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QUALITY ASSURANCE OF PET/CT FOR RADIATION THERAPY

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Abstract

Recent advances in radiation delivery techniques, such as intensity-modulated radiation therapy, provide unprecedented ability to exquisitely control the 3D dose distribution. The development of on-board imaging and other image-guidance methods significantly improve our ability to better target a radiation beam to the tumor volume. In reality, however, accurate definition of the location and boundary of the tumor target is still problematic. Biological and physiological imaging promises to solve the problem in a fundamental way and plays a more and more important role in patient staging, treatment planning and therapeutic assessment in radiation therapy clinics. Indeed, the last decade have witnessed a dramatic increase in the use of PET and CT in radiotherapy practice. To ensure safe and effective use of nuclide imaging, a rigorous quality assurance (QA) protocol of the imaging tools and integration of the imaging data must be in place. The application of nuclide imaging in radiation oncology occurs at different levels of sophistication. Quantitative use of the imaging data in treatment planning through image registration and standardized uptake value (SUV) calculation is often involved. Thus QA should not be limited to the performance of the scanner, but also include the process of implementing image data in the treatment planning, such as data transfer, image registration, and quantitation of data for delineation of tumors and sensitive structures. This presentation will discuss various aspects of the nuclide imaging as applied to radiotherapy and describe the QA procedures necessary for the success of biological image guided radiation therapy.

Keywords

IGRT; PET; SPECT; Quality Assurance; Molecular Imaging

I. Introduction

To 'see' the extent of disease more clearly and define the tumor target volume relative to the patient's anatomy have been one of the most important tasks in radiation oncology. CT and MRI have played pivotal roles in this process. Many radiation oncology departments acquired dedicated CT and/or MRI scanners. In reality, CT and MRI do not always provide an accurate picture of the tumor extent, especially in the zone of infiltration that may be a limiting factor in the attempt of radical treatment approach. It is also problematic when attempting to determine the volume of residual tumor for additional therapies owing to the shortcomings of CT/MRI in differentiating post-therapy changes from the residual tumor. Indeed, the CT and MRI are anatomic in nature - they provide a snapshot of patient's anatomy without the biological information of various organs or structures. Biological imaging, defined as *in vivo*

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characterization and measurement of biological processes at the cellular and molecular level, is an emerging disciplinary field resulting from the developments of molecular biology and diagnostic imaging and shows significant promise to revolutionize cancer detection, staging/re-staging, treatment decision-making, and assessment of therapeutic response.

Positron emission tomography (PET) and single photon emission tomography (SPECT) are valuable biological imaging modalities for radiation therapy planning. They have been harnessed into the planning process in many clinics. In general, PET and SPECT have lower image resolution than CT and MRI and, with the commonly used FDG tracer, it contains little anatomy information of the normal structures (bony structure shows up clearly in PET imaging with some tracers due to the high uptake of bone matrix, which can be utilized to facilitate registration of the images with CT or other imaging data). Information derived from PET needs to be fused with CT or MRI images for treatment planning. Fusion of PET and CT images is made easy with the use of a hybrid PET/CT scanner¹⁻³. PET/CT is a hardware-based image-fusion technology that virtually eliminates the uncertainty and inconvenience of the currently available software fusion of separate PET and CT images. Many radiation therapy departments now house dedicated PET/CT scanners for radiotherapy applications.

Several studies incorporating FDG-PET into treatment planning have been reported⁴⁻⁷. Radiation targeting with fused PET and CT images resulted in alterations in the treatment planning of over 50% of patients, as compared with CT targeting. Changes included alterations in the AJCC TNM stage and modification of target volume. The recent development of ¹⁸F-fluorothymidine (FLT)^{8, 9} and other novel tracers (such as ¹¹C-Acetate¹⁰, ¹⁸F-choline¹¹, ¹¹C-choline^{12 13}, ⁶⁴Cu-DOTA-[Lys³]Bombesin¹⁴, ¹⁸F-FMISO and -FAZA¹⁵, ⁶⁴Cu-ATSM¹⁶) provided new opportunities to improve the sensitivity and specificity of PET imaging of cancer.

