J Cancer Res Clin Oncol (2000) 126:560–574

REVIEW

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Positron emission tomography with 2-[^{18}F]fluoro-2-deoxy-D-glucose in oncology

Part II. The clinical value in detecting and staging primary tumours

Received: 7 December 1999 / Accepted: 1 February 2000

Abstract The tumoral uptake of 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}FdGlc) is based upon enhanced glycolysis. Positron-emission tomography (PET) using ^{18}FdGlc provides the physiological and metabolic information. ^{18}FdGlc PET has been used successfully for assessing primary tumours and metastases, prognosis, and planning and for monitoring tumour therapy as well as for early detection of recurrent tumour growth. This review summarises the uptake mechanism of ^{18}FdGlc in benign and malignant lesions, its relation to histolopathology, and its clinical value for detecting and staging primary tumours.

Key words Fluorodeoxyglucose · Positron-emission tomography · Tumour

Introduction

Over the past decade nuclear medicine techniques have been developed for evaluating biochemical and physiological characteristics of tumours such as blood flow, glucose metabolism and receptor status. These techniques have added unique functional information to the anatomical characterisation of disease provided by conventional imaging methods including radiography, ultrasonography, computed tomography and magnetic resonance imaging.

Positron-emission tomography (PET) using 2-[^{18}F]-fluoro-2-deoxy-D-glucose (^{18}FdGlc) is a technique being used for the assessment of primary tumours and metastases, prognostic stratifications and planning and monitoring of tumour therapy, as well as for the early detection of recurrent tumour growth. This review summarises the uptake mechanism of ^{18}FdGlc in benign and malignant lesions and its relation to histolopathology. Furthermore, we discuss its present and clinical value in detecting and staging primary tumours.

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^{18}FdGlc uptake mechanism

Use of the ^{18}FdGlc in tumour imaging is based on the observations by Warburg in the 1920s that neoplastic cells exhibit increased glucose metabolism compared with normal cells, and that this increased glucose utilisation is greatest in the most rapidly growing tumours (Warburg 1956). The increased glucose metabolism was primarily thought to be solely the result of increased glucose uptake, in fact, this altered uptake was demonstrated in experiments with mouse cells infected with murine sarcoma virus (Hatanaka 1974). Just like glucose, ^{18}FdGlc uptake in cells is followed by phosphorylation to ^{18}FdGlc 6-phosphate (^{18}FdGlc-6-*P*) by hexokinase, the first enzyme of glycolysis. In contrast with glucose, however, glucose-6-phosphate isomerase does not react with ^{18}FdGlc-6-*P*, so further metabolism is not possible. In addition, ^{18}FdGlc-6-*P* is cleared slowly from the cell because of low membrane permeability. Owing to a very low concentration of glucose-6-phosphatase in the cell, degradation of ^{18}FdGlc-6-*P* is minimal, resulting in the accumulation of ^{18}F activity. This trapping of ^{18}FdGlc in the malignant cells is the rationale for its common use in PET imaging (Gallagher et al. 1978).

The uptake of glucose and ^{18}FdGlc into malignant cells is facilitated by an increased expression of glucose transporter (GLUT) molecules at the tumour cell surface. There is experimental evidence that malignant transformation results in an increased expression of the gene encoding the glucose transport system (Flier et al.

1987). As a result, the membrane of transformed cells contains a large number of glucose transporters compared with normal cells. The rapid and high glucose uptake by the glucose transporters correlates with the high glycolytic activity of tumour cells (Oheir 1999). Seven genes encoding glucose transporters are currently known (*GLT1–7*). However, it has been suggested that overexpression of the *GLUT1* and *GLUT3* genes is responsible for increased uptake of glucose in malignancies (Yamamoto et al. 1990). Increased expression of GLUT-1 is also seen in conditions that induce greater dependence on glycolysis as an energy source, such as ischaemia, hypoxia or both (Minn et al. 1993; Wahl and Clavo 1993). These data suggest that overexpression of GLUT-1 may have an important role in the survival of cancer cells by promoting an adequate supply of energy to support their high metabolism and fast growth in an often less than ideal physiological environment (Clavo et al. 1995; Kalff et al. 1992). Brown et al. (1996) assessed the relationship between GLUT-1 and ^{18}FdGlc uptake in a rat mammary cancer, an animal tumour model that closely mimics human breast carcinoma. ^{18}FdGlc uptake in areas of high cancer cell density was consistently higher than the average tumour uptake. There was a positive correlation between estimates of ^{18}FdGlc uptake and the intensity of staining of the GLUT-1 antigen. Overexpression of the GLUT-1 was also demonstrated by Reske et al. (1997) in pancreatic carcinoma. A detailed overview of the biological factors influencing ^{18}FdGlc accumulation in tumour has been published as the preceding paper in this journal forming part I of this series of three articles (Pauwels et al. 2000).

^{18}FdGlc uptake in benign and malignant lesions

The distribution of ^{18}FdGlc is not limited to malignant tissue. Kubota et al. investigated its uptake in mouse tumours with microautoradiography (Kubota et al. 1992). Newly formed granulation tissue and macrophages, which were massively infiltrating the marginal areas surrounding necrotic area of the tumour, showed a higher ^{18}FdGlc uptake than viable tumour cells, suggesting that this uptake may be associated with the inflammatory reaction. A maximum of 29% of the glucose used was derived from non-tumour tissue within the tumour. In a study by Brown et al. (1995), using a breast carcinoma animal model, cancer cells were found to be the main site of uptake, with about 20% occurring in non-neoplastic components. Yamada et al. (1995) studied the ^{18}FdGlc accumulation in experimental inflammatory tissue in rats. The highest concentration was seen in areas with fibroblasts, endothelial cells from blood vessels, macrophages, and neutrophils. The ^{18}FdGlc uptake may be variable, as the number of macrophages within the same tumour type may vary substantially (Steele et al. 1985).

The uptake of ^{18}FdGlc in metabolically active macrophages would explain its increased accumulation in benign inflammatory lesions. Although the exact uptake mechanism of ^{18}FdGlc in infectious diseases is still not fully elucidated, accumulation has been demonstrated in abscesses (Strauss 1996; Tahara et al. 1989), sinusitis (Yasuda et al. 1998a), and acute pancreatitis (Shreve 1998). Healing bone (Meyer et al. 1994) and osteoarthritis (Delbeke 1999) also may demonstrate ^{18}FdGlc uptake. Active granulomatous diseases, such as tuberculosis, and also sarcoidosis cause high ^{18}FdGlc uptake (Lewis and Salama 1994; Strauss 1996). The amount of ^{18}FdGlc accumulation in sarcoidosis probably reflects disease activity, as the uptake was found to decrease during anti-inflammatory therapy (Brudin et al. 1994). Diffuse thyroidal ^{18}FdGlc uptake may be a sign of subclinical chronic thyroiditis or Hashimoto's thyroiditis (Yasuda et al. 1998b).

