AIRO Lombardia

Tumori del distretto cervico-cefalico

dalla definizione dei piani di trattamento alla adaptive radiotherapy

Milano, 22 giugno 2013

La stadiazione mediante imaging

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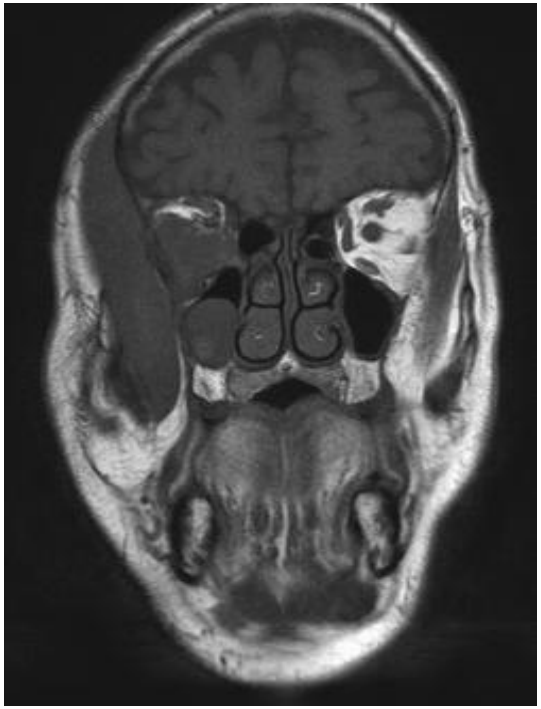
Role of imaging

- Complex anatomy
- Dedicated acquisition protocols (PET/CT)
- Minor role in diagnosis (biopsy)
- Essential in staging
  - Local extension
  - Regional lymph node
  - Distant metastases
  - Other malignancies
- Assessment of response
- Detection of relapse

Role of imaging – MR/CT

- Exact definition of T
  - T volume on PET is generally reduced when compared to morphologic imaging
- 3D target volume definition
  - RT or navigation, evaluation of adjuvant treatment
- Accurate of N definition
  - Specificity CT=39% / MRI=48%
  - New contrast media
- Optimization of restaging accuracy

Anatomical imaging



Spiral CT

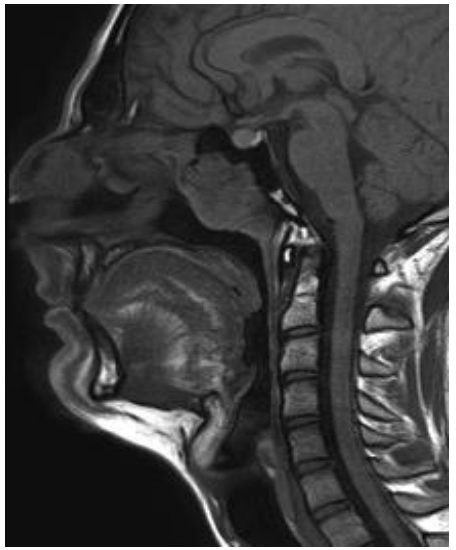
- High spatial resolution
- Unsurpassed definition of the bone structures
- Good cost/benefit ratio

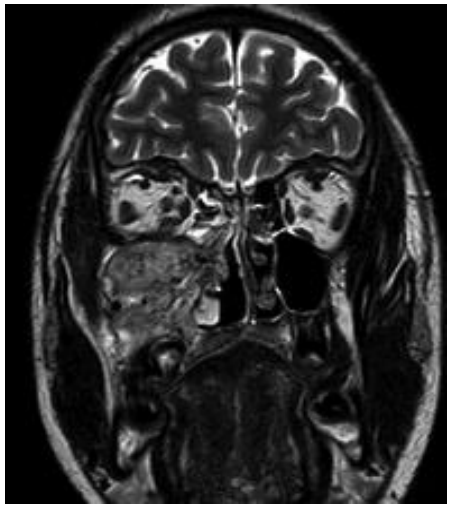
- Low contrast resolution for soft tissue

- 3D reconstruction – navigation SW
- No geometric distortion
- Measure of absorbed dose

MRI (1.5 T)

- High contrast resolution for soft tissues
- High multiplanar anatomical details
- 3D reconstruction – navigation SW
- Magnetic artifacts, bone/air interface, distortions at field margins
- No information on tissue density
  - Cannot be used alone in RT planning





Radiopharmaceuticals

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Amino acid transport and protein synthesis	Methionine	C-11	Liver, salivary glands, lachrymal glands, bone marrow, pancreas, bowels, renal cortical, urinary bladder	In-house production/cyclotron
	Fluoroethyltyrosine	F-18	Pancreas, kidneys, liver, heart, brain, colon, muscle	In-house production/cyclotron[b]
	FDOPA	F-18	Pancreas, liver, duodenum, kidneys, gallbladder, biliary duct	Commercially available
Glucose metabolism	FDG	F-18	Brain, myocardium, breast, liver, spleen stomach, intestine, kidney, urinary bladder, skeletal muscle, lymphatic tissue, bone marrow, salivary glands, thymus, uterus, ovaries, testicle, brown fat	Commercially available
Proliferation	FLT	F-18	Bone marrow, intestine, kidneys, urinary bladder, liver	In-house production/cyclotron[b]
Hypoxia	FMISO	F-18	Liver, urinary excretion	In-house production/cyclotron[b]
	FAZA	F-18	Kidneys, gallbladder, liver, colon	In-house production/cyclotron
	Cu-ATSM	Cu-64	Liver, kidneys, spleen, gallbladder[c]	In-house production/cyclotron[b]
Lipid metabolism	Choline	C-11	Liver, pancreas, spleen, salivary glands, lachrymal glands, renal excretion, bone marrow, intestine	In-house production/cyclotron
	Fluoroethylcholine	F-18	Liver, kidneys, salivary glands, urinary bladder, bone marrow, spleen	In-house production/cyclotron[b]
	Acetate	C-11	Gastrointestinal tract, prostate, bone marrow, kidneys, liver, spleen, pancreas	In-house production/cyclotron
Angiogenesis/integrin binding	Galacto-RGD	F-18	Bladder, kidneys, spleen, liver	In-house production/cyclotron
	AH111585	F-18	Bladder, liver, intestine, kidneys	In-house production/cyclotron
SSTR binding	DOTATOC	Ga-68	Pituitary and adrenal glands, pancreas, spleen, urinary bladder, liver, thyroid	In-house production/generator

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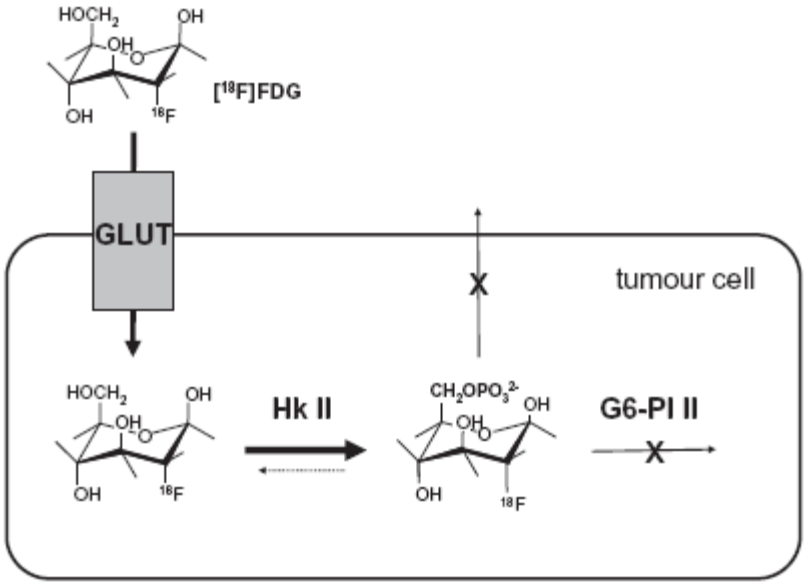
^{18}FDG uptake mechanism



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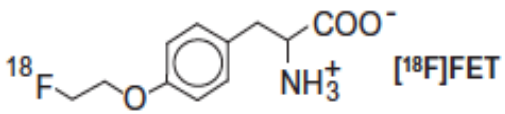
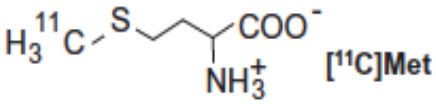
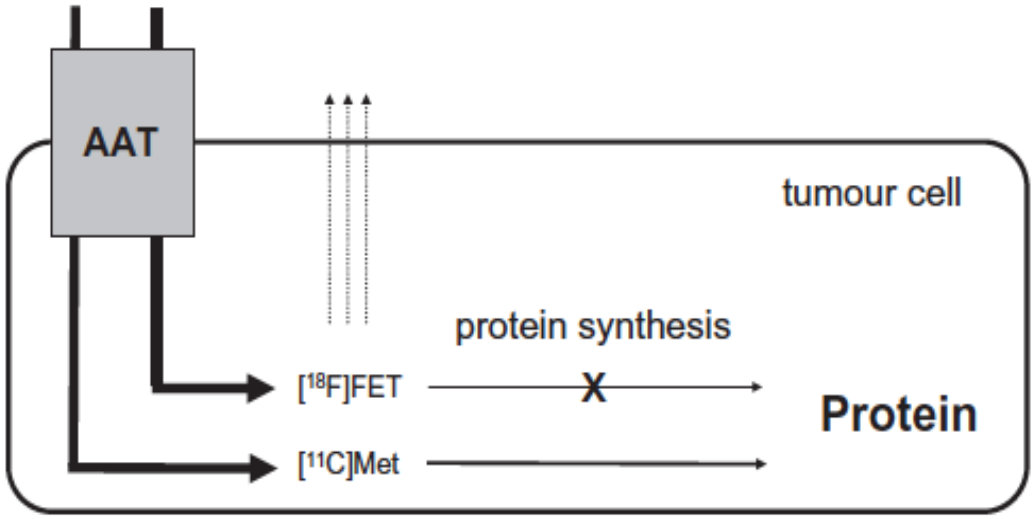
BEYOND FGD

