Nuclear Medicine

Giovanni Paganelli and Lisa Bodei

SCINTIGRAPHIC STUDIES IN BREAST CANCER

Lymphoscintigraphy and sentinel node biopsy in breast cancer

Sentinel lymph node (SLN) localisation and biopsy (SLNB) represent one of the most important developments in surgery and has already produced important changes in the management of patients affected by early breast carcinoma. This technique was proposed as a method of disease staging in breast cancer patients (Giuliano et al. 1997) in order to permit the use of less aggressive surgical treatment that would not compromise quality of life. In fact, removal of axillary nodes in the presence of breast cancer is performed for staging and not with curative intent (Fisher et al. 2002), and axillary dissection is burdened by a significant rate of immediate and delayed possible complications such as lymphoedema, paraesthesia, pain and restriction of arm motion. Several studies have demonstrated that lymphoscintigraphy in combination with gamma probe-guided surgery is the best procedure to identify and remove the SLN in breast cancer patients [Veronesi et al. J Natl Cancer Inst. 1999 17;91(4):368-73], being more suitable and sensitive than blue dye mapping.

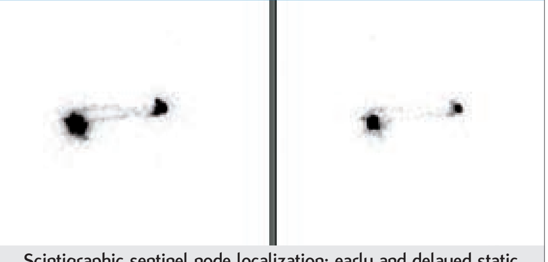
We have already described a reliable lymphoscintigraphic technique in previous works [Paganelli et al. Q J Nucl Med. 1998;42(1):49-53, De Cicco et al. J Nucl Med. 1998;39(12):2080-4]. Today, more than 10 years after the pioneering reports of Krag (1993) and Giuliano (1994), SLNB has become a new standard of care for axillary node staging in breast cancer. A widely accepted consensus exists in literature that SLNB is "feasible and accurate, works well in a wide range of practice settings, is sufficiently robust to withstand variations in technique, increases staging accuracy by allowing enhanced pathologic analysis, has less morbidity than complete axillary lymph node dissection (CAD), and gives local control comparable of that of CAD" (Cody 2003).

Despite since several years SLNB is routinely performed in the clinical practice, the correct indications for SLNB still represent an unsolved question. In fact, to ensure a high SLN accuracy and a low false-negative rate, in the early experience of the 90's (the developmental phase of validation) SLNB was strictly limited to patients with small unique invasive tumours and clinically negative axillary lymph nodes. Nevertheless, with the increased experience gained and the widespread use of the technique, the indications for SLNB have since been extended to encompass most patients with non-metastatic disease previously excluded for technical or theoretical reasons. So, most of the "historical" relative contraindications for SLNB are now being questioned and the initial restrictive selections of patients are now progressively enlarging. Several new clinical situations are presenting in the clinical practice as possible, previously unexpected, indications so that someone is actually asking if "does anybody not need a SLNB?". The suitability of SLNB has been studied and established in the settings of DCIS, in multifocal and multicentric disease, following neo-adjuvant chemotherapy, after excisional or core-needle biopsy or after small or large volumes of resection and finally after a previous SLNB when a local recurrence occurs. SLNB has been recently demonstrated to be safe and sure in pregnancy and can be also considered in patients with clinically suspicious axillary nodes if preoperative palpation or US-guided FNA is nondiagnostic. Only for a small subset of patients at both ends of the tumoral spectrum, those with pure low grade DCIS radically resected and those with inflammatory cancer or previous radiotherapy treatment the jury is still out.

Nowadays, in the sentinel lymph node era, CAD for uninvolved axillary lymph nodes should be considered unnecessary and inappropriate. Between January 2000 and August 2005, 3487 out of 10,031 invasive breast cancer patients consecutively operated at the European Institute of Oncology were considered not suitable for sentinel lymph node biopsy (SNB) (for suspicious nodes, neoadjuvant treatments, large tumours, multifocality, or previous excisional biopsies), and were directly submitted to CAD. In 2875 cases (82%) a variable grade of axillary involvement was shown, while in 612 patients (18%) no evidence of axillary metastases was documented. According to the wider extension of the indications for SNB over the time, the number of unnecessary CAD" progressively decreased from 26% (in 2000) to 9% in 2005 [Intra M. et al. Eur J Cancer. 2007 Dec;43(18):2664-8].

