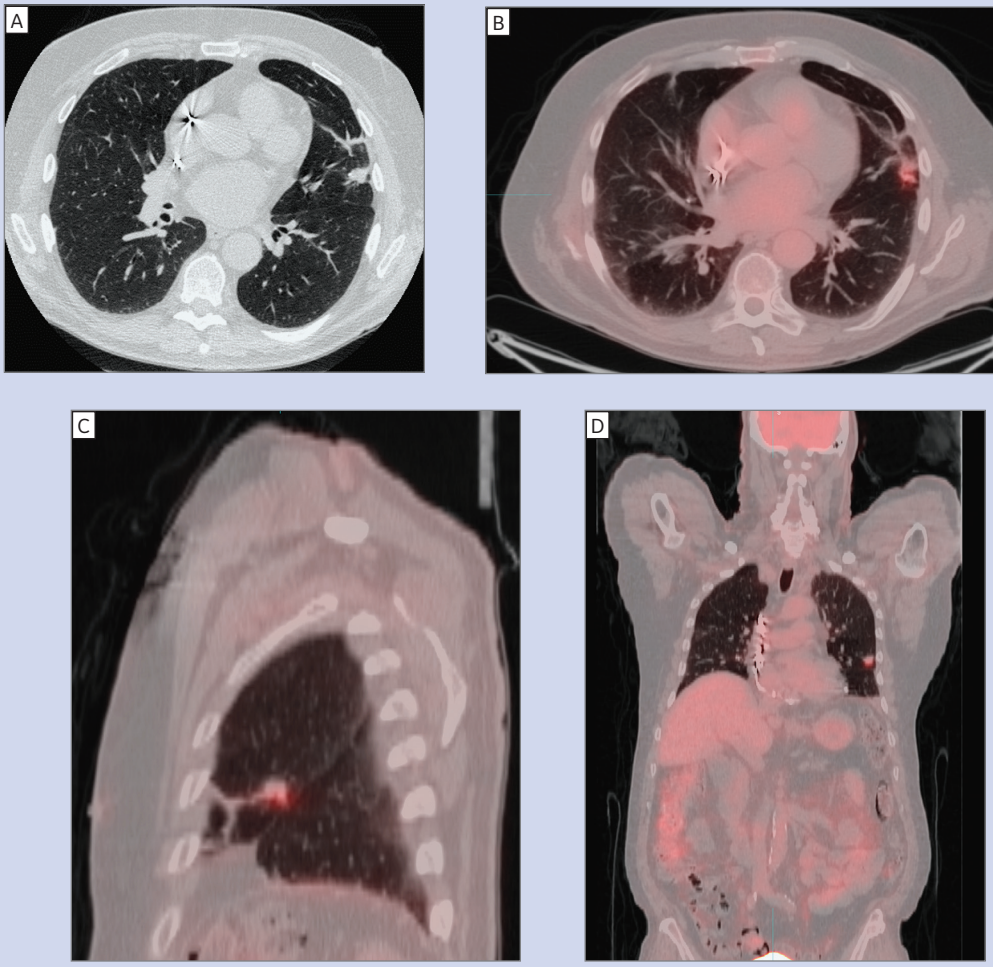

Figure 1. A 70-year-old man with a long smoking history was referred to the Duke Lung Cancer Screening Clinic by his internist. (A) The lung cancer screening low-dose CT performed at that time showed a 1.4 cm spiculated nodule in the left upper lobe, for which a PET was recommended. (B, C, D) PET demonstrated a hypermetabolic nodule (SUV_{max} 2.8) with FDG uptake above medastinal blood pool.

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>
> *Dr. Brandon Howard*

Lung-RADS recommends that nodules classified as 4A be further examined with PET/CT while nodules classified as 4B be further examined with either PET/CT or tissue sampling.

Duke University's low-dose CT lung cancer screening program was launched in early 2015 and is a multi-disciplinary team effort comprised of thoracic surgeons, radiologists, medical oncologists, and nurse practitioners/tobacco treatment specialists. As of March 2016, 16 patients with nodules classified as 4A or 4B received a PET/CT study. The patients were imaged either on the Discovery™ PET/CT 690 or Discovery IQ PET/CT scanners.

