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REVIEW

Role and Cost Effectiveness of PET/CT in Management of Patients with Cancer

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PET/CT is a relatively new imaging technology, whose undoubted advantages are valuable in clinical oncology as well as in all fields of diagnosis, staging, and treatment. The hardware combination of anatomy and function has been the true evolution in imaging. PET using ^{18}F-fluorodeoxyglucose (FDG†) is increasingly used for the staging of solid malignancies, including colon, lung, etc., but anatomic information is limited. Integrated PET/CT enables optimal anatomic delineation of PET findings and identification of FDG-negative lesions on computed tomography (CT) images and might improve preoperative staging. However, controversy still exists in relation to the application of PET/CT in clinical practice, mainly because of its high cost. It is evident that apart from additional costs, potential savings also are associated with PET/CT as a result of avoiding additional imaging examinations or invasive procedures and by helping clinicians make the optimum treatment decisions. The authors review the literature on the role of PET/CT in management of various tumors and discuss the medicoeconomic usefulness.

INTRODUCTION

For the past decades, Computed Tomography (CT) has been the gold standard imaging method in oncology. It has been used for initial staging, tumor evaluation after treatment, and follow-up of patients with cancer. The method depicts intricate morphological changes with the use of intravascular contrast, abnormal contrast enhancement, and blood flow due to pathological circumstances. However, this conventional imaging technique is not always efficient in the differentiation between benign and malignant lesions [1,2].

Positron Emission Tomography (PET), on the other hand, is a non-invasive molecular imaging technique that uses various radiolabeled compounds and visualizes metabolic differences between tissues, thus depicting the functional status of a suspicious lesion. PET was developed in the early 1970s and was approved in the United States for limited use in the oncological

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†Abbreviations: CT, Computed Tomography; PET, Positron Emission Tomography; ^{18}F-FDG, ^{18}F-fluorodeoxyglucose; NSCLC, non-small cell lung cancer; GVT, gross tumor volume.

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clinical practice in 1998 [3,4].The development of this method was based on the observation that malignant cells are associated with an increased glycolytic rate and increased cellular glucose uptake. In order to visualize this biochemical procedure, radiolabeled ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is used. FDG is a glucose analogue that has the same cellular uptake as glucose but is metabolically trapped within the cell after enzymatic phosphorylation to FDG-6-phosphate. Therefore, FDG can be used to quantify glucose metabolic rates [5,6].

One of the most important limitations of PET is that most anatomic structures are poorly depicted, if not completely absent, thus making it difficult to localize tumor lesions precisely. Furthermore, FDG accumulates in various normal tissues, such as the brain, muscles, salivary glands, thyroid gland, myocardium, gastrointestinal tract, and the urinary tract. It is, therefore, at times difficult to interpret the images when the neoplasm is located near an organ with physiological FDG uptake [1,7,8]. It is also challenging to differentiate lesions due to malignancy from lesions due to inflammation in which FDG accumulation is equally intense due to increased glucose metabolic rates. Finally, FDG uptake is variable in some types of cancer, thus limiting the diagnostic value of PET [9-11]. For example, most well-differentiated, hypocellular, and mucous-producing tumors demonstrate low uptake of the tracer [12].

Consequently, FDG-PET could not be used as an independent imaging method in oncology. In order to interpret the PET images correctly, the clinician has to correlate them with images of a more morphologically oriented imaging technique.

DEVELOPMENT OF PET/CT

In oncological imaging, the goals are lesion detection and localization — including anatomical correlation with structures such as vessels — lesion characterization, proper staging, and treatment success. Some of these goals require precise anatomical imaging, whereas others demand molecular techniques [5-11]. It was, therefore, easily acknowledged that FDG-PET and CT are complementary, and the employment of the two is imperative in the oncological clinical practice. Visual imposition of the images was often considered sufficient, but the development of software fusion algorithms provided more accurate localization [13].

However, fusion was difficult and sometimes outright unsuccessful when it involved structures outside the brain: Errors were observed with deformable soft-tissue organs as well as with organs in which time difference mattered between imaging procedures as seen with the dynamic motion of the gastrointestinal organs [1,2,9,13-15].

