PET/CT applications in head and neck cancer

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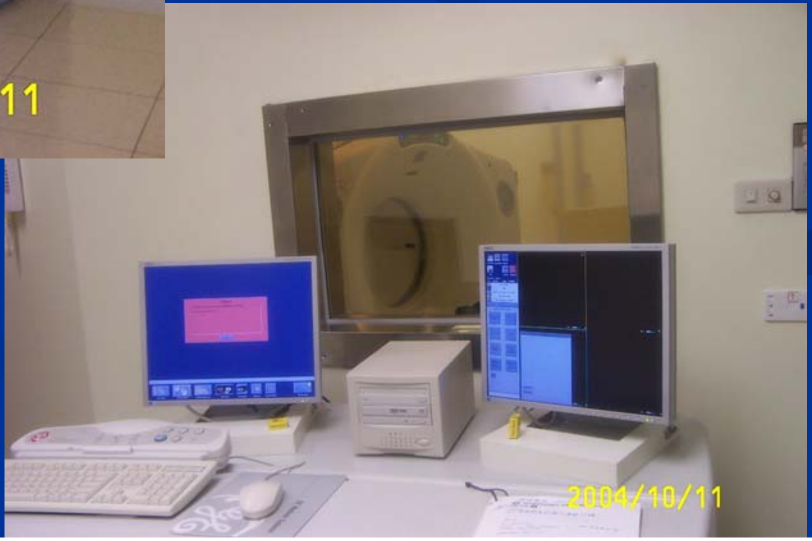
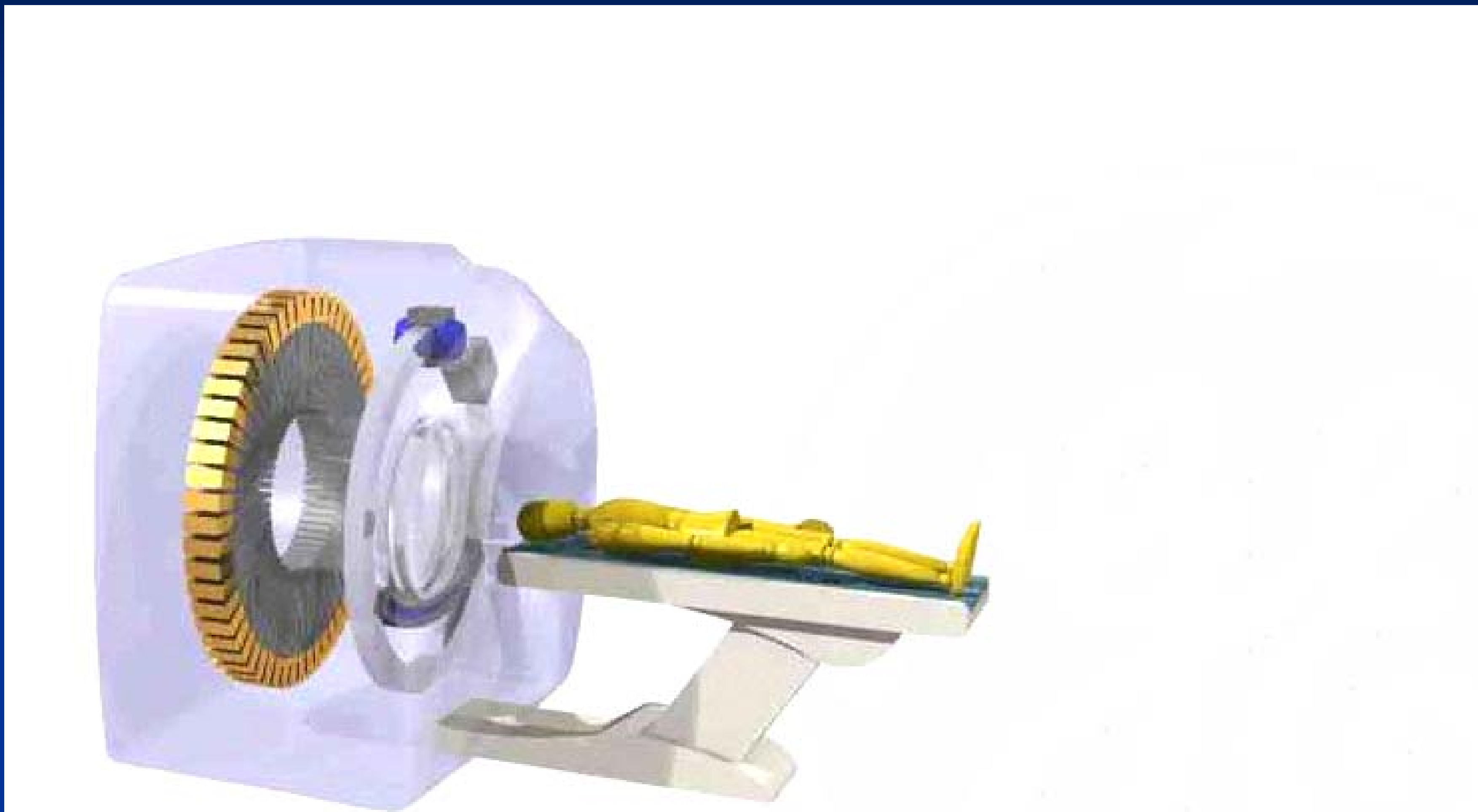




Positron Emitters (Cyclotron)

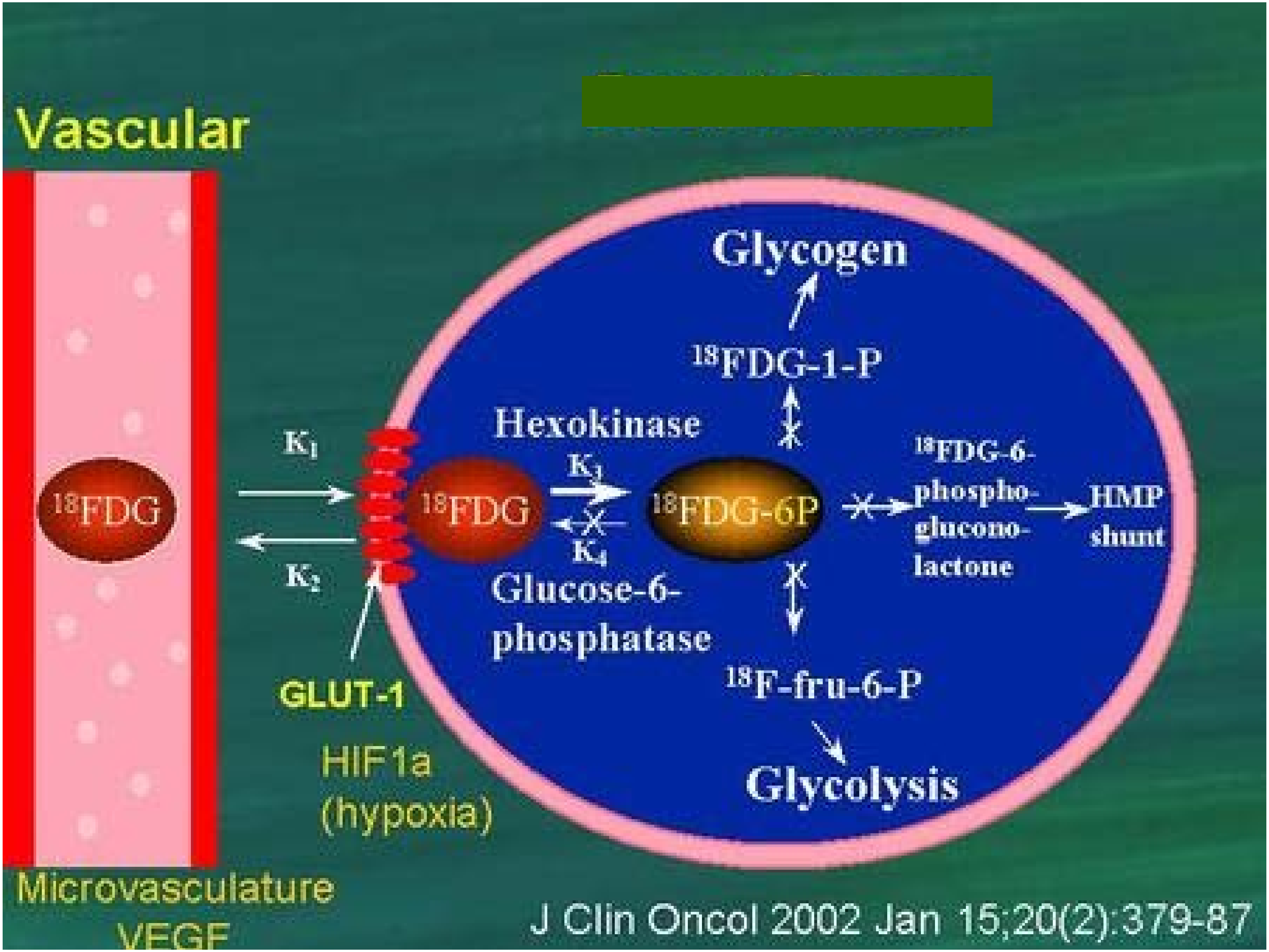
- F-18 (108 min)

