Breast carcinoma may be detected as the result of screening applied within a high-risk population, where the risk may be as general as a particular age group or as specific as in carriers of specific genetic mutations. It may also be incidental, for example as a finding in large field of view imaging performed for other indications, or it may be detected in response to a clinical concern.

In addition to the primary carcinoma, there may also be metastases. Metastatic breast carcinoma is usually found within the regional lymph nodes, chest wall, lungs, liver, and skeleton. Accurate staging relies on the ability to identify lesions within these organs and then the feasibility to access these lesions for biopsy.

Metastases may be divided into two categories according to imaging considerations. The first are those that are regional and superficial in location (e.g. to axillary and internal mammary lymph nodes). The rest may be regional though deeper from the skin surface (e.g. to supraclavicular lymph nodes) or distant, the latter often at significant distance from the skin surface and the primary lesion.

Each location or organ of dissemination has its particular imaging specifics that further influence the identification and characterization of metastatic lesions. Whenever possible, imaging protocols should be so tailored as to search and identify the “threshold” lesions, i.e. those lesions that when confirmed would lead to stepwise intra- and/or intermodality therapy changes.

**Imaging options**

There are several imaging options capable of identifying and defining breast cancer. These include X-ray mammography, ultrasound, computer tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET). Newer modalities such as positron emission mammography (PEM) or near infrared spectroscopy (NIRS), recently or soon to be available in clinical practice, may replace MRI or PET for the detection of the primary lesion.

The best applications of PET to the diagnosis and local-and-superficial staging rely on the high positive predictive value of this exam to indicate the presence of breast cancer. PET that uses fluorodeoxyglucose (FDG-PET) assesses a lesion’s rate of glycolysis. Lesions with a high rate of glycolysis found within breast parenchyma or the axillary and the internal mammary lymph nodes are almost always malignant. The FDG-PET exam is also the single most important modality within any imaging protocol to identify and localize additional sites of distant metastasis.

This article reviews the recent literature on breast imaging with FDG-PET and FDG PET-CT. It addresses the current and likely future role of this imaging technique vis-à-vis complementary and competing current and emerging technology as applied to the diagnosis, staging and restaging of breast cancer.

Imaging protocols that assess response to therapy and attempt to separate between residual tumor, tissue repair or post therapy inflammation, are not addressed in this article.

**Recent PET studies**

In 2000, Avril et al. studied 185 breast masses with FDG-PET (132 malignant and 53 benign) and reported that, depending of the preset threshold uptake, the sensitivity of cancer detection ranges between 64.4% and 80.3%. They describe a lower false negative rate for IDC when compared to ILC (23.7% vs. 65.2%) and conclude that PET positive findings have a high (96.6%) positive predictive value for primary breast carcinoma [1].

Schirmeister et al. studied 117 patients preoperatively, and reported in 2001 that for almost constant specificity, PET sensitivity for the detection of multifocal breast carcinoma was almost twice that of combined X-ray mammography and ultrasonography [2].

In 2001, Samson et al. published their meta-analysis of 13 studies that included 606 patients. The authors chose large tumor size (pT2 or larger) and moderate to high pre-test probability for breast cancer (53% to 95%) as their main...
selection criteria. Their statistical analysis yields a cross-study PET sensitivity of 88% and specificity of 79%. The authors concluded that PET has 12.1% negative predictive value (NPV) when the pre-test probability for breast cancer is between 20-50% and 29.2% NPV when the pre-test probability is at least 75% [3].

Avril et al. addressed the relationship between the FDG uptake of the primary breast cancer and various tumor characteristics, and in 2001 published their finding that the observed rate of glycolysis may not be used to predict the biological behavior such as differentiation or histopathology or the axillary lymph node status. They also reported that a lower density of blood tumor vessels corresponds to a higher rate of FDG uptake [4].

In 2002, Buck, Schirmeister et al. reported a direct relationship between FDG uptake and the Ki-67 proliferative index for ductal cancers, that is not found for lobular ones, and the lack of significant correlation between primary tumor uptake and receptor status, c-erb B2 or p53 tumor expression [5].

Beaulieu et al studied the dynamic rate of FDG uptake of untreated breast carcinoma and reported in 2003 that the standardized uptake value (SUV) of the primary tumor changes linearly at a rate of -0.02 to +0.15 per minute after approximately 30 minutes from the time of FDG administration [6].

