ROLE OF 18F-FDG-PET/CT SCANNING IN MANAGEMENT OF PATIENTS WITH LOCALLY ADVANCED HEAD AND NECK CANCER

Thesis

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18.F-FDG- PET / CT	:	18 F- Fluorodeoxyglucose positron Emission Tomography/ computed temography
CECT	:	Contrast-enhanced computed tomography
CI	:	Conformity Index
CR	:	Complet Response
CT	:	Computed Tomography
CTV	:	Clinical Target volume
DVH	:	Dose Volume Histogram
ECOT	:	Eastern Cooperative Oncology Group
FNAB	:	Fine Needle Aspiration Biopsy
FNAC	:	Fine Needle Aspiration Cytology
GTV	:	Gross target volume
H&N	:	Head and Neck
HNC	:	Head and Neck Cancer
HNSCC	:	Head and Neck Squamous Cell Carcinoma
HPV	:	Human Papilloma Virus
IMRI	:	Intensity Modulated Radiation Therapy
MBI	:	Narrow Band Imaging
MRI	:	Magnetic Resonance Imaging
MRS	:	Magnetic Resonance Spectroscopy
NCCN	:	National Comprehensive Cancer Network
NTCP	:	Normal Tissue Complication Probability
OAR	:	Organs at Risk
OB	:	Open Biopsy

PD	:	Progressive Disease
PET	:	Positron Emission Tomography
PR	:	Partial Response
PTV	:	Planning Target Volume
RECIST	:	Response Evaluation Criteria in Solid Tumors
RT	:	Radio-Therapy
SD	:	Stable Disease
SPECT	:	Single Photon Emission Computed Tomography
TCP	:	Tumor Control Probability
TNM	:	Tumor- Nodes- Metastases
TSH	:	Thyroid Stinulating Hormon
US	:	Ultrasound
USCB	:	Ultrasound-Guided Core Biopsy

INTRODUCTION

Head and neck cancers accounted for approximately 4% to 5% of all the malignant diseases ***(Al-Ibraheem et al., 2009).*** Head and neck squamous cell carcinoma (HNSCC) comprises the vast majority of head and neck cancer (HNC). Unfortunately, at the time of initial diagnosis more than 50% of patients already present with regional nodal metastases or even distant metastases. For all stages, the 5-year survival is approximately 50%. Of patients for whom therapy fails, 90% will have recurrent disease within the first 2 years after treatment. The median survival of patients with local or metastatic recurrent disease is 6 months ***(Bujenovic, 2004).***

Oncologic imaging plays an important role in head and neck cancers as imaging findings can aid significantly detection, staging, restaging, and therapy response assessment of these tumors ***(Bujenovic, 2004, Al-Ibraheem et al., 2009).***

Morphologic imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI) with intravenous contrast are often performed either prior to pan-endoscopy to noninvasively assess the aero-digestive tract or afterwards to provide information about primary tumor size, infiltration,

involvement of surrounding structures, and regional nodal involvement. There is growing evidence, however, that these modalities have limitations in their diagnostic accuracy. CT and MR imaging rely on criteria of contrast-enhancement patterns and nodal size for detection of lymph node metastases which are not specific and may escape detection of metastases within normal size lymph nodes ***(Al-Ibraheem et al., 2009).***

Treatment is complex for head and neck cancer. The specific site of the disease, stage and pathologic findings guide the treatment i.e the appropriate surgical procedure, radiation targets, dose, fractionation and indication of chemotherapy (NCCN guidelines-2013, head and neck cancer). Single modality treatment with surgery or radiotherapy is generally recommended for approximately 30-40% of patients diagnosed with early stage disease (stage I-II). The two modalities result in similar survival in these individuals. In contrast, combined modality therapy is generally recommended for the approximately 60% of the patients with locally or regionally advanced disease at diagnosis (NCCN guidelines-2013, head and neck cancer). This is because for most cases radiation is at least equivalent to surgery and preserves a greater degree of function ***(Sessions et al., 2005)***.

