Head & Neck cancer management with emphasis on clinical management using FDG PET/CT

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Head & Neck tumors

Carcinoma
- Nasopharyngeal carcinoma
- Squamous cell carcinoma
  - HPV + or -

Cutaneous
- Melanoma
- Squamous cell carcinoma
- Merkel cell carcinoma

Salivary gland tumors*
- Mucoepidermoid
- [illegible]
- [illegible]
- Salivary ductal carcinoma
- Pleomorphic adenoma
- Warthin tumor

*risk of malignancy is inversely proportional to the size of the gland
perineural spread common

Cysts and cyst like lesions
- Branchial cyst
- Thyroglossal duct cyst

Neurogenic
- [illegible]
- [illegible]

Neuroendocrine
- Well differentiated
- [illegible]
- Poorly differentiated (small or large cell type)

Paraganglion tumors
- Carotid body
- Jugular foramen
- Glomus vagale
- Glomus tympanicum

Odontogenic

Sinonasal papilloma
- Inverted
- Oncocytic

Haemato-lymphoid
- FDG avid disease
- Low grade FDG uptake
- [illegible]
- Photopenic

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- Adenoid cystic
- Acinic cell
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- Pleomorphic adenoma
- Warthin tumor

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- Low grade FDG uptake
- Variable FDG uptake
- Photopenic

Squamous cell carcinoma of the neck

- Preferentially spreads to regional lymph nodes
- Distant metastatic disease at the time of diagnosis has been reported in 10% to 18% of patients
- The lungs are the most frequent site for distant metastatic disease
- Skeletal metastases are most frequently in the ribs and vertebrae
- Detection of distant metastatic disease at initial staging is crucial because it will change prognosis and typically change the management strategy toward more systemic options.
- An increased rate of second primary malignancy and concurrent lung malignancy

ACR Appropriateness Criteria® Staging and Post-Therapy Assessment of Head and Neck Cancer, Journal of the American College of Radiology, Volume 20, Issue 11, Supplement, 2023, Pages S521-S564, ISSN 1546-1440, https://doi.org/10.1016/j.jacr.2023.08.008. (https://www.sciencedirect.com/science/article/pii/S1546144023006063)

Head & Neck cancer management overview

SQUAMOUS CARCINOMAS OF THE LIP AND ORAL CAVITY (MaxFacs)	**This group includes cancers of the lip, anterior two-thirds of the tongue, floor of mouth, gum (alveolus) and hard palate**	**Surgery is the preferred initial treatment. Those with disease beyond the scope of surgery or those not sufficiently fit for surgery may be considered for radical radiotherapy +/- chemotherapy; neo-adjuvant chemotherapy can be considered for rare selective cases**
SQUAMOUS CARCINOMAS OF THE OROPHARYNX, HYPOPHARYNX AND LARYNX (ENT)	Primary radiotherapy +/- concurrent chemotherapy is the preferred treatment for such cases. Neo-adjuvant (induction) chemotherapy is recommended for locally advanced squamous cancers, such as T3/T4 disease and bulky nodal disease, prior to concurrent chemo-radiotherapy.	Surgery for early T1 larynx (TLM) or advanced T4 larynx/hypopharynx or early stage oropharynx (TORS)

NHS
Kent and Medway Cancer Collaborative

Head & Neck cancer management overview

SINO-NASAL AND EAR CANCERS (Skull Base MDT)	**This group includes cancers of the nasal cavity, maxillary or ethmoid sinuses (rarely frontal or sphenoidal sinuses), auditory canal and middle ear. Cancers of the pinna and nasal ala are considered as skin cancers**	**Surgery is the preferred initial treatment; followed by postoperative radiotherapy. Those with disease beyond the scope of surgery or those not sufficiently fit for surgery may be considered for radical radiotherapy. Concurrent chemoradiotherapy may be considered for those with locally advanced squamous sino-nasal cancer and a good response to induction chemotherapy.**
NASOPHARYNGEAL CANCER (Oncology)	Radiotherapy can be offered alone for T1/T2 N0M0 disease. All other stages should be considered for radiotherapy +/- chemotherapy	

NHS
Kent and Medway Cancer Collaborative

Surgery for head and neck cancer

Primary Tumor Resection: Removal of the tumor with clear margins.
Neck Dissection: Removal of lymph nodes to assess or treat regional metastasis.
Reconstructive Surgery: Free flap reconstruction (e.g., radial forearm, fibula) for large defects. Local flaps for smaller reconstructions.
Minimally Invasive Techniques: Transoral Laser Microsurgery (TLM) Transoral Robotic Surgery (TORS) – especially for oropharyngeal cancers.
Emerging Trends Organ preservation protocols. Enhanced recovery protocols post-surgery.

Common surgical procedures and reconstruction

Surgical procedures
Panendoscopy
Laryngectomy (hemi/total)
Pharyngolaryngectomy
Neck dissection
Maxillectomy
Mandibular resection/rim resection
Mucosectomy
Glossectomy partial/total
Parotidectomy (superficial/total)
Mastoidectomy

Surgical reconstruction techniques
Radial forearm
Pectoral rotation
Anterolateral thigh
Latissimus dorsi
DCIA

Category	Free Flap	Reconstructs
Muscular	Latissimus dorsi	Skull base, scalp
Fascial	Radial forearm	Oral cavity, tongue, palate, nose, face, scalp, lip, pharynx, larynx
	Anterolateral thigh	Oral cavity, tongue, palate, pharynx, larynx, cervical oesophagus
Osseous	Fibula	Mandible
	Iliac crest	Mandible & midface
Visceral	Jejunum	Pharynx, oesophagus

Adapated from:
Imaging of Surgical Free Flaps in Head and Neck Reconstruction. J.L. McCarty, A.S. Corey, M.W. El-Deiry, H.M. Baddour, B.M. Cavazuti, P.A. Hudgins. American Journal of Neuroradiology Jan 2019, 40 (1) 5-13; DOI: 10.3174/ajnr.A5776

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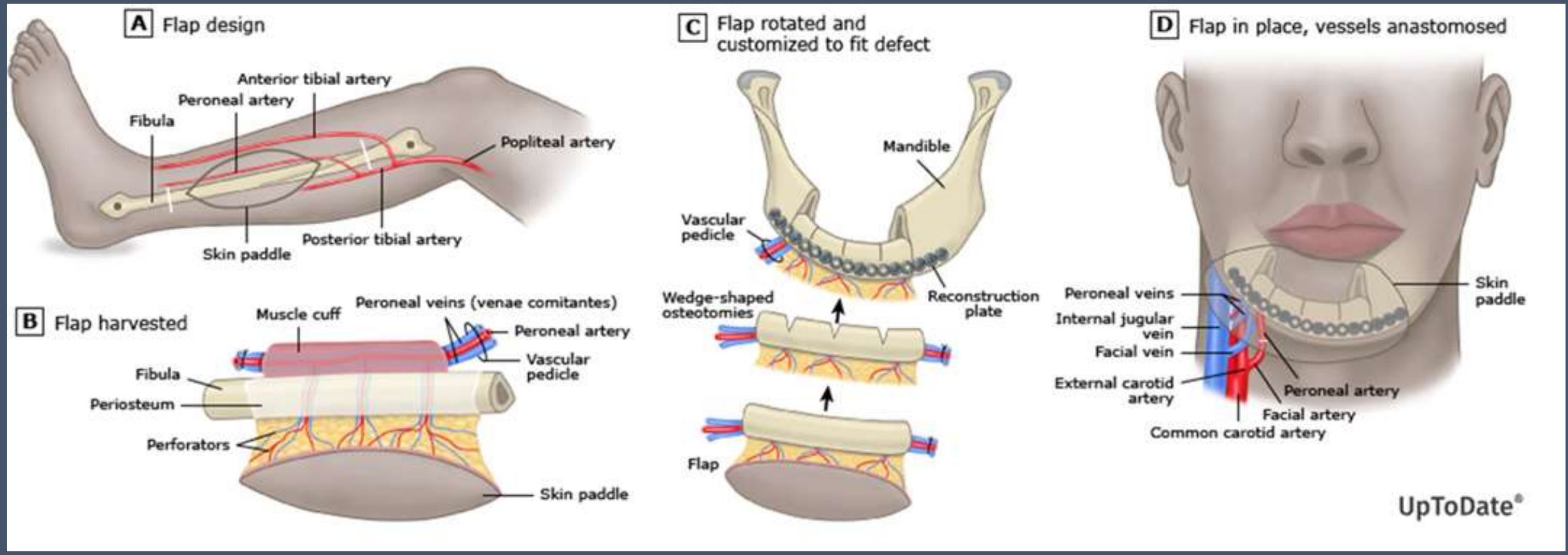
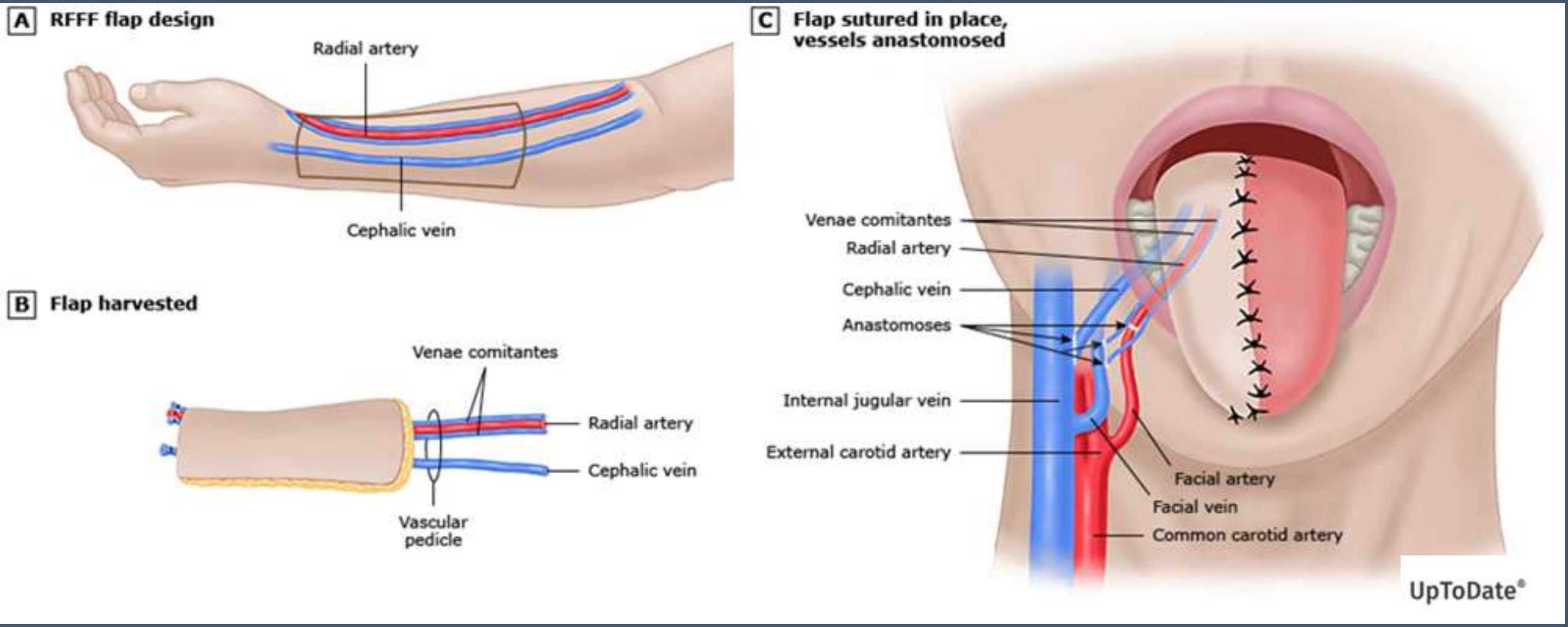
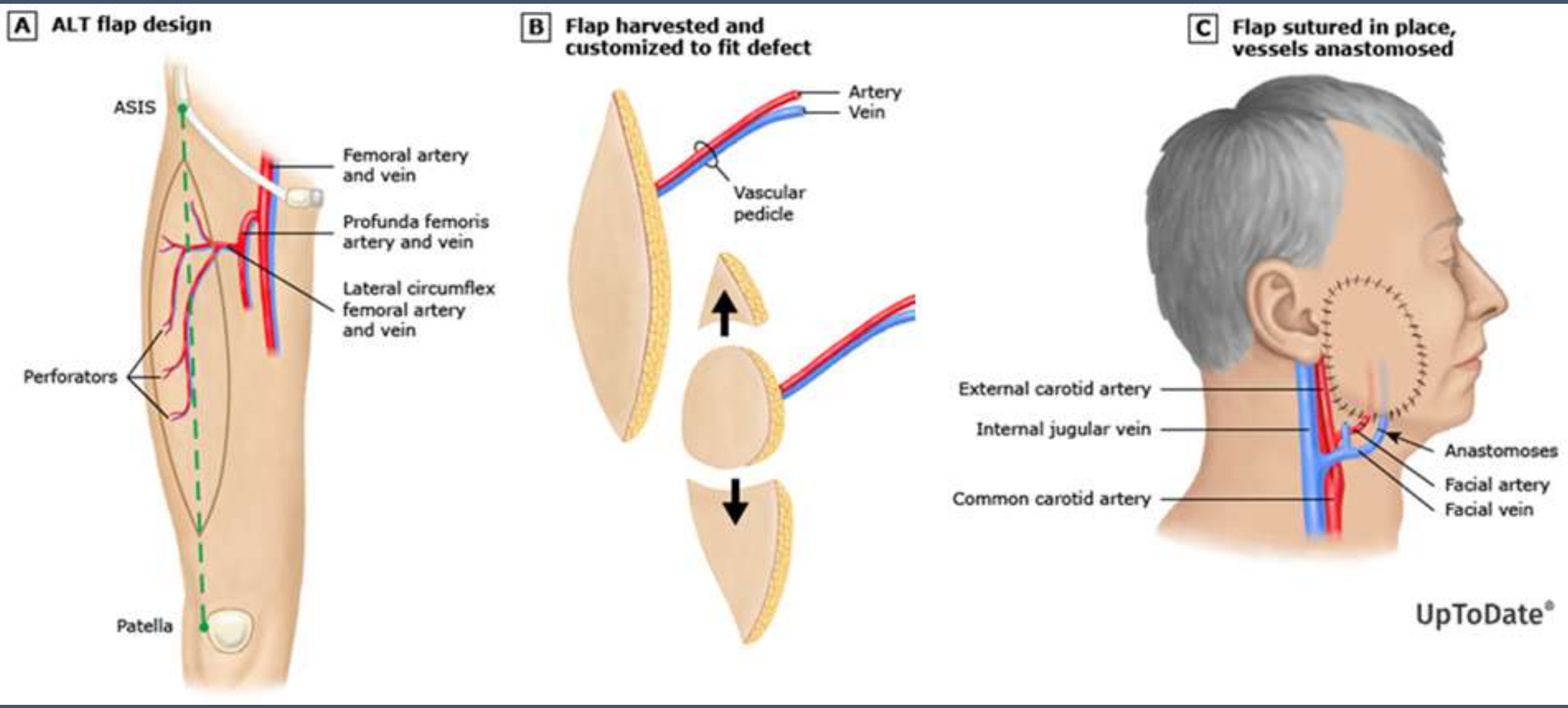
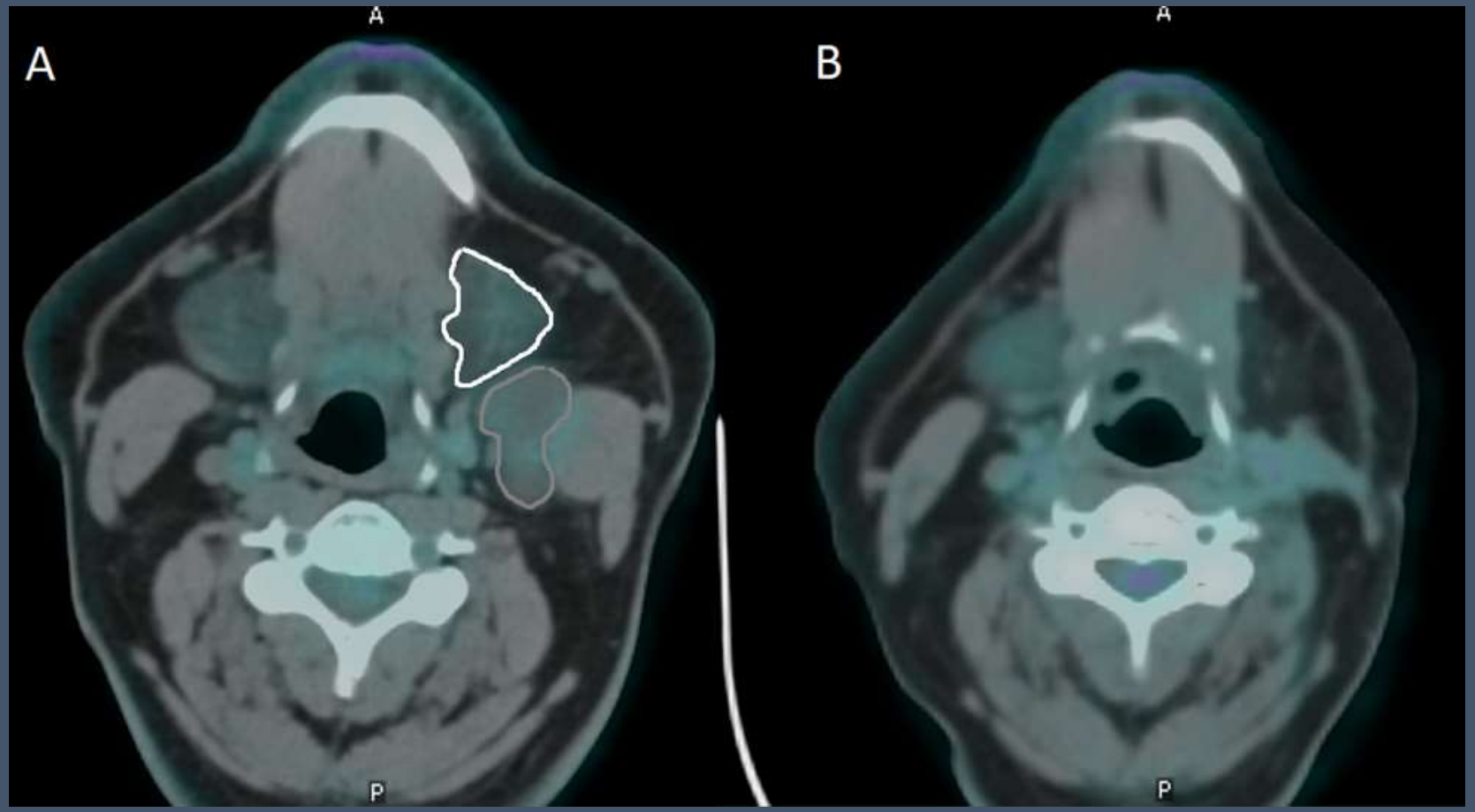

A Flap design
Anterior tibial artery
Peroneal artery
Fibula
Popliteal artery
Skin paddle
Posterior tibial artery
B Flap harvested
Muscle cuff
Peroneal veins (venae comitantes)
Peroneal artery
Vascular pedicle
Fibula
Periosteum
Perforators
Skin paddle
C Flap rotated and customized to fit defect
Mandible
Vascular pedicle
Reconstruction plate
Wedge-shaped osteotomies
Flap
D Flap in place, vessels anastomosed
Skin paddle
Peroneal veins
Internal jugular vein
Facial vein
External carotid artery
Peroneal artery
Facial artery
Common carotid artery
UpToDate®

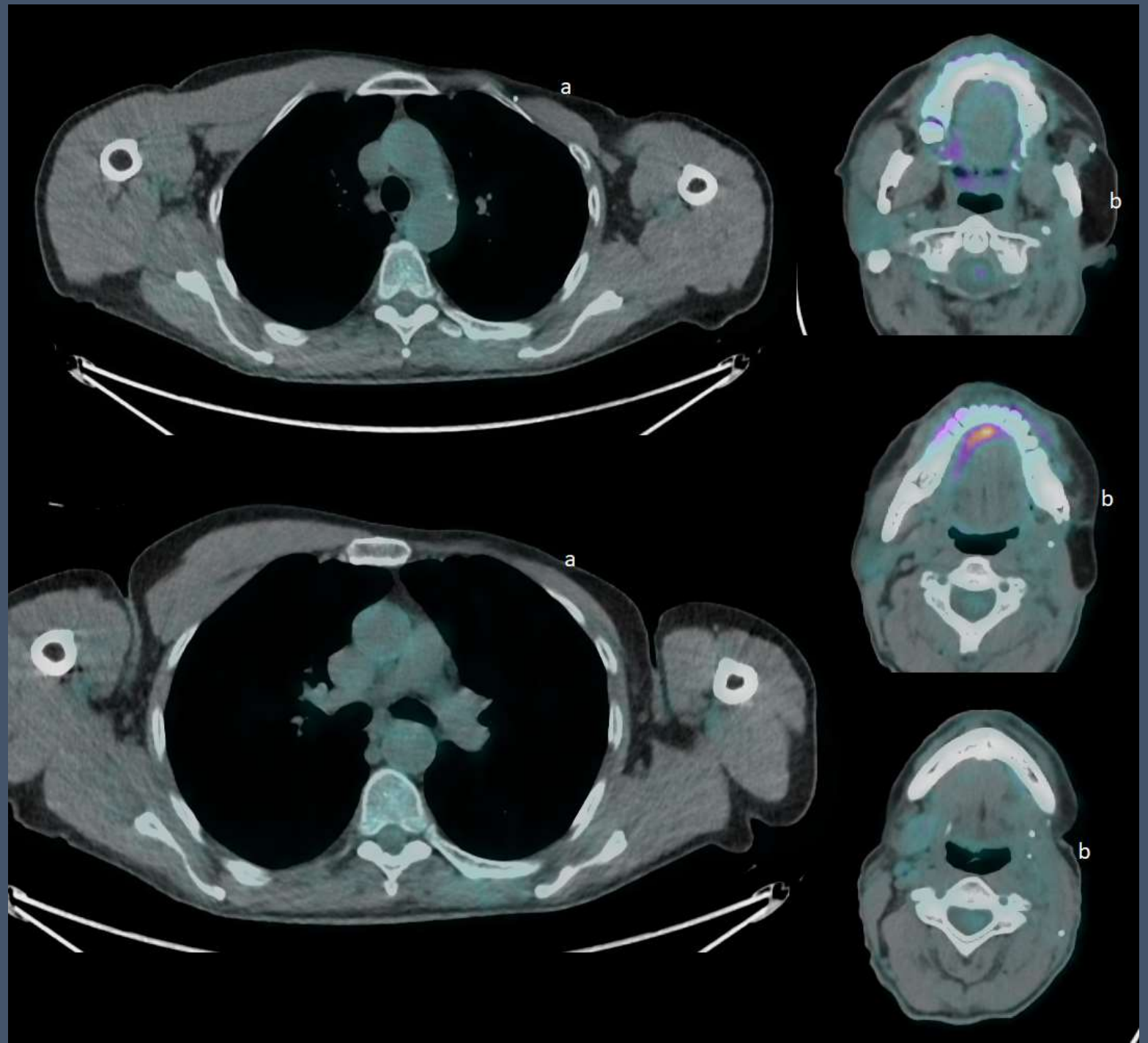

A RFFF flap design
Radial artery
Cephalic vein
B Flap harvested
Venae comitantes
Radial artery
Cephalic vein
Vascular pedicle
C Flap sutured in place, vessels anastomosed
Venae comitantes
Radial artery
Cephalic vein
Anastomoses
Internal jugular vein
External carotid artery
Facial artery
Facial vein
Common carotid artery
UpToDate®


A ALT flap design
ASIS
Femoral artery and vein
Profunda femoris artery and vein
Lateral circumflex femoral artery and vein
Perforators
Patella
B Flap harvested and customized to fit defect
Artery
Vein
Vascular pedicle
C Flap sutured in place, vessels anastomosed
External carotid artery
Internal jugular vein
Common carotid artery
Anastomoses
Facial artery
Facial vein
UpToDate®

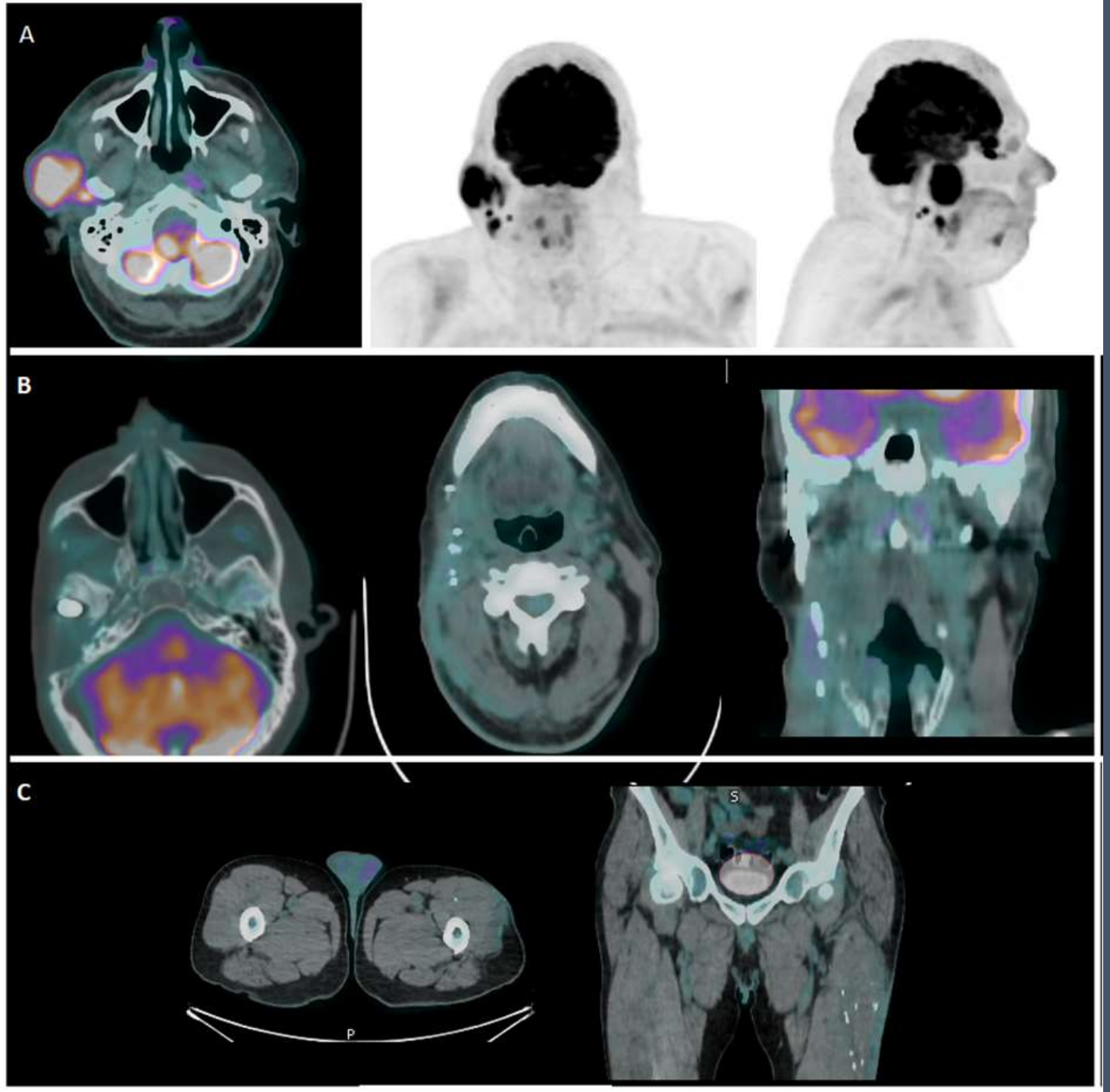


(A) presurgery: left submandibular gland (white outline), necrotic nodal metastasis (gray outline).