The need for data hardware, rather than software, fusion of the functional PET with the morphologically oriented CT remained apparent. In 1998, Townsend and his colleagues introduced the first PET/CT prototype — a single integrated device — combining the two techniques in order to minimize temporal and spatial differences [5]. Imaging manufacturers made PET/CT scanners commercially available in 2001 [7]. The most important advantage of this hardware fusion was that it made images available from one device in a single patient positioning. Since the patient remains on the same bed for both scans, spatial and temporal differences are eliminated [16]. Internal organ movement is minimal since both scans are acquired roughly in sync. CT is used for attenuation correction of PET, and the imposed anatomical and functional images are available immediately after the scan for corroboration [5,17-19].

INDICATIONS IN ONCOLOGY

Currently, PET/CT has mostly found its application in the clinical practices of oncology (97 percent) and much less in infection (2 percent) and cardiology (1 percent). The primary areas of interest are diagnosis, staging, treatment-effectiveness monitoring, and radiotherapeutic planning — practically all fields of tumor management [20,21].

Diagnosis

In the area of diagnosis, the PET/CT is not frequently used. It is mostly indicated in

the evaluation of single pulmonary nodules — especially those that are not amenable to percutaneous biopsy — and the assessment of lymphadenopathy [2,20,21]. It also may be helpful in cases of abnormalities that are "intermediate," according to imaging criteria and the patient, if the clinician is hesitant to proceed with an invasive procedure or in cases of suspicious lesions examined pathoanatomically but with no definite diagnosis. Furthermore, PET/CT may be used in cases of pyrexia of unknown origin and suspected paraneoplastic syndromes [22,23].

Staging and Restaging

When PET/CT was first introduced, the oncological indications approved by Medicare included staging and restaging of non-small cell lung cancer, esophageal cancer, colorectal cancer, pancreatic cancer, ovarian cancer, head and neck cancer, breast cancer, melanoma, and lymphoma. In 2003, the additional indications of monitoring breast and thyroid cancer were approved, and it is expected that more indications will be approved in the future [3,24,25].

Poor co-registration of PET and CT images due to motion of the diaphragm also may lead to inaccurate interpretation of chest tumors. However, recent data have shown that integrated PET/CT images, regarding tumor staging, are superior to PET images alone and PET and CT images viewed side by side. Lardinois et al. were the first who found a diagnostic advantage for PET/CT over all the other methods in regard to the determination of T and N stage. In regard to non-small cell lung cancer (NSCLC), PET/CT scans have proven to be statistically more accurate than any other method, as far as tumor staging is concerned. As a result of the exact correlation between anatomy and functional disorder, focal chest wall infiltration, mediastinal invasion (with the ability to distinguish between contiguity of tumor and mediastinum from the direct invasion of the walls of the mediastinum), and differentiation of tumor from atelectasis have largely improved with PET/CT [26-28]. Although mediastinoscopy remains the standard procedure for mediastinal nodal staging, PET/CT has proven to be a very sensitive noninvasive staging technique and may even determine the exact location of a solitary lymph node, thus concluding the precise classification as N1 or N2 [29]. Unsuspected extra thoracic soft tissue or skeletal metastases also may be revealed by PET/CT in cases where other imaging methods failed to demonstrate distant metastasis [30]. Adrenal enlargement is often a diagnostic problem that can be solved with PET/CT. One limitation is cerebral metastasis, because the brain shows the highest normal FDG accumulation. Overall, it has been demonstrated that PET/CT is an important feature for precise NSCLC staging. The extent of tumor spread is the primary factor that determines whether the patient will undergo surgery or will be offered a non-surgical treatment. Studies have concluded that PET/CT resulted in an alteration of treatment management in up to 30 percent of NSCLC patients [20,27,30-34].

The value of PET/CT in patients undergoing restaging after treatment is equally apparent. Recurrence, whether local, intrathoracic, or distant, is successfully detected by PET/CT. Furthermore, with this imaging modality, it is now possible to distinguish between malignancy and post-therapeutic change [33]. Surgical resection may cause scarring and anatomical distortion, which can conceal early changes caused by tumor spread. Likewise, radiation-induced pneumonitis may provoke mass-like changes. PET/CT helps in the differential diagnosis by enabling the exact localization of increased FDG uptake [20,22,35,36].

