ORIGINAL ARTICLE:

ROLE OF PET-CT IN MODERN RADIOTHERAPY PLANNING PROCESS OF SOLID TUMOURS

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Abstract:

Positron emission tomography (PET) allows functional imaging of structures by virtue of their ability to metabolise glucose and concentrate specific molecules which are labelled with positron emitting Radionuclides. Integrated computed tomography (CT) and PET more accurately characterise the metabolically active tissue. Together PET-CT has shown more sensitivity and specificity for diagnosis, staging, response assessment, during follow up for early detection of recurrence and target volume delineation in radiotherapy planning.Aim: Aim of the study is to evaluate the technical challenges in the image registration of PET/CT and planning CT done in our hospital.Methods& Materials: Our study includedpatients who have attended our hospital and received Radiotherapy (RT) for various sub-sites. The PET/CT images of the respective sub-sites were fused with the planning CT images using rigid registration and the target was delineated using the registered images.Conclusion: Apart from few technical difficulties, rigid registration fusion algorithms of PET/CT images to the planning images after careful patient positioning helps the radiation oncologist in proper delineation of target volume.

Keywords—Non-Deformable Image Registration,FDG, PET/CT, Rigid Registration, Treatment, Planning.

INTRODUCTION

Advances in imaging revolutionarised the diagnosis and management of cancer. Imaging modalities like Positron Emission Tomography (PET) and Computed Tomography (CT) are now widely used for staging and tumour delineation for cancers of various sites. Imaging has always been the backbone of radiotherapy planning whether it might be a portal film or CT, MRI or more recently the PET and SPECT scans. RT planning has evolved from the era of 2D planning using the portal films and taking wide margins around the tumour, firing more of normal tissue to avoid geographical miss, to the present era of modern treatment planning using advanced imaging modalities with lesser margin around the tumour leading to minimum normal tissue dosage and precise and higher target volume dosage. While PET images provide details on the extent and intensity of the metabolically active tumour, the conventional imaging modalities like CT, MRI etc are anatomical imaging modalities which provide the anatomic details of the tumour and surrounding structures like bone, soft tissue, lymph nodes etc. But many a times difficulty arises in differentiating between an actual tumour from benign conditions like fibrosis, gliosis etc. In such situations and many other situations PET scan plays an important role.

In particular, accurately defining target volumes in radiation treatment planning is crucial to ensure proper coverage of the tumour and spare organs at risk.The PET/CT scan can be used for precise tumour delineation and planning of the radiation therapy. To better correlate the location of the ^{18}F-fluorodeoxyglucose (FDG) avid tumours from the combined PET/CT images with the planning CT scan, software can be deployed to co-register the images. Rigid image registration (RIR) of the two images can effectively align the PET to the planning CT images to accurately define the volumes for radiation treatment.

AIMS AND OBJECTIVES:

The purpose of this retrospective study is to asses the utility and efficacy of the Rigid Image Registration (RIR) between PET/CT and planning CT images for radiotherapy patients. The impact of RIR on the tumor volume delineation is investigated in this work.

METHODS AND MATERIALS

45 Patients underwent curative and palliative radiotherapy at the Queen's NRI Hospital in Visakhapatnam, India, between Sep 2013 and Dec 2015 using Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated Radiotherapy (VMAT).

The CT simulation for the patients was performed at the treatment site with a Philips MX-16 CT scanner and the patients were immobilized with a thermoplastic mask. Full body scans were acquired with the patients immobilized on a flat couch top and a PET/CT was generated for radiotherapy treatment purposes. The DICOM imaged are imported into the treatment-planning database. The PET/CT images were fused with the planning CT scans within the treatment planning system (Eclipse, Varian Medical Systems, Palo Alto CA). Rigid registration of the PET/CT and planning CT images was carried out using the Varian Rigid registration application (Version-10.0.42). Routine treatment planning was done and treatment plan was generated.

OBSERVATIONS AND RESULTS

Head and Neck:

PET-CT can influence the treatment strategy of head and neck cancer patients greatly from changes of nodal status before therapy, detection of distant metastasis and/or treatment evaluation.[1-4]PET may also be of use in patients presenting with metastatic squamous cell carcinoma of neck nodes from unknown primary.[5] Even though primary tumourdetection rate ranges from 24%-44% [6], PET-CT helps in dilenation of GTV Nasopharyngeal carcinomas (fig 2) and in metastatic nodal disease (fig 1).