**Dual-point PET imaging**

Dual-point PET imaging has been previously evaluated as an imaging protocol to improve PET specificity in head and neck cancer [7] and to differentiate malignant pulmonary nodules from inflammatory lung lesions [8]. The protocol variation of a single delayed acquisition, in the context of lung carcinoma, did not improve sensitivity and reduced specificity in comparison to dual-point imaging [8].

In 2006, Kumar, Alavi et al. reported that dual-point PET imaging could also separate breast carcinoma from benign causes of FDG uptake [9]. One year later, this same group reported that 95% of normally dense breasts have an SUV\textsubscript{max} of 1.62 or less [10].

**Prone breast imaging**

Prone breast imaging is another protocol likely to improve PET sensitivity. When normal breast tissue is spread apart its radiographic density and measured metabolism decrease, while these changes are not observed in an adjacent cancer. Lesions adjacent to chest wall activity may also be better resolved. Prone PET imaging allows same breast geometry co-registration with MRI. In a small group of patients, prone PET imaging improved the MRI specificity for the detection of primary breast cancer [11].

**Positron emission mammography (PEM)**

The current positron emission mammography (PEM) camera has LSO-crystal planar detectors integrated with conventional mammography, and is capable of direct image co-registration. The first prospective multi-center trial completed in 2005 reported PEM sensitivity of 89%. Two of the lesions missed, a 1 mm DCIS and 1 cm IDC, suggest that tumor metabolism is an independent factor that affects sensitivity [12].

The next prospective multi-center trial, completed in 2006, reports PEM sensitivity, specificity, PPV, NPV and accuracy all in the range of 90%. In this group of 61 patients with breast carcinoma, PEM detected 10 of 11 DCIS, 1 of 2 T1a tumors, 4 of 6 T1b tumors and 7 of 7 T1c tumors [13]. A cylinder-shaped PEM camera (CYBPET) with BGO-crystal detectors and 20 cm port diameter is currently under development [14].

**MRI breast imaging**

MRI breast imaging relies on detailed morphological information (high spatial resolution in the range of 1 mm coupled with high signal-to-noise ratio) and dynamic contrast enhancement kinetics. Compared with X-ray mammography, MRI has less spatial and contrast resolution, but provides additional information that defines aberrant tumor perfusion. There is recent consensus gathering that the morphological presentation with MRI may provide the best clinical information, as there is significant overlap between the enhancement kinetics patterns of breast tumors and benign lesions.

On March 28, 2007, the American Cancer Society released MRI guidelines for breast cancer screening as an adjunct to X-ray mammography in high-risk patients. The evidence submitted draws from the study of over 3800 patients in 6 countries, all with BRCA mutation or a very strong family or personal history of breast cancer. Within this population, MRI detection sensitivity is expected to be 77% to 100%, significantly higher than that of X-ray mammography, which is estimated as being in the 16% to 40% range. This statement paper reports reduced MRI specificity for the detection of carcinoma in situ and points out that a lower MRI specificity when compared to X-ray mammography may lead to more patient recalls and likely increase in false negative biopsies [15].
Melanoma is considered to be the most FDG avid tumor.

Near infrared optical imaging

An emerging technology, near-infrared (NIR) tomographic optical imaging, provides information on blood flow kinetics and the level of tissue oxygenation. Limited depth light penetration reduces the potential for human uses to only few applications such as breast imaging. Indocyanine green (ICG), approved for use in humans in the United States, provides fluorescent information that is limited to the presence of angiogenesis and tumor vessel “leakiness”. Reports from pilot studies suggest improved tumor detection rates when MRI and NIR optical imaging are combined as a single imaging device [16].

SPECT

A meta-analysis of scintimammography in 3049 patients yielded 85% sensitivity and 83% specificity for the detection of breast cancer [17]. Recent improvements in SPECT image reconstruction, SPECT–CT as single imaging device or dedicated gamma cameras integrated with mammography aim at enabling the use of SPECT to detect “pre-anatomic” lesions.

Compared with PET or PEM, SPECT has reduced image quality, but SPECT imaging agents interrogate tumor physiology at a more basic level than glycolysis. The mechanism of technetium-99m methoxyisobutylisonitrile (MIBI) uptake in breast cancer is uncertain, but is linked to the grade of the tumor [18], directly correlated to the Ki-67 proliferative index, and inversely related to the expression of estrogen receptors [19].

