Additive Value of PET-CT in Detecting the Primary Site of Unknown Primary in Head and Neck Squamous Cell Cancer.

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Background
A proportion of histology confirmed squamous cell cancer from cervical lymph nodes have unknown primary site despite clinical examination and examination under anaesthetic (EUA) and MRI and/or CT. PET-CT has been widely used to detect primary site, with reported primary detection rate ranging 37-44% in the published literature***. We present our experience from a large tertiary centre for head and neck cancer to look at the additive value of PET-CT in detecting primary site in cancer of unknown primary in head and neck squamous cancer.

Conclusion
In our experience, the overall yield of PET-CT in detecting a primary site in CUP-HNSCC is 18% which is less than published literature (range 37-44%). Proposed reasons would be that not all of the studies had comprehensive cross sectional imaging and often not all of the had histological reference standards. There is a false positive rate of 10% in patients where a primary is suggested, but not found on further evaluation.

Despite the low yield, use of PET-CT is quite useful in CUP-HNSCC where primary is identified and confirmed as appropriate targeted treatment can be delivered.

Methods and Materials
Patients with proven SCC in cervical nodes with unknown primary, not detected by prior MRI/CT and clinical examination+/- EUA who had a subsequent PET-CT from 2010 to 2016 were included.

A positive case was defined as concordance between the primary site suggested by the PET-CT and subsequent histology or in cases where histological confirmation was not achieved but tumour was treated based on PET-CT, these (i.e. Radiological and pathological discordance) were also considered true positive based on MDT decision.

False positive was defined as if PET-CT has suggested a primary site but has confirmed on subsequent EUA sampling/histology. False negative was defined as the PET-CT has not identified a primary and primary was found on subsequent EUA.

Results
• Total of 65 patients had PET-CT for unknown primary with cervical nodal metastases. 2 patients had a primary detected in the lung, 1 patient was excluded due to prior imaging in another centre demonstrated the primary.
• Of 62 remaining patients- male 54(87%) and female 8(13%), 11(18%) had a primary identified. 2 of these cases, the histological confirmation was not achieved but sites identified by the PET-CT treated as the primary site after MDT review. The rest of the cases, there were histological confirmation. Primaries were located in tonsil 6, base of tongue 3, mandibular alveolus 1 and 1 vocal cord.
• 6 of the patients (10%), PET-CT raised potential primary sites in the head and neck region, needing further evaluation. These cases had further evaluation and examination with histological sampling and subsequently treated as unknown primaries. Such suggested sites were 3tonsil, 1 hypopharynx, 1nasopharynx, 1 oropharynx. None of these patients had targeted radiotherapy to the site the PET suggested and subsequently treated as cancer of unknown primary.
• In 2 cases (3%), the patients had primaries detected at EUA after no primaries were found on PET-CT- 1in tonsil and 1 in the base of tongue.
• Therefore, PET-CT had 18% positive detection rate, 10% false positive and 3% false negative rate in our patient cohort.

References
1. 18F-Fluorodeoxyglucose positron emission tomography-computed tomography as a diagnostic tool in patients with cervical nodal metastases of unknown primary site: a meta-analysis- Zhu, Wang, Surgical Oncology Volume 22, Issue 3, September 2013, Pages 190-194

Fig 1- A comparison of CT and PET-CT showing increased FDG uptake in the right base of tongue with cervical nodal metastasis.

Fig 2. Primary sites identified with cancer of unknown primary in head and neck squamous cancer presenting with cervical nodal metastases

1. Tonsil
2. Tongue base
3. Hypopharynx
4. Nasopharynx
5. Oropharynx
6. Base of tongue