

THERANOSTICS AUSTRALIA

High Sensitivity and Specificity of Ga⁶⁸ Octreotate PET compared with F-18 FDG PET in Head and Neck Squamous Cell Carcinoma

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Theranostics Australia's Philosophy

Mission

To develop and provide powerful and innovative therapies

Vision

To improve quality of life and restore hope.

Values

Courage, Education, Excellence, Hope and Innovation.

About Theranostics Australia

- The first PRIVATE theranostics facility in Australia
- Established in May 2015 and Opened in August 2015
- Based at Diagnostic Nuclear Imaging at Hollywood Private Hospital, Perth, Western Australia.
- Providing patients with contemporary cancer treatment options
- “Offering Integrated Molecular Imaging and Cancer Therapy Services”
- Focusing particularly on cancers which are difficult to treat or are becoming resistant to conventional therapies.

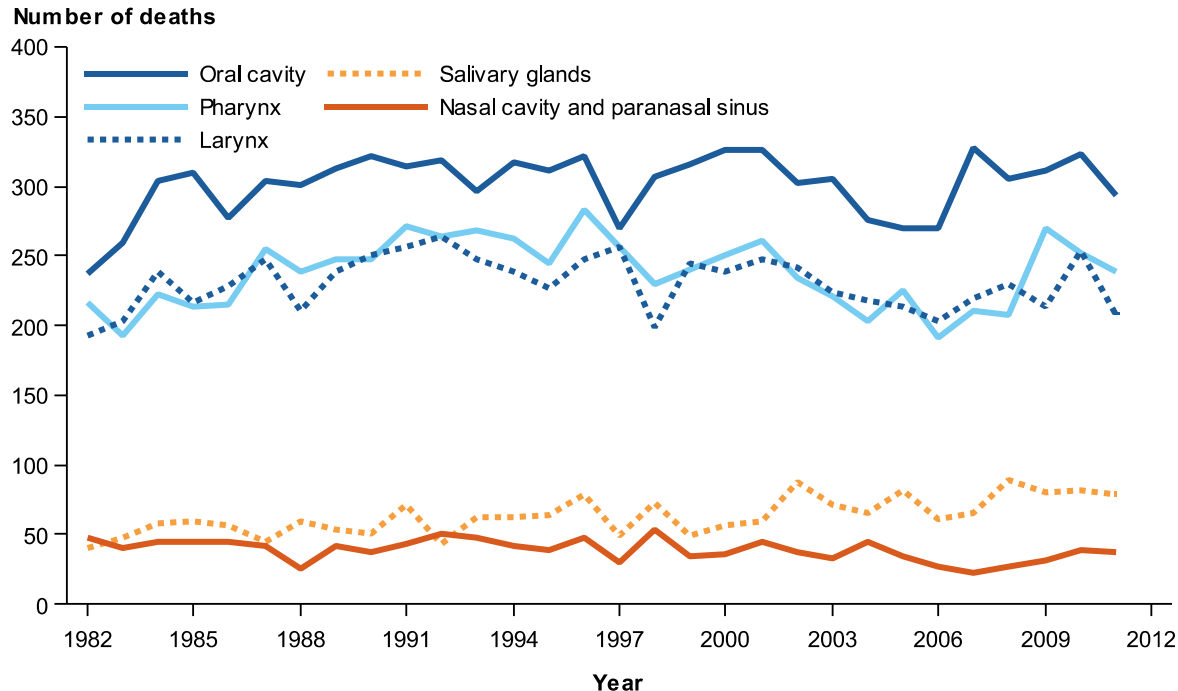
Disclosures

- Professor Harvey Turner – conference travel and research grants : Novartis
- Somatostatin receptor staining : Novartis
- The Garnett Passe and Rodney Williams Memorial Foundation
- The Fremantle Hospital Medical Research Foundation