"Right from the start we reconstructed the images using the Q.Clear algorithm," Dr. Howard explains. Q.Clear is a pioneering full-convergence reconstruction technology that enables fast and efficient reading for greater confidence in evaluating a patient's response to treatment. It provides up to 2x improvement in both PET quantitation accuracy (SUVmean) and image quality (SNR).

"With Q.Clear and time-of-flight, we have a lot of tools to work up these small nodules," Dr. Howard says. Along with colleagues, Dr. Howard is conducting research to better understand how to characterize the performance of PET/CT in cases where low-dose CT has been used for lung cancer screening.

"The Q.Clear reconstruction algorithm has the potential to give us the true metabolic activity of the nodule," Dr. Howard says. "In lung cancer, the SUVmax is a very helpful parameter in determining how the patient will do over time."

In a 2015 study, Dr. Howard and co-authors demonstrated that patients with a lower or decreasing SUVmax had improved survival and a longer time to recurrence—independent of the treatment the patient received.[2] Dr. Howard and co-authors conclude that this data may help identify early-stage cancer patients who would benefit from a more aggressive therapy after surgical resection.

"SUV is a promising biomarker for FDG PET in determining patient management," Dr. Howard adds. "The real question is to know precisely what that SUV value is—that the low uptake I'm seeing in a lung nodule is, in fact, truly low compared to a nodule that is too small to characterize and may possibly lead to underestimation of the cancer. Q.Clear could potentially give us a more accurate SUV value and a better idea of how aggressive a tumor will be."

That's not to say that radiologists should use a certain SUV value to report a tumor as benign or malignant, he adds. However, a surgeon could use the information to help determine whether a biopsy or wedge resection is most appropriate for that patient.

With Q.Clear, the SUV values are slightly higher than with non-Q.Clear reconstructed images. It's not a significant change, Dr. Howard says—an SUV of 2 might be 3 or 4 with Q.Clear—but it may be enough of a difference to indicate to the radiologist that the lesion is more aggressive. That, he says, is important, as it can change patient management.

The nodule size is also a consideration, as some studies have reported that PET is not as accurate in nodules less than 10 mm. However, Dr. Howard says these studies were performed on prior generation PET/CT scanners; he believes there is evidence to suggest that today's more advanced systems may enable better characterization of smaller nodules.

"We would really like to optimize characterizing nodules between 6 and 9 mm," Dr. Howard explains. Nodules below 5 mm are often seen incidentally on PET scans and are unlikely to be cancer unless the patient has a significant smoking history or a primary malignancy. The typical course of action is to follow these very small nodules (under 5 mm) over time.

Dr. Howard and his colleagues have also utilized Q.Static on solid pulmonary nodule workups. Q.Static is a motion management tool that can help eliminate motion artifacts in PET imaging. Motion can degrade the quality of the image and, therefore, the accuracy of the quantitation. This can be particularly important when examining nodules at the lung base near the diaphragm where motion blurring can lead to underestimation of the biologic nature of the nodules.

"If we can confidently say a nodule is negative, even with a small nodule, and the patient could be followed (with imaging) rather than undergo a biopsy, that would be a great benefit," Dr. Howard says. "These procedures are not innocuous; many of these patients will have pneumothoraces after lung biopsy and some may require placement of a chest tube."

While FDG-PET is inherently non-specific, Dr. Howard believes that it can help guide patient management.

"FDG as a biomarker is powerful. I think when used with CT imaging, patient history, and risk factors it can help raise suspicions when appropriate. If we can reduce the equivocal results, then that would be very helpful."

Looking forward, Dr. Howard would like to see the development of additional tracers for predictive imaging.

"If we could image a receptor to see whether the tumor is expressing that receptor, we could determine whether or not the patient would benefit over the long term from a very expensive targeted immunologic or biologic agent. That's a role where PET could have a real impact," Dr. Howard says. ■

References

1. Nickson C, Mason KE, English DR, Kavanagh AM. Mammographic Screening and Breast Cancer Mortality: A Case-Control Study and Meta-analysis. Cancer Epidemiol Biomarkers Prev. 2012 Sep;21(9):1479-88.