When lesions are non-palpable, the localization and removal may be troublesome. When such lesions are malignant, axillary node status must be determined. We used radio-guided occult lesion localization (ROLL) for locating and removing non-palpable breast lesions together with sentinel node biopsy (SNB) to assess axillary status (the "SNOLL technique"). From March 1997 to April 2004 we studied 1046 consecutive patients with suspicious non-palpable breast lesions and programmed for conservative surgery and SNB. In 87 patients intraoperative histological examination revealed a benign lesion and SNB was not performed. The remaining 959 patients, with cytologically or histologically proven cancer, underwent SNOLL with immobile radiotracer injected under mammographic or ultrasound (US) guidance into the lesion, and subsequent injection of mobile tracer subdermally to localize the sentinel node (SN). Patients then underwent breast surgery and SNB. Breast lesions were localized by ROLL in 99.6% of cases and were removed radically with negative margins in 91.9% of cases. Sentinel nodes were detected in all but one case. Intraoperative or definitive histological examination revealed 776 invasive/microinvasive carcinomas and 182 with in situ disease. Sentinel nodes were positive in 154 (19.8%) of 776 invasive/microinvasive cancers and in two with ductal intraepithelial neoplasia (1.1%). In SNOLL the injection procedures are performed separately, but both lesion and SNs are removed together; axillary dissection is performed if the SN is positive, thus definitive treatment of malignant non-palpable lesions occurs in a single surgical session [Monti S et al. Ann Surg Oncol. 2007;14(10):2928-3].

Scintigraphic sentinel node localization



Scintigraphic sentinel node localization: early and delayed static images in left oblique anterior view. Note: injection site (bigger spot) and two lymphatic vessels draining to two close lymph nodes.

Mammoscintigraphy

Mammoscintigraphy (MMS) with MIBI has been indicated as a useful tool in predicting response to therapy in cancer. However, contrasting results have been reported in the literature for breast cancer patients. We studied the role of MMS in 51 patients with locally advanced breast cancer (LABC) scheduled for neoadjuvant therapy. Breast tumour status was evaluated at baseline, during therapy and at the completion of therapy by radiological techniques and by MMS. Pre-therapy (MMS1) and post-therapy scintigraphic images (MMS2-3) were analyzed. MMS1 was performed in all pts, 41 carried out MMS2 and 27 had MMS3. Tumour uptake and washout in MMS1 did not show any correlation with the therapy response. The absence of any association between tumour uptake and washout with respect to therapy response suggests that MMS is not a reliable technique to predict therapy response in LABC [Travaini L.L. et al. Breast. 2007;16(3):262-70].

SCINTIGRAPHIC STUDIES IN OTHER MALIGNANCIES

Lymphoscintigraphy and sentinel node biopsy in head and neck cancer

Cervical lymph node status is the most important pathological determinant of prognosis and decision making in head and neck squamous cell carcinoma (SCC). In order to demonstrate that lymphoscintigraphy (LS) can supply a complete map of the lymphatic drainage before surgery, allowing planning of the type of intervention and serving to guide lymphadenectomy, we studied 14 patients with T2-4 SCCs of the tongue and clinically negative lymph nodes in the neck (cN0) who were scheduled to undergo tumour resection and selective level I-IV neck dissection extended to level V. LS was performed in all patients following the injection of (99m)Tc-colloidal sulphide in three aliquots around the primary lesion. Dynamic, static and tomographic images of the head and neck were acquired. The operative specimens were subjected to lymphoscintigraphic evaluation. Preoperative and postoperative imaging results were compared with the pathological findings. Preoperative LS was successful in all patients. Preferential pathways of lymphatic drainage were identified: level II of the neck was the most common lymphatic drainage pattern, followed by levels IV and III. Contralateral drainage occurred in 11 patients and in two of them metastatic nodes were found on the contralateral side. Metastases were observed only in radioactive lymph nodes. LS is able to supply a complete map of the lymphatic drainage before surgery, making it possible to tailor selective neck dissection to each individual patient based on the results of preoperative mapping, thereby sparing healthy lymphatic tissue and reducing surgery-related morbidity [De Cicco C. et al. Eur J Nucl Med Mol Imaging. 2006].

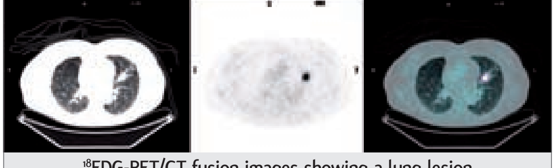
FDG-PET STUDIES

FDG-PET in lung nodules

Indeterminate noncalcified lung nodules are a frequent finding when low-dose computed tomography (LD-CT) is used for lung cancer screening. The best clinical management for such nodules remains uncertain. We present results using positron tomography scanning (CT-PET) to evaluate LD-CT-detected lung nodules during the first year of the

Continuing Observation of Smoking Subjects (COSMOS) early detection trial for lung cancer in 5200 asymptomatic current or former smokers (> or = 20 pack-years) older than 50 years of age, enrolled in a single-institution screening trial using annual LD-CT. Growing nodules and those with a maximum diameter exceeding 8 mm were studied with CT-PET. Transthoracic needle biopsy was not a routine part of the protocol. During the first year of study, 157 subjects underwent CT-PET, 66 of whom underwent surgical biopsy. Of the 58 lung cancers found on surgical biopsy, 51 were positive (PET standard uptake value > 2.0) and seven were negative for malignancy by CT-PET. Sensitivity was 88% overall, but 100% in the subgroup with solid nodules of 10 mm or more. Among the 8 patients with benign disease at surgical biopsy, CT-PET was positive in 6 and negative in 2. CT-PET is a highly promising modality for identifying potentially malignant lesions in screening-detected lung nodules and appears particularly useful as an alternative, in the screening setting, to invasive procedures for the further investigation of uncertain nodules. Our findings also indicate that the standard uptake value threshold for positivity should be lowered for small nodules (< 10 mm). Longer follow-up and larger prospective studies are necessary to confirm these preliminary findings [Veronesi G. et al. Ann Thorac Surg. 2007;84(3):959-65].