  - FDG (glycolysis/cardiac viability/cerebral metabolism)
- C-11 (20 min)

  - Methionine (amino acid metabolism)
- N-13 (10 min)

  - Ammonia (myocardial perfusion)
- O-15 (2 min)

  - water (cerebral perfusion)



Vascular
[redacted]
Glycogen
^{18}FDG-1-P
Hexokinase
K_1
K_3
K_4
K_2
^{18}FDG
^{18}FDG
^{18}FDG-6P
^{18}FDG-6-phospho-glucono-lactone
HMP shunt
Glucose-6-phosphatase
^{18}F-fru-6-P
Glycolysis
GLUT-1
HIF1a (hypoxia)
Microvasculature VEGF
J Clin Oncol 2002 Jan 15;20(2):379-87

- Oncologic application
- Neurologic application
- Psychologic disorders
- Cardiac application

Applications of PET/CT

- Lung cancer
- Head and neck tumor
- Colorectal
- Lymphoma
- Melanoma
- Thyroid cancer
- Breast cancer
- Esophagus
- Seizure disorder

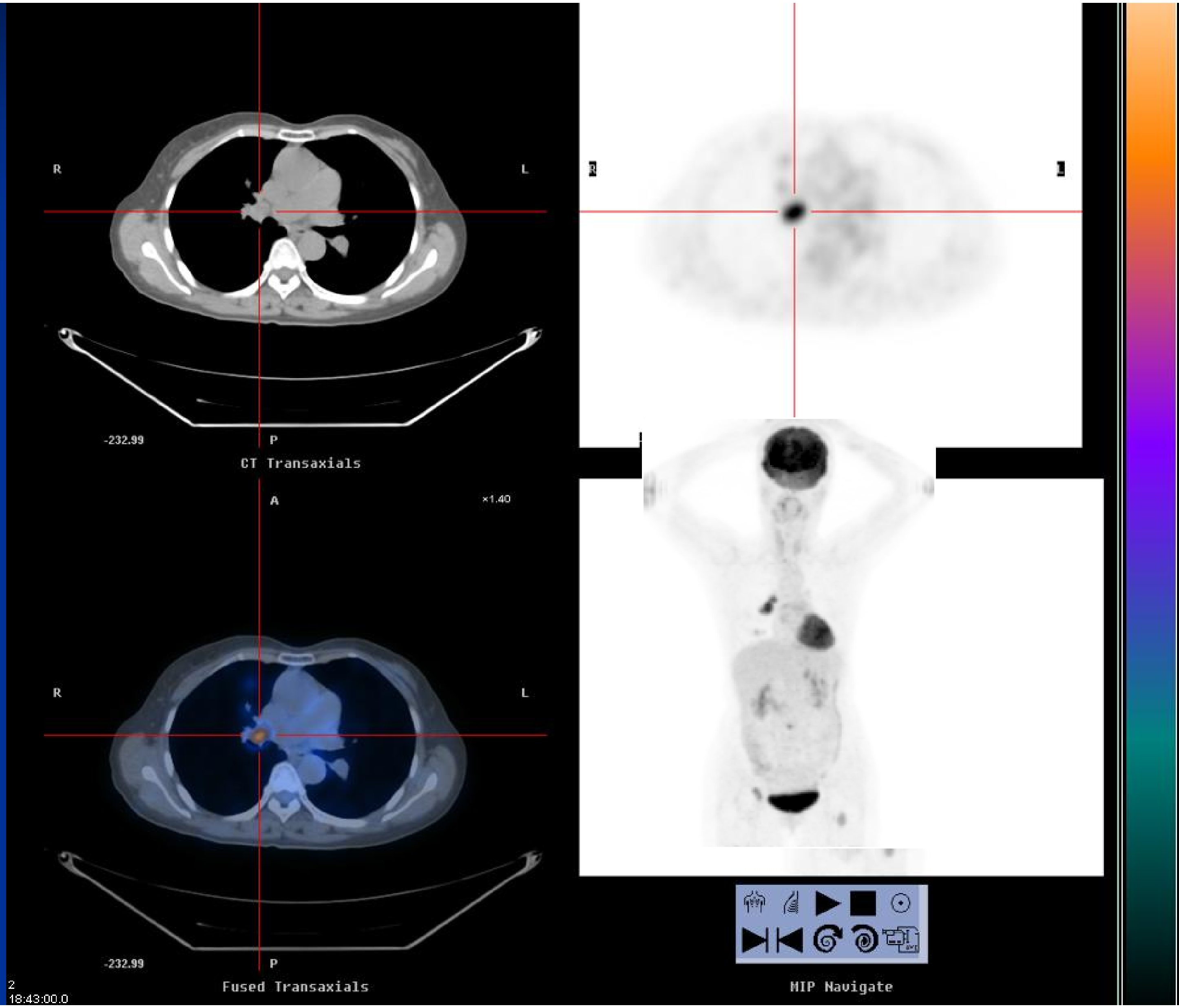
Patient preparation

- No vigorous exercise for one day
- Fasting> 4 hours except water
- Early morning appointment for DM patient
- No pregnancy for female patient
- Check Blood sugar < 150 mg