Although, the mechanisms associated with increased ^{18}FdGlc uptake during hypoxia are not certain, the uptake in prenecrotic or hypoxic cells in tumour is high. In vitro studies by Clavo et al. (1995) showed that hypoxia increases the cellular uptake of ^{18}FdGlc in different malignant human cell lines (HTB 63 melanoma and HTB 77 IP3 ovarian carcinoma). Immunochemical assays showed an increase in the membrane expression of GLUT-1 transporter in cells exposed to hypoxia. The uptake of ^{18}FdGlc into tumour cells was evaluated in a normoxic and a hypoxic atmosphere (Clavo and Wahl 1996). Again, ^{18}FdGlc uptake in both cell lines increased significantly (23% and 38% respectively) over normoxic levels when cells were exposed to moderate hypoxia. Relevant ^{18}FdGlc uptake by non-malignant elements of the tumour will increase the detectability of smaller tumours in pre-treatment evaluation, but increments of activated macrophages and prenecrotic/hypoxic cells may induce a higher uptake even in the presence of non-viable tumour cells. Furthermore, treatment may induce hypermetabolic inflammatory changes, making it difficult to differentiate between persistent tumour and treatment effects (Haberkorn et al. 1991a). In sarcomas treated with combined radiotherapy and hyperthermia, well-defined central regions where uptake is absent as well as a reduction of peripheral uptake were seen on ^{18}FdGlc PET images 1–3 weeks after the start of therapy (Hautzel and Muller-Gartner 1997).

Distribution of the ^{18}FdGlc is affected by high blood glucose levels. In hyperglycaemia, ^{18}FdGlc competes with blood glucose, resulting in its decreased accumulation in neoplastic cells (Wahl et al. 1992). PET studies are generally performed when the subject is in a fasting state. Insulin-induced hypoglycaemia may impair tumour identification by reducing tumour uptake and increasing the background muscle activity (Torizuka et al. 1997).

Normal distribution of ^{18}FdGlc

In tissues with a low concentration of glucose-6-phosphatase, such as the brain and myocardium, ^{18}FdGlc-6-*P*

accumulates intracellularly in proportion to the glycolytic rate of the cell. Some tissues, such as liver, spleen, bone marrow, kidney, intestine and muscle may have different levels of glucose-6-phosphatase, and therefore do not accumulate ^{18}FdGlc-6-*P* to the same extent.

The brain uses glucose as its substrate; therefore, ^{18}FdGlc accumulation is normally high especially in the cortex, basal ganglia and thalamus. The total uptake in the brain is approximately 6% of the injected dose. Normal myocardial uptake of ^{18}FdGlc, approximately 4% of the injected dose, depends on free fatty acids and glucose. After eating, the myocardium preferentially uses glucose. When the chest is evaluated with ^{18}FdGlc to assess the presence of malignant lesions, a long fasting state (12 h) is preferable to avoid artefacts caused by cardiac ^{18}FdGlc uptake (Delbeke 1999; Shreve et al. 1999). In the resting state, there is little accumulation of ^{18}FdGlc in the muscular system but, after exercise, its increased accumulation in selected muscular groups may obscure the interpretation (Shreve et al. 1999). Exercise should be prohibited on the day of scanning to avoid muscle artefacts, and benzodiazepines may used to abolish the characteristic paraspinal and posterior cervical muscle uptake often seen in tense patients (Barrington and Maisey 1996). ^{18}FdGlc appears to accumulate in laryngeal muscles in proportion to contractile activity during speech (Kostakoglu et al. 1996). Because ^{18}FdGlc is excreted in the urine, intense ^{18}FdGlc activity is encountered in the intrarenal collecting system, ureters and bladder. This may interfere with the study of renal or pelvic tumours either by obscuring local tumours or by causing reconstruction artefacts. Also the gastrointestinal system may show uptake of ^{18}FdGlc, which is partly due to smooth-muscle activity. It is most noticeable in the large bowel and, to a lesser extent, in the stomach and small intestine (Cook et al. 1996). Glandular breast tissue often demonstrates moderate uptake of ^{18}FdGlc in premenopausal women. After menopause there is little breast activity, but women on oestrogen-replacement therapy may also show enhanced ^{18}FdGlc uptake (Cook et al. 1999). ^{18}FdGlc accumulation can be observed in the uterus during menstruation (Yasuda et al. 1997). Lymphoid tissue may demonstrate significant uptake of ^{18}FdGlc and the normal appearance of the tonsils and adenoids must be recognised. It is also possible that coecal activity, which is often seen as a normal variant, may in part be due to lymphoid tissue present in this region (Cook et al. 1999).

^{18}FdGlc uptake and the relation to histopathology

Malignancy grade is determined by mitotic rate, differentiation, and the amount of necrosis (Coindre et al. 1986). In patients with soft-tissue tumours, a clear relation was found between the amount of ^{18}FdGlc uptake and malignancy grade (Adler et al. 1991; Griffeth et al. 1992; Nieweg et al. 1996). Low-grade tumours have lower ^{18}FdGlc uptake than intermediate- and high-grade tumours. No significant difference was found between intermediate- and high-grade tumours. Nieweg et al. (1996) found a correlation between the histopathological malignancy grade and median glucose consumption measured by ^{18}FdGlc PET in 18 patients with soft-tissue sarcomas. In patients with intracranial tumours, ^{18}FdGlc uptake was shown to be related to the malignancy grade, which in brain tumours merely depends on differentiation (Watanabe et al. 1989). Watanabe et al. investigated glucose utilisation in rat brain tumours, using an autoradiographic technique, and reported that the malignancy grade of the tumour correlates with glucose utilisation (Watanabe et al. 1989). Patronas et al. (1982) have shown that high-grade astrocytomas (III and IV) demonstrate a higher glucose consumption, measured by ^{18}FdGlc PET in patients with cerebral gliomas, than that of low-grade (I and II) gliomas. Also in liver cancer, uptake of ^{18}FdGlc is higher in poorly differentiated tumours (Okazumi et al. 1992). Yoshioka et al. demonstrated that ^{18}FdGlc uptake in various gastrointestinal tumours increases with the loss of differentiation. However, no correlation was found between the ^{18}FdGlc uptake and the differentiation grade in patients with head and neck cancer and in patients with breast cancer (Crove et al. 1994; Minn et al. 1988).

