



FDG-PET and PET/CT in Radiation Therapy Simulation and Management of Patients Who Have Primary and Recurrent Breast Cancer

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Precise anatomical information regarding the location and extent of tumor tissue is essential for radiation treatment planning. In the past, anatomical imaging has greatly improved the accuracy of delineating target structures and is currently the basis of modern three dimensional (3D)-based radiation treatment [1]. Plain radiography, CT, and MRI provide structural or morphological information based on tissue density, size, vascularity, and fat or water content, and are routinely being used for radiation treatment planning. The excellent spatial resolution of anatomical imaging techniques allows the detection of subcentimeter lesions

(eg, in the lungs); however, definition of tumor involvement, in lymph nodes for example, based on the increased size is more difficult. Some enlarged lymph nodes may be reactive, whereas smaller nodes may harbor metastatic foci. MRI is better at outlining soft tissues, particularly in the brain, and has been valuable in complementing CT-based radiation treatment planning [2].

Over recent years, functional imaging with positron emission tomography (PET) has gained increased importance in determining biological or molecular abnormalities in specific tumors. PET using [F-18] fluorodeoxyglucose (FDG) allows the

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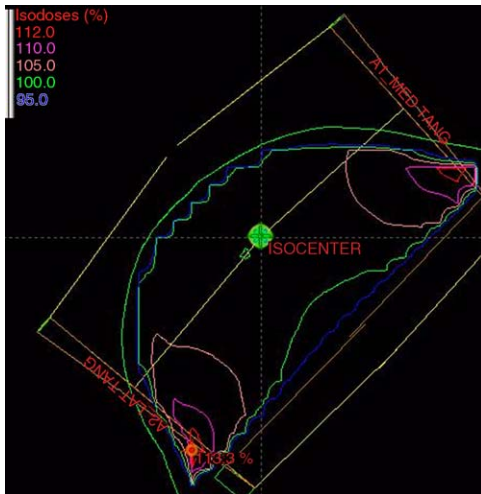


Fig. 1. 2D tangential beam showing the isodose lines in the central axis.

characterization of suspicious masses as well as determination of the spread of disease to loco-regional lymph nodes and distant sites [3]. The metabolic information derived from FDG-PET can influence the radiation treatment planning in several ways. First, FDG-PET may reveal a tumor target that was previously not detected by anatomical imaging. Second, FDG-PET may detect additional tumor regions outside the tumor volume defined by CT or MRI. Third, FDG-PET may show subregions or foci with increased or altered biological activity within the gross tumor volume that could be preferentially targeted and treated with escalated radiation doses. Therefore, the more precise 3D delineation of tumor volumes could translate into improved loco-regional control with radiation therapy.

Breast cancer is the most common malignancy among women in the United States, with approximately 211,240 cases expected in 2005 [4]. Breast irradiation was first used to minimize the risk of loco-regional recurrence in patients who had locally advanced cancers [5]. Beginning in the late 1970s, breast irradiation has evolved into the mainstay of therapy in patients treated with breast conservation surgery. In recent years, breast conservation therapy consisting of a segmental mastectomy and definitive breast irradiation has assumed an increasing role in the management of patients who have both invasive and noninvasive breast cancer. No fewer than six prospective, randomized controlled trials have shown equivalent outcomes of breast conservation therapy compared with mastectomy [6–11]. Distant metastases of breast cancer are frequently found in lymph nodes, lungs, liver, and bones.

In the metastatic setting, radiation therapy is currently used for treatment of soft tissue and bone

metastasis as well as for intracranial disease. Palliative radiation has been shown to be effective in improving the quality of life and providing relief of symptoms, especially the pain of bone metastasis.

Conventional radiation therapy planning

For the last half a century, breast irradiation has been performed through parallel opposing tangential beams with wedges, with matching anterior supraclavicular and posterior axillary fields whenever appropriate. Radiation simulation, the process of selecting the area to be treated and beam selection, is routinely performed through fluoroscopic placement of the tangential beams, based upon clinically determined breast tissue borders. Treatment planning has been single-slice, two-dimensional (2D) dosimetry, applying wedge beam data onto manually obtained breast central axis contours [Fig. 1].