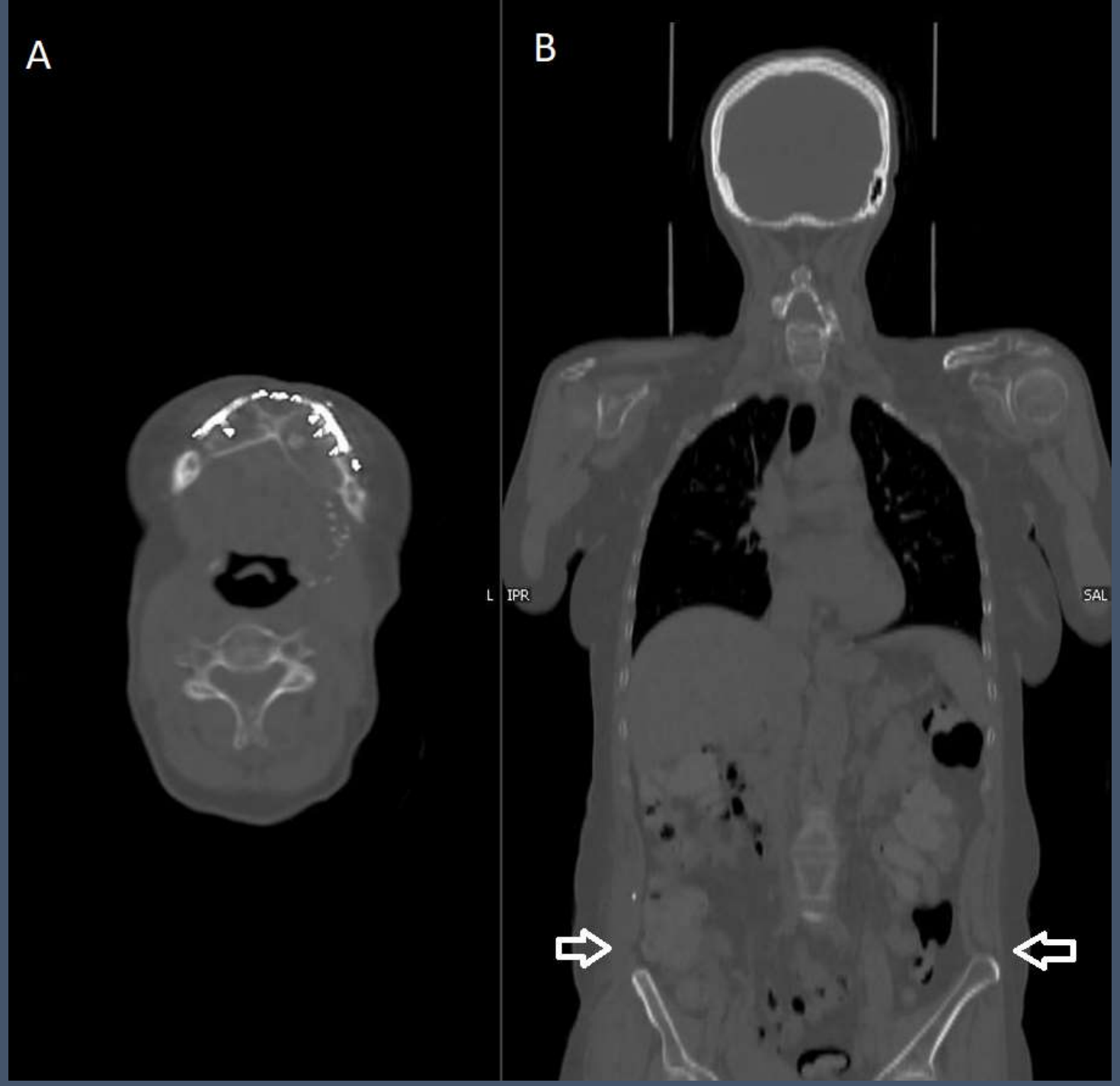
(B) post-surgical excision of gland and node



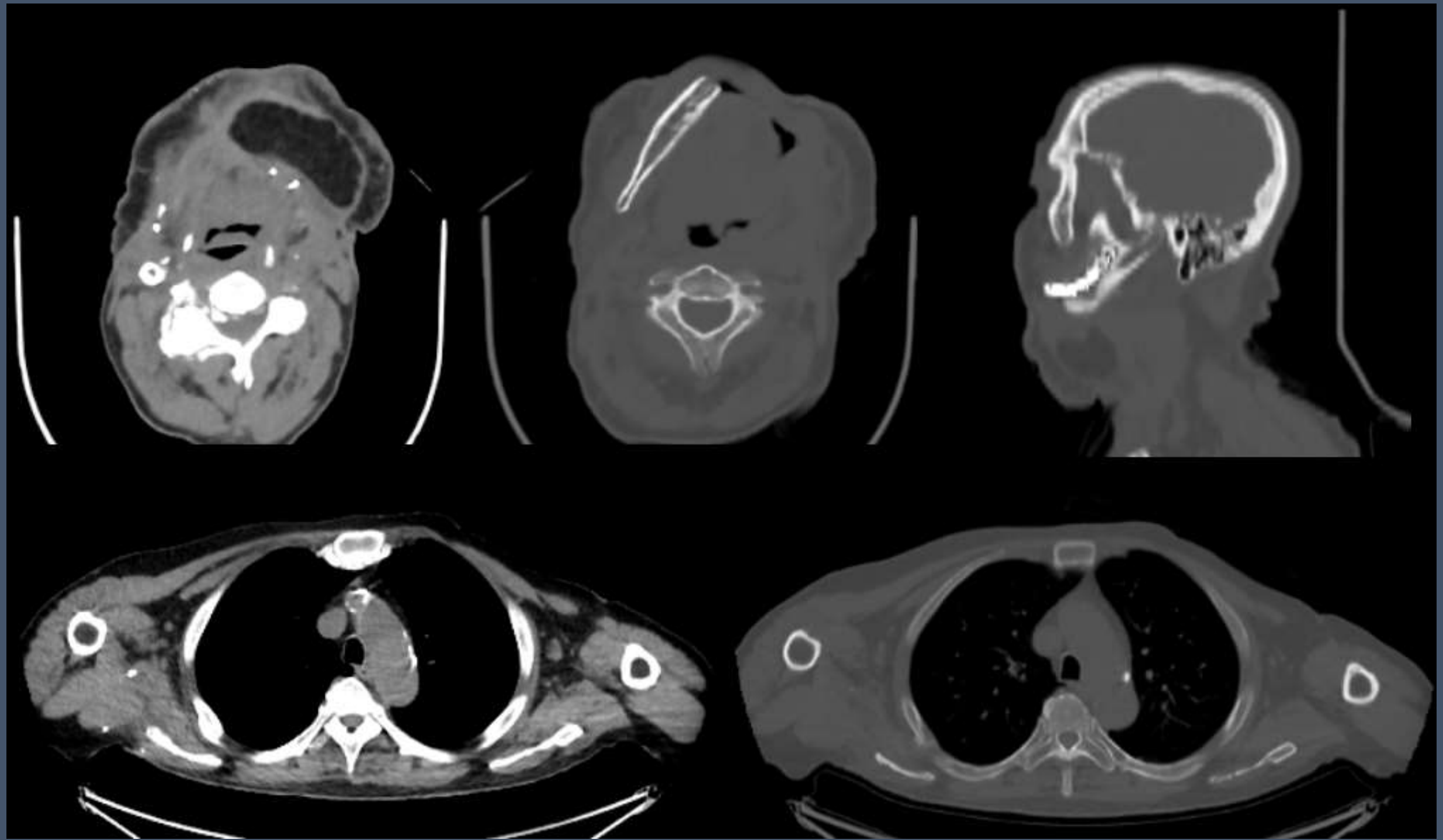
Left parotidectomy, neck dissection, resection of sternomastoid with a left pectoral (a) rotation myocutaneous free flap reconstruction (b)

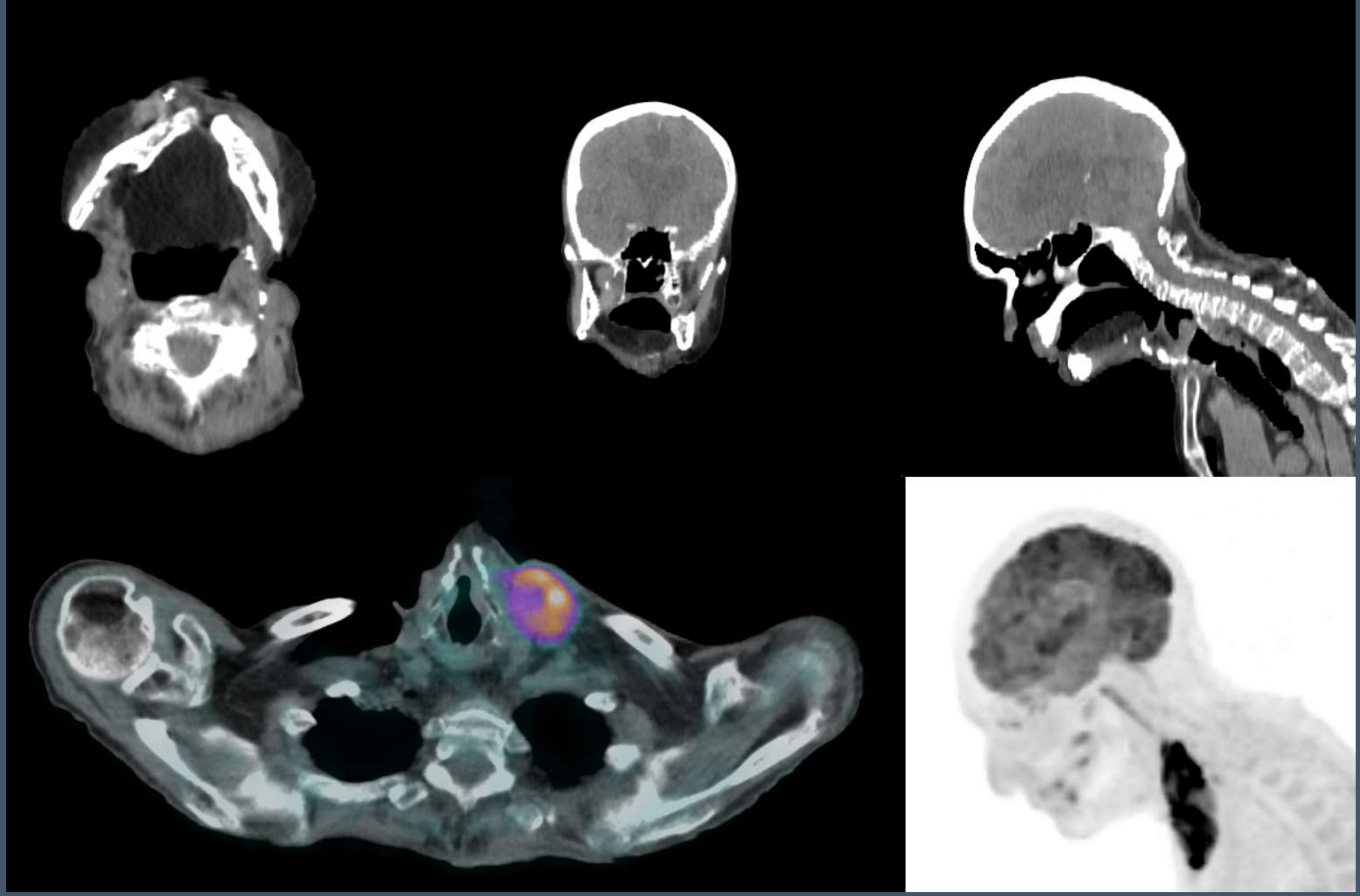


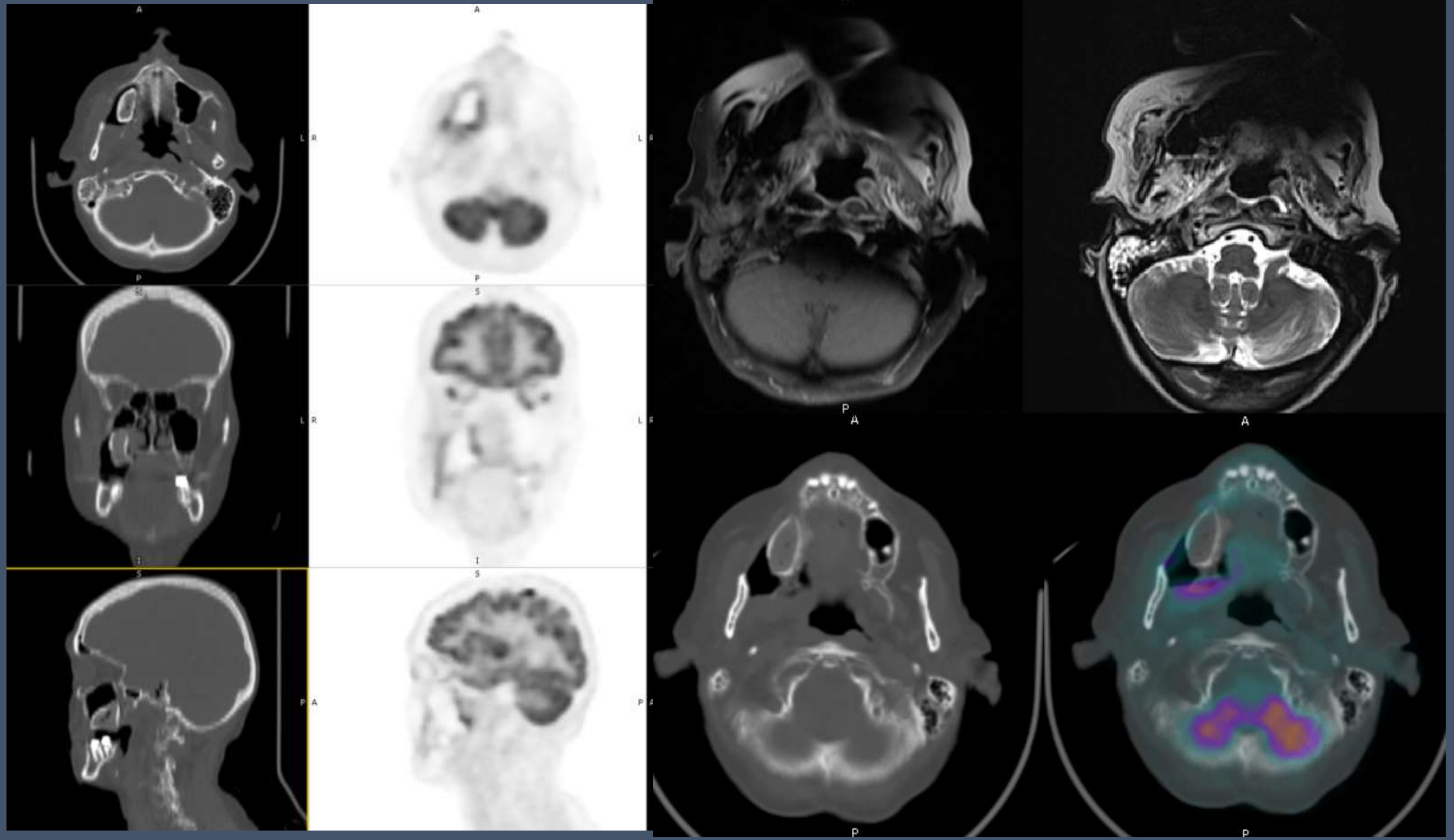
Neuroendrocrine tumor right parotid, locally advanced with nodal disease (A). Post parotidectomy, mandibular resection and prosthetic reconstruction, right neck dissection and right mastoid resection (B), free flap reconstuction left anterolateral thigh donor site (C).

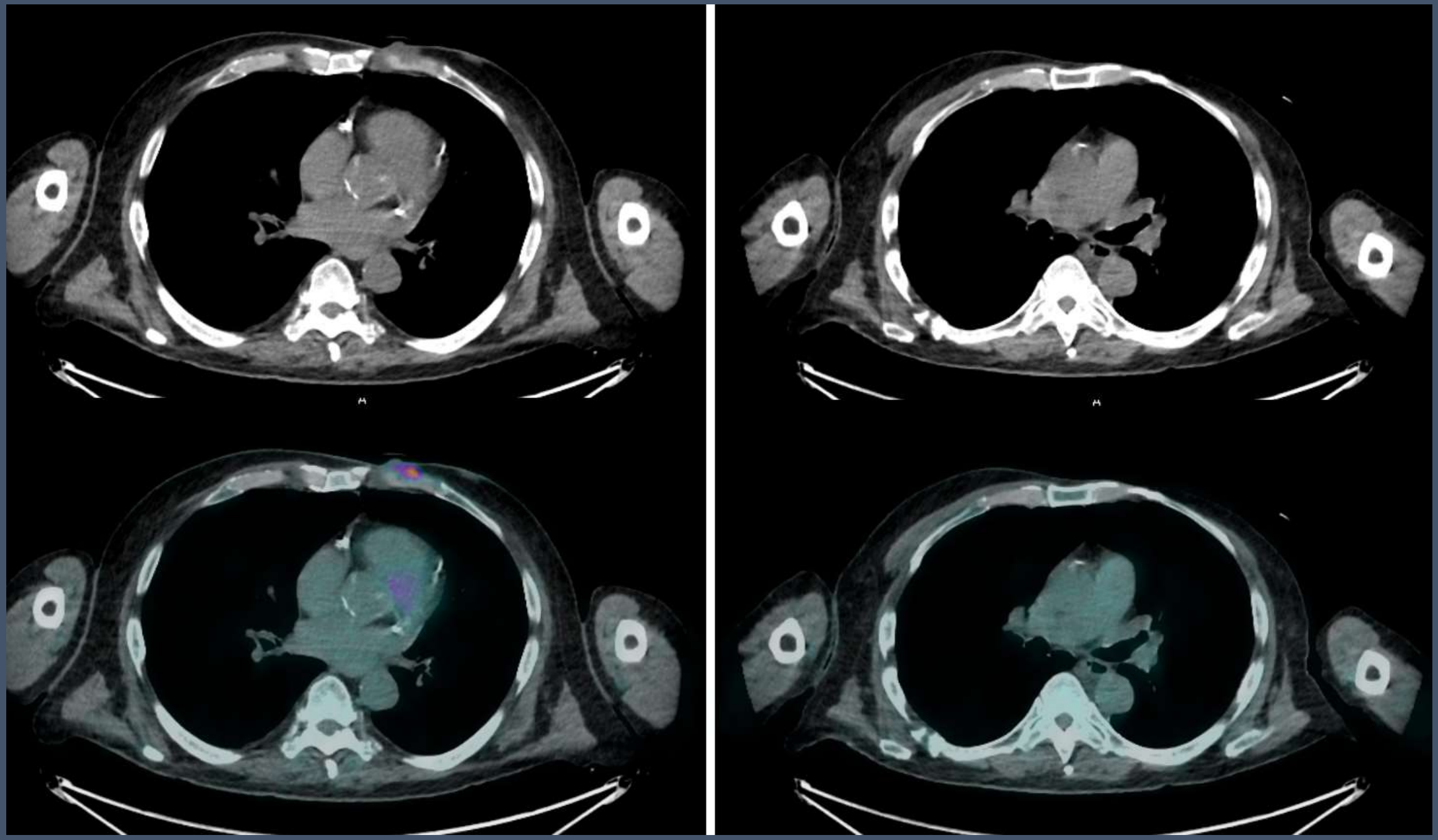


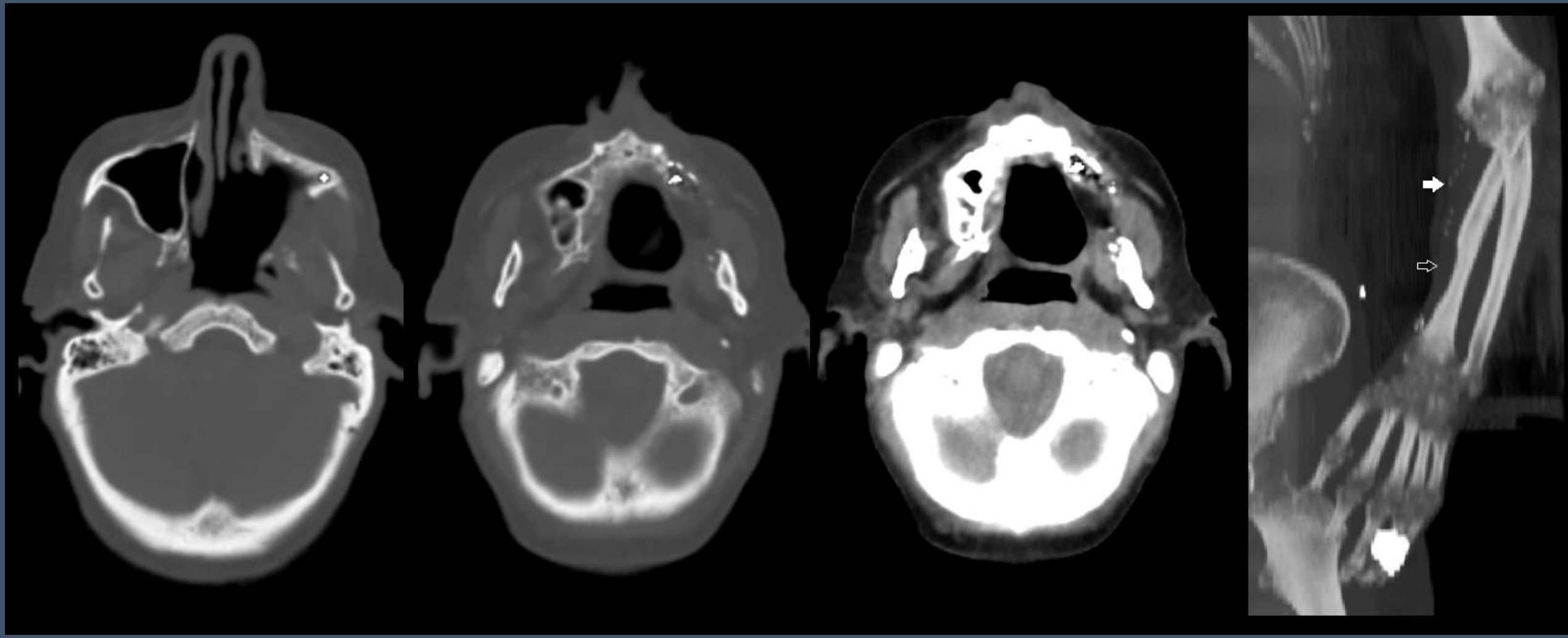
(A) Mandibular reconstruction,
(B) donor site right DCIA free flap (arrows)

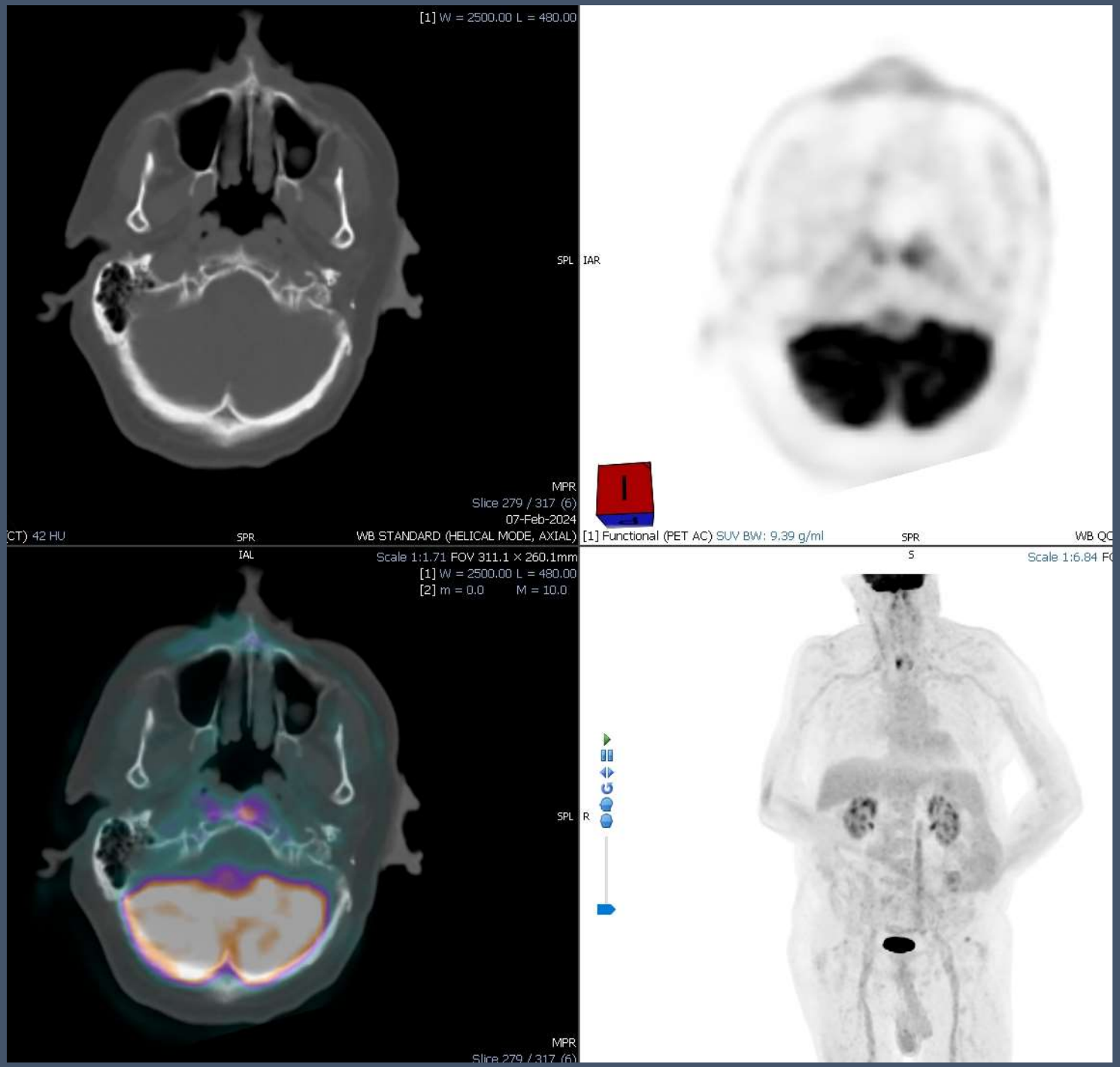


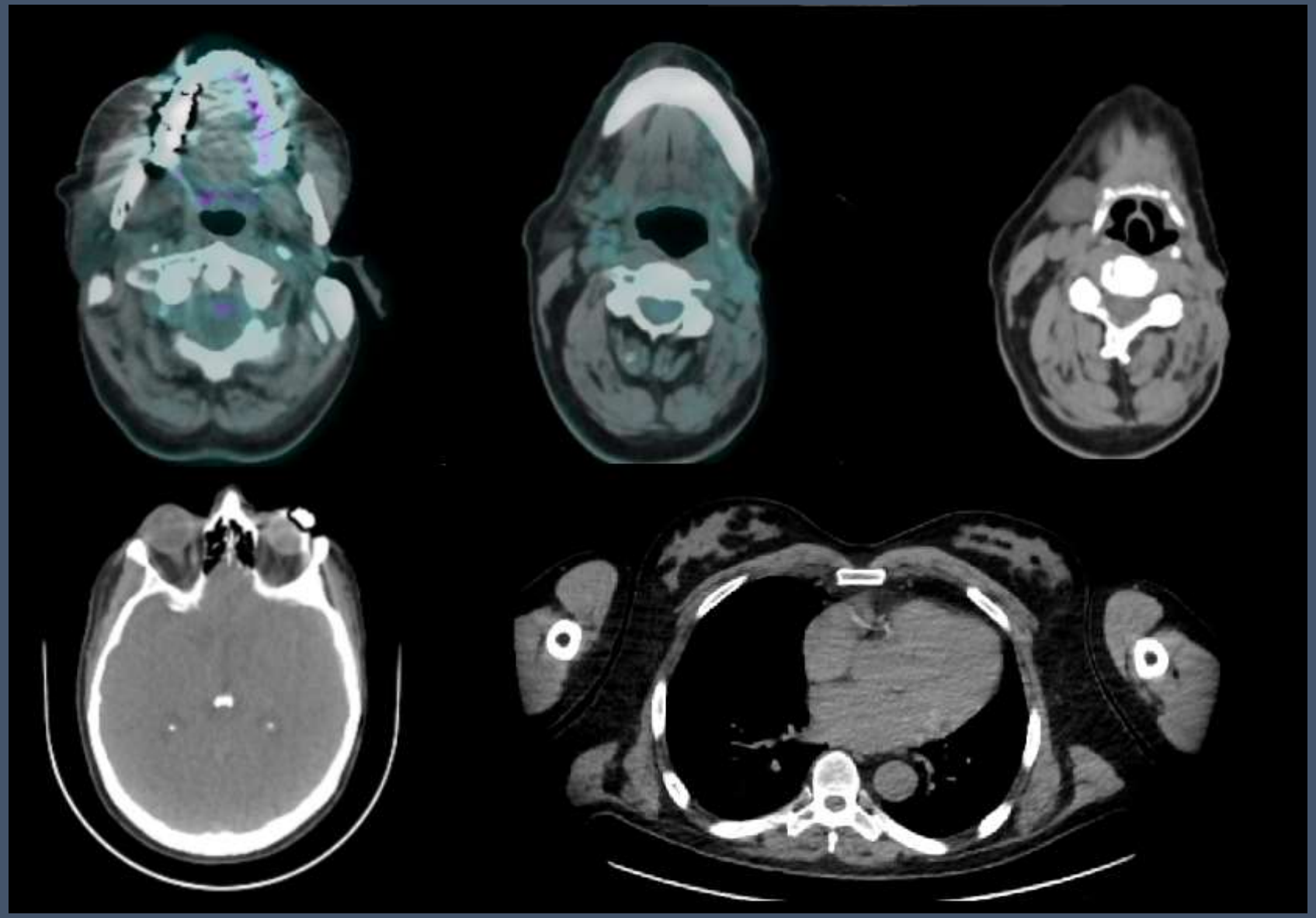


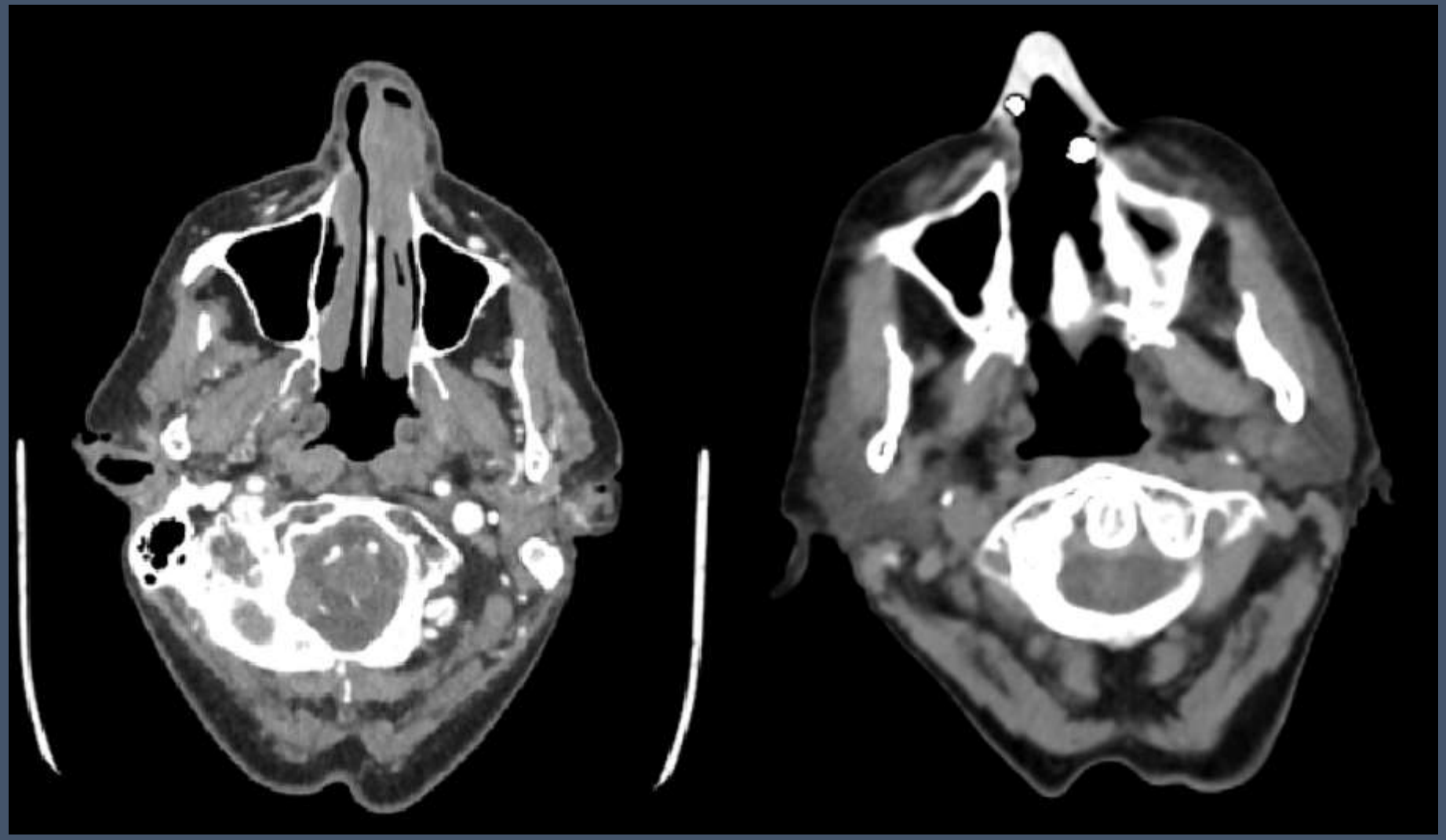


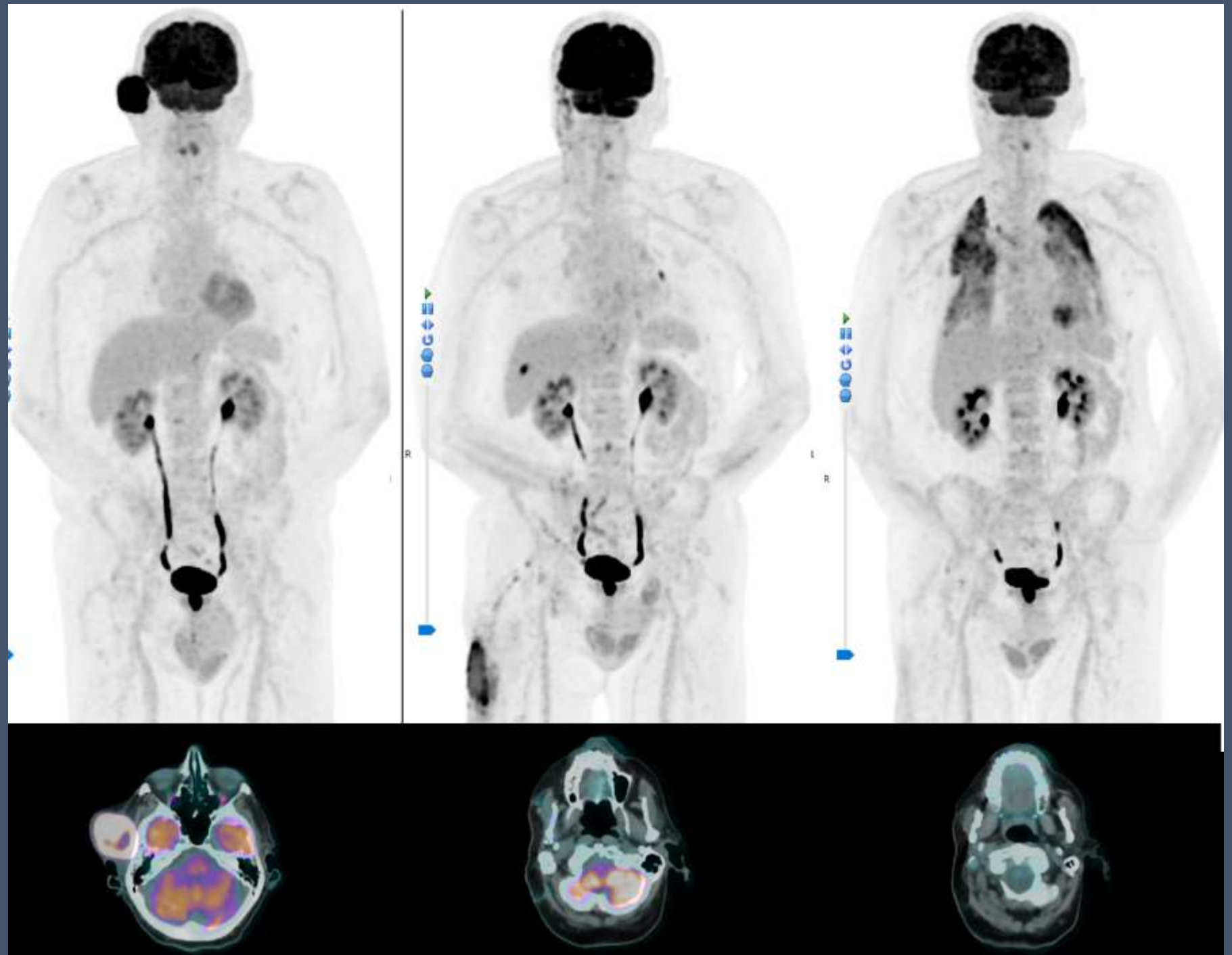





[1] W = 2500.00 L = 480.00
SPL
IAR
MPR
Slice 279 / 317 (6)
07-Feb-2024
CT) 42 HU
SPR
WB STANDARD (HELICAL MODE, AXIAL)
[1] Functional (PET AC) SUV BW: 9.39 g/ml
SPR
WB QC
IAL
Scale 1:1.71 FOV 311.1 × 260.1mm
[1] W = 2500.00 L = 480.00
[2] m = 0.0 M = 10.0
S
Scale 1:6.84 F
SPL
R
MPR
Slice 279 / 317 (6)







Oncological treatment for head & neck cancer

Radiotherapy

Definitive: As primary treatment for certain tumors (e.g., early laryngeal cancer).
Adjuvant: Post-surgery to reduce recurrence risk.
Palliative: For symptom control in advanced disease.
Techniques: IMRT (Intensity-Modulated Radiotherapy) is standard for precision.