The amount of ^{18}FdGlc uptake in primary lung lesions has been shown to have a direct relation to tumour growth rate (Duhaylongsod et al. 1995). Immnunohistochemical analysis of cell membrane glucose transporters (GLUT-1 and GLUT-3) demonstrated that protein overexpression was correlated with a poor prognosis (Younes et al. 1997). These data suggest that tumours with increased glucose uptake are more metabolically active and more biologically aggressive.

Minn et al. (1988) compared the ^{18}FdGlc tumoral uptake with the nuclear DNA content and the percentage of proliferative cells (S + G2/M), measured by flow cytometry in patients with head and neck tumours. There was a distinct correlation between the degree of ^{18}FdGlc accumulation and the proportion of the cells in the S + G2/M phases of the cell cycle. The ^{18}FdGlc uptake by tumours also correlated with the percentage of S-phase cells. Haberkorn et al. (1991b) also reported that ^{18}FdGlc uptake correlated with the proliferation rate of squamous cell carcinoma of the head and neck region. Initially it was suggested that the increase in glucose utilisation is mainly needed for nucleic acid synthesis (Minn et al. 1988; Watanabe et al. 1989) and that enhanced glucose metabolism, measured by the ^{18}FdGlc uptake, is associated with the proliferative activity of the tumour. However, larger changes in proliferation rate resulted in only moderate changes in ^{18}FdGlc uptake (Higashi et al. 1993; Slosman et al. 1993). Therefore, these data suggest that the glucose uptake is not directly regulated by the need for DNA synthesis (Haberkorn et al. 1991). Beside proliferation, other factors probably play a major role in the ^{18}FdGlc uptake in tumours. From these results it was

hypothesised that the number of viable tumour cells is another major determinant in ^{18}FdGlc accumulation.

Clinical applications of ^{18}FdGlc PET in staging primary tumours

Lung cancer

Lung cancer is a leading cause of death in many countries, and its incidence is increasing globally. The disease now claims approximately 150 000 lives each year in the U.S. (Magrath and Litvak 1993). Most patients present with advanced disease. Despite aggressive treatment protocols, the 5-year survival rate of patients with lung cancer is still approximately 14% and has not changed over the past several years (Boring et al. 1993). The classification of lung cancer by the World Health Organisation is widely accepted (Ginsberg et al. 1997). Small-cell lung cancer (SCLC) accounts for 17%–29% of all lung cancers, and it has almost always spread systemically by the time of diagnosis. Non-small-cell lung cancer (NSCLC) accounts for 70% of all lung cancers. Squamous cell carcinoma, the most common type of NSCLC, tends to be slow growing (Ginsberg et al. 1997). Adenocarcinoma, the second most common type, arises from alveolar surface epithelium or bronchial mucosal glands. Most adenocarcinomas are peripheral in origin (Ginsberg et al. 1997). Large-cell carcinoma is the least common type of NSCLC, the prognosis of large-cell undifferentiated carcinomas being similar to that of adenocarcinoma (Ginsberg et al. 1997). Staging of these tumours by the anatomical measures of primary lung tumour (T), regional lymph nodes (N), and metastases (M) has been used in the management of lung cancer.

Patients who have lung cancer often present with solitary pulmonary nodules on chest radiographs obtained as preoperative evaluations or as part of routine physical examinations (Coleman 1999). Further radiographic evaluation is often performed with computed tomography (CT) and magnetic resonance imaging (MRI) of the chest. Chest radiography, CT and MRI provide anatomical and morphological information, but do not accurately characterise abnormalities as benign or malignant. Therefore, the diagnosis has to be established by cytology or biopsy.

The presence of nodules or non-specific opacities as well as mediastina and hilar changes suggesting the lymphadenopathy on chest radiography can indicate malignancy. CT can detect smaller lesions than those detected by chest radiography. In addition, it can determine the invasiveness of the tumour into the chest wall, vertebrae or mediastinum, which can also be used to stage the extent of disease. Any lymph node greater than 1 cm in diameter is regarded as abnormal. CT can also detect the distant metastases to the liver, adrenal glands and brain (Coleman 1999). Bronchoscopy achieves a sensitivity of only 65% in the detection of malignant nodules, whereas transbronchoscopic biopsy increases the sensitivity to only 79% (Salathe et al. 1992). The most accurate method for staging the superior mediastinal lymph nodes is mediastinoscopy. Peripheral lesions can be biopsied percutaneously with the help of CT guidance. CT-guided transthoracic fine-needle aspiration has a sensitivity and specificity of 94% and 91% respectively (Salathe et al. 1992). Video-assisted thoracoscopy can be used to excise peripheral nodules for histological evaluation (Ginsberg et al. 1997).

An accurate and non-invasive diagnostic test could avoid the morbidity and cost of invasive tissue sampling. After identification of a pulmonary abnormality by an anatomical study, ^{18}FdGlc PET imaging could be performed to evaluate the metabolic activity of the lesion in an attempt to distinguish a benign from a malignant process. In the first account of this procedure, Dewan et al. (1993) reported a sensitivity and a specificity of 95% and of 80%, respectively, in the assessment of focal pulmonary nodules with ^{18}FdGlc PET. Patz et al. (1993) investigated focal opacities that could not be characterised as benign or malignant by chest radiography or CT in 51 patients. The sensitivity and specificity of ^{18}FdGlc PET for malignancy were found to be 100% and 89% respectively. In a prospective multicentre study of 89 patients who underwent evaluations of solitary pulmonary nodules where malignancy could not be determined, ^{18}FdGlc PET had an overall sensitivity and specificity of 92% and 90% respectively (Lowe et al. 1998). They reported that the sensitivity and specificity were not statistically significantly different when nodules 0.7–1.5 cm in diameter and greater than 1.5 cm in diameter were compared. In a study by Gupta et al., sensitivity, specificity, and positive predictive value were 93%, 88% and 92% respectively (Gupta et al. 1996). The overall sensitivity, specificity and accuracy of ^{18}FdGlc PET in differentiating benign from malignant lesions range from 82% to 100%, from 75% to 100% and from 79% to 94% respectively (Dewan et al. 1993; Gupta et al. 1996; Lowe et al. 1998; Patz et al. 1993).

