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Prospective Comparison of CT scan, MRI and PET/CT in the Diagnosis of Oral Cancer and Nodal Metastasis

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Abstract

Objectives: Combining functional PET scans with anatomical CT imaging displays improvements in clinical staging of intra-oral squamous cell carcinoma (OSCC) [1-3]. In this study, we are comparing and contrasting this technology to the conventional assays of CT and MRI in detecting the primary lesion, nodal and distant metastases.

Study design: Fifty-four primary OSCC cases over a six-month period were staged for their primary lesion, nodal metastases and distant metastases with CT, MRI and FDG-PET/CT scanning. Histology results were the control.

Methods: Fifty-four consecutively newly diagnosed patients with OSCC were recruited. Sensitivity for each of the radiological modalities was calculated using the binary classification equation.

Results: PET/CT showed most sensitivity to identification of the primary OSCC, followed by MRI imaging and lastly, CT scanning. MRI was most sensitive to detecting neck disease, followed by PET/CT and then CT. Whole body CT and PET/CT imaging identified 6 and 3 distant metastases respectively.

Conclusion: PET/CT proved most superior to identifying primary OSCC, while MRI identified most nodal metastases. CT alone has little place.

Level of evidence: 1b (Individual prospective cohort study).

Keywords

Radiology, MRI, CT, PET/CT, Oral cancer staging, Head and neck oncology

Introduction

The addition of the CT/PET scans to achieve both an anatomical aspect to the image via the CT component and a functional aspect via the PET component has been shown to improve clinical staging of Oral Squamous Cell Carcinoma (OSCC)/oral cancer over Positron Emission Tomography (PET) or Computerized Tomography (CT) alone [1-3].

Hafidh, et al. [4] in 2003 carried out a study and assessed the sensitivities of PET, CT and MRI scanning in the clinical staging of Head and Neck cancers and showed that PET scanning had some promise, but required more information to confirm significance. With the introduction of PET/CT fusion images, there was an opportunity to compare and contrast the sensitivities of the three staging modalities commonly used in oral cancer, while also retrospectively comparing the results achieved by the PET scanning from the 2003 study to the results achieved using PET/CT, a modality that is now widely available. By doing this, an attempt is made to define any advantage in having PET/CT fusion images vs. CT or PET alone and put this argument to rest.

Fifty four primary OSCC cases over a six month period, were staged for their primary lesion, nodal metastases and distant metastases with CT, MRI and FDG-PET/CT scanning. The results of the scans with respect to primary disease and nodal metastases identification

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predominantly were compared to histopathology results, set as the control/gold standard.

Materials and Methods

Consecutive newly diagnosed patients with oral cancer; Oral Squamous Cell Carcinoma (OSCC), confirmed by histology, attending the Maxillofacial Unit were included in the study. Only confirmed oral cancer tumours were included. This totaled a sample of 54 patients in six months. The ages of the patients ranged from a minimum of 28 years to a maximum of 95 years, with a mean age of 65 years. There were 34 males and 20 females.

All patients went through a thorough pre-operative work up encompassing MRI, CT, and PET/CT fusion scans. Histological examination included an oral biopsy to confirm the diagnosis and post surgical histological analysis of the tumour and neck nodes, where neck dissection was performed.

Sensitivity values were calculated for each diagnostic modality examining the primary tumour and confirmed neck metastasis. However, any suspected distant lesions/metastases were referred to the relevant specialty, which then carried out the necessary examinations to confirm whether it was a true metastasis or a new lesion. Therefore, no sensitivity values were attributable to distant metastases.

Sensitivity was calculated using the Binary Classification defining equation of;

$$[(\text{True Positives})/(\text{True Positives} + \text{False Negatives})]*100.$$

The Specificity values for the three diagnostic tests with regard to the primary tumours were not relevant as only confirmed true intra-oral cancers were included in the study, meaning the amount of true negative findings were zero from the beginning.

CT and MRI scans were arranged through the Radiology department in the hospital. All patients had CT scans of the brain, head and neck, thorax and upper abdomen. MRI scanning was of the head and neck region with only distant scans requested when metastasis was suspected.

CT scanning was carried out via a multislice scanner with an IV contrast injection. Axial and coronal slices of 5 mm thickness were produced. MRI imaging protocols were also standard to all patients; multiplanar imaging with contrast enhancement. Axial and coronal planes were obtained with 5 mm slices.

Whole body FDG-PET/CT scanning was carried out on all patients prior to and sometimes after therapy to assist in visualizing the primary tumour, neck nodes and distant metastasis. FDG was injected intravenously and patients were advised not to exercise and to limit voice use for 60 minutes post FDG intake to avoid false positive uptake because of increased voice activity. Muscle activity causes increased vascularity and increased uptake. Scanning for the PET/CT was then carried out from mid-thigh to base of skull. The nuclear physician was aware of the patient's clinical history in all cases to try to avoid misdiagnosis. One nuclear medicine physician evaluated all the FDG-PET images.

