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Positron Emission Tomography Computed Tomography: A Guide for the General Radiologist

Clare Beadsmoore, MBBS, MRCP, FRCR*, David Newman, MBBS, FRCR, Duncan MacIver, MBChB, FRCR, Davina Pawaroo, MBChB, MRCP, FRCR

Department of Radiology, Norfolk & Norwich University Hospital, Norwich, United Kingdom

Abstract

Cancer remains a leading cause of death in Canada and worldwide. Whilst advances in anatomical imaging to detect and monitor malignant disease have continued over the last few decades, limitations remain. Functional imaging, such as positron emission tomography (PET), has improved the sensitivity and specificity in detecting malignant disease.

In combination with computed tomography (CT), PET is now commonly used in the oncology setting and is an integral part of many cancer patients' pathways. Although initially the CT component of the study was purely for attenuation of the PET imaging and to provide anatomical coregistration, many centers now combine the PET study with a diagnostic quality contrast enhanced CT to provide one stop staging, thus refining the patient's pathway.

The commonest tracer used in everyday practice is FDG (F18-fluorodeoxyglucose). There are many more tracers in routine clinical practice and those with emerging roles, such as 11C-choline, useful in the imaging of prostate cancer; 11C-methionine, useful in imaging brain tumours; C11-acetate, used in imaging hepatocellular carcinomas; 18F-FLT, which can be used as a marker of cellular proliferation in various malignancies; and F18-DOPA and various 68Ga-somatostatin analogues, used in patients with neuroendocrine tumours. In this article we concentrate on FDG PETCT as this is the most commonly available and widely utilised tracer now used to routinely stage a number of cancers.

PETCT alters the stage in approximately one-third of patients compared to anatomical imaging alone. Increasingly, PETCT is being used to assess early metabolic response to treatment. Metabolic response can be seen much earlier than a change in the size/volume of the disease which is measured by standard CT imaging. This can aid treatment decisions in both in terms of modifying therapy and in addition to providing important prognostic information. Furthermore, it is helpful in patients with distorted anatomy from surgery or radiotherapy when there is suspicion of recurrent or residual disease.

FDG PETCT is not specific for malignancy and can also be used for diagnosing and monitoring a number of inflammatory and infectious conditions that can be difficult to diagnose on anatomical imaging, some of which carry significant morbidity. FDG PETCT is increasingly used in patients with pyrexia of unknown origin and in patients with metastatic malignancies of unidentified primary on conventional imaging. This article reviews the uses of PETCT including an overview of the more common incidental lesions and conditions. It also provides guidance of how to approach a PETCT as a nonradionuclide radiologist and how to interpret a study in the multidisciplinary team setting.

Résumé

Le cancer est l'une des principales causes de mortalité au Canada et ailleurs. Malgré des avancées en matière d'imagerie anatomique visant la détection et la surveillance des affections malignes au cours des dernières décennies, certaines limitations subsistent. L'imagerie fonctionnelle, comme la tomographie par émission de positrons (TEP), a mené à une sensibilité et spécificité diagnostiques accrues des affections malignes.

Conjointement à la tomodensitométrie, la TEP est désormais couramment utilisée en oncologie et fait partie intégrante du cheminement clinique de nombreux patients atteints d'un cancer. Initialement, le recours à la tomodensitométrie avait uniquement pour but les corrections d'atténuation pour la TEP et de permettre la coregistration de l'image anatomique, mais de nombreux centres combinent aujourd'hui la TEP à une TDM avec injection de produit de contraste de qualité diagnostique pour permettre la stadification en une seule étape et ainsi simplifier le cheminement clinique du patient.

Le marqueur le plus couramment utilisé dans la pratique quotidienne est le fluorodésoxyglucose (^{18}F) (^{18}F-FDG). Il existe de nombreux autres marqueurs utilisés dans la pratique clinique courante ou émergents, comme la choline (^{11}C), utilisée en imagerie du cancer de la

* Address for correspondence: Clare Beadsmoore, MBBS, MRCP, FRCR, Department of Radiology, Colney Lane, Norwich, Norfolk NR4 7UY, United Kingdom.

E-mail address: clare.beadsmoore@nnuh.nhs.uk (C. Beadsmoore).

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prostate, la méthionine (^{11}C), utilisée en imagerie des tumeurs du cerveau, l'acétate (^{11}C), utilisé en imagerie des carcinomes hépatocellulaires, le ^{18}F-FLT, qui peut servir de marqueur de la prolifération cellulaire de diverses affections malignes, ainsi que le ^{18}F-dopa et diverses substances analogues à la somatostatine (^{68}GA), utilisées chez les patients atteints de tumeurs néoendocrines. Le présent article porte plus précisément sur la TEP-TDM avec ^{18}F-FDG, puisqu'il s'agit du marqueur le plus facilement accessible et le plus couramment utilisé pour établir le stade d'un certain nombre de cancers.