False-negative ^{18}FdGlc PET scans have been reported to occur in primary pulmonary carcinoid tumours (Gupta et al. 1996) and in bronchoalveolar lung cancers (Higashi et al. 1998). ^{18}FdGlc PET established four false negatives in seven bronchoalveolar lung carcinomas. The carcinoid tumours are slow-growing and demonstrate a minimal mitotic rate. The authors reported that these cancers have a less proliferative potential and longer mean doubling times than NSCLC. Although the sensitivity for detecting lung malignant lung lesions is high, it is less than optimal. Some active infectious or inflammatory lesions, such as tuberculous granulomas, cryptococcosis, histoplasmosis and other infections, may result in false positive PET scans in assessing the focal opacities (Lowe and Naunheim 1998).

While gross invasion of the mediastinum and major structures such as chest wall, pleura, diaphragm, spine, or large vessels can be easily demonstrated with CT and MRI, assessment of subtle invasion of the mediastinum

remains a problem. In a comparative study on the evaluation of chest wall invasion, Yokozaki et al. found a sensitivity, specificity and accuracy of 67%, 75% and 73%, respectively, for MRI, 67%, 63% and 64%, respectively, for CT and 33%, 75% and 64%, respectively, for ultrasonography (Yokozaki et al. 1997). However, ^{18}FdGlc PET is also not very accurate in determining even gross invasion into adjacent structures (Lowe and Naunheim 1998). The identification of pleural metastasis is perhaps the most useful, if highly frequent, discovery that can be made accurately by PET imaging when dealing with the determination of the T status. Consequently, an anatomical imaging modality remains necessary for treatment planning.

The amount of ^{18}FdGlc uptake in primary lung lesions has been shown to have a direct relation to tumour growth rate. Duhaylongsod et al. found that the standardised uptake value (SUV) was significantly correlated with tumour doubling time (Duhaylongsod et al. 1995). These data suggest a direct relation between tumour growth and ^{18}FdGlc uptake in lung cancer. Ahuja et al. (1998) documented a relationship between prognosis and the amount of ^{18}FdGlc uptake in nodules of patients with lung cancer. SUV were calculated for primary lesions on the basis of PET evaluation and these were correlated with clinical information to determine prognostic significance. In 76% of the patients with primary lung lesions, SUV < 10 was calculated. In this group, the median survival was 24.6 months. In 24% of the patients with SUV > 10, the median survival was 11.4 months. Multivariate analysis demonstrated that SUV > 10 provided prognostic information, which was independent of the clinical stage and lesion size. These data show that the amount of ^{18}FdGlc uptake within the primary tumour lesion correlates with survival.

Staging of lung cancer requires accurate evaluation of the mediastinum. Mediastinoscopy is the most reliably technique for staging lung cancer, and has a sensitivity of 87%–91% (Patterson et al. 1987). CT and MRI have a sensitivity of 52% and 48% and a specificity of 69% and 64%, respectively, for evaluation of the mediastinum (Webb et al. 1991). ^{18}FdGlc PET is superior to CT for the assessment of mediastinal lymph node involvement. Sasaki et al. (1996) found a sensitivity of 76%, a specificity 98% and an accuracy of 93% for ^{18}FdGlc PET in the assessment of mediastinal lymph node involvement. On the other hand, for CT a sensitivity of 65% and specificity of 87% and an accuracy of 82% were observed. In another study (Tatsumi et al. 1999), ^{18}FdGlc PET was 100% sensitive, 84.2% specific and 87% accurate in the evaluation of mediastinal involvement. Since nodal size is the only useful criterion for evaluating lymph node metastases, CT and MRI show a similar, poor accuracy in lymph node staging resulting from both low sensitivity (normal-sized nodes may contain micrometastases) and low specificity (enlarged lymph nodes may be reactive).

Whole-body PET imaging can be used to assess the distant metastases and provides information that can not be obtained by any other radiological technique. Bury et al. (1997) found a sensitivity of 100%, a specificity of 94% and an accuracy of 96% for the detecting distant metastases in lung cancer. In a study by Valk et al. (1995), previously unsuspected metastases were identified in 11% of 99 patients with lung cancer using whole-body PET imaging. In addition, normal PET findings were obtained at sites assessed to be malignant by CT in 19 patients. Lung cancer frequently leads to metastases in the adrenal glands and benign enlargement of the adrenal glands is difficult to distinguish from metastatic disease in patients with lung cancer. Some studies have shown that ^{18}FdGlc PET imaging is able to differentiate between benign enlarged glands and those containing malignancy (Boland et al. 1995; Maurea et al. 1996). Erasmus et al. (1997) showed a 100% sensitivity and an 80% specificity for detecting metastases in the adrenal glands with PET. Unenhanced CT scans revealed a sensitivity and specificity of 96% and 73%, respectively, for detecting metastatic disease at these sites (Korobkin et al. 1996). Finely, Schwartz et al. (1997) reported that MRI can distinguish benign from malignant enlarged adrenal glands with nearly 100% accuracy.

Because of the high cost and limited availability of ^{18}FdGlc PET, alternative methods to detect the high-energy photons (511 keV) of positron emitters have been sought. Weber et al. (1999) have reported that using a ^{18}FdGlc coincidence-mode gamma camera (GCI) is an accurate technique for differentiating between benign and malignant pulmonary lesions. In 96 patients with lung disease, an overall sensitivity of 97% and specificity 80% was achieved. False positive results were due to inflammatory processes. Tatsumi et al. demonstrated that ^{18}FdGlc GCI yielded results comparable to ^{18}FdGlc PET in a visual analysis to detect pulmonary lesions and lymph node metastases. However, lesion-to-background contrasts were lower in ^{18}FdGlc GCI than those in ^{18}FdGlc PET (Tatsumi et al. 1999). Stokkel et al. (1999a) assessed the feasibility of mediastinal lymph node staging with a dual-headed PET camera in 33 newly diagnosed patients with primary NSCLC. ^{18}FdGlc GCI is considerably more sensitive and specific than CT for the assessment of individual lymph node involvement. A sensitivity of 90% and a specificity of 97% for ^{18}FdGlc GCI in assessing lymph node involvement are values comparable to those reported in the literature on dedicated PET cameras (Chin et al. 1995; Guhlmann et al. 1997; Sazon et al. 1996).

Breast cancer

Breast cancer is the commonest malignancy in women, with an estimated incidence in the US of 180 000 cases (Landis et al. 1999). In most patients, physical examination or mammography contributes to the clinical diagnosis of breast cancer. However, despite the important role of mammography as a screening and diagnostic tool, it is of limited value in several situations such as

detecting malignancy in women with dense breasts or with breast implants, early detection of tumour recurrence after surgery, and monitoring response to therapy. Recently, breast MRI has attracted significant attention and initial results are very promising.

