Continuing Education Course
Use of CT and PET in Radiation Therapy

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I. INTRODUCTION

The modern practice of radiation therapy relies on volumetric patient images. Computed tomography (CT) imaging has been the primary imaging modality used in radiation oncology for over two decades. However, magnetic resonance imaging (MRI) and positron emission tomography (PET) are increasingly becoming an important component of the treatment planning process.

CT studies provide information not only about target volumes but about critical (normal) organs as well. Using CT images for radiation therapy treatment planning has enabled us to improve dose delivery to target volumes while reducing the dose to critical organs. CT images also provide density information for electron density corrected dose calculations. A major weakness of CT imaging is a relatively limited soft tissue contrast. This, limitation can be overcome by using CT images in conjunction with MRI studies. PET studies provide functional information about patient's anatomy which can aid in target volume definition.

The first portion of this refresher course reviews CT-simulation technology, tools, and process; and discusses the QA requirements for CT-simulation process and recommendations of the upcoming TG66 report on CT-simulation QA. The second part discusses registration of CT and PET images for treatment planning purposes and describes PET scanning process for radiation therapy. The third portion of presentation reviews the current status of PET based treatment planning for several treatment sites.

II. CT-SIMULATION

1. CT-Simulator Technology

CT simulator consists of a CT scanner, laser patient positioning / marking system, virtual simulation / 3D treatment planning software, and different hardcopy output devices, Figure 1. The CT scanner is used to acquire a volumetric CT scan of a

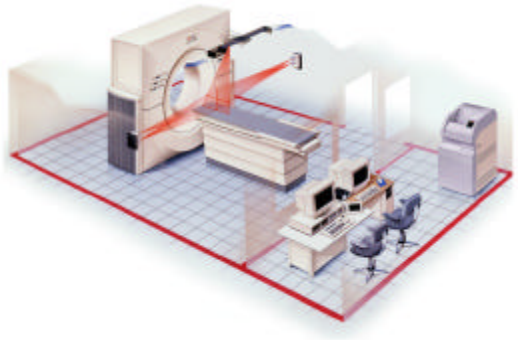


Figure 1. CT-Simulator. (Courtesy Philips Medical Systems, Inc.)

patient which represents the virtual patient and the simulation software creates virtual functions of a conventional simulator. Proper selection of components of a CT-simulator or a CT-simulator as a commercial package is very important, as they will notably affect the rest of the treatment planning and delivery process in a clinic.

a) CT scanner

Generation - Scanners commercially available today are either 3rd or 4th generation. Both scanner generations give excellent images with no significant advantages of one over the other.

X-ray tube - Two characteristics of CT simulation process guide requirements for the X-ray tube selection:

a) Large number of images per study
b) Rapid study acquisition time

CT simulator X-ray tube must have large heat anode loading and heat dissipation capabilities to withstand the

very high heat loads associated with the large number of images acquired in a rapid sequence.

Single-slice and multi-slice scanning- The main advantage of multi-slice scanners is the ability to acquire images faster than single slice scanners[2-4]. A four-slice system with a 0.5 second rotation can acquire volume data up to 8 times faster than a single slice machine with a 1 second rotation. Due to the longer length of imaged volume per tube rotation (multiple slices simultaneously), the tube heat loading during a scan of a certain patient volume is lower for multi-slice than for a single-slice scanner. This allows thinner slice thickness to be used for scanning or longer volumes to be scanned. Faster acquisition times, decreased tube loading (which will allow longer volumes to be scanned in a single acquisition), and thinner slice thickness associated with multi-slice scanners can potentially provide advantage over single-slice systems for CT simulation purposes.

Bore (gantry opening) size- CT scanners typically have 70 cm bore openings. This is quite adequate for diagnostic scans. For CT-simulation purposes, patients are often in positions that can prevent them from entering the 70 cm bore opening. For example, breast treatments where the ipsilateral arm is subtended at close to a 90° angle frequently have difficulty entering the 70 cm bore. Inability to simulate all patients in an optimal treatment position due to restricted bore opening has often been cited as on of the major weaknesses of the CT simulation process[5-8]. A CT-scanner specifically designed for radiation oncology purposes with an 85 cm bore opening has been introduced almost two years ago.