Histological analysis was carried out by a Consultant Oral/Head and Neck pathologist. All resections were pinned in a fresh state to a corkboard and orientated. The lymph nodes were dissected while fresh. Small nodes over 10 mm were bisected and submitted in total; grossly positive nodes were sampled to confirm the presence of carcinoma and to assess extra capsular spread. After fixation the blocks were processed in the usual way and reported as per the Royal College of Pathologists' Guidelines [5].

Results

Some of the tumours affected more than one site. Of the 54 tumours, seven affected more than one site (sixty one sites in total). The sites that were involved in total were as follows; twenty one (21) primary tumours were located on the tongue, mainly on the lateral surfaces, making the tongue, the most common site for intra-oral cancers. Sixteen (16) primaries were in the floor of mouth region, 8 on the buccal mucosae and 7 in the retromolar areas. Two (2) tumours were found on the lips, one being on the upper lip and another on the lower lip. Four (4) tumours were found on the mandibular alveolus and 3 on the maxillary alveolus. Two (2) were located on the soft palate, making it the least common site in this study for intra oral SCC.

Primary tumour

Of the 54 primary tumours, thirteen (13/54) had no post-resection histology report as no primary resection was done. For these thirteen cases, the biopsy results were used as the histological gold standard to identify whether oral SCC was actually present. These patients had radiotherapy as their primary course of treatment or were deemed to be for palliative measures from the outset.

The remainder of the primary tumours (41/54) had typical TNM staging following post resection histological analysis. Nineteen (19/41) were T1 stage, thirteen (13/41) were T2, one case (1/41) was T3 and eight (8/41) were T4 stage.

MRI scans correctly identified 37/54 primary tumours, while producing 17 false negatives, giving a sensitivity of 69% (Table 1).

CT scanning correctly identified 25/54 primaries while attaining 29 false negatives, giving a sensitivity of 46% (Table 1), making CT scanning less sensitive than MRI scanning in identifying primary tumours.

PET/CT scanning however correctly identified 39 of the 54 primaries (Table 1), with 15 false negatives,

Table 1: Numbers of true positive cases identified for each of the imaging modalities and the respective sensitivities.

	PET/CT true pos	PET/CT sensitivity	MRI true pos	MRI sensitivity	CT true pos	CT sensitivity
Primary Tumour	39/54	72% ($p < 0.01$)	37/54	69%	25/54	46%
Nodal	13/19	68%	14/19	74%	12/19	63%
Metastases	6	N/A	2	N/A	3	N/A

confirmed positive by histology. This makes PET/CT scanning the most sensitive diagnostic modality (72%) with respect to detecting primary tumours.

Nodal metastases

With regards to neck (nodal) disease/metastases, histology was only available for 34 of the 54 subjects, who underwent bilateral neck dissections. Of these 34 cases histology confirmed the presence of positive nodal disease in 19 of them. MRI scanning correctly identified 14/19 true positive nodal disease cases. This gives MRI scanning a sensitivity of 74%. CT scanning identified positive nodes in 12/19 cases, producing a sensitivity of 63%. PET/CT scanning correctly identified 13, implying six cases with true nodal involvement was not identified, giving 68% sensitivity to PET/CT imaging.

With regards to negative nodes, histology confirmed the negativity of the nodes in 15/34 of cases that underwent neck dissections. MRI scanning identified 20/34 to be node negative, identifying in the process 5 false negative cases. PET/CT scanning identified 6 false negatives and CT identified 7 false negatives.

MRI scanning had the best sensitivity with regards identifying nodal metastases, at 74%. PET/CT scanning came second at 68%. CT alone produced 63% sensitivity.

Distant metastases

CT scanning found 3/54 cases to be positive for distant metastases - three lung metastases (5.5%). PET/CT Scanning found 6/54 positives - five lung metastases and a second neoplasm identified in the rectum (11%).

MRI found 2/54 patients to have distant metastases (2%). MRIs were taken of the head and neck only and are used to cover the rest of the body only where indicated by PET/CT e.g. colon.

Discussion

Primary tumour

Positron emission tomography (PET), since its inclusion in the staging of OSCC, has been shown to greatly improve clinical staging [6-8]. In this study, PET/CT has the highest sensitivity of all the diagnostic tests; 72% versus 46% for CT and 69% for MRI in detecting primary tumours. This is in stark contrast to the similar study carried out by another Head and Neck team, where Hafidh, et al. in 2003 found that PET scanning was of similar sensitivity to CT scans and MRI, all ranging around 90%. They used a different method to determine sensitivity and specificity rather than the conventional binary system and also included pharyngolaryngeal tumours. Therefore it is important to realize that a direct comparison between the two studies cannot be made.