Although this unsophisticated technique initially produced a breakthrough in breast conservation therapy, a number significant limitations of this technique are now apparent, including excess cardiac and lung sequelae of breast irradiation [12]. In addition, patients desire better cosmetic results and shorter treatment times. Increased scatter radiation to contralateral breast from wedges may increase the incidence of second malignant neoplasm [13]. Furthermore, some have suggested that poor dose distribution may contribute to late in-breast tumor failures. Data from Bhatnagar and colleagues [14] suggest significant reduction of scatter radiation to the contralateral breast with the use of intensity-modulated radiation therapy (IMRT). As a result, newer techniques using CT-based treatment planning have been used to create “beam’s eye” views to avoid these underlying critical structures [Fig. 2].

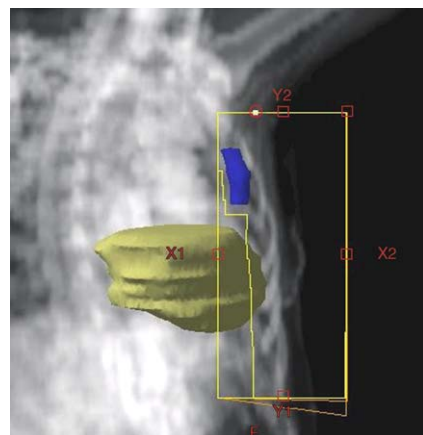


Fig. 2. Beam’s eye view of 3D partial wide tangent covering chest wall and internal mammary nodes (blue) and sparing heart (green).

These beams eye views allow the radiation oncologist to examine the target and nearby critical structures from the perspective of the beam's path.

Image guidance for radiation therapy planning

CT-based, 3D treatment planning represents an evolution from 2D planning, and provides volumetric information that permits a greater assessment of the beam's path and subsequent dose to target tissues and normal structures [Fig. 3]. CT-based approaches also permit virtual simulation, a process in which the CT data set is acquired rapidly, thus significantly reducing the time the patient is spending on the simulation table. Treatment of chest wall and regional nodes poses significant challenges to radiation oncologists, particularly in the postmastectomy setting. The range of body habitus and close proximity of the internal mammary nodes to the heart often necessitates individualized treatment planning, with complex field arrangements. 3D treatment planning with volumetric information helps in clinical decision-making

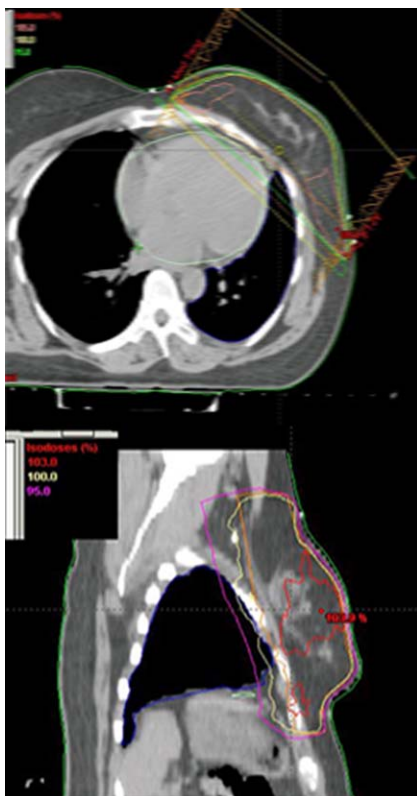


Fig. 3. 3D radiation treatment plan showing isodose distribution covering the breast in axial and sagittal planes.

when selecting field arrangements for treatment of these patients, and has become standard of care.

Radiation therapy planning: use of F-18 fluorodeoxyglucose-positron emission tomography and positron emission tomography/computed tomography

Currently, CT-assisted volume definition remains the gold standard for external beam radiation therapy with curative intent [1]. Accurate localization of the gross tumor volume (GTV) is critical to optimizing the therapeutic ratio, by sparing normal tissues and maximizing coverage of tumor volumes in conformal radiation techniques. Using current available anatomical imaging for treatment planning has several limitations. These include the visualization and precise delineation of tumors in certain areas of the body, such as the head and neck, but also in postsurgical distorted anatomy, and in residual scar tissue after chemotherapy, specifically in previously irradiated areas. The incorporation of metabolic FDG-PET imaging in radiation treatment planning has raised hopes for further improvement, which would lead to so-called "multidimensional conformal radiotherapy."