MIBI behaves in vivo like a P-glycoprotein substrate. The study of its initial uptake and subsequent washout in breast tumors has been used to identify the multidrug resistance (MDR) phenotype [20, 21,22]. The presence and density of estrogen receptors varies with each site of tumor involvement, over time within each tumor site, and difficult to define with biopsy if a large lesion or multifocal disease is present. In vivo imaging of the estrogen receptors’ status may prove to be a more accurate assessment than biopsy, and I-123 labeled tamoxifen SPECT [23] or FES-PET imaging [24] have been used for this purpose.

Axillary lymph node staging

Axillary and internal mammary lymph nodes are most often the only initial metastases. The superficial location of these nodes invites the most sensitive applications of imaging, allows for accurate mapping procedures with precise anatomical localization, and facilitates safe and fast surgical access for definite tissue confirmation.

Van der Hoeven et al. reported that FDG-PET performance for axillary lymph node staging is dependent on the local nodal tumor load and the FDG avidity of the primary tumor [25]. Greco et al. reported 94.4% sensitivity, 86.3% specificity and 89.9% accuracy for 167 consecutive patients, and concluded that FDG-PET would be able to select patients who might avoid ALND [26].

Wahl et al. reported that in a multicenter prospective study of 360 women with newly diagnosed breast carcinoma, FDG-PET had much lower sensitivity for axillary node metastasis, estimated as 25% to 32% when SUV-lead image analysis was controlled for an almost perfect specificity. This group does not recommend FDG-PET for axillary lymph node staging, but reported that PET has a 78%-83% positive predictive value for malignancy when multiple axillary lymph nodes were involved [27].

Chung et al. reported that axillary lymph node(s) uptake with SUV of 2.3 or higher could obviate the need for surgical staging [28]. This difference in reported staging sensitivity, borne out by other smaller studies, is explained by a change in the gold standard, from ALND with histopathologic analysis to SNB with step sectioning and IHC [29].

Sloka et al. identified 20 original articles in Medline, Embase and Cochrane databases that address FDG-PET axillary lymph node staging in the context of breast carcinoma. These studies are graded on methodological quality: five studies use SNB as the gold standard, sixteen studies are prospective, and all were published between 1992 and 2004. This meta-analysis concludes that FDG-PET may have better than 85% sensitivity and specificity for axillary lymph node metastasis in select patient populations when imaging conditions are optimized [30].

Melanoma is considered to be the most FDG avid tumor. Inductive reasoning suggests that lymph node staging as a PET imaging application would be best suited for melanoma. In their study of melanoma, Wagner et al report 98.6% sensitivity for occult LN metastasis with SNB and 16.7% for PET [31]. This same group reports that in the case of melanoma, PET sensitivity for staging is directly proportional to the initial tumor burden (threshold defined as 80 mm³), condition likely fulfilled in stage III or IV disease [32].

Based on a meta-analysis of sixteen prospective studies published between 1986-2003, Alvarez et al. concluded that sonography is only “moderately” sensitive, and that it cannot be used in isolation.
for deciding whether to perform axillary node dissection [33].

Murray et al. reported that in 47 women with primary breast cancer, dynamic contrast enhanced MRI of the axilla achieved 100% NPV and 38% PPV for the diagnosis of lymph node metastases [34]. Stets et al. reported that MRI with ultra-small particles of iron oxide improves the accuracy of axillary lymph node staging [35]. MRI for IMLN staging has been described in reference to lymph node morphology and size, the latter as mean major diameter. A threshold of 5 mm produced 90.7% accuracy when referenced to dissection followed histopathologic evaluation [36] (Figure 1).

Whereas PET may always fail to identify micrometastases or small (less than 3 mm) macrometastases, PEM may be able to identify the latter. Morphological imaging would provide support as anatomic localization. Optical imaging abilities in the evaluation of the breast may also be extended to the axilla.

In a group of 203 breast cancer patients, Pritivelis et al reported a 9.36% failure rate for lymphoscintigraphic mapping. Their analysis suggests that failure is related to advanced age, elevated body mass index, prior breast surgery, or a short period of time from breast biopsy. It does not appear to be influenced by the size of the primary tumor [37].

Extensive tumor involvement of the sentinel lymph node, previously suggested as a source of mapping failure, was not addressed.

The ALMANAC Trialists Group evaluated 803 patients who received both peritumoral injection of Tc-labeled albumin and Blue V dye. The authors reported that successful SBN compared to follow-up standard axillary treatment had a 10% FN rate if one sentinel lymph node was harvested and 1% FN rate when three or more lymph nodes are removed [38]. Torrenga et al. reported that SNB with immunohistochemistry and step-sectioning upstages 30% of the patients initially considered negative for metastasis with ALND and H&E staining [39].