FDG PET in head and neck cancer

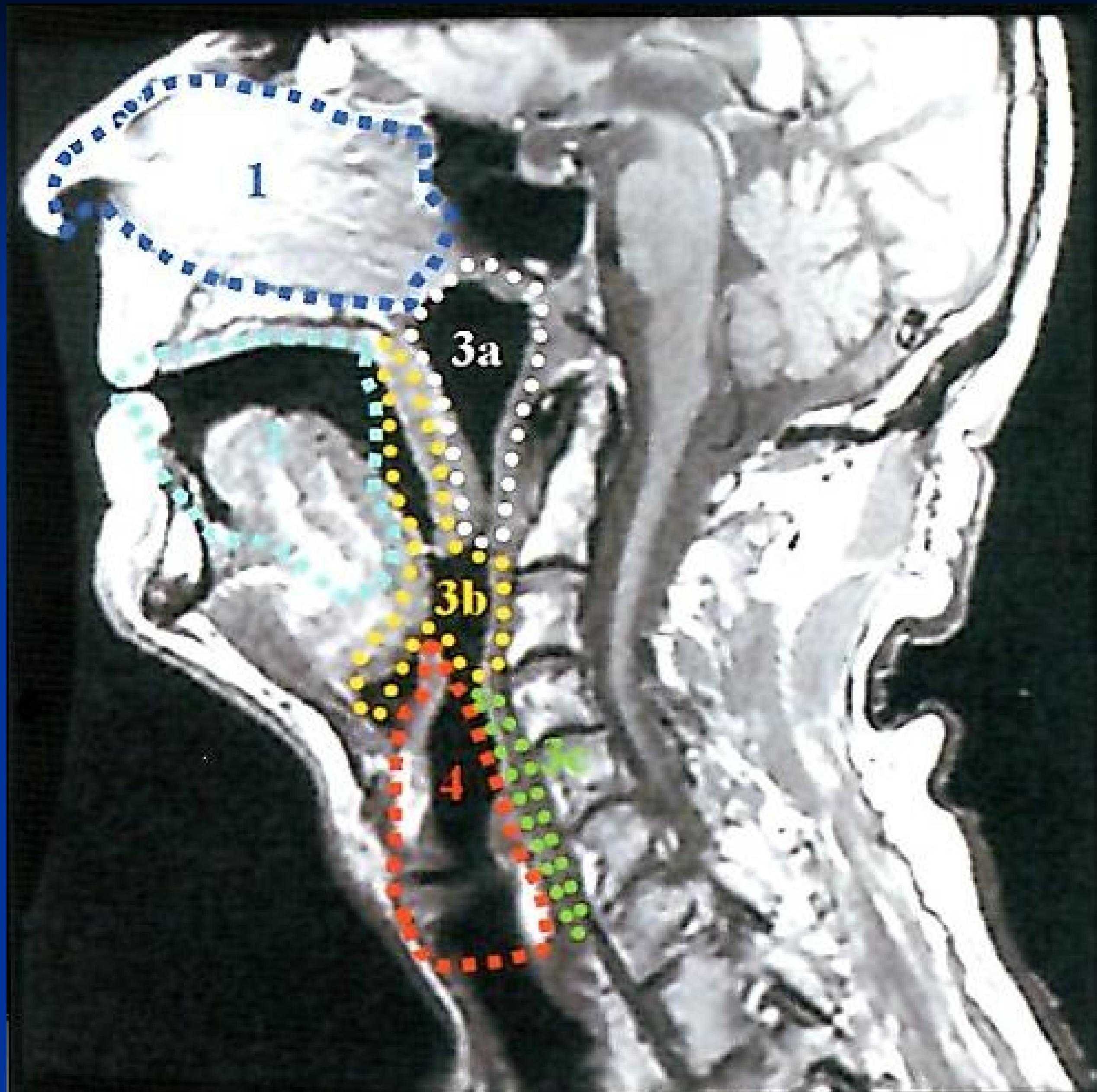
- Staging of head and neck cancer
  - Primary tumor evaluation by PET
  - Regional nodal staging by PET
  - Distant staging by PET
- Diagnosis of unknown primary tumor
- Treatment planning
- Therapeutic monitoring
- Assessment of recurrent head and neck cancer

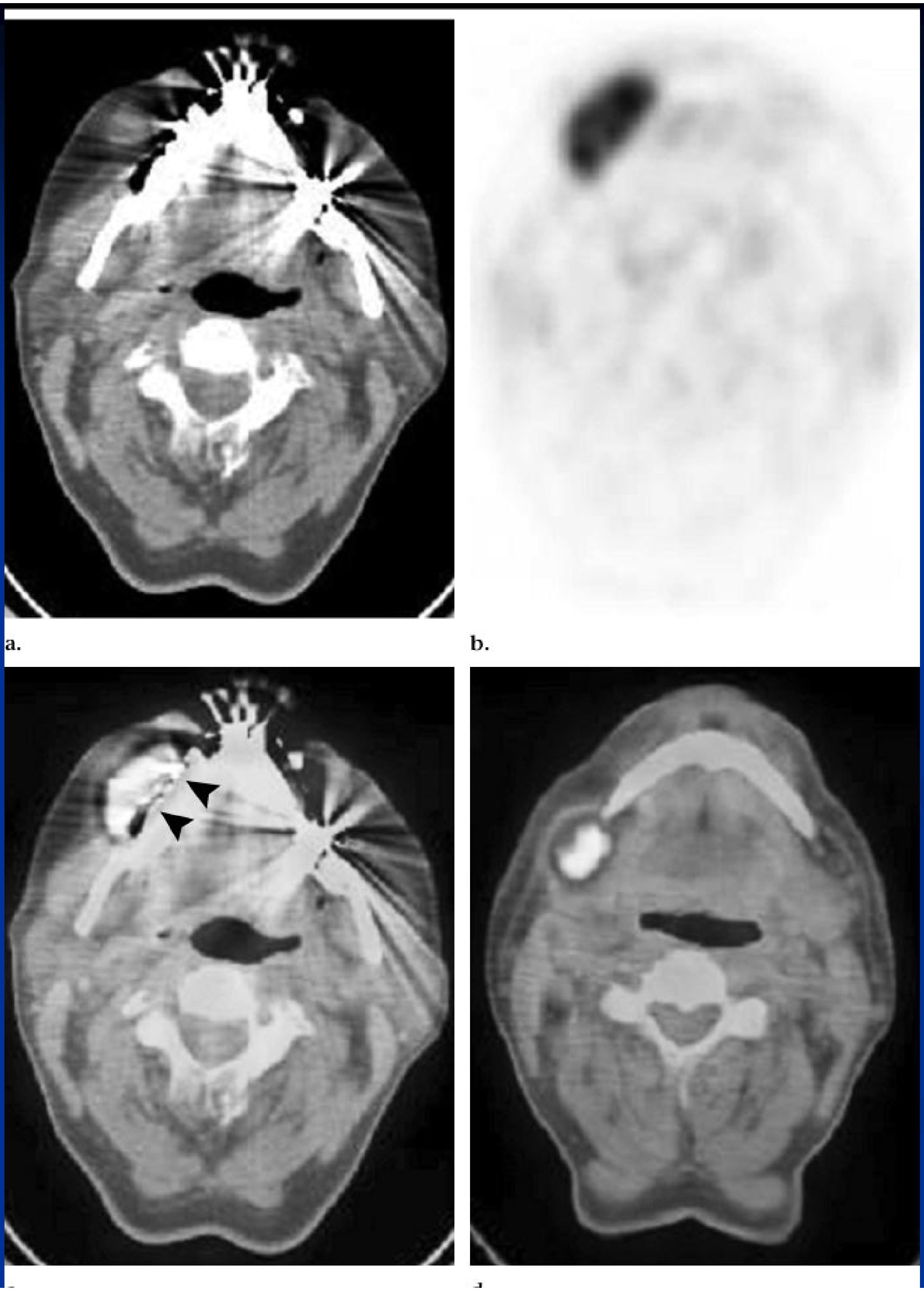
Normal FDG uptake, variants, and pitfalls