- Overcome FDG limits
  - Biodistribution
  - Glucose metabolism
- Increase specificity and sensitivity
- Visualize specific pathways

Amino Acids uptake mechanism







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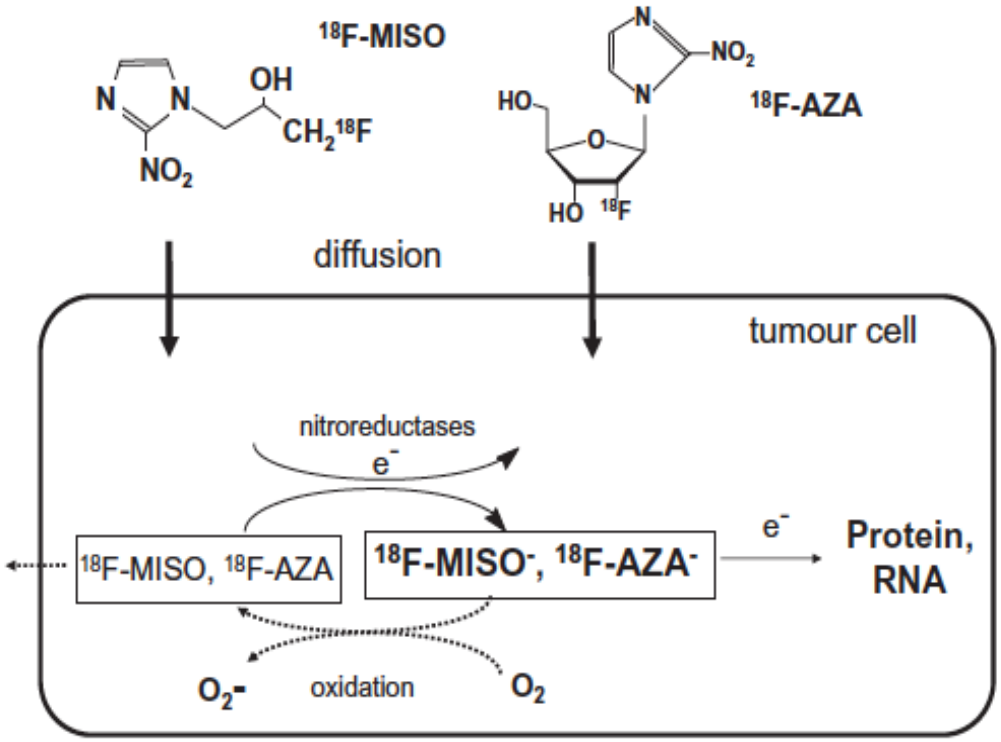
^{18}FMISO and ^{18}FAZA uptake mechanism



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Staging

- Several published studies
  - Old detection systems
- FDG PET accurately detects primary tumors without advantages over CT/MRI.
- At this stage of technology FDG PET alone is not appropriate to evaluate local extension

N staging

- PET cannot detect micro mestastases
- Better than CT/MR to detect metastases in normal sized lymph nodes
- Correlative imaging is mandatory
  - Level and size
  - Number and distribution (ipsilateral or contralateral)
  - Extra-capsular spread

Evaluation of the negative neck

Author and Year	No. Patients	Specificity, %	Sensitivity, %
Wensing, et al, 2006	28	33	76
Schoder, et al, 2006	36	67	85
Stoekli, et al, 2002	12	25	88
Myers, et al, 1998	12	78	100

Agarwal V, Otolarygol Clin N Am 2008

N staging

	SN	SP
FDG PET	**90%**	**94%**
CT	**82%**	**85%**
MR	**80%**	**79%**
US	**72%**	**70%**

Distant metastases

- Low prevalence at presentation (< 5%)
- Whole body staging
- Detection of a second primary tumor
  - Common risk factors
  - Areodigestive tract
  - Esophagus
  - Lung

Cervical metastases from unknown primary

- CUP syndrome
- Localize a focus of uptake to guide biopsy
- FDG PET detection rate: 30-50%
- CT/MR detection rate: 10-20%

Post-therapy evaluation

- Imaging plays a major role
- PET has greater accuracy than CT/MRI in detecting residual or recurrent disease
  - FDG biological properties
  - Volume changes occur late
  - New therapies aim to stabilize the tumor
  - FDG images are not affected by post-therapy anatomical distortions

Detection of recurrence

- Most recurrences appears in the first 2 years
- FDG PET results
  - Sensitivity 88-100%
  - Specificity 75-100%
- CT/MR results
  - Sensitivity 70-92%
  - Specificity 50-57%
- FDG false positive
- Semi-quantitative evaluation (SUV)
- Whole body evaluation

Clinical use of PET in Head & Neck tumors

Summary of available data on the use of PET–CT in radiotherapy planning.

Tumour site/ pathology/tracer	Target volume selection	Target volume delineation	Isodose distribution	Adaptive treatment	Patient outcome
HNSCC and ^{18}FDG	Limited (lymph nodes) or no use (primary tumour) of ^{18}FDG. Potential benefit for unknown primary tumour	Potentially interesting for primary tumour GTV using automatic segmentation. Decision aid for lymph nodes	Preliminary study indicating more conformed ^{18}FDG-PET-based plans	Promising preliminary data. No routine use yet	No prospective data available comparing CT-based and ^{18}FDG-PET-based plans
Undifferentiated NPC	No use of ^{18}FDG (primary tumour)	No data available	No data available	No data available	No data available
HNSCC and ^{18}FMISO	Three successful theoretical studies on selection of subvolume	Three successful theoretical studies on delineation of subvolume	Theoretical study indicating an increased TCP with same toxicity	No data available	Prognostic and predictive value shown in small clinical studies
HNSCC and ^{18}FLT	Limited (primary tumour) and no use (lymph nodes) of ^{18}FLT	No data available	One theoretical planning study on dose escalation to ^{18}FLT subvolume	One study on oropharyngeal tumours	Results on prognostic value awaited

HNSCC, head and neck squamous cell carcinoma; ^{18}FDG, ^{18}F-fluorodeoxyglucose; GTV, gross tumour volume; NPC, nasopharyngeal carcinoma; ^{18}FMISO, ^{18}F-fluoromisonidazole; TCP, tumour control probability; ^{18}FLT, 3′-deoxy-3′-^{18}F-fluorothymidine.

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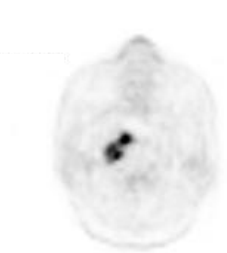
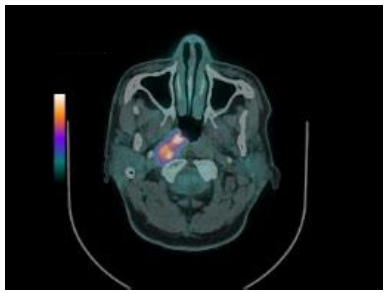
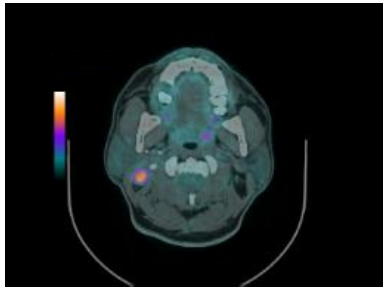
Adding PET-CT to a radiotherapy plan

- Reduction of inter-observer variability in GTV delineation
- Reduction in GTV
- Identification of tumor extensions missed by CT or MRI
- Identification of GTV sub-volumes