FDG-PET is complementary to conventional methods of staging in that it has been shown to have both higher sensitivity and specificity in detecting nodal metastases and distance in a variety of malignancies, including breast cancer, when compared with CT alone [15]. The sensitivity of FDG-PET in the detection of axillary lymph node metastasis from breast cancer varies from 20% to 100% when compared with sentinel lymph node (SLN) biopsy or axillary node dissection [16–22]. This variation in the sensitivity of FDG-PET to detect tumor-involved lymph nodes depends primarily on the tumor stage, and subsequently on the extent of disease. Step sectioning and immunohistochemical staining of sentinel lymph nodes detected micrometastases in up to 45% of cases [21]. FDG-PET can miss micrometastases in lymph nodes when the number of tumor cells is too small to provide a signal above the background activity. Avril and coworkers [17] studied 51 patients and found an overall sensitivity and specificity for detection of axillary lymph node metastases of 79% and 96%, respectively. In patients who had primary breast tumors larger than 2 cm (>stage pT1), the sensitivity increased to 94%, with a corresponding specificity of 100%; however, in patients who had small primary breast cancer (stage pT1), the sensitivity of FDG-PET was only 33%. In a prospective multicenter study including 360 women [23] who had newly diagnosed invasive breast cancer, the largest patient group so far, the sensitivity for

FDG-PET was 61%, with a corresponding specificity of 80%. Despite the limitations of FDG-PET discussed above, specifically in detecting micrometastases, its accuracy for detecting tumor-involved axillary lymph nodes is superior to those of CT or MRI alone.

Studies have consistently demonstrated that FDG-PET is better than CT in the detection of internal mammary as well as mediastinal lymph nodal metastases [Fig. 4]. In 73 consecutive patients who had recurrent or metastatic disease, PET was able to correctly identify 40% of the patients who had intrathoracic lymph node metastases, resulting in a sensitivity of 85% and a specificity of 90% [24]. Only 23% of the patients had suspiciously enlarged lymph nodes in CT, leading to a sensitivity of 54% and a specificity of 85%. Therefore, the overall diagnostic accuracy of PET (88%) was higher compared with that of CT (73%) [24]. In locally advanced breast cancer patients, the prevalence of internal mammary FDG uptake can be as high as 25% [25]. The potential importance of internal mammary nodal drainage has also been brought to the forefront with the widespread use of axillary sentinel node mapping, which frequently shows internal mammary lymph drainage on lymphoscintigraphy. There is some speculation that a subset of patients who have "sternal metastases" may in fact be internal mammary node failures with erosion of the sternum. If detected at

initial diagnosis, this area could be effectively targeted with conformal radiation techniques.

Several reports have suggested that FDG-PET is superior to conventional imaging for detection of distant metastatic disease. The use of FDG-PET in patients who have locally advanced breast cancer frequently results in the detection of unexpected distant metastases, and has been shown to substantially change the clinical management [25]. Recently, Dose and colleagues [26] compared FDG-PET with chest radiograph, bone scintigraphy, and ultrasound of the abdomen for detection of metastatic disease in 50 breast cancer patients. FDG-PET identified metastatic disease with a sensitivity and a specificity of 86% and 90%, respectively, as compared with 35% and 95%, respectively, for conventional imaging procedures. In another retrospective analysis of 62 patients [27], sensitivity and specificity for detecting local recurrences or distant metastases were 97% and 82%, respectively, for FDG-PET, versus 84% and 60% for conventional imaging.