Ga-68 Octreotate in H&N Cancer

- Includes cancers of oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx
- Relatively common cancer in Australia (3.4% of all cancers); 6th most common cancer worldwide
- Approximately 4000 patients per year in Australia (>650, 000 worldwide)
- Increasing incidence in Australia (aging population; HPV)
- Males 74%, Females 26%
- Risk factors: Tobacco, Alcohol, Diet, Genetics, Occupational irritants, EBV & Human Papilloma Virus (HPV) infections

Ga-68 Octreotate in H&N Cancer



Trends in number of deaths, groups of head and neck cancers, persons, Australia, 1982-2011

Notes

1. Deaths registered in 2009 and earlier are based on the final version of cause of death data; deaths registered in 2010 and 2011 are subject to further revision.
2. Cancers coded in ICD-10 as C00-C13, C30-C32.
3. The mortality data in AIHW National Mortality Database were provided by the Registers of Births, Deaths, Marriages and the National Coronial Information System and coded by the Australian Bureau of Statistics.
4. Years in table refer to year of occurrence of death except for the most recent year, which refers to the year of registration of death.

Source:
AIWH National Mortality Database 2014

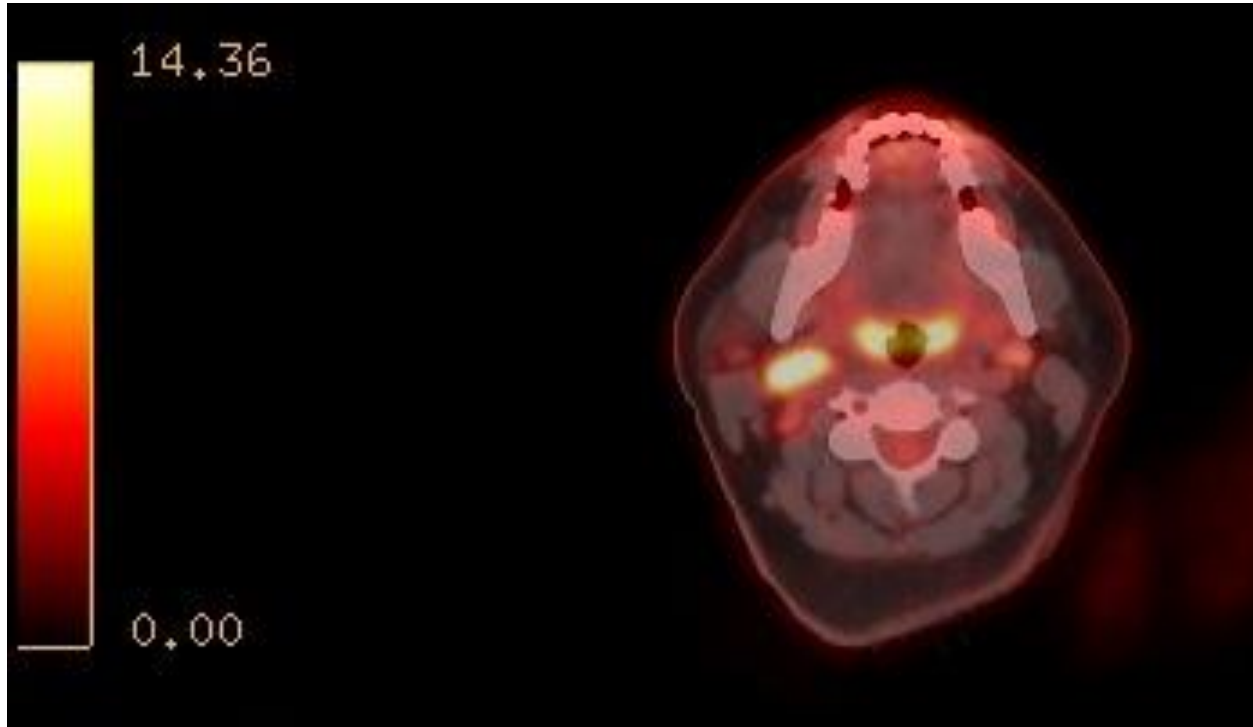
Ga-68 Octreotate in H&N Cancer

- 30% present with stage I or stage II surgically resectable disease; 60% present with stage III disease; 10% present with metastatic disease (stage IV)
- Standard treatment is surgery or radiotherapy for early stage disease; combined surgery and chemoradiotherapy for more advanced disease
- Overall 5 yr survival 68% however stage IV disease only has median survival of 5-9 months.
- Relapse post curative therapy also has poor survival with limited treatment options

