S020 EVALUATION OF TUMOR HYPOXIA AND METABOLISM IN HNSCC USING [18F]HX4 AND [18F]FDG PET IMAGING.

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Objective:

Increased tumor hypoxia and metabolic uptake levels are prognostic factors for worse overall survival and increased radioresistance in patients with head and neck cancer. [18F]HX4 is a novel promising PET tracer for visualization and quantification of tumor hypoxia. The aims of this study were to evaluate the [18F]HX4 uptake, its changes and spatiotemporal stability during treatment and the correlation between [18F]HX4 and [18F]FDG PET. We hypothesize that [18F]HX4 will contribute to a better identification of therapy resistant areas for radiotherapy dose-escalation.

Materials and Methods:

PET/CT images of 12 HNSCC patients (11 male, 1 female, T2-4, any N, M0) from an ongoing trial (NCT01347281) were included in the analysis. Before the start of radiotherapy, baseline [18F]HX4 and [18F]FDG PET/CT scans were performed. During radiotherapy (after ±20Gy) [18F]HX4 PET was repeated. Patients were treated with radiotherapy (N=2), in combination with chemotherapy (N=8) or cetuximab (N=2). All gross tumour volumes (GTV; primary lesions and pathological lymph nodes > 5cm³) were included in the analysis. The maximum standardized uptake values (SUVmax) within the GTV were determined. The hypoxic fraction (HF), defined as the relative fraction of the GTV with a tumor-to-muscle ratio (TMR)>1.4, were calculated for both [18F]HX4 PET scans. In addition, baseline [18F]FDG and [18F]HX4 PET/CT images taken during treatment were registered rigidly to the baseline [18F]HX4 PET/CT. Spatial correlations were evaluated using a Pearson's correlation coefficient estimation.

Results:

PET/CT scans including 11 primary and 7 involved lymph nodes > 5cm³ were analyzed. The average lesions size was 19±14 cm³ (primary) and 37±34 cm³ (lymph nodes). On baseline [18F]HX4 PET scans a significant uptake was observed in 8/11 primary lesions and in 7/7 lymph nodes. The average SUVmax, TMR and HF were 1.4±0.4, 1.9 ±0.4 and 14±11%, respectively, for the primary lesions and 1.7±0.3, 2.3±0.4, 41±21% for the lymph nodes. Voxel wise comparison of the [18F]HX4 and [18F]FDG uptake within these GTVs showed a large diversity for the primary lesion (R=0.45±0.36, range -0.04 to 0.85), however a good correlation was observed for the lymph nodes (0.76 ±0.12, range: 0.59 to 0.91).

During treatment 63% (5/8) of the primary tumors and 29% (2/7) of the involved lymph nodes showed persistent hypoxia (TMR >1.4). However a decrease in SUVmax (primary -30±12%, lymph nodes -22±16%), TMR (primary -24±13, lymph nodes -22±6) and HF (-97±3% primary, -51±29% lymph nodes) were observed. Voxel-wise comparison of the [18F]HX4 uptake pattern before and during treatment showed a relative stable distribution for the lymph nodes (R: 0.74±0.15) and primary lesions (R: 0.58±0.09).

Conclusion:
The majority of HNSCC lesions shows significant hypoxia before treatment. There is a spatial correlation between [18F]HX4 and [18F]FDG uptake for the lymph nodes, but this is less pronounced for primary lesions. During treatment the [18F]HX4 uptake in all lesions is decreased, although the location of persistent hypoxia is stable. These findings are relevant for ongoing radiotherapy dose-escalation trials, using dose-painting strategies based on PET-uptake patterns.

Figure: Example patient 12. Transverse view of the baseline [18F]HX4 (left), [18F]FDG PET/CT (middle) and the voxel-wise comparison of the [18F]HX4 and [18F]FDG uptake within the gross-tumour volumes (right). For the primary lesion there is no correlation (R=-0.04), for the lymph node a good correlation is observed (0.85).
ASSESSMENT OF A NOVEL MULTIMODAL CT/OPTICAL CONTRAST AGENT FOR IMAGE-GUIDED HEAD AND NECK SURGERY

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Introduction

Head and neck cancer surgery involves resection tasks in close proximity to critical structures, which can potentially limit surgical performance even for the experienced surgeon. Clinicians must also contend with complex 3D anatomical structures which are subject to variations across the patient population and morphological changes. The need for precise surgical guidance that accounts for intraoperative anatomical deformation and tissue excision has motivated the development of imaging systems for intraoperative guidance. We report here for the first time, the successful development, preclinical characterization and performance assessment of a liposome-based dual-modality nano-agent (Nanovista-CF800) for CT and near-infrared (NIR) fluorescence imaging. This agent, fabricated from regulatory-approved components, is designed for longitudinal intraoperative tumor, blood vessel, and malignant lymph node localization and visualization. This study describes the surgical assessment of this agent in an animal model for head and neck cancer.