PET/CT in T staging

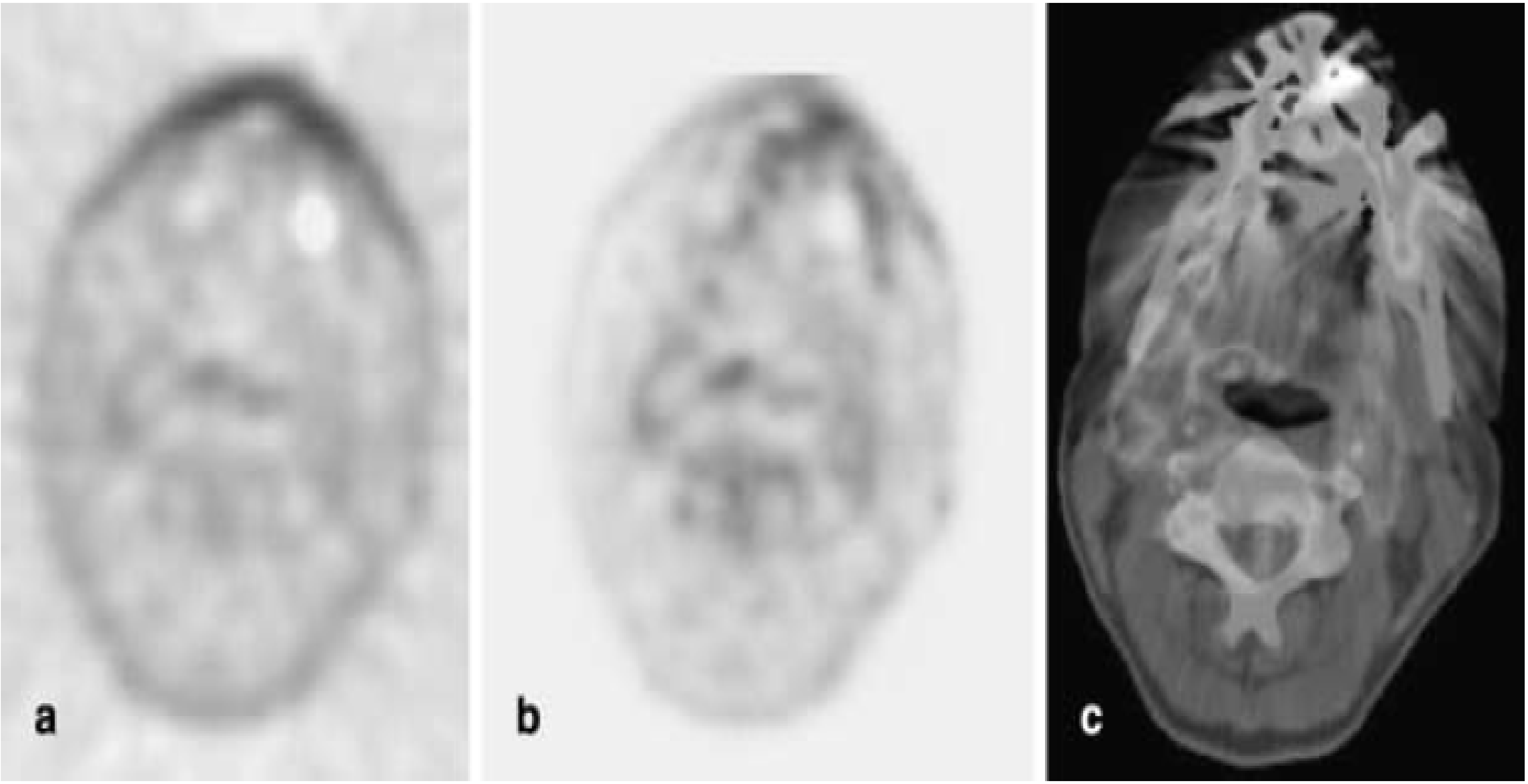
- Sensitive and specific: more than 90% to 95%
- Limited in primary tumor extension delineation.
- Dental artifacts on CT or MR images.
- The radiotherpy planning especially by delineating the gross tumor volume in intensity-modulated raidation therapy (IMRT)


1
3a
3b
4

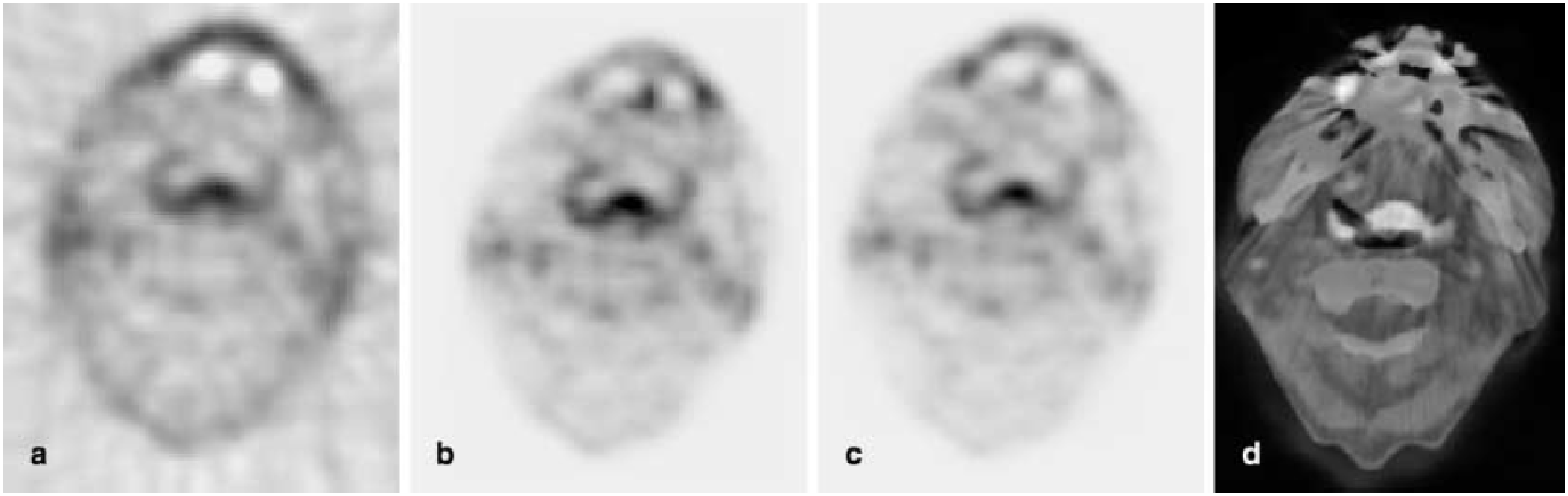


Bone Invasion in Patients with Oral Cavity Cancer: Comparison of Conventional CT with PET/CT and SPECT/CT