Ga-68 Octreotate in H&N Cancer

- Diagnostic Pathway: CT neck and thorax, MRI neck and whole body FDG PET (if > stage I disease)
- FDG PET – High sensitivity and specificity for staging and re-staging head and neck cancer
- Useful also for localising primary in squamous cancer of unknown primary in head and neck region
- Limitations: High background in tonsillar region (normal lymphoid tissue); post-surgical and post-radiotherapy inflammation and healing response; infection e.g. tonsillitis

Ga-68 Octreotate in H&N Cancer



FDG PET-CT

HOT TONSIL

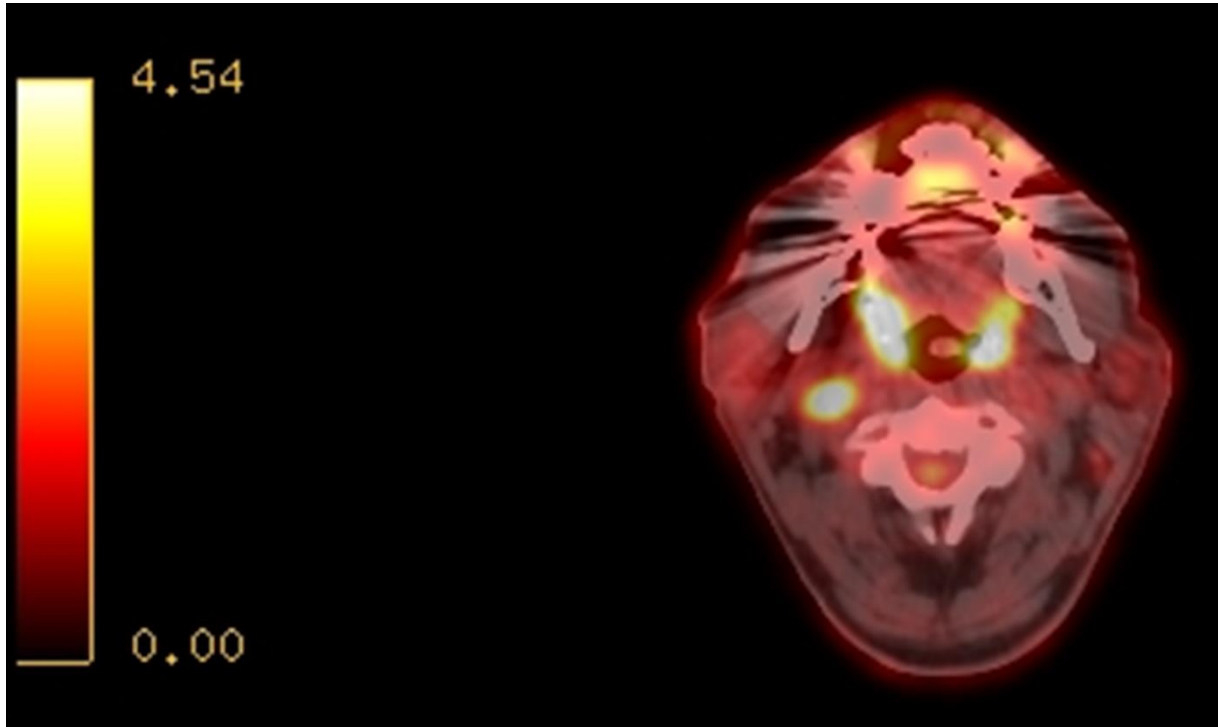
FOSSAE POST-OP

34yo T1N2c R

Tonsil SCC HPV+



Ga-68 Octreotate in H&N Cancer



FDG PET-CT

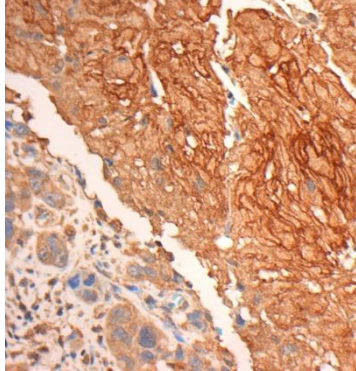
CO-MORBID
TONSILITIS

57M. TxN2bMO
SCC CUP HPV+

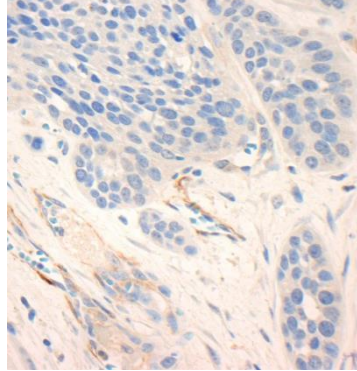


Ga-68 Octreotate in H&N Cancer

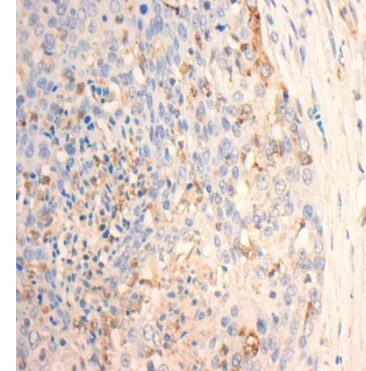
- Somatostatin receptor (in particular SSTR 5) expression frequent in squamous cell head and neck cancer. (Shartinger et al J Laryngol Otol 2012)