The assessment of residual disease in the neck by PET-CT after chemoradiotherapy in some patients can help avoid unnecessary neck dissection.[7] PET-CT performed 3 months post chemoradiation, exhibit very high negative predictive value (97-100%)[7], and a metabolic complete response is predictive for disease- free and overall survival. [8]

Thorax and Abdomen:

Addition of FDG- PET in radiotherapy planning has a significant impact on target volume delineation (in 20–94% of patients), resulting in either reduction or increase in target volumes based on CT images (Muijs et al).[9] However, FDG uptake in pathologic areas on one side can be compensated on the other side by inflammation. [9] Some studies [10,11] reported that PET-based tumourdelineation prevented geographic miss by identifying unsuspected malignant involvement in 30–60% of patients in Thorax (fig 3) , Butbecause of the poorer sensitivity of FDG-PET for primary tumour, the irradiated volume should not be reduced based on a negative FDG-PET finding in a region with suspect malignant involvement on other diagnostic investigations. [12]

FDG-PET in RT treatment planning can also be used to reduce inter-and intra-observer variability. Toya et al.showed significantly increased similarity in GTV definition in inter- and intraobserver comparison, when incorporating FDG-PET-CT images in comparison to CT images of cervical oesophageal carcinoma. [13]

The potential prognostic value of FDG uptake in oesophageal cancer patients was evaluated [14],in which most of 31 reviewed studies showed that FDG uptake in pre-treatment and post-neoadjuvant treatment PET scans, as absolute values, are predictors for survival in univariate analysis. During neoadjuvant therapy an early decrease in FDG uptake is also predictive for pathologic response and survival in most studies.

PET/CT is preferred medical imaging modality for detecting atelectasis from intra-tumorheterogeneity in non-small cell lung cancer, and has higher sensitivity and specificity for identifying lymph node involvement. [15] Several planning studies showed that adding PET/CT information was associated with smaller size on tumor volume than compared to radiotherapy pCT[16-18], thus allowing radiation oncologists to escalate the dose with slightly lower doses on organs at risk with promising high curability rates. In lung and other thoracic malignancies, the problem of target motion is an important issue. Artifacts due to respiratory motion can cause deterioration of the quality of images and the appearance of tumor with resulting misdiagnosis and mislocalization. [19,20] In this regard, nowadays, the use of gated PET/CT and 4-dimensional CT acquisition are becoming more popular.

In the management of lymphoma (both non-Hodgkin's and Hodgkin's), the use of FDG-PET has become standard with its high sensitivity for defining disease.[21,22] It has a well-accepted role in staging, radiation therapy field design and response evaluationand may predict disease outcome. Recent findings showed that staging with PET/CT is superior to CT or MRI. Use of PET/CT in involved field radiation therapy field design in Hodgkin's lymphoma leads toreduced target volumes while avoiding geographic miss. [21,23]

Pelvis:

In cervical cancer, the current gold standard for primary tumourstaging, especially in determining tumour extension in the parametria is T2 weighted MRI (reported accuracy of MRI is 80 to 90% compared to 60 to 69% for CT). [24,25]Whereas, in nodal staging, in patients with locally advanced cervicalcarcinoma (i.e.FIGOstage is ≥IB2) PET-CT is an effective imaging technique, with significantly better sensitivity and specificity in comparison to other morphological imaging (PET-CT sensitivity ranging from 77% to 96% for pelvic lymph nodes and 50% to 100% for paraaortic lymph nodes, specificity from 55% to 75% for pelvic and 83% to 95% for para aortic lymph nodes respectively).[26] The presence of metastatic lymph nodes in the pelvic (fig 6)andpara aortic regions alter the clinical stage of disease and it definitely alters radiation treatment strategy (either by extending irradiated volume to the common iliac or para-aortic areas(fig 4) or by escalating irradiated dose to the involved lymph nodes), [25] and also the presence and extent (i.e. the most distant level of involved lymph nodes) of PET positive nodal metastases correlate well with recurrence-free and disease-free survival. [27]

By using PET CT guided IMRT dose escalation can be done to pelvic and positive para aortic lymphnodes(fig 5) without adversely affecting adjacent organs at risk. [28,29, 30]

It has been demonstrated that even post-treatment metabolic response immediately after RT and 3 months after RT are predictive of patient outcome. [31,32]

DISCUSSION

The crucial points in use of PET/CT for radiotherapy planning are patient positioning and image registration. As the quality of image fusion has been shown to be significantly better when CT and PET have been acquired in identical position, irrespective of the type of scanner used, the correct registration of PET data with the CT data should be verified. It is impotant to bear in mind that patient position may change during PET/CT acquisitions. Uncorrected or improperly corrected PET-derived GTVs when transmitted to CT datasets without critical evaluation of the quality of coregistration, results in a geographical miss. This correction can be done by comparing anatomical landmarks detectable on both the imaging techniques, like carina tracheae, spine, sternum, thoracic wall and—with care due to breathing mobility—diaphragm.