Similarly as seen in lung cancer, PET/CT can also help in the management of malignant pleural mesothelioma. In this case, PET/CT is useful in documenting the extent of pleural effusion, the possible involvement of the lymph nodes, and the infiltration of the pulmonary parenchyma as well as the thoracic wall. It also has an important part in the diagnosis of distant metastases and the assessment treatment response [20,37].

Few studies have been performed to determine the role of PET/CT in breast cancer.

Since this is a potentially curable type of cancer if diagnosed at an early stage, pre-operative staging is extremely important as it influences the choice of surgical treatment [35]. Sensitivity, specificity, and accuracy of PET/CT for the diagnosis of the primary tumor and detection of axillary lymph node metastasis is limited [38,39]. However, this method seems to be superior to mammography, ultrasound, or PET alone. The sensitivity of PET/CT to diagnose micrometastases is limited, and therefore restricting, as far as the initial staging of breast cancer and axillary node infiltration are concerned. Furthermore, the histological characteristics of the tumor may affect FDG-PET imaging enough to fail to visualize the primary tumor [22]. In clinical practice, PET and PET/CT are useful in restaging and demonstration of distant metastases. The increased localization accuracy of PET/CT results in the detection of metastases in the internal mammary node chain, which have been previously disregarded as nonspecific with PET [40]. PET/CT also may be helpful in the evaluation of treatment. However, in the screening and diagnosis of primary breast tumors, the high cost of PET/CT does not allow wide application [20,25,39].

As far as esophageal and gastric carcinomas are concerned, PET/CT has limited accuracy in the identification of the primary tumor. This is because a variety of benign conditions of the esophagus, such as Barrett esophagus, also lead to high FDG uptake [20,25]. Furthermore, focal areas of brown fat, asymmetric uptake in the vocal cords, and vessel atherosclerosis may lead to false positive results, although these areas are generally better differentiated from areas of esophageal uptake on PET/CT, rather than on PET images [41,42]. False negative FDG-PET images in regard to the identification of primary tumors have been reported up to 20 percent. As far as staging is concerned, many studies have been carried out, and the results indicate a major benefit of PET/CT as opposed to FDG-PET in the determination of M stage. Tumor size and local-regional lymph node involvement can be evaluated with a sensitivity of only 30 percent by PET, while PET/CT has slightly improved this percentage [42]. On the other hand, the detection of gastric cancer depends on the histological type. After the diagnosis has been made, PET/CT can be used to determine the depth of invasion of the primary tumor and evaluate the nodal spread of the disease, including distant metastasis. The utility of this technique in esophageal cancer is most evident in the evaluation of the response to chemotherapy. Patients responding to treatment had a significant reduction of tumor FDG accumulation in relation to those not responding [20,41,43-45].

Although PET images alone are difficult to interpret in the evaluation of abdominal and pelvic tumors — due to the absence of anatomical landmarks and the nonspecific FDG uptake in the gastrointestinal tract — PET/CT fusion images may be of great importance. PET/CT was more accurate than PET alone in staging and restaging of colorectal cancer [1,22,46]. It also has proved to be equally effective as a contrast-enhanced CT in detecting distant metastasis, but more sensitive in the detection of local recurrence and liver metastasis in patients with prior hepatectomy. PET/CT also can be useful in patients with liver lesions that cannot be clearly characterized by CT [47,48]. Early detection of liver metastases may affect patient management, providing the opportunity for neoadjuvant chemotherapy and tumor resection. It is important to point out that in several trials, after PET/CT imaging was performed, the treatment strategy was altered in 20 percent to 35 percent of patients [24,49-50].

Stromal tumors of the gastrointestinal tract may show heterogeneity in FDG accumulation between different lesions of the same patient. PET/CT is, therefore, complementary to CT in terms of staging and detection of metastasis. There are studies, however, that have confirmed its superiority in assessing response to treatment with imatinib. Patients without FDG uptake and after the initiation of therapy have better prognosis than patients with residual activity [1,20,51,52].