Chemotherapy

Concurrent chemoradiotherapy: Standard for locally advanced disease.
Neoadjuvant (induction): Sometimes used to shrink tumors before surgery or radiation.
Adjuvant: Postoperative in high-risk cases (e.g., positive margins, extracapsular spread).
Palliative chemotherapy: for recurrent/metastatic disease to control symptoms and prolong survival.
Common agents:
Cisplatin, cornerstone agent often used with RT
Carboplatin as alternative when cisplatin not tolerated
5-FU, taxanes used in combination regimes

Immunotherapy

Checkpoint inhibitors (e.g., pembrolizumab, nivolumab, PD1 inhibitors)
First-line for recurrent/metastatic disease, especially in PD-L1–positive tumors.
Second-line after platinum failure.
Perioperative setting: Pembrolizumab was recently approved for resectable, locally advanced HNSCC with PD-L1 expression, marking a shift toward neoadjuvant immunotherapy
Targeted Therapy
Cetuximab: an EGFR inhibitor used In combination with radiotherapy for patients unsuitable for cisplatin. Occasionally used in recurrent/metastatic settings, often with chemotherapy.

Treatment Selection Considerations

HPV status: HPV-positive tumors may respond better to treatment and are candidates for de-escalation trials.
PD-L1 expression: guides immunotherapy use.
Performance status and comorbidities: influence choice between cisplatin, cetuximab, or immunotherapy.
Multidisciplinary team input: essential for tailoring systemic therapy.

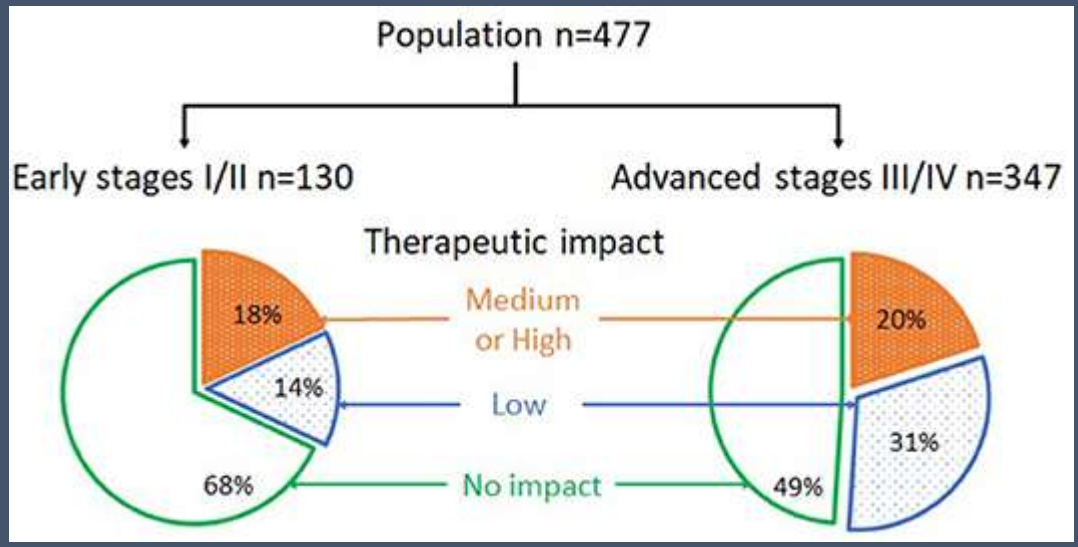
Emerging trends

De-escalation strategies for HPV-positive oropharyngeal cancers.
Personalized medicine based on molecular profiling.

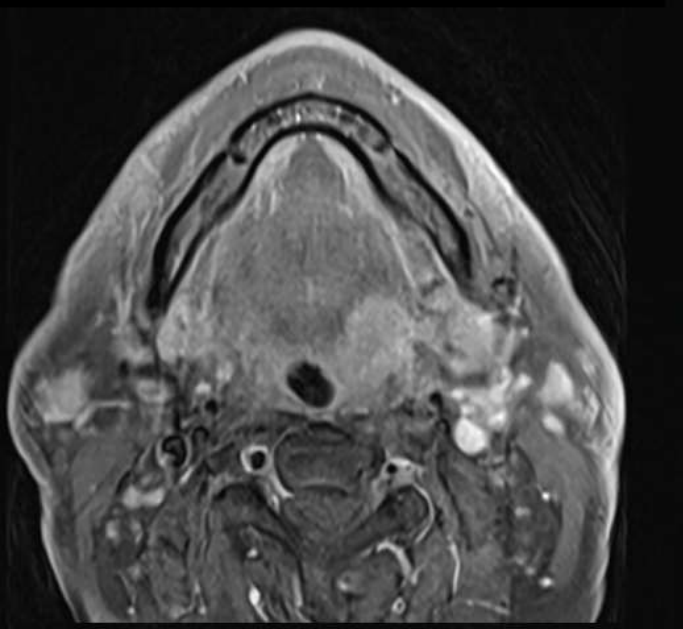
Primary staging

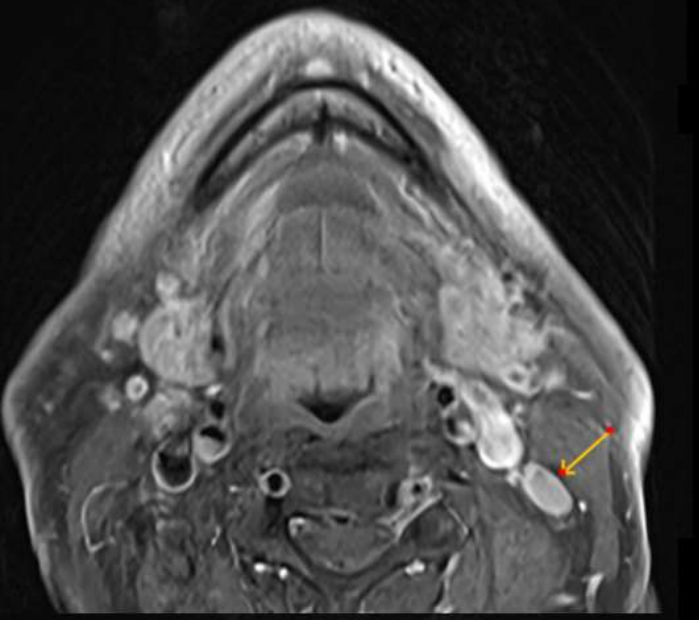
- Using FDG PET/CT in initial workup of HNSCC improves staging, provides prognostic information
- FDG PET/CT altered patient management for all disease stages and impact on survival
- FDG PET/CT driven changes were due to nodal upstaging or rarely second primary cancer or occult metastases

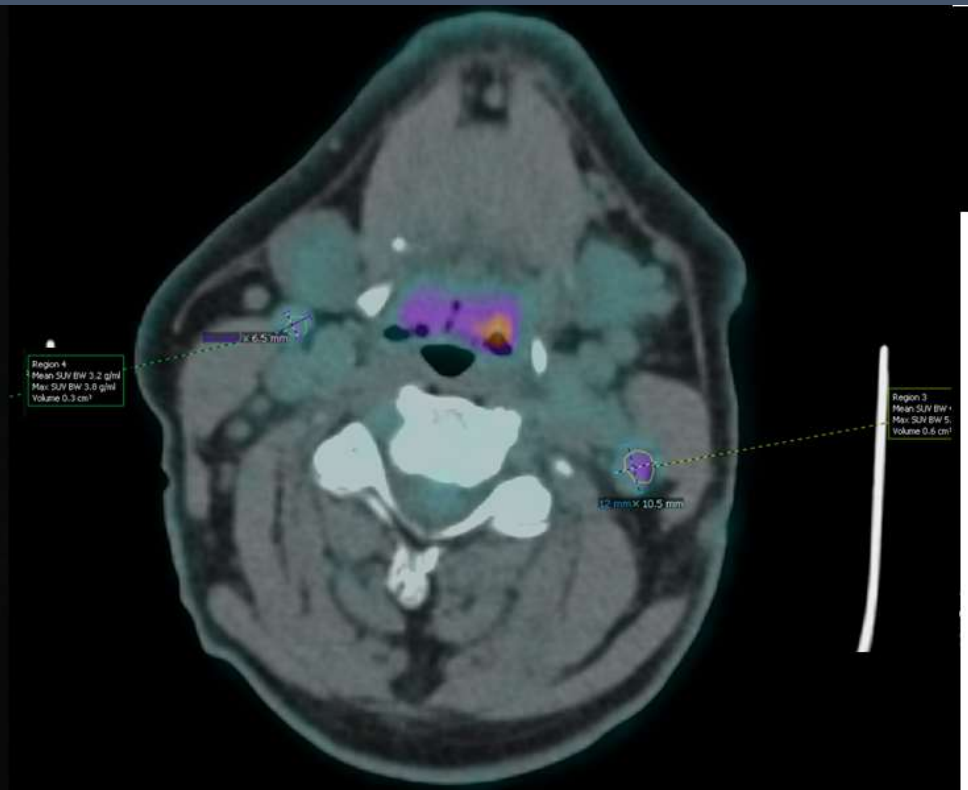
Characteristics		*n* (%)
Gender	Male	414 (86.8)
	Female	63 (13.2)
Age (average in years ± SD)	62.3 ± 9.7	
Primary location	Oral Cavity	99 (20.8)
	Oropharynx	187 (39.2)
	Larynx	103 (21.6)
	Hypopharynx	88 (18.4)
CWU staging	Early stages I/II	130 (27.3)
	Advanced stages III/IV	347 (73.7)

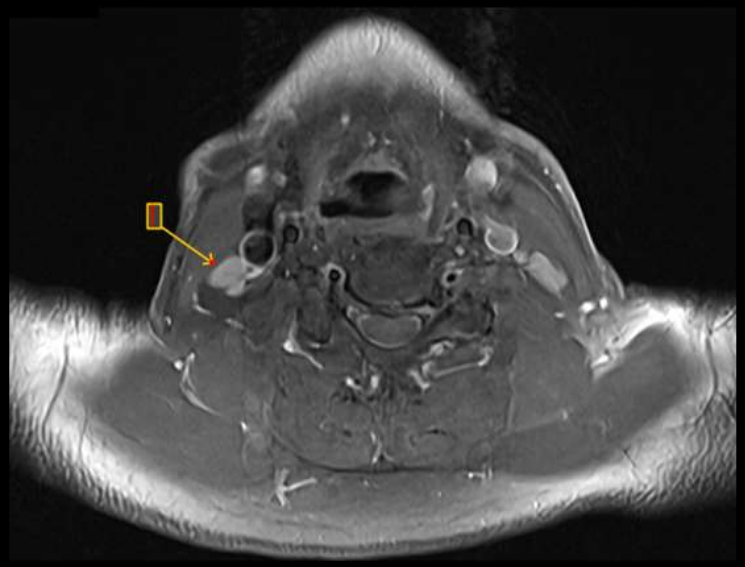


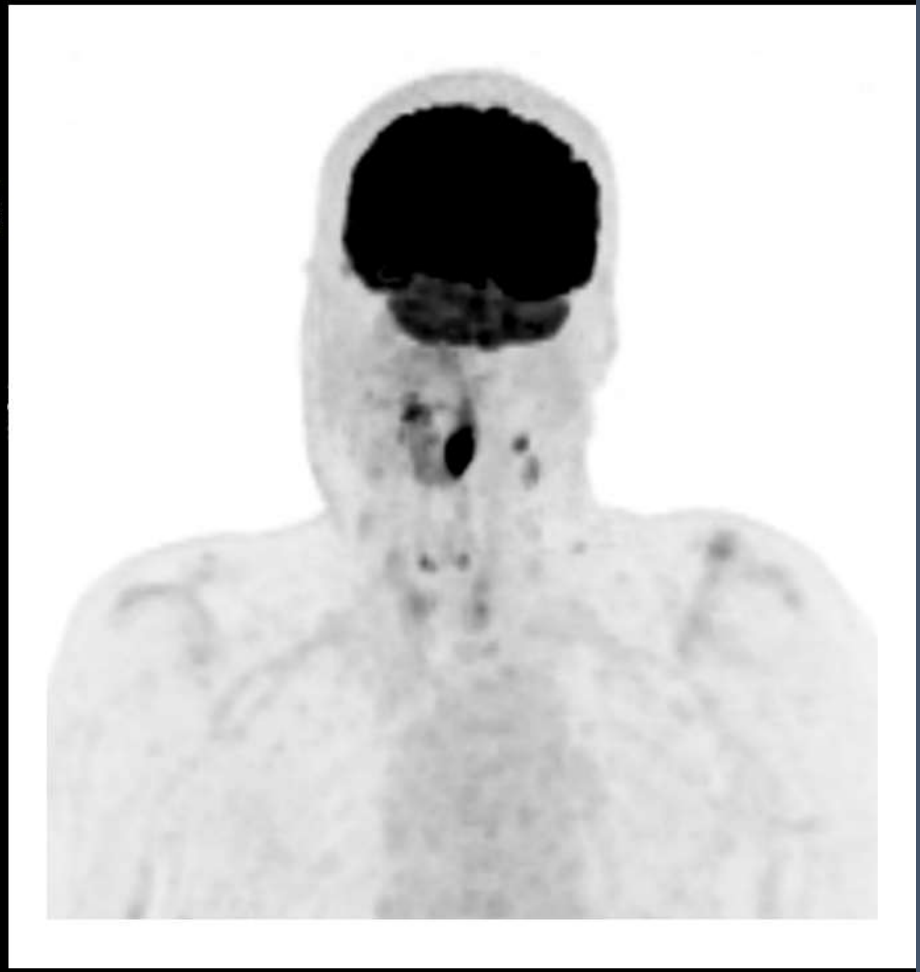
Leclere Jean-Christophe et al, Integration of 18-FDG PET/CT in the Initial Work-Up to Stage Head and Neck Cancer: Prognostic Significance and Impact on Therapeutic Decision Making. Frontiers in Medicine 2020 Vol 7 URL=https://www.frontiersin.org/articles/10.3389/fmed.2020.00273



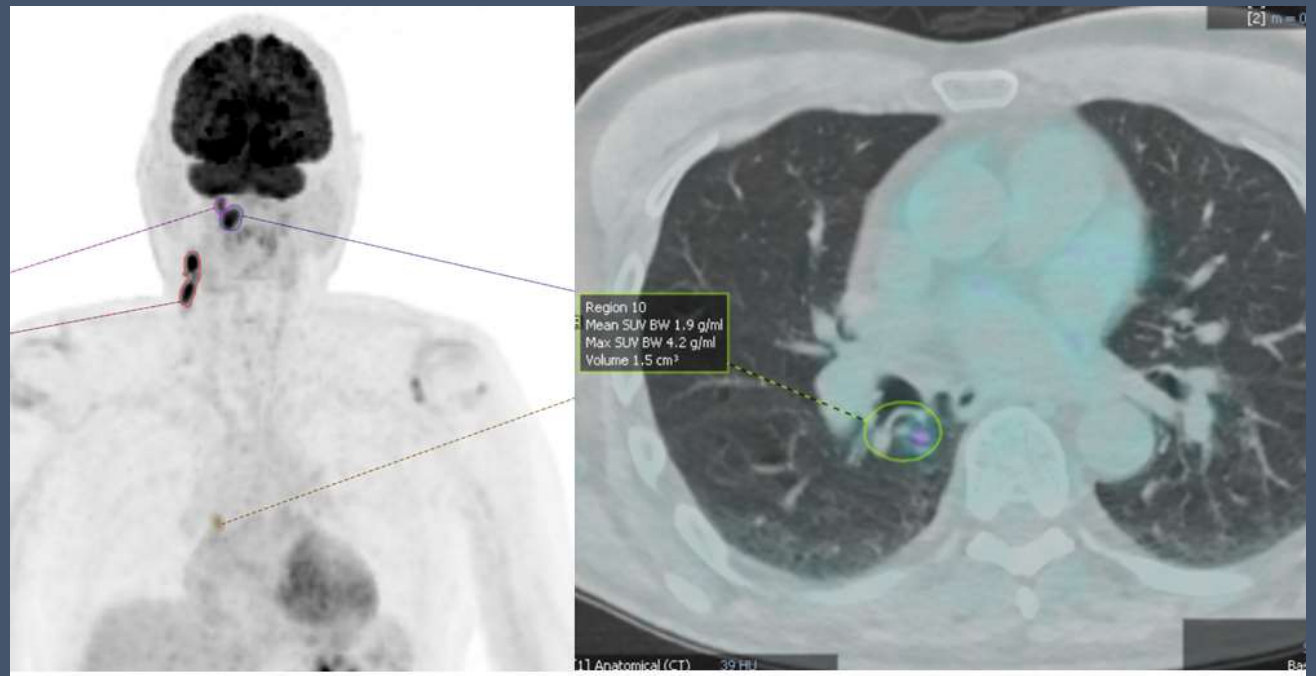


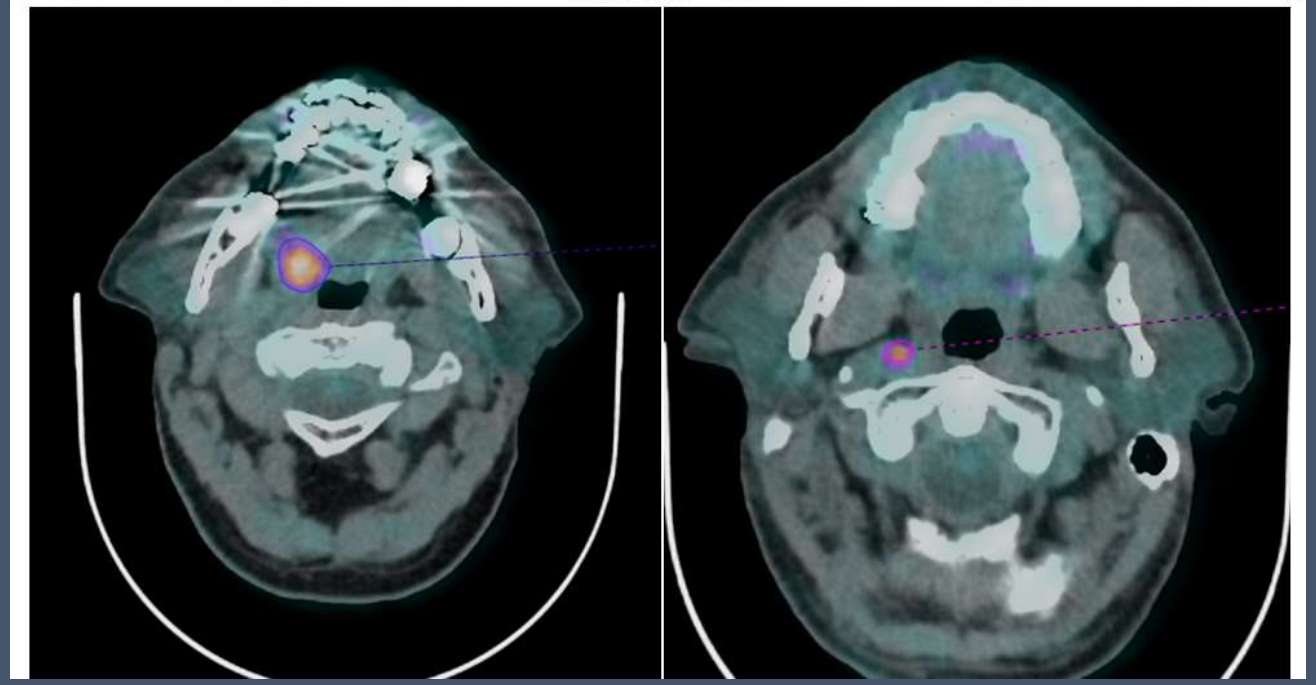

Region 4
Mean SUV BW 3.2 g/ml
Max SUV BW 3.8 g/ml
Volume 0.3 cm³
Region 3
Max SUV BW 5.
Volume 0.6 cm³

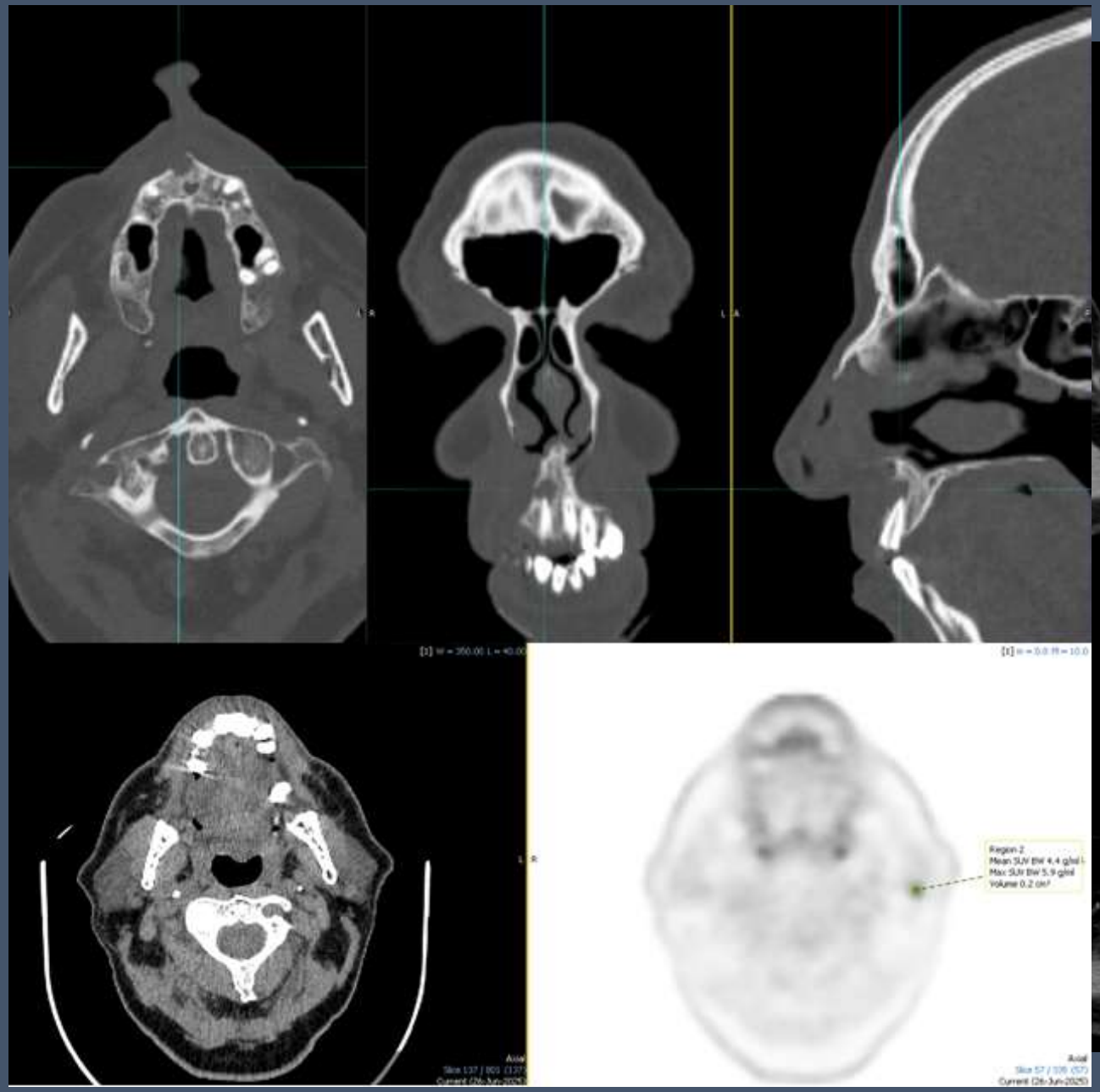


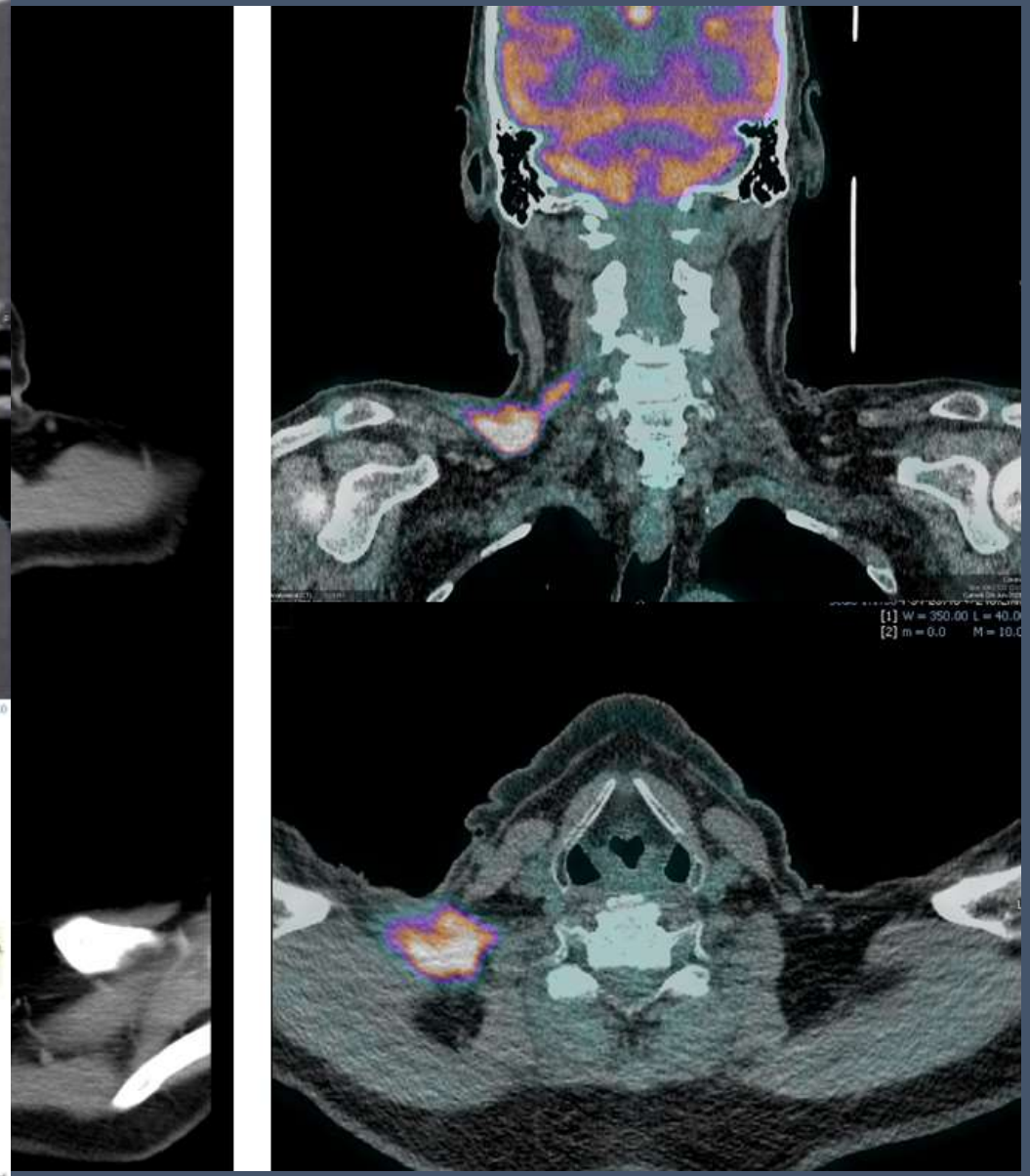


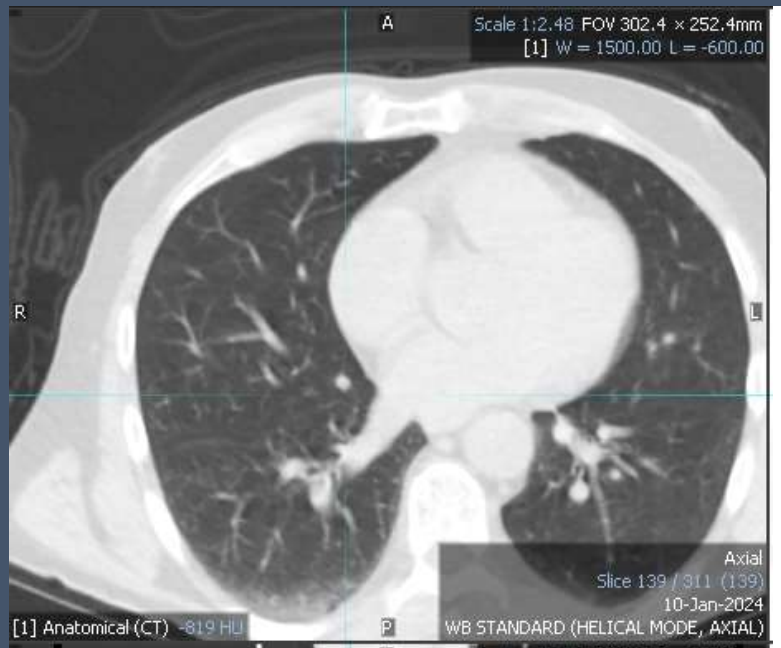
MRI/CT	FDG PET/CT
Short-axis diameter ≥10 mm is generally considered suspicious	
Level II nodes (subdigastric region): threshold increases to ≥11 mm.	
Lateral retropharyngeal nodes: ≥5 mm.	
Medial retropharyngeal nodes: any visible node is abnormal.	
A cluster of three or more borderline nodes (each ≥8 mm, or >9 mm in level II) also raises concern.	
Round nodes (long-to-short axis ratio <2) are more suspicious than oval ones.	
Necrosis or cystic change: high T2 signal intensity with rim enhancement is highly specific for metastasis.	Necrotic nodes can be missed on PET so careful review of CT is needed. Small volume nodal disease (focus of 5mm or smaller) will be missed on PET, typically a lesion of about 10mm will identify of metastatic or not
Loss of fatty hilum or heterogeneous enhancement may also indicate malignancy.	
Extranodal Extension (ENE) signs include irregular nodal margins, capsular enhancement, and infiltration into adjacent fat or muscle—all suggestive of aggressive disease.	ENE can be difficult on non-ceCT but increasing SUVmax level increases likelihood of ENE
Diffusion-weighted imaging (DWI): restricted diffusion (low ADC values) can support malignancy.	FDG avid uptake (criteria vary) SUVmax >2.5-3.0, asymmetry in uptake, clustering of FDG avid nodes. The probability of neck metastasis increases with increasing SUVmax values and higher T stage of the primary. The probability of occult metastases increases above an SUVmax of approximately 10
DOI:10.2214/AJR.12.8960	https://doi.org/10.3390/cancers16172954;doi:10.1016/j.tripleo.2009.07.054;https://doi.org/10.1016/j.oooo.2019.09.005 https://doi.org/10.1155/2020/6241637