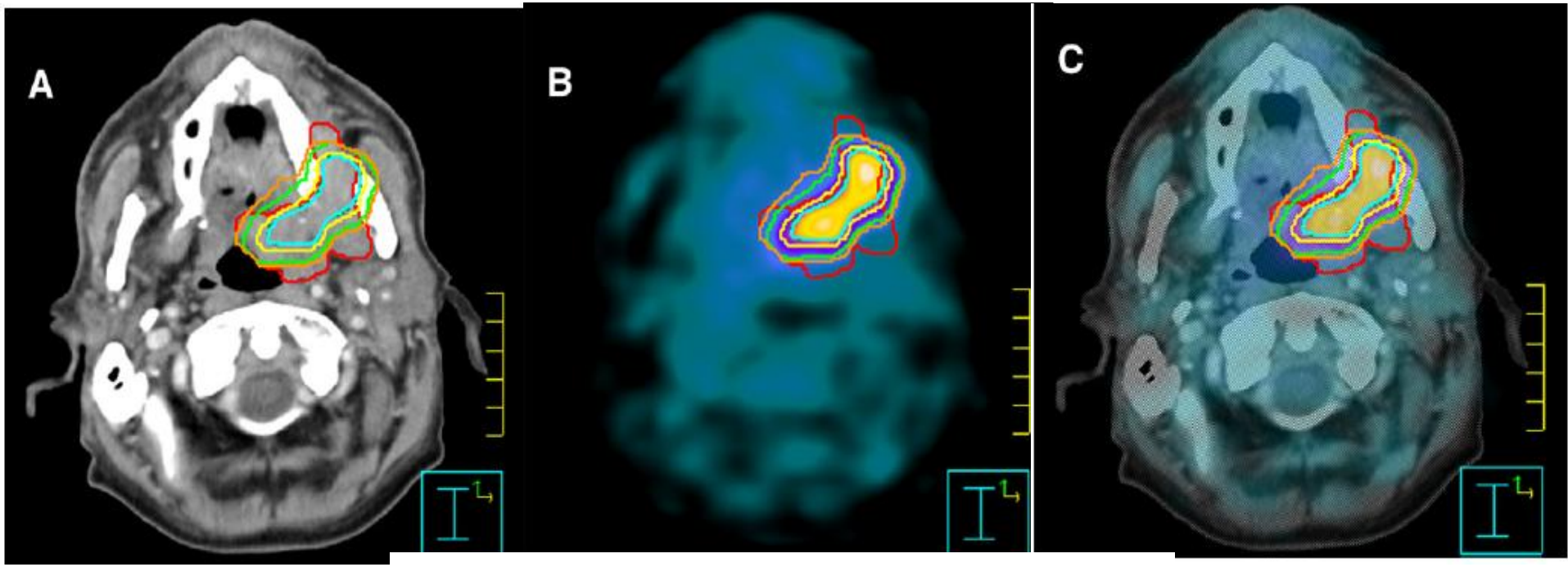




PET-CT provides extra info for GTV delineation

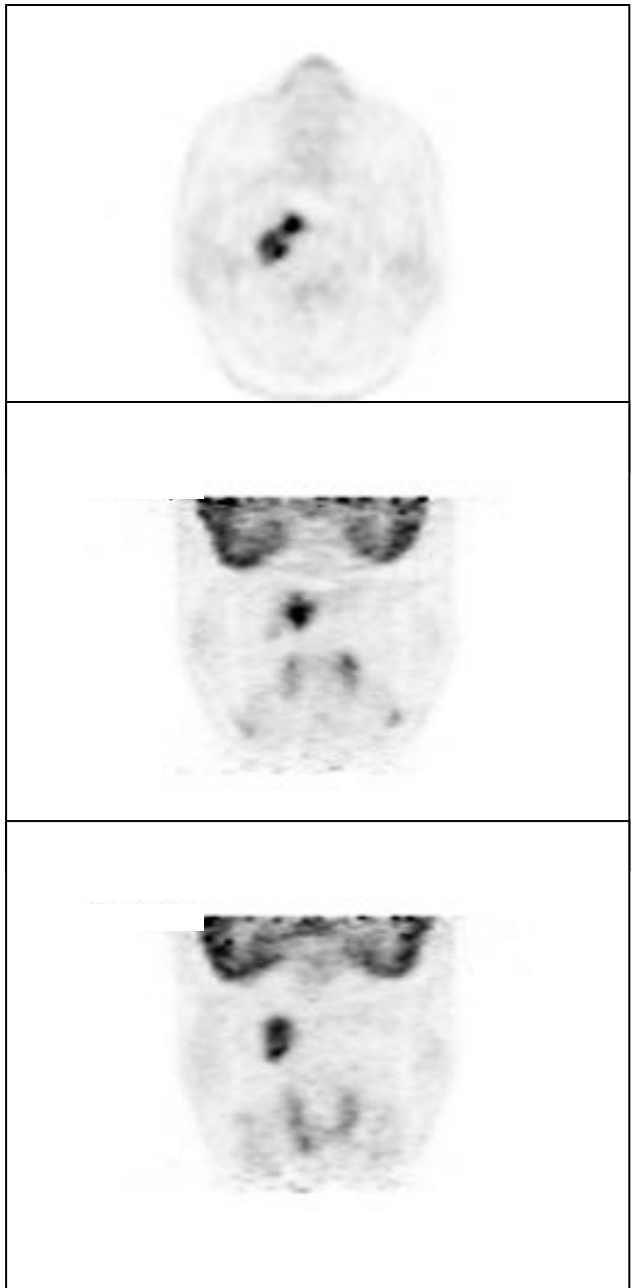
Thresholding

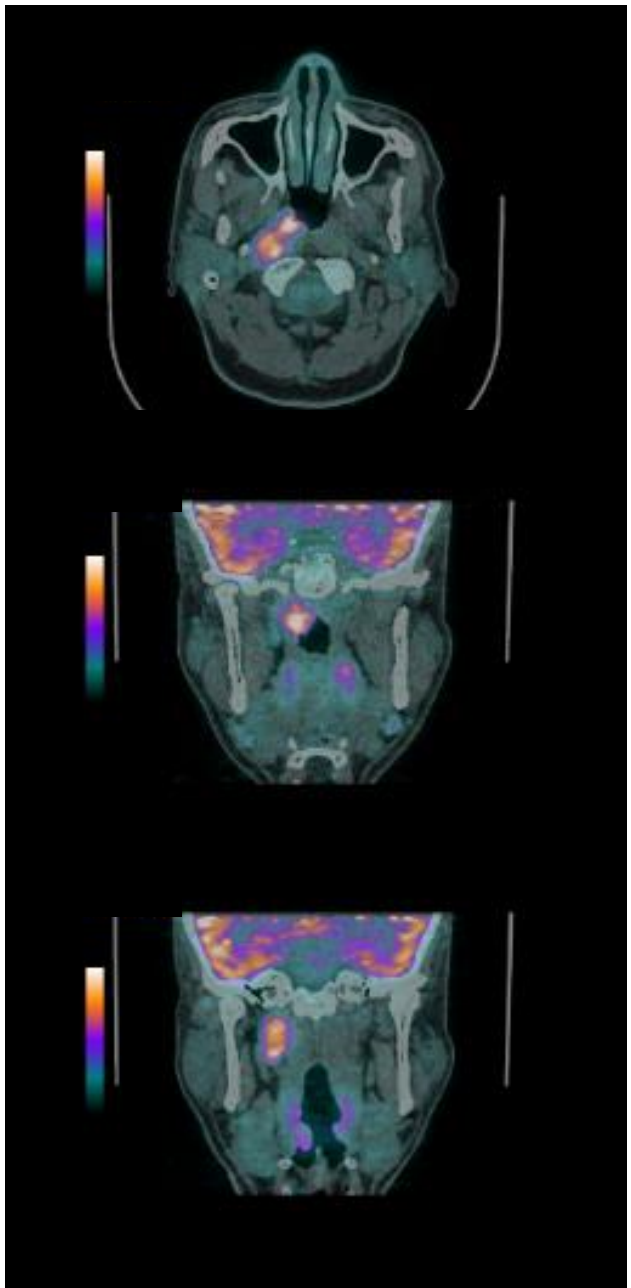
Clinical evidence on PET–CT for radiation therapy planning in head and neck tumours