Radiology 2005

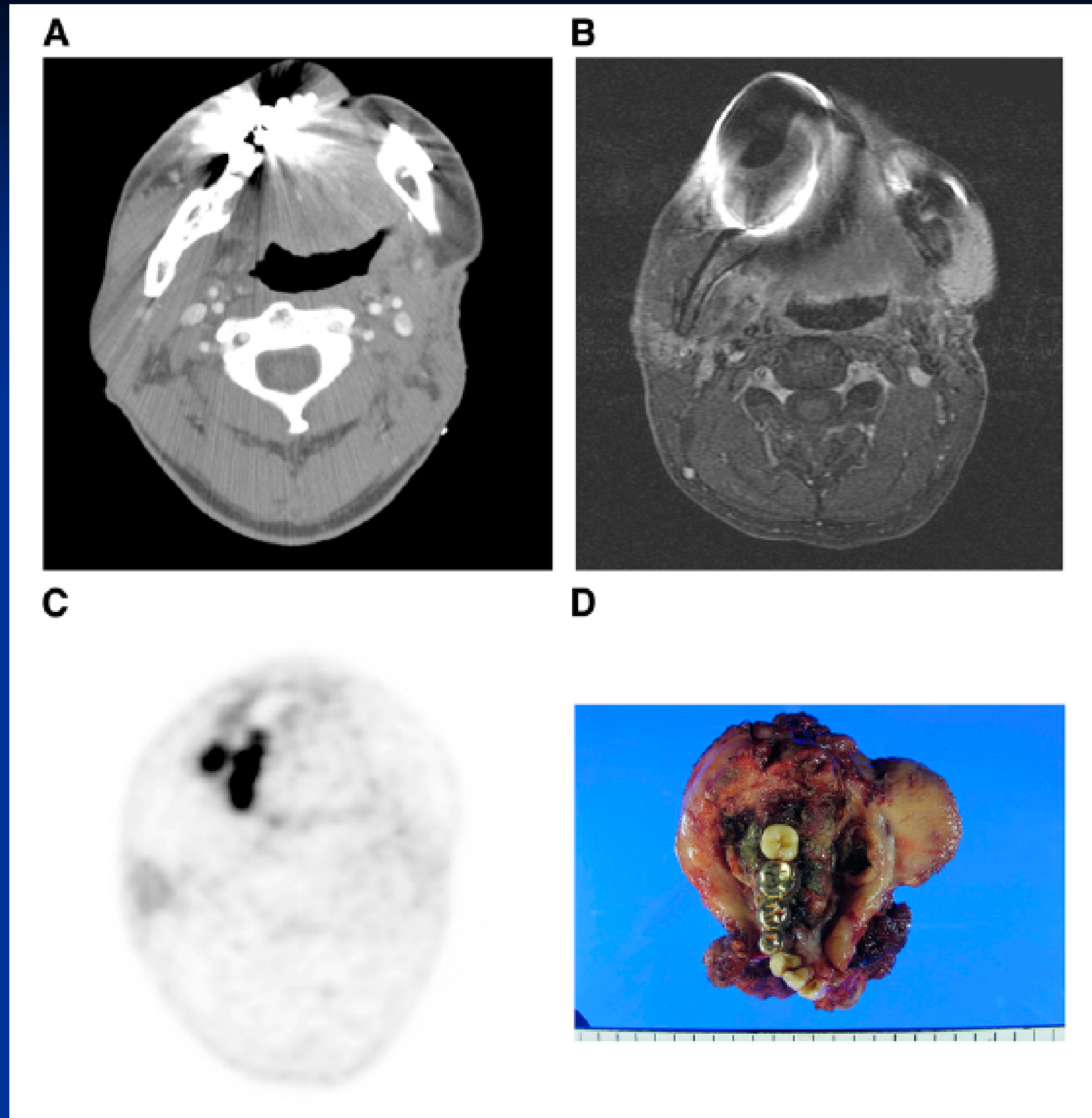


a In the non-attenuation-corrected PET image (filtered back-projection), white spots at the site of non-removable metallicdental artwork are visible.
b An artefact mimicking FDG uptake adjacent to the metallic foreign body is present on the identical slice when using attenuation correction (iterative reconstruction).
c In the co-registered PET/CT image, interpretation of this region is impossible.



a Dental fillings in a non-attenuation-corrected PET image in another patient.
b, c After applying attenuation correction, pseudo-uptake is present adjacent to the metallic dental bridgework. There is a difference between the PETGe68 image (**b**) and the PETCT scan (c)

• 54-y-old male patient with squamous cell carcinomas of right retromolar area



Standardized uptake value

$$\text{SUV} = \frac{\text{Tissue activity (uCi/cc)}}{\text{Administered activity (uCi/g)}}$$

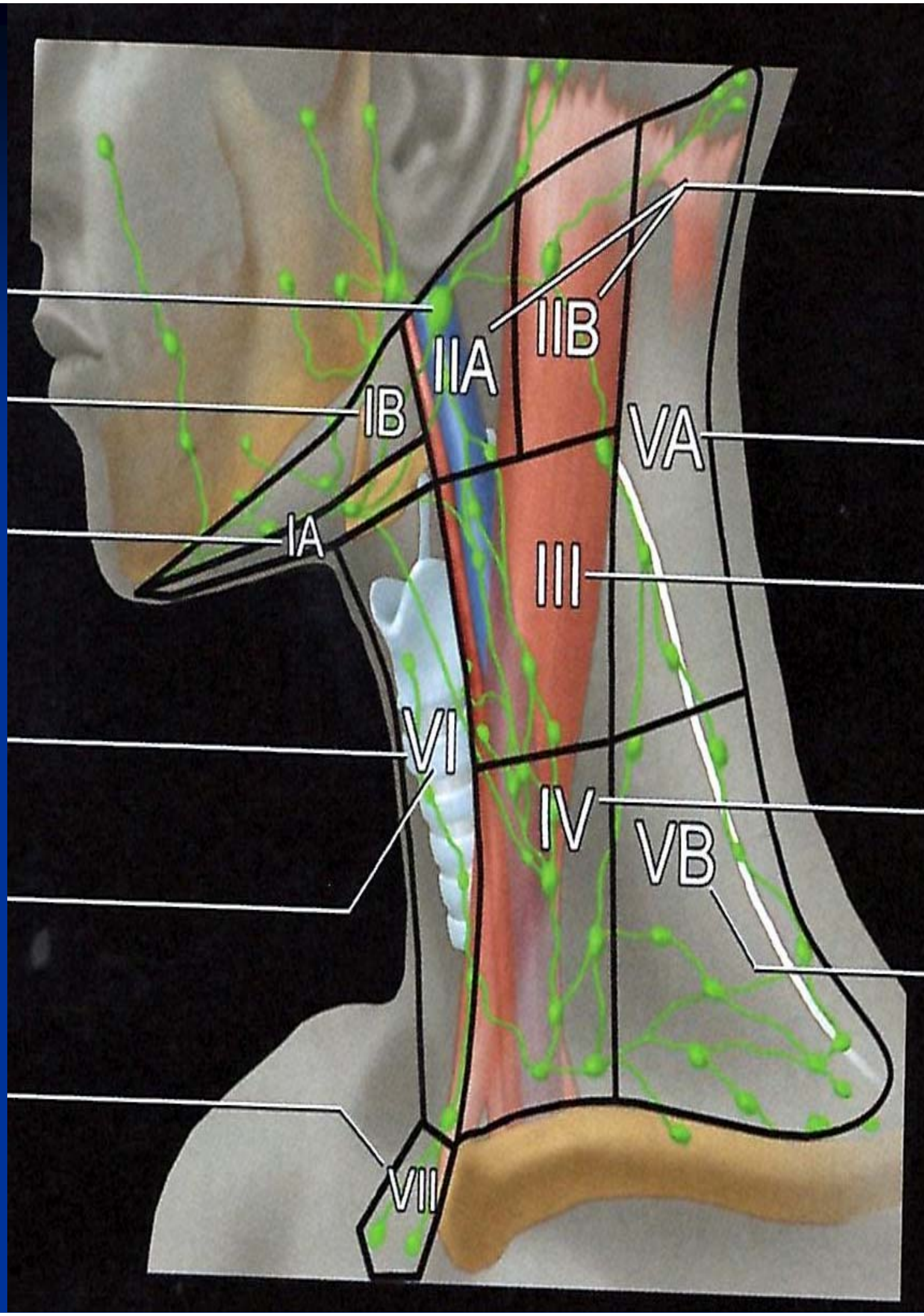
$$= \frac{\text{Mean ROI activity (mCi/ml)}}{\text{Injected dose (mCi)/body wt(g)}}$$

Factor affecting SUV

- Body composition and habitus
- Length of uptake period
- Glucose & insulin level ,renal function
- Partial volume effect
- Recent physical activity
- Inflammation can have elevated SUV

PET/CT in N staging

- PET has a high positive predictive value, greater than 90% to 95%, and is superior to CT and MRI with respect to sensitivity and specificity in the detection of nodal disease.