SSTR₁ IHC



SSTR_{2a} IHC



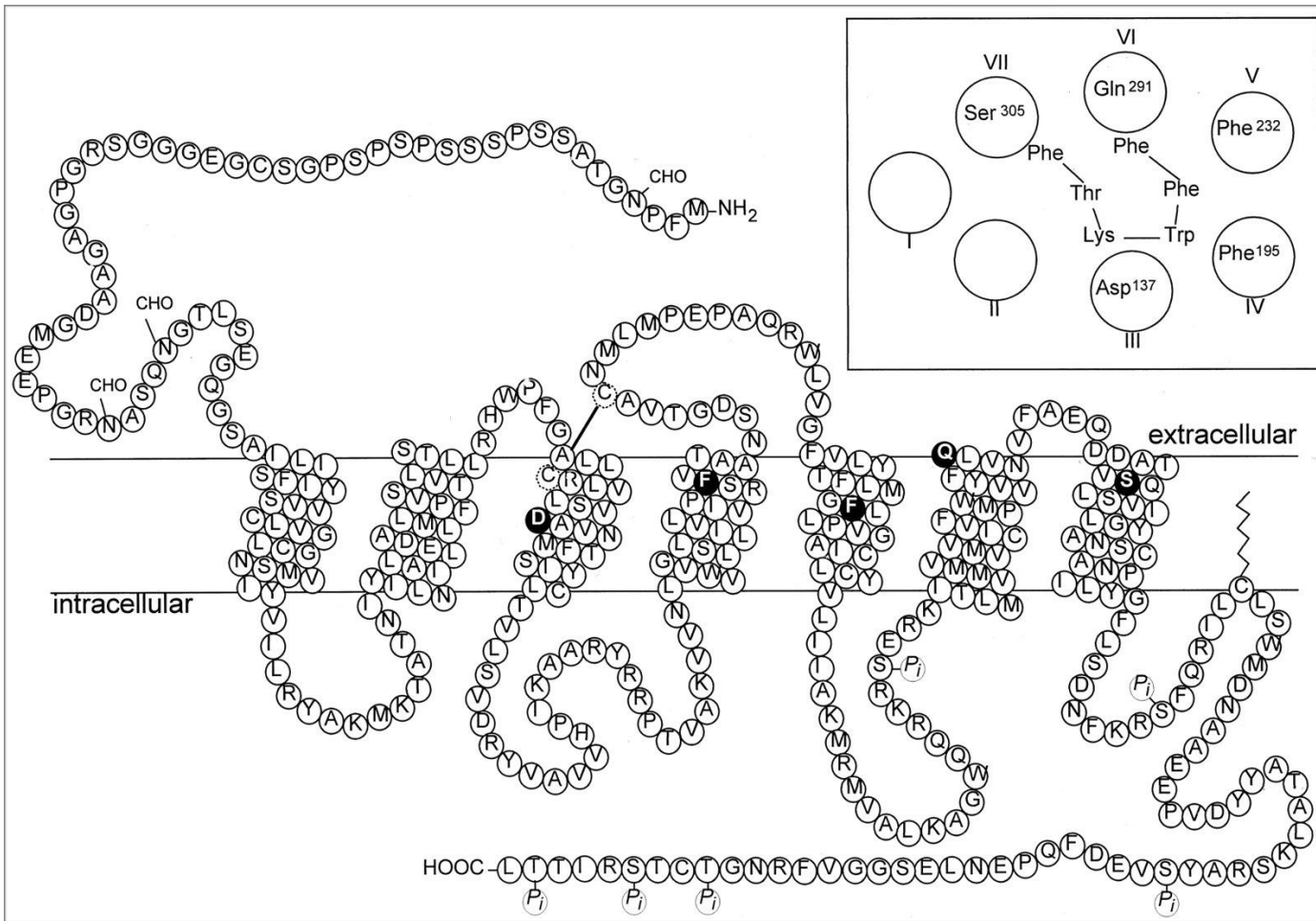
SSTR₃ IHC

THE TARGET

SSTR₁₋₅:

A G-coupled 7
Transmembrane