2. Kwon W, Howard BA, Herndon JE, Patz Jr EF. FDG Uptake on Positron Emission Tomography Correlates with Survival and Time to Recurrence in Patients with Stage I Non-Small-Cell Lung Cancer. J Thorac Oncol. 2015;10: 897–902.

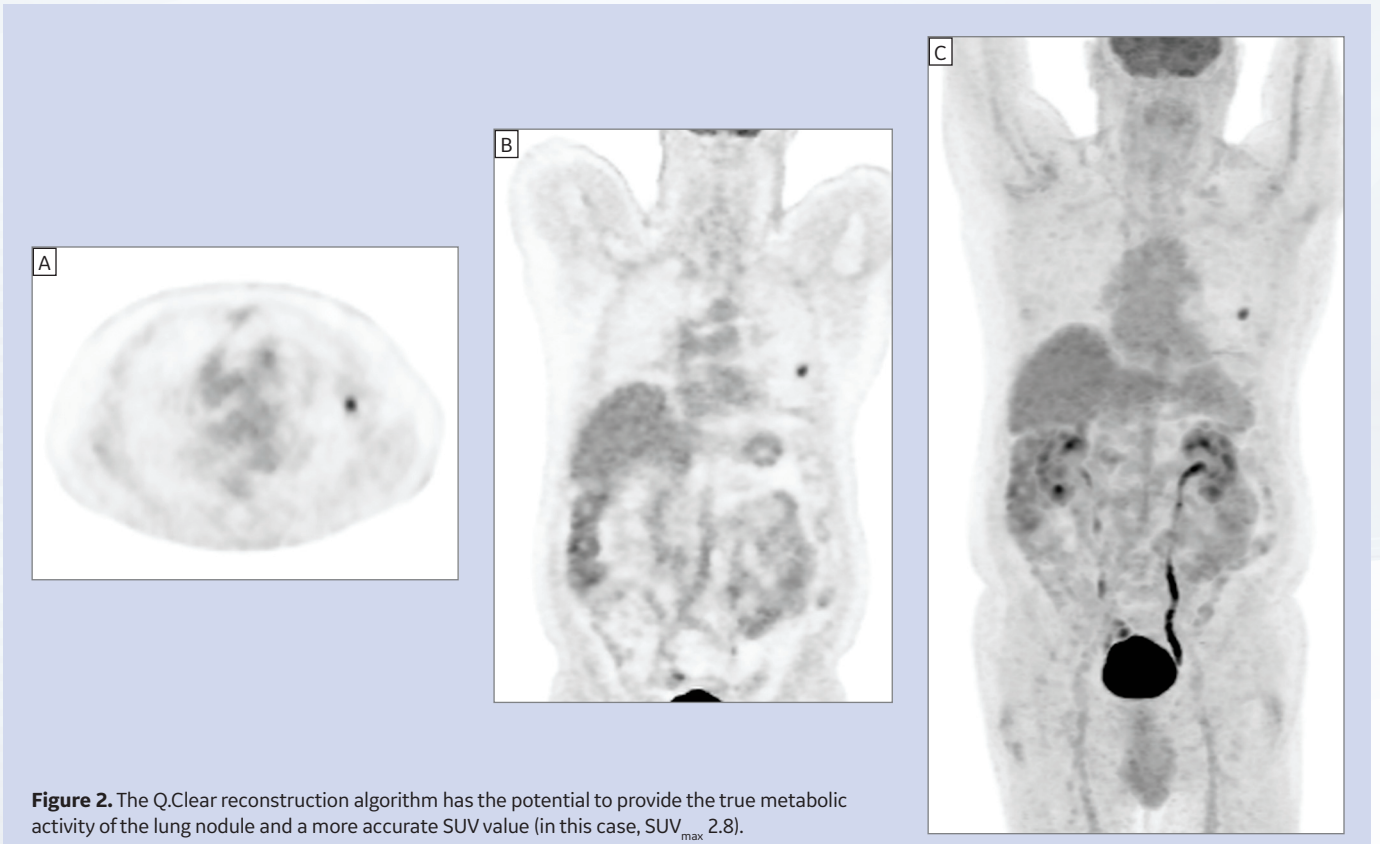

Figure 2. The Q.Clear reconstruction algorithm has the potential to provide the true metabolic activity of the lung nodule and a more accurate SUV value (in this case, SUV_{max} 2.8).