Methods and results

The CT/optical liposome formulation, Nanovista-CF800, is composed of phospholipids (phosphotidylcholine and phosphotidylethanolamine), cholesterol and polyethylene glycol (PEG). The commercially-available contrast agents iohexol (Omnipaque®, GE Healthcare, a clinically used CT contrast agent) and indocyanine green (ICG, a clinically approved near-infrared optical dye) are encapsulated within the internal aqueous volume of the liposomes.

The performance of Nanovista-CF800 for image-guidance in surgical applications was evaluated in a rabbit model of VX-2 buccal mucosa carcinoma. A VX-2 carcinoma cell suspension was injected into the buccinator muscle of male New Zealand white rabbits. Tumors were formed at the site of VX-2 cell injection and all rabbits presented with at least one cervical lymph node metastasis at two weeks post-inoculation. Pre-operative CT scans were performed every day post Nanovista-CF800 IV administration, followed by intra-operative cone-beam CT (CBCT) and NIR fluorescence imaging at 4 days post-administration for tumour and lymph node detection. An endoscopic NIR fluorescence imager (PINPOINT®, Novadaq) was employed for intraoperative fluorescence imaging. All surgical procedures were scheduled between day 4 and day 7 post-liposome administration, based on the CT imaging results, in order to maximize the tumor-to-blood signal ratio, as high ICG signal in the bloodstream can interfere with target lesion visualization due to vessel rupture during surgery. Blood samples were collected for hematology and comprehensive biochemistry testing as well as for contrast agent concentration analysis.

Successful CT visualization of the contrast-enhanced tumor and involved lymph nodes was achieved in the pre-operative setting. All 10 animals investigated displayed significantly higher NIR fluorescence signal in the tumor lesions compared to background. Intra-operatively, NIR fluorescence imaging also
demonstrated successful detection of the surgical site containing the tumor and malignant lymph nodes enhanced with Nanovista-CF800. Lymph node involvement information provided by fluorescence imaging was compared to that provided by pathological evaluation.

Conclusions

Our results demonstrate the development of a long-circulating contrast agent for near real-time surgical imaging with capability to sustain multiple imaging sessions. This dual-modality nano-agent provides improvements to both CT and optical imaging contrast, which appeared with high specificity and sensitivity for tumour and regional disease detection. The next step is clinical translation of the contrast agent into human studies for further evaluation.
Figure: Pre-operative and intra-operative imaging of Nanovista-CF800 in a rabbit buccal mucosa carcinoma model. a) pre-operative CT images of the tumor cross-section in the rabbit head region pre-liposome administration (left) and 4 days post liposome administration (right); b) CT images showed the metastatic cervical lymph node 4 days post liposome administration (left), confirmed by pathology analysis (right); c) intra-operative NIR fluorescence imaging of the multiple tumor sections and well-defined margins (right); d) NIR fluorescence images (superimposed over white light images) of a contrast enhanced malignant lymph node near the primary tumor site (left) and a non-contrast enhanced healthy popliteal lymph node away from the tumor site (left). The vascular half-life of the liposomes in rabbits is roughly 80 hours and therefore clear visualization of the vessels can still be achieved at 4 days post-injection.
OPTIMAL TIMING OF FIRST SURVEILLANCE FDG-PET/CT IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Importance: Patients with head and neck squamous cell carcinoma undergo post-treatment surveillance to detect recurrent disease at the earliest possible stage. The optimal timing of initial surveillance imaging after definitive treatment remains undefined.

Objective: To determine the optimal timing for initial surveillance 18F-fluorodeoxyglucose positron emission tomography/computed tomography scan after definitively treated head and neck squamous cell carcinoma.