The skeleton is a common site for distant metastases in breast cancer. Bone scintigraphy is an established screening method for bony metastases, and allows determining the extent of disease; however, tracer uptake in bone scintigraphy reflects osteoblastic activity, and is therefore limited in the detection of osteolytic lesions. Cook and coworkers [28] studied 23 breast cancer patients who had known skeletal metastases, and FDG-PET was able to de-

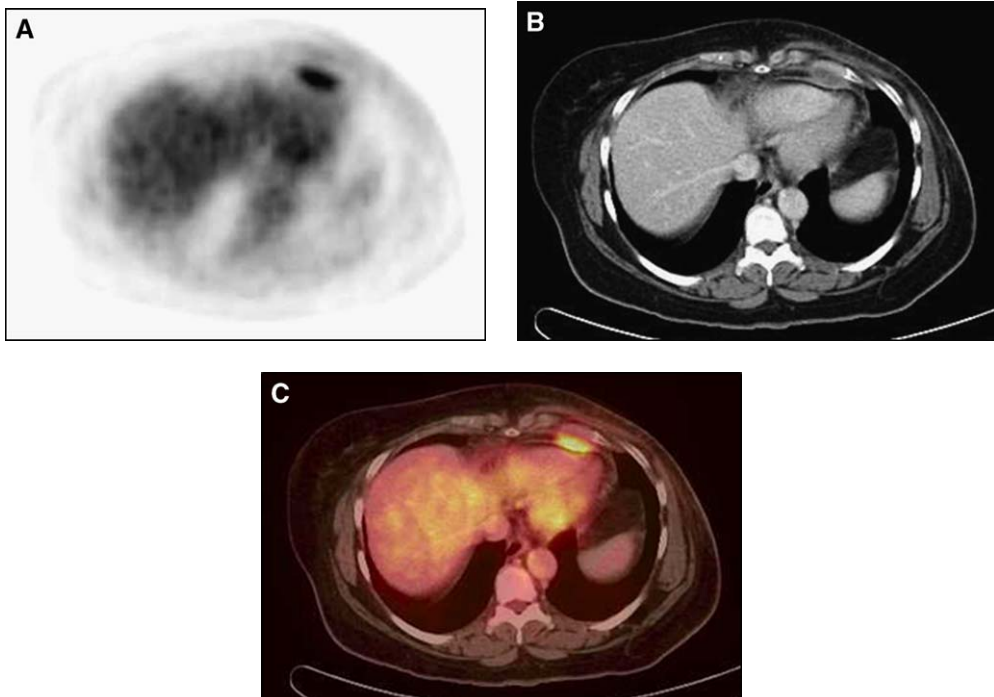


Fig. 4. (A–C) PET, CT, and PET/CT demonstrating FDG-avid left chest wall metastasis.

tect more lesions than bone scintigraphy overall. Higher FDG uptake was observed for osteolytic than for osteoblastic bone metastases, and FDG-PET also detected more osteolytic lesions. On the other hand, PET detected fewer bone metastases than bone scintigraphy in patients who had osteoblastic metastases. In a larger series of 48 breast cancer patients [29], a total of 127 bone lesions, including 105 metastatic and 22 benign lesions, were found by either FDG-PET or bone scintigraphy. The sensitivity and diagnostic accuracy of FDG-PET were 95.2% and 94.5%, respectively, versus 93.3% and 78.7% for bone scintigraphy. Although the overall sensitivity for bone scintigraphy and PET are reported as comparable, bone scintigraphy seems to be superior in the detection of osteoblastic disease, whereas FDG-PET is superior in osteolytic metastases, suggesting a complementary role for the imaging procedures.

F-18 fluorodeoxyglucose-positron emission tomography for radiation therapy of the breast and loco-regional lymph nodes

Breast cancer may be unique in that there are numerous loco-regional treatments using various combinations of surgical techniques and radiotherapy regimens. Surgery may vary from excisional biopsy with microscopically involved margins, to lumpectomy, which usually indicates a more generous resection (again with or without positive margins), to quadrantectomy, simple mastectomy, modified radical mastectomy, and even to radical mastectomy. There are several accepted radiation therapy techniques, ranging from treatment of the entire breast with or without a boost to the lumpectomy cavity following breast conservation surgery, to more comprehensive techniques including the regional nodes [30]. These nodal areas include the axilla, supraclavicular region, and the upper internal mammary region. Similarly, following the mastectomy, radiotherapy may be administered to just the chest wall, or to the chest wall with or without one or more of the regional nodal areas. Currently, FDG-PET cannot provide additional information in the radiation treatment planning of primary breast cancer following breast conserving surgery, because there is no macroscopic (residual) disease. In the setting of local recurrence, FDG-PET may aid in determining more precisely the extent of tumor tissue, and may identify additional lymph node involvement in the axilla or internal mammary chain, as well as assess metastatic tumor to the chest wall.