Several reports have shown that ^{18}FdGlc PET scanning is both sensitive and specific in detecting primary breast cancers and differentiating cancers from benign lesions. Reported sensitivities have ranged from 66% to 96% and specificities from 83% to 100% (Adler et al. 1993; Avril et al. 1996b; Moon et al. 1998; Scheidhauer et al. 1996; Tse et al. 1992; Wahl et al. 1991). According to these studies, the main advantage of ^{18}FdGlc PET over other currently used imaging techniques is its high specificity. Although false-positive results may occur, especially in patients with inflammatory processes such as a breast abscess, mastitis, or early after biopsy and surgery (Kubota et al. 1992), these conditions are often easily clinically recognised. Sensitivity in the detection of small lesions is limited by partial volume effects (Avril et al. 1996b). In most published reports, the cancers detected were at least 1 cm in diameter (Adler et al. 1993; Scheidhauer et al. 1996; Tse et al. 1992; Wahl et al. 1991) and the majority of false-negative results occurred in tumours with a diameter below 1 cm.

Slowly growing or well-differentiated tumours, such as tubular carcinomas (Nieweg et al. 1993) and ductal carcinoma in situ (Avril et al. 1996a), often show less ^{18}FdGlc uptake than the more common invasive ductal carcinoma. The glycolytic rate of these tumours is not sufficiently different from that of normal breast tissue to permit reliable detection of these lesions by ^{18}FdGlc PET (Tse et al. 1992).

Mammographic evaluation of postsurgical breast tissue, particularly in patients who have had a lumpectomy or excisional biopsy and in patients with augmented breasts, is very difficult because of scar formation or the high density of implant. Mammographic evaluation of dense breast, which is commonly seen in younger women or in women undergoing hormone replacement therapy, is also difficult. In this situations, ^{18}FdGlc PET appears to be useful and may obviate biopsy (Flanagan et al. 1998). Wahl et al. have demonstrated a possible role of ^{18}FdGlc PET in patients with silicone-gel breast implants (Wahl et al. 1994).

Avril et al. (1996a) reported that quantitative analysis of FdGlc uptake in tumours using SUV showed a significant difference between benign (1.4 ± 0.5) and malignant (3.3 ± 1.8) breast tumours. Furthermore, the possible value of SUV as a prognostic factor for breast cancer has been examined by Crippa et al. (1998). In this study, it was shown that high SUV values were more frequently associated with high-grade infiltrating ductal carcinoma. In addition, they found that high SUV values in primary breast cancer were often associated with metastases in the axilla, but the overlap of SUV between patients with and without axillary metastasis did not allow a cut-off value to be determined with which to establish the axillary status.

A ^{18}FdGlc PET examination prior the treatment would help when planning the treatment of individual patients. The detection of multiple malignant breast lesions, either multicentric or multifocal, is important to ensure that proper local treatment is initiated. Since the axillary lymph node status is the single most important prognostic indicator in patients with breast cancer, accurate staging of regional lymph node metastases is also important in patients with breast cancer. The presence and number of regional lymph node metastases influence the selection of an appropriate treatment regimen for the individual patient and provide valuable prognostic information (Harris et al. 1993). In 1989, Wahl et al. (1991) observed that ^{18}FdGlc uptake in lymph nodes corresponded with the presence of metastases. Utech et al. reported that ^{18}FdGlc PET correctly categorised all 44 tumour-positive axillary lymph nodes in 124 patients, a sensitivity of 100%; 60 tumour-negative axillary lymph nodes were found to be negative and 20 tumour-negative axillary lymph nodes were positive, resulting in a specificity of 75%. No false-negative PET findings were encountered (Utech et al. 1996). Although early studies have reported a high sensitivity and specificity (Adler et al. 1993, 114; Tse et al. 1992, 115; Wahl et al. 1991, 116), later studies have demonstrated a slightly lower sensitivity and specificity (Avril et al. 1996b; Scheidhauer et al. 1996). Avril et al. (1996) have reported a sensitivity of 79% and specificity of 96% for the detection of axillary nodal involvement. However, axillary lymph node metastases in small-cell breast cancer could not be diagnosed with sufficient accuracy by ^{18}FdGlc PET. The reported sensitivity was only 33%. Thus, detection of micrometastases and small tumour-infiltrated lymph nodes is limited by the spatial resolution of PET imaging.

Another role of ^{18}FdGlc PET could help to detect internal mammary nodal involvement in patients with breast cancer, which may occur in medially localised tumours. At present, no technique is routinely used to image these nodes and sampling is not routinely performed (Flanagan et al. 1998). Data on the sensitivity and specificity of ^{18}FdGlc PET for detecting internal mammary lymph nodes are not available.

Whole-body PET imaging has the ability to evaluate the entire body in one examination. Thus, it can be used for the detection of the primary tumour and nodal metastases, but also skeletal and visceral metastases. In a study by Wahl et al. (1991), all of five known soft-tissue metastases and four previously unsuspected nodal lesions were detected in 12 patients by whole-body PET. In another study by Jansson et al. (1995), PET detected 12 of 14 primary breast lesions. In addition, lymph node status (11 of the 14 patients) and distant metastases (in 2 patients) were correctly determined.

Head and neck cancer

Head and neck (HN) carcinomas originating from the upper aerodigestive tract account for approximately 5%

of all malignant tumours (Parker et al. 1996) and their frequency is increasing. Squamous cell carcinomas represent the majority of all malignant HN tumours, and non-squamous cell HN carcinomas (salivary gland carcinoma, lymphogenous and odontogenic tumours etc.) account for only 5% of HN cancers. About 40% of the patients have localised disease, while the remaining 60% of the patients already have advanced disease. Lymph node involvement is the most important prognostic factor affecting the survival of patients with HN cancer (Sham and Choy 1990). The early stages of HN cancers are usually treated by surgery or radiotherapy as a single treatment, advanced stages by surgery and concomitant chemotherapy (Forastiere 1994). The effectiveness of surgical treatment depends on the complete excision of all tumour tissue, and accurate preoperative TNM staging is therefore mandatory. Although local and regional control of HN tumours has improved significantly, the increase in long-term survival has remained modest because of the development of distant metastases or second primary tumours (Jones et al. 1995; Schwartz et al. 1994).