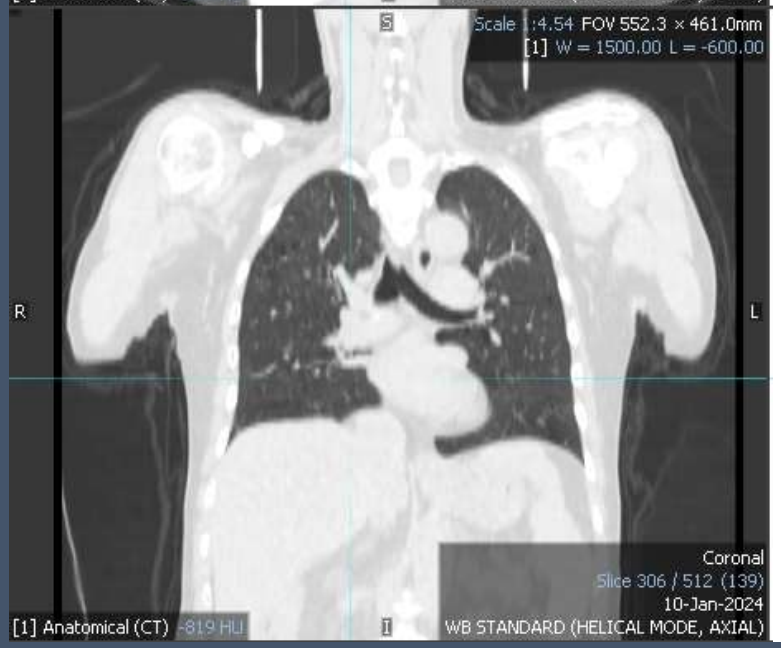

Region 10
Mean SUV BW 1,9 g/ml
Max SUV BW 4,2 g/ml
Volume 1,5 cm³

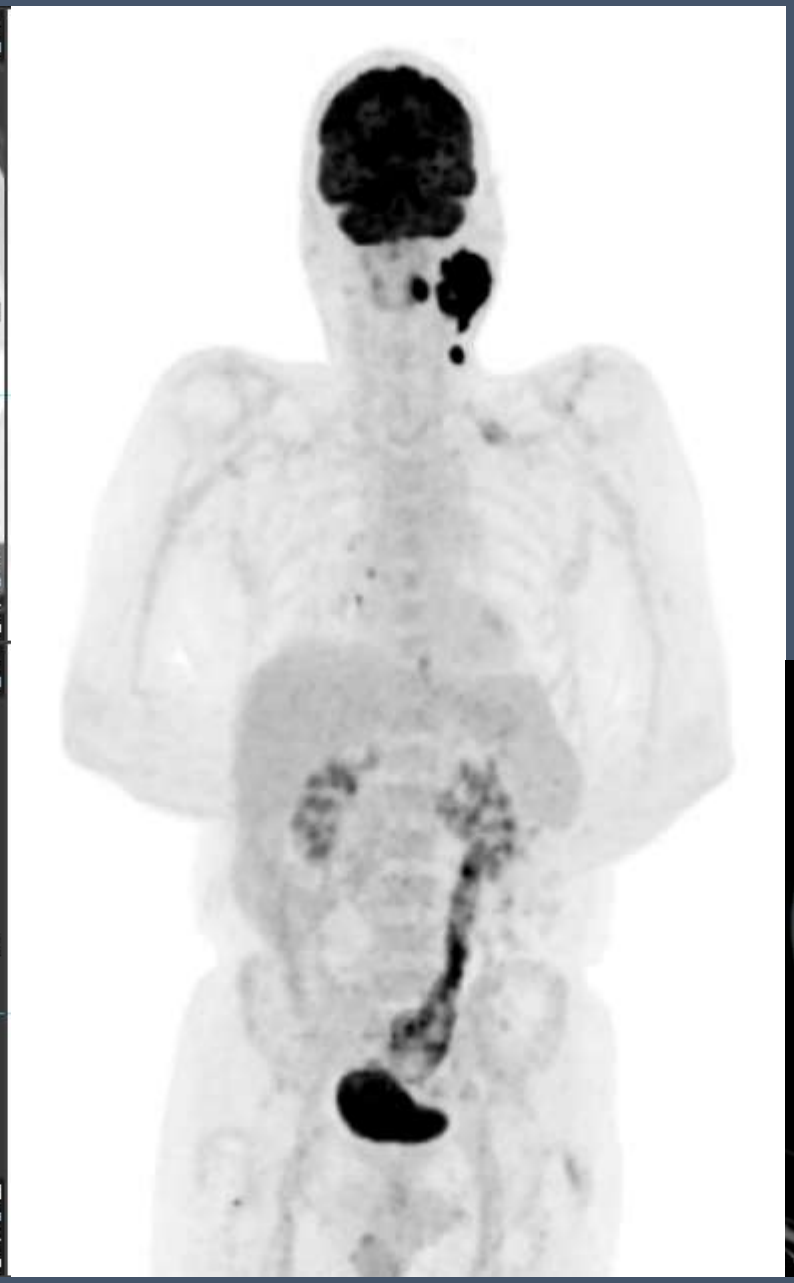


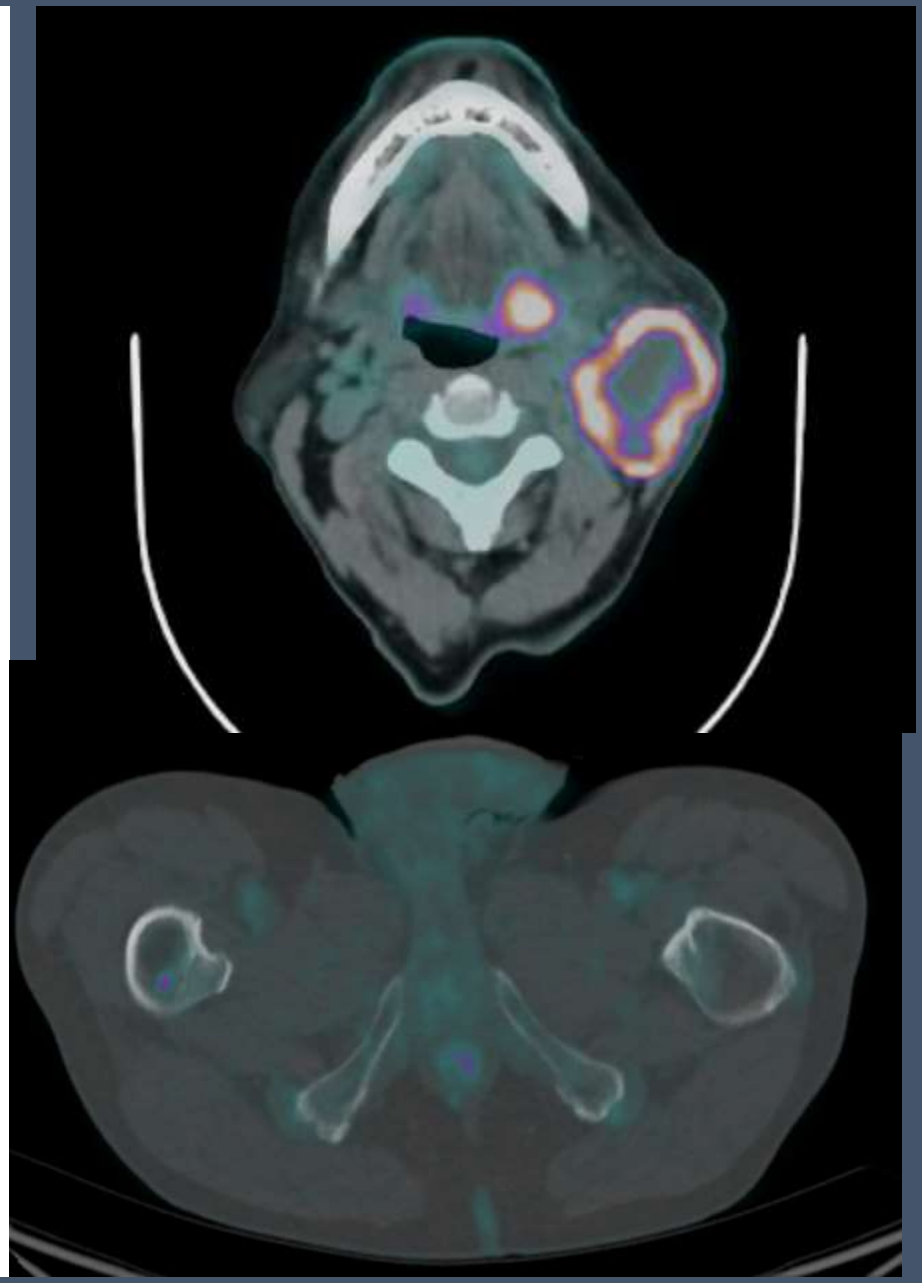

Region 2
Mean SUV BW 4.4 g/ml
Max SUV BW 5.9 g/ml
Volume 0.2 cm³
Axial

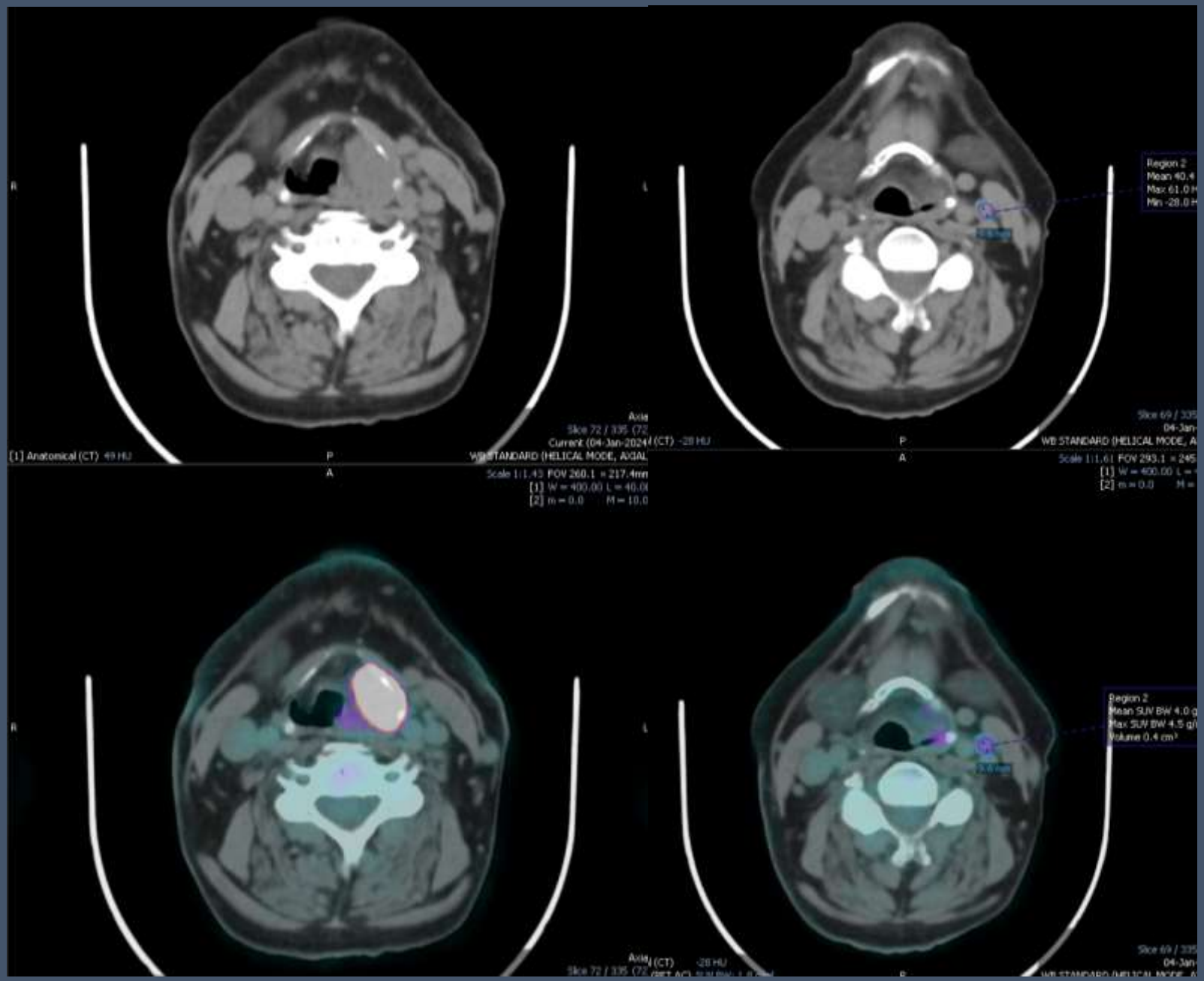


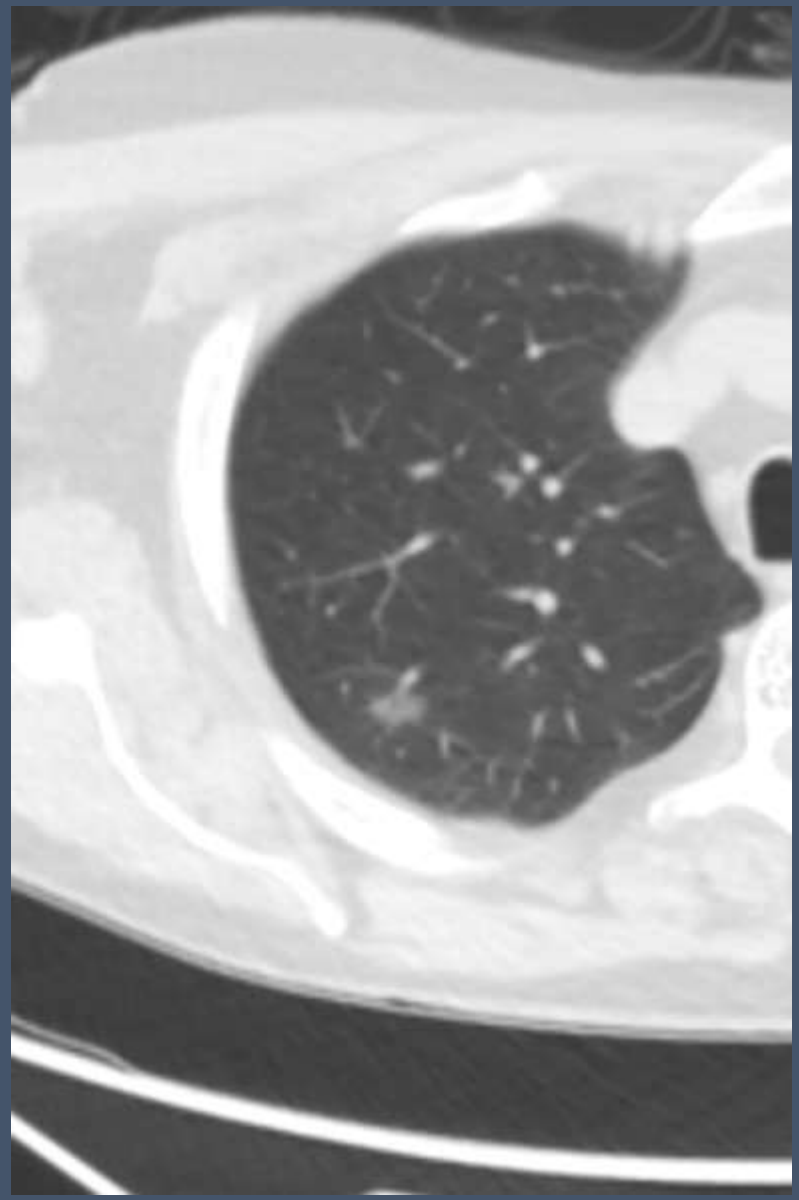

A
Scale 1:2.48 FOV 302.4 × 252.4mm
[1] W = 1500.00 L = -600.00
R
L
Axial
Slice 139 / 311 (139)
10-Jan-2024
[1] Anatomical (CT) -819 HU
P
WB STANDARD (HELICAL MODE, AXIAL)

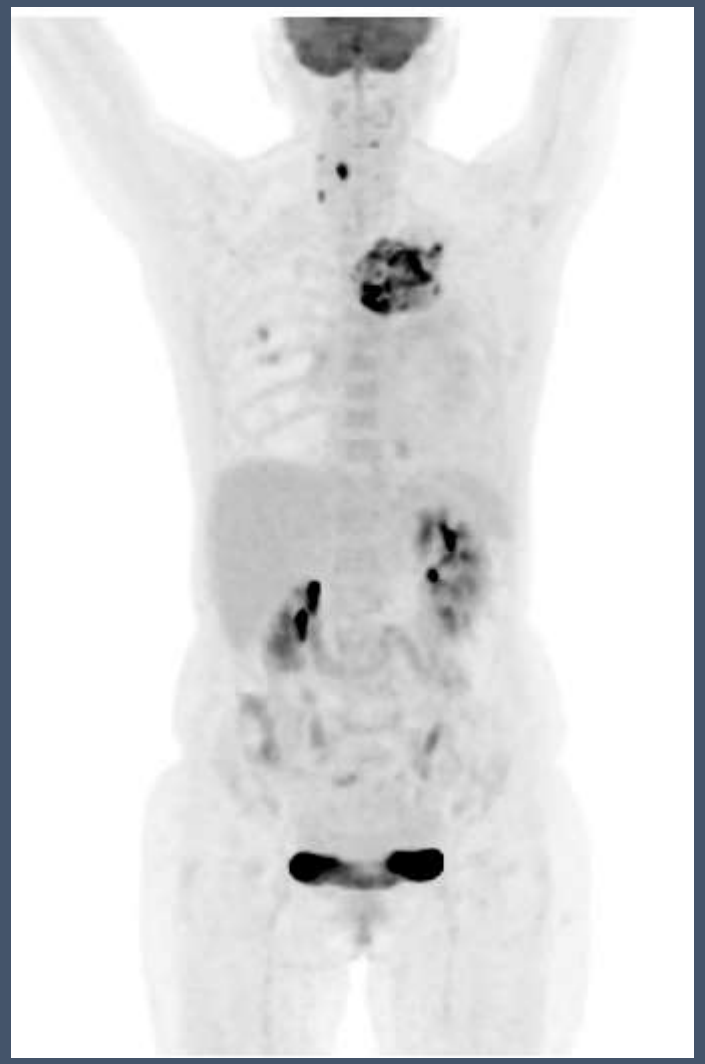

S
Scale 1:4.54 FOV 552.3 × 461.0mm
[1] W = 1500.00 L = -600.00
R
L
Coronal
Slice 306 / 512 (139)
10-Jan-2024
[1] Anatomical (CT) -819 HU
I
WB STANDARD (HELICAL MODE, AXIAL)