The enlarged opening allows entry of immobilization devices and patients in positions that are commonly used in radiation oncology, Figure 2. Image performance of the large bore scanner is comparable to 70 cm bore diagnostic scanners[9]. The 85 cm bore scanner also has increased *scanned field of view* (SFOV)--60 cm compared to 48 cm on most 70 cm bore units. Increased SFOV allows for full visualization of larger patients and immobilization devices. This feature is important to fully assess patient external dimensions which are necessary for accurate dose and monitor unit calculation.

Couch- CT simulator couch should have a flat top similar to radiation therapy treatment machines. Additionally, it should accommodate commercially available registration devices. The registration device allows patient immobilization device to be moved from the CT simulator to a treatment machine, in a reproducible manner. The couch should have sag of less than 2 mm. This is in accordance with specifications for linear accelerators[10]. The couch weight limit should be comparable to those of medical linear accelerators (at least 400 to 450 lbs).

Patient marking lasers- A laser system is necessary to provide reference marks on patient skin or on the immobilization device. Figure 1 shows the laser system for a CT simulator:

Wall lasers – Vertical and horizontal, mounted to the side of the gantry

Sagittal laser – Ceiling or wall mounted single laser, preferably movable. Scanner couch can move up/down and in/out but can not move left/right, therefore the sagittal laser should move left/right to allow marking away from patient mid line.

Scanner lasers – Internally mounted, vertical and horizontal lasers on the either side of the gantry and an overhead sagittal laser.

Lasers should be spatially stable over time and allow for positional adjustment.

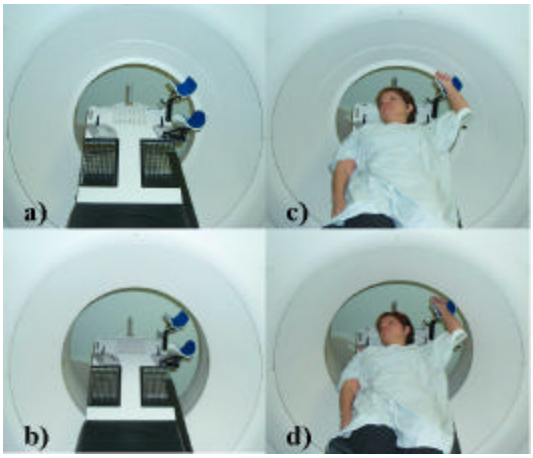


Figure 2. Comparison of 70 cm and 85 cm bore opening; a and b) breast board in front of 70 cm and 85 cm bore, respectively, c and d) breast CT simulation with a breast board in front of 70 cm and 85 cm bore, respectively.

Image quality performance- The corner stone of 3D conformal radiation therapy (3DCRT) treatment planning are patient images. These should be high quality diagnostic type images. When purchasing a CT simulator, image quality should be one of the top concerns. At the very least, the following image quality indicators[1] should be considered:

Spatial resolution – measure of the scanner's ability to discriminate objects of varying density a

small distance apart against a uniform background. Specified in line pairs per cm (Lp/cm).

Low contrast resolution – the ability of an imaging system to demonstrate small changes in tissue contrast. Specified as the ability of the CT unit to image objects 2 to 5 mm in size which vary slightly in density from a uniform background.

Noise – the fluctuation of CT numbers from point to point in the image of a uniform object.

Cross-field uniformity – the uniformity of CT numbers throughout the entire scan field. This performance characteristic can potentially be important in heterogeneity-based dose calculations.

Hard copy printers **–** DRRs can be printed on paper or on film using laser film printers. DRRs printed on film are generally much easier to use and often preferred.

b) Virtual simulation/3D treatment planning software and workstation

As with all software programs, user-friendly, fast, and well functioning virtual simulation software with useful features and tools will be a determining factor for the success of a CT simulation program. Several features are very important when considering virtual simulation/3D treatment planning software:

I. Contouring and localization of structures
II. Image processing and display
a) Digitally reconstructed radiographs (DRRs)
b) Digitally composited radiographs (DCR)
c) Multiplanar reconstruction
d) Various other displays
III. Simulator geometry
IV. Fusion/Multimodality imaging registration -
V. Connectivity
V. Dose calculation

2. CT-Simulation Process

CT simulation process has been described by several authors[6-8, 11, 12]. The process includes the following steps:

- Patient positioning and immobilization
- Patient marking
- CT scanning
- Transfer to virtual simulation workstation
- Localization of initial coordinate system
- Localization of targets and placement of isocenter
- Marking of patient and immobilization devices based on isocenter coordinates
- Contouring of critical structures and target volumes
- Beam placement design, design of treatment portals
- Transfer of data to treatment planning system for dose calculation
- Prepare documentation for treatment
- Perform necessary verifications and treatment plan checks

This process and its implementation vary from institution to institution. The system design is dependent on available resources (equipment and personnel), patient workload, physical layout and location of different components and proximity of team members.

a) CT Scan, Patient Positioning and Immobilization

The CT simulation scan is similar to conventional diagnostic scans. Patient positioning and immobilization are very important. Scan parameters and long scan volumes with large number of slices often push scanners to their technical performance limits.

I. Patient positioning and immobilization
II. Scan protocol
III. Scan Limits
IV. Contrast
V. Reference Marks
a) No shift method
b) Shift method

b) Virtual simulation

Virtual simulation process typically consists of contouring target and normal structures, computation of the isocenter, manipulation of treatment machine motions for placement of the beams, design of treatment portals, printing of DRRs and documentation. This process is largely dependent on the software capabilities. Also there are well designed methods for simulating specific treatment sites. Several publications describe these methods in detail[6-8, 13-16].

3. Quality Assurance

Quality assurance (QA) for CT simulators consists of procedures for QA of (1) CT scanner, (2) CT simulation software, and (3) QA of the overall process. Several publications have addressed QA needs for CT scanners and CT simulators [8-10, 12, 17-27]. The American Association of Physicist in Medicine (AAPM) Task Group 66 has been charged with addressing the QA process for CT simulation. The task group is currently in the process of preparing a comprehensive document that will address all of the above-mentioned QA procedures.

The goals of the quality assurance program should be concentrated on the imaging performance and mechanical integrity of the CT scanner, accuracy of the virtual simulation software in reconstruction of the virtual patient and treatment machine and other functions[26], and the overall correct positioning and treatment of the patient. As often suggested by the AAPM[10, 17], the QA procedures are separated into daily, weekly, monthly, quarterly, and annual procedures. The frequency of a QA task depends on its significance for the overall program accuracy and reliability and other factors (past performance, etc.)[10]. Tolerance and action levels for various components of the QA program depend on the institutional policies and national and international organization recommendations[10, 17, 26] and current standard of practice.

The CT scanner used in the CT-simulation process can be located in the radiation oncology department or in the diagnostic radiology department. Depending on the scanner location and primary use, the acceptance testing, commissioning, and QA of the actual scanner can be the sole responsibility of the therapy medical physicist or a joint responsibility of diagnostic and therapy physicists. The commissioning and periodic QA of the accompanying software and the QA of the CT-simulation process is always the responsibility of the therapy physicist. This report does not address each of the two scenarios individually (scanner located in diagnostic radiology or radiation oncology), but rather establishes a set of QA procedures that are applicable to scanners used for CT-simulation regardless of their location and primary purpose. It is the responsibility of the respective diagnostic and therapy physicists to determine how the QA program will be implemented and how the responsibilities are assigned. The primary responsibility for implementation of recommendations for QA of scanners used for CT-simulation in this document rests with the radiation oncology Quality Assurance Committee (QAC) as specified by the AAPM task group 40.

Quality assurance of CT scanners: The AAPM Report Number 39, "Specification and acceptance testing of computed tomography scanners"[17] has describe in great detail acceptance testing and QA procedures for CT scanners. Several other references have been published that address this issue[20-22]. A valuable source of information is also the www.impactscan.org website. Until publication of the AAPM TG66 report, the above referenced documents should be used for designing a CT simulator QA program. The QA Program should address radiation safety, CT scanner dosimetry, electromechanical performance, x-ray generator operation, and imaging performance.

Quality assurance of the CT simulation software: The QA of the virtual simulation software is in many aspects similar to QA procedures for 3D treatment planning systems as many functions and features are common to these two types of software. The AAPM TG53 report "Quality assurance for clinical radiotherapy treatment planning" has addressed in detail the QA needs for clinical radiation oncology treatment planning. This document can be applied when designing a virtual simulation software QA program. Additionally, the AAPM TG66 will address QA issues more specific to virtual simulation. The QA should include verification of spatial and geometric accuracy of the software (contour delineation, isocenter localization, treatment port definition, virtual treatment machine operation, etc.), evaluation of DRRs and DCRs, and accuracy of the multimodality image fusion and registration process. .