The initial diagnosis of HN carcinomas is based on physical and endoscopic examination. Conventional imaging modalities (CT, MRI) have been applied for the assessment of bone involvement and extension into adjacent tissue. Morphologically oriented imaging techniques result in correct tumour staging in approximately 80%–90% of cases for both CT (Lenz et al. 1989; Steinkamp et al. 1993) and MRI (Lenz et al. 1989). CT and MRI have an accuracy of 77% and 81%, respectively, for assessing T stage in HN cancer (Steinkamp et al. 1993). Many studies (Braams et al. 1995; Laubenbacher et al. 1999; Rege et al. 1994; Stokkel et al. 1998) show that HN cancers exhibit an extraordinarily high ^{18}FdGlc uptake. In this respect, however, the additional value of PET is limited by the lack of the exact anatomical information necessary for T staging and for surgery. (Stokkel et al. 1998).

Minn et al. (1997) found that high uptake of ^{18}FdGlc in untreated HN cancer was associated with advanced disease. After 3 years, 73% of patients with SUV < 9 in the primary tumour were still alive compared to only 22% of the patients with SUV > 9. A multivariate analysis of these data was not able to identify extend of ^{18}FdGlc uptake as an independent prognostic factor. In this study, however, uptake of ^{18}FdGlc correlated poorly with the histological grade.

The evaluation of cervical lymph nodes plays an important role in the management and prognosis of patients with HN cancer. Therefore, correct lymph node staging is important in patients in whom neck dissection is being considered. (Dillon and Harnsberger 1991). In addition, a radical neck dissection affects both the function and appearance of patients. Methods available for lymph node staging include palpation and also morphologically oriented imaging techniques such as ultrasonography, CT and MRI. In patients found to be N0 by palpation of the neck it was found that both CT and MRI increased the identification of metastasis from 60%–75% to 85%–94% (Hillsamer et al. 1990). Adams et al. reported a sensitivity and specificity of 82% and 85%, respectively, for CT, and 80% and 79%, respectively, for MRI in detecting the lymphatic metastasis (Adams et al. 1998). Ultrasonography of the cervical region has been applied for the detection of lymph node metastases with an accuracy between 70% and 89% (Gritzmann et al. 1987; van den Brekel et al. 1991). Adams et al. reported a sensitivity of 72% and a specificity of 70% for localising the regional lymph node metastases (Adams et al. 1998). The main limitation of this diagnostic modality is that tissue can only be detected to a depth of 4–6 cm and the results are dependent on the experience of the investigator (Brinkmann et al. 1990). Furthermore, it is not possible to differentiate between reactive lymph nodes and enlargement due to metastatic involvement with radiological techniques. Eichhorn et al. (1987) showed that up to 40% of all lymph node metastases are localised in lymph nodes smaller than 1.0 cm in diameter, which limits the use of the size-dependent criterion of radiology.

^{18}FdGlc PET attains a sensitivity of 72%–91%, and a specificity of 88%–99% when applied to individual lymph nodes, thus being clearly superior to morphologically orientated imaging techniques (Benchaou et al. 1996; Laubenbacher et al. 1995). The smallest lymph node detected by ^{18}FdGlc PET reported in the literature was about 4 mm (Braams et al. 1995), which may result in an increased justification for performing neck dissection in these patients. In a recent report by Stokkel et al. (1999b), two cases were described in which tumours with a diameter of 4 and 5 mm, respectively, were detected with a dual head coincidence camera. In another study, Stokkel et al. (2000) also describe a high sensitivity of 96% in the preoperative evaluation of patients with HN cancer using ^{18}FdGlc dual-head PET.

In 5% of patients presenting with metastatic disease in cervical lymph nodes, a primary tumour cannot be found (Laubenbacher et al. 1999). These patients with cervical metastases of unknown primary tumours may benefit from ^{18}FdGlc PET. Rege et al. (1994) reported the successful detection of a primary tumour in 2 out of 4 patients by ^{18}FdGlc PET. In a total group of 8 patients with cervical metastases of unknown origin, Braams et al. (1997) demonstrated three unknown primary tumours, two by ^{18}FdGlc PET and one by endoscopy. In another study (Mukherji et al. 1996), ^{18}FdGlc PET revealed 9 of 11 histologically prove occult primary tumours. Stokkel et al. (1999c) reported that, in 5 out of 10 patients with cervical lymph node metastases of unknown origin, a primary tumour was identified by dual-head ^{18}FdGlc PET.

In up to 60% of cases in which local therapy has failed, haematologically distant metastases may be seen (Laubenbacher et al. 1999). These metastases can be detected with a high degree of diagnostic accuracy by conventional diagnostic methods. Owing to the high

cost, there is only a limited indication for using PET to search for distant metastases in patients with HN cancers. Data on this subject are not available.

Second primary neoplasms are a particular feature of HN cancers. Approximately one-half of the deaths of patients with a successfully eradicated HN cancer have been attributed to a second primary cancer (Licciardello et al. 1989). In patients with a high risk for HN cancers, a high incidence of second tumours of the upper aerodigestive tract is expected (Halpern 1997). This appears to be related to the synergistic effects of ingesting and inhaling multiple carcinogens. The most important carcinogens are the aromatic hydrocarbons of tobacco and alcohol, acting on a field of growth resulting in "field cancerization" (Slaughter et al. 1953). The reported incidence of second malignancies in patients with primary HN tumours ranges from 6% to 36% (Jovanovic et al. 1994; Schwartz et al. 1994). Early detection of these second primary tumours may offer opportunities to reduce their related morbidity and mortality. However, methods for early identification are often limited to close clinical observation and radiography, which have been found to be insufficient for this indication. Halpern (1997) evaluated the contribution of computed CT of the chest in patients with negative plain chest X-rays in 24 patients with HN cancer. Out of 24 patients, 9 (37.5%) had positive findings on chest CT. All lesions were biopsied and reported to be squamous cell carcinomas; 4 of the 24 patients (16.6%) were assessed to have a second primary lung tumour.

Endoscopic assessment of local recurrence or second synchronous tumours can be more difficult in patients previously treated for HN cancer, which could justify the use of PET. Data on use of ^{18}FdGlc PET in the detection of second primaries are scarce. Stokkel et al. found a second simultaneous primary malignant tumour in 12 of 68 (18%) patients with HN cancer by ^{18}FdGlc PET. In none of the 68 patients studied were additional simultaneous or synchronous (detected within 6 months of the initial diagnosis) primary tumours found during the follow-up. The prevalence of 18% of the simultaneous second primaries in the present study is significantly higher than the 3% reported in the literature and higher than the 7% detected with the diagnostic modalities used in this study. Although not enough studies have yet been published, ^{18}FdGlc PET imaging seems to be an important additional diagnostic tool in patients with HN cancer for the detection of second primary tumour.