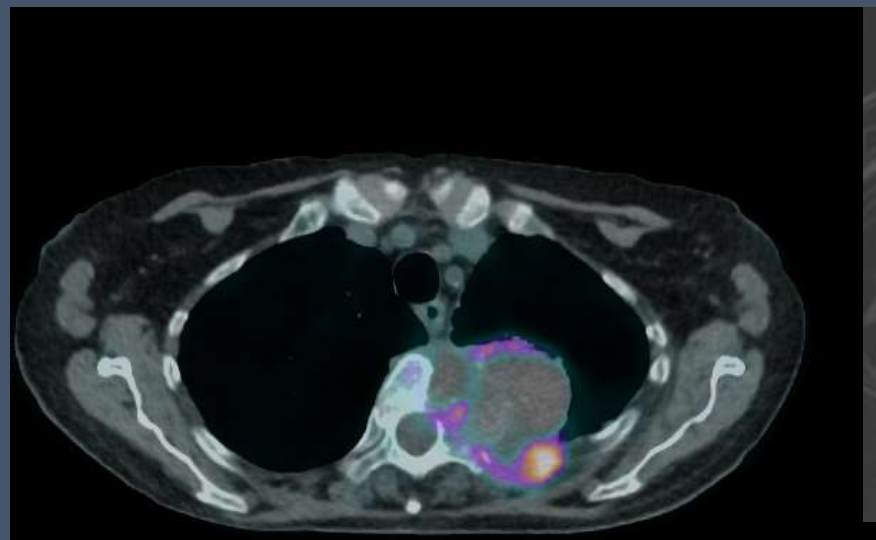


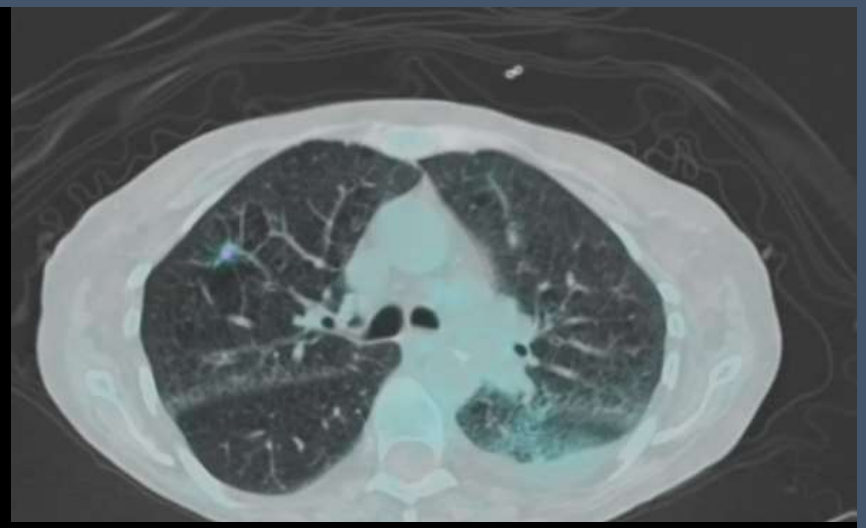


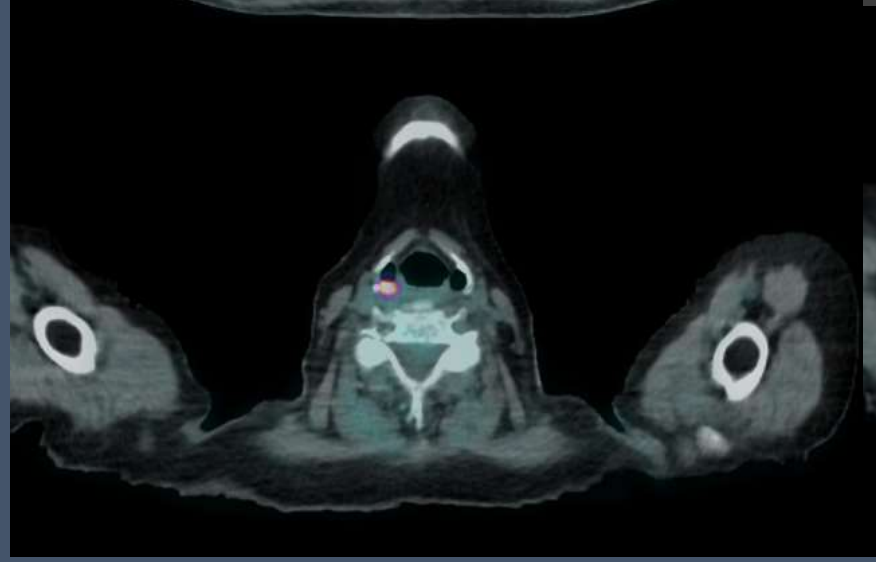


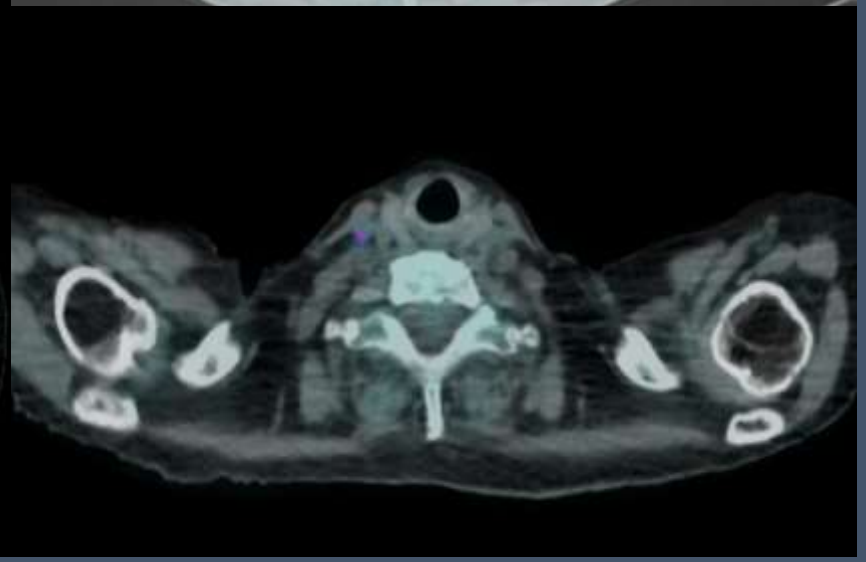


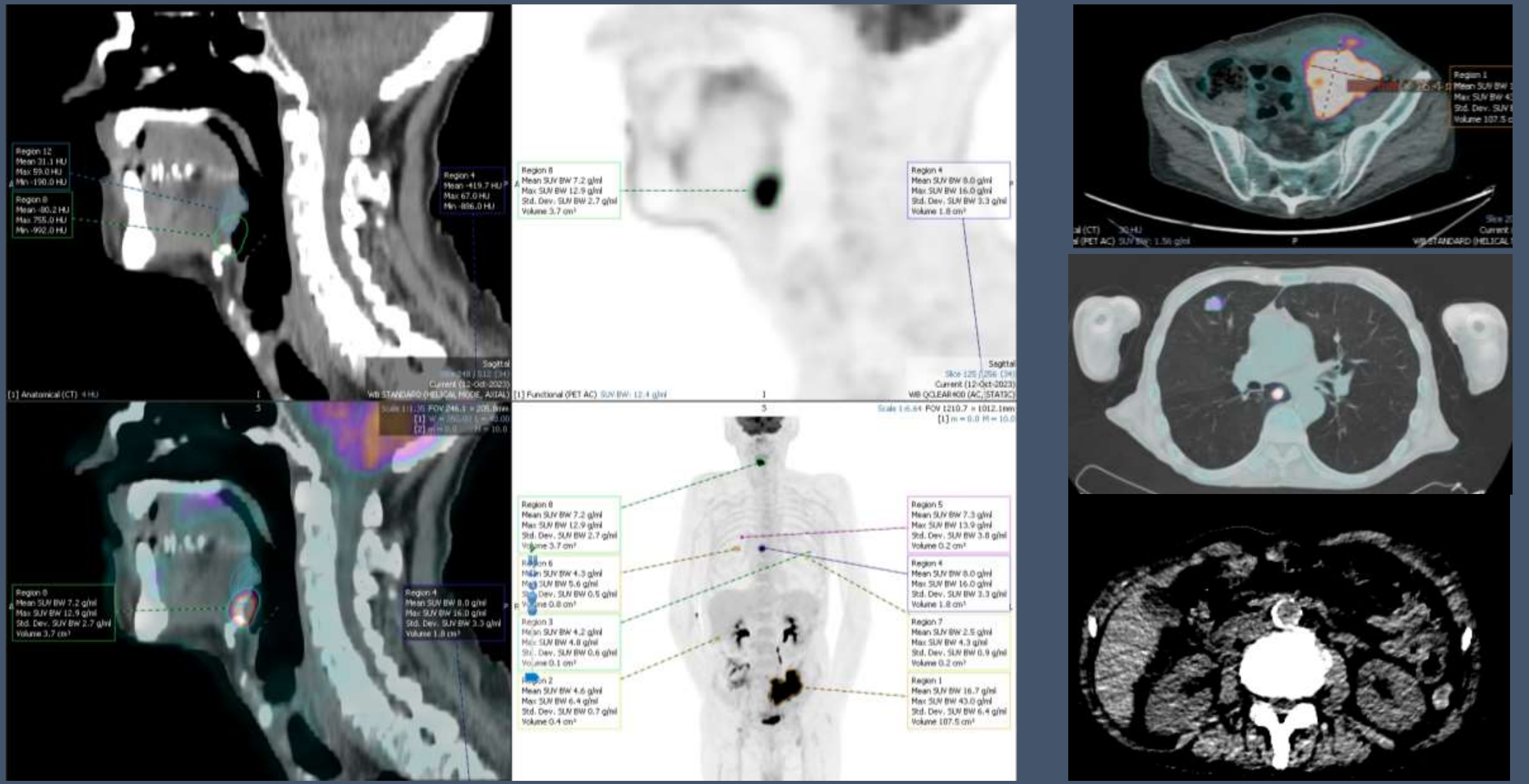




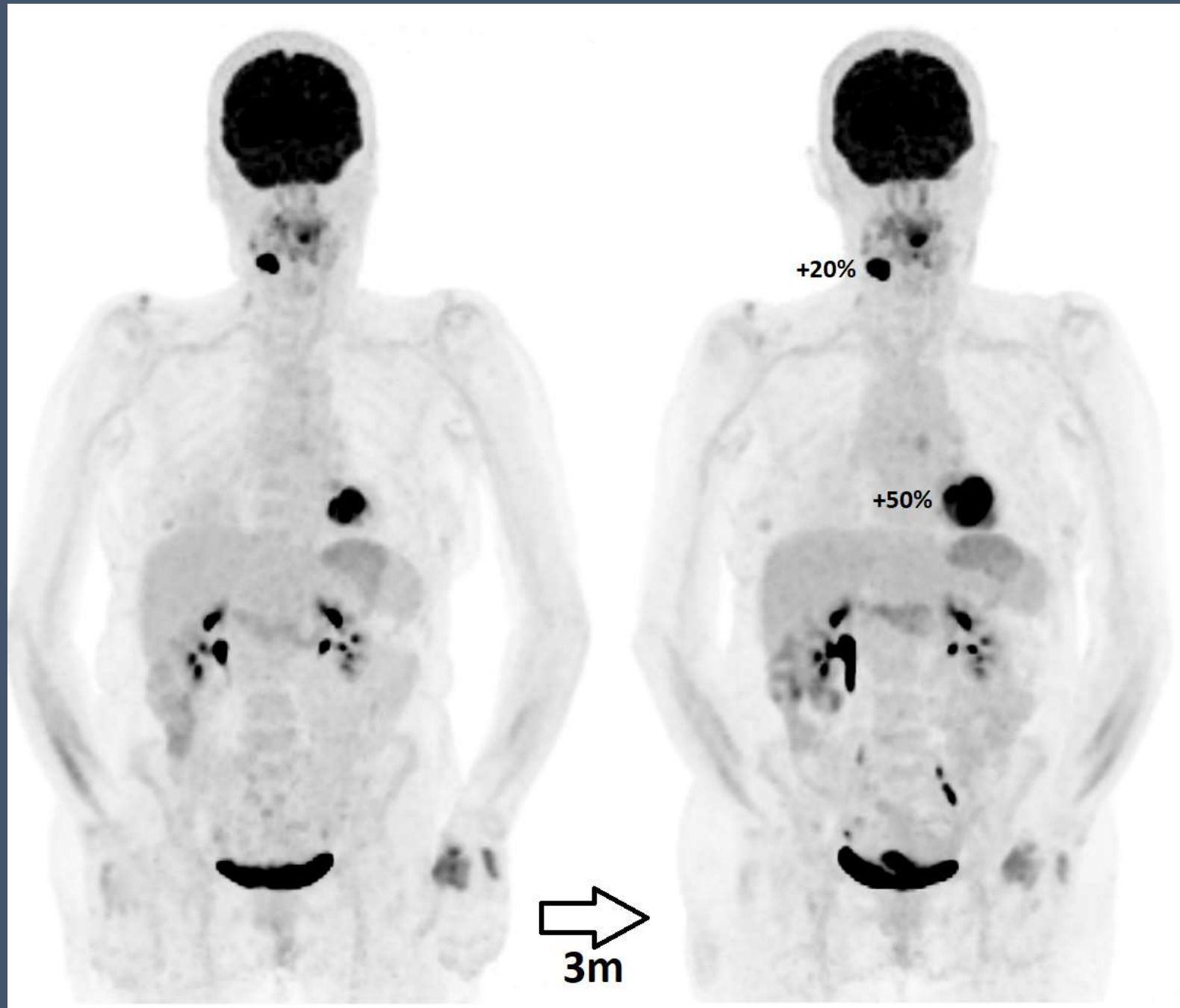







Region 12
Mean 31.1 HU
Max 59.0 HU
Min -190.0 HU
Region 8
Mean -80.2 HU
Max 755.0 HU
Min -992.0 HU
Region 4
Mean -419.7 HU
Max 67.0 HU
Min -886.0 HU
[1] Anatomical (CT)
Region 8
Mean SUV BW 7.2 g/ml
Max SUV BW 12.9 g/ml
Std. Dev. SUV BW 2.7 g/ml
Volume 3.7 cm³
Region 4
Mean SUV BW 8.0 g/ml
Max SUV BW 16.0 g/ml
Std. Dev. SUV BW 3.3 g/ml
Volume 1.8 cm³
[1] Functional (PET AC) SUV BW: 12.4 g/ml
Region 8
Mean SUV BW 7.2 g/ml
Max SUV BW 12.9 g/ml
Std. Dev. SUV BW 2.7 g/ml
Volume 3.7 cm³
Region 4
Mean SUV BW 8.0 g/ml
Max SUV BW 16.0 g/ml
Std. Dev. SUV BW 3.3 g/ml
Volume 1.8 cm³
Region 6
Mean SUV BW 4.3 g/ml
Max SUV BW 5.6 g/ml
Std. Dev. SUV BW 0.5 g/ml
Volume 0.8 cm³
Region 3
Mean SUV BW 4.2 g/ml
Max SUV BW 4.8 g/ml
Std. Dev. SUV BW 0.6 g/ml
Volume 0.1 cm³
Region 2
Mean SUV BW 4.6 g/ml
Max SUV BW 6.4 g/ml
Std. Dev. SUV BW 0.7 g/ml
Volume 0.4 cm³
Region 5
Mean SUV BW 7.3 g/ml
Max SUV BW 13.9 g/ml
Std. Dev. SUV BW 3.8 g/ml
Volume 0.2 cm³
Region 7
Mean SUV BW 2.5 g/ml
Max SUV BW 4.3 g/ml
Std. Dev. SUV BW 0.9 g/ml
Volume 0.2 cm³
Region 1
Mean SUV BW 16.7 g/ml
Max SUV BW 43.0 g/ml
Std. Dev. SUV BW 6.4 g/ml
Volume 107.5 cm³

Region 1


+20%
+50%
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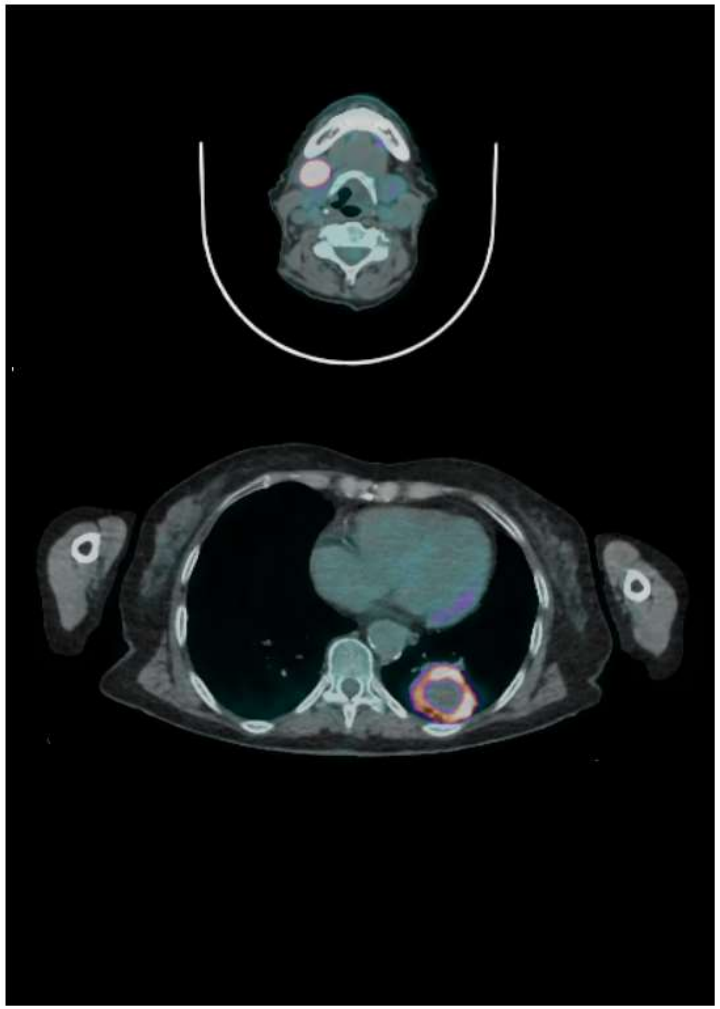

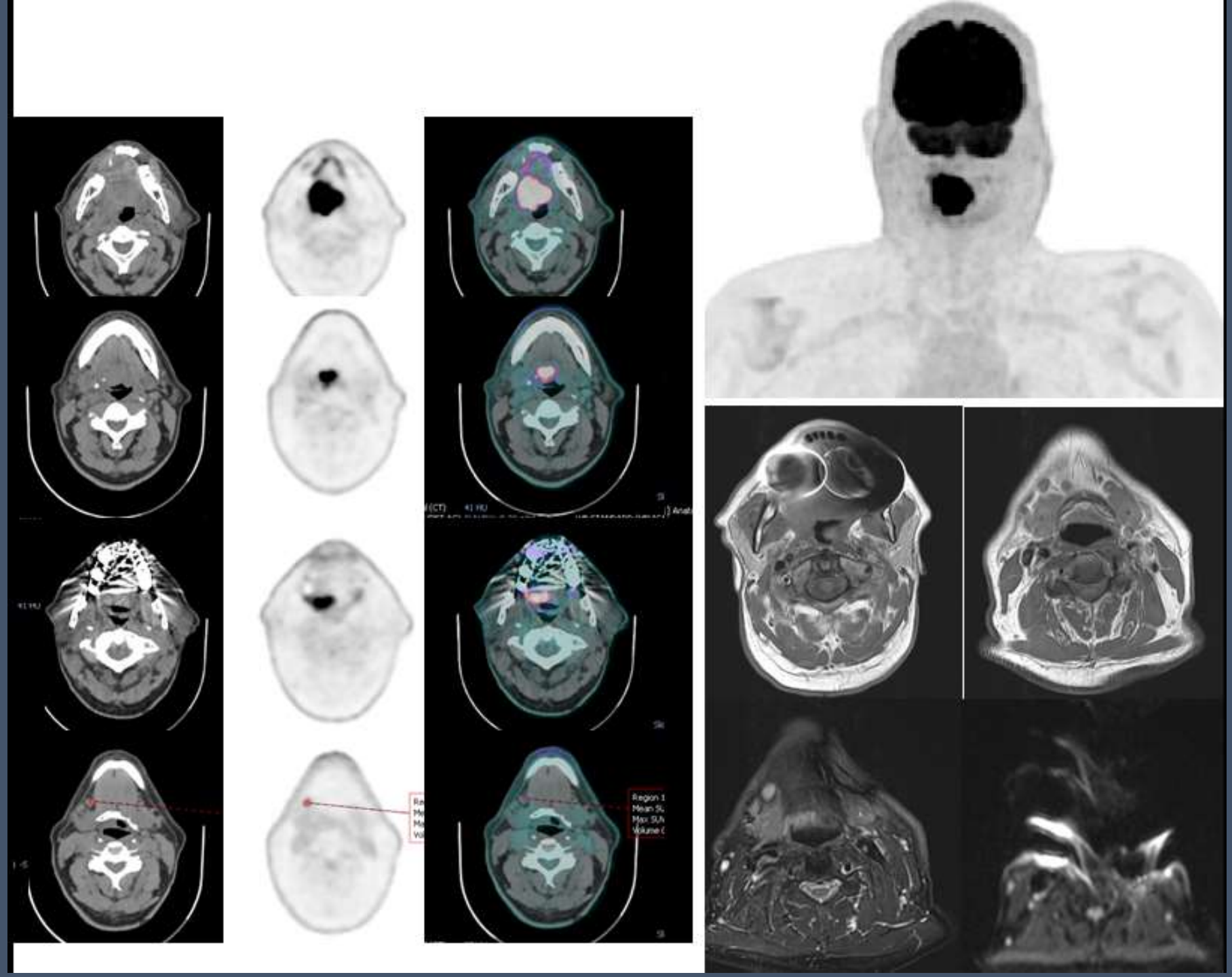

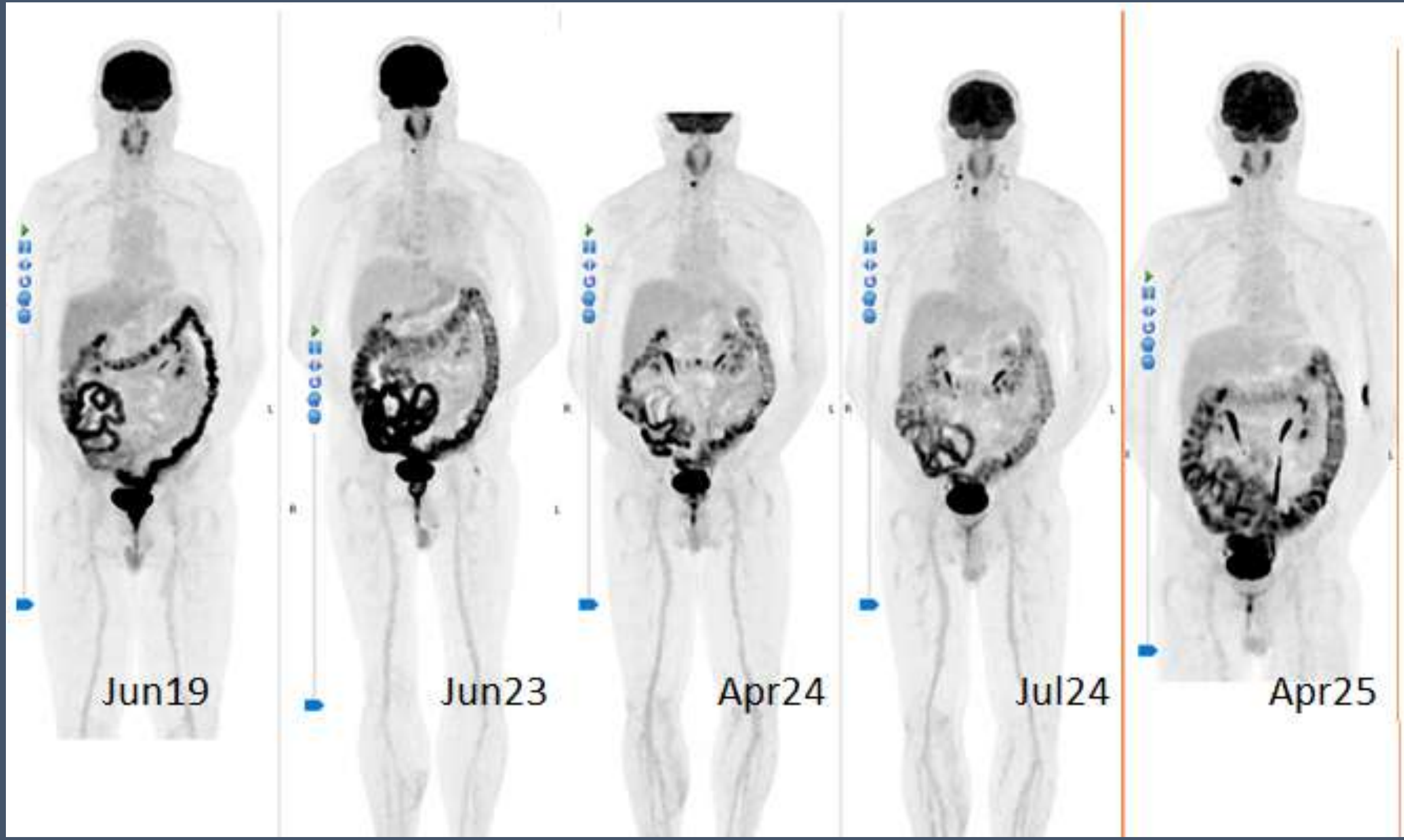
Jun19
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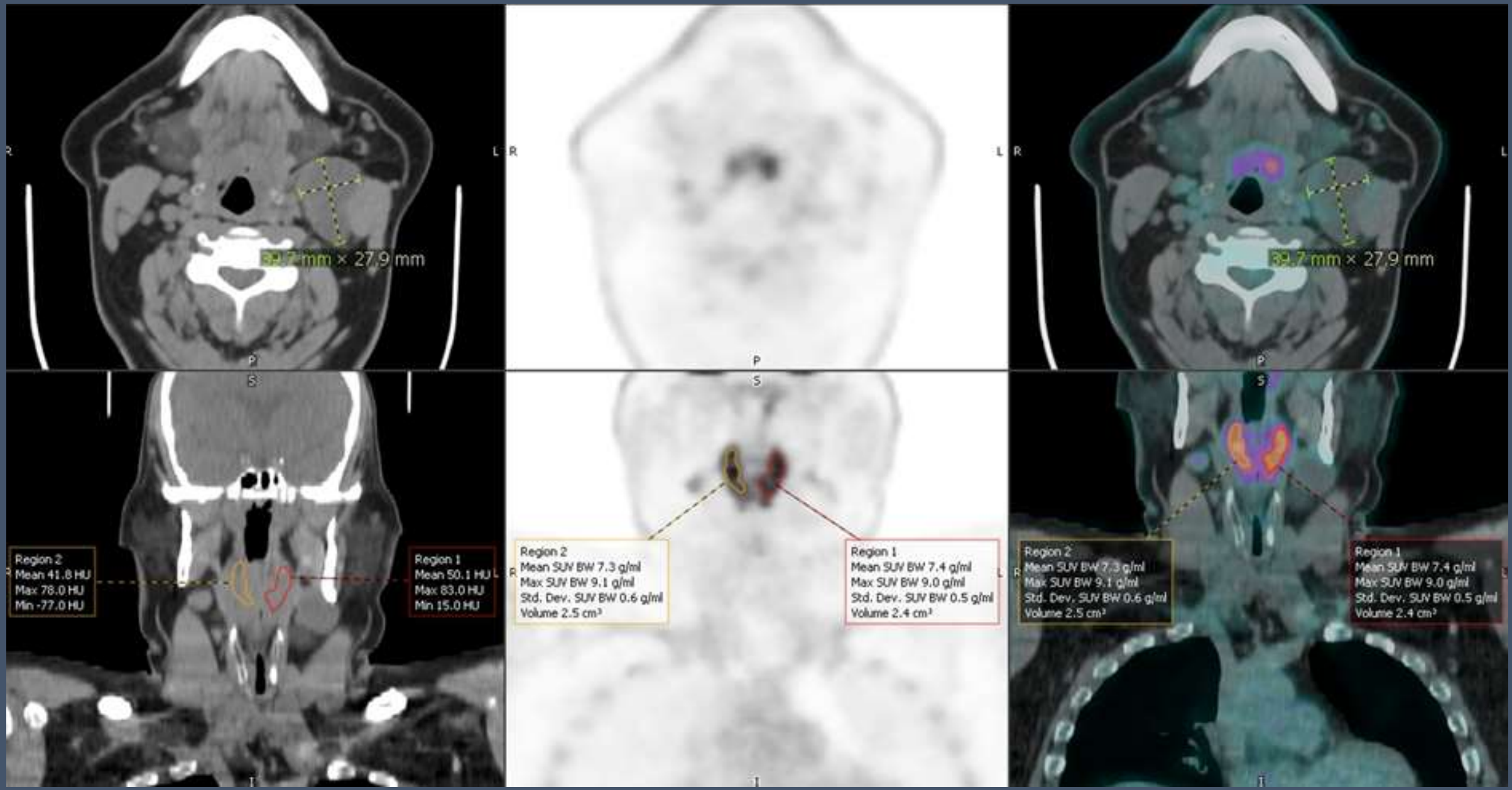
Strategy for FDG PET/CT use in CUP

- Use US nodal biopsy for diagnosis and HPV status
- ceCT and MRI can identify up to 44% of occult tumors
- PET/CT is the most sensitive modality for detection of CUP, perform after MRI and prior to panendoscopy
- Knowing HPV status can help at the time of imaging reporting
- Ratio >1.6 to raise suspicion of palatine tonsil disease
- 68Ga-FAPI PET/CT outperforms 18F-FDG PET/CT in detecting primary lesions

- Gitta Madani, Zoya Arain, Zaid Awad The radiological unknown primary of the head and neck: Recommendations for imaging strategies based on a systematic review Clin Otolaryngology Volume49, Issue1 January 2024 Pages 16-28 https://doi.org/10.1111/coa.14111
- Pencharz D et al Palatine tonsil SUVmax on FDG PET-CT as a discriminator between benign and malignant tonsils in patients with and without head and neck squamous cell carcinoma of unknown primary Clin Rad VOLUME 74, ISSUE 2, P165.E17-165.E23, DOI:https://doi.org/10.1016/j.crad.2018.10.007
- Bingxin Gu et al Imaging of Tumor Stroma Using 68Ga-FAPI PET/CT to Improve Diagnostic Accuracy of Primary Tumors in Head and Neck Cancer of Unknown Primary: A Comparative Imaging Trial, Journal of Nuclear Medicine Jan 2024, jnumed.123.266556; DOI: 10.2967/jnumed.123.266556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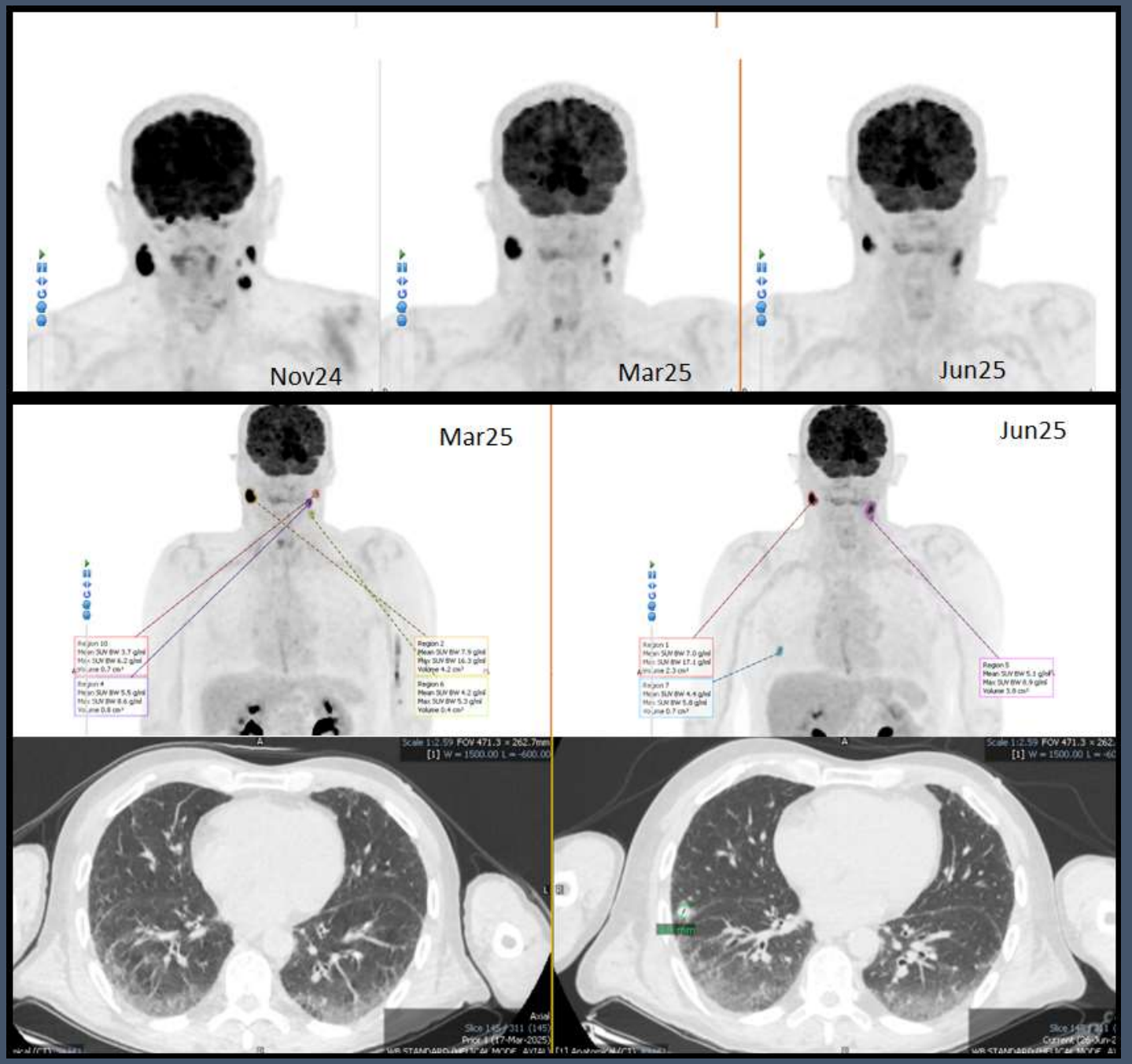
Region 2
Mean 41.8 HU
Max 78.0 HU
Min -77.0 HU
Region 1
Mean 50.1 HU
Max 83.0 HU
Min 15.0 HU
Region 2
Mean SUV BW 7.3 g/ml
Max SUV BW 9.1 g/ml
Std. Dev. SUV BW 0.6 g/ml
Volume 2.5 cm³
Region 1
Mean SUV BW 7.4 g/ml
Max SUV BW 9.0 g/ml
Std. Dev. SUV BW 0.5 g/ml
Volume 2.4 cm³
39.7 mm × 27.9 mm
Region 2
Mean SUV BW 7.3 g/ml
Max SUV BW 9.1 g/ml
Std. Dev. SUV BW 0.6 g/ml
Volume 2.5 cm³
Region 1
Mean SUV BW 7.4 g/ml
Max SUV BW 9.0 g/ml
Std. Dev. SUV BW 0.5 g/ml
Volume 2.4 cm³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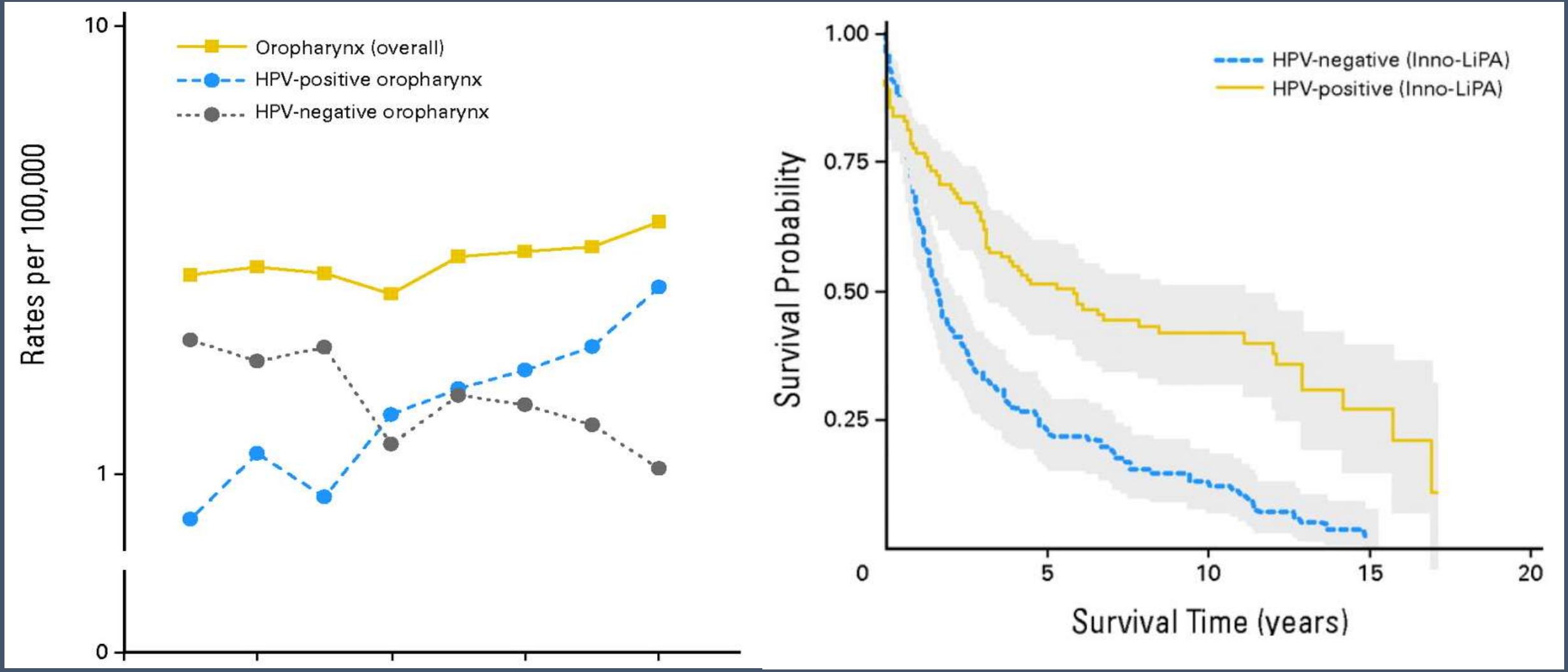
HPV+ vs HPV – disease



Anil K. Chaturvedi et al., Human Papillomavirus and Rising Oropharyngeal Cancer Incidence in the United States. JCO 29, 4294-4301(2011). DOI:10.1200/JCO.2011.36.4596

HPV+ vs HPV – disease

HPV negative	HPV positive
Linked to tobacco and alcohol use. Strong correlation with smoking history.	Primarily caused by high-risk HPV strains, especially HPV-16
More common in the oral cavity, larynx, and hypopharynx.	Strongly associated with oropharyngeal sites (tonsils, base of tongue).
More common in older individuals (median ~66 years)	Tends to affect younger, non-smoking males.
Frequent TP53 mutations and EGFR overexpression. Higher mutational burden and genomic instability.	Overexpression of p16 (used as a surrogate marker). Fewer genetic mutations; often lacks TP53 mutations. More immune-infiltrated tumor microenvironment.
More likely to present with larger primary tumors and locally advanced disease.	Often presents with small primary tumors but large cystic lymph nodes.
Poorer prognosis: 5-year survival around 25–40%. More aggressive treatment often required.	Better response to radiation and chemotherapy. Excellent prognosis: 5-year survival rates of 85–90%. De-escalation of therapy is being explored to reduce long-term toxicity.