Design, Setting, and Participants: Retrospective chart review at a tertiary care referral center. We identified 247 patients from the tumor registry with definitively treated non-metastatic head and neck squamous cell carcinoma between 2002 and 2012 who underwent at least 1 year of post-treatment follow-up. Post-treatment initial surveillance positron emission tomography/computed tomography scans were grouped into the following intervals based on time elapsed from treatment: <7 weeks, 7 to 10 weeks, 11 to 14 weeks, and >=15 weeks. Scans were categorized as negative, probably benign, suspicious, and malignant based on the probability of the presence of primary, neck or metastatic disease. Accuracy of scans were calculated for each time interval using biopsy, subsequent imaging, or clinical follow-up for 1 year as the reference standard. Radiologist confidence at different time intervals was additionally analyzed.

Intervention: None

Main Outcomes and Measures: Ability of scans to predict eventual recurrence. Radiologist confidence was studied by comparing the rate of definitive interpretations ("negative" and "malignant") versus tentative interpretations ("probably benign" and "suspicious").

Results: Follow-up data was available for all 247 patients. Of the 45 patients who were scanned at <7 weeks, 35 had accurate scan results (78%). Of the 122 patients who were scanned at 7 to 10 weeks, 113 had accurate scan results (93%). Of the 38 patients who were scanned at 11 to 14 weeks, 35 had accurate scan results (92%). Of the 42 patients that were scanned at >=15 weeks, 36 had accurate scan results (86%). Only scans performed at <7 weeks were significantly different in accuracy (p<0.05). Scans performed at 7 to 10 weeks (2-months) were similar in accuracy to scans performed at 11 to 14 weeks (3-months) and later. There were 67 (27.1%) cancer recurrences in the study population. There were no differences in radiologist confidence between the different follow-up intervals.

Conclusions and Relevance: First surveillance positron emission tomography/computed tomography scan may be obtained as early as 2 months after the conclusion of definitive therapy for head and neck squamous cell carcinoma without adversely affecting the accuracy of the results or the confidence of the interpreting radiologist. Scans performed earlier than 2 months have lower accuracy.
COMPARING STAGING BASED ON POSITRON EMISSION TOMOGRAPHY WITH CONTRAST-ENHANCED COMPUTED TOMOGRAPHY AND PATHOLOGY IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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These authors contributed equally.

Objective: To evaluate the ability of positron emission tomography (PET) with contrast-enhanced computed tomography (CT) to correctly stage head and neck squamous cell carcinoma (HNSCC), as compared to the gold standard of pathologic staging, by retrospectively reviewing radiology and pathology reports of HNSCC patients. To our knowledge, most recent studies have compared PET to CT or magnetic resonance imaging (MRI) and there are a limited number of studies that have examined the correlation of PET/CT and pathology for both the primary and nodal disease in HNSCC.

Design: Retrospective cohort study.

Setting: Tertiary medical center.

Patients: Eighty-five patients with HNSCC.

Main Outcome Measures: Pre-operative PET-CT imaging studies were retrospectively compared to operative pathology reports to look for any differences in staging in eighty-five HNSCC patients who were treated with primary surgical therapy between July 2007 and January 2013 at the Johns Hopkins Medical Institutions. PET-CT determined Tumor-Node-Metastasis (TNM) classification and overall stage was compared to that based on pathology evaluation of the surgical specimen. Agreement between PET-CT and pathologic TNM-classification and overall staging was examined with univariate and multivariate analysis overall, and within each primary tumor sub-site.

Results: PET-CT was able to identify regional cervical metastases with a sensitivity and specificity of 87.5% and 44.8%, respectively, when compared to the gold standard of pathology review of surgical resections. The positive predictive value was 75.4% and negative predictive value was 65.0%. PET-CT had a false positive rate of 18.8% and false negative rate of 8.2%. Univariate analysis of agreement between PET-CT and pathologic N-classification revealed significant odds ratios (95% CI) of 1.07 (1.02-1.12) for age and 2.62 (1.08-6.58) for oral cavity sub-site. Backward variable selection of age and oral cavity with multivariate modeling revealed odds ratios (95% CI) of 1.07 (1.02-1.13) for age and 2.94 (1.11-7.74) for oral cavity sub-site. Univariate analysis of agreement between PET-CT overall stage and pathologic overall stage revealed significant odds ratios (95% CI) of 1.04 (1-1.09) for age and 2.73 (1.11-7.01) for PET-CT T-classification greater than or equal to 3. Backward variable selection of age and PET-CT T-classification with multivariable modeling revealed odds ratios (95% CI) of 1.04 (1-1.09) and 2.85 (1.11-7.31), respectively. All other anatomic tumor subsites and clinical factors such as human papilloma virus/p16 tumor positivity, gender, race, smoking, and alcohol were not significantly associated with PET-CT to pathology staging agreement.