III. FUNCTIONAL IMAGE REGISTRATION: TECHNICAL AND CLINICAL ASPECTS

Computed tomography (CT) images have historically been and still remain the primary imaging modality used for treatment planning. Magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), single photon emission computed tomography (SPECT), and positron emission tomography (PET) are imaging modalities which can provide unique target information, that is not contained in CT images, and may improve overall radiation therapy patient management. Due to their individual shortcomings (CT-limited soft tissue contrast, MRI-susceptible to spatial distortions and lack of electron density information, PET-relatively poor resolution) it is required that multiple imaging studies be used for patient treatment planning to complement each other.

When multiple imaging studies are employed for treatment planning they must be spatially registered to accurately aid in target volume delineation, this applies to PET and CT registration as well. Registration of multimodality images is a several-step process requiring multi-function software capable of image set transfer, storage, coordinate transformation, and voxel interpolation. These features enable image study registration (transforming images to a common reference frame and resampling to a common pixel grid) and fusion (the display of a combination of pixel intensities from registered image studies).

The image registration process consists of the following steps: patient positioning and immobilization, use of fiducial markers, image acquisition, data transfer, and the actual registration process. This process typically involves cooperation between several hospital groups. Good organization and understanding of all components of the registration process are crucial for efficient clinical operation. The registration process is also prone to errors that can in turn cause serious patient treatment errors. Quality assurance of the image registration process is essential for the verification of post-transfer image data integrity, image spatial integrity, image orientation, image chirality (i.e. absence of image mirroring), image registration accuracy, and other system functionality. This process applies to registration of CT and PET studies.

1. Patient Positioning and Immobilization

Flat tabletop - Typically, diagnostic CT scanners and PET units have curved tabletops whose radius of curvature is designed to conform to scanner opening. As described earlier, scanners used for CT-simulation are equipped with flat tabletops to represent treatment machine geometry. This is also required for PET scanners which are used radiation oncology imaging. The flat tabletop can be an overlay, which is mounted on the top of the curved table, or it can be an insert which conforms to the curved tabletop. Figure 3, shows a PET scanner with a flat tabletop insert.

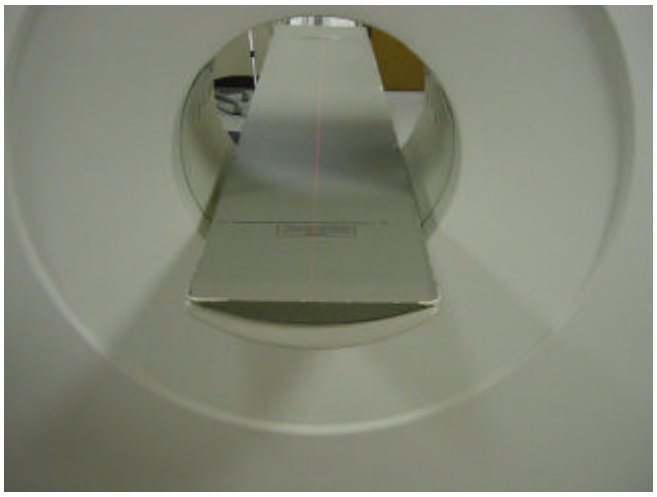


Figure 3. PET scanner with a flat tabletop insert.

Patient immobilization and registration devices - Devices, which allow patient immobilization and registration to the treatment machine table, increase the patient positioning accuracy, setup reproducibility and rigidity, and patient setup efficiency. These devices also allow accurate transfer of patient setup from the scanner to treatment machine. Scanners used for CT-simulation are commonly equipped with such devices, Figure 4. When registering CT and PET studies for treatment planning purposes, use of patient immobilization and registration devices greatly simplifies the process and increase registration accuracy. Figure 5a shows a registration device attached to the PET scanner. Then device allows registration of thermoplastic masks and body moulds to the PET scanner table. Figure 5b shows a body mould attached to the registration device.