CT and MRI imaging have been the cornerstone of diagnosis and staging of pancreatic cancer. However, differentiation of masses such as chronic pancreatitis and carcinoma remains difficult with these modalities [22,25,50]. In their study, Heinrich et al. showed that PET/CT in pancreatic cancer is equally sensitive as CT, but has an increased specificity. PET/CT showed a positive and negative predictive value of 91 percent and 64 percent, respectively [53]. It also proved to be more effective than standard staging in detecting distant metastasis, thus altering the therapeutic plan in 16 percent of patients. In addition, PET/CT can guide biopsies to the most active lesion, allowing for a more precise diagnosis [20,22].

Little evidence from selected case reports has shown superiority of FDG-PET in imaging of ovarian and fallopian tube carcinoma. Malignant lesions often accumulate FDG but cannot be detected by CT. Exact localization of the neoplasm in order to define the therapeutic procedure is crucial and can be achieved with fusion PET and CT images [54]. PET/CT also was effective in demonstrating peritoneal disease specificity and sensitivity much higher than those of CT alone. The sensitivity of PET/CT for staging and restaging of endometrial and cervical cancer has been compared to conventional imaging, and the results were very encouraging [55-57].

Loco-regional evaluation of head and neck cancer is extremely complex by definition. The limitations are due to the normal or questionable size of the lymph nodes, which with the conventional imaging techniques cannot be classified as either normal or pathologic [24]. FDG-PET, on the other hand, is not efficient enough because of physiologic FDG uptake in muscular, lymphoid, glandular and fatty tissue, and proximal to metal dental work. The problem is even more serious in patients who have undergone surgery [58,59]. Thus, interpretation of both anatomical and functional images is of great importance. Even though data on the use of PET/CT is locoregional, staging of head and neck cancer is limited. This modality seems to offer an easier distinction between lymph nodes of normal FDG uptake and those that are abnormal which may have normal sizes but actually contain malignant cells. Therefore, it is more accurately possible to be upstaged to N1 [60-63]. Although distant metastasis is infrequent in head and neck carcinomas, PET/CT is helpful in their identification. Relevant tumors, such as lung and esophageal carcinoma and precancerous or cancerous lesions in the large bowel, may be present in patients with head and neck carcinomas and are readily defined by PET/CT [64]. All the information acquired is used in order to give the patient the treatment indicated. In most cases, extensive surgery and radiotherapy are used as standard treatment procedures. As a result, the anatomy of the site is largely altered, while persistent sterile inflammation is often present. PET/CT cannot always distinguish between inflammation and malignancy, but it can be used in order to identify the best biopsy site, if biopsy is necessary [61-63].

Most well-differentiated thyroid malignancies show high iodine uptake, but are not FDG avid. In cases of dedifferentiation, these more aggressive tumor cells lose their ability to accumulate iodine. If thyroid cancer is iodine negative, other imaging methods are required for staging and restaging [25,30]. FDG-PET has proven valuable in this case. It allows for precise metastatic localization and allows differentiation between tumor and scar tissue, thus preventing unnecessary interventions [65,66]. In one study, PET/CT findings altered the treatment plan in 67 percent of patients with thyroid cancer. Most of these patients had markedly elevated serum thyroglobulin levels and negative 123I scans. No false positive scans occurred [25]. In patients with suspected differentiated but iodine negative tumors, PET/CT proved to be more accurate than CT for the detection of disease, with a sensitivity of 93 percent [67].

Malignant melanoma and its metastases are highly FDG-accumulative. PET/CT is not useful for initial staging or for patients with early disease with no nodal or distant metastasis [68]. Even though the primary le-

sions are often seen in PET/CT images, the technique is not currently used to determine the T stage. Several studies and meta-analyses report that the sensitivity and specificity of FDG/PET in detecting recurrent melanoma ranges from 70 percent to 100 percent. With the exception of the brain, FDG-PET can successfully locate metastases and micrometastases at unusual sites that may be missed with conventional imaging modalities. PET/CT will determine the exact location of metastasis. Surgical resection is the treatment of choice in the case of regional lymph node spread or a single distant metastasis [50,69,70]. However, only palliative symptomatic treatment is indicated in the presence of distant lesions. Unexpected findings in PET/CT have been reported in 15 percent of cases. Therefore, PET/CT should be performed not only in patients scheduled for surgery to exclude occult metastases, but also to achieve the most minimally invasive excision possible [50,71].