Step-sectioning may still be inadequate, as the slice thickness is at least an order of magnitude larger than the neoplastic cell diameter. Reverse transcription-coupled polymerase chain reaction has been suggested as a more sensitive staging method [40].

The sentinel lymph node is most often within the ipsilateral axilla, but may also be found as an internal mammary lymph node. Drainage to the internal mammary lymph nodes is from channels deeper within the breast that course along subdivisions of intercostal arteries [41]. Metastasis to IM lymph nodes has been considered as usually concomitant with axillary node involvement and isolated IM chain metastasis as an infrequent occurrence [42].

Byrd et al. reported scintigraphic documentation of radiocolloid drainage to the internal mammary lymph nodes in 37 of 220 (17%) studied patients with tumors located in all breast quadrants, but this is less common when the primary is within the upper outer quadrant [43].
In 2002, in a pilot study of 182 patients, Galimberti et al. described stage migration from N0 and N1 to N3 in 14 patients (7.7%) after biopsy of internal mammary chain lymph nodes in breast cancer patients. This group concluded that IM lymph nodes can be quickly removed with insignificant risk and no increase in postoperative hospitalization, with the benefit of improved staging and prompting modification of both local and systemic therapy [44].

Four years later, in 2006, Carcoforo et al. published similar results for a study population of 741 women with breast cancer [45]. Tran et al. reported that within a sample of 42 patients with the primary tumor located within the inner quadrants, 61.9% had only extra-axillary metastases and that 11.9% had both extra-axillary and axillary metastases. The likelihood of understaging with conventional approaches, and the higher risk for disease progression when the primary breast lesion is within the inner quadrants, were invoked as grounds for potential benefit from additional PET staging in these cases [46]. Zucali et al. retrospectively evaluated 2,396 breast cancer patients and conclude that those with primary tumors within the internal quadrants or subaureolar locations have a 30% higher chance of distant metastasis and 20% higher mortality than those with the primary tumor within the outer breast quadrants. The authors suggest that the higher mortality may be at least partially related to the reduced ability to detect disease at extra-axillary sites [47].

The prognostic significance of micrometastases and the question of whether microscopic amounts of tumor found by SNB always justify adjuvant local or systemic therapy has to be defined. Regional lymph node filter function has traditionally been assumed to be critical in the prevention of the systemic spread of malignant cells shed from the primary cancer but laboratory studies indicate that lymph node filter function may be incomplete and that lymphatic and lymphovenous shunts exits that bypass regional lymph nodes and allow for simultaneous lymphatic and hematogenous dissemination of malignant cells [48].

Inoue et al. reported that high SUVmax and PET “node (+)” indicates a significantly worse prognosis than for other patients (5-year disease free survival rates of 44.4% vs. 96.8%) and could preoperatively select patients for adjuvant chemotherapy independently of TNM staging [49].

In the 2001 National Institute of Health Consensus Development Conference Statement, 44 medical experts disseminated the data from 2,230 references published between 1995 and 2000. They concluded that adjuvant polychemotherapy improves survival and should be recommended to the majority of women with localized breast cancer, that adjuvant dose-dense chemotherapy should be offered to high-risk breast cancer women, and that post-operative radiation should be given to women with a high risk for locoregional tumor recurrence. High-risk cancer was defined as advanced primary cancer or the presence of at least four positive lymph nodes [50]. In March 2003, the same group published “Practice Outcomes” for breast cancer, with an imaging algorithm that includes mammograms, ultrasound, CXR, CT abdomen and bone scan, but with no mention of diagnostic chest CT, breast/marrow MRI, PET or PET-CT [51].

**Distant dissemination**

Distant dissemination of breast cancer may be the initial presentation of a rather aggressive cancer. When new lesions lack geographic adjacency to the primary tumor, this weakens the implied clinicopathologic connection. Metastasis to deep location or to strategic anatomical spaces may limit the technical feasibility or safety of a biopsy procedure. The possibility for variable histopathological phenotypes within different metastatic lesions and the implied sampling error for larger lesions further add to the complexity of fully assessing the disease process. Such complexities result in...
an increased reliance on tomographic imaging for cancer surveillance and characterization (Figure 2).

