Is there a role for PET/CT parameters to differentiate thyroid cartilage invasion from penetration?

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ABSTRACT

Background: Assessment of thyroid cartilage invasion (tumor extension through inner cortex) and thyroid cartilage penetration (tumor involving both the inner and outer cortices of thyroid cartilage) may be challenging with CT (Computed Tomography) and MR imaging (Magnetic Resonance Imaging). Positron Emission Tomography/Computed Tomography (PET/CT) is a non invasive imaging modality that provides both anatomic and metabolic information. Quantitative data obtained from PET/CT, also known as PET/CT parameters, include maximum, mean or peak standardized uptake values (SUVmax, SUVmean, SUVpeak), metabolic tumor volume (MTV), total lesion glycolysis (TLG), standardized added metabolic activity (SAM) and normalized standardized added metabolic activity (NSAM). Our aim was to examine if FDG PET/CT parameters could differentiate thyroid cartilage invasion from penetration.
Methods: 50 patients who underwent PET/CT before laryngectomy for squamous cell carcinoma of the larynx, had SUVmax, SUVmean, SUVpeak, TLG, MTV, SAM and NSAM calculated on a dedicated workstation. Univariate and multivariate analysis was performed. ROC analysis was used to determine the ability of PET/CT parameters to predict pathologically proven thyroid cartilage invasion or penetration.
Results: Of the 50 patients, 50% (25/50 patients) had history of prior radiation therapy. Among the previously irradiated group, 24% had thyroid cartilage invasion and penetration. 8% of the patients in this group had thyroid cartilage invasion only. Among the non-irradiated group, 76% had thyroid cartilage invasion and penetration, 8% had thyroid cartilage invasion without penetration. ROC analysis revealed that none of the PET/CT parameters had enough power to predict thyroid cartilage penetration, but TLG, MTV and SAM had enough power to predict thyroid cartilage invasion in non-irradiated patients. TLG, MTV, SAM and NSAM had enough power to predict thyroid cartilage invasion and penetration in irradiated group.
Conclusion: TLG, MTV and SAM have enough power to predict thyroid cartilage invasion and penetration in irradiated patients. PET/CT parameters do not have enough potential to differentiate thyroid cartilage invasion from penetration.

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1. Introduction

Since the US Department of Veterans Affairs (VA) laryngeal study group and the radiation therapy oncology (RTOG) 91-11 trials, there has been significant change in the management of T3 and T4a laryngeal squamous cell carcinoma (SCCa) [1–3].

Extent thyroid cartilage involvement is a defining factor between T3 and T4a stages. Laryngeal SCCa with involvement of only inner cortex of the thyroid cartilage (thyroid cartilage invasion) is staged as T3 and those involving both inner and outer cortices of the thyroid cartilage (thyroid cartilage penetration) are staged as T4a [1–3]. Currently American Society of Clinical Oncology and the National Comprehensive Cancer Network expert panels

Fig. 1. 67 year old male, previously irradiated. T4a transglottic laryngeal carcinoma with pathologically proven thyroid cartilage penetration. Axial fused PET/CT (1A) shows the location and extent of the metabolic activity of the tumor. Sagittal and coronal PET/CT images (1B, 1C) show the primary VOI (red) and two outer VOIs (light blue and dark blue). SUV max, SUV mean, MTV, and TLG were calculated from VOI_{PET} (defined by a gradient method using the PET uptake, red contour). SUV peak was centered on the voxel defined by SUV max. SAM was calculated as the total SUVs from VOI_{SAM} less the normal tissue SUVs calculated from the volume between VOI_{SAM} (light blue contour) and VOI_{BKG} (dark blue contour).
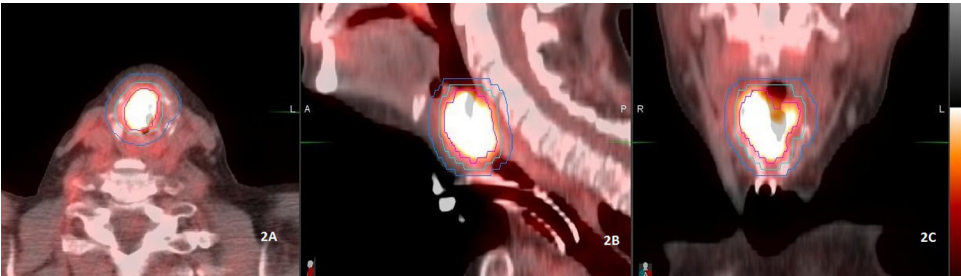

Fig. 2. 62 year old female, previously irradiated. T3 transglottic laryngeal carcinoma with pathologically proven thyroid cartilage invasion. Axial fused PET/CT (2A) shows the location and extent of the metabolic activity of the tumor. Sagittal and coronal PET/CT images (2B, 2C) show the primary VOI (red) and two outer VOIs (light blue and dark blue).

Table 1
Descriptive statistics.

Variable	Level	N (%) = 50
age 65	<65	28 (56.0)
	> = 65	22 (44.0)
Sex	Female	13 (26.0)
	Male	37 (74.0)
Path T stage	T1–T2 (including Tx)	9 (18.0)
	T3–T4	41 (82.0)
Path N stage	N0	31 (62.0)
	N1–N2 (including Nx)	19 (38.0)
Primary location	Glottic	21 (42.0)
	Supraglottic/subglottic/transglottic	29 (58.0)
T.cart.penetration	No	25 (50.0)
	Yes	25 (50.0)
T.cart.invasion	No	21 (42.0)
	Yes	29 (58.0)
Rthistory	No	25 (50.0)
	Yes	25 (50.0)
Age	Mean	63.58
	Median	62.50
	Minimum	42.00
	Maximum	91.00
	Std dev	9.83
	Missing	0.00

recommend initial laryngectomy for patients with T4a laryngeal carcinoma. T3 laryngeal SCCa can be treated with radiation therapy as initial treatment strategy.

Before the VA and RTOG 91-11 trials, the primary question for the patient with advanced laryngeal carcinoma was whether the patient was operable [2]. Identification of imaging findings such as thyroid cartilage invasion, penetration, or extralaryngeal spread were not important, as the management was total laryngectomy, regardless of degree of cartilage involvement [2]. As a result of these trials, the impact of thyroid cartilage invasion (T3) versus penetration (T4a) has been recognized as important, as cartilage penetration is usually treated surgically [1–3].

18F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG PET/CT) imaging has been increasingly used in the assessment head and neck SCCa [4], as it provides both anatomical and functional information. There are a variety of parameters that can be acquired from quantitative analysis of FDG PET/CT. PET/CT parameters can be used as biomarkers that may have prognostic and diagnostic value [4].

Anatomic imaging alone, computed tomography (CT) and magnetic resonance imaging (MRI), has become extremely important in clinical decisions about whether to proceed with radiation therapy (RT) or total laryngectomy. The differentiation between thyroid cartilage invasion versus penetration can be difficult, even with the most advanced imaging technique. However, the myriad of metabolic markers available with PET/CT are rarely used to direct treatment. Our goal, therefore was to examine if FDG PET/CT parameters could impact treatment planning by differentiating thyroid cartilage invasion from penetration.

2. Methods and materials

2.1. Patients

After institutional review board approval and waiving for informed consent for this retrospective study we performed a database review of the Department of Pathology to identify patients who had undergone total laryngectomy for SCCa of the larynx between November 2002 and April 2014. Fifty patients were iden-