Figure 4. Use of a registration device. (Courtesy of MED-TEC, Inc, Orange City, IA)

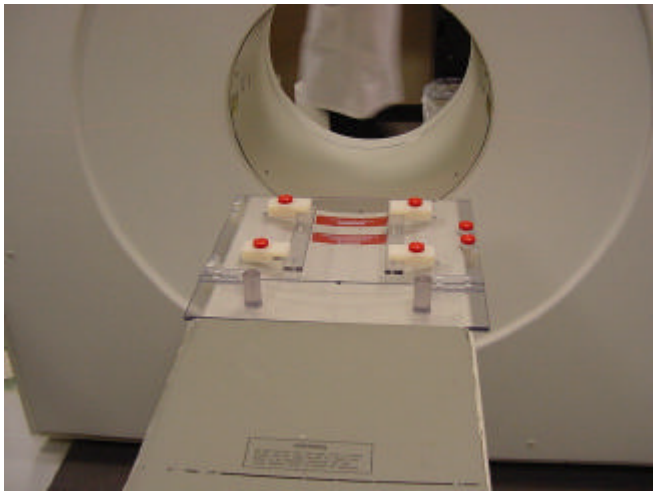
External patient positioning lasers - Scanners used for CT simulation are routinely equipped with external patient positioning/marking lasers, Figure 1. Availability of external lasers on the PET scanner increases patient setup reproducibility from the CT scan which is usually first acquired.

2. Fiducial Markers

There are several methods which can be used for PET and CT image registration, surface based registration (internal and external), image based registration, point based registration, and there are also automatic and semi-automatic algorithms which can be used for this task.

Due to relatively poor PET resolution, registration methods which relay on patient anatomy can not always produce satisfactory registration accuracy (dependant on physician preferences, treatment site, treatment technique, etc.). It is also sometimes difficult to evaluate registration accuracy based on the patient anatomy data alone. PET/CT compatible fiducial markers which are placed on patient skin during scanning can be used for point based registration and to evaluate accuracy of other registration methods.

Figure 6 shows CT/PET compatible fiducial markers. The fiducial markers are made with 0.5 cm diameter, 3 cm long plastic centrifuge ampoules commonly found in chemistry and biology laboratories (VWRbrand Disposable Microcentrifuge Tubes, VWR Scientific Products, West Chester, PA). One end of the ampoules is conical and the other end can be opened and closed with a small cap. For CT scans,



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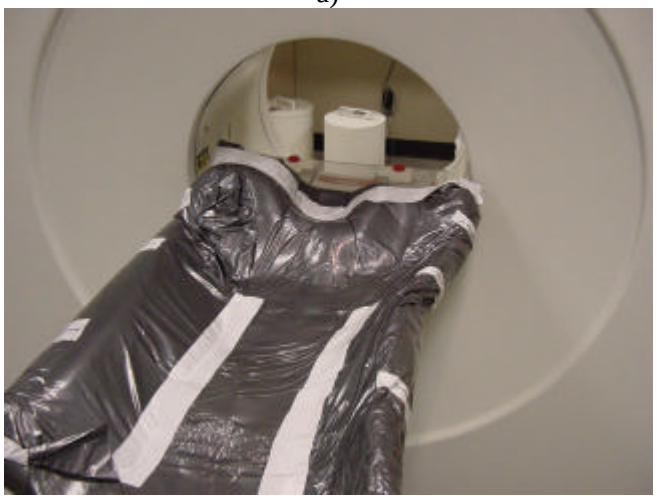


b)

Figure 5. a) Registration device attached to the PET scanner table, b) body mould placed on the registration device.

two small pieces of aluminum wire are placed at the pointed end of the ampoules and secured in place with dental wax. The bottom ampoule in Fig. 6 has two aluminum wires at the tip and dental wax in place to hold the wires. For PET scans, a small drop of ^{18}F-FDG is placed at the pointed end of the fiducial marker. The drop is held in place by the liquid surface tension. The surface tension is strong enough that the fiducial marker can be handled without worry that the drop may be displaced. Also for PET scans, the radioactive material is safely contained in the plastic ampoules.