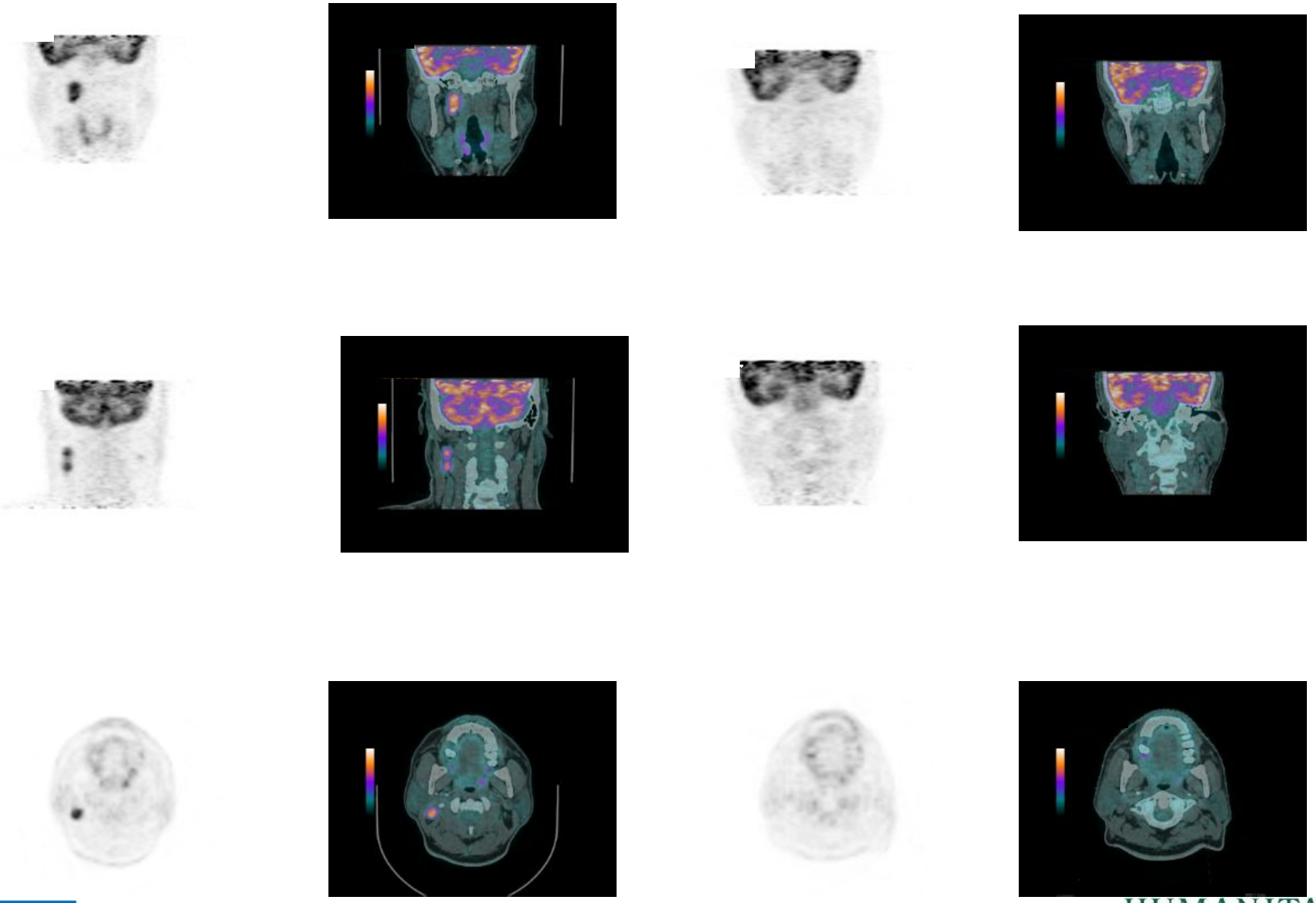
E.G.C. Troost et al. / Radiotherapy and Oncology 96 (2010) 328–334