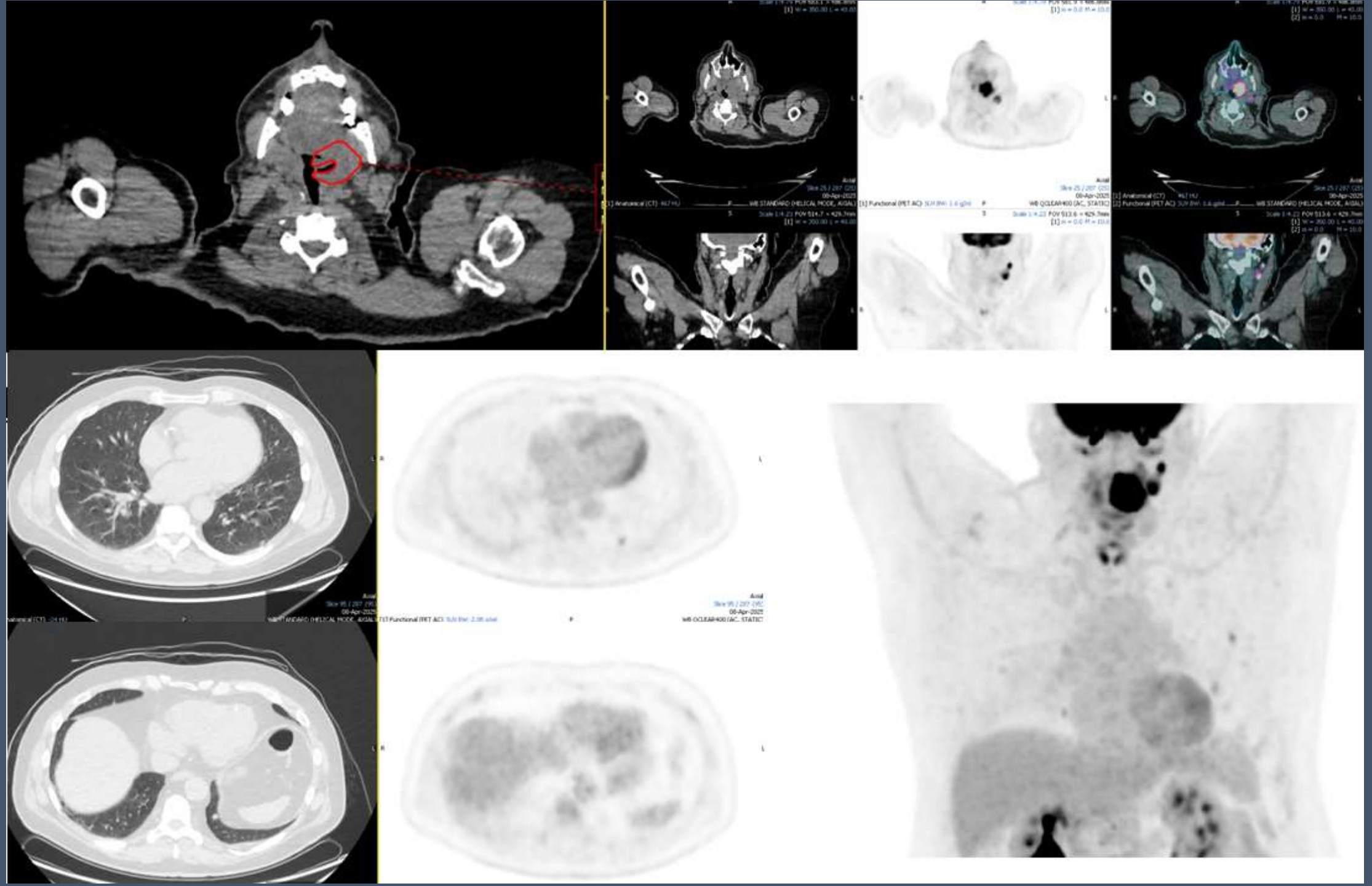
HPV and head and neck cancer

- TNM for HPV+ HNSCC differs from HPV- due to high survival rates in previously called stage IV disease
- N staging depends on knowledge of HPV status
- Extracapsular spread is a clinical finding but imaging can offer supportive evidence, both on MRI and PET/CT
- Extra nodal extension has huge prognostic significance for HPV- disease
- Over 90% of CUP on neck nodal biopsy are HPV related oropharyngeal SCC

Christine M. Glastonbury Critical Changes in the Staging of Head and Neck Cancer Radiology: Imaging Cancer Vol 2 No 1 Jan 31 2020
https://doi.org/10.1148/rycan.2019190022

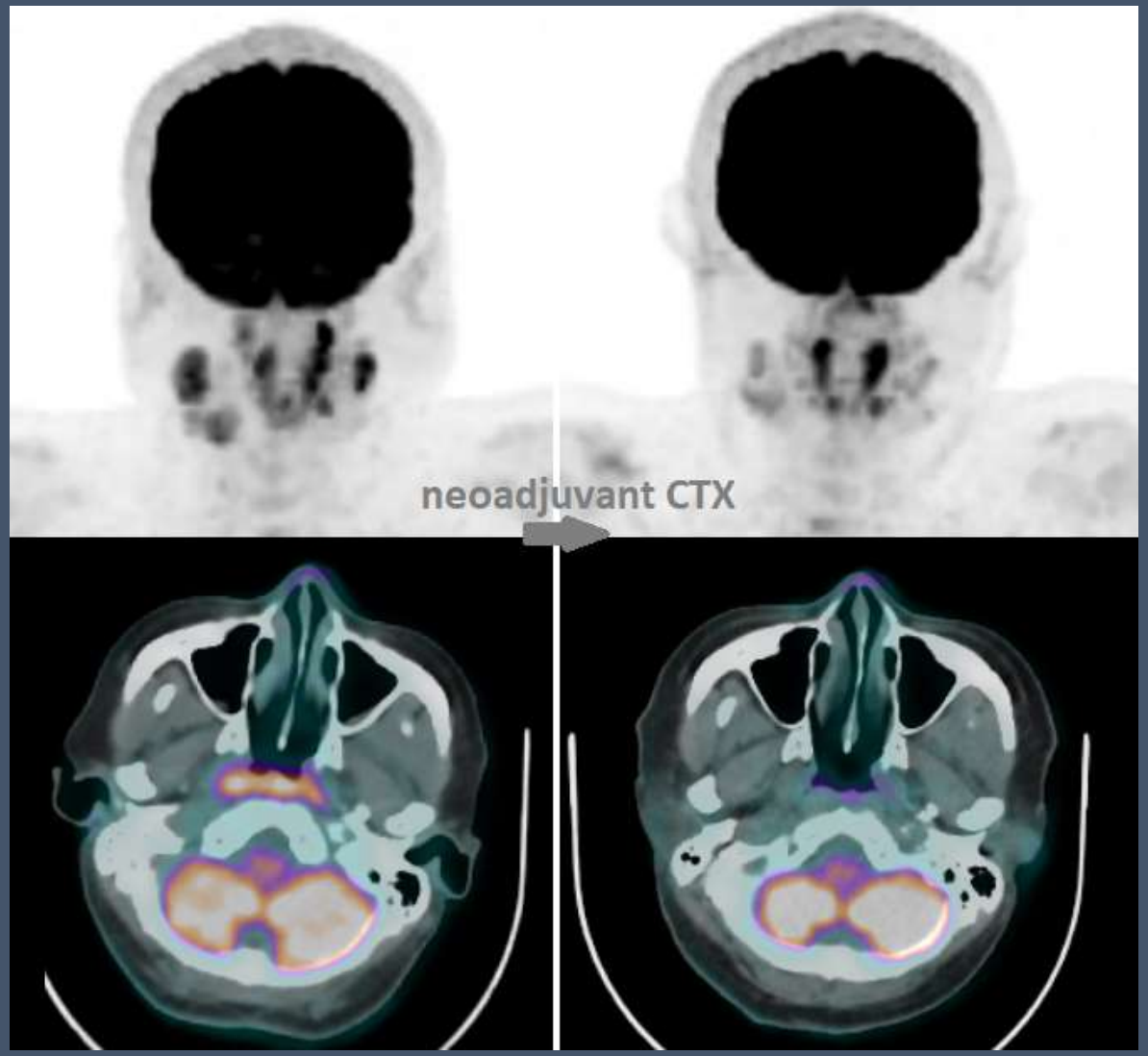
HPV and head and neck cancer

- A move to minimise treatment toxicity, whilst maintaining disease control
- Whilst the negative predictive value (NPV) of a post treatment PET/CT has been well demonstrated with the PET-NECK trial the positive predictive value (PPV) is less well characterised
- In HPV positive patients treated with chemo-radiotherapy treatment (CRT) the PPV is significantly lower compared to the HPV negative patients, and this divergence is even more pronounced with single modality radiotherapy.
- HPV positive patients take longer to achieve a complete response on imaging and a strategy of surveillance may be more appropriate than surgery.



Nasopharyngeal carcinoma

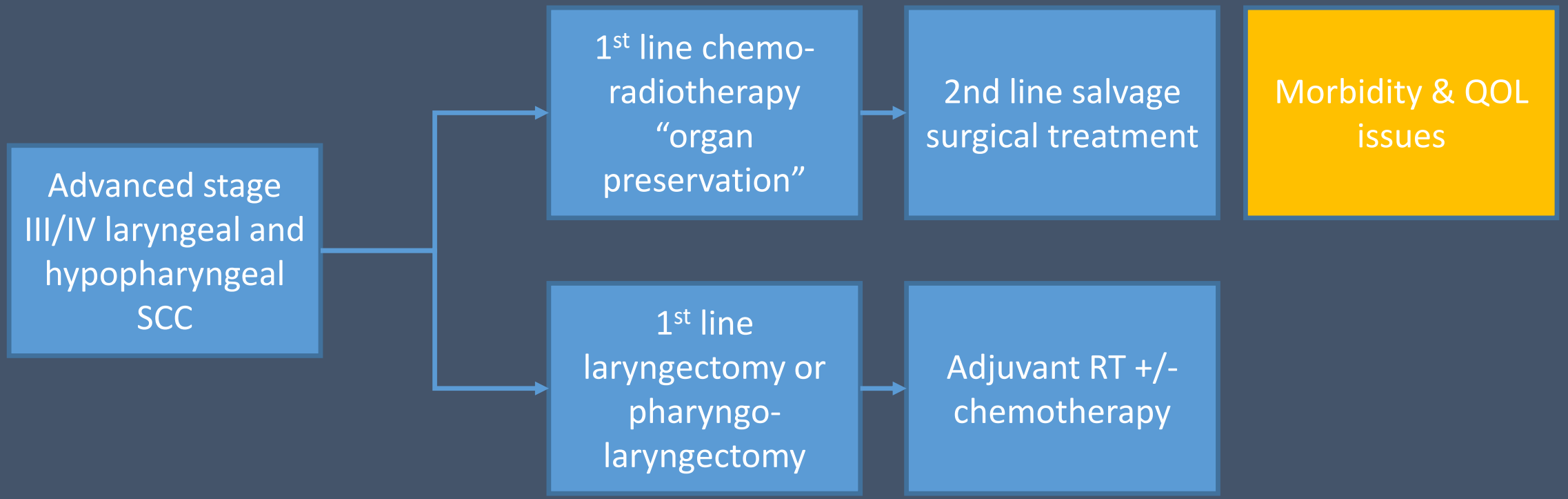
- Amongst the most aggressive of the head and neck cancers
- High rates of locally invasive disease, metastatic spread, treatment failure
- Can metastasise early
- Current mainstay of treatment is chemoradiotherapy
- Challenging to deliver radiotherapy
- Half of recurrences occur in the 1st 2 years
- Distant metastatic disease post treatment most common cause of death

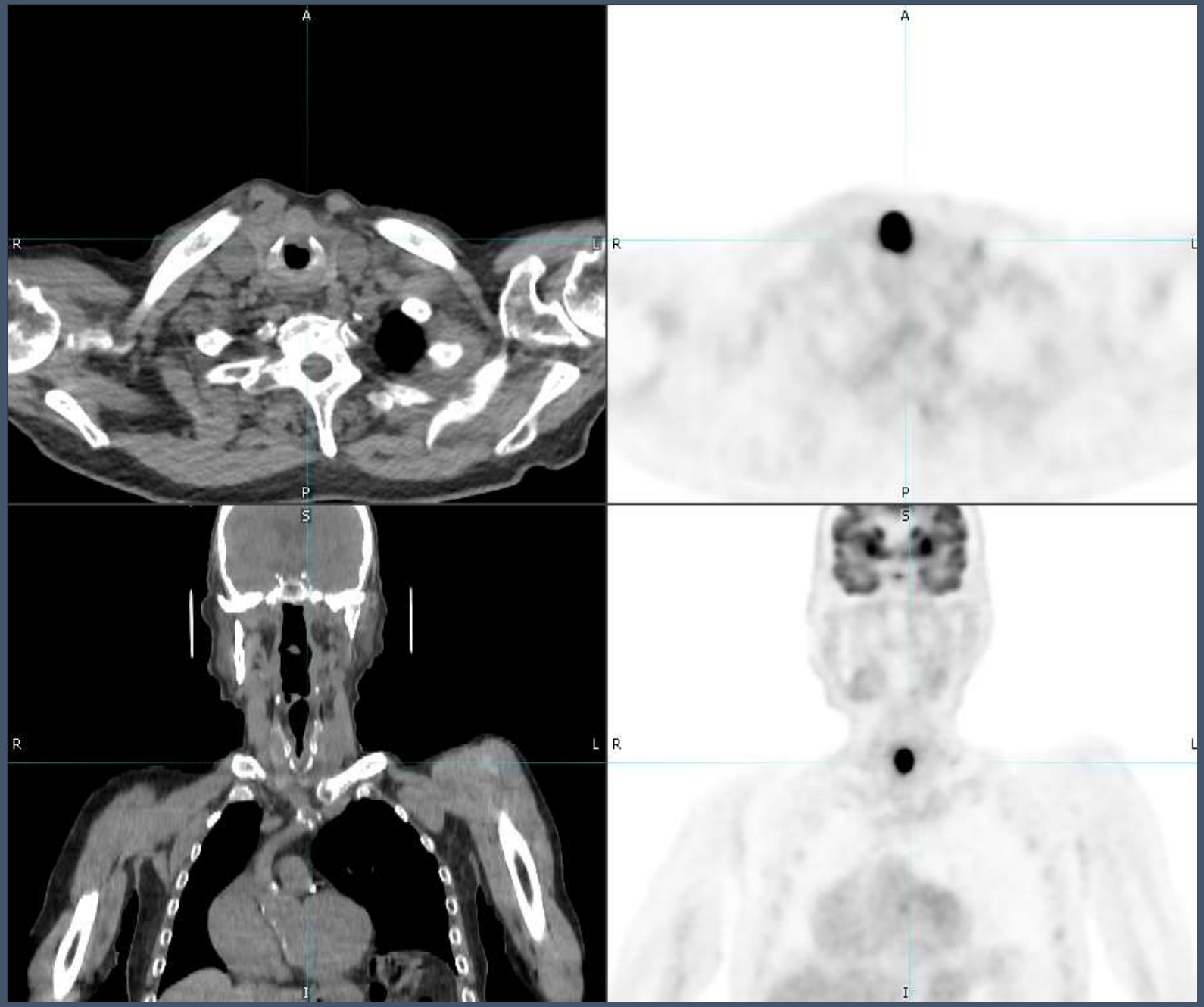


Nasopharyngeal carcinoma

- FDG PET/CT has advantages over MRI
  - more accurate nodal staging
  - may be more sensitive detection of locoregional invasion
  - improved tumor delineation for radiotherapy with associated improved recurrence rates
  - useful for prognostication where higher SUVmax levels (primary ≥ 9.3 and nodal disease ≥ 7.4) have significantly worse distant metastasis free survival , prognosis is linked to metabolic tumor volume (worse with disease ≥4.0ml)
  - high NPV for predicting residual/recurrent disease at 6 months post treatment
  - distant metastatic spread is common especially when compared to other head and neck cancers and FDG PET/CT is an accurate modality in identifying distant disease.

Laryngeal/hypopharnygeal cancer

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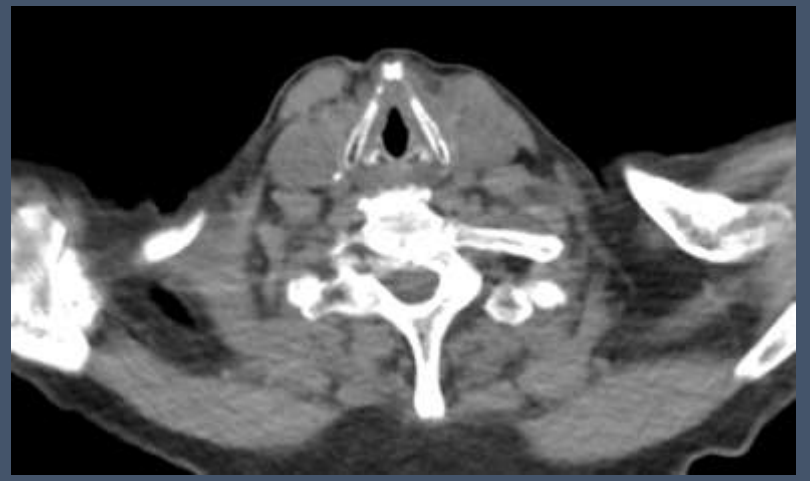
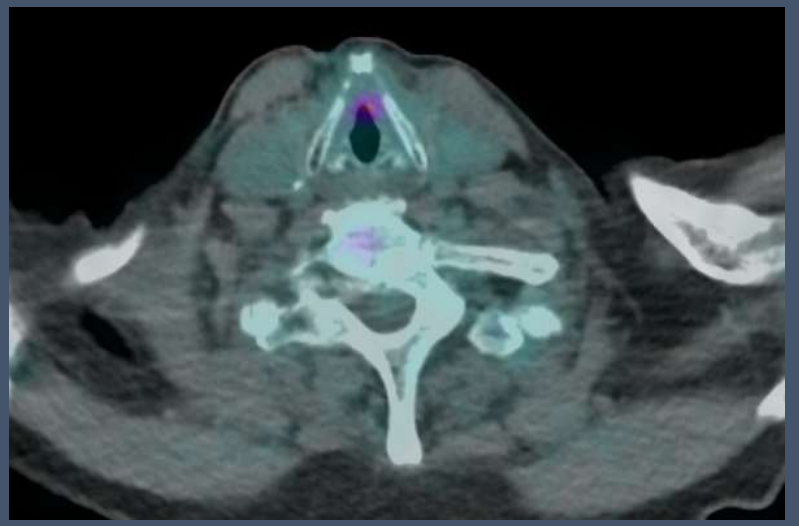
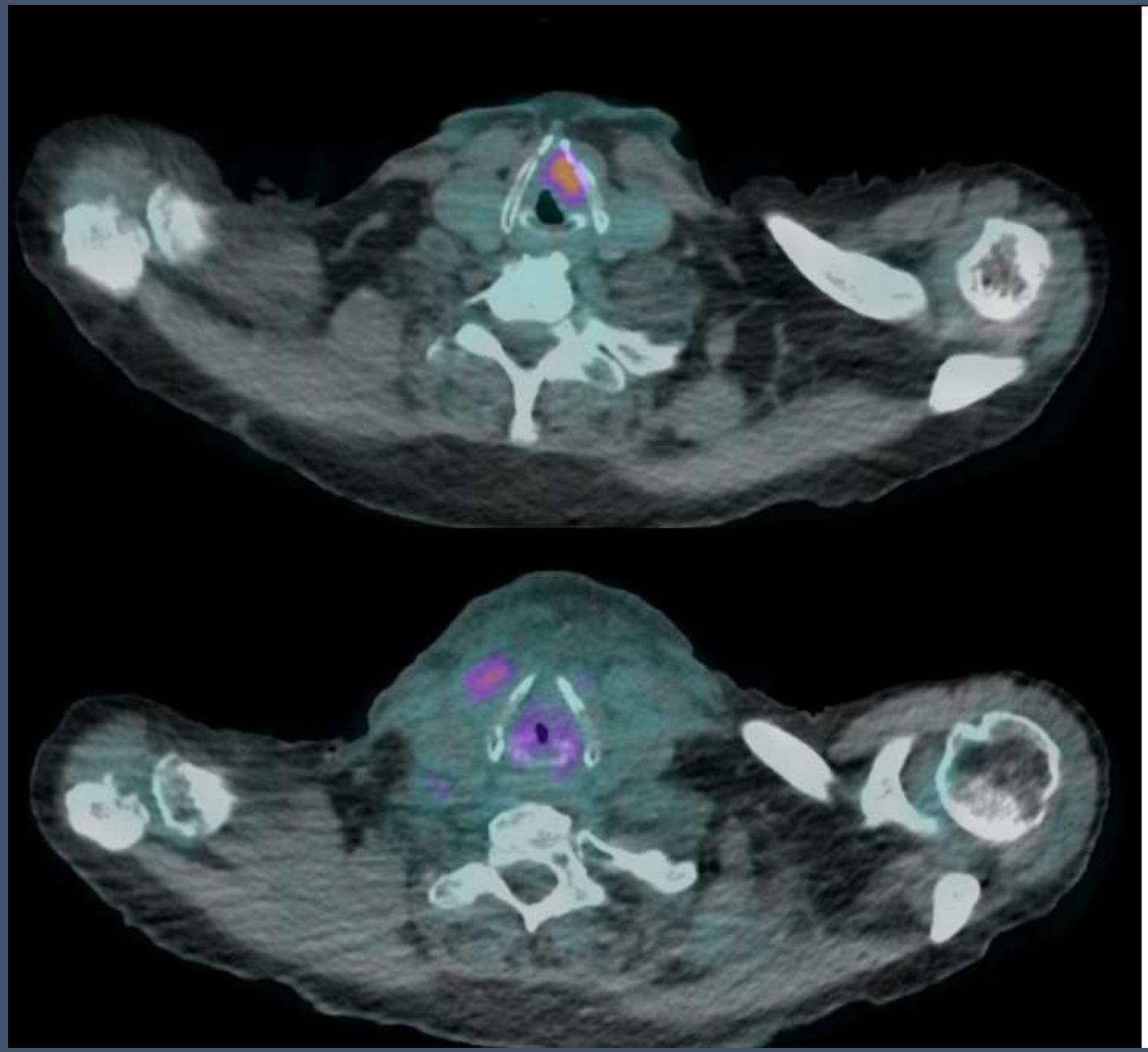
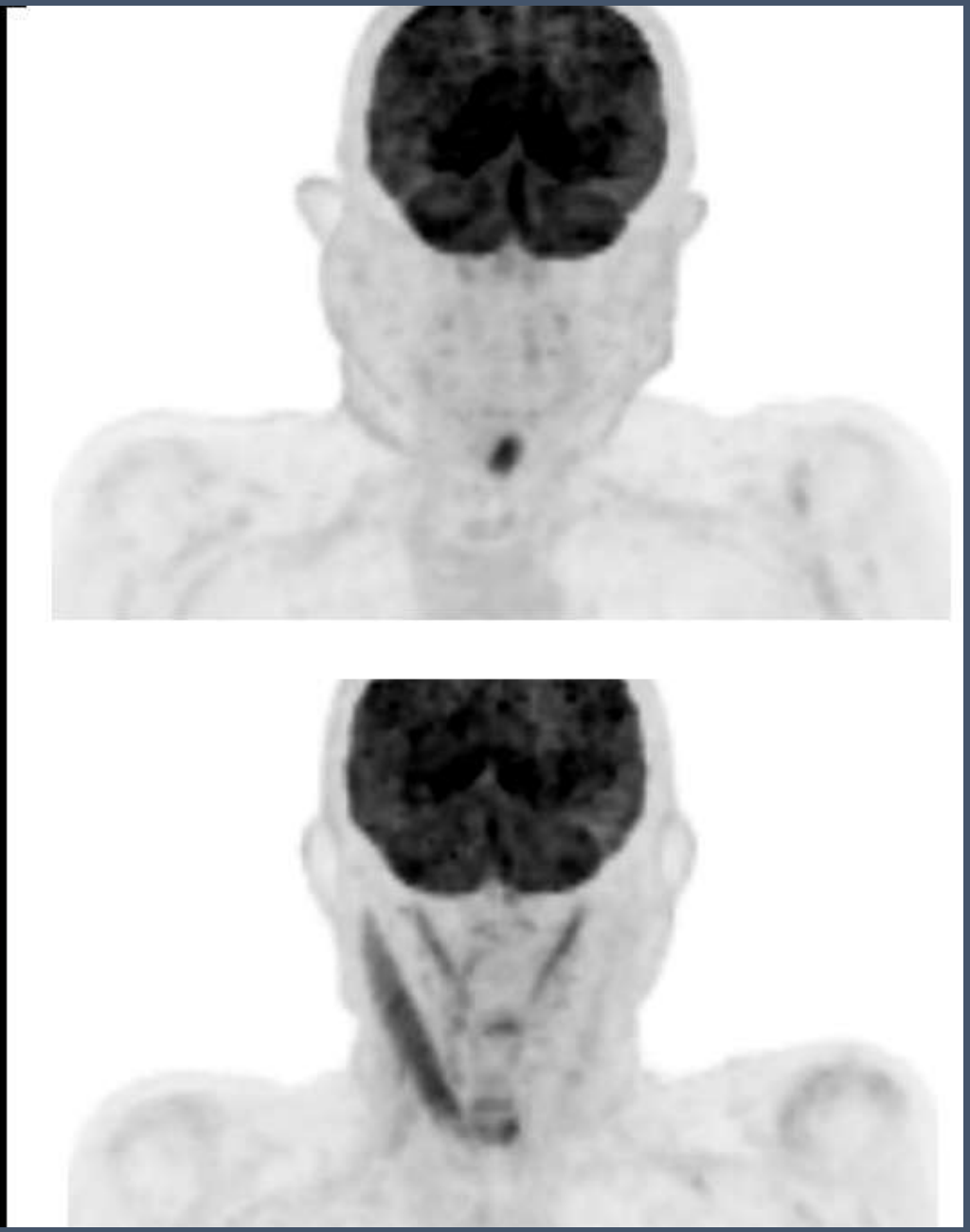
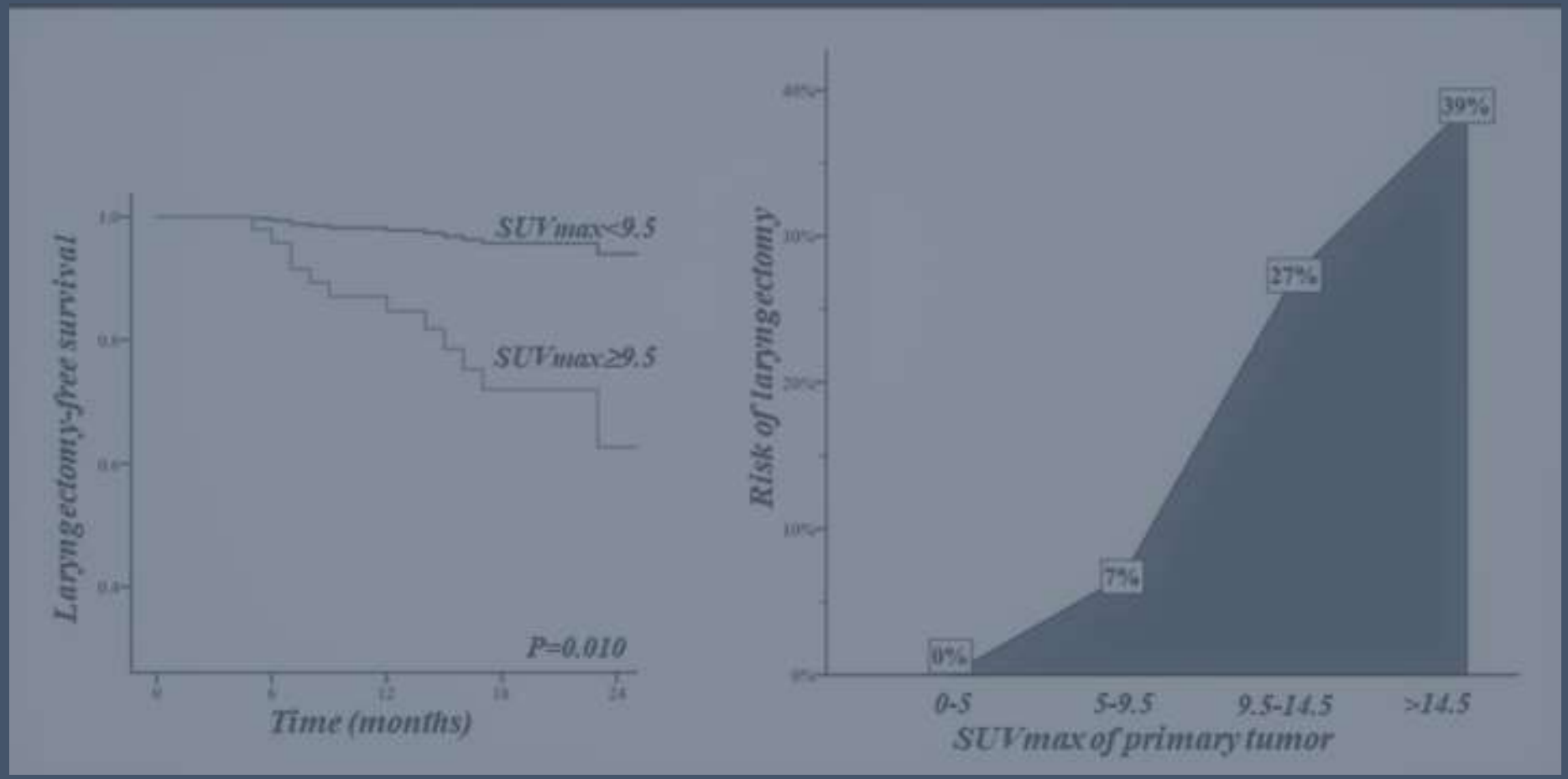








Hypopharnygeal cancer



- Werner, J., Hüllner, M.W., Rupp, N.J. et al. Predictive Value of Pretherapeutic Maximum Standardized Uptake Value (Suvmax) In Laryngeal and Hypopharyngeal Cancer. Sci Rep 9, 8972 (2019). https://doi.org/10.1038/s41598-019-45462-y

Prognostication and hypopharyngeal cancer

- Hypopharyngeal SCC has a high rate of distant metastatic disease
- Patients with high SUVmax values displayed significantly shorter distant metastasis-free survival and OS.

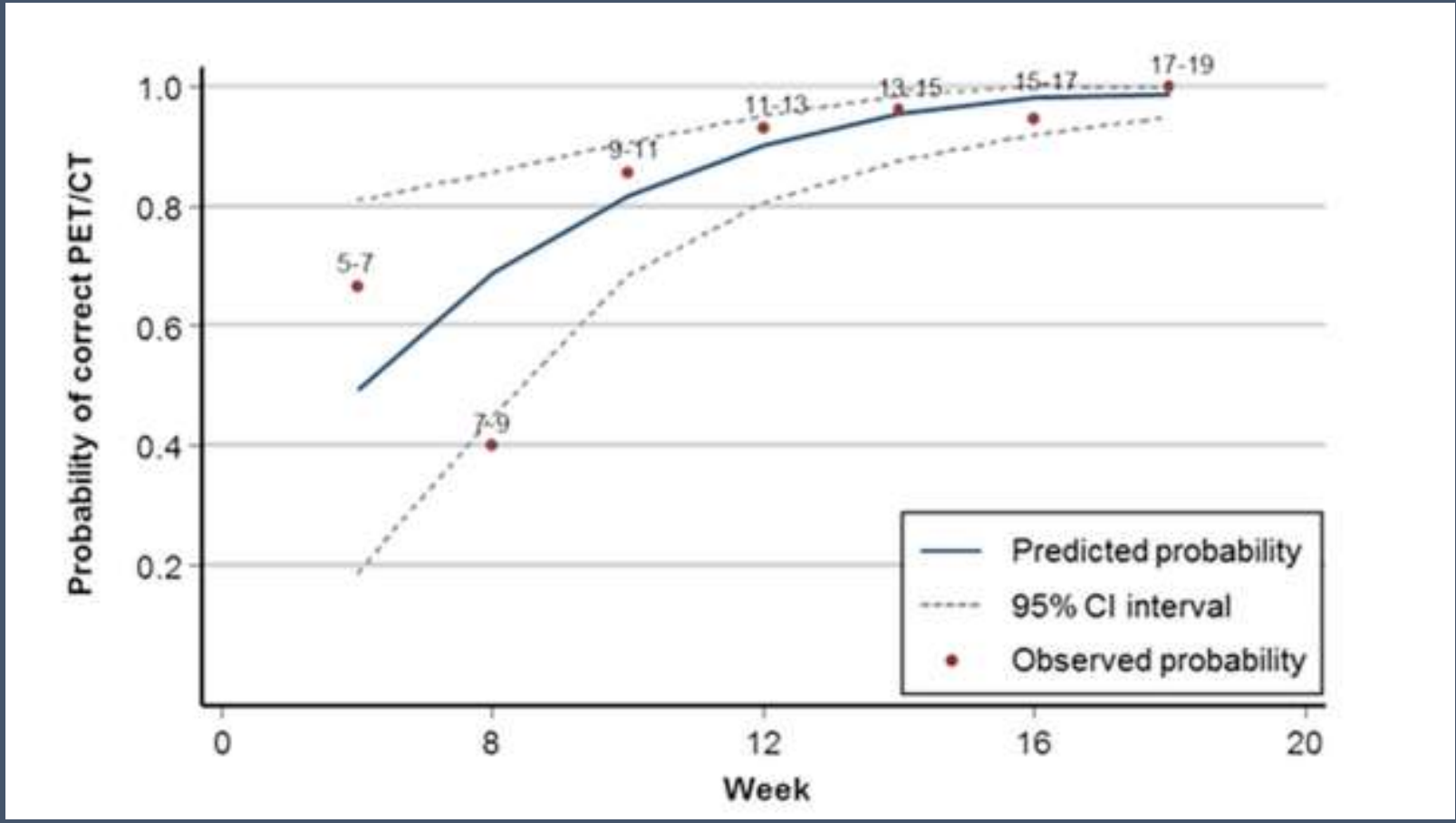
Suzuki S, Toyoma S, Abe T, Endo T, Kouga T, Kaswasaki Y, Yamada T. 18F-FDG-PET/CT can be used to predict distant metastasis in hypopharyngeal squamous cell carcinoma. J Otolaryngol Head Neck Surg. 2022 Apr 1;51(1):13. doi: 10.1186/s40463-022-00568-8. PMID: 35365214; PMCID: PMC8973647.