receptor

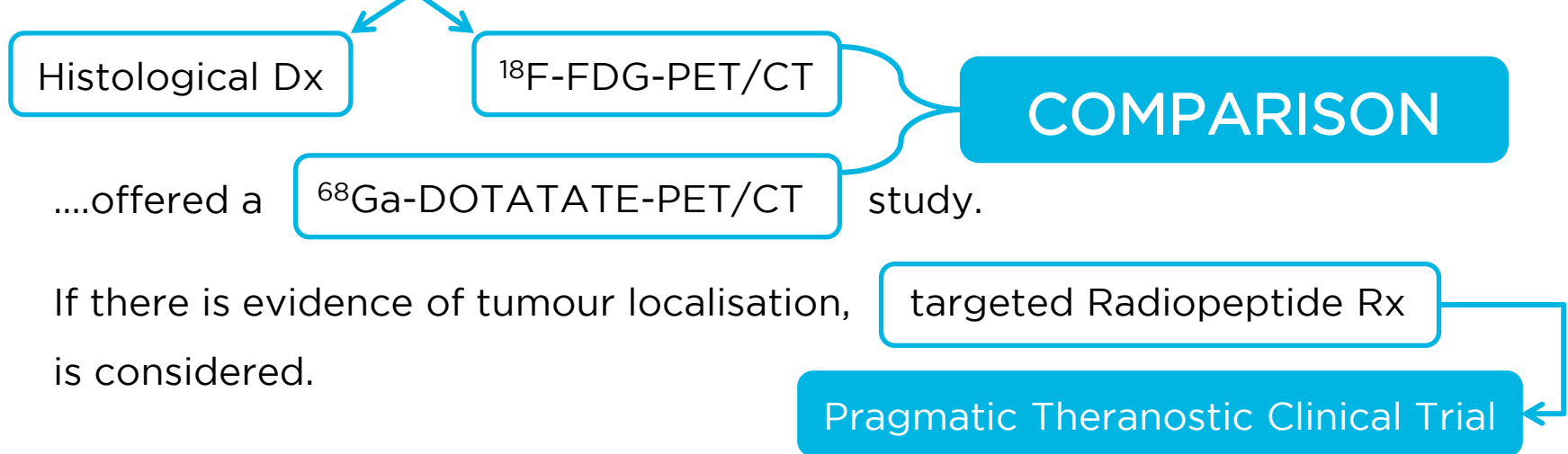
*Sheridan et al. Integrative and
Comparative Biology 2000;
40(2):269-86*