PET/CT: PET/CT scanning (72%) was significantly more effective than CT alone (46%) ($p < 0.01$) and slightly more effective than MRI (69%). This study confirms that PET/CT scanning has a valuable place in identifying primary tumours and by experience, may possibly be valuable in detecting new or recurrent disease.

PET/CT fusion scans allows fusion of the anatomical data of CT scans and the functional data of PETs, which has been shown in other studies to be more accurate than PET alone or CT alone in detecting malignancy [2-4].

CT: CT scanning proved the weakest with regards sensitivity to detecting primary tumours (46%). This was due to both a low number of true positives identified (24/54 primary tumours) and a high count of false negatives (30/54). Eight of the primaries were not detected by CT due to artifacts on the CT images from dental amalgam. Dental artifacts have been shown to have a negative impact on CT imaging in the literature [9]. Another reason might be the fact that the majority of the tumours were soft-tissue masses at a T1 size. Only one of the T1 primary tumours was identified by CT. This was on the palate, close to the thin maxillary bone complex. Only some of the T2 tumours were detected with conventional CT, mainly the tumours that were close to bone margins on the buccal mucosa and sometimes the floor of mouth. Interestingly, one T4 tumour with extensive mandibular involvement was not identified on conventional CT scan but was easily identified with PET/CT fusion image. Overall, this evident correlation of bone proximity with detection of primary OSCC via conventional CT alone has been documented in several studies [10,11]. The superiority of PET/CT images in the detection of the smaller T1 and sometimes T2 primary soft tissue tumours, over conventional CT has also been documented in the literature and is further advocated in this study [11,12].

MRI: MRI scanning (69%) produced better sensitivity than CT (46%); in detecting the primary cancers. In comparison to PET/CT, MRI identified a slightly smaller number of true positives 37/54 (69%) as opposed to 39/54 (72%) for PET/CT. Seven of the false negative cases with MRI were due to the fact that the tumours were small, often presenting as a dysplasia with foci of invasive SCC, which the MRI scanner was not able to pick up. Most of the T1 tumours were not

picked up by the MRI scanner. In 4 cases, the patients moved, making it difficult to identify discrete masses, indicating how technique sensitive MRI imaging can be. Dental amalgam was a culprit in another 4 cases, acting as an artifact, obscuring the MRI image, which is a well-documented phenomenon [13]. Three other cases were not identified by MRI without any evident reason. All the primary oral cancers with bone involvement were accurately picked up by MRI, and a proposed TNM staging was reported back by the radiologist. This would indicate that MRI scanning appears to fail in identifying the small or early tumours, however accurately identifies larger masses, especially if involving bone. This has been shown to be the case in the literature [14,15].

Nodal disease

With regards to nodal metastases, MRI was the most sensitive in this study, producing 74% sensitivity; as opposed to 68% sensitivity for PET/CT and 63% sensitivity for CT. It is worth noting however, that the 6% difference between the results of MRI and PET/CT scanning clinically denotes only 1 of 19 cases. The clinical significance of such a small difference is questionable and it probably can be assumed that PET/CT is a powerful adjunct to MRI imaging, which at present remains the study of choice for neck disease.

These results are in contrast to a study carried out by Ng SH, et al. [15] where 18F-FDG PET and CT/MRI were analysed for their sensitivity and specificity in detecting primary tumour and nodal metastases in 124 histologically confirmed oral squamous cell carcinoma cases. Ng SH, et al. found 75% sensitivity with PET scanning in detecting nodal disease and 53% with MRI/CT scanning. The results from our study show MRI to be much higher in sensitivity than in Ng SH, et al. study (74% vs. 53%). Our study shows PET/CT to be lower in its sensitivity to nodal disease. PET/CT showed 68% sensitivity in our study compared to 75% in Ng SH, et al.

Bearing in mind that a direct comparison cannot be made as the sample sizes and patient groups were different and only PET scanning was used by Ng SH, et al. as opposed to our PET/CT fusion scanning, it can be deduced that no one modality can be taken solely as being the most accurate in detecting nodal disease and also that the addition of CT images to PET scanning may not carry a significant advantage over PET alone.

PET/CT: A PET scan sensitivity of 73% was produced in Hafidh, et al.'s study of oro-pharyngeal and laryngeal cancers in 2003. This is slightly higher than the sensitivity produced in our study (68%). While the significance of a 5% difference in sensitivity is questionable, it is however evident again that there would not seem to be a significant advantage of using a PET/CT as opposed to a PET image alone in detecting nodal disease.