Nasopharingeal carcinoma

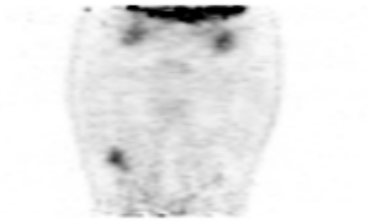


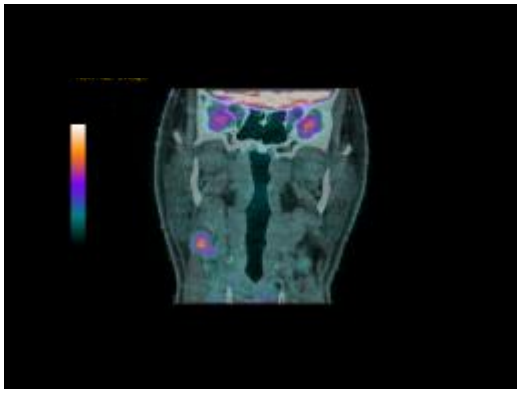


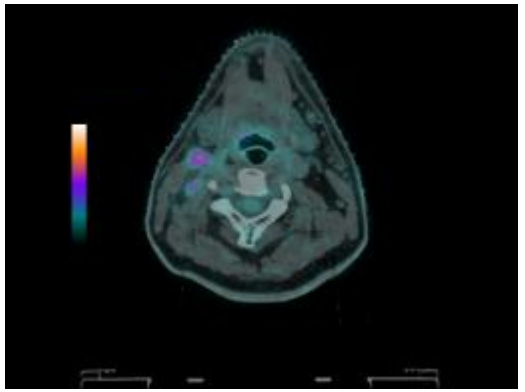
Nasopharingeal carcinoma

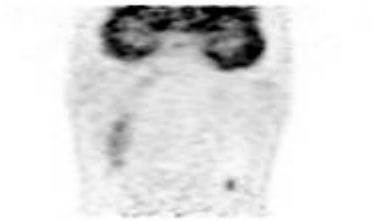


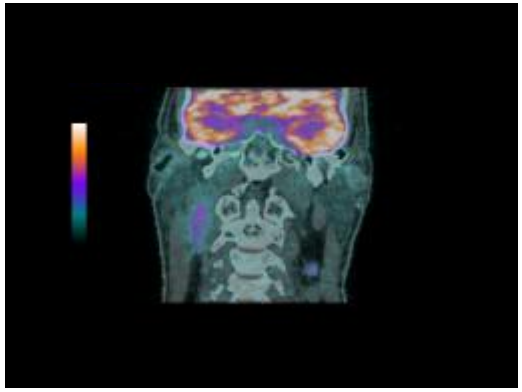
Nasopharingeal carcinoma

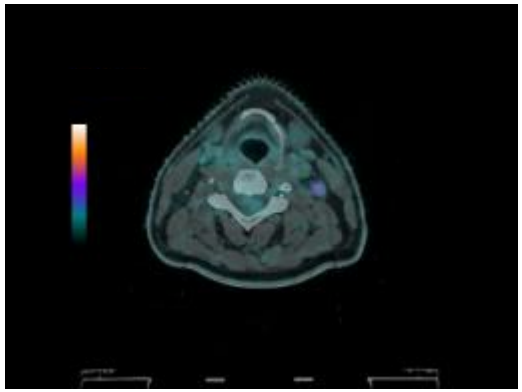




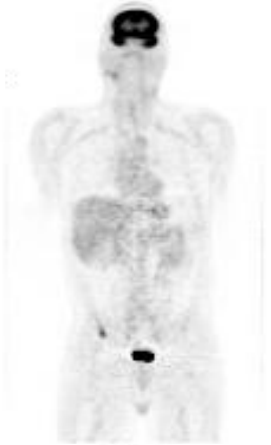


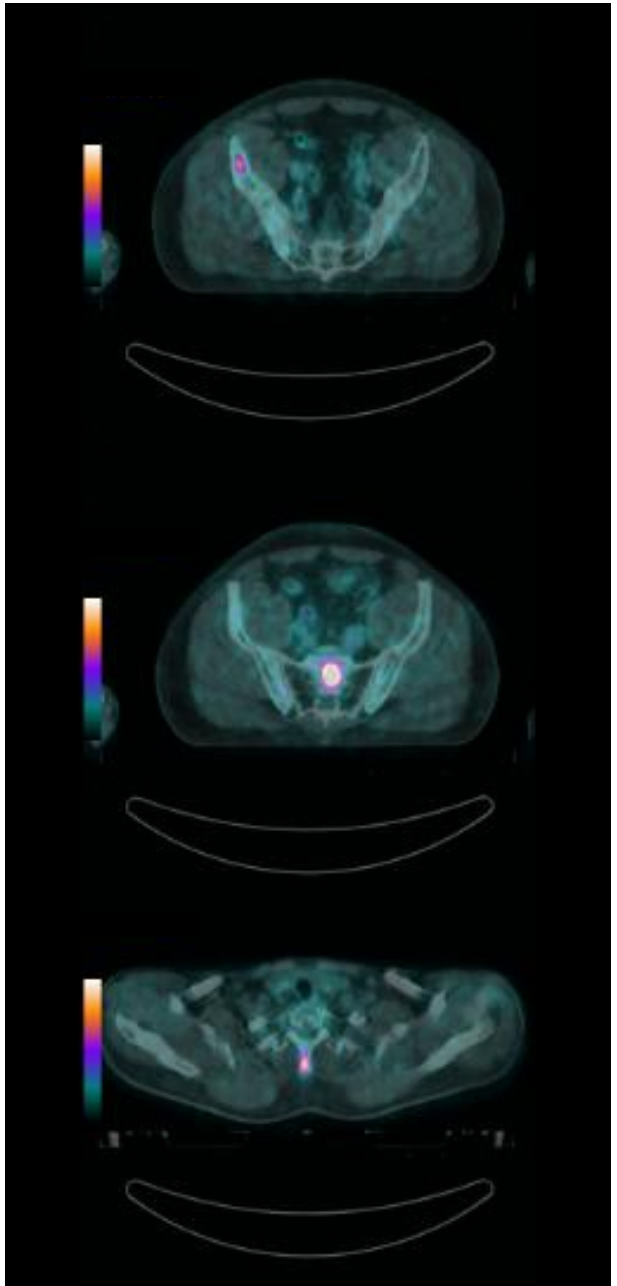






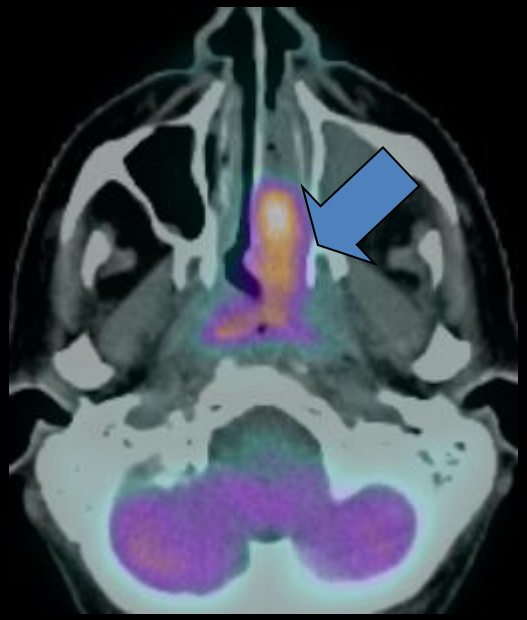
Nasopharingeal carcinoma



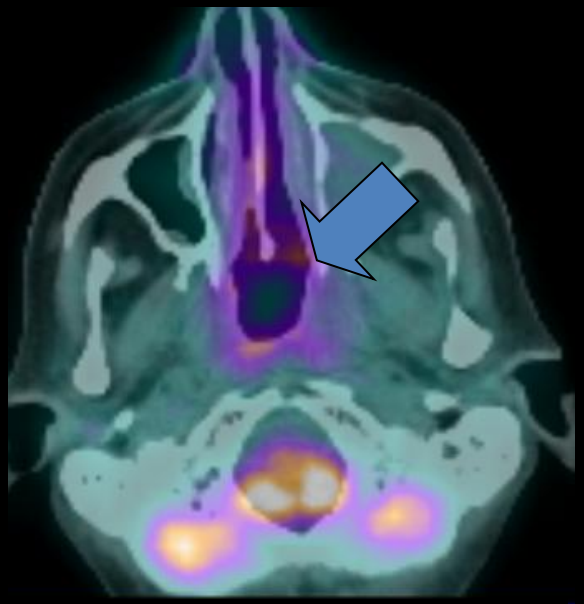


PT.60 y. Nasopharynx carcinoma. Prior RT (56 Gy neck+8 Gy brachy in 2007).
local recurrence: CR after TrueBeam Reirradiation with FFF

Dose:30 Gy/5 fr



PET/CT before SBRT



PET/TC after 6 months

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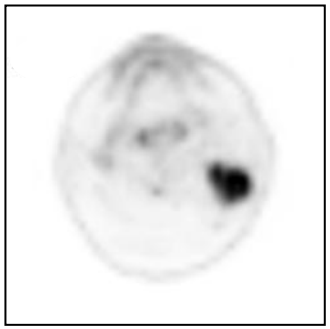
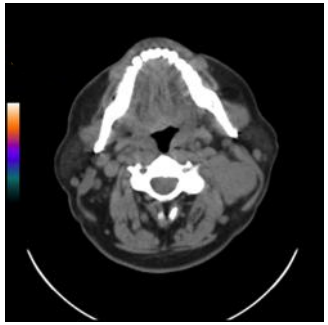
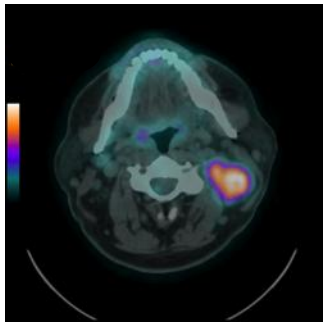
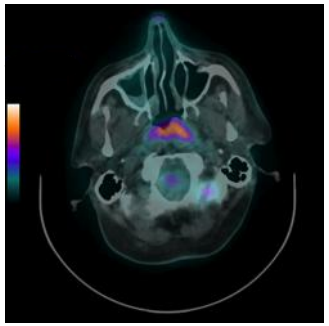
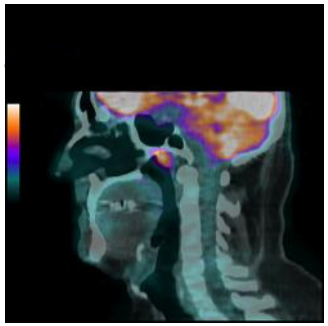
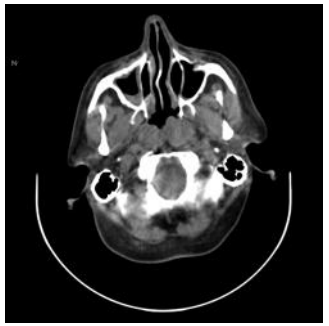
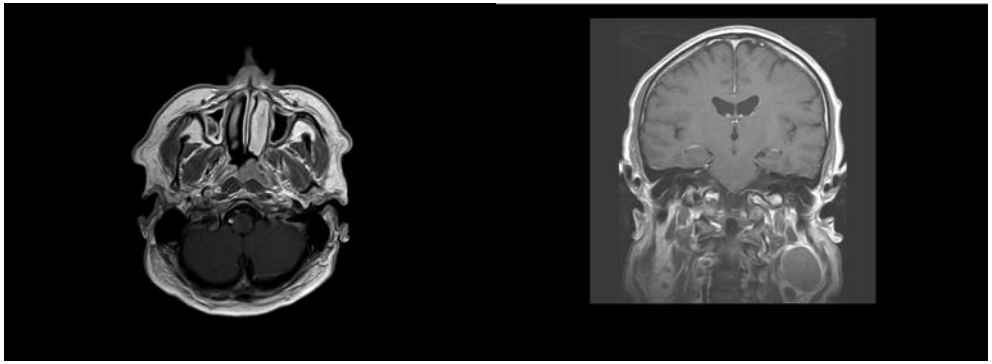
CUP: Poorly Differentiated Carcinoma

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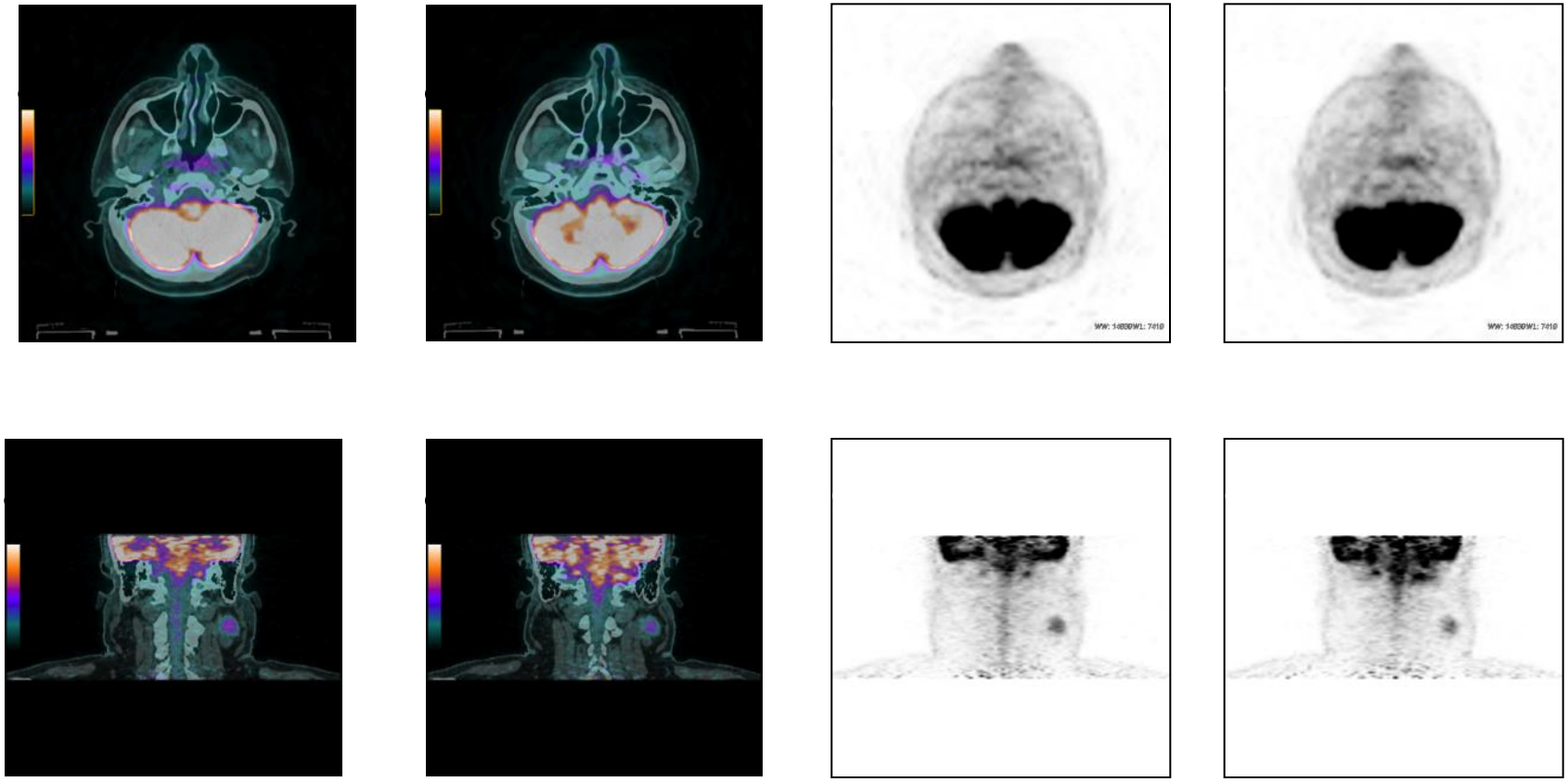
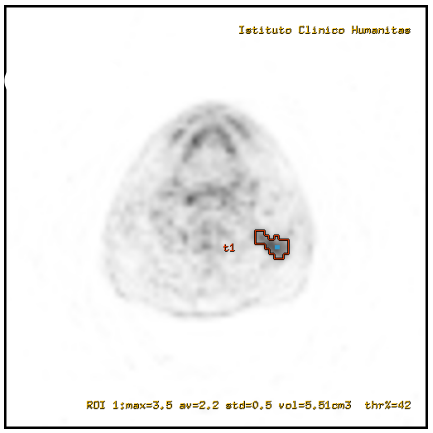
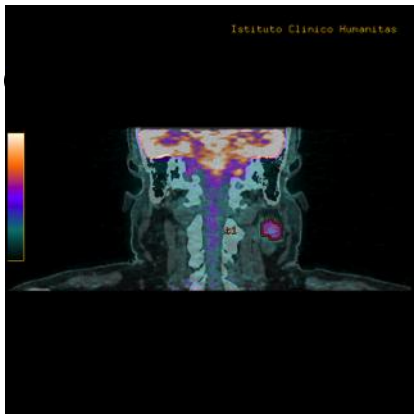
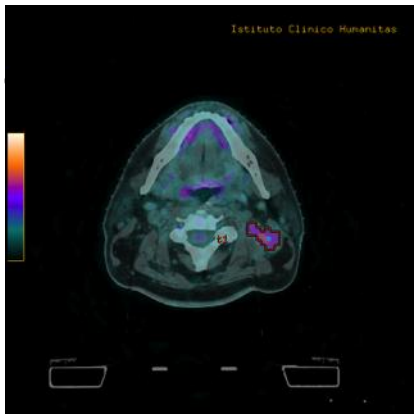