Treatment response

- FDG PET/CT is accurate and cost effective for response assessment, sparing neck dissection in about 80% of patients, and with high NPV [1]
- High post-treatment SUVmax is indicative of poor metabolic response to chemoRT with high NPV but suboptimal PPV [2]
- The time interval between end of treatment and scan has a significant impact on diagnostic accuracy [3]
- Imaging at 11-12 weeks post treatment is optimal but a further PET/CT at one year to identify late recurrence [4]

1 Mehanna H, Wong W-L, McConkey CC, et al. PET-CT surveillance versus neck dissection in advanced head and neck cancer. N Engl J Med. 2016;374:1444–54
2 Gupta, T. et al. Diagnostic performance of post-treatment FDG PET or FDG PET/CT imaging in head and neck cancer. A systematic review and meta-analysis. European journal of nuclear medicine and molecular imaging 38, 2083–2095, https://doi.org/10.1007/s00259-011-1893-y (2011).
3 Phylannie K. F. Cheung et al Detecting Residual/Recurrent Head Neck Squamous Cell Carcinomas Using PET or PET/CT Systematic Review and Meta-analysis Dec 2015 https://doi.org/10.1177/0194599815621742
4 Helsen N et al. (2017) 18F-FDG-PET/CT for the detection of disease in patients with head and neck cancer treated with radiotherapy. PLoS ONE 12(8): e0182350. https://doi.org/10.1371/journal.pone.0182350

Treatment response



Helsen N et al. (2017) 18F-FDG-PET/CT for the detection of disease in patients with head and neck cancer treated with radiotherapy. PLoS ONE 12(8): e0182350. https://doi.org/10.1371/journal.pone.0182350

PET/CT timing post treatment

	Local Residual/Recurrent Disease		Nodal Residual/Recurrent Disease	
Subgroup	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Imaging modality				
PET	90.7 (82.5-95.9)	76.5 (72.0-80.6)[a]	72.0 (60.4-81.8)	87.7 (83.9-90.8)
PET/CT	80.8 (69.9-89.1)	89.8 (85.8-92.9)[a]	73.0 (55.9-86.2)	89.4 (84.5-93.2)
Image analysis				
Visual	86.7 (78.4-92.7)	80.2 (75.5-84.4)	63.9 (50.6-75.8)	88.4 (83.4-92.4)
Semiquantitative	85.2 (73.8-93.0)	84.2 (80.1-87.8)	81.8 (64.5-93.0)	88.6 (84.3-92.0)
Timing of scan				
<12 wk	84.8 (75.0-91.9)	79.9 (76.1-83.4)[b]	67.5 (56.1-77.6)	86.2 (82.6-89.3)[c]
>12 wk	87.5 (77.6-94.1)	88.4 (83.0-92.6)[b]	82.6 (61.2-95.0)	96.0 (90.1-98.9)[c]

[b]Statistically significant difference ($P = .009$).

[c]Statistically significant difference ($P = .004$).

Imaging time point

- Short time difference of 15 minutes in uptake time between scans can introduce significant changes in SUVmax and skew clinical interpretation[1]
- Biphasic acquisition[2]
  - Treatment naïve
  - @60 and 90 min post injection
  - ↑SUV (5.7%) implies malignancy and ↓↔ SUV implies more likely benign
  - Comparable to a delayed protocol at 120min

The RI-SUVmax evaluation		
Lesions/value	mean RI-SUVmax ± S.D.	Range
SCC Oropharynx	11% ± 10%	−10% to 36%
SCC Nasopharynx	12% ± 14%	−9% to 51%
SCC Hypopharynx	17% ± 19%	−14% to 66%
Inflammation	1% ± 10%	−18% to 28%
Postoperative lesions	6% ± 10%	−13% to 24%
Blood vessels	−13% ± 12%	−53% to 2%
Benign lesions	2% ± 10%	−18% to 28%
Malignant lesions	12% ± 14%	−14% to 66%

1 Wendy Ni et al, Significant impact of FDG plasma kinetics and uptake time on tumor SUV in oncology clinical trials. JNM May 2014, 55 (supplement 1) 2072
2 AK Pietrzak et al Sequential delayed [18F]FDG PET/ CT examinations in the pharynx Scientific Reports (2020) 10:2910 doi.org/10.1038/s41598-020-59832-4

Scoring systems

	Hopkins	Deauville	Cuneo	
sens	87	93	47	
spec	86	79	93	Node size/morphology, ceCT
PPV	76	70	78	Image later than 12 weeks esp for HPV+
NPV	92	96	76	
acc	86	84	77	repeat PET @16 weeks?

1	Minimal uptake < IJV	No uptake	No uptake	All 3 scales correlate significantly with PFS and OS Combining CT and PET findings can improve treatment response evaluation
2	Minimal uptake > IJV but < liver	Minimal uptake < MBP	Residual uptake > MDP but < liver + absent local background	
3	Diffuse uptake > IJV and liver	Low-grade uptake > MBP but < liver	Residual uptake > MDP but < liver + local background	
4	Moderate focal uptake > liver	Moderate focal uptake > liver	Focal uptake > liver + local background	
5	Intense focal uptake > > liver	Intense focal uptake > 2 × liver or new lesions	Focal uptake > liver + absent local background	
6			Focal uptake > > liver	

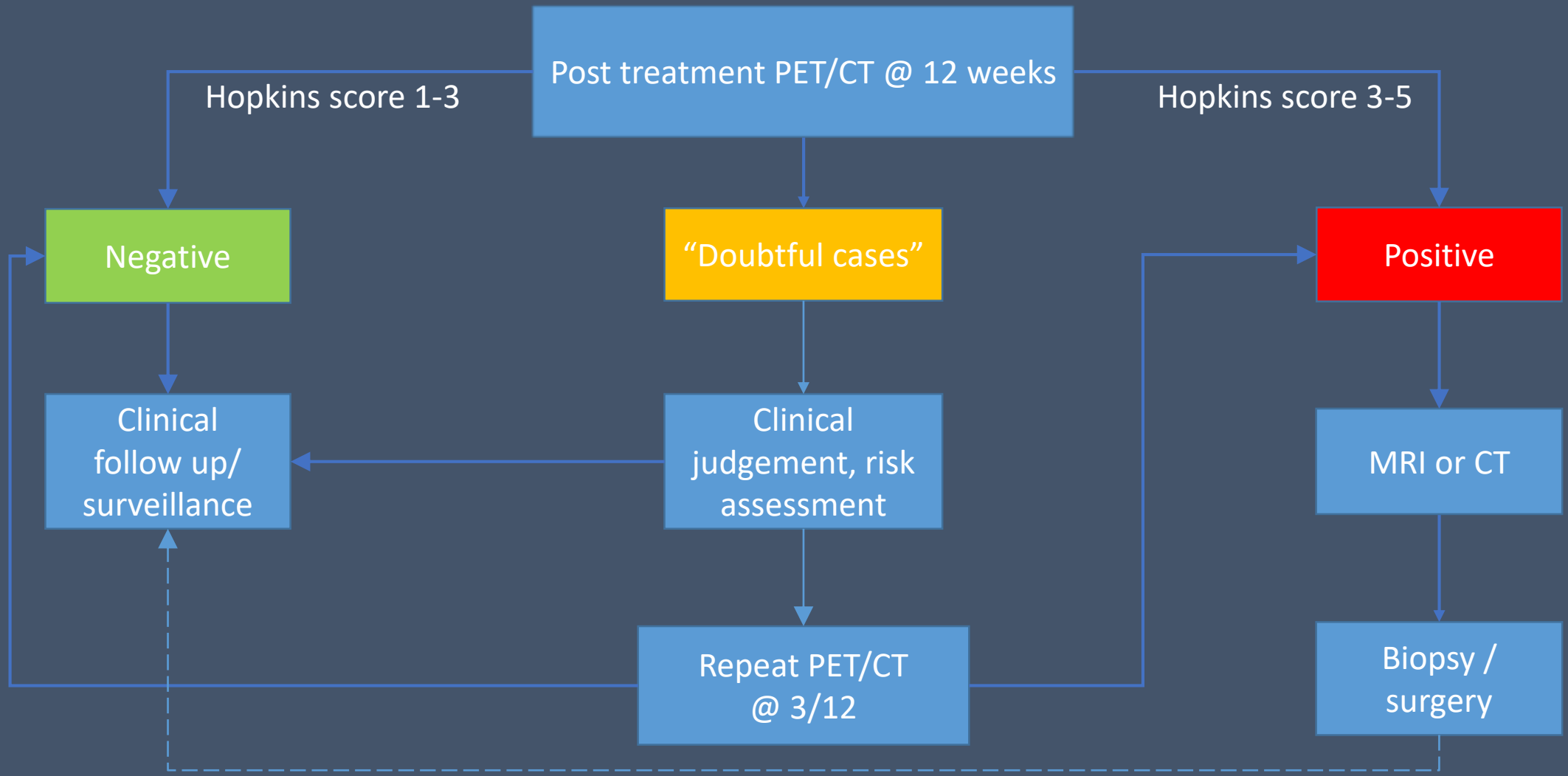
Ferrari, C., Santo, G., Mammucci, P. et al. [18F]FDG PET/CT in head and neck squamous cell carcinoma: a head-to-head between visual point-scales and the added value of multi-modality imaging. BMC Med Imaging 23, 34 (2023). https://doi.org/10.1186/s12880-023-00989-5

Hopkins scoring system

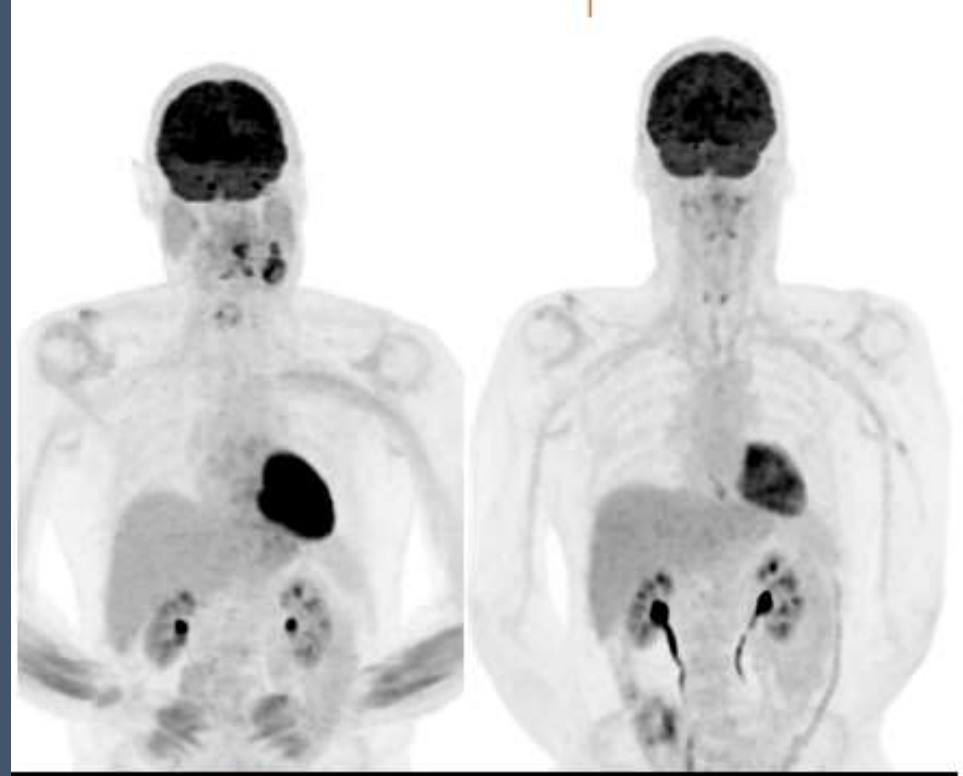
TABLE 1: Five-Point Qualitative Posttherapy Assessment Scoring System (Hopkins Criteria) for Head and Neck PET/CT

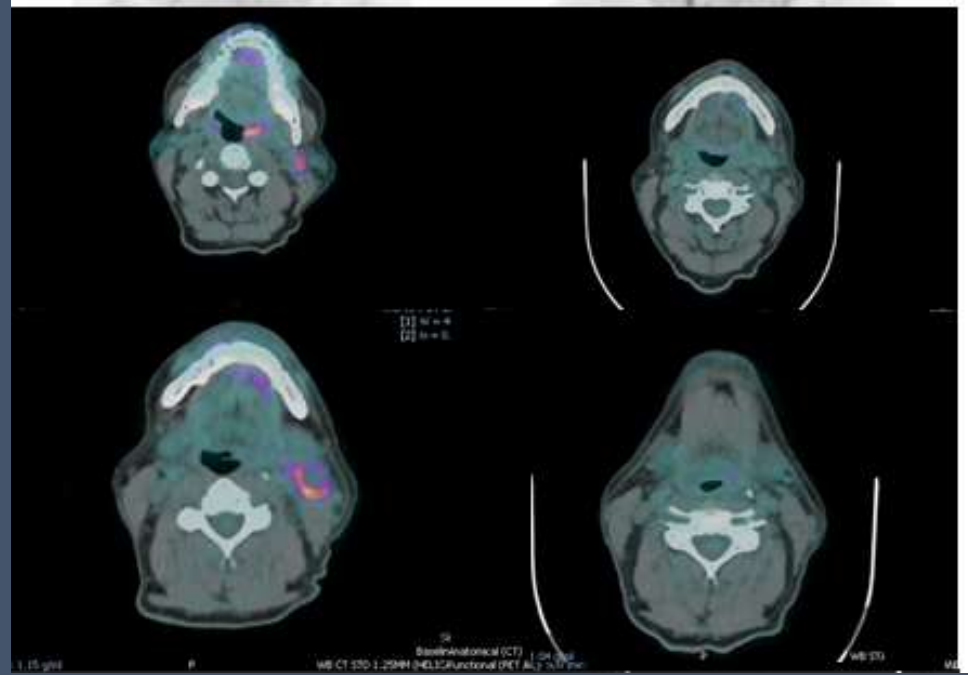
Score	^{18}F-FDG Uptake Pattern	Response Category
1	^{18}F-FDG uptake at the primary site and nodes less than IJV.	Complete metabolic response
2	Focal ^{18}F-FDG uptake at the primary site and nodes greater than IJV but less than liver.	Likely complete metabolic response
3	Diffuse ^{18}F-FDG uptake at the primary site or nodes is greater than IJV or liver.	Likely postradiation inflammation
4	Focal ^{18}F-FDG uptake at the primary site or nodes greater than liver.	Likely residual tumor
5	Focal and intense ^{18}F-FDG uptake at the primary site or nodes.	Residual tumor

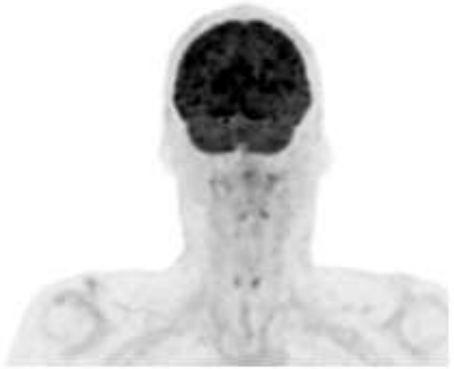
Note—Scores 1, 2, and 3, which represent complete metabolic response, likely complete metabolic response, and likely postradiation inflammation, respectively, are considered negative for tumor. Scores 4 and 5, which represent likely residual tumor and residual tumor, respectively, are considered positive for tumor. New lesion would be considered as progressive disease. IJV = internal jugular vein. (Reprinted with permission from [61]: This research was originally published in *JNM*. Marcus C, Ciarallo A, Tahari AK, et al. Head and neck PET/CT: therapy response interpretation criteria (Hopkins criteria)—interreader reliability, accuracy, and survival outcomes. *J Nucl Med* 2014; 55:1411–1416 © by the Society of Nuclear Medicine and Molecular Imaging, Inc.)

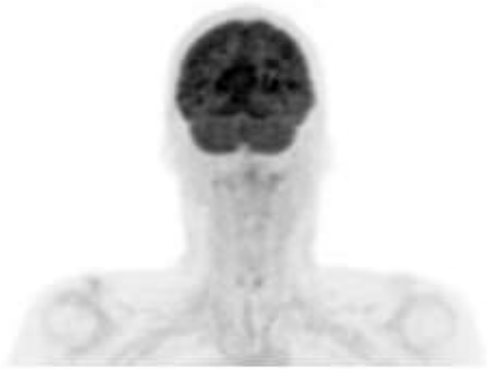


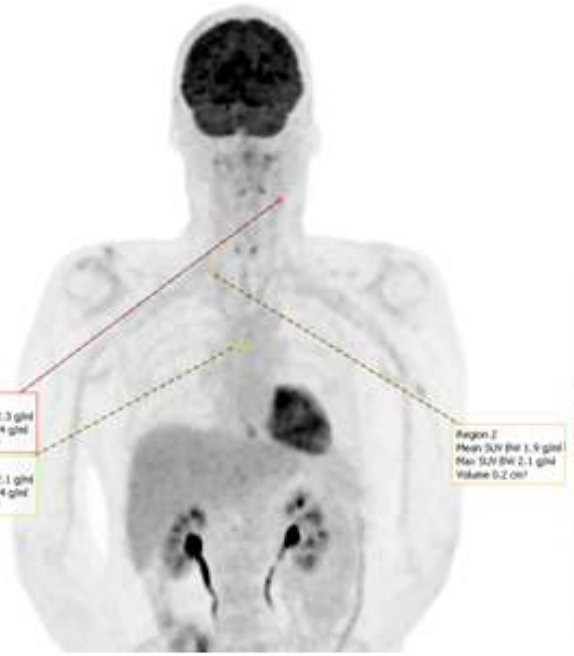
Head and Neck Cancers, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network J Natl Compr Canc Netw, 18(7), 873-898. Retrieved Apr 7, 2024, from https://doi.org/10.6004/jnccn.2020.0031







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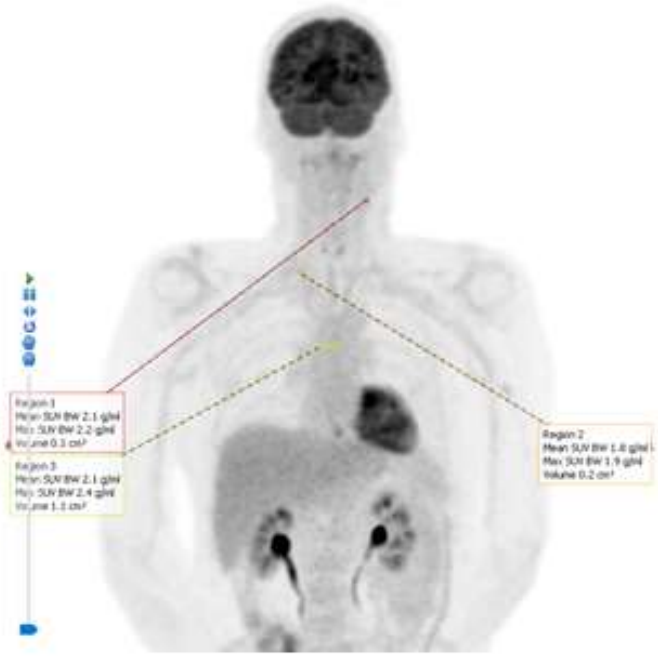
Max SUV BW 2.1 g/ml
Volume 0.2 cm³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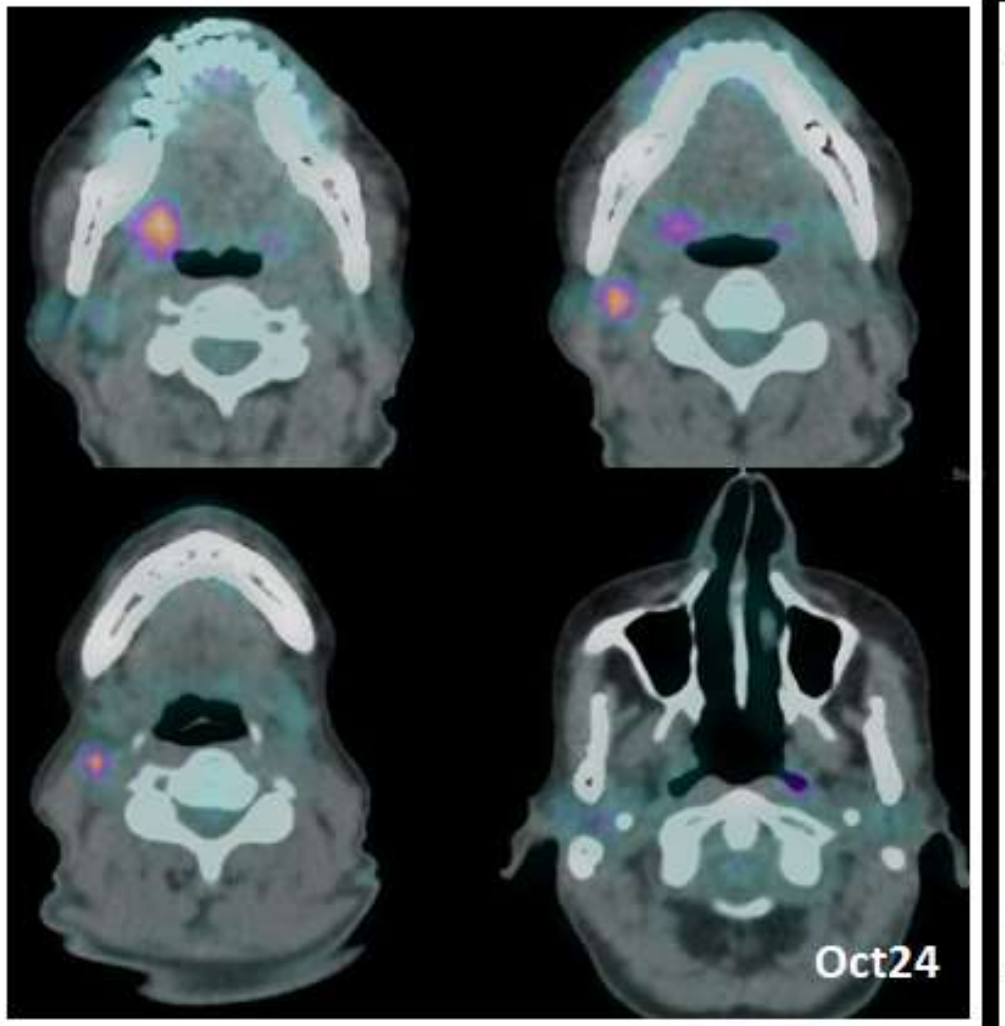
Max SUV BW 1.9 g/ml
Volume 0.2 cm³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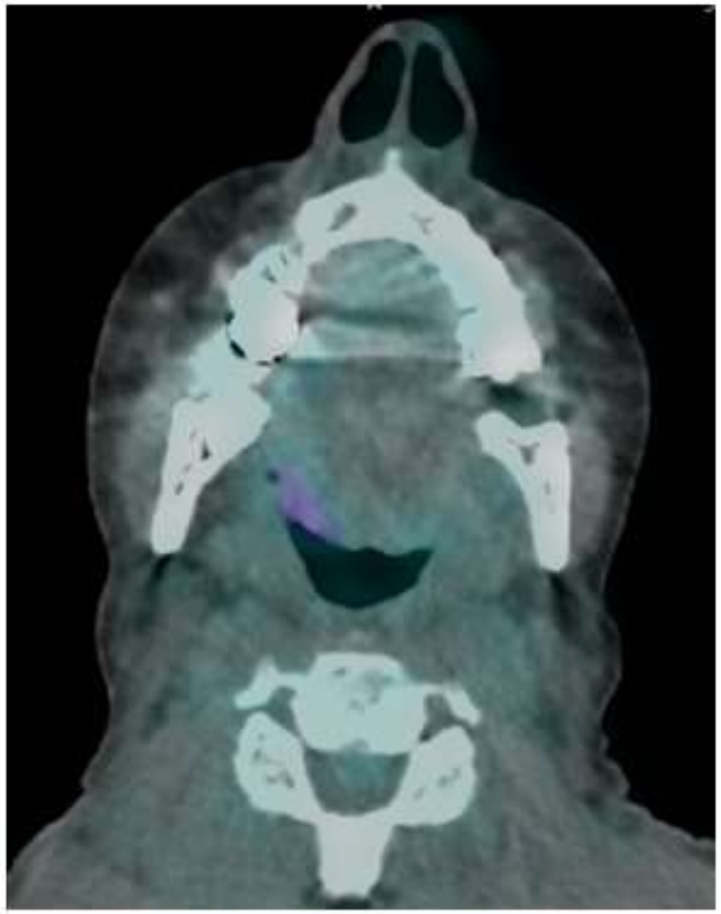

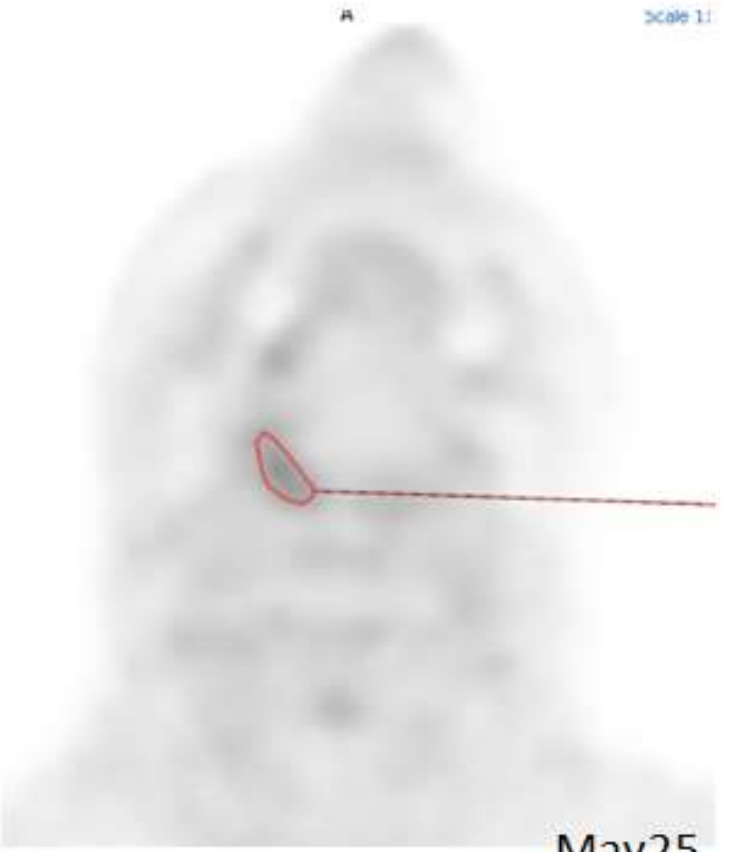
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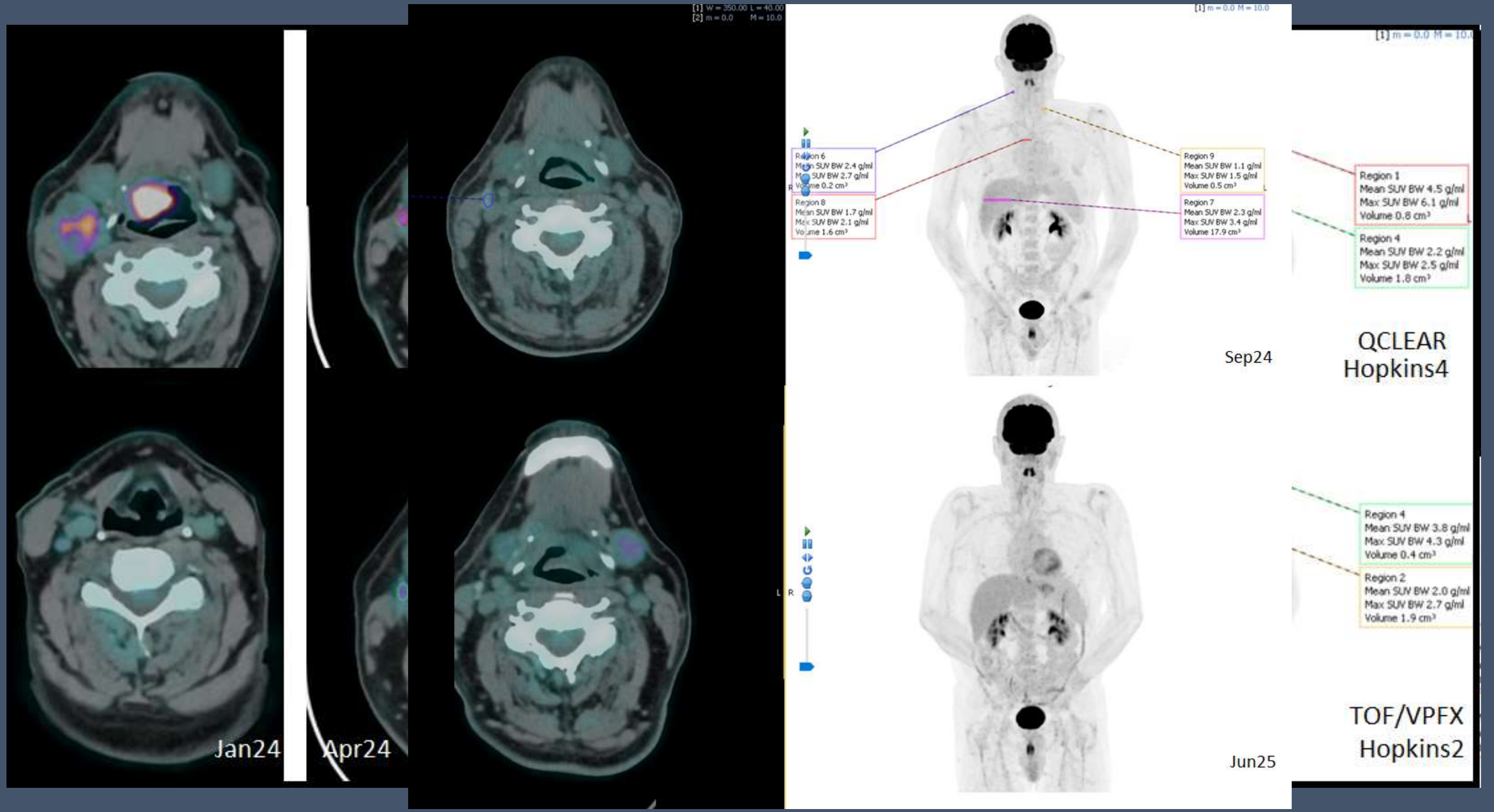
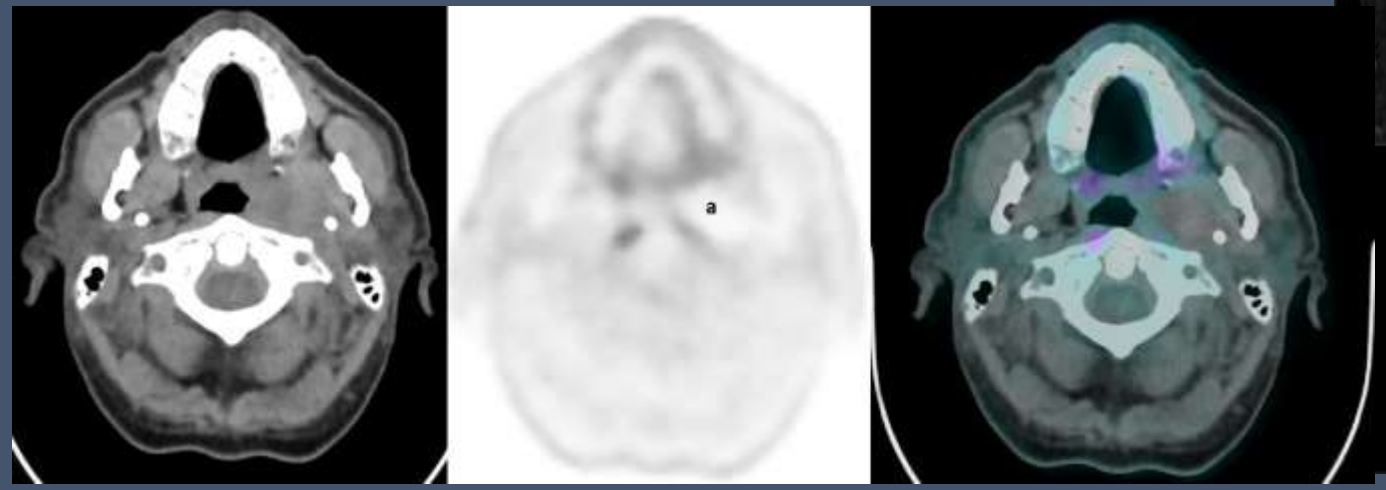