The added value of FDG-PET body surveillance across many malignancies has been addressed with success in numerous publications and has gained acceptance by medical regulatory bodies worldwide. In 2001, Yap et al. published the referring physician’s perspective on staging patients with breast cancer. This group reports that the addition of PET to the current imaging algorithm upstaged 28% and downstaged 8% of their study patients. Management impact was seen in 86% of patients who were upstaged [52].

In 2004, Eubank et al. reported that FDG-PET after CT imaging alters therapy in 32% of patients [53]. This distinct difference in staging ability between conventional imaging (mostly CT) and PET had been addressed by Vranjesvic et al. as early as 2002, in their analysis of the clinical outcome following primary treatment for breast cancer. For example, their data indicates that negative PET restaging has 80% likelihood for disease free survival at 36 months whereas negative conventional imaging likelihood is 40% [54] (Figure 3).

In 2005, Isasi et al. published a meta-analysis on FDG-PET for the evaluation of breast cancer recurrence and metastases. The group found that in a sample size of 808 patients, the pooled sensitivity was 90% and the pooled FPR was 11%. They concluded that FDG-PET is a valuable tool in these circumstances [55].

Liu at al. reported a 96% sensitivity and 90% accuracy for FDG-PET in asymptomatic patients with elevated serum tumor markers (CA 15-3 above 32 U/ml and CEA above 5 mg/ml) [56].

Radan L et al. re-addressed re-staging for patients with elevated serum tumor markers, replacing PET with PET-CT. They reported in 2006 that the addition of PET-CT to contrast-enhanced CT further changed management in 51% of their study patients [57].

Discussion

Clinical practice

Current clinical practice follows the sequence of tumor identification, localization and in vitro characterization. Once a cancer is identified, management and prognosis are derived from staging information that is addressed to fit the TNM decision grid. At the core of this system is the attempt to establish merit for local therapy and to stratify current systemic therapy options. The main assumption of the TNM system is that the process of metastasis may solely assume a stepwise progression along the draining lymphatic system or, for reasons not fully understood, disseminate rapidly or extensively.

Lesion detection may be improved through further technological refinement and a better understanding of the early breast cancer biology. The current designs of US, CT, MRI and PET are very close to their theoretical spatial resolution and further refinements would necessitate disproportional expenditure to achieve any further imaging improvements. Thus hardware development, at least in the near future, will make a lateral move and proceed to re-pack current systems as hybrid ones, then market them as simultaneous multi-modality imaging devices with implied spatial co-registration.

Larger leaps in medical progress will come from future software developments. Recent advances in imaging technology have generated large data sets that cannot be fully integrated by the human
Computer-aided reference to patient specific or normal-population databases is expected to enhance interpretation. Biopsy targeting systems now available with mammography or ultrasound imaging need to be integrated with the newer technology.

The few-millimeter-to-sub-centimeter lesions detected only with the newer PET (-CT), PEM, and NIR optical imaging systems require wire localization prior to surgical resection. The widespread availability of mammography and the low relative cost associated with it, fine spatial resolution and the ability to detect ominous microcalcifications, the recent enhancements of digital imaging and computer-aided detection are all factors that provide clinical and economic value to sustain its use for many more years.

MRI has recently crossed the threshold to a screening role, albeit limited to a high-risk population. MRI, like ultrasound, does not use ionizing radiation and is likely to be better suited to answering the clinical questions now addressed with ultrasound. In this role as a problem solving technique, MRI may replace ultrasound utilization when or if its availability and cost become more favorable. PEM coupled with a biopsy gun, available later this year, will provide competition to MRI for screening high-risk patients. PEM will surpass PET ability to detect primary breast cancer and, where available, will displace it. NIR optical imaging, when clinically available, will compete with PEM and MRI.

The future of PET(-CT) in cancer detection, best described by Korn et al., is that it attributes a very high likelihood of IDC to any incidental hot focus of breast uptake [58] (Figure 4).

**Detection of metastatic lesions**

Breast parenchyma and axillae are superficial structures that could be imaged in relative isolation from the rest of the body, and are thus less influenced by body habitus or the imaging method (e.g. the use or type of attenuation correction or planar imaging versus SPECT imaging). All PET systems report their best spatial resolution in the center of the field of view that then deteriorates by approximately 1 mm in the region of the axillae. PET imaging of IM lymph nodes has higher spatial resolution than within the axillae, but in clinical practice this advantage is offset by lower contrast resolution in the adjacency of chest wall activity.