Colorectal cancer

Colorectal cancers are among the commonest tumours in the western world with an incidence of approximately 12%–13%, and they are second only to lung cancer as the most frequent cause of cancer mortality in the US (Landis et al. 1999). Environmental factors appear to influence the aetiology of most colon cancers. About 25% of patients have a positive family medical history. Colon cancer is a frequent complication of long-standing inflammatory bowel disease and the majority of all colorectal cancers are presumed to develop from adenomatous polyps (Ruhlmann and Oheir 1999). The prognosis of colorectal cancer depends on the depth of penetration into the bowel wall, the involvement of regional lymph nodes, and the presence of distant metastases. The optimal treatment of colorectal cancer appears to be total resection of the tumour. Irradiation of the pelvis is generally necessary, since there is a 30%–40% risk of local recurrence after total resection of the tumour (Ruhlmann and Oheir 1999).

The data reported in the literature support the use of ^{18}FdGlc PET for detecting primary tumours and the metastases. Reported sensitivities range from 87% to 96% and specificities from 67% to 97% (Abdel-Nabi et al. 1998; Falk et al. 1994; Haberkorn et al. 1991a; Ruhlmann et al. 1997; Vitola et al. 1996). In the study by Abdel-Nabi et al. (1998), 48 patients with primary colorectal carcinomas were evaluated by ^{18}FdGlc PET. The method detected all known intraluminal carcinomas in 37 patients, including two in situ carcinomas, but false positive finding were seen in 4 of 7 patients. The specificity and negative predictive value were 43% and 100% respectively. In addition, ^{18}FdGlc PET detected liver metastases in 7 of 8 patients, and was superior to CT, which detected the liver metastases in 3 patients. ^{18}FdGlc PET detected lymph node involvement in 4 of 14 patients, a sensitivity of 29%. Results were similar to those obtained with CT (sensitivity 29%).

In cases where there is reason for a strong clinical suspicion, such as an increased level of tumour markers (CEA or CA19-9), but conventional diagnostic techniques yield unclear results (Ruhlmann et al. 1997), it may be possible to diagnose the primary tumour with ^{18}FdGlc PET.

A considerable ^{18}FdGlc accumulation can often occur in segments or large sections of the colon after colonoscopy, most often accompanying an unspecific inflammatory reaction. For this reason, the chronological relationship between colonoscopy and the PET examination should be considered carefully (Ruhlmann and Oheir 1999). Since inflammatory changes are shown as positive findings on a PET scan, additional information must be considered in order to avoid false positive results.

Lai et al. (1996) reported that unsuspected extrahepatic metastases, including retroperitoneal nodal metastases ($n = 6$), pulmonary metastases ($n = 3$) and locoregional recurrences ($n = 2$), which were missed by conventional imaging modalities, were detected by PET in 11 patients (32%). Findlay et al. (1996) assessed the presence of liver metastases in 20 patients with colorectal cancer. PET detected a total of 27 metastatic lesions. In this study, ^{18}FdGlc PET had a high sensitivity and specificity for the detection of both primary colorectal

cancer and liver metastases and appeared to be superior to CT in the staging of colorectal carcinoma.

Ovarian cancer

Ovarian epithelial cancer is one of the leading causes of cancer deaths in women; it starts in the surface epithelium and spreads locally into adjacent structures such as the fallopian tube, uterus and contralateral ovary. The pelvic wall, bladder, rectum and Douglas's pouch may also be involved (Zimny et al. 1999). Metastases in pelvic, paraaortic as well as inguinal lymph nodes develop in as many as 75% of all patients, depending on tumour stage (Burghardt et al. 1991). Whereas an exclusively surgical procedure is justified in stage I, advanced tumour stages require extensive surgery and chemotherapy (Zimny et al. 1999).

Although the CA-125 tumour marker is elevated in the majority of patients with advanced ovarian cancer (Brooks 1994), an established screening procedure for early detection of ovarian cancer is not yet available. A mass lesion of the ovaries is usually detected at gynaecological examination, whereas imaging methods are necessary for evaluating the tumour status and spread. Chou et al. reported quite a high diagnostic accuracy of about 90% for transvaginal colour Doppler ultrasonography (Chou et al. 1994).

CT and MRI are not very reliable in evaluating tumour spread since lymph node metastases and smaller peritoneal implants may be missed. Immunoscintigraphy, which is thought to be the most specific imaging technique, has not been accepted as a routine method. Krag (1993) reported a sensitivity and a specificity of 69% and 57%, respectively, for immunoscintigraphy and 44% and 79%, respectively, for CT in patients with ovarian cancer. The first report on ^{18}FdGlc accumulation in ovarian cancer was by Hubner et al. (1993). They found a sensitivity of 93% and a specificity of 82% for assessing primary tumours. Zimny et al. (1997) evaluated ^{18}FdGlc PET in 26 patients suspected of having primary ($n = 7$) or recurrent ($n = 9$) ovarian cancer. Quantitative analysis revealed a mean SUV of 6.8 ± 2.3 in primary ovarian carcinoma compared to 2.6 ± 1.2 in benign masses. The sensitivity, specificity and diagnostic accuracy were 88%, 80% and 85%, respectively, for evaluating peritoneal metastases and 50%, 95% and 80%, respectively, for lymph node staging. However, PET is also of limited value for the detection of microscopic seeding. No study comparing PET and immunoscintigraphy directly has been carried out yet, but PET is supposed to be superior to immunoscintigraphy because of its higher spatial resolution and its better image contrast in the liver and kidney regions (Zimny et al. 1999). Special attention is required to differentiate peritoneal seeding from increased bowel activity in ^{18}FdGlc PET studies, and the clinical value of this approach in primary ovarian cancer still has to be established. Owing to the limited number of studies, it is not possible to draw any conclusion.

Hodgkin's disease and non-Hodgkin's lymphomas

Lymphomas manifest themselves in lymph nodes or lymphatic tissue of paranchymatous organs. Approximately 90% of all cases of Hodgkin's disease (HD) exhibit initial manifestation in lymph nodes, compared with only about 60% of non-Hodgkin's lymphomas (NHL) (Menzel 1999). NHL, like HD, have their origin in the lymphoreticular tissue but they differ histologically and clinically from HD (Menzel 1999). Accurate staging is essential for therapy planning, particularly for HD.

The current staging routine includes a thorough clinical examination followed by a conventional chest X-ray for detecting or excluding thoracic or mediastinal lymphomas. If there is suspicion of intrathoracic or abdominal disease, a CT scan and/or ultrasonography of these sites is performed in order to detect any involvement of lymph nodes or extralymphatic organs. CT evaluates the nodes according to number, size, anatomical location and environmental reaction.