La TEP-TDM vient modifier le stade chez le tiers environ des patients comparativement à l'imagerie anatomique utilisée seule. Elle est de plus en plus utilisée pour évaluer la réponse métabolique précoce au traitement. La réponse métabolique peut être détectée beaucoup plus tôt que la variation de la taille ou du volume de la tumeur, laquelle est mesurée par TDM standard. En plus de fournir d'importantes données pronostiques, la TEP-TDM peut faciliter les décisions relatives à la modification du traitement. Elle est de plus utile chez les patients qui présentent une déformation anatomique en raison d'une chirurgie ou d'une radiothérapie et chez qui on soupçonne la présence de tumeurs résiduelles ou récidivantes.

Le recours à la TEP-TDM avec ^{18}F-FDR ne se limite pas aux affections malignes. Cette technique peut également être utilisée pour diagnostiquer et traiter diverses maladies inflammatoires et infectieuses qui sont difficiles à diagnostiquer par imagerie anatomique et dont certaines présentent un taux élevé de morbidité. Elle est de plus en plus utilisée chez les patients souffrant d'une fièvre d'origine inconnue et chez ceux qui présentent des affections malignes métastatiques provenant de sites primaires non détectées par examen d'imagerie classique. Le présent article examine le recours à la TEP-TDM et passe en revue les lésions et affections accessoires les plus courantes. Il présente également des directives à l'intention des radiologistes non spécialisés en imagerie isotopique et concernant l'interprétation d'une étude par une équipe multidisciplinaire.

Key Words: Positron emission tomography computed tomography; Positron emission tomography/computed tomography; F18-fluorodeoxyglucose; Radionuclide; Oncology

Cancer remains the leading cause of death in Canada, accounting for nearly 30% of all deaths [1], despite recent medical advances. For the last 100 years, since Wilhelm Roentgen produced and detected the first x-ray in 1895, we have used anatomical imaging to detect cancer and monitor its response to treatment. Anatomical imaging whilst useful has limitations. It can identify masses but small tumour deposits are often not detectable when surrounded by normal tissue or when the normal anatomy is distorted by previous surgery. The sensitivity of detecting metastatic lymph nodes is notoriously limited with conventional cross-sectional anatomical imaging using size-based criteria. For example, sensitivities of 55% have been reported for detecting colorectal nodal metastases on computed tomography (CT) [2]. When trying to assess response of tumours to therapy, anatomical imaging is often slow to demonstrate a change and with the increasing use of cytostatic drugs is unable to demonstrate their efficacy at all.

There are many different functional alterations in cancer cells including increased glucose metabolism and amino acid transport, increased protein, membrane and DNA synthesis, overexpression of receptors and antigens, and increased blood flow. It is these properties of cancer cells that functional imaging seeks to exploit. The most widely available, broadly applicable functional imaging technique worldwide is F18-fluorodeoxyglucose (FDG) positron emission tomography (PET); this is combined with CT to create a hybrid imaging modality. The technique involves the intravenous injection of FDG, which is taken up by cells, incorporated into the metabolic cycle and metabolized to FDG-6-phosphate. It cannot be metabolized further by glucose-6-phosphate isomerase and becomes trapped in the cell. The amount of glucose and its analogue FDG that gets taken up into a cell is dependent on the cell's metabolic activity, GLUT1 receptor expression on the cell surface membrane and levels of glucose phosphorylation enzyme type II (hexokinase II). The majority of cancer cells are highly metabolically active, preferentially using glucose, and thus have a relative over expression of GLUT1 receptors which are responsible for the movement of glucose and hence also FDG across the cell membrane [3]. Increased levels of hexokinase II with a relative decrease in the levels of glucose-6-phosphatase in cancer cells leads to accelerated glucose phosphorylation and hence increased glucose metabolism [4].

FDG is a positron emitter. Positrons are positive electrons (antimatter electrons), and do not travel far (1 mm) before they collide with negatively charged electrons resulting in an annihilation reaction producing 2 high energy gamma ray photons (511 KeV) at 180° to one another. Patients are imaged lying supine in a ring of detectors. A computer registers the counts that occur within a narrow time frame (coincidence imaging), at 180° to one another (ie, only photons which trigger the opposite detectors in the ring will be counted). A greyscale image is then constructed from the data acquired. In addition a low-dose nonenhanced CT or contrast enhanced diagnostic CT is performed, depending on the local protocols. The CT data set is used to attenuation correct the PET data to compensate for the fact that the human body is not a tube of uniform size and density. It has the additional advantage of providing anatomical coregistration for the functional PET scan. This improves the specificity of the PET scan interpretation by accurately identifying the site of uptake [5].