Tissue spreading improves the detection of primary breast lesions (prone/gravity or mechanical compression) and that of axillary lymph node metastasis (arms above head) as it generates improved contrast resolution and better signal-to-noise ratio.

If axillary staging is the only consideration, PET, as molecular imaging, may be a better choice than US or MRI, as anatomical/function imaging, although less sensitive than PEM or NIRS. If combined axillary and internal mammary nodal staging is required, PET(-CT) may prove to be the best single imaging option.

Most imaging has its domain in the millimeter-to-centimeter range, and is thus unlikely to replace in vitro tissue analysis, although even the latter does not have perfect sensitivity. SNB may only reflect local tumor “seeding”, and does not exclude microscopic dissemination into the vascular system. Early microscopic metastasis may one day become an axiom, and the need for confirmation may be substituted by the assessment of macroscopic local disease burden. PET and its variants may then become the gold standard.

A normal submillimeter resolution CT series may have the best NPV for cancer staging within non-mesenchymal locations. When the exam is not normal, CT imaging lacks both sensitivity and specificity for small lesions. PET usually has better target-to-background cancer conspicuity, that is a significant advantage over CT in daily practice.

PET-CT continues to replace PET in clinical practice. Current imaging protocols promote the incorporation of single or multi-body section diagnostic/enhanced CT exams into a single oncology examination with PET-CT. The
recognition that cancer imaging is multifactorial and PET and CT imaging features are synergistic should eliminate the need for further study of the individual merits, and acknowledge (fully diagnostic) “PET-CT” as the first full-body cancer staging test of this century.

Optimal lung surveillance is the domain of submillimeter CT imaging, further aided by MIP variations and HRCT reconstructions that aid in the detection of tiny nodules or lymphatic spread as carcinomatosis.

Liver lesions are difficult to identify or characterize when small. The protocol and execution may be the limiting factor for today’s high-end CT (e.g. phases) or MRI (e.g. pulse sequences). Selective PET improvements are high signal strength (3-D imaging and time-of-flight), scatter reduction (septae and window of photon acceptance) and improved data analysis (recent 3-D iterative reconstructions).

Skeletal lesions are the most common site of post-systemic therapy metastasis and have a significant prognostic contribution (Figure 5). Staging of the skeleton presents imaging intricacies stemming from tumor location and rate of tumor growth or bone repair. CT offers advantages in cortical lesions, as it can detect even tiny cortical breaks; the amplitude of bone repair influences visualization with matrix agents such as Tc-MDP/HDP or Na-F. In general, lesions surrounded by marrow are better seen with CT if sclerotic, or with MRI if aggressive and lytic. MRI is regarded as the most sensitive modality for detecting marrow-based lesions, although this modality has limitations as a skeletal survey in the absence of a full body scanner, and for small sclerotic lesions.

FDG-PET specificity surpasses that of MRI because marrow edema, a change not specific to tumor, is not associated with increased FDG uptake. Current understanding suggests that lytic breast metastasis may accompany an aggressive primary cancer and usually represents an early recurrence. Staging and surveillance in these cases favors the use of MRI and FDG-PET imaging. Late recurrences that are likely to be indolent and sclerotic may be better detected with the bone matrix agents. Published data suggests relative merits for each of FDG-PET, Tc-MDP/HDP either planar or SPECT [59].

A large study comparison between high end CT, MRI, or PET-CT is not yet available. Na-F PET appears to be a better test than Tc-MDP/HDP imaging in all respects, but is more expensive.
At our institution we have performed cocktail (Na-18F + 18F-FDG) PET imaging with the intent to improve the detection of all breast metastasis in a single examination (Figure 6).

Gene microarrays have been recently used to subtype breast cancers and predict survival. Oncotype Dx (21-gene assay) is commercially available in the USA and a 70-gene assay is under development in the Netherlands. It is foreseen that genetic characteristics of tumors will surpass clinical characteristics in the development and employment of tailored therapeutic strategies [60]. The multitude and complexity of interactions that occur between host genotype and tumor phenotype cannot be decoded with a blood test, no matter how sophisticated. To best understand the disease process and tailor the most efficient therapy will require increasing use of multimodality imaging.

**Conclusion**

Multimodality imaging integration is complex, powerful and in continuous flux. It represents the pivotal decision point for clinical oncology as understood and practiced in reference to the TNM staging system. PET (and its variants) as a technology and as an imaging tool is integral to what is regarded as today’s best cancer management.

**Acknowledgement**

This paper was supported by an educational grant from Philips Medical Systems.

---

**References**