Conclusions: Pre-operative PET-CT has a substantial false positive rate of 18.8% in the evaluation of regional metastasis in HNSCC. When compared to the gold standard of pathologic evaluation of neck dissection specimens, PET-CT imaging evaluation of regional metastases in HNSCC is most reliable in
older patients with oral cavity primary tumors. Furthermore, overall PET-CT staging is most reliable in older patients with large T3 and greater oral cavity primary tumors.
PET-CT FOR METASTATIC HEAD AND NECK SQUAMOUS CARCINOMA WITH UNKNOWN PRIMARY; CORRELATION WITH TARGETED AND SURVEILLANCE BIOPSY IN 40 CASES

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INTRODUCTION

Metastatic cervical nodes containing squamous carcinoma (SCC) presenting as presumed head and neck SCC (HNSCC) with an unknown primary (UP) site is an important clinical problem. There is little agreement in the literature as to the precise definition of this entity and the literature on the subject is similarly heterogeneous in terms of the definition used. Multiple modalities are used in the detection of the primary tumour in such cases and FDGPET-CT may be a useful adjunct in diagnosis by targeting biopsies which would otherwise be blind. In order to assess usefulness of this imaging modality we compared biopsy histological information from patients diagnosed with HNSCC with UP with FDGPET-CT findings. This case series includes data from 2009-2013. The FDGPET-CT highlighted areas allowed targeted biopsy compared with FDGPET-CT negative cases where routine surveillance biopsies were taken.

METHODS

Patients classified by two head and neck MDTs as HNSCC with UP were identified from our prospectively completed database. The classification of UP in both MDTs were the same and in total 40 patients were identified over four years. Case records, FDGPET-CT reports, and histopathology results were obtained and analysed for further data and to corroborate database entries. The chronological sequence of management and outcome was also assessed.

RESULTS

Eleven cases had positive FDGPET-CT imaging and positive targeted biopsies. Eight cases results showed positive FDGPET-CTs but negative targeted biopsies. Eighteen patients were both FDGPET-CT and surveillance biopsy negative. One patient did have a negative FDGPET-CT but positivesurveillance biopsy. FDGPET-CT showed 92% sensitivity and 70% specificity.

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<tr>
<th>PET-CT vs Biopsies</th>
<th>Biopsy results positive</th>
<th>Biopsy results negative</th>
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<tr>
<td>Positive PET-CT</td>
<td>11 (28.9%)</td>
<td>8 (21.1%)</td>
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<tr>
<td>Negative PET-CT</td>
<td>1 (2.6%)</td>
<td>18 (47.4%)</td>
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CONCLUSION

Our study shows a high sensitivity and negative predictive value for FDGPET-CT in the detection of the primary site of the unknown primary head and neck carcinoma. FDGPET-CT appears to be a useful
adjunct in the work up of the unknown primary head and neck cancer patient. It should be considered to be included as part of the routine MDT management pathway for these cases.
Early PET Post Radical Radiotherapy in N+ HNSCC to Select Patients for Neck Node Dissection, A Prospective Study.

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Purpose:

To evaluate if neck node dissections (ND) can be safely omitted by an early scheduled FDG-PET 6 weeks after radiotherapy in N+ (node-positive) HNSCC (head and neck squamous cell carcinoma).

Background:

Following radical radiotherapy a ND for clearance of residual tumor has been standard of care in patients with N+ HNSCC. In the majority of cases no viable tumor is found in the neck specimen. Remaining pathological tumor metabolism depicted by FDG-PET can select patients benefitting from a ND. The optimal timing of the post-radiotherapy PET has been a subject of discussion. An early PET would allow for surgery, before onset of post-radiotherapeutical fibrosis and offer early clearance of remaining viable tumor.

Method:

In all 111 N+ HNSCC patients referred for radical radiotherapy at Lund University Hospital, a tertiary referral center entered the study between Sept 2009 - July 2012. 105/111 patients were evaluable. The majority of patients (89%) had oropharyngeal tumors, approx. 70% p16/HPV + tumors. The study includes a baseline FDG PET CT, PET1, for radiotherapy planning purposes, PET2 6 weeks after completed therapy, as guidance for biopsy when assessing T-site response as well as evaluation of neck disease. If CR at T-site and a positive PET indicating remaining node disease a ND is performed. In cases of negative or equivocal PET2 a PET3 is performed 12 weeks later in order to confirm the remission. We hypothesized that a late PET3 would be able to detect minimal residual disease not revealed in PET2. The endpoints were neck control and survival.