IIB
IIA
IB
VA
IA
III
VI
IV
VB
VII

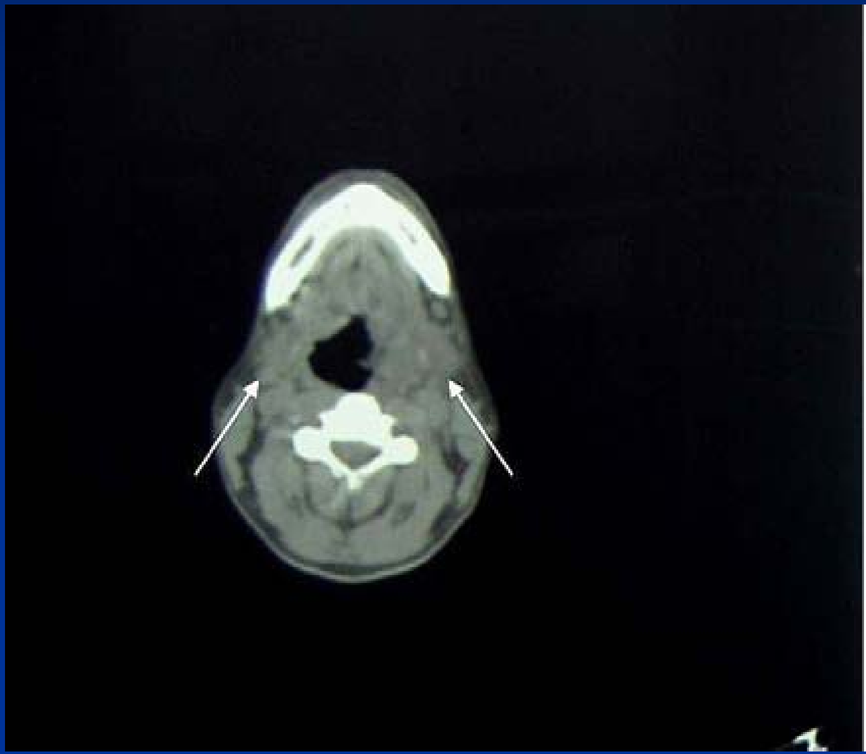



Table 1

Sensitivity and specificity of positron emission tomography (PET/CT) compared with CT or MRI in the detection of nodal disease in the neck confirmed on pathologic findings

Author	No. of patients	PET[a] or PET/CT[b] Sens/Spec (%)	CT Sens/Spec (%)	MRI Sens/Spec	Significance
Adams et al (1998)[6a]	60	90/94	82/85	80/79	S
Benchaou et al (1997)[58a]	48	72/99	67/97	NP	NS
Braams et al (1995)[59a]	12	91/88	NP	36/94	NP
Di Martino et al (2000)[60a]	50	82/87	82/94	NP	NS
Hannah et al (2002)[61a]	40	82/100	81/81	NP	NP
Jeong et al (2007)[5b]	47	92/99	90/94	NP	S
Laubenbacher et al (1995)[13a]	22	90/96	NP	78/71	S
Mattei et al (1998)[62a]	24	87/99	53/87 (CT/MRI)	—	S
Myers et al (1998)[63a]	14	78/100	57/90	NP	NS
McGuirt et al (1998)[12a]	45[c]	83/82	95/86	NP	NP
Ng et al (2005)[64a]	134	74/95	74/93 (CT/MRI)	—	S
Nowak et al (1999)[65a]	71	80/92	80/84 (CT/MRI)	—	NS
Paulus et al (1998)[66a]	25	50/100	40/100	NP	NP
Schwartz et al (2005)[67b]	63	100/96	96/99	NP	NS
Stuckensen et al (2000)[68a]	106	70/82	66/74	64/69	NP
Wong et al (1997)[14a]	16	67/100	—	67/25 (CT/MRI)	NP

Distant Metastases Staging (M0) and Detection of Synchronous Primary Tumors

- PET is useful in identifying distant metastases and synchronous second malignancies that may not have been detected on routine conventional imaging.
- Some series have reported a detection rate of previously unrecognized distant metastases of 27%.

Limitations

- Low grade malignancies
- Small lesion

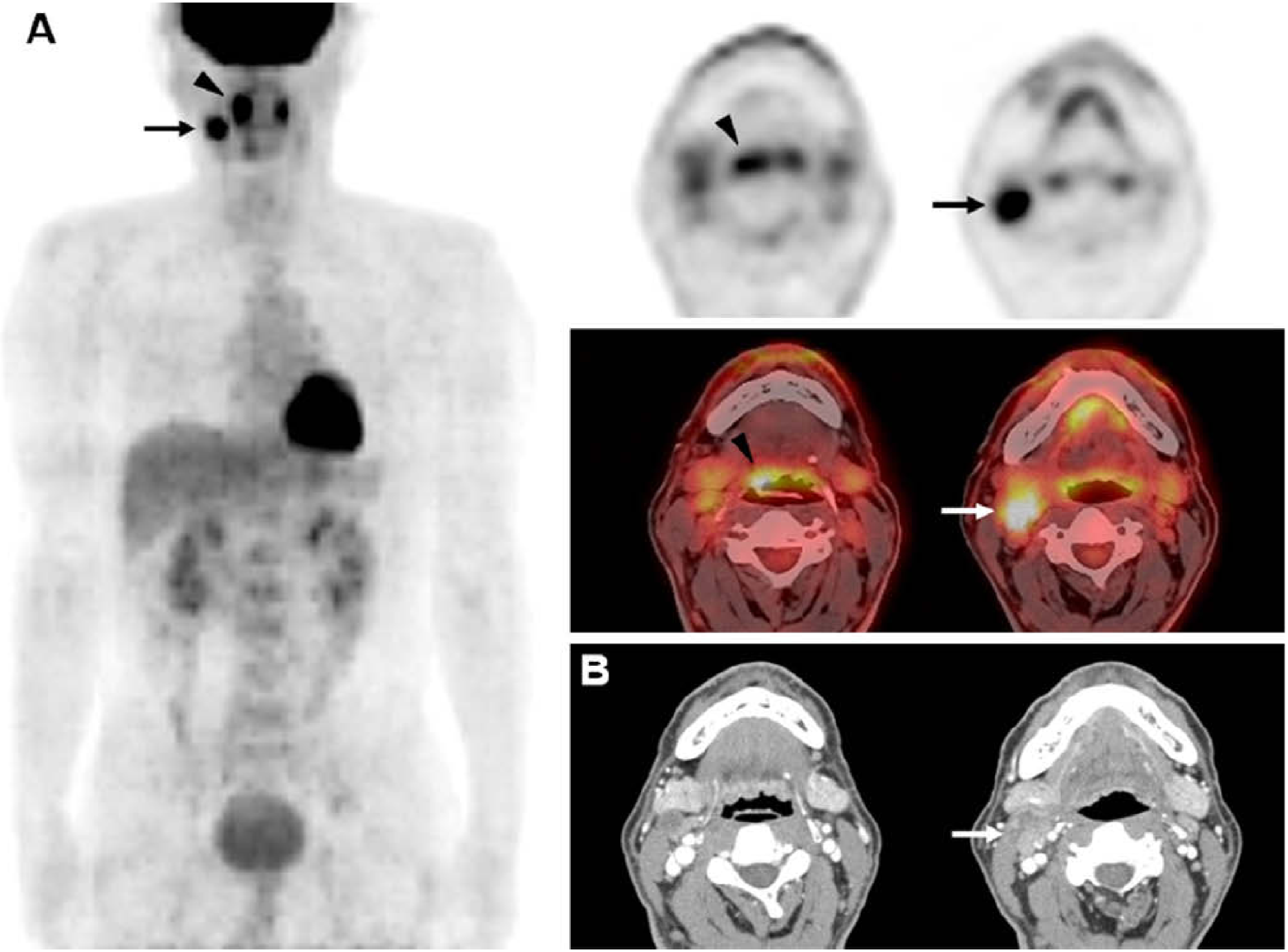
  - Size detectable is a function of reconstructed resolution and contrast