As reported in several studies (Lapela et al. 1995; Leskinen-Kallio et al. 1991; Newman et al. 1994; Okada et al. 1992), malignant lymphomas demonstrate high ^{18}FdGlc uptake. It has been clearly shown that the ^{18}FdGlc uptake of NHL is directly correlated with the degree of tumour malignancy (Rodriguez et al. 1995). Okada et al. (1992) have demonstrated a positive correlation between the proliferative activity of malignant lymphomas and intratumoural ^{18}FdGlc accumulation. They also reported that the response to therapy and the mean survival time were reduced in patients who initially exhibited a high metabolic rate, i.e. a high ^{18}FdGlc uptake in PET scans.

The advantage of ^{18}FdGlc PET is that additional information can be obtained with whole-body scanning. Hoh et al. (1997) used whole-body ^{18}FdGlc PET for staging HD and NHL. Accurate staging was achieved in 17 of 18 patients (7 HD, 11 NHL) compared to 15 of 18 patients when conventional staging methods were used. Whole-body PET detected 33 out of 37 lesions. In 5 out of 18 patients, whole-body PET showed additional lesions not detected by conventional staging modalities, whereas in 4 out of 18 patients conventional staging demonstrated additional lesions that were not detected by whole-body PET. In the thorax and especially in the abdominal region, PET proved to be superior to CT in staging lymphomas, which was also confirmed by Thill et al. (1997). Compared with CT, ^{18}FdGlc PET revealed almost 25% more lesions. In another study, 49 tumour foci were identified equally well by both techniques and there were 5 additional foci that were only imaged by ^{18}FdGlc PET (Newman et al. 1994). Moog et al. (1997) evaluated 60 untreated patients with HD or NHL using ^{18}FdGlc PET and CT for nodal staging. PET not only identified all nodal involvement seen on CT (160 of 740 lymph node regions), but also showed 25 additional lesions (7 were true positive, 2, false positive, and 16 were unresolved), this resulted in a change of tumour stage in

8% of the patients. There were no false negative PET findings.

It is known that steroids, in the majority of therapeutic approaches for malignant lymphoma, lead to lower ^{18}FdGlc accumulation in malignant lymphoma than in the surrounding tissue, because of their anti-insulin effect on carbohydrate metabolism (Rosenfeld et al. 1992).

Indications for ^{18}FdGlc PET in malignant lymphomas include the staging and re-staging of HD and the detection or exclusion of residual disease after completion of therapy. With respect to the various histological subtypes of lymphoma, specific data on ^{18}FdGlc PET are still relatively few.

Malignant melanoma

Cutaneous melanoma is a highly malignant tumour of melanocytes presenting characteristic metabolic and biological features. The Auckland region of New Zealand has the highest documented incidence of malignant melanoma, with a crude annual rate of 77.7/100 000 and an age-standardised annual rate of 56.2/100 000 (Jones et al. 1999). Factors indicating a risk of developing melanoma include multiple atypical naevi, freckles, ease of burning, inability to tan and a history of severe sunburn. Other factors include the presence of familial melanoma, disorders of DNA repair and excessive exposure to the sun (Anonymous 1993).

The classification of malignant melanoma, including superficial spreading, nodular, lentigo maligna and acral lentigious types, is of little relevance in the clinical management of patients with melanoma (Cascinelli et al. 1995). Accurate staging is important for treatment and prognosis. The most predictive factor for recurrence and prognosis of melanoma is the tumour thickness, measured in millimetres, the so-called Breslow thickness (Cascinelli et al. 1995). The regional lymph nodes are the most frequent site of melanoma metastases and the surgical excision of these involved nodes is the most effective treatment for either cure or local disease control. An increased thickness is strongly associated with more lymphatic and distal metastases at first presentation, and during follow-up. Surgery is the treatment of choice when melanoma is confined to the site of origin and does not extend beyond the regional lymph node basin. In the early stages, treatment is usually curative (Cascinelli et al. 1995), whereas in disseminated disease therapy is always palliative.

The first report on the clinical evaluation of melanoma with ^{18}FdGlc PET was in primary uveal melanoma. In this setting, ^{18}FdGlc uptake was observed in 3 of 12 lesions (Lucignani et al. 1992). Compared with radiological techniques, ^{18}FdGlc PET has been shown to be superior for the staging of melanoma patients (Damian et al. 1996; Gritters et al. 1993; Rinne et al. 1998; Steinert et al. 1995). In a small study by Gritters et al. (1993) for staging of melanoma, ^{18}FdGlc PET had an overall accuracy of 100%, detecting 7 of 7 metastatic lesions and correctly predicting 13 of 13 negative lymph node regions. Damian et al. studied 100 patients with cutaneous malignant melanoma and found a sensitivity of 93% for detecting metastatic disease. Twenty-four metastases were shown with ^{18}FdGlc PET up to 6 months earlier than with conventional imaging (Damian et al. 1996). Rinne et al. (1998) investigated the primary staging in 52 melanoma patients by ^{18}FdGlc PET. In 4 patients, PET detected 9 lymph node metastases that had not been detected by conventional imaging. Mcfarlane et al. reported an 88% accuracy for predicting residual/occult lymph node status with ^{18}FdGlc in 21 patients undergoing lymph node dissection (Macfarlane et al. 1998). Holder et al. have performed 103 ^{18}FdGlc PET examinations on 76 patients having stage II to IV melanoma. ^{18}FdGlc PET had a sensitivity of 94.2% and a specificity of 83.3% for the detection of metastases compared to 55.3% and of 84.4% respectively (Holder et al. 1998) for CT.

Wagner et al. compared ^{18}FdGlc PET with sentinel lymph node biopsy in patients with stage I, II and III melanoma. In the detection of occult regional lymph node metastases, sentinel lymph node biopsy was found to have a sensitivity and specificity of 94.4% and 100%, respectively, compared with 16.7% and 95.8%, respectively, for ^{18}FdGlc PET (Wagner et al. 1999). ^{18}FdGlc PET has been shown to be better than CT scanning in the early detection of melanoma metastases and for staging melanoma patients. However, ^{18}FdGlc PET is an insensitive indicator of occult regional lymph node metastases in patients with minute tumour volumes in this population.

Conclusion

The current applications of ^{18}FdGlc PET in oncology have been in differentiating and characterising indeterminate lesions, staging of disease and differentiating recurrent disease from treatment effects. Because benign lesions can exhibit hypermetabolism and because of physiological ^{18}FdGlc uptake, false positive findings can be seen. The potential sites and imaging characteristics of these conditions should be well recognised, to avoid the false positive interpretations. The development of coincidence technology on gamma cameras makes the usage of ^{18}FdGlc more widely available.

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