The DEMISSTify HNSCC Trial

Diagnostic Evaluation via Molecular Imaging of SSTR in HNSCC

Consecutive **eligible** patients, August 2013 to January 2015.



DEMISSTify Trial

Aims:

To:

- Compare the utility of ^{68}Ga -OCT PET/CT compared to F-18 FDG in localization and staging of H&N SCC and;
- Evaluate the potential for neoadjuvant or salvage radiopeptide therapy.

DEMISSTify Trial

- Physician sponsored trial
- Period: 6/9/2013 - 6/1/2015
- Ethics approval from Fremantle Hospital Medical Research Ethics committee
- Patients recruited from Head and Neck Surgical Unit Fremantle Hospital
- FDG PET and Ga-68 octreotate PET performed at OMI Hollywood PET-CT centre on 128 slice GE 710 PET scanner
- Ga-68 octreotate PET performed within 2 weeks of FDG PET
- Tissue samples from surgical specimen taken for tumour grade, HPV analysis and SSTR analysis (1,2a,3,4,5) in subset of 8 patients
- SSTR analysis - blinded assessment by independent pathologist

DEMISSTify Trial

Demographics:

- N=35; Male: 27 (55yrs ave) ; Female: 8 (51yrs, ave)

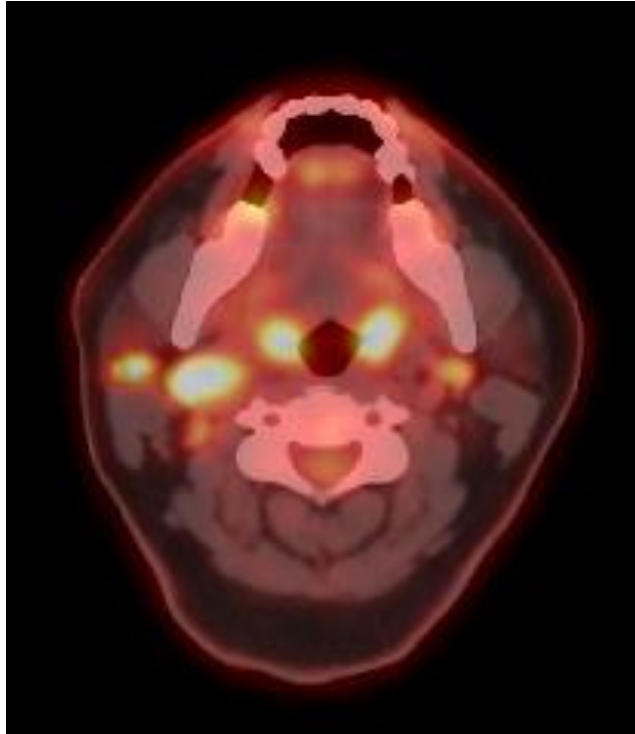
Results:

- 34 SCC (2 Basaloid SCC), 1 Verrucous Ca.
- 37% HPV positive disease (13/35)
- 88% + Ga68-DOTATE PET/CT (31/35) - based on tumour to background
- 4 negative included 1 Verrucous cancer + 3 SCC cases
- FDG-PET/CT unable to identify primary in 3 cases - all in oropharynx and all identified on tumour to background with Ga-68-DOTATATE PET/CT (confirmed on histopathology)