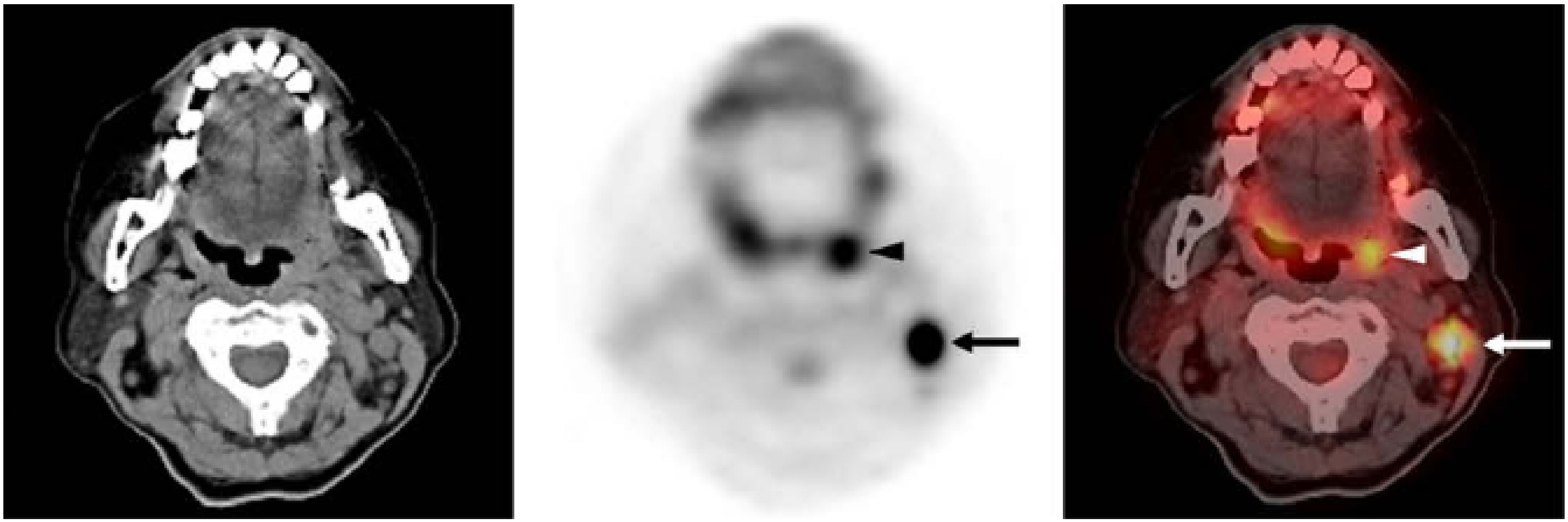
  - Partial volume effect or respiratory motion

  - <1mm
- Limited ability to distinguish between residual or recurrent tumor from scar
- Inability to biologically characterize disease
- Inflammatory diseases

Diagnosis of unknown primary tumor

- There have been conflicting reports with respect to the usefulness of PET in this setting.
- In a review of the published series by Rusthoven and colleagues17 the overall ability of PET to detect the occult primary was 25-49%, with a sensitivity, specificity, and accuracy of 88%, 75%, and 79%, respectively.


A
B



INITIAL MANAGEMENT

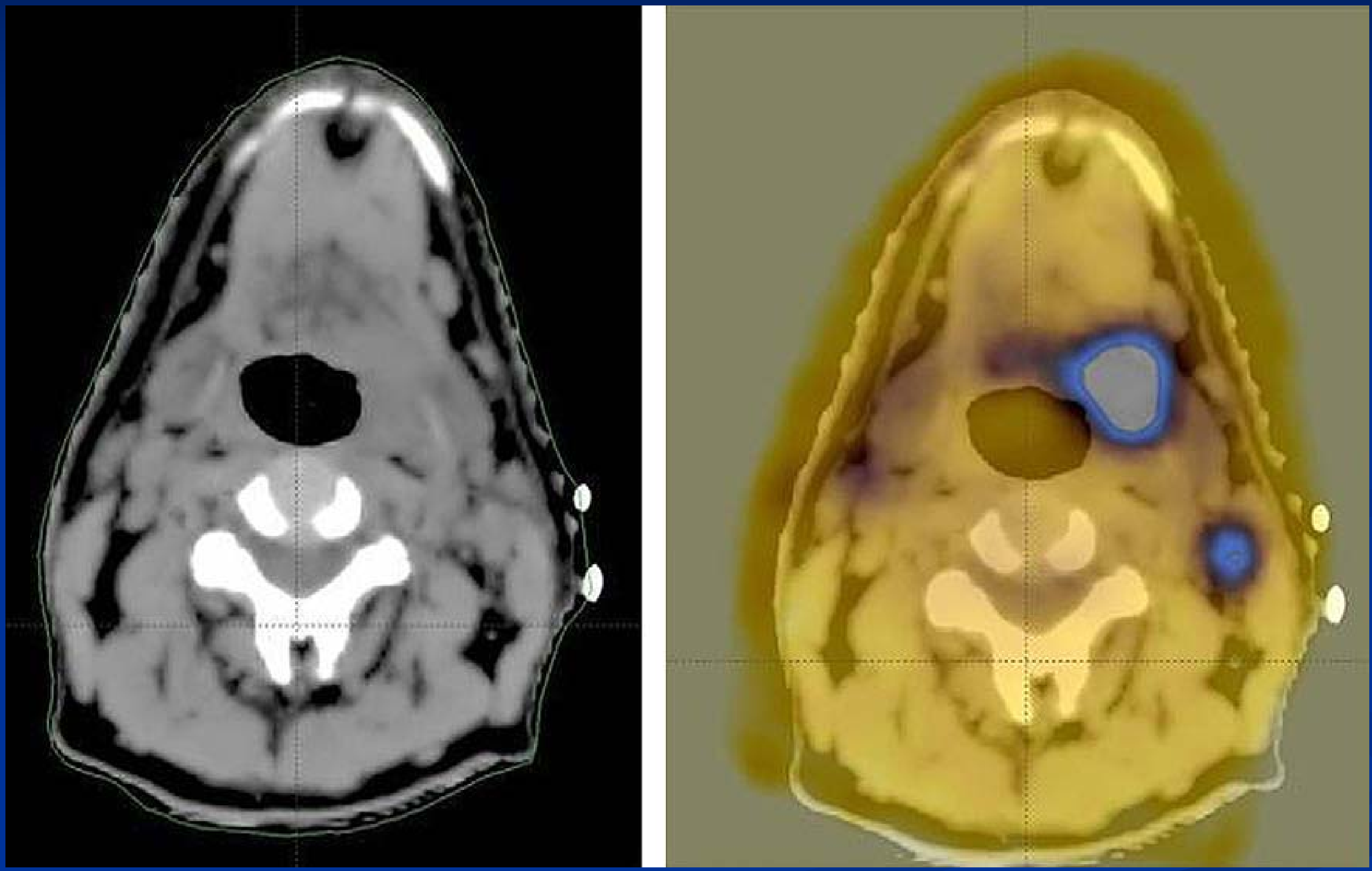
- The ability of PET to alter the TNM staging following conventional imaging, mainly N and M staging
- Connell and colleagues found PET/CT altered the TNM staging in 34% of patients, with 10/35 patients up-staged and 2/35 down-staged. In most cases the alteration was attributable to a change in N staging.

Clinically Node-Negative Neck (N0)

- clinical/radiologic N0 is based on perceived risk for less than 15% to 20% occult neck disease
- PET: Positive predictive value : 90% ~ 95%;

  Negative predictive value : 50% ~ 85%.
- Ng and colleagues assessed the usefulness of PET, CT, and MRI in patients who had oral cavity SCC and a palpably N0 neck
  - 134 patients, 26% were found to have neck metastases
  - The sensitivity of PET was 51% and this increased after visual correlation with CT/MRI to 57%.