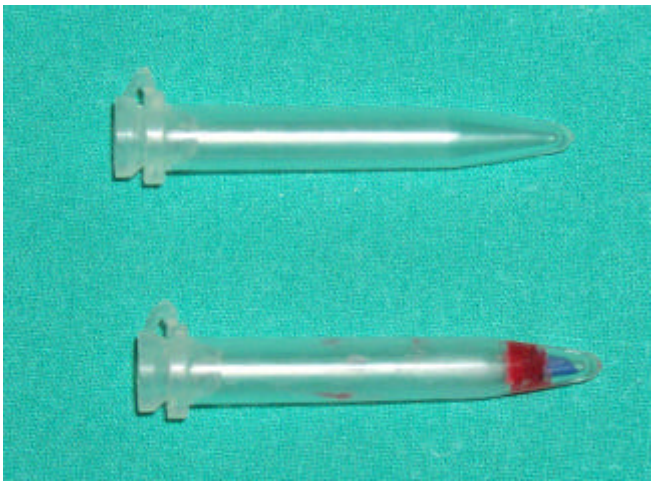


Figure 6. PET/CT compatible fiducial markers.

3. Image Acquisition and Data Transfer

Scan protocols and scan limits should be site specific and defined in advance for both CT and PET. Well-understood scan parameters greatly simplify the registration process and improve the scan acquisition efficiency.

Data transfer between CT and PET scanners and treatment planning software is prone to errors. These scanners are usually located in different departments and equipment is often manufactured by different vendors. The data transfer process involves multiple computers and networks. Because of this, quality assurance (QA) of the image registration process is essential for the verification of post-transfer image data integrity, image spatial integrity, image orientation, image chirality (i.e. absence of image mirroring), image registration accuracy, and other system functionality[23]. As outlined in the American Association of Physicists in Medicine Task Group Report #53[26], general commissioning and routine procedural quality assurance checks of a multimodality image registration process used for treatment planning are recommended.

IV. FUNCTIONAL IMAGE BASED TREATMENT PLANNING: CURRENT STATUS

Functional imaging can improve target delineation for several treatment sites and can also introduce novel treatment techniques which could allow dose escalation to target volumes, better sparing of normal structures, and hopefully better outcomes with reduced complications.

A number of publications have addressed PET based target volume delineation and treatment techniques which are designed to improve delivered dose distributions based on PET information. Nonsmall cell lung carcinoma (NSCLC), brain tumors, head and neck cancer, and cervical tumors have been the focus of several studies [28-45].

1. Nonsmall Cell Lung Carcinoma

Studies have shown that PET imaging demonstrates that conventional staging methods frequently underestimates the true extent of NSCLC[33, 35, 36, 39, 43, 44]. As often noted, tumor stage in NSCLC is the strongest prognostic factor and the most important parameter that guides treatment decision-making. FDG-PET imaging is superior to conventional imaging in staging of NSCLC, it improves treatment planning and provides valuable prognostic information. FDG-PET information has been reported to change patient management strategy from radical to palliative which avoided futile treatments[35, 36]. It has also been reported that patients staged with FDG-PET have been downstaged and became candidates for potentially curative resections[35]. Most frequently, FDG-PET study provided information resulted in modification of radiation therapy treatment planning volumes. These modifications include enlargement and reduction of CT-defined treatment volumes and inclusion of volumes previously unsuspected of disease.

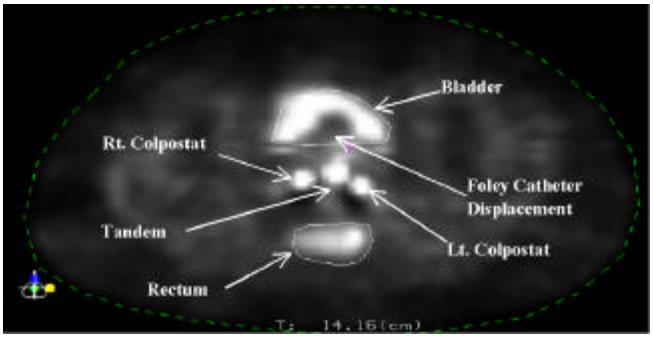
Treatment planning issues regarding NSCLC include target edge definition, image registration, patient positioning, and patient motion.

2. Cervical Cancer

Studies have demonstrated PET imaging benefits for staging and definition of cervical tumors[31, 38, 42]. Treatment planning techniques have been developed to use FDG-PET information for radiation dose delivery[37, 40, 41].

