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ARTICLE

Intra-operative use of PET probe for localization of FDG avid lesions

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Abstract

Localizing positron emission tomography (PET)/computed tomography (CT) findings in heavily scarred surgical fields can be challenging. A high energy gamma probe (PET probe) can be used to guide surgery in those difficult areas. We describe our experience localizing and removing fluorodeoxyglucose (FDG) avid lesions in different body areas. Between 2004 and 2007, we used the PET probe to localize and remove 12 lesions from 9 patients. The lesions were removed confirming ex vivo and tumor bed FDG activity. Five patients had lesions in previously operated and sometimes radiated fields. One patient had FDG avid spots in the retroperitoneum. Two lymphoma patients had been previously treated and had new FDG avid spots in a background of scarred nodes. The last patient had a core biopsy suspicious for lymphoma but a repeat CT was non-specific. One patient with gastric cancer patient, two patients with melanoma patients and two patients with breast cancer had 10 metastatic lesions easily identified and removed. After a median follow-up of 14 months all five patients are alive. The two patients with lymphoma had their FDG avid lymph nodes easily identified and biopsied. In one patient with melanoma and one patient with suspected lymphoma, the preoperative scan revealed no FDG avid lesions. The PET probe confirmed this finding in the operating room. Clinical applications of PET probe guided surgery include restaging for previously treated lymphoma patients, localization and resection of metastatic FDG avid nodules especially in previously operated or radiated fields and biopsy of PET findings difficult to localize.

Keywords: *PET scan; PET probe; FDG avid lesions.*

Introduction

The introduction of whole body positron emission tomography (PET) using [^{18}F]fluorodeoxyglucose (FDG) in the 1980s for localization of colon metastasis has led to significant advances in nuclear medicine and oncology enabling more differentiation between benign and malignant processes on other imaging modalities and helping detect more occult metastases. This technology is based on the principle of increased glucose consumption by the tumor cells and the ability to detect the photon produced by the breakdown of [^{18}F]FDG inside the cancer cells[1]. Currently, the applications of this technology have broadened to include a large number of tumors such as melanoma, lung cancer, gastrointestinal stromal tumor, lymphoma, head and neck tumors, thyroid cancer, colon cancer, breast cancer, stomach cancer, pancreatic cancer, esophageal cancer and others to confirm the extension of the tumor, cancer recurrence and to follow up the response of chemotherapy with excellent sensitivity and specificity.

In parallel, new surgical challenges have emerged. Surgeons are often asked to biopsy or remove an FDG avid lesion in an effort to analyze the nature of the lesion, restage, check for possible tumor recurrence or even prolong survival. However, those lesions are not always easily detectable on the other imaging modalities and localizing findings identified by an abnormal PET/CT

Table 1 Diagnosis, PET CT findings, operative results and follow-up.

Patient	Diagnosis	PET findings	Operative result	Follow-up
1	Gastric cancer	1 lesion porta hepatis	1 lesion removed	15 months NED
2	Melanoma	4 lesions right neck	4 lesions removed	7 months AWD
3	Melanoma	1 lesion left axilla	Negative PET	54 months NED
4	Melanoma	2 lesions retroperitoneum	2 lesions removed	10 months NED
5	Breast cancer	2 lesions left axilla	2 lesions removed	16 months DOD
6	Breast cancer	1 lesion left interpectoral area	1 lesion removed	33 months AWD
7	Breast cancer	1 lesion left subclavicular	1 lesion removed	7 months NED
8	Lymphoma	1 lesion right axilla	1 lymph node removed	12 months NED
9	Lymphoma	1 lesion right groin	1 lymph node removed	7 months NED
10	Suspected lymphoma	1 lesion right axilla	Negative PET	Lost

AWD, alive with disease; DOD, dead of disease; NED, no evidence of disease.

scan in a heavily scarred surgical field can be challenging. Low energy gamma probes (140 keV) routinely used for sentinel node biopsy procedures are not capable of detecting the high energy rays of 511 keV emitted by FDG. Recent technological developments have led to the production of a high energy gamma probe (PET probe) that can be used to guide surgery in those difficult areas of the body[1].

This article describes our experience localizing and removing FDG avid lesions in the head and neck, chest, abdomen and retroperitoneum. In addition, the possible clinical indications for this exciting new technology are discussed.