Jan24
Apr24
Region 6
Mean SUV BW 2.4 g/ml
Max SUV BW 2.7 g/ml
Volume 0.2 cm³
Region 8
Mean SUV BW 1.7 g/ml
Max SUV BW 2.1 g/ml
Volume 1.6 cm³
Region 9
Mean SUV BW 1.1 g/ml
Max SUV BW 1.5 g/ml
Volume 0.5 cm³
Region 7
Mean SUV BW 2.3 g/ml
Max SUV BW 3.4 g/ml
Volume 17.9 cm³
Sep24
Jun25
Region 1
Mean SUV BW 4.5 g/ml
Max SUV BW 6.1 g/ml
Volume 0.8 cm³
Region 4
Mean SUV BW 2.2 g/ml
Max SUV BW 2.5 g/ml
Volume 1.8 cm³
QCLEAR
Hopkins4
Region 4
Mean SUV BW 3.8 g/ml
Max SUV BW 4.3 g/ml
Volume 0.4 cm³
Region 2
Mean SUV BW 2.0 g/ml
Max SUV BW 2.7 g/ml
Volume 1.9 cm³
TOF/VPFX
Hopkins2

Checklist for reading head and neck cancer PET/CT

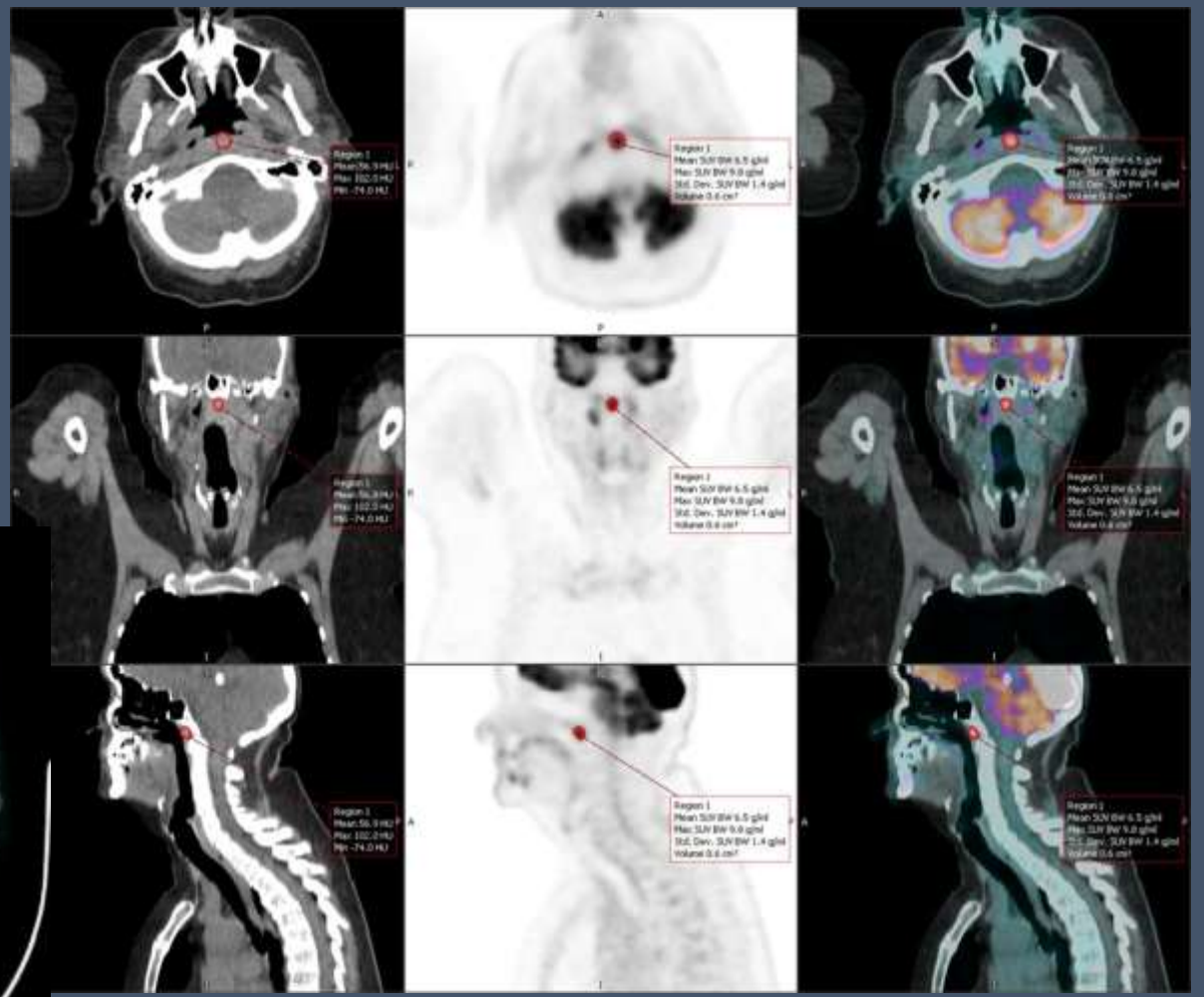
Clinical history of tonsillectomy
Identify surgical excision, free flap reconstruction including donor site review, use of obturator or other prostheses
Neck mucosal surfaces, special attention to Waldeyer's ring
Effacement of fossa of Rosenmuller, glosso-tonsillar sulcus, vallecula, pyriform fossa
Salivary glands
Sinonasal spaces, mastoid air cells, dentition
Named spaces review
Lymphadenopathy
Skull base, clivus, neural foramina
Orbits, globe of the eye, extraocular muscles
Floor of mouth
Neck muscle activation
Cutaneous review including external auditory meatus, ears, scalp
Percutaneous gastric feeding tube placement / removal / complications

Finding	Notes
Branchial cyst	Can be misinterpreted as a necrotic nodal metastasis, especially if there is associated secondary inflammatory change
Thornwaldt cyst	Typical finding in the midline as a small volume low attenuation FDG avid lesion in the nasopharynx The use of nasopharynx to palatine ratio of ≤1.1 to discriminate benign nasopharyngeal uptake from malignant uptake has been described .
Periodontal disease	Usually self-evident periodontal disease but if there is a soft tissue component a primary mucosal lesion is possible. In post radiotherapy scenario consider the possibility of osteoradionecrosis. Maxillary molar eruption with associated inflammatory changes in not uncommon.
Trichilemmal cysts	Scalp lesions, sometimes calcified, with associated FDG avid uptake. Clinical correlation is always advised especially if lesion enlarging.
Inverted sinonasal papilloma	This is a benign sinonasal papilloma. Malignant transformation is possible but FDG PET/CT has no accepted defined role in this context.
Muscular activity	This is usually self-evident, often easiest to identify on MIP type PET images, asymmetry or unusual activation is seen post-treatment and in the context of trismus
Salivary gland inflammation	Asymmetric changes related to neck irradiation, incidental benign salivary duct stone, systemic related inflammation are typical examples.
Benign parotid tumors	The most common are Warthin's tumor and pleomorphic adenoma. There is significant diagnostic difficulty in distinguishing benign from malignant parotid tumors using FDG PET/CT. There is evidence to try to distinguish benign lesions such as Warthin's tumor from malignancy
Brown fat activation	Usually self-evident, localises to fat attenuation areas on CT, high uptake with scatter artefact or misregistration artefact can cause diagnostic difficulty.

Typical inflammatory FDG uptake in left molar maxillary eruption



Photopenic left 2nd branchial cyst



Typical appearance of a benign Thornwaldt cyst

Surveillance – why bother?

- Locoregional recurrence is common in the first 2 years post treatment in 2/3 of patients
- PET/CT vs CWU (regular clinical f/u and chest CT) x3 follow up[1]
- Overall survival at 3 years significantly better in PET/CT group, especially for stage III-IV disease and oropharyngeal disease
- Increased detection of subclinical/occult disease using PET/CT

Surveillance methods[2]
Self referral/symptoms
Clinical examination
Imaging
Biomarkers, HPV ctDNA, EBV ctDNA

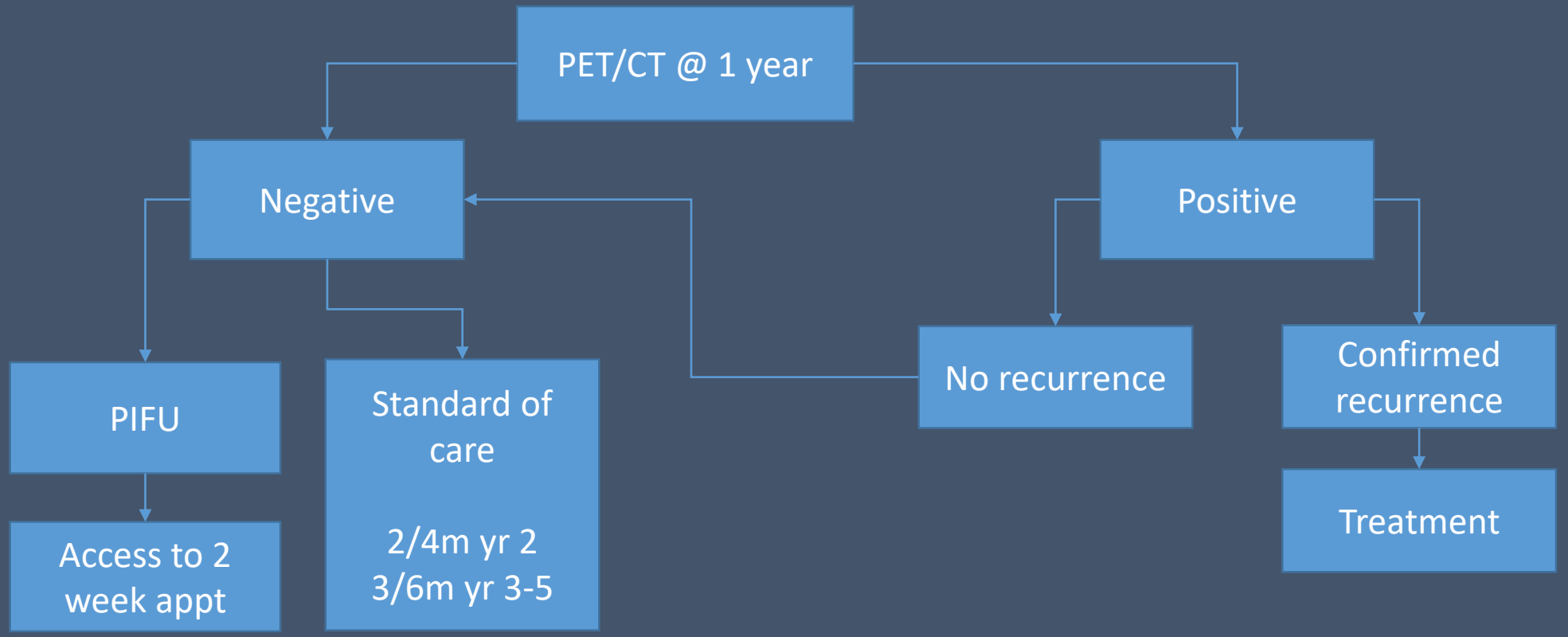
Risk stratification[2]
Original T staging
Tobacco use (poorer local disease control, increased risk of progression and death)
HPV status, HPV ctDNA

1 Leclère. An Intensive 18F-Fludeoxyglucose–Positron Emission Tomography With Computed Tomography–Based Strategy of Follow-Up in Patients Treated for Head and Neck Squamous Cell Carcinoma Who Are Clinically Asymptomatic. JAMA Netw Open. Published online Aug 2023. doi:10.1001/jamanetworkopen.2023.26654
2 Glenn J. Hanna et al., Personalizing Surveillance in Head and Neck Cancer. Am Soc Clin Oncol Educ Book 43, e389718(2023). DOI:10.1200/EDBK_389718

PETNECK2

Does PETCT-guided, patient-initiated follow-up (PIFU) result in similar overall survival compared to current post-treatment routine surveillance for head and neck cancer patients?

oral
laryngeal
nasopharyngeal
hypopharyngeal
oropharyngeal



Post treatment surveillance - guidance

Organization	Guidelines
NCCN 2022	• Imaging only in locoregionally advanced disease and only if clinically indicated • PET-CT may be the most sensitive imaging modality • If a PET/CT at 3 months post-treatment is negative, there are no data to support substantial benefit for further routine imaging in an asymptomatic patient with negative clinical exam • Routine annual imaging (repeat use of pretreatment imaging modality) may be indicated to visualize areas inaccessible to routine clinical examination (deep-seated anatomic locations or areas obscured by extensive treatment change)
eviCore 2.1 Clinical Guidelines 2021	• No imaging surveillance after first post-treatment scan • Exceptions: in case of nasopharyngeal primary site or physical exam unable to visualize deep-seated primary site: annual CT or MRI for 3 years • In smokers: CT chest only if lung cancer screening criteria are met
AWMF (Germany)	• Imaging every 6 months in the first and second year, every 12 months in years 3–5
BAHNO (UK) 2001	• None (symptom-directed only)
EHNS-ESMO-ESTRO	• Imaging should be carried out if symptoms occur or in cases of abnormalities found at the clinical examination
ASCO 2019	• Only if initial PET-CT shows possibly suspect lymph node
AHNS 2016	• Consider in case of smoking history, nasopharyngeal primary, or tumor site inaccessible to clinical examination • Endorses NCCN guidelines
NI-RADS 2018	• CT, MRI, or PET-CT every 3, 6, or 12 months depending on initial post-treatment imaging findings
ACS 2016	• No definite recommendations

*Van Hoe, S., Hermans, R. Post-treatment surveillance imaging in head and neck cancer: a systematic review. Insights Imaging 15, 32 (2024). https://doi.org/10.1186/s13244-023-01578-4

Surveillance post treatment

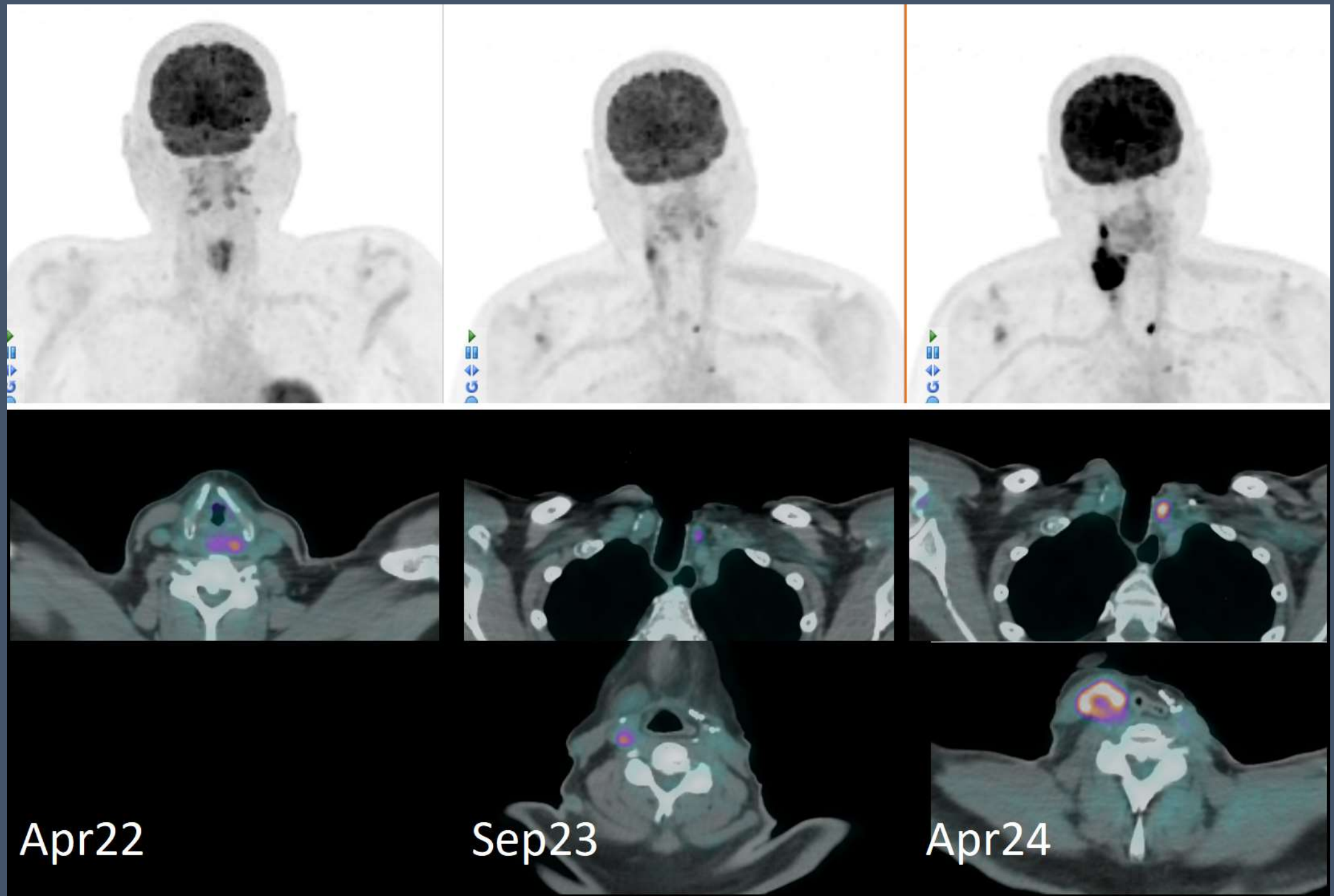
- systematic review on the usefulness of long-term systematic imaging surveillance in patients treated for head and neck cancer*
- almost half of cases of locoregional recurrences and/or metastases were only detected by imaging (40.9%)
- the mean time of detection of recurrent or metastatic disease was 11.5 months
- superior results with PET-CT when compared to other imaging techniques
- in favour of systematic imaging surveillance in locoregional advanced head and neck cancer during at least one and preferably up to 2 years after treatment
- Strengthen the NPV if 2 consecutive PET/CT studies in a 6m period are negative, from 91% to 98%

*Van Hoe, S., Hermans, R. Post-treatment surveillance imaging in head and neck cancer: a systematic review. Insights Imaging 15, 32 (2024). https://doi.org/10.1186/s13244-023-01578-4

Surveillance post treatment PET/CT

- The added value of ceCT in a PET/CT protocol is minimal[1]
- In patients with oral, oropharyngeal and hypopharyngeal cancers with no clinical symptoms of recurrent disease, follow up PET CT is more sensitive than MRI in identifying treatment failure, both locoregional and distant disease[2]

1 Suenaga, Y., Kitajima, K., Ishihara, T. et al. FDG-PET/contrast-enhanced CT as a post-treatment tool in head and neck squamous cell carcinoma: comparison with FDG-PET/non-contrast-enhanced CT and contrast-enhanced CT. Eur Radiol 26, 1018–1030 (2016). https://doi.org/10.1007/s00330-015-3902-1
2 Omar Breik, Anand Kumar, James Birchall, Sean Mortimore, David Laugharne, Keith Jones,
Follow up imaging of oral, oropharyngeal and hypopharyngeal cancer patients: Comparison of PET-CT and MRI post treatment, Journal of Cranio-Maxillofacial Surgery, Volume 48, Issue 7,2020, Pages 672-679, ISSN 1010-5182, https://doi.org/10.1016/j.jcms.2020.04.008.


Apr22
Sep23
Apr24

Take home messages

- Accurate disease staging is critical to determine prognosis and to manage/treat appropriately
- PET/CT characterises local, regional and distant disease in a primary staging role, treatment reponse assessment, identifying recurrence and metastases at follow up when suspected by clinical symptoms
- CUP represents 5-10% of node positive disease and an added detection rate of about 25% over CWU, commonly palatine tonsils and BOT
- PET/CT T staging is limited by poor spatial resolution and soft tissue contrast but can be helpful with dental artefact on MRI and can be supplemented by ceCT

Take home messages

- PET/CT N staging is superior to CT and MRI with an approximate 5-10% improvement in performance
- PET/CT M staging has a very high NPV of 99% and specificity and sensitivity for metastatic disease identification of 92% and 93% respectively. The incidence of metastatic disease is low (2-18%) mainly in the lungs, liver and bone. Patients with HNSCC have a higher incidence of synchronous and metachronous primary disease.
- Most patients with HNSCC present with advanced disease to be treated curatively with combined modalities. Treatment varies by site and staging. Options include CRT with surgery for residual disease or surgery plus neck dissection followed by CRT

Take home messages

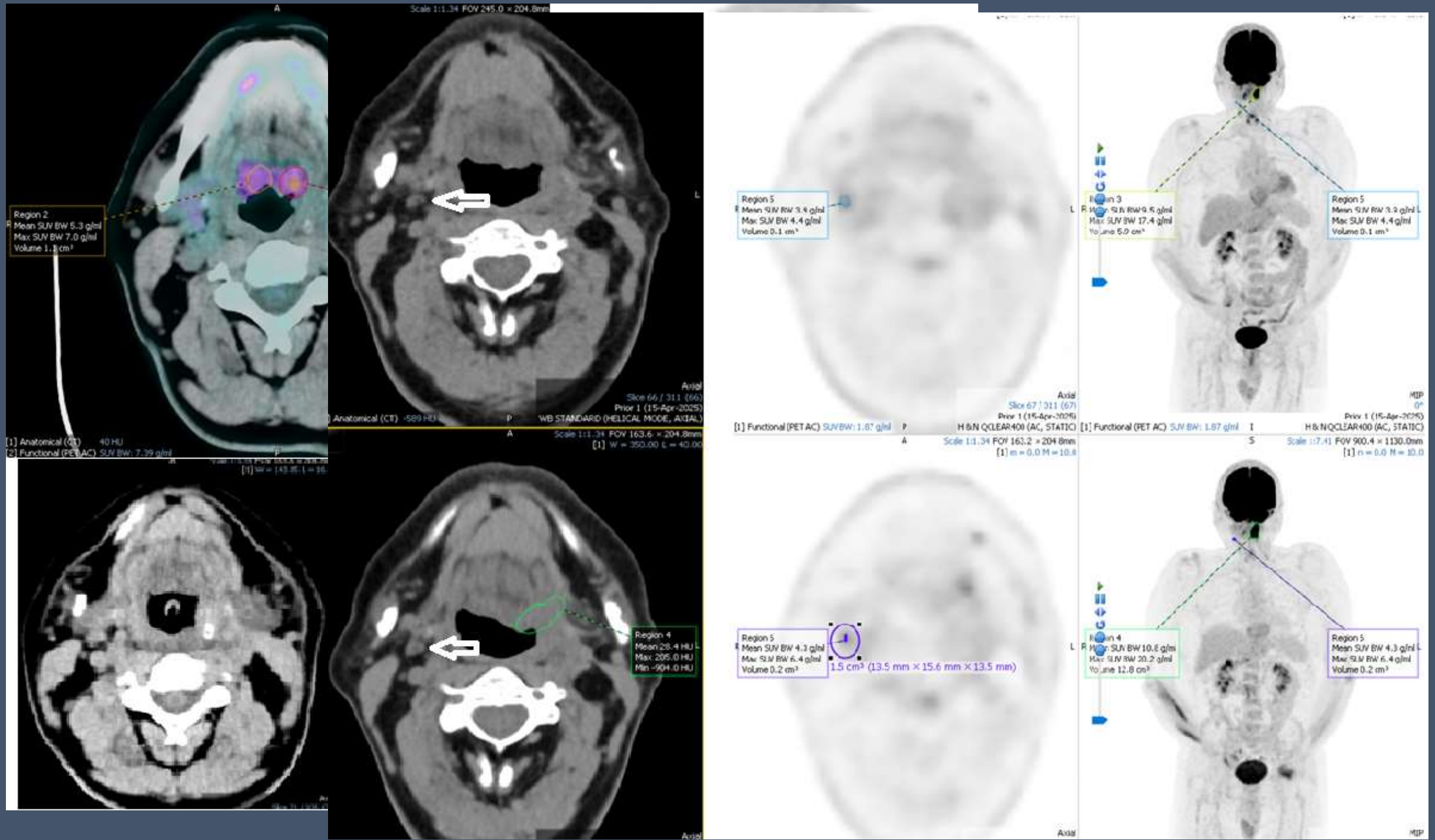
- PET/CT is useful in treatment response assessment. A large meta-analysis of 51 studies involving 2335 patients, the sensitivity, specificity, positive predictive value (PPV), and NPV of FDG PET/CT for the detection of residual primary HNSCC were reported to be 94%, 82%, 75%, and 95%, respectively
- Negative post treatment PET/CT in P16+ disease may select a subset of patient for less frequent surveillance
- PET/CT with high primary disease SUVmax at primary staging is associated with worse outcome . High nodal disease SUVmax is associated with higher risk of disease recurrence

Extra slides

Nodal staging FDG PET/CT

- Sensitivity and Specificity: FDG PET/CT has shown higher sensitivity and specificity in detecting nodal metastases compared to MRI alone. A metaanalysis encompassing 32 studies and 1236 patients that evaluated the performance of FDG PET in N staging showed an overall sensitivity of 82% and specificity of 86% for FDG PET and an approximate 5–10% improvement in both performance values compared with CT, MRI, or both CT and MRI in absolute values
- Impact on Treatment Planning: The superior diagnostic performance of FDG PET/CT has been shown to significantly impact treatment planning, leading to more tailored and effective therapeutic strategies
- It also holds its own when compared to PET/MRI for a variety of different cancers PET/CT had a pooled sensitivity of 86% and specificity of 86% for detecting regional nodal metastases, compared to 88% sensitivity and 92% specificity for PET/MRI. This suggests that while PET/MRI may offer slightly better specificity, FDG PET/CT remains highly effective.

Subha ST, Nordin AJ. The impact of multimodality integrated positron emission tomography-computed tomography on improving the staging and management of head and neck malignancy: a cross- sectional study. Sao Paulo Med J. 2022 May-Jun;140(3):454-462. doi: 10.1590/1516-3180.2021.0599.R1.15092021. PMID: 35507996; PMCID: PMC9671254. (PET/CT vs ceCT)
Rohde M, Nielsen AL, Johansen J, et al. Up-front PET/CT changes treatment intent in patients with head and neck squamous cell carcinoma. Eur J Nucl Med Mol Imaging. 2018;45(4):613–21. doi: 10.1007/s00259-017-3873-3 (PET/CT vs MRI)
Head-to-Head Comparison of the Diagnostic Performance of FDG PET/CT and FDG PET/MRI in Patients With Cancer: A Systematic Review and Meta-Analysis. Amit Singnurkar, Raymond Poon, and Ur Metser American Journal of Roentgenology 2024 223:3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Max SUV BW 7.0 g/ml
Volume 1.1 cm³
[1] Anatomical (CT) 40 HU
[2] Functional (PET AC) SUV BW: 7.29 g/ml
Scale 1:1.34 FOV 245.0 × 204.8mm
Axial
Slice 66 / 311 (66)
Prior 1 (15-Apr-2025)
Anatomical (CT) -589 HU
WB STANDARD (HELICAL MODE, AXIAL)
Scale 1:1.34 FOV 163.6 × 204.8mm
[1] W = 350.00 L = 40.00
Region 4
Mean 28.4 HU
Max 295.0 HU
Min -904.0 HU
Axial
Region 5
Mean SUV BW 3.9 g/ml
Max SUV BW 4.4 g/ml
Volume 0.1 cm³
Axial
Slice 67 / 311 (67)
Prior 1 (15-Apr-2025)
[1] Functional (PET AC) SUV BW: 1.87 g/ml
H&N QCLEAR400 (AC, STATIC)
Scale 1:1.34 FOV 163.2 × 204.8mm
[1] W = 0.0 M = 10.0
Region 3
Max SUV BW 17.4 g/ml
Volume 5.0 cm³
Region 5
Mean SUV BW 3.9 g/ml
Max SUV BW 4.4 g/ml
Volume 0.1 cm³
MIP
0°
Prior 1 (15-Apr-2025)
[1] Functional (PET AC) SUV BW: 1.87 g/ml
H&N QCLEAR400 (AC, STATIC)
Scale 1:7.41 FOV 900.4 × 1130.0mm
[1] W = 0.0 M = 10.0
Region 5
Mean SUV BW 4.3 g/ml
Max SUV BW 6.4 g/ml
Volume 0.2 cm³
1.5 cm³ (13.5 mm × 15.6 mm × 13.5 mm)
Axial
Region 4
Mean SUV BW 10.8 g/ml
Max SUV BW 20.2 g/ml
Volume 12.8 cm³
Region 5
Mean SUV BW 4.3 g/ml
Max SUV BW 6.4 g/ml
Volume 0.2 cm³
MIP