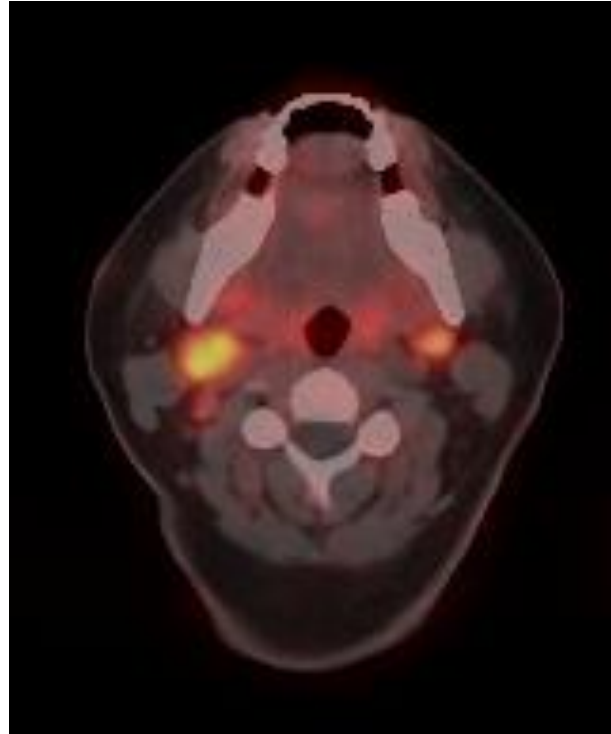
DEMISSTify Trial

Results:

- Mean SUV 8.2 (primary + nodal) FDG PET compared with mean SUV 4.3 Ga-DOTATATE.
- Mean tumour to background ratio (T:B) 5.3 FDG PET compared mean T:B 4.9 Ga-DOTATATE
- SSTR assessment strong positive in 4 cases positive for Ga-DOTATATE , negative in 1 case negative for Ga-DOTATATE (verrucous) and low grade in 3 cases with positive Ga-DOTATATE
- 2 cases with metastatic head and neck cancer with positive Ga-68 octreotate PET offered neoadjuvant radiopeptide therapy with Lu-177 octreotate