Radiotherapy Planning



PET fusion with RT planning CT scans to assist with definition of tongue base tumor

Summary of Studies Dealing with PET or PET-CT Radiotherapy Target Delineation

First Author (Reference)	N	Type of Tumors	Method of Target Delineation	Findings
Nishioka (44)	21	12 oropharyngeal and 9 nasopharyngeal	Visualization	GTV altered in 11% of cases by fusion of PET with CT-MRI. Parotid sparing was able to be performed in 71% of patients.
Paulino (37)	40	22 oropharyngeal, 6 paranasal/nasal cavity, 4 nasopharyngeal, 3 laryngeal, 5 other	50% isointensity level	25% of patients under-treated with IMRT when PET-defined GTV was incorporated into CT-GTV-based treatment plan.
Riegel (35)	16	5 nasopharyngeal, 5 oropharyngeal, 2 laryngeal, 2 paranasal/nasal cavity, 2 other	SUV 3–4	Significant differences in GTV delineation were found between multiple observers contouring on PET-CT fusion.
Heron (43)	21		Visualization	8/21 patients had additional disease on PET and not visualized on CT.
Schwartz (42)	20		Visualization	Elimination of prophylactic coverage to PET-CT negative neck levels markedly reduced mean dose to contralateral parotid and to laryngeal cartilage.
Wang (36)	28	16 oropharyngeal, 6 hypopharyngeal, 3 nasopharyngeal, 3 other	SUV 2.5	In 50% of cases, PET-CT-based GTV different from CT-based GTV.
Scarfone (38)	6	Not stated	50% isointensity level	In 1 of 6 patients, PET found lymph nodes not found on CT. The CT-based GTV was modified in all patients using PET-CT-GTV.
Ashamalla (33)	25	6 oropharyngeal, 4 laryngeal, 4 nasopharyngeal/paranasal, 4 unknown primary, 3 oral cavity, 4 other	Halo	68% had significant GTV modification based on use of PET/CT. Interobserver variability was lower for PET-CT-GTV compared to CT-GTV.
Ciernik (45)	12	Not stated	Visualization	GTV increased in 17% and decreased in 33% of cases by at least 25% of volume.
Geets (46)	18	9 oropharyngeal, 5 hypopharyngeal, 4 laryngeal	Segmentation algorithm based on signal-to-background ratio	PET-GTV significantly smaller than CT- or MRI-based GTV. Decreased dose to ipsilateral parotid glands when PET-GTV was used.

Post-Radiotherapy Restaging

- Assessment of the neck following chemotherapy and RT can be difficult because of residual clinical or radiologic abnormalities.
- Following RT, PET/CT has the ability to distinguish whether there is ongoing metabolic activity within residual structural abnormalities and has a high negative predictive value, in excess of 95%.
- Yao and colleagues assessed the role of PET at a median of 15 weeks following definitive RT and found the negative predictive value was 100%.
- The optimal time for a restaging PET seems to be 12 to 15 weeks following treatment.

THERAPEUTIC MONITORING AND PROGNOSTICATION

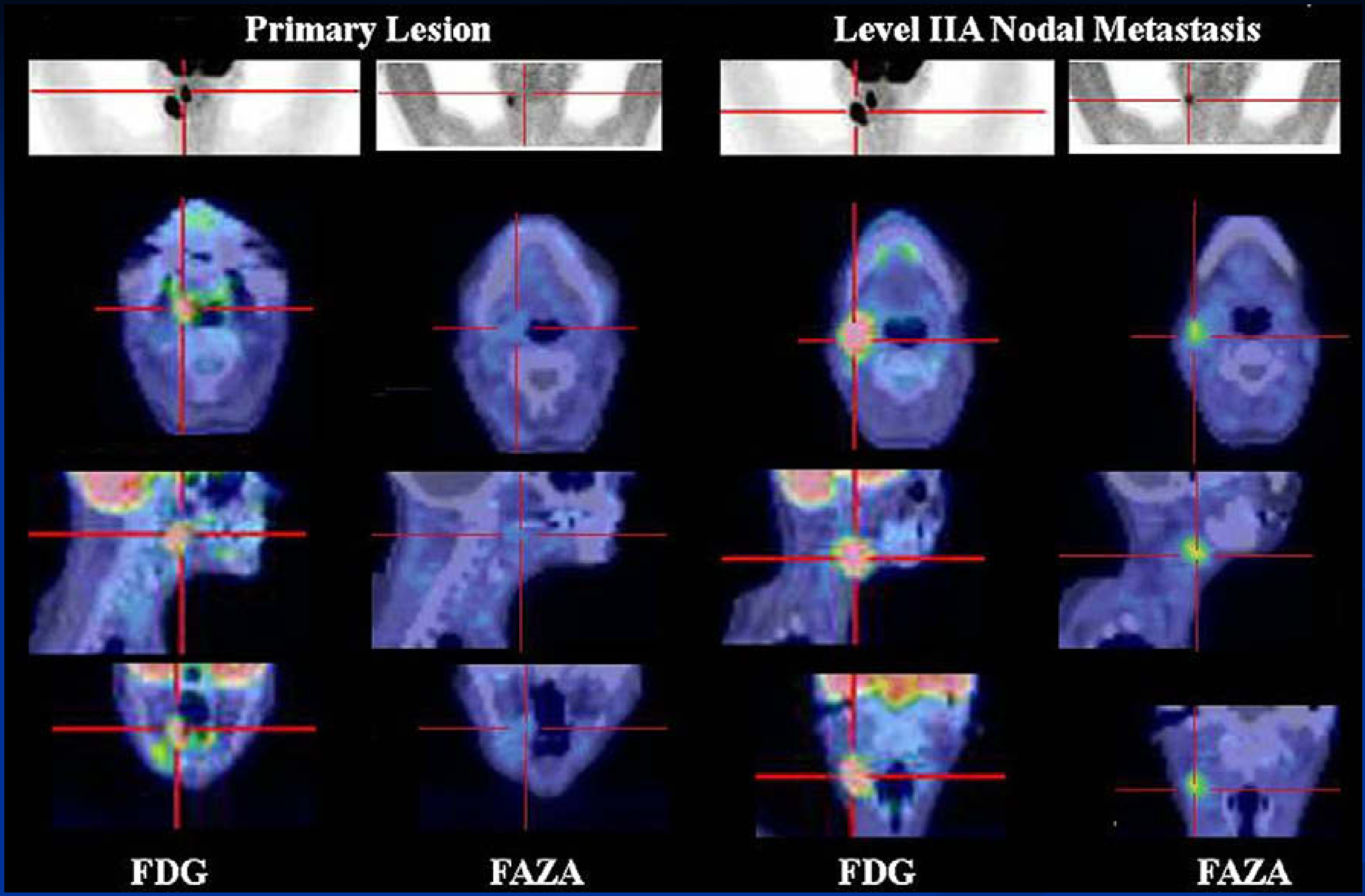
- PET response following RT seems to have some role in predicting long-term outcome.
- Brun and colleagues evaluated the metabolic response (MR) and standardized uptake value (SUV) in 47 patients who had HNSCC
  - Patients underwent a preatment PET followed by another PET after 1 to 3 weeks of radical RT
  - Low and high MR FDG PET, with median value as cutoff, was associated with complete response in 96% and 62% (P =0 .007)
  - 5-year survival, 72% versus 35% (P 5 .0042)

RESTAGING AT RELAPSE AND SURVEILLANCE

- In patients treated with HNSCC the 5-year rate of locoregional recurrence, second malignancy, and development of distant metastases are 40% to 50%, 10% to 30%, and 15% to 20%, respectively.

NOVELTRACERS AND CLINICAL IMPLICATIONS

- Hypoxia imaging
  - Hypoxia has long been recognized as an adverse determinant of RT treatment outcome in head and neck cancer
  - 18F-labelled FMISO PET
  - fluorine-18 fluoroazomycin arabinoside (FAZA) PET



FDG PET demonstrating uptake at the tongue base and level II node with the FAZA PET demonstrating hypoxia in the node only.

- Proliferation Imaging
  - Increased proliferation is one of the hallmarks of cancer cells.
- fluorine-18 fluoro-deoxy-L-thymidine (FLT)

- Novel tracers, such as fluorine-18 fluoromisonidazole (FMISO) and fluorine-18
- fluoro-deoxy-L-thymidine (FLT), are being evaluated in their ability to biologically characterize
- disease and provide prognostic information

Thank You for your attention