Results:

Median follow-up is 26 months, 2 year overall survival is 84%. 92% of the patients were treated with radiotherapy alone, only 8 patients received chemo-radiotherapy. Following PET2, 6 weeks after completed radiotherapy 17 patients underwent a neck-dissection (one bilaterally) and additionally 4 patients were operated on after PET3. Following PET2 viable tumor was found in 10/18 specimens, and in 3/4 following PET3. NPV was 94% and 97% at PET2 and PET3, respectively. PPV was 56% and 75% at PET2 and PET3, respectively.

During the follow up period 4 isolated neck recurrences occurred, all have undergone salvage surgery and 2 are alive without any signs of disease whereas 2 are alive with disease.

Other PET findings were synchronous tumors of other origin in 5 patients and dissemination of the head and neck cancer in 2 patients.

Conclusion:
High NPV:s are achieved 6 weeks and 18 weeks post radiotherapy, 94% and 97% respectively. Neck dissections can safely be omitted by this selection, although the power of a 6 week study is lower than after 18 weeks.

We postulate that the later follow-up PET reveals progression of minimal residual disease in the few false negative early PET scans. Furthermore PET added clinical information about tumor stage and synchronous tumors.
**S025 INFLUENCE OF FDG-PET ON PRIMARY NODAL TARGET VOLUME DEFINITION FOR HEAD AND NECK CARCINOMAS**

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**Purpose/Objective**

With IMRT more focused radiotherapy to the (possible) positive nodes in patients with head and neck cancer is feasible, without substantial increase in risk on complications. In this study we analyzed the influence of FDG PET-CT versus CT alone on defining nodal target volume definition and to analyze its long term clinical results. Secondly, since smaller radiation fields may lead to more marginal failures, the location of nodal recurrences was related to the radiation regional dose distribution.

**Materials and Methods**

This retrospective descriptive study included 283 patients with head and neck carcinoma scheduled for primary radiotherapy (RT) between 2002 and 2010, with a mean follow-up of 50 months. The primary tumor was located in the pharynx in 76%, in the larynx in 9%. T3-4 stage was noted in 50%, 64% were node positive, based on CT-scan and ultrasound. RT was combined with chemotherapy in 43%. FDG-PET scan was performed in the RT mould and fused with the planning CT-scan. FDG-PET scans were visually analyzed. The mean irradiation dose for each suspected lymph node was recorded. In case of nodal recurrence, determined by histology and/or imaging, date of nodal recurrence free survival was calculated. In addition, to review the location of our recurrences, the imaging of disease recurrence was compared to the initial imaging for IMRT planning.

**Results**

In 125 cases (44%) N-stage and/or number of neck nodes varied between CT only and PET-CT findings. The extent of N+ decreased in 14% and increased in 29% with FDG-PET. FGD-PET was N0 in 15 CT N+ cases, CT was N0 in 34 FDG-PET N+ cases. In 39 cases, CT results alone were the decisive factor for clinical policy. In 86 cases, clinical policy was based on the additional FDG PET imaging. RT fields were mainly expanded based on a higher number, and contralateral nodes. We found 38 nodal recurrences (13.5%) after a mean of 10 months FU. Actuarial 3 year nodal control rate correlated with N-stage, with the most significant correlation based on FDG-PET staging compared to CT only, 97% vs. 93%, 87% vs. 90%, 79% vs. 75%, and 51% vs. 68% for FDG-PET-CT based vs. CT only, respectively. Three years nodal control was 88% in cases were FDG-PET showed more nodes, compared to 89% in cases were FDG-PET showed less nodes. 18 (56%) of the nodal recurrences were localized in high-dose field, thirteen recurrences (41%) were found in the elective dose area and one recurrence (3%) out field.