Technically, a number of advancements in radionuclide imaging have been made in the past decade. Efforts continue to develop new scintillation-based and solid state detectors to enhance the performance of nuclide imaging devices. Advances in computing technology are making it increasingly feasible to implement the state-of-art iterative algorithms, which promise to significantly reduce reconstruction artifacts and to better model or correct scatter and attenuation. In particular, the development of 4D PET imaging and image enhancement techniques have found natural applications in image guided radiation therapy^{17, 18}. Clinically, to maximize the efficacy of nuclide imaging and to ensure safe and effective use of the technology, a rigorous QA protocol of the imaging tools and integration of the imaging data must be in place. Overall, the goal of QA program is to identify and minimize the sources of uncertainties and errors, taking into consideration the economic, medical, legal, and regulatory implications. In this paper, the issues important to the clinical implementation of nuclide imaging in radiation oncology will be identified, and QA procedures necessary for the success of biological image guided radiation therapy will be described.

II. Issues related to the quality assurance of nuclide imaging

The application of nuclide imaging in radiation oncology occurs at different levels of sophistication. Quantitative use of imaging data in the treatment planning through image registration and SUV calculation is often involved. The QA should not only be limited to the performance of the scanner, but also include the whole implementation process of the imaging data, from image acquisition, data transfer, image fusion, quantitation of data in the delineation of tumor and sensitive structure, and treatment planning.

II.1. Performance assessment

The task of performance assessment is to define an experimental setup that allows to determine the image characteristics of a scanner, to compare different scanners, and to understand and predict the scanner's behavior for patient studies. The National Electrical Measurement Association (NEMA) has introduced a standard, NU 2-2001¹⁹, for assessing PET system performance. Most manufacturers' specifications of imaging devices are based on NEMA recommendations. As described in NU2-2001, this standard utilizes a solid polyethylene cylinder with line sources positioned parallel to the axis of the tomograph at a few radial distances to measure scatter fraction. The sensitivity expresses the correlation between activity within the field-of-view (FOV) and the number of counts acquired in the absence of dead-time effects. Sensitivity measurement is usually conducted with a line source surrounded by known absorbers, and the sensitivity with no absorbers is determined by extrapolation. The spatial resolution is determined using point source measurement. The NEMA standard should be followed for acceptance testing and comparison of different systems.

II.2 Routine QA

Routine QA is performed to ensure normal operation of the scanner and the integrity of acquired images^{20, 21}. The routine QA should track system stability and detect any change in scanner's functionality. For a PET scanner, detector and electronic characterizations, such as adjustment of the gains of the photomultiplier tubes (PMTs), definition of crystal and energy maps and coincidence timing calibration, are parts of the QA and calibration procedure of a scanner. System corrections such as normalization and calibration are examined during the course of QA. Calibration correction is used to convert the reconstructed image pixel values into activity concentration and may be used to compensate the axial sensitivity variation of the scanner.

Evaluation of PET image quality is in general adequately addressed by procedures established in diagnostic imaging²⁰. The PET QA as recommended by the manufacturer is generally divided into daily, weekly, and quarterly procedures. The documents provide practical guideline for a QA program of the scanner. The PET/CT scanner has a radioactive rod source mounted in a shielded container behind the scanner that may be used for calibration and QA purpose as well as transmission scanning. The daily QA program quantitatively monitor the image quality of the scanner over time. In daily QA, single events, coincidence, deadtime and peak energy spectrum of the detectors are measured. During weekly QA, all detectors are irradiated and corrections are made for the detector outputs. The quarterly calibrations provide the system with a benchmark for counting variations and optimizes the system performance. The type of measurements includes the position of single events, update gain, and energy. The detector coincidence timing characterization, 2D normalization, 3D geometric and 2D/3D well counter calibrations, are also performed. The details of all these routine QA tasks are well described in the manufacturers' manuals.