Treatment-related toxicities in breast cancer patients treated with radiation therapy have improved over the last 2 decades. Nevertheless, meta-analysis

has suggested more late cardiac death in patients treated with radiation therapy compared with those treated surgery alone [31]. This effect appeared to be more pronounced in younger women who had left-sided breast cancer and who were treated with anthracycline-based chemotherapy. The excess cardiac mortality is thought to be due to a combined toxicity of chemotherapy and radiation of the left ventricle and major coronary vessels. The introduction of intensity-modulated radiation therapy (IMRT) technology in breast treatment has the potential to provide uniform dose coverage to the left breast while limiting dose to the underlying heart and lungs [Fig. 5]; however, this issue is complicated by the respiratory motion of the chest wall and physiologic cardiac motion. These motions may cause geometric deviations of the heart from the intended location, causing undesired higher doses to the heart. The use of four-dimensional (4D) CT and beam gating systems in radiation therapy has proven effective in limiting the motion impacts to radiation treatments in lung cancer [32]. Similar techniques may be used to manage chest wall and cardiac motion by the selection of phases that minimize the overlap of the treatment portal with the heart and lungs.

The accurate evaluation and diagnosis of internal mammary metastases is of great importance in radiation treatment planning. The diagnosis of internal mammary metastases can facilitate directed radiation or surgical intervention, thus allowing for treatment planning tailored more closely to each individual patient's disease and risk. Similarly, chemotherapy choices may also be affected, particularly in the patient who appears to have node-negative disease by conventional staging of the axilla, but is found to have internal mammary involvement. The routine use of radiation to treat the internal mammary lymph nodes in women who have locally advanced breast cancer remains controversial; however, internal mammary disease has been associated with higher rates of distant metastases and lower overall survival [33]. Although older extended radical mastectomy series did not

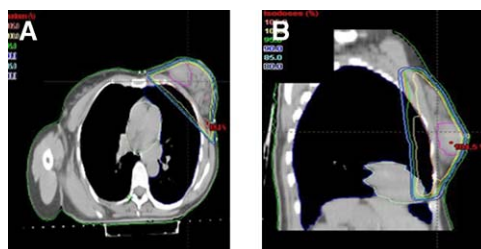


Fig. 5. (A, B) IMRT plan showing homogenous dose to the breast in axial and sagittal plane with sparing of heart.

demonstrate a survival advantage to internal mammary dissection, they did demonstrate that for medially located tumors the incidence of involvement was up to 30% to 40%, especially when the axilla was also positive for metastases [34,35]. In subset analyses, there was a suggestion of a potential disease-free advantage in patients who had medially located primary tumors and axillary metastases, those most likely to have internal mammary involvement when these areas were subjected to treatment. Moreover, a recent large retrospective review from the British Columbia Cancer Agency [36] found a poorer overall survival and distant metastases-free survival in high-risk women who had medial tumors, again indicating the presence of untreated internal mammary disease. Despite an overall trend to less extensive surgery, interest in the detection and treatment of internal mammary nodes has resurfaced in recent years. Two large randomized trials published in the *New England Journal of Medicine* [37,38] demonstrated a survival benefit to postmastectomy chest wall and regional nodal radiation that included the internal mammary nodes. The relative contribution of internal mammary treatment, however, remains unclear.

FDG-PET can contribute in significant ways to the clinical management and radiation planning of patients who have suspected loco-regional recurrences. The most common sites of loco-regional recurrence among patients treated with mastectomy, axillary node dissection, or radiation therapy are the chest wall and supraclavicular nodes. Because it provides biological and functional information, FDG-PET often is complementary to conventional staging methods such as physical examination or cross-sectional imaging (CT or MR), which rely more on changes in morphology to detect disease recurrence. This is particularly true in the evaluation of anatomic regions that have been previously treated by surgery or radiation, where the discrimination between post-treatment scar and recurrent tumor is often problematic. Brachial plexopathy, for example, is difficult to assess on conventional anatomical imaging. FDG-PET and MRI were compared in 10 patients who had clinical findings suggestive of breast cancer metastases [39]. Out of 9 patients who had loco-regional breast cancer metastases, MRI was positive in 5 patients and indeterminate in 4 patients, whereas FDG-PET was positive in all patients. Similar results were found in 19 breast cancer patients who had symptoms referable to the brachial plexus, and it was concluded that FDG-PET may particularly be useful in distinguishing between radiation-induced and metastatic plexopathy [40]. Van Oost and colleagues [25] recently corroborated the need for a more sensitive staging tool in patients who