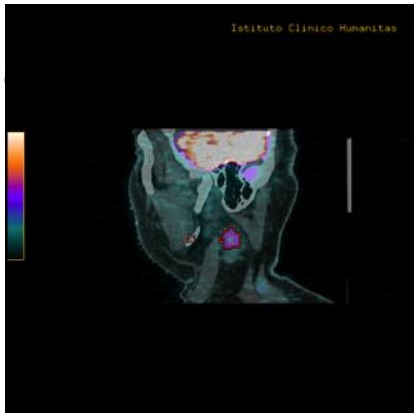
FDG-PET after TCF x 2 cycles

CUP: Poorly Differentiated Carcinoma









• CT/RT with taxotere, cisplatinun, fluorouracile (6 cycles) and IMRT SIB (VMAT RA) on primary rinopharingal lesion + cervical lymph nodes, (Total Dose 69.96 Gy and 54.4 Gy)

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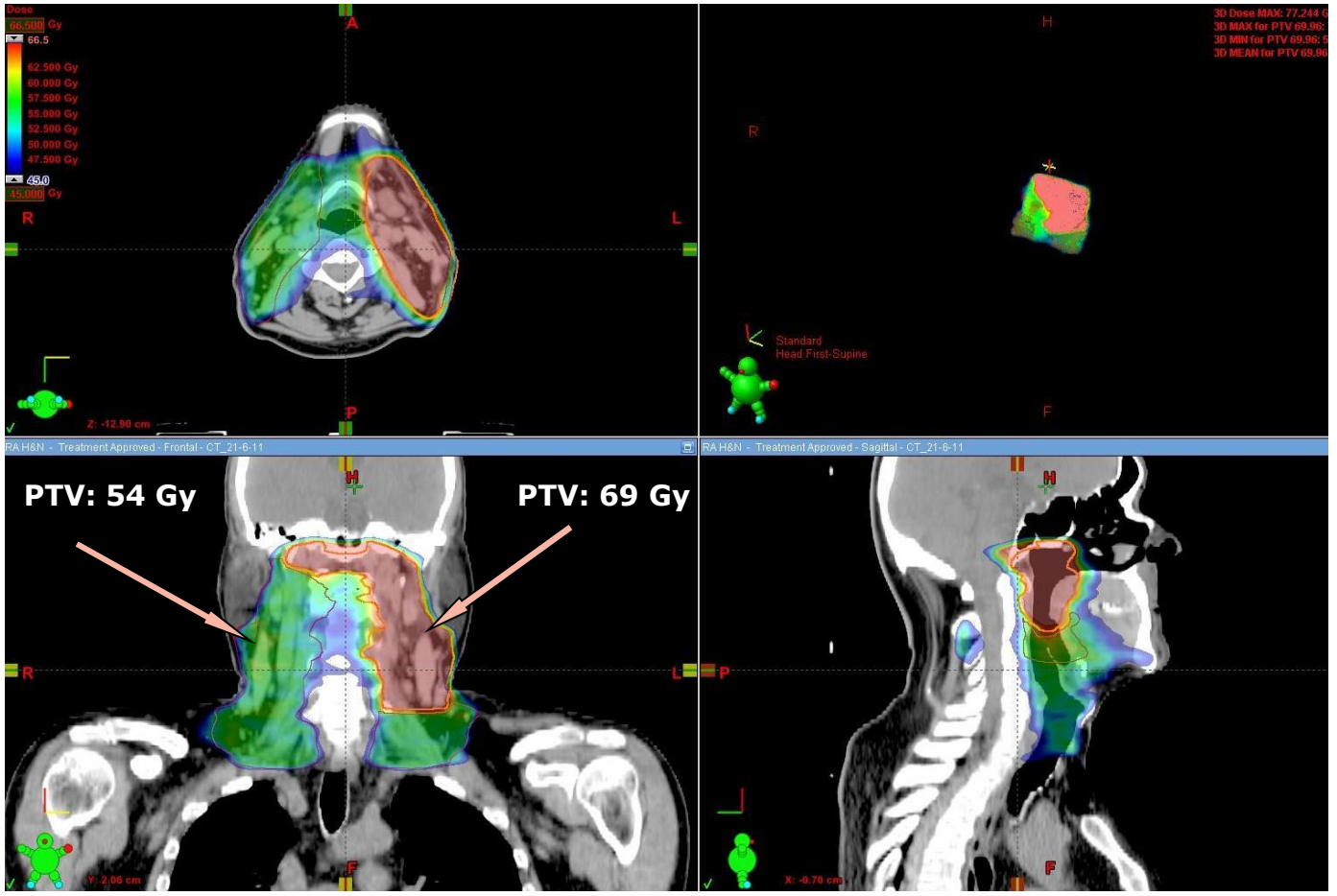

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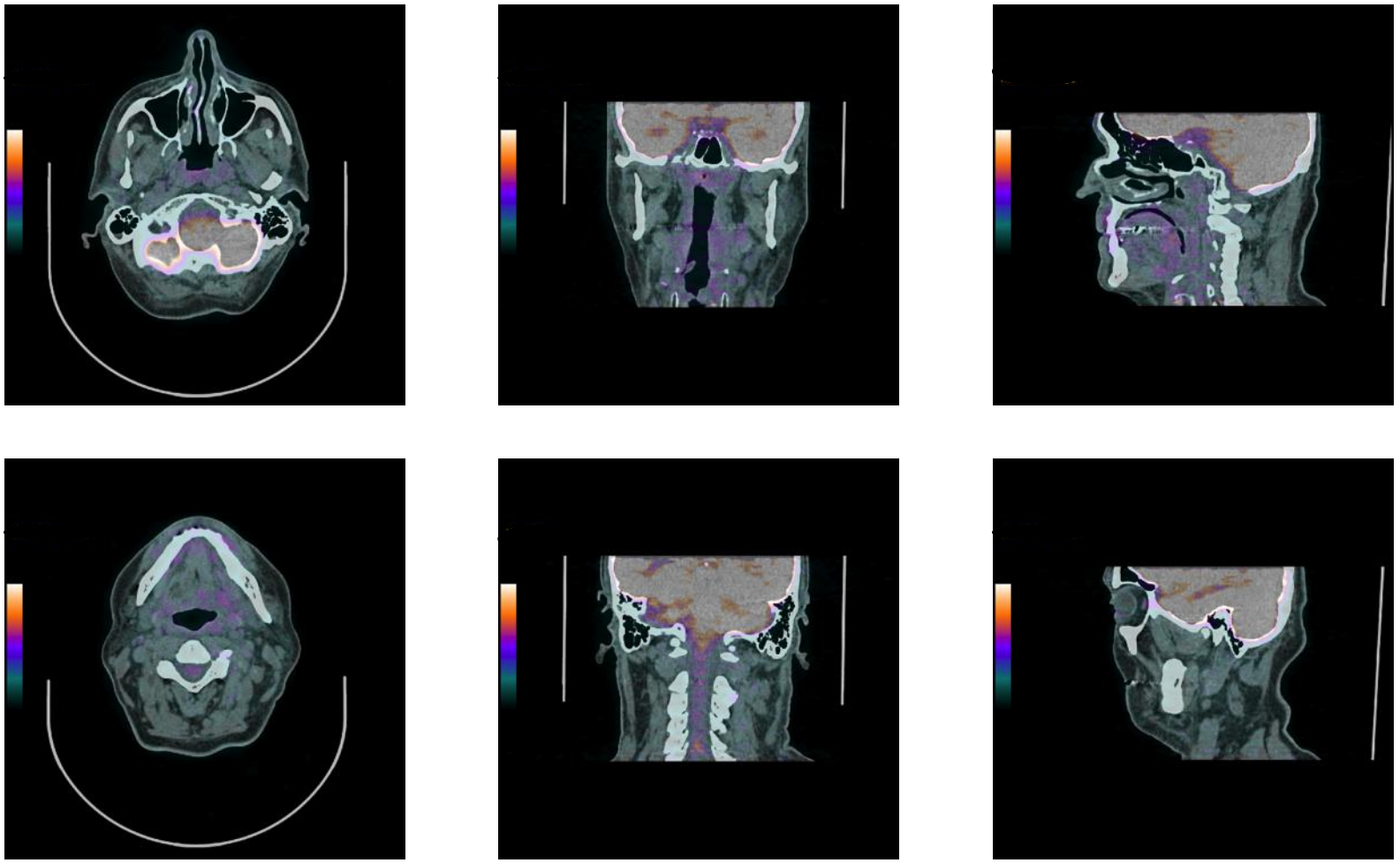