Both Hodgkin and non-Hodgkin lymphoma usually show high FDG accumulation. FDG-PET, where available, already has replaced gallium scan in the detection of lymphatic lesions. The assessment of lymphoma distribution is of great importance for the choice of the optimal treatment [72,73]. Non-enhanced CT is very accurate in defining lymphadenopathy, based on anatomical criteria. However, nodes of normal size may contain disease. PET is the indicated imaging method to determine the presence or absence of disease. However, non-Hodgkin's disease is often extra nodal and may occur in almost any site of the human body. PET/CT is the indicated modality to provide confidence in identifying and localizing the lesion. It also may be helpful on occasion when no CT findings correlate with the PET abnormality. Biopsy sites, when needed, can also be determined by PET/CT [50]. While lymphomatous masses usually respond dramatically to treatment, residual masses are often present after therapy. It is of great importance to distinguish viable lymphoma from necrotic tissue and fibrosis. Morphological imaging methods are not at all effective for this purpose, as opposed to PET/CT. It is very interesting to mention that in the case of a low-grade lymphoma, an unexpected increase in FDG accumulation in any or all known parts of the disease during follow-up suggests transformation to a higher grade lymphoma [74-77].

PET/CT, by searching the whole body for anatomic and metabolic alterations, may lead the physician to incidental findings of unsuspected malignancies. Normal structures show ^{18}F-FDG uptake, which, in contrast with the uptake of pathologic tissues, is usually symmetric. In the study by Osman et al., non-contrast enhanced PET/CT revealed unexpected lesions in 3 percent of patients [78]. Other studies reported unsuspected hypermetabolic lesions, which were confirmed as malignant in at least 1,2 percent of patients [25,79].

It is conceivable that PET/CT could be used in the management of cancer in regard to the detection of occult metastasis. In some cases, during follow-up after treatment, tumor markers may be elevated, but no site of residual disease can be detected by conventional imaging. PET/CT may detect and localize successfully the malignant lesion with increased FDG uptake.

Treatment monitoring

It has been discussed previously that PET/CT can be very effective in treatment response assessment due to its characteristics of functional or metabolic imaging. The assessment of residual tumor after a course of therapy (surgery, chemotherapy, or irradiation) is usually made by conventional anatomical imaging procedures, although FDG-PET is sometimes used in clinical practice during restaging. However, metabolic changes within the tumor have been documented very early after treatment. For example, FDG uptake reduction in patients with lymphoma can be monitored within a few hours after treatment [37,38]. Evidently, a metabolic response, reflecting the malignant cells' viability, may precede an alteration in the size of a tumor lesion. As a result, reduced FDG uptake may demonstrate treatment effectiveness much earlier

than a CT image, even after only one chemotherapy infusion. Studies demonstrated that the decrease of FDG uptake after a single infusion of chemotherapy was a predictor of eventual response to this regimen [80]. Similarly, no decrease of tumor FDG uptake after the first infusion was a predictor of non-response. Morphological changes in the tumor usually occur after a certain interval following therapy. As a result, multiple doses of antineoplastic agents are administered, even if they are ineffective. The early identification of response via PET/CT helps the clinician decide whether the same treatment should be continued or another alternative is required [20,22]. Clinical studies have demonstrated that PET can readily predict response to chemotherapy in cases of breast cancer, lymphoma, NSCLC, head and neck, esophageal, and gastric cancer, as well as liver metastasis [81-83]. Early decrease of FDG uptake has been monitored and seen in molecular targeted therapy (with imatinib) and radiotherapy as well [84].

