

REVIEW

FDG–PET and colon cancer

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Date accepted for publication 18 December 2002

Abstract

Imaging colorectal cancer has become a major indication for positron emission tomography using fluorodeoxyglucose (FDG–PET). In primary diagnosis and staging, the role for this technique is limited but FDG–PET has proved highly accurate in the detection of recurrent tumour. The three main indications are (i) characterisation of a residual structural lesion after definitive therapy, (ii) pre-operative staging prior to resection of apparently isolated metastasis, and (iii) investigation of rising carcinoembryonic antigen (CEA) in a patient with normal structural imaging. The diagnostic accuracy of FDG–PET translates to changes in management in a large number of patients, resulting in improved cost-effectiveness. FDG–PET is fast becoming the standard of clinical care for patients with recurrent colorectal cancer.

Keywords: *Colonic neoplasms; recurrence; FDG–PET; tumour staging; cost-effectiveness.*

Introduction

Imaging colorectal cancer has become a major indication for positron emission tomography (PET), following the transition of this technology from the research arena into clinical practice. Colorectal cancer is the second commonest tumour to be evaluated at the Wesley PET centre, reflecting the high prevalence of this disease. PET is a functional imaging technique that exploits the increased glucose metabolism that occurs in colorectal cancer, and many tumours, by depicting the distribution of the radio-labelled glucose analogue, fluorine-18 fluorodeoxyglucose (^{18}F -FDG). The high impact of PET results from its ability to detect tumour foci too small to be confidently diagnosed by CT or other structural imaging methods. This ability arises from the fact that lesion detection on PET is determined by the magnitude of metabolic change in the tumour, rather than tumour size.

Following a 6-hour fast to normalise serum glucose levels, patients receive 185–370 MBq ^{18}F -FDG intravenously, with imaging performed 45–60 min later. Whole-body images are acquired using attenuation

correction to improve detection of deeply located lesions. Iterative algorithms should be used for image reconstruction to improve image quality and prevent streak artefacts from areas of high activity, such as excreted activity within the bladder. Combined PET/CT systems allow for more rapid attenuation correction and improved anatomical localisation of PET abnormalities in some cases.

Role of FDG–PET in primary diagnosis and staging

Primary colorectal cancers occasionally present as an incidental finding on FDG–PET, and FDG uptake has been reported in adenomatous polyps, a precursor to colon cancer^[1]. However, the presence of physiological gut uptake of FDG combined with false-positive uptake in inflammatory disease, along with low sensitivity to lesions less than 1 cm, precludes a significant role for FDG–PET in primary diagnosis or screening^[2]. There is evidence that FDG–PET is more accurate than CT

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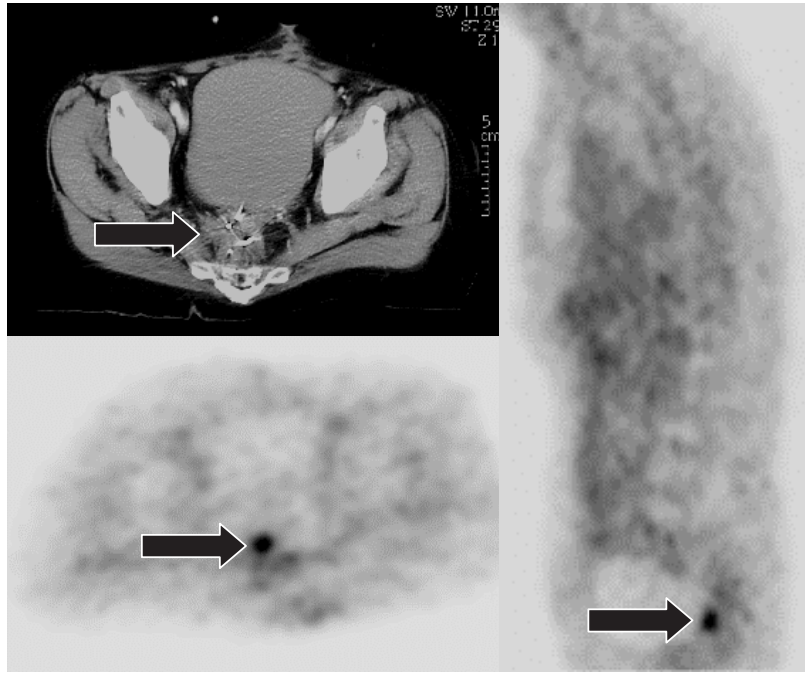