FDG PET



Ga⁶⁸ DOTATATE PET

HOT TONSIL

FOSSAE

POST-OP

34yo T1N2c R Tonsil

SCC HPV+



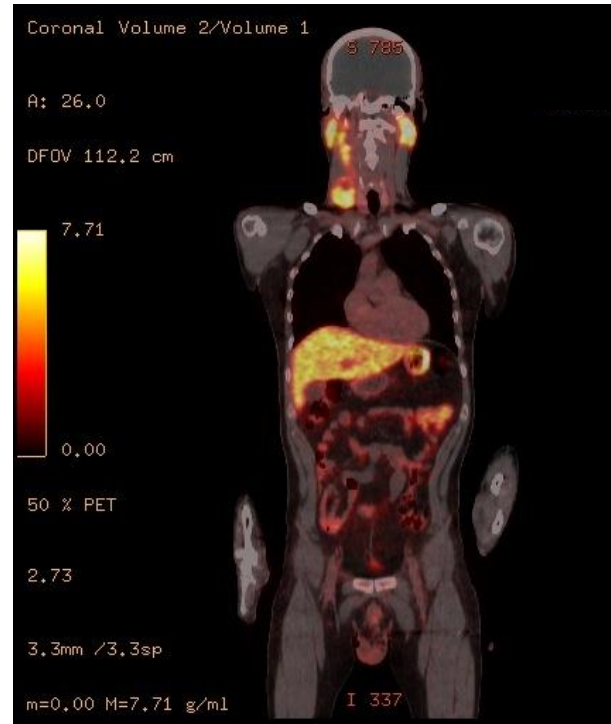
FDG-PET/CT AGREEMENT

50M. T3N2bM0

Right lingual
tonsil/BoT



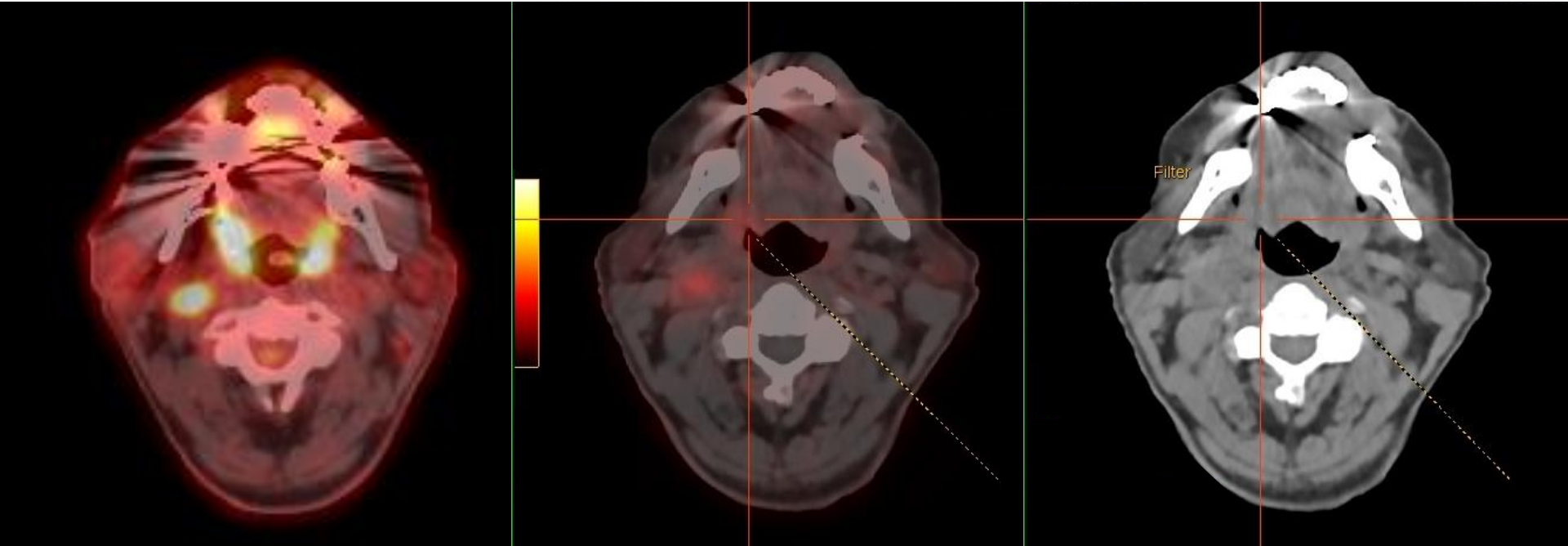
FDG PET



Ga⁶⁸ DOTATATE PET

CO-MORBID TONSILLITIS

67M. TxN2bM0 SCC CUP HPV+



FDG PET

Ga⁶⁸ DOTATATE PET

CT

Limitations

- Small study
- High gallium octreotate uptake in:
 - Adrenals
 - Salivary glands
 - Liver
 - May limit assessment of metastatic disease at these sites
- Cost and availability of Ga-68 octreotate

Conclusions

- Ga-68 octreotate PET shows positivity in most head and neck squamous cancers (in keeping with previous in-vitro histochemical findings)
- SSTR immunohistochemistry not as sensitive as Ga-68 octreotate PET (though subtype may be cause)
- Ga-68 octreotate PET may have a role in:
 - Helping assess for tumour of unknown primary in non-diagnostic FDG PET/in early post-op/inflammation
 - Assessing patients suitable for salvage radiopeptide therapy with Lu-177 octreotate

Concluding Remarks

- We have established that H&N cancers imaged with Ga-68 octreotate:
 - Often show somatostatin receptor positivity with equivalent T:B ratios as FDG PET;
 - May be of benefit in inflammatory/post-surgical situations
- We have also established a proof of concept for a novel nuclear theranostic approach to the management of metastatic recurrent HNSCC.

Acknowledgements

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