II.3 QA of image acquisition and data transfer

Imaging acquisition parameters can directly or indirectly affect the use of the image set in treatment planning. A standard disease specific image acquisition protocol should be developed, optimized, and used routinely, and should be confirmed by routine inspection of clinical procedures^{22, 23}. In the case of PET/CT scanning, for example, attention should be paid if CT contrast agent is to be used since CT data are also used for PET attenuation correction^{24–26}. In many institutions, sets of CT images are acquired with and without contrast media, and the former is employed for PET attenuation correction. Hyperconcentrated positive contrast in the enhanced region can cause spurious apparent increased tracer activity on the attenuation corrected PET images when the contrast-enhanced CT scan is used for attenuation correction. In some institutions, however, it is claimed that no perceptible artifacts in image or significant changes in SUV measurements are encountered when the contrast-enhanced CT is

used for attenuation correction^{27–29}. In general, PET images are susceptible to CT artifacts. When designing an acquisition protocol, assessment of the PET/CT images is recommended for patients with CT contrast media or with implanted artificial materials, such as prostheses, dentures or implanted fiducials. The clinical protocols which are used for PET/CT must try to minimize the creation of artifacts.

Data transfer and computer interface often present practical problems to the clinical implementation of biological imaging modalities. The nuclide imaging devices should be equipped with appropriate hardware and software interfaces to allow them to be a part of an integrated network environment within the radiation therapy department. An efficient and robust data transmission network is critical to the effective use of multimodality imaging data. Although the use of DICOM standard has greatly facilitated the image transfer to third-party image workstations, there is still some lack of correspondence between the various DICOM implementations released by different manufactures. Specific to the nuclide images, special attention should be paid to the spatial resolution, volumetric or 2D slice format, and the coordinate system of the scanner. It is recommended that specific tests should be designed to verify that each of these functions works as expected.

II.4 Consistency of SUV

SUV is a semi-quantitative index used in PET to express the uptake of a radiopharmaceutical in a region of interest of a patient's scan. It is typically calculated as the ratio of the radioactivity in the region to the injected dose, corrected for body weight³⁰. Numerous publications have showed that changes in **SUV** over approximately two hours can be used in some settings to separate benign from malignant disease, and help to distinguish patients with post-biopsy inflammation or tumor³⁰. **SUV** is the basis for quantitative use of nuclide imaging data and automated segmentation. The delineation of tumor contours in radiation oncology is usually done by: (i) visual interpretation; (ii) using a threshold **SUV**; (iii) thresholding by percentage (e.g., 40%) of the maximum uptake; and (iv) the source-to-background ratio. The visual inspection is subjective as the results depend on the window and level as well as the individual physician's experience. Automated PET segmentation tools have been proposed, but most, if not all, have limited clinical utility. Comparisons of different methods were recently performed by Nestle et al³¹ and Kirov et al³². Substantial differences in the delineated tumor volumes were found, especially in patients with inhomogeneous tumors. It seems that rigorous validation tests and adaptations to each clinic's PET scanner and procedures are needed for reliable automated tumor delineation^{31, 32}. Because of its important role in tumor volume definition, it is crucial to ensure the consistency of **SUV**. It should be emphasized that **SUV** may be influenced by organ motion and 4D PET should be used when dealing with lesions in the thorax or upper abdomen^{16,17,33}.

II.5 QA of multimodality imaging fusion

Image registration is a process of determining the optimal spatial transformation that maps one image to another, which is a necessary step to utilize PET/SPECT information for treatment planning. Computer-based rigid image registration has gained widespread popularity in the last decade and is used in routine clinical practice. In this approach, the matching of the two input images is formulated into an optimization problem and the best registration of the two images is obtained by iteratively comparing various possible matches until no better registration can be found^{34–39}. Rigid and deformable image registrations are two main categories of registration models. The former one assumes that the transformation consists only of translations and rotations, whereas the latter allows localized stretching of images. There are circumstances in medical applications where non-rigid registration is necessary. For example, respiratory motion causes non-rigid distortion of the lungs and other organs and necessitates deformable model to map information from one phase to another³⁸.