Materials and methods

All the surgical interventions were performed between 2004 and 2007. The patients' medical history, imaging studies and clinical indications were carefully reviewed and discussed for all cases. Initially, initial detection of FDG avid lesions was considered sufficient for surgical intervention, however, thereafter and in most cases, persistence of FDG avidity on a minimum of two sequential studies was required before surgical intervention. All patients were injected with 10–12 mCi of FDG 3–4 h prior to the procedure. Intra-operatively, the lesions were localized using a PET probe (Intramedical Imaging/GE, California) for navigation. All localized lesions were removed confirming the FDG activity outside the body and a final background count was obtained in the tumor bed. The final pathologic reading of the lesions, and any operative and post-operative complications were recorded. Follow-up was available on all cancer patients. Institutional review board approval was obtained for the study.

Results

Nine patients underwent surgical intervention with the intra-operative use of the PET probe to navigate and localize previously identified FDG avid lesions. The underlying cancer diagnosis, PET findings, operative results and follow-up are presented in Table 1. In all cases except one, the surgical field had undergone previous surgery, radiotherapy, heavy chemotherapy or a combination of those (Table 2). Twelve lesions were identified and removed.

Table 2 Surgical field.

Patient	Surgery	Radiation	Chemotherapy
1		−	+
2		+	−
3		−	−
4		−	+
5		+	+
6		+	+
7		+	+
8		−	+ (scarred nodes)
9		−	+ (scarred nodes)
10		−	−

The first patient had undergone a subtotal gastrectomy with lymphadenectomy 20 months before the PET probe guided surgery. A few months after surgery PET/CT revealed a single FDG avid lesion in the porta hepatis. The patient was treated with chemotherapy and radiation, however the lesion grew slowly on follow up PET/CT without evidence of additional lesions. At surgery, a metastatic lymph node was found on the hepatic artery and removed. At 9 months follow-up the patient had no evidence of disease.

The second, third and fourth patients had previous diagnosis of melanoma. All patients had wide local excision of their melanoma and clearance of their lymph nodes. The second patient had a lesion removed from his right ear with negative sentinel nodes 5 years previously with recurrence in the parotid gland and in the neck after 4 years treated with a parotidectomy and neck dissection. A follow-up PET scan a year later, found 4 lesions in the right neck. All 4 lesions were identified intra-operatively with the PET probe and removed. At 18 months follow-up the patient is alive with stable recurrent disease in the neck. The third patient had a melanoma removed from his upper back and bilateral neck dissections, 4 years previously. A follow-up PET scan showed a questionable lesion in the left axilla. This lesion was not identified with the PET probe and no tissue was removed.

At 48 months follow-up the patients had no evidence of disease.

The fourth patient had a melanoma removed from his right foot 5 years before the PET guided intervention. He experienced a few episodes of in transit recurrences on his right leg but was free of disease 24 months before a PET scan identified 2 lesions in the retroperitoneum. At 4 months follow-up the patient had no evidence of disease.

The fifth and sixth patients had previous diagnosis of breast cancer. The fifth patient had a left modified radical mastectomy 6 years earlier. A follow up PET scan identified two lesions in the left axilla. These two lesions were localized and removed using the PET probe. At 13 months follow-up the patient is alive with distant disease. The sixth patient had a lumpectomy with axillary dissection 22 months before. A follow-up PET showed a lesion in the left interpectoral region. The lesion was localized and removed successfully. The patient was free of disease for 17 months and at 27 months is alive with new FDG avid lesions in the mediastinum. The seventh and eight patients were diagnosed with lymphoma previously and were treated but in a follow-up PET scan were found to have FDG avid lesions in the right axilla and in the right groin, respectively. Both patients underwent exploration with PET probe guidance; in both cases no recurrence was found in the FDG avid node. The last patient had a positive PET scan in the right axilla with a core needle biopsy suspicious for lymphoma. Repeat CT imaging was equivocal. The PET scan on the day of surgery did not show the lesion and this was confirmed in the operating room where no activity was detected by the PET probe. Patient number 7 had a wound infection. There were no other complications.

Discussion

Advances in medicine in general and in surgery in particular are closely related to advances in technology. Progress in technology opens new horizons and new opportunities to explore the merit of procedures that would not otherwise be possible. The clinical scientist plays a key role in the development and investigation of the indications and procedures within the clinical knowledge and management of the disease process.

In 1994, Daghighian *et al*. described the intra-operative used of a beta probe able to detect the 511 keV photons derived from radioactive decay of ^{18}F left free inside the tumor cell after phosphorylation of the attached glucose molecule[2,3]. The development of high energy gamma probes by Haigh *et al*. in 2000 and Raylman *et al*. in 2001 with excellent sensitivity in detecting [^{18}F]FDG avid lesions initiated the era of PET probe guided surgery for removal of occult lesions and lesions in re-operative scarred tissues[4–6]. [^{18}F]FDG enters the tumor cells using facilitative glucose transporters (glucose transporter-1) and undergoes phosphorylation to phosphodeoxyglucose (PDG)-6 by hexokinase, which accumulates in the tumor cells secondary to a slow dephosphorylation. The ^{18}F molecule is released and its radioactive decay produces two 511 keV photons traveling at 180° from each other. The detection of these photons is the basis of the PET scan and high energy gamma probes[7]. The half-life of [^{18}F]FDG is 110 min.