A technique for treatment planning of brachytherapy gynecologic (GYN) implants based on PET imaging information alone has been shown to be clinically feasible[37, 40]. In this technique, patients undergo PET scanning with GYN brachytherapy applicators in place. During scanning, small tubes containing FDG are place inside the applicators. The acquired PET scans show tumor volumes and applicators in relationship to those volumes, Figure 7.

Another proposed treatment technique involves PET-guided-IMRT treatment of cervical carcinoma with positive para-aortic lymph nodes (PALN)[41]. The treatment technique goal is to escalate doses delivered to PALN bed while maintaining doses to critical structures at acceptable levels. The positive PALN are identified on PET study which has been registered with a CT study, Figure 8.



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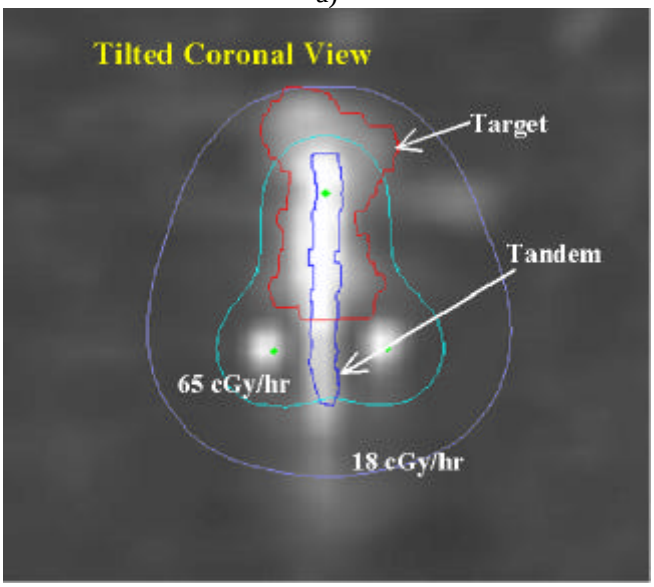

b)

Figure 7. a) axial PET image showing bladder, rectum, and brachytherapy applicators, b) coronal PET image showing target volume, applicators, and isodose distribution lines. PET based brachytherapy treatment plans can be used to evaluate 3D target volume dose distribution. This treatment planning method is supported by recent NCI recommendations regarding new direction in brachytherapy[46].

IMRT delivery is then used to escalate dose to PALN to 60 Gy compared with conventional 45 Gy.

3. Brain Tumors

Studies have compared PET defined brain tumors with volumes identified on MRI images[32, 34, 47]. These studies revealed that PET imaging does not provide significant amount of additional information compared with MRI studies. PET target volumes were typically contained with MRI defined volumes. A potential use

for PET imaging of brain tumors may be identification of boost volumes. Undoubtedly, further studies will evaluate PET utility for treatment planning of brain tumors.

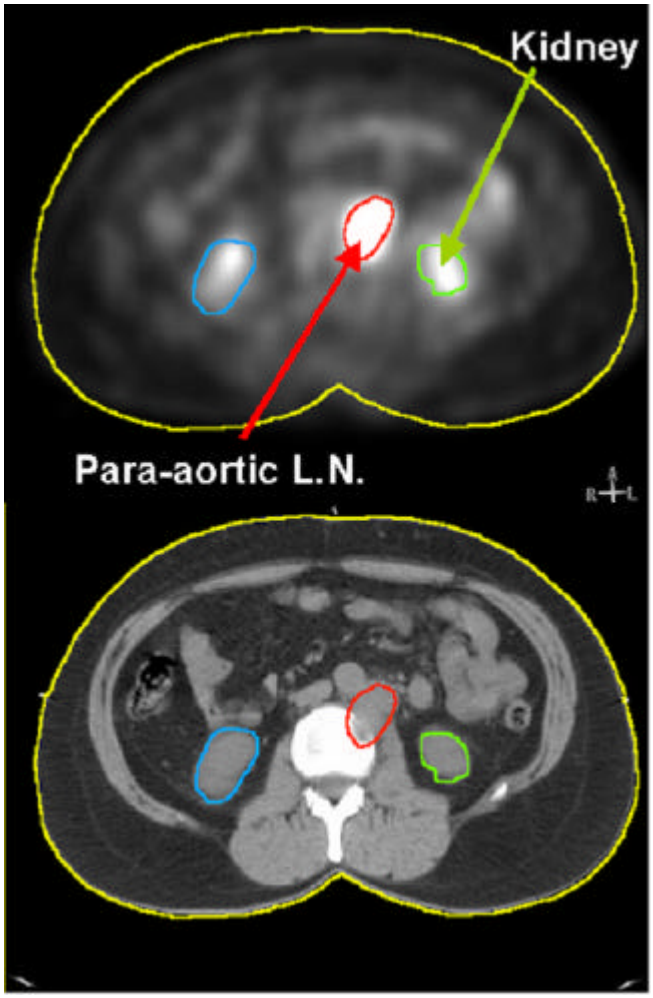

Figure 8. Corresponding PET and CT images with positive PALN.