FDG-PET 2 months after CT/RT → Metabolic response

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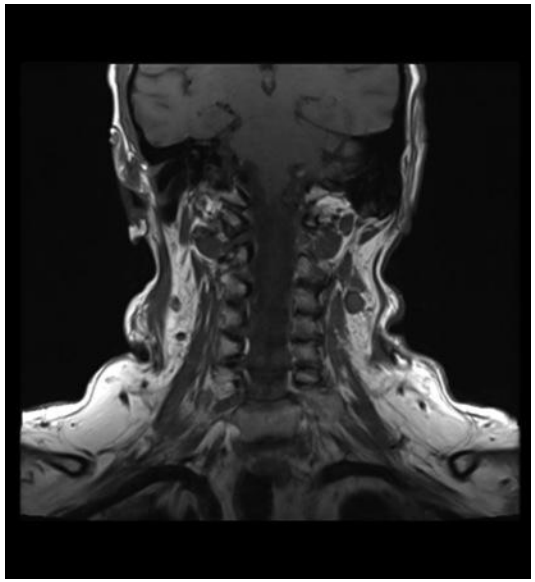
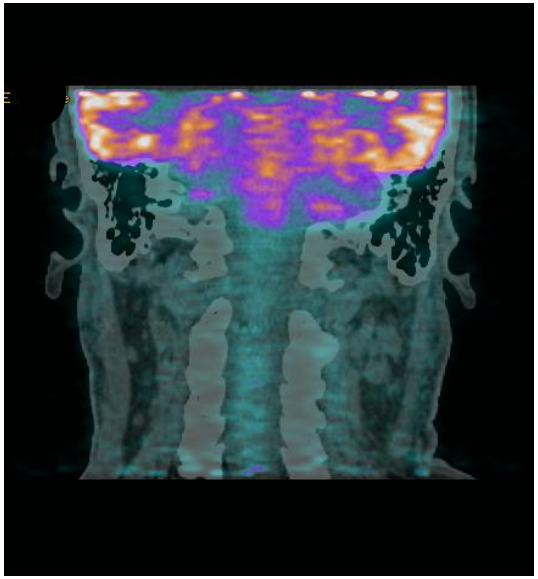