Intra-operative detection of [^{18}F]FDG avid metastatic and recurrent lesions is the main application of radio guided surgery using PET probes. This concept applies particularly to the exploration and localization of these lesions in highly scarred tissue from re-operation or secondary to radiotherapy. The localization of occult lesions not seen by any of the other available imaging studies is another indication when lesions are particularly enhanced using PET probes, which can guide the surgeon to lesions not easily visualized or palpated[10].

In this study we describe our experience localizing and removing FDG avid lesions in the head and neck, chest, abdomen and retroperitoneum. It is important to notice the accuracy of localizing the FDG avid lesion once the PET scan confirms their presence. From 14 lesions seen in PET/CT, 12 of them were localized and removed using PET probe guidance. The two lesions that were not identified also had negative PET scans on the day of surgery. The intra-operative accuracy of PET probe finding FDG avid lesions approximates 100%. In our experience, the probe was very helpful navigating into scar tissue and confirming complete removal of the lesions after the tumor bed activity reached the background counts.

As can be seen from the results, on two occasions, mostly at the beginning of our experience, the FDG injection on the day of the surgery did not confirm the presence of an avid lesion. For that reason our recommendation is to confirm the presence of FDG avid lesions on at least two sequential PET scans.

The next question is how to select the patients who would benefit from PET probe guided removal of metastatic lesions. We have tried to adhere to the general principles guiding the indications for surgical removal of metastatic lesions. Only patients who could potentially be rendered disease free and who could benefit from improved survival were offered the procedure. In some cases, as with the gastric cancer patient, a preoperative course of chemotherapy was requested to establish disease stability and non-appearance of other disease sites. In addition, all the patients were offered systemic therapy after the surgical removal of their metastatic disease. Despite the fact that some patients did develop subsequent new sites of disease, all the patients remained radiologically disease free for significant periods of time after the PET probe guided intervention. Because of the strict criteria of eligibility the number of patients offered the procedure is limited.

An interesting application of PET probe guidance pertains to the diagnosis or restaging of lymphoma patients. Directing the biopsy to the FDG active lesions has a

better chance of obtaining a diagnostic sample. This is especially true in areas that are difficult to access such as the mediastinum or retroperitoneum and after previous treatment when a repeat PET scan reveals an FDG avid spot in the background of large scarred down lymph nodes.

The use of this technology for the removal of FDG avid metastatic breast cancer to axillary nodes especially in the re-operative setting and with difficult anatomy has been described by others[8].

The role of high energy gamma probes for the resection of recurrent melanoma was described by Frac *et al*. demonstrating a sensitivity of 89% with a specificity of 100%[14].

Localization of metastatic lymph nodes in head and neck tumors, especially in re-operative and radiated fields, has become an area of special interest since the guidance provided by the PET probes can avoid damage to important nerves and vital organs in this area especially during difficult dissections. This particular topic was addressed by Meller *et al*. comparing the accuracy of PET, ultrasound and PET probes localizing metastatic lymph nodes in head and neck malignancies. PET probes and ultrasound demonstrated a 95% sensitivity for both but the PET probe had a 60% specificity when compared with ultrasound with only 40% specificity[11]. This study showed the superiority of this technique in the head and neck area. Curtet *et al*. described the used of PET probes for detection of iodine in scans negative for recurrent thyroid tumors with 100% accuracy in 7 patients[12].

Sarikaya *et al*. studied the accuracy of high energy gamma probes in the detection of recurrent colon cancer. The accuracy was 81% with tumors <1 cm and with a mean standardized uptake value of 8.27 for true positive lesions and 3.65 for false negative lesions. This study included 21 patients with recurrent lesions in the rectum, peritoneum, abdominal wall, porta hepatis, retroperitoneum, pelvis, lung and liver. The carcinoembryonic antigen level was elevated only in 11 patients[13].

Recent reports of the use of laparoscopic resection of occult metastasis in patients with ovarian cancer using a laparoscopic high energy gamma probe by Barranger *et al*. introduce the application of high energy probe guided surgery to the field of laparoscopy. This technique combines the accuracy of the PET probes with the advantages of minimally invasive surgery[15].

Conclusion

The development of FDG imaging and its application in a growing number of malignancies has led to the clinical need for a high energy gamma probe. The applications for this device are rapidly expanding and new surgical possibilities are probably on the horizon. A careful and stepwise evaluation of the clinical indications and benefits remains primordial.

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