**Conclusions**

In literature published specificity of FDG-PET for detection of positive neck nodes ranges around 80%. Based on these results, we included FDG-PET, performed in a RT mould, in our decision to treat suspected lymphnodes regions with a boost dose, resulting in a 89% nodal control rate. A boost dose for FDG-PET negative nodes, although suspicious on CT, maybe be omitted, based on our 97% nodal control rate in these cases. Outfield recurrences were rare.
**S026 18F-FDG-PET REDUCES THE NUMBER OF DIRECT LARYNGOSCOPIES IN PATIENTS WITH SUSPECTED RECURRENT LARYNGEAL CARCINOMA AFTER RADIOThERAPY: RELAPS RANDOMISED, PARALLEL, SUPERIORITY TRIAL**

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BACKGROUND. There is limited evidence as to the efficacy of 18F-FDG-PET as first-line diagnostic investigation, prior to performing a direct laryngoscopy with biopsy under general anesthesia, in patients suspected of recurrent laryngeal carcinoma after radiotherapy.

METHODS. This study was conducted between February 2005 and February 2009, at eight Dutch hospitals and one in Belgium. One-hundred-fifty patients older than 18 years and suspected of recurrent T2-4 laryngeal carcinoma at least two months after prior (chemo)radiotherapy with curative intent for resectable disease were randomised to direct laryngoscopy (CWU: conventional workup strategy) or to 18F-FDG-PET only followed by direct laryngoscopy if PET was assessed ‘positive’ or ‘equivocal’ (PWU: PET based workup strategy), to compare the effectiveness of these two strategies. Primary endpoint was the number of indications for direct laryngoscopies classified as unnecessary based on absence of recurrence, both on laryngoscopy and on 6 (or 12) months follow up. Safety endpoints comprised resectability of recurrent lesions and completeness of surgical margins following salvage laryngectomy. Randomization was centralised, computer-generated, with allocation concealment.

RESULTS. Intention-to-treat analyses were performed on all randomised patients (CWU: n=74, PWU: n=76), followed by per-protocol analyses, excluding three patients (two CWU, one PWU). Tumor recurrence was similar in both groups: 45 patients (30%; 21 CWU, 24 PWU) within 6 months and 48 (32%; 23 CWU, 25 PWU) within 12 months. In 53 patients in the CWU arm (72%, 95%CI: 60-81) unnecessary direct laryngoscopies were performed compared to 22 in the PWU arm (29%, 95%CI: 19-40) (p<0.0001). PET scanning resulted in a true-negative in 30 patients and false-negative in one. The percentage of salvage laryngectomies (resectability) and positive surgical margins were similar between CWU and PWU (81%, 63% respectively, p=0.17, and 29%, 7%, respectively, p=0.20).

CONCLUSIONS. In patients with suspected laryngeal carcinoma after radiotherapy, PET as first diagnostic procedure can reduce the need for direct laryngoscopy by more than 50% without jeopardizing quality of treatment for potentially resectable recurrences.
Background: Traditionally clinical staging has been one of the most important prognostic factors in predicting treatment outcome in patients with head and neck cancer (HNC). Metabolic tumour volume (MTV) obtained from pre-treatment 18F-fluorodeoxyglucose positron emission tomography with computed tomography (PET-CT) has been recently validated as an independent predictive factor of outcomes in HNC treated with primary chemoradiotherapy (CRT). However, its role in patients treated with primary surgery has not yet been studied.

Objective: To evaluate the prognostic value of MTV in patients treated with primary surgery for oral cavity squamous cell carcinoma (OCSCC).

Method: Demographic and survival data was obtained from patients diagnosed with OCSCC from 2008-2012 in Alberta, Canada. All patients included in the study had PET-CT scan before curative surgical resection. MTV and maximum standardized uptake value (SUVmax) value was delineated from pre-treatment PET-CT scans using Segami Oasis software (Columbus, OH).

Results: A total of 80 patients were analyzed using SPSS (SPSS Inc, Chicago, IL). Five-year overall, disease-specific, and disease-free survival using Kaplan-Meier curves were 72%, 79%, and 78% respectively. An increase in MTV of 17.5 mL (difference between the 75th and 25th percentile) was associated with a 1.9 fold increase in risk of disease recurrence (p<0.001) and a 2.0 fold increase in the risk of death (p<0.05). SUVmax was not associated with either outcome. Cox-Regression analysis showed MTV predicted overall (hazard ratio [HR] = 1.22; p<0.0001), disease-specific (HR = 1.62; p<0.0001), and disease-free (HR = 1.97; p<0.0001) survival.

Conclusions: This study shows that MTV is an adverse prognostic factor for death and disease recurrence in OCSCC treated with primary surgery and may be used along with tumour staging when counselling patients on treatment expectations and prognosis.