Radiotherapy planning

It is becoming obvious that PET/CT will have an important role in radiotherapy planning in the future. Successful radiation planning requires accurate evaluation of the extent of the disease. Traditionally, this is performed with a CT scan prior to radiotherapy simulation [22,25]. The anatomical information is used in order to determine the radiation boundaries. However, the microscopic extension of the tumor around the gross tumor volume (GVT) cannot be determined by CT. In order to overcome this problem, the volume treated is much greater than the gross tumor volume. On the other hand, precise and accurate localization of RT targeted to GTV is critical for optimizing the therapeutic ratio [85-88]. By measuring the metabolically active tumor volume, PET on its own provides functional data that can be used in order to improve tumor coverage, including the involved lymph nodes, and thus reduce normal tissue exposure [89]. Feasibility studies have shown that a PET/CT scan may provide valuable information for accurate staging and decision making in the field of radiotherapy, changing treatment strategies in about 25 percent of patients. Treatment changes include prevention of inappropriate radiotherapy, changes in radiation dose or target volume, and changes in planning regarding curative or palliative radiation therapy. Data from a CT may be used for volume planning and delineating tumor margins; whereas, PET differentiates viable from non-viable and aggressive from non-aggressive lesions. In NSCLC, for example, PET/CT helps distinguish tumor involvement from atelectasis. By demonstrating the most active tumor lesions, PET/CT may play a role by adjusting regional radiation dosages accordingly [86,89-92].

The evaluation of local response after RT with conventional imaging may be of limited accuracy, because the presence of fibrosis, atelectasis, or radiation-induced pneumonitis may be falsely interpreted as disease. Inflammed lymph nodes also may be misinterpreted [88]. Even though RT-induced inflammation accumulates ^{18}F-FDG, there is data suggesting that a viable tumor shows higher uptake, thus making the differentiation feasible. The optimal timing to perform PET/CT in order to minimize both false positive (due to inflammation) and false negative results (in case residual disease has not yet reached the threshold of resolution by PET) has not yet been determined. All the above suggest that PET/CT could successfully become the first imaging study for a more rational approach to radiation treatment planning for cancer patients [22,86,87,90].

COST CONSIDERATIONS

PET/CT has only been available in clinical practice for approximately five years and is expanding rapidly. The hardware fusion of the morphological CT-acquired data and the metabolic PET images has proven to be more efficient and less time consuming than visual or software fusion, and no extra personnel needs to be involved [1]. The contemporary acquisition of images reduces problems due to misalignment or possible change of the disease in the interval between

the two imaging procedures [1,11]. It appears that PET/CT is more accurate in tumor localization and cancer staging as compared to PET alone, CT alone, or CT plus PET [11]. Several studies have reported a change in the management of up to 18 percent to 25 percent of cases after PET/CT scan [1,11,93-95].

Cost calculations show that there are savings from the integration of PET and CT in one system. First, there are several occasions in which FDG-PET leads to equivocal findings, and follow-up imaging studies (usually CT scans) are required. If patients undergo both examinations in one session, in addition to having more accurate results, costs will be lower [1,3]. Second, PET is a quite lengthy procedure, as it requires both emission and transmission scans. Image fusion between PET and CT has resulted in an average time savings of 20 to 30 minutes per patient. In this case, transmission scans are not required because the CT data are used for attenuation correction. It has been estimated that patient output has increased by approximately 40 percent. Furthermore, a shorter scanning time results in more efficient use of FDG, since it decays rapidly due to its short half-life. Consequently, an increase in patient throughput and a simultaneous decrease in FDG requirements for the same number of patients may bring additional income to the institution. Even with fewer FDG requirements, a better price for the radiopharmaceutical is negotiable, as the examination sequence gets faster [1,11,93,96].