^{18}FDG-PET/CT



^{18}FDG-PET/CT fusion images showing a lung lesion with increased metabolism.

FDG-PET in thymic masses

Thymic masses may represent an unsolved diagnostic problem, which often require surgical procedures for an accurate staging. We tested the possible role of ^{18}FDG PET/CT as a non-invasive way to determine the nature of thymic lesions candidated for surgery. We retrospectively analyzed through contrast-enhanced multidetector computed tomography (MDCT) and ^{18}FDG PET/CT twenty consecutive patients presenting with a thymic mass. CT scans were focused on morphologic features and invasiveness characteristics. Qualitative and semi-quantitative analyses by maximum standardized uptake value corrected for body weight (SUVbw max) were performed on ^{18}FDG PET/CT. In all cases, readers were blinded to pathology findings. Both imaging techniques were correlated to final pathology. In the group of benign lesions MDCT correctly identified well-defined margins of masses in 8 out of 8 patients whereas ^{18}FDG PET/CT was negative in 6 out of 8 patients. Amongst malignant lesions, MDCT revealed mediastinum fat or infiltration of adjacent organs in 10/12 patients. On the other hand, ^{18}FDG PET/CT showed increased radiotracer uptake in 12/12 patients. We concluded that MDCT and ^{18}FDG PET/CT alone are not able to differentiate the nature of thymic lesions. However they are two non-invasive complementary techniques which can be used to differentiate benign from high risk malignant thymic lesions. These findings should be taken into account before surgery is performed as a diagnostic procedure [Travaini LL et al. Lung Cancer 2008].

FDG-PET after radiofrequency ablation of liver metastases

Focal metastasis may be treated with radiofrequency ablation (RFA), a low invasive method yet limited by the lack of direct evidence of radicality of treatment. We, hereby, aimed at assessing the role of ^{18}FDG PET/CT in RFA treatment success evaluation and early diagnosis of local relapse of liver metastasis after RFA procedure. RFA was performed in nine patients on 12 liver metastasis, serially imaged through ^{18}FDG PET/CT and multidetector CT (MDCT) at 1, 3, 6, and 9 months after treatment. Eight lesions were also scanned with ^{18}FDG PET/CT at 1 week after treatment. Imaging analyses were performed on 47 ^{18}FDG PET/CT and 51 MDCT. Imaging reading outcomes were compared to each other and to biopsy tissue results when available. In one case, ^{18}FDG PET/CT revealed radiotracer uptake at RFA site a week after procedure. Negative concordant outcome was obtained on eight lesions at 1 month after RFA, on eight cases at 3 months, on four at 6 months, and on two cases at 9 months. Extra-liver (peritoneal) disease was detected in one case by both ^{18}FDG PET/CT and MDCT. In seven cases, ^{18}FDG PET/CT revealed the presence of local recurrence earlier than MDCT. In no cases did MDCT detect local relapse earlier than ^{18}FDG PET/CT. ^{18}FDG PET/CT may detect RFA treatment failure as well as local relapse after RFA earlier than MDCT [Travaini L.L. et al. Eur J Nucl Med Mol Imaging. 2008, in press].

CT and FDG-PET/CT in the diagnosis of local and distant recurrence of resected rectal cancer

The aim of this study was to compare the diagnostic value of multidetector computed tomography (MDCT) and ^{18}FDG PET/CT for the detection of local and distant recurrence in patients operated on for rectal cancer. Sixty-seven patients who underwent radical surgery for rectal cancer and were followed up with ^{18}FDG PET/CT and MDCT were included in this retrospective study. The ^{18}FDG PET/CT and MDCT findings were independently compared with histological sampling or 2 years' follow-up. Local recurrence occurred in 15/67 patients. MDCT diagnosed local recurrence in 15/15 cases and ^{18}FDG PET/CT in 14/15. Sensitivity and specificity were 100% and 98% for MDCT and 93% and 98% for ^{18}FDG PET/CT, respectively. Hepatic lesions were found in 17/67 patients. All hepatic metastases were detected by both techniques. Pulmonary metastases occurred in 8/67 patients: they were correctly identified in all cases by MDCT and in 6/8 by ^{18}FDG PET/CT. MDCT and ^{18}FDG PET/CT showed high sensitivity and specificity for the detection of local recurrence of rectal cancer. Both techniques were equally accurate for the detection of hepatic metastases. MDCT showed slightly higher sensitivity and positive predictive value in detecting pulmonary metastases compared with ^{18}FDG PET/CT [Bellomi M. et al. Radiol Med (Torino). 2007 Aug;112(5):681-90].