have first-episode loco-regional recurrence. In their study of 175 patients, they found that 16% had distant metastases at the time of loco-regional recurrence, and 24% developed distant metastases within 18 months of confirmation of recurrent disease. They estimated that FDG-PET would upstage and likely change the therapeutic plan in up to 29% of patients who have negative conventional staging studies.

F-18 fluorodeoxyglucose-positron emission tomography/computed tomography for radiation treatment planning

Combining two imaging devices, PET and CT, into one integrated PET/CT scanner has substantially broadened the clinical use of metabolic PET imaging, specifically in oncology, and particularly for radiation treatment planning [41–46]. PET/CT is unique because it allows the acquisition of spatially and temporally registered PET and CT data in one imaging procedure, providing combined anatomical and functional imaging information that allows accurate tissue characterization and determination of the exact localization and extent of tumor tissue. The diagnostic accuracy of PET/CT is generally higher compared with either imaging procedure performed separately, because of the exact anatomical correlation of abnormal FDG uptake and the functional correlation of suspected morphological abnormalities [47]. The accuracy of FDG-PET/CT is specifically higher in the neck and abdomen, because it distinguishes physiological from pathological uptake by confirmation of metabolic abnormality with anatomic correlation. Several reports indicate a distinct advantage of PET/CT in breast cancer as well [47].

Fused FDG-PET and CT images provide radiation oncologists with two pieces of critical information with a single study: the extent of viable tumor, and its exact location. Initial studies in patients who had various tumor types have confirmed that using FDG-PET/CT both in pretreatment planning and in follow-up evaluations has a significant impact on radiotherapy management in up to 56% of patients [46]. In 24 patients who were planned with 3D conformal radiation therapy for lung cancer, FDG-PET clearly altered the radiation therapy volume in 14 (58%) patients. FDG-PET also helped to distinguish tumor from atelectasis in 3 patients. Unsuspected nodal disease was detected in 10 patients, and 1 patient had a separate tumor focus detected within the same lobe of the lung [45]. Similarly, Heron and colleagues [42] showed that in head and neck cancer, FDG-PET/CT simulation provided valuable information that resulted in greater delineation of normal tissues from

tumor-bearing areas at high risk for recurrence. In this study of 21 consecutive patients, the FDG-PET portion of PET/CT demonstrated the primary tumor in all cases, whereas the coregistered CT did not delineate the primary in three cases. In 8 patients, additional areas of disease were identified by FDG-PET. Because of the often poor anatomical delineation of head and neck tumors, the volumes for the primaries were significantly larger on CT treatment planning than on FDG-PET, which provided more precise metabolic definition of the tumor extent. In contrast, the volumes for nodal regions were smaller on CT because FDG-PET demonstrated tumor outside the CT-defined target volumes. The additional metabolic information from FDG-PET resulted in a more accurate characterization of the extent of disease for both primary tumors and nodal regions, with the potential clinical implication of improved radiation treatment. Ciernik and coworkers [46] investigated the usefulness of FDG-PET/CT imaging for target volume definition in 39 patients who had solid tumors. The gross tumor volume increased by 25% or more because of FDG-PET in 17% of cases who had head-and-neck and lung cancer, and in 33% of cases who had cancer of the pelvis. The gross tumor volume was reduced 25% or more in 33% of patients who had head-and-neck cancer, in 67% who had lung cancer, and in 19% who had cancer of the pelvis. Overall, in 56% of cases, gross tumor volume delineation was changed significantly if information from metabolic PET imaging was used in the planning process. The modification of the gross tumor volume translated into altered planning target volume (PTV) changes exceeding 20% in 46% of cases.