In cases of biopsy sampling, PET/CT is the most adequate method to demonstrate the area that is most likely to be of diagnostic value. This avoids unnecessary invasive procedures [1,3,9,11]. With regard to surgical treatment, the method contributes to accurate decision making. There is now substantial evidence that PET/CT is an extremely sensitive imaging modality in the detection of malignant tissues and that it presents a higher specificity than PET alone, which is the main reason for fewer equivocal scans and better diagnostic results. Precision in staging may be prohibitive of surgical excision. In most cases, the patient is upstaged by PET/CT [20,53]. Considering the median length of pre- and post-operative hospital stays (including intensive care unit costs when necessary), the cost of surgical resections and biopsies, and the cost of PET/CT scan, the avoidance of surgery was found overall to be cost beneficial [3,20]. More specifically, in the Heinrich et al. trial, patients with pancreatic tumors underwent PET/CT scan for disease staging. Metastases were found in 16 percent of patients with cancer initially deemed resectable, leading to different management and cost savings of $1,066 per patient [53]. An estimated cost for a Whipple procedure is in the range of $35,000 to $40,000 in the United States [97,98]. The expenses related to a hospital stay for 12 to 20 days in the United States is approximately $34,350 [84,85]. Neither shortening the length of the hospital stay nor the use of CT guided FNA and surgical assessment of metastasis (by a thoracoscopic or laparoscopic approach) would reverse the cost effectiveness of PET/CT [97,98].

Likewise, radiotherapy and chemotherapy strategies also can be adjusted according to staging, therapy-response evaluation, and restaging. The potential of early response detection with PET/CT helps avoid possible ineffective and expensive drugs, thereby tailoring treatment for each individual patient [1,3,20,53,93]. Use of PET/CT scan in colorectal cancer and melanoma restaging has resulted in a cost savings of approximately $3,000 and $4,400 per patient, respectively [3].

As PET/CT is the combination of PET and CT, the major advantage of PET/CT is the simultaneous availability of both functional and anatomic information that facilitates an optimal fusion of both imaging techniques. It is only by this improved imaging fusion that FDG-positive findings, e.g., lymph node metastases, can be exactly identified. Though there is little data to comment on cost, PET/CT scan detects unknown distant metastases and rules out suspicious lesions. Subsequently, surgery is performed in cases in which respectability of tumors has been confirmed. Thus, survival after surgery is increased, and overall cost might be reduced [99].

It is important to stress that not all medical institutions need a PET/CT scanner. For a cancer center, however, it could prove quite valuable for patient management [1,11,93]. Even in this setting, the need for a PET/CT scanner would depend on the patient population served in this particular imaging center. Furthermore, the price of PET/CT systems is likely to decline as the method gains acceptance and continues to spread [93].

FUTURE DEVELOPMENTS

PET/CT scan has the potential to change clinical practice in numerous malignancies. In prostate cancer, ^{18}F-choline seems to be a promising PET-tracer, useful in the detection of disease recurrence and bone metastases [100]. In sarcomas, PET/CT can play a significant role in tumor grading, staging, follow-up, and as a prognostic factor [101]. PET/CT scan also seems valuable as a response biomarker in order to monitor not only cytotoxic but predominantly cytostatic cancer therapies [102]. As targeted therapies are expensive and cause considerable toxic adverse events, PET/CT scan can be useful in identifying potential responders [102]. It also offers original information concerning tumor biology [102]. Its indications in clinical oncology are constantly being expanded in carcinomas such as cervical [103], rectal [104], and lymphoma [105], and it constitutes the future gold standard of care in lung cancer [106]. Development of new PET-tracers will increase the number of indications of this multimodality imaging technique. More randomized multicenter clinical trials are necessary in order to establish standardized clinical algorithms and guidelines that include PET/CT scan.

CONCLUSION

PET/CT is a relatively new imaging technology, whose undoubted advantages are valuable in clinical oncology as well as in all fields of diagnosis, staging, and treatment. The hardware combination of anatomy and function has been the true evolution in imaging. PET/CT is a technique with high sensitivity and specificity as far as malignant lesions are concerned. It has dramatically improved PET interpretation; it has reduced equivocal interpretations; and it has increased diagnostic accuracy. More accurate staging, restaging, and prompt evaluation of therapy may lead to appropriate changes in patient management. However, controversy still exists in relation to the application of PET/CT in clinical practice, mainly because of its expense. It is evident that apart from additional costs, potential savings are associated with PET/CT as a result of avoiding additional imaging examinations or invasive procedures and by helping clinicians make the optimum treatment decisions. The evidence continues to accumulate on its usefulness in clinical practice as a profound imaging modality with expanding applications in a variety of oncological fields.

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