Problems associated with PET-CT and tumor delineation

There are several sites of the normal physiologic accumulation with the FDG, the most intense tracer accumulation is found in the brain, heart and urinary tract. Elsewhere in the body, tracer activity is distributed at low levels on attenuation-corrected images in the liver, spleen, bone marrow, and renal cortex. In the head and neck, significant muscle uptake can be observed in the skeletal muscles with exercise, in the breathing muscles with hyperventilation, in cervical muscles with tension, and in the laryngeal muscles with vocalization. Low to moderate FDG uptake occurs in the lymphatic tissues in the nasopharynx, base of tongue, and palatine and lingual tonsils. Low to moderate FDG uptake is noted in the salivary glands. Physiologic FDG uptake in the normal thyroid gland is usually absent or minimal. These areas of physiologic uptake should be interpreted with caution and not assumed to be pathologic and delineated for radiotherapy.

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Inflammatory conditions can be manifested with increased FDG uptake. In postoperative patients, normal wound healing and inflammatory response associated with tissue resorption should not be misinterpreted as malignant processes. Prior radiotherapy can be associated with increased FDG uptake even months after therapy. Some have recommended performing a PET-CT no sooner than three months after radiotherapy to assess persistence of cervical nodal disease. The classic example of increased uptake secondary to radiation treatments is radiation pneumonitis, which can mimic an infectious pneumonia or a malignant neoplasm.

One of the problems with PET-CT is movement of the patient between the CT and PET scans, creating artifacts on fused images that may cause misregistration and confusion as to where the tumor is located. Attenuation corrections artifacts can also occur where there are highly attenuating objects in the path of the CT beam such as a dental device or contrast-enhanced vessel.

The position of the patient during radiotherapy simulation should be the same as the position during PET-CT to minimize misregistration. Immobilization masks should be brought to PET-CT to reproduce the setup, and arm position, which can affect placement of the shoulder, should be kept the same. A flat board should be inserted and used during PET-CT to replicate the linear accelerator tabletop.

Image registration:

Proper registration is required to precisely identify gross tumor volume. As the quality of image fusion has been shown to improve significantly when CT and PET have been acquired in identical position, it becomes essential, that a FDG-PET acquisition for RT treatment planning must be done in RT treatment patient position. [33] Here, photo documentation and laser systems are of great help. Whatever may be the kind of scanner used (PET or PET/ CT) the correct registration of PET data with the CT dataset used for RT-planning must be verified. Without critical evaluation of the quality of registration, differences in the tumour localization in the PET-CT and planning CT may lead to geographical miss. Rigid and deformable image registrations are the most commonly used subtypes of registration.

Rigid registration is the overlap of the two imagedata set based on bony structures. But, the potential differences between image data set, such as variations in anatomical positioning, are still continued by rigid fusion. The probability of mismatch between PET/CT and pCT caused by different recumbent position, unintended organ movements and different respiratory phases is still disadvantage of rigid fusion. Non-rigid coregistration algorithms may solve a part of the positioning problems. However, although these methods have been proposed for the use in radiotherapy [34] the resulting image datasets have not been evaluated concerning the correct position of pathologic tissues, especially tumors until now. It may well be, that the deformation of image data caused by non rigid algorithms may result in geometrical inexactnesses or geographical misses, predominantly in cases, where the tumours are not unequivocally depicted by the morphological method.[35]Unless a dedicated PET/CT scanner is used for radiation treatment simulations, the patient anatomy on the PET/CT does not always correspond to that of the planning CT. This can be further complicated by changes in the positioning of the patient and displacements due to patient breathing, cardiac motion or involuntary motion. When performing a PET /CT scan, it is of greater importance that the patient lies still for the entire study. This requires that the patient is postioned as comfortably as possible and is well established. A PET/CT scanning session, even with the modern scanner will typically take 10-15 minutes. The PET images will be corrected for attenuation, reconstructed and then fused with the CT images; therefore the patient must not move between the two procedures. In our experience of fusion of PET-CT and planning CT images using rigid registration there was good target coverage and no geographical miss in almost all subsitesas care was taken during PET-CT imaging to maintain treatment planning position.It is well known that if the diagnostic PET/CT is aquired the patient lying on a flat table like RT Planning position, the accuracy of rigid registration increases. [15]

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CONCLUSION:

Apart from few technical difficulties, rigid registration fusion algorithms of PET/CT images to the planning images after careful patient positioning helps the radiation oncologist in proper delineation of target volume without any geographical miss. The interdisciplinary nature of this approach requires cooperation at multiple levels between imaging and radiation oncology departments. The disadvantages are the influence of time delay between the diagnosis and referral for radiotherapy on tumor volume and tracer uptake, the effects of induction systemic therapy on FDG uptake, the differences in patient position and immobilization devices between diagnostic and therapeutic sets. Careful image registration and validations are needed before delineation of the tumor.