Verifications of the dataset registration and multiple dataset functionality involve general commissioning tests, as well as development of routine procedural checks to make sure the information is used properly for each particular case. In general, the accuracy of image registration depends on a number of factors, such as the quality of images to be registered, imaging artifacts, and intensity contents. PET images are usually noisy and have little anatomic information to aid registration with CT images. However, the transmission scan and the CT-PET co-visible fiducials are useful to facilitate the registration. In special cases when FLT tracer (or alike) is used for PET imaging, the patient's bony structures have high tracer uptake, facilitating auto-registration algorithm to register the PET and CT images³⁷. There are cases where the feature(s) on one image do not have correspondence to the other image (for pelvic PET imaging, for example, the bladder shows up as a high intensity region because of tracer accumulation, which has no correspondence in CT images). To deal with image artifacts or modality-specific image features, regional algorithms such as control volume-based techniques³⁷ seem to be extremely valuable. As usual, any image fusion algorithm needs to be validated before its clinical use.

II.6 QA of system integration

Just minimizing the uncertainties in each of the many steps involved in using biological imaging data is not enough to accomplish our QA goal. The system integration should be part of the QA tests, which is particularly important in today's multi-vendor clinical environment. In addition to the above mentioned issues, there should be tests examining the performance of the whole system to ensure the functionality of the system integration. This should be reevaluated each time after a major system upgrade or a new device is introduced.

II.7 QA of emerging 4D PET/CT-guided radiation therapy

Respiratory motion poses a challenge in nuclide imaging, where data often must be acquired over many respiratory cycles to obtain adequate statistics. Intra-scanning organ deformation results in lesion motion, thereby spreading the radiotracer activity over an increased volume, distorting apparent tumor shape and location, and reducing signal-to-noise ratio (SNR). The artifacts are particularly worrisome for modern radiation therapy, which is aimed to achieve millimeter precision. One solution is to gate the data either prospectively or retrospectively, limiting the image analysis to a single phase of the respiratory cycle. The feasibility of gated PET has been well demonstrated on both phantom and patient data in several excellent recent publications^{17, 18, 40}. More effective 4D PET image acquisition technique has been developed to ease the competition between spatial and temporal resolutions. In essence, the signal data are acquired over many short timesteps, and retrospectively grouped into several bins along a measured amplitude of respiratory motion. These bins are then registered one-by-one through either rigid or deformable transformation methods, and stacked on top of one another to form a composite image at a single point in the respiratory cycle.

Clinically, 4D imaging and 4D radiation therapy entail additional QA steps⁴¹. It is important to note that a 4D image set is not simply a stack of 3D images and the functionality of the scanner in 4D acquisition mode needs to be examined routinely. The related informatics and data storage are also unique to 4D imaging and therapy. The support of 4D imaging and planning data from the treatment planning vendors is still at an early stage and this situation may last several years. Given the inherent complexity of the problem, it is essential to establish a rigorous QA procedure as we develop reliable 4D radiation therapy techniques.

III. Conclusions

The success of radiation treatment relies on the use of biological imaging, and accurate and robust integration of the imaging data. Biological imaging will play a more and more important

role in patient staging, treatment planning and therapeutic assessment in radiation therapy clinics. Biological imaging is also the foundation of future biologically conformal radiation therapy, where the goal of BCRT is to take the inhomogeneous biological information derived from biological imaging into account and to produce customized nonuniform dose distributions on a patient specific basis. To ensure safe and effective use of the nuclide imaging technology, a rigorous QA protocol must be in place. QA of biological imaging equipment and the integration of the imaging data should be parts of a comprehensive QA program in radiation oncology. It is emphasized that the goals of nuclide imaging for radiation therapy treatment planning may be different from that of diagnostic imaging. Hence QA should not only be limited to the performance of the scanner, but also include the whole treatment planning process, such as data transfer, image registration, and delineation of tumors and sensitive structures.

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