Figure 1 Pelvic recurrence of colorectal cancer on CT (top left) and FDG-PET: transaxial (bottom left) and sagittal (right) images.

in the primary staging of colorectal cancer. However, FDG-PET in this setting appears to have little impact on clinical management, due to the need for most patients to undergo surgical resection of the primary tumour in order to prevent subsequent bowel obstruction and due to the importance that the results of pathological staging have in determining prognosis and post-operative management.

Role of FDG-PET in recurrent colorectal cancer

Recurrence rates after apparently curative resection of colorectal cancer remain high, up to 40% in some series^[3]. Some patients will have a localised recurrence that is amenable to surgical resection and potential cure. The aim of imaging in such patients is to diagnose the local recurrence and confirm the absence of other disease sites that would preclude curative surgery. The performance of current imaging strategies in this setting has proved disappointing, with many patients thought suitable for surgery being found to have unresectable disease at operation^[4]. FDG-PET is proving to have a pivotal role in identifying those patients most likely to benefit from surgical intervention.

Characterisation of residual structural lesion after definitive therapy

Differentiation between pelvic recurrence and post-operative fibrosis after excision of rectal tumour can be problematic for CT and MRI (Fig. 1). A meta-analysis of

FDG-PET literature^[4] determined a 95% sensitivity and 97% specificity for PET in this setting, whilst a direct comparison of CT and FDG-PET reported sensitivity values of 52 and 91% for CT and PET respectively, along with enhanced specificity for PET (CT 80%, PET 100%)^[5]. Post-irradiation inflammatory change can result in falsely positive uptake with PET^[4], particularly within 6–12 weeks of therapy.

FDG-PET can also be useful in characterising hepatic or pulmonary lesions in patients who have previously undergone resection of colon cancer. Although FDG-PET often demonstrates hepatic metastases undetected by CT, the overall accuracy for PET is only marginally better than CT^[5–8]. This finding is partly due to the background hepatic uptake of FDG, which creates difficulty in diagnosing hepatic metastases, particularly for lesions less than 2 cm in diameter. For this reason, an FDG-PET scan that is negative for hepatic metastases should not be considered to exclude this diagnosis. There has been little research to investigate the factors that determine background hepatic uptake of FDG, although our experience suggests background levels of FDG activity are lower in patients with advanced disease and poor survival.

Pre-operative staging prior to resection of apparently isolated metastasis

Surgical resection of apparently isolated hepatic or pulmonary metastasis from colorectal cancer results in improved survival^[3]. Accurate pre-operative staging

of such patients is essential to avoid the morbidity of surgery for patients with otherwise unsuspected additional metastatic sites. There are now several reports indicating superiority of PET over CT in this clinical context^[5-8], the greatest benefit arising from detection of additional extra-hepatic tumour foci (Fig. 2). Comparative sensitivity values for extra-hepatic disease range from 58 to 74% for CT, vs. 90-100% for FDG-PET, whilst specificity values are similar for the two modalities. Exclusion of extra-hepatic metastases may also be useful prior to aggressive local treatments for hepatic metastases such as radiofrequency ablation or intra-arterial microsphere-based radiotherapy.