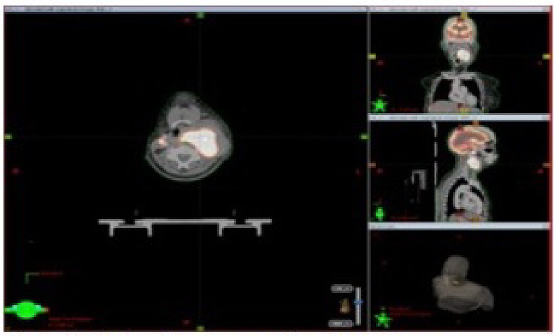

Figure 1: A 49year female case of carcinoma breast with cervical lymph nodal recurrence planned for radiotherapy.

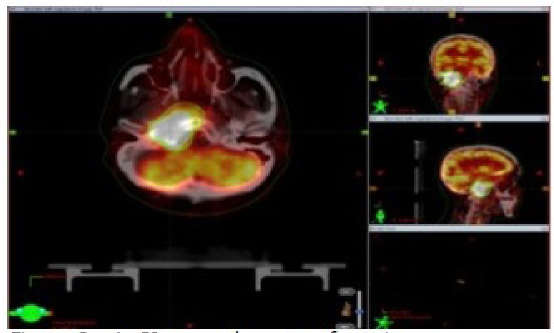

Figure 2: A 59year male case of carcinoma nasopharynx with extension into petrous apex treated with IGRT 70Gy/35#.

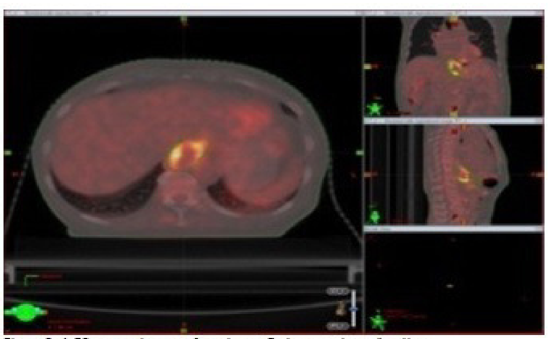

Figure 3: A 72 year male case of carcinoma Gastro-oesophageal junction treated with radiotherapy 55.8Gy/31#.

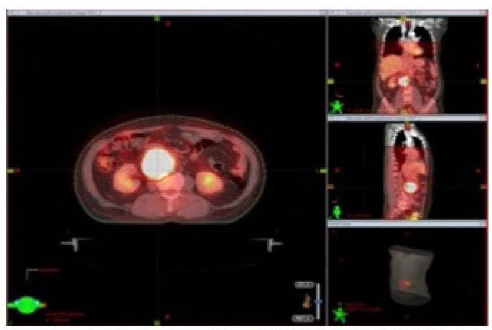

Figure 4: A 68year male case of NHL testis post 6 cycles of chemotherapy with recurrence with in 6 months in the retroperitoneum treated with IGRT 45Gy/25#.

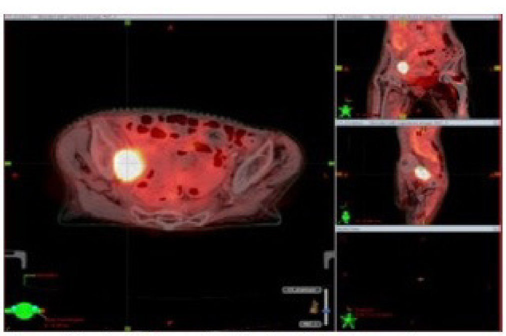

Figure 5: A 65year female treated case of carcinoma cervix (post RT) with pelvic lymph nodal recurrence. Treated using rapid arc technique to a dose of 46.71Gy/27# @ 1.73Gy/#.

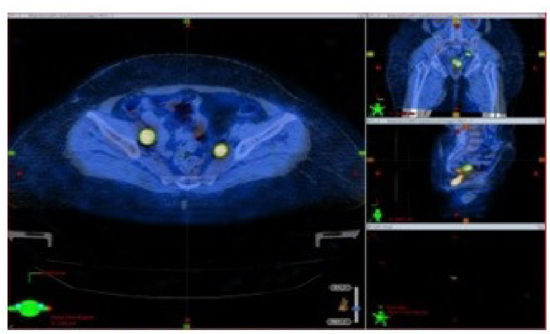

Figure 6: A 47year female case of carcinoma cervix post simple hysterectomy with gross residual disease and pelvic lymphadenopathy.Treated with IGRT 61.20Gy/34# @ 1.8Gy/#.

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