An important implication from improved target definition is avoiding geographic misses and unnecessary exposure of nontarget tissue to radiation. In addition, improved target definition may also allow dose escalation in 3D and IMRT. The authors found a close correlation between the metabolic activity on pretreatment FDG-PET and the subsequent risk of treatment failure (unpublished data, 2005). If this observation is confirmed in larger trials, the intensity of FDG uptake in tumor tissue could guide and tailor the radiation dose delivered by IMRT, and therefore improve radiation treatment outcomes.

Current limitations of F-18 fluorodeoxyglucose-positron emission tomography and positron emission tomography/computed tomography for radiation therapy planning

There are important differences between the currently used anatomical-imaging-based radiation

treatment planning and potential FDG-PET treatment planning. Although FDG-PET offers unique metabolic information about the tumor activity, the limited spatial resolution of PET compared with CT or MRI may not characterize small lesions with sufficient accuracy. Current PET technologies do not allow identifying micrometastases, which limits its use for narrowing the treatment volume in lymph nodes areas at risk. The specificity of FDG-PET is in the range of 80% to 95%, and generally higher than that of CT or MRI; however, the uptake of FDG is not specific for tumor tissue, and granulomatous or acute inflammatory processes can result in false-positive PET findings. An important limitation of FDG-PET in radiation treatment planning is the precise delineation of tumor tissue based on the PET images. Unlike anatomical imaging, the size of metabolic abnormalities varies depending on the scaling of the PET display. Whereas tumors often have well-defined anatomic borders on CT images, the edges of tumors on FDG-PET imaging appear indistinct to the contouring physician. Some have arbitrarily defined the FDG-avid volume as the region encompassed by the 40% to 50% [45] intensity level relative to the tumor maximum, whereas others have normalized to the FDG uptake in the liver without background subtraction [42]; hence the FDG-avid volume may have significant interobserver variability. The use of standardized uptake value (SUV) normalized parametric images may help to overcome this problem. Major limitations of FDG-PET for radiation treatment planning are the limited anatomical landmarks, which are necessary for exact tumor target definition on the treatment planning system.

As discussed above, the use of coregistered FDG-PET and CT images obtained from combined PET/CT scanners may greatly improve the use of PET for radiation treatment planning, by providing the metabolic tumor activity and the precise anatomical information. The sequential nature of the PET/CT acquisition does not completely prevent misregistration between the PET and the CT portion of the examination. In most PET/CT scanners, a CT scan is acquired first from the base of the skull through the pelvis, followed within approximately 20 to 60 seconds by PET data acquisition. Because a PET emission scan takes between 3 and 5 minutes per bed position (which is approximately 15–20 cm, depending on the scanner manufacturer) the PET images represent an average over the period of data acquisition, whereas as the CT represents a snapshot from a fraction of a second. Misregistration of tumors on the PET compared with the CT portion of PET/CT is common because of respiratory motion, specifically at

the base of the lungs and in the upper abdomen (liver). In breast cancer, differences in the breathing cycle can cause misregistration, specifically of tumor lesions in the breast, chest wall, and internal mammary lymph node chain. Different filling of the renal collecting system and the urinary bladder are also frequently observed because of the sequential imaging of CT and PET. Finally, patient movement may occur between the PET and the CT portion, specifically in the head and neck region. Heron and colleagues [42] have used a thermoplastic mask for radiation treatment planning with FDG-PET/CT of head and neck cancers, and successfully immobilized patients to improve the precise coregistration between PET and CT. Laser-assisted localization for treatment planning is often used for current CT-based radiation treatment planning, and might also be necessary for PET/CT radiation treatment planning.

Radiosurgery treatment planning and positron emission tomography/computed tomography

There are several techniques being developed to extend radiosurgery from the brain to the body. The CyberKnife (Accuray, Sunnyvale, California) system [48] for example, consists of a lightweight linear accelerator mounted on a robotic arm with 1-mm spatial accuracy. Real-time radiograph imaging tracking allows for correction of patient movement by bringing the radiation beam into alignment with the observed position of the treatment target. An important advantage of this type of radiosurgery is that each beam is delivered independently, without a fixed isocenter. Because of the spatial precision with which radiation can be delivered, it is feasible to administer a tumoricidal radiation dose in a single outpatient treatment. Radiosurgery is specifically helpful in spinal metastases from breast and other cancers, but can potentially be used for any tumor localization within the body [49]. Because of the high precision and the steep decline in delivered tumor dose, extension beyond the anatomical abnormality would lead to underdosing of the tumor.