4. Other Imaging Agents

The majority of above described studies rely on ^{18}F fluorodeoxyglucose radiopharamceutical as imaging agent. Other PET tracers have a potential for providing information which can be used for target definition for radiation therapy. For example, Cu(II)-diacetyl-bis (N^{14}-methylthiosemicarbazone) (Cu-ATSM) has been shown to identify hypoxic areas of the tumor. IMRT can then be used to boost the Cu-ATSM identified hypoxic volume to higher doses[29] to potentially overcome inherent hypoxia-induced radioresistance without compromising normal tissue sparing, Figure 9.

Though it has been shown that treatment of hypoxic areas with IMRT is feasible, clinical-pathologic correlation between ^{60}Cu-ATSM retention and radiation curability remains to be established.

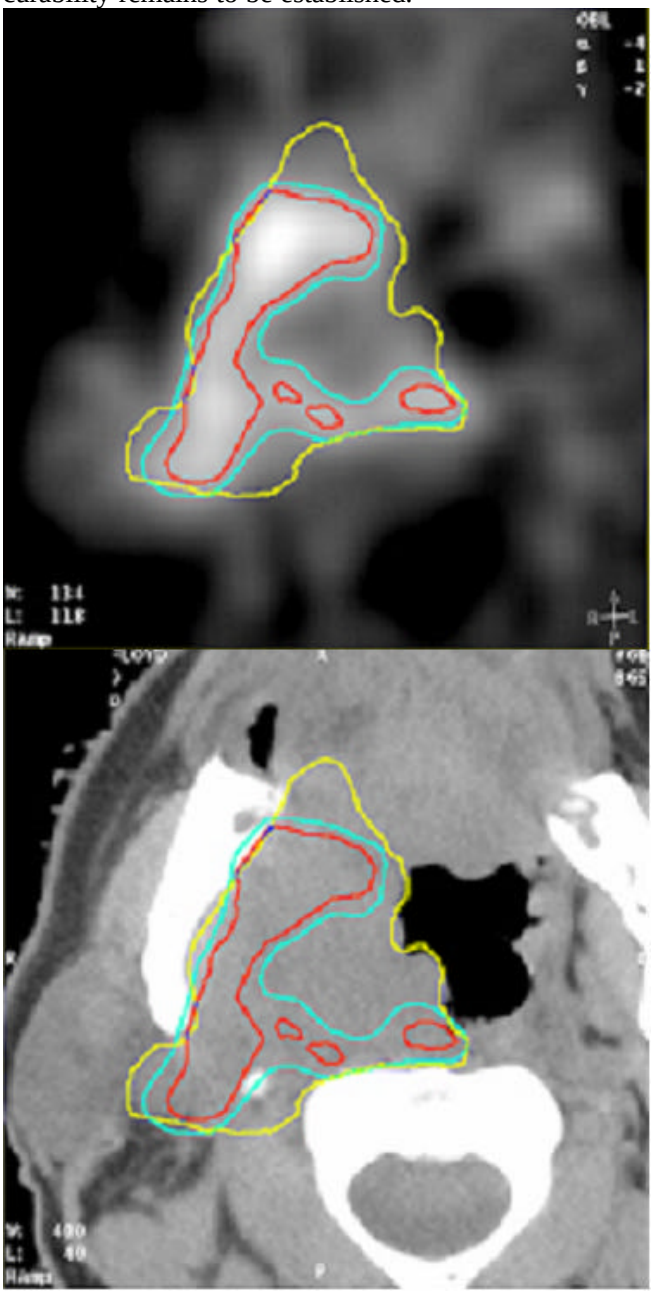

Figure 9. Cu-ATSM identified hypoxic region and the corresponding CT area.

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