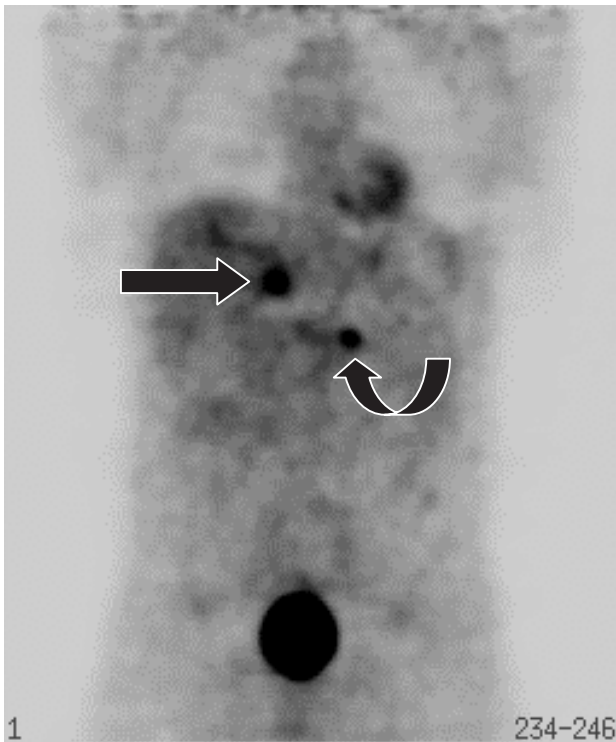


Figure 2 Coronal FDG-PET image in a patient with an hepatic metastasis from colorectal cancer (straight arrow). A retro-peritoneal deposit undetected by CT is also seen (curved arrow). (Note normal myocardial and bladder activity.)

Investigation of rising carcinoembryonic antigen (CEA) with normal structural imaging

The aim of imaging for patients with rising tumour markers is to identify a localised tumour recurrence that is potentially resectable with hope of a survival benefit. CT typically provides the initial investigation in such patients. However, when conventional imaging is negative, the positive yield of FDG-PET ranges between 38 and 77%^[5,9,10]. Although FDG-PET may reveal extensive inoperable disease in some cases, a localised tumour deposit potentially amenable to surgery is found in others. However, in a significant

proportion of these patients (25% in one series^[10]), PET is found to have underestimated the extent of disease at surgery. Also, false-positive diagnoses, most commonly inflammatory conditions, occasionally arise amongst patients investigated for a rising CEA^[9,10].

Therapeutic impact and cost-effectiveness

Demonstration of therapeutic impact and cost-effectiveness is becoming increasingly important in the evaluation of new diagnostic tests, and is often required before funding can be obtained from governments or health purchasers. A meta-analysis of PET literature in recurrent colorectal cancer concludes that management is altered in 29% (95% confidence interval 25-34%)^[4]. In most patients, FDG-PET results in upstaging of disease with deferment of surgery^[4,10]. Reported experience and modelling approaches, such as decision-tree sensitivity analysis, can demonstrate that these management changes translate to improved cost-effectiveness (Fig. 3).

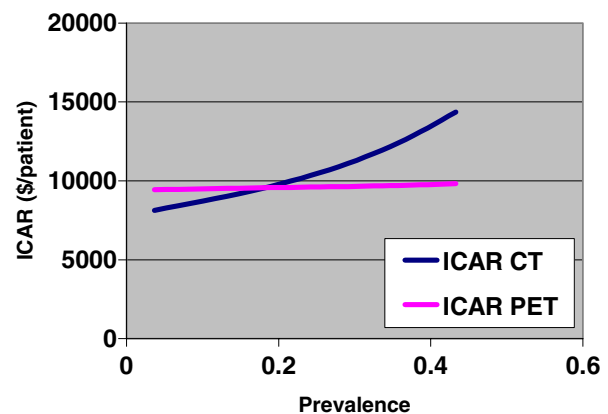


Figure 3 Results from a decision-tree sensitivity analysis for the use of FDG-PET to detect extra-hepatic metastases prior to resection of an apparently isolated hepatic metastasis. Using Australian medical costs, the graph plots the incremental cost-accuracy ratio (ICAR: i.e. the additional cost per additional correctly managed patient) against the prevalence of extra-hepatic disease for CT- and PET-based management strategies. PET is more cost-effective if the prevalence is above 0.18. (Typical reported prevalence values are 0.3 or greater).

Summary

FDG-PET demonstrates high accuracy in detection of recurrent colorectal cancer. This diagnostic performance leads to changes in clinical management for a significant proportion of patients, resulting in improved cost-effectiveness. FDG-PET is fast becoming the standard of clinical care for patients with known or suspected recurrence of colorectal cancer.

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