The major potential benefits of radiosurgery are the short treatment time in an outpatient setting, with rapid recovery and good symptomatic response. Tumor target definition and dose planning are currently based on CT, however, which frequently provides poor delineation of tumor involvement, specifically in bone. When possible, MRI is being used to more accurately define the extension of tumor tissue; however, in previously irradiated areas, MRI frequently demonstrates un-

specific increased signal intensity in the bone marrow, limiting the definition of viable tumor.

The potential advantage of FDG-PET and PET/CT is in providing more accurate treatment planning compared with CT and MRI alone. This could result in improved local control rates after radiosurgery, and reduce subsequent tumor recurrence rates. There is only very little information so far describing the role of FDG-PET and PET/CT for CyberKnife treatment planning, however. Prospective studies are needed comparing volumetric dose planning for target definition and radiosurgical treatment planning using FDG-PET and PET/CT with currently used CT and MRI. For potential clinical application, it is important to demonstrate that the metabolic information is different from the anatomical tumor delineation, and provides specific additional information. It has also to be shown that the ability to tailor radiation doses to a specific metabolic activity, as opposed to using conventional doses based upon histology alone, results in improved local control. It is also important to determine specific features of FDG-PET and PET/CT that would predict local failure to standard radiosurgical dose prescriptions.

Future perspectives

Preliminary data provide early proof of the principle that multimodality imaging can facilitate individualized treatment by better delineation of target. In theory, better delineation of the target should mean better tumor coverage, and hence better local control. Better target delineation will not help if we are missing the target because it moves as a result of physiological or other mechanical forces. Future studies are needed to integrate respiratory gating with PET/CT scanning to account for target motion in radiation treatment planning and delivery. The use of 4D PET/CT can correct for respiratory motion artifacts seen in conventional PET/CT imaging. It has potential to reduce smearing and improve the accuracy in PET/CT coregistration.

The metabolically active disease seen by PET can be treated with escalated dose to improve chances of local control. Prospective trials are needed to evaluate and validate the role of dose escalation in this setting using IMRT-based technique. Besides, the studies performed to date using PET/CT in radiation planning have only shown that treatment volume changes significantly with the use of functional imaging. It has yet to be determined whether the PET-defined target volume leads to improved outcomes in terms of local control, survival, and reduced toxicities.

PET/CT also has application in assessment of treatment response. The utility of post-therapy FDG-PET

to monitor tumor response also has been evaluated in several tumors, including lymphoma, breast, cervix, and colorectal cancers [50–53]. There are also encouraging results available for treatment evaluation of radiation therapy. The concept of assessment and prediction of treatment response by sequential FDG-PET imaging needs to be validated in larger studies to help in early identification of treatment failure. This can lead to early intervention with potential for salvage therapy, which might improve outcome.

From the authors' perspective, there is no doubt that FDG-PET/CT will become an important part of modern radiation treatment planning in the near future; however, it should be emphasized that currently, FDG-PET can only be used as complementary imaging modality for detecting disease not identified by CT. The routine use of FDG-PET or PET/CT for radiation treatment planning requires a thorough and careful evaluation in large prospective studies as it relates to the promise of improving local control or increasing disease-free and overall survival.

Summary

PET-CT based imaging is a valuable tool, and one of the most useful tools in the staging and restaging of breast cancer, especially in patients who have recurrent or locally advanced breast cancer. Its greatest clinical applications are in detection and definition of extent of recurrent or metastatic disease, and in monitoring response to therapy. The role of PET-CT in radiation treatment planning for breast cancer is still in the nascent stages, lacking controlled randomized trials data; however, the potential to improve radiation treatment planning by allowing for the tailoring of comprehensive radiation portals, particularly for locally advanced breast cancer, makes this one of the most promising tools as we enter the era of image-guided radiation therapy.

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