

Editorial

Is an FDG-PET Scan the New Imaging Standard for Colon Cancer?

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In this issue of the *Annals of Surgical Oncology*, Libutti et al. from the National Cancer Institute (NCI) report the results of a well-designed prospective study that examines the role of the 2-[¹⁸F] fluoro-2-deoxy-D-glucose (FDG) and positron emission tomography (PET) scan (the FDG-PET scan), carcinoembryonic antigen (CEA) scan, and “blind” second look laparotomy for the detection of recurrent colon cancer in patients with increasing CEA levels.¹ They concluded that the FDG-PET scan predicts the patients who will have resectable disease. How does FDG-PET work? The motivation to develop PET came from the understanding that the molecules of organic matter—carbon, oxygen, and nitrogen—can be imaged in their radioactive forms only as positron-emitting isotopes. PET imaging took a leap forward with the use of 2-[¹⁸F] fluoro-2-deoxy-D-glucose (fluorodeoxyglucose or FDG) which is distributed in the body similar to glucose. The inefficient metabolism of glucose in malignant tumors noted by Warburg 70 years ago allowed detection *in vivo* of this compound. Because the rate of glycolysis increases proportional to the growth rate of a tumor, FDG-PET imaging potentially provides information regarding the growth rate and tumor grade.² Does FDG-PET imaging work? The evidence in the literature became so compelling that in 1998 the Health Care Finance Administration and Medicare endorsed PET imaging to differentiate benign pulmonary nodules from non-small lung cancer. In 1999, reimbursement was approved for this imaging modality for the evaluation of lymphoma, melanoma, and recurrent colon cancer.²

Libutti et al. performed an extremely well-designed prospective study to evaluate FDG-PET, CEA scanning, and “blind” second look laparotomy to evaluate colon cancer patients who had both increasing CEA levels and conventional imaging that showed no disease or one site of disease. Of 30 patients who entered the trial, 28 were explored and 26 (94%) had disease discovered. FDG-PET found unresectable disease in 9 of 10 (90%) patients who had unresectable disease and resectable disease in 81% of 16 patients who had resectable disease. The CEA scan performed miserably: sensitivity of 18% and specificity of 33%. Interestingly, a “blind” look laparotomy by a second surgeon who was unaware of the results of the FDG-PET and CEA scans was associated with a 92% sensitivity and 100% specificity. This study adds to a growing literature of FDG-PET and CEA scintigraphy in the evaluation of patients with colon cancer. In the 1980’s, CEA scintigraphy seemed promising, but the recent experience suggests the practice has not matched the theory. Investigators in Germany compared FDG-PET and CEA scintigraphy by using a CEA Fab’ fragment to evaluate 28 patients with suspected recurrent colorectal cancer.³ Local recurrence was identified in 8 of 9 (88.9%) patients with CEA scintigraphy but metastases were identified in only 1 of 15 (6%) patients. In contrast, FDG-PET correctly identified the local recurrences in all 9 patients and metastases in all 15 patients. Although Libutti et al. appropriately focused their conclusion on the value of FDG-PET, their results regarding the use of the CEA scan—added to those in the literature—suggest that we should put the CEA scan to rest; unless the CEA scan can be improved, it simply should not be used to evaluate patients with suspected recurrent colorectal cancer.

FDG-PET previously has been used in patients with increasing CEA levels. Flanagan et al.⁴ reported on the use of FDG-PET in 22 patients with both abnormal CEA levels and normal conventional imaging studies. Overall,

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the positive predictive value was 89% (15 of 17) and the negative predictive value was 100% (5 of 5). The number of patients examined in the Flanagan study was small, and the design was not as precise as that of the Libutti et al. study; however, the combined data of the Flanagan and Libutti studies suggest that FDG-PET is useful in the evaluation of the colorectal cancer patient with an increasing CEA level.

The report by Libutti et al. will prove useful to clinicians, but it does raise questions. How do the investigators define "resectable?" Does carcinomatosis fall into the category of "resectable" because the NCI has a protocol for treatment of carcinomatosis? How do the investigators define resectable metastases in the liver? Do we have sufficient follow-up and numbers to demonstrate that their "resectable" group truly benefited by detection of disease? Conversely, how do the investigators define unresectable? What happened to this group? On a per patient basis, FDG-PET performed admirably. On a per lesion basis, the value of FDG-PET was not as obvious. Of the 119 lesions in the 28 patients, which lesions were missed by FDG-PET? Was there a difference in detection rates for patients with mucinous versus non-mucinous tumors? The literature suggests that mucinous tumors do not accumulate FDG differently than background. This is a well-designed small study with relatively short follow-up. Will the results change with longer follow-up and larger numbers? Finally, what is the cost? With the answers to these questions, FDG-PET scans probably will become part of the standard for imaging patients with colorectal cancer and suspected recurrent or metastatic disease. At the same time, it was not too long ago when CEA scintigraphy looked promising.

The study by Libutti et al. is well-designed and is useful in several respects. First, it gives useful data regarding the utility of FDG-PET in evaluating colon cancer patients with increasing CEA levels; it suggests that this technique can determine resectable versus unresectable disease. Second, it adds to the literature that unfortunately demonstrates the lack of utility of CEA scintigraphy. Finally, possibly the most important strength of the study is its design and execution. This study should be read in detail by all surgical investigators. The role of the second surgeon who did not know the results of the FDG-PET and CEA scans was invaluable and demonstrated the type of collaboration that is necessary to determine the added benefit of the technology to a thorough laparotomy. The investigators should be congratulated for executing this trial; the design and execution, as well as the results and conclusion, will further the science of clinical investigation.

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