Treatment of cancer with radiation aims at eradication of the tumor while preserving normal tissue (organ) function. This requires spatially accurate visualization of tumor in relation to the surrounding healthy structures. Computed tomography forms the primary imaging modality for image based radiotherapy treatment planning. With the inclusion of many newer imaging modalities, each with unique diagnostic capabilities, multi-modality imaging is the current buzzword in radiotherapy. Imaging modalities like magnetic resonance imaging (MRI) & magnetic resonance spectroscopy (MRS), single photon emission computed tomography (SPECT), ultrasound imaging and molecular imaging are being increasingly incorporated into radiotherapy treatment planning. Additionally, treatment evaluation tools in radiotherapy such as dose volume histogram (DVH), tumor control probability (TCP), normal tissue complication probability (NTCP) and conformity index (CI) completely depend upon the imaging modality used for treatment planning ***(Prabhakar et al., 2007; Al-Ibraheem et al, 2009).***

Positron Emission Tomography (PET) has been increasingly used in various fields of medicine. It has found its role in the diagnosis, staging, prognosis, treatment planning and evaluation of treatment response. The incorporation of PET in

radiotherapy treatment planning has revolutionized the field of radiation oncology ***(Prabhakar et al, 2007).***

With the introduction of advanced radiotherapy treatment techniques like 3-D conformal radiotherapy (3-D CRT) and intensity modulated radiotherapy (IMRT), it is of utmost importance to delineate the target volume precisely in order to achieve a good tumor control ***(Prabhakar et al, 2007).*** As of now, CT is the best imaging modality for 3-D treatment planning as it provides information about the tissue densities in the form of electron density which is required for radiotherapy dose calculation. To utilize PET in radiotherapy, it should be fused either with CT or MRI. An integrated PET-CT is the best option, it provides precise localization of lesions and improves the standardization of volume delineation compared with that of CT alone ***(Solberg et al, 2004).*** Using PET-CT in radiotherapy planning reducing interobserver variability in target delineation, and modifying the extension of gross tumor volume (GTV), clinical tumor volume (CTV) and planning target volume (PTV) for both primary tumor and regional lymph nodes, potentially, allowing additional dose escalation. In some cases, the intent of treatment could also change from curative to palliative when distant metastases have been detected by PET ***(Alauddin, 2012; Al-Ibraheem et al., 2009).***

In order to use the PET-CT data for radiotherapy treatment planning, the scanner must be equipped with a flat-bed insert as the radiation treatment is performed with patients on a flat couch ***(Ireland et al., 2007).***

One of the most controversial and challenging issues in applying PET/CT in radiation planning is contouring the outline of the tumor. Changing the PET window level can lead to a considerable overestimation or underestimation of the target volume. However, several techniques including threshold-based methods have been suggested and used, but still consensus needs to be met. Forty or fifty percent of the tumor/image maximum intensity (SUVmax) has been used for contouring by several groups ***(Scarfone et al., 2004).*** Others used normalized volumes according to liver uptake ***(El-Bassiouni et al., 2007).*** Wang et al. used an arbitrary SUV of 2.5 as a basis for contouring ***(Wang et al., 2006).*** Berson et al. suggested in a recent report that developing an institutional contouring protocol for PET/CT treatment planning is highly recommended to reduce inter-observer variability ***(Berson et al., 2009).***

Even with PET, one must not only consider the GTV but also must continue to estimate subclinical involvement (the

CTV). Subclinical disease usually is lymphatic or perineural invasion and by lowering the upper threshold of the PET data this can be detected. In a study done by Breen et al, the addition of PET-CT to GTV (primary site) delineation of head and neck cancers does not change the volume of the GTV as observed on CT but it may demonstrate differences in neck node delineation and in other disease sites ***(Breen et al., 2007).***

Schwartz et al has shown that the addition of 18F-FDG-PET is superior to CT alone in geographic localization of diseased neck nodes, with sensitivity of 96% and specificity of 98.5% in nodal level staging ***(Schwartz et al., 2005).***

FDG-PET has also been demonstrated to be a prognostic indicator of recurrence in head and neck cancer ***(Min et al., 2016).*** The quantitative assessment of changes in tumor metabolic activity provided by FDG-PET allows monitoring of response to cancer treatment ***(Doot et al., 2014).***