A disappointing accuracy for PET/CT fusion images was reported by Gourin, et al. [16] in 2009 where the ability of PET/CT to predict the need for neck dissection was studied. Out of 32 patients who had received chemoradiation for head and neck squamous cell carcinoma, only 10 were found to be positive histologically for occult nodal disease. PET/CT had found 20/32 to be node positive. Six of the 20 were truly node positive and 12/20 were negative on histological testing, giving PET/CT a low sensitivity of 60% and a specificity of 36%. This study was however looking for occult nodal disease, and had a small sample size. Despite these limitations, when comparing our results of 68% sensitivity of PET/CT images with those of Gourin, et al. (60%), it would seem that PET/CT is limited as a predictor of nodal metastases from amongst the current investigative modalities available today.

CT: Conventional CT scanning in this study was 63% sensitive for neck disease. Hafidh, et al. reported a sensitivity of 42% with CT scanning identifying 8 out of 20 positive cases identified as neck node positive while 8/12 cases were truly N0. Our study shows a considerable improvement with regards to picking up N+ nodes. However, it is evident from this study and previous studies [15,17,18], that conventional CT shouldn't be used as a single predictor for nodal metastases in OSCC.

MRI: MRI scanning was most sensitive (74%) with regards nodal metastases with 14/34 true node positive cases identified and only five false negative cases reported. In this study, it is felt that MRI was reasonably accurate with regards nodal disease identification and is probably more successful than PET/CT and/or CT alone, yet is not perfect and also cannot be considered solely as a predictor for nodal disease in the staging process.

While only the identification of nodal metastases was examined in our current study, radiological identification of extra nodal extension should be considered in future trials. Extra nodal extension has been shown to be a poor prognostic indicator - being one of the most important prognostic indicators in Head & Neck Squamous Cell Carcinoma and its radiologic identification remains difficult to achieve [19]. The importance of extra nodal extension has been recognized and incorporated into the American Joint Committee on Cancer (AJCC) staging manual for Head & Neck Squamous Cell Carcinoma [20] in addition to other forms of cancer such as colorectal cancer [21] and pancreatic cancer [22]. Future prospective trials should assess the sensitivities of the latest functional MRI techniques in addition to PET scanning techniques to assess extra nodal extension, while using histology as control.

Distant metastases

With regards to distant metastases in this study, PET/CT scanning and CT scanning alone were most sensitive. This is for the simple reason that MRI scanning mainly only involves the head and neck region. MRI of distant metastases sites was only undertaken when these lesions

were suggested by other tests. The Radiology department is now establishing a full body MRI protocol to increase the sensitivity/specificity of picking up distant metastases or occult primaries elsewhere in the body.

CT scanning detected 6/54 distant metastases, three more than PET/CT. Most of the distant metastases were lung metastases, at early stages. There is overwhelming evidence in the literature that PET/CT imaging is proving more effective at distant metastases detection, especially pulmonary metastases than conventional imaging [23]. As such, due mainly to the method used (larger slices) and a small sample size of distant metastases in the cohort of patients in this study, the results of distant metastases sensitivities produced here cannot be taken as counter evidence.

Conclusion

PET/CT

PET/CT is the most effective radiological modality in determining the presence of primary disease. In addition, from clinical experience, it may have a part to play in detecting recurrent or new oral cancer primary disease, and has an ability to highlight colonic or other inflammatory disease, which aids in earlier diagnosis in these areas. As a result, PET/CT will provide better outcomes and helps avoid surgery in patients with disseminated disease. However, PET/CT alone in a screening mode cannot be used to identify distant metastases.

MRI

MRI is the most effective radiological modality in nodal metastases detection. It is superior to both PET/CT and CT alone, with a sensitivity of 74%. However, MRI was not found to be very accurate in detecting the presence or size of small primary tumours. It was more effective in detecting primary tumours than CT, yet not as effective as PET/CT. Technique sensitivity, movement, dental artifacts and small tumour sizes were the reasons. Therefore, MRI needs to be assessed further in its ability to identify recurrent or new oral primary disease.

CT

CT scanning alone came out weakest in the sensitivity of detecting primary sites and nodal metastases, due to low true positive counts and high false negative counts. The small size of the T1 and some T2 tumours plus their soft tissue characteristics as well as the discreteness of some of the sub-centimeter nodes seemed to be the reasons for this shortfall. In addition, the presence of dental artifacts obscured several images, making detection of the primary tumour difficult. Most of the larger tumours and obvious bony involvement were picked up as well as the larger nodes.

Overall, the authors feel that MRI and PET/CT scans remain important investigations with the staging of SCC of the oral cavity. It is essential for future research to look at whole body MRI and PET/CT scanning at higher intensity in the most relevant clinical areas (head/neck/lungs).

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Conflicts of Interest

None.

Informed Consent

Verbal informed consent for use of the results of staging scans was obtained from every respective case staged for Oral SCC in the study. No identifying features were included in any part of the study requiring ethical approval.

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