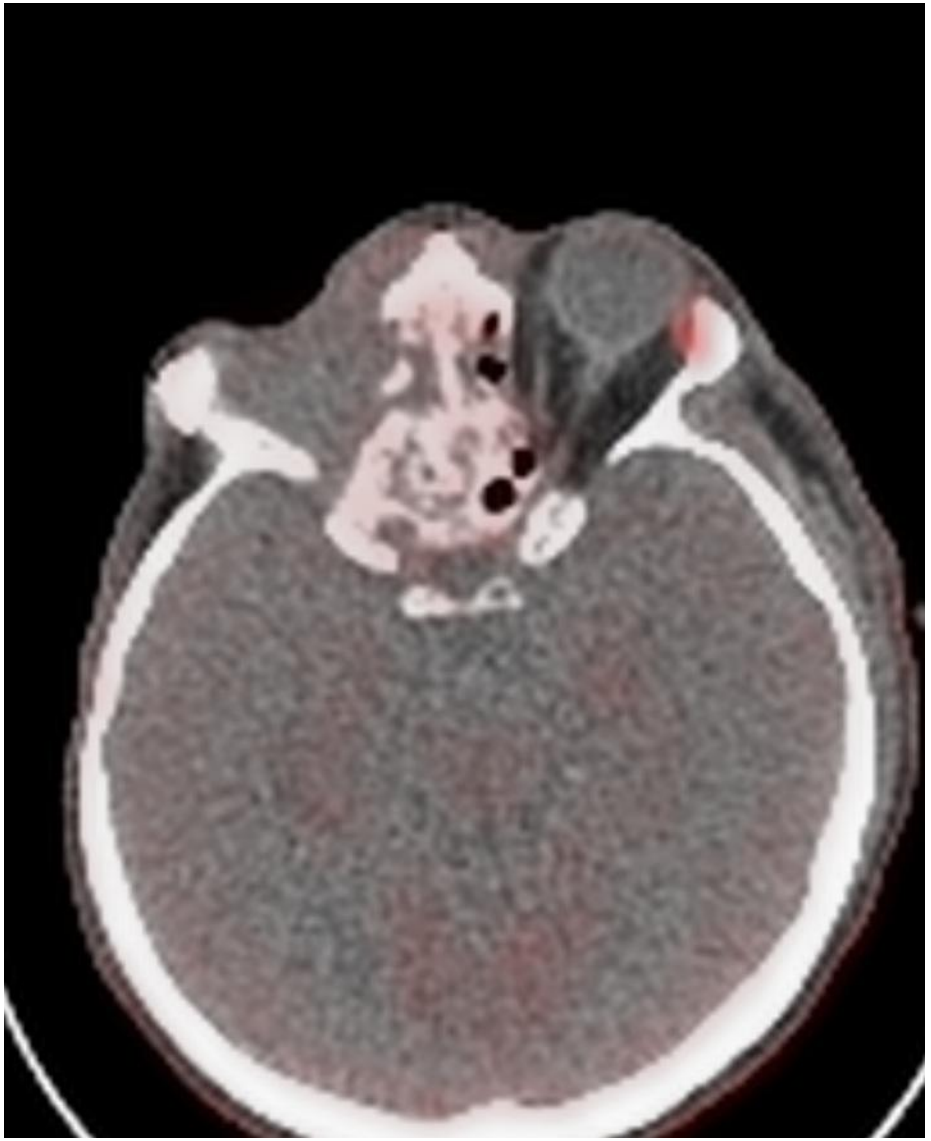
MRI 2 month after CT/RT

MRI 6 month after CT/RT



PET 6 month after CT/RT

Adron Therapy in Adenoid cystic carcinoma



11C-methionine

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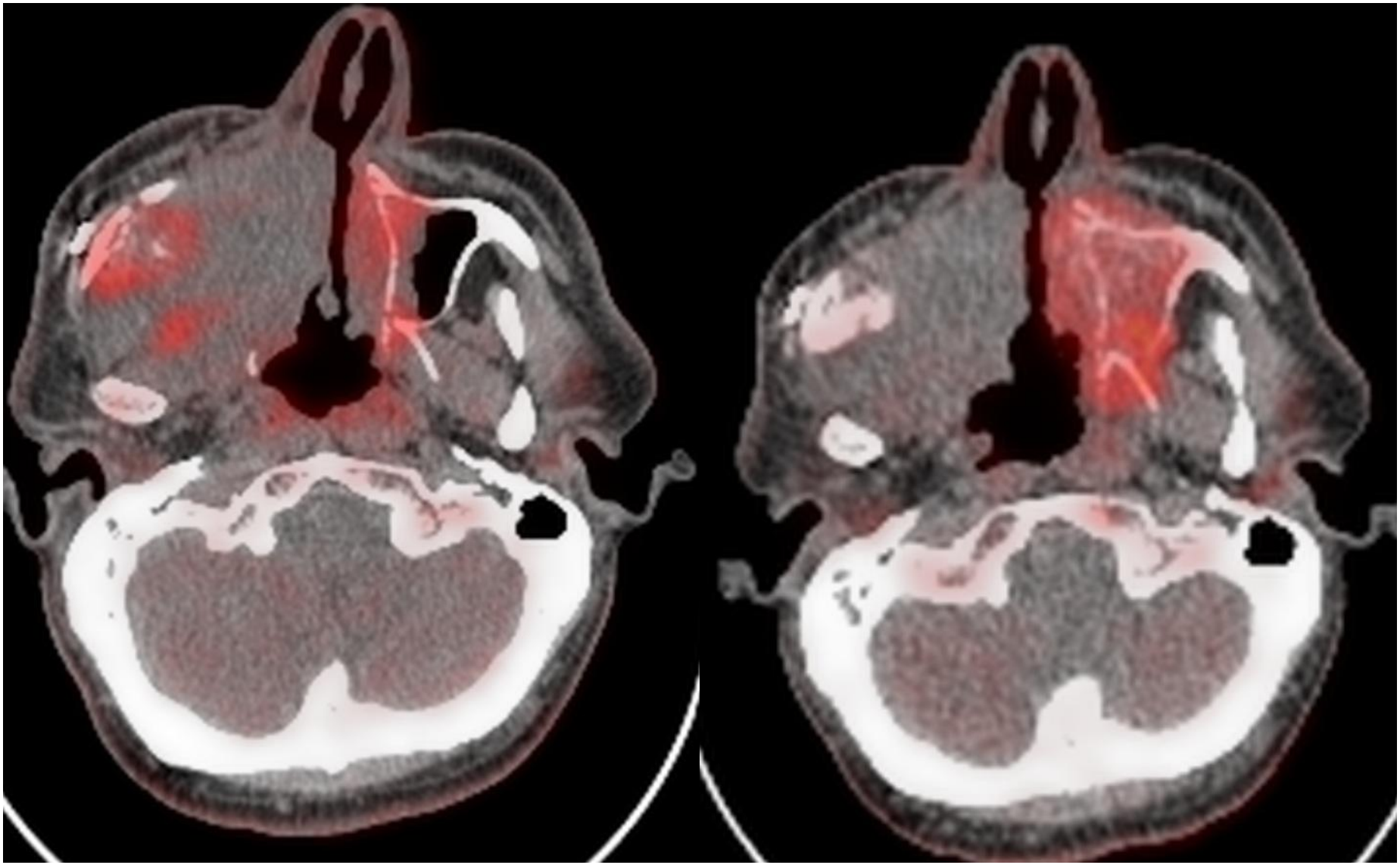
HUMANITAS CANCER CENTER

Adron Therapy in Adenoid cystic carcinoma



11C-methionine

EANM European Association of Nuclear Medicine

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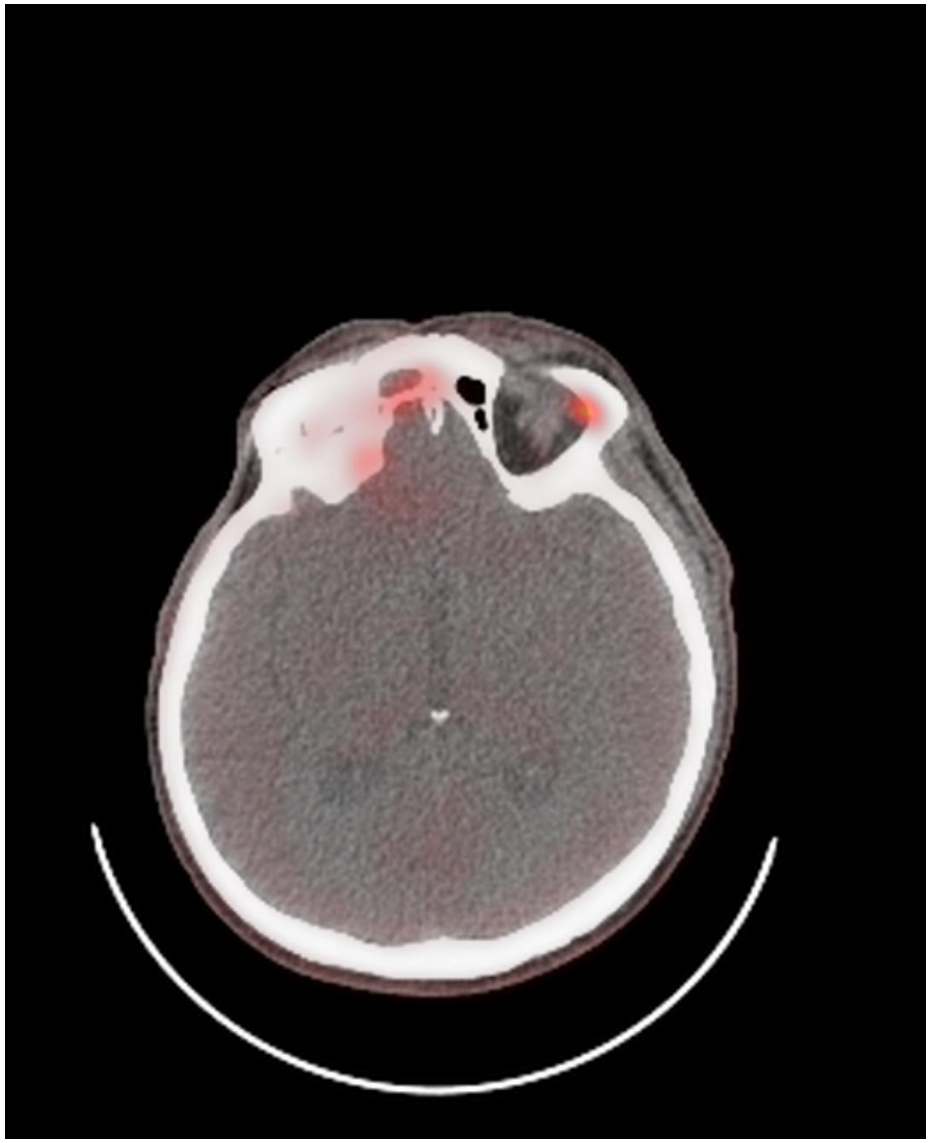
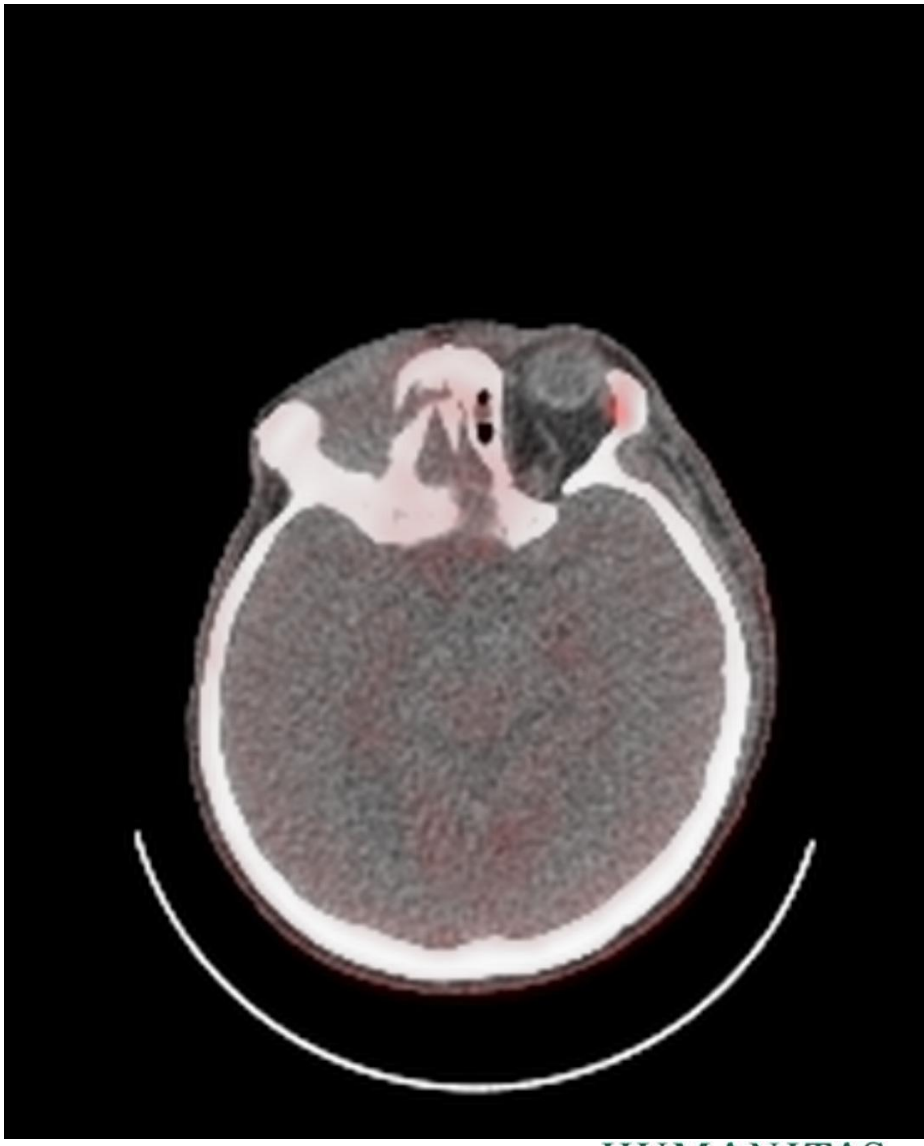
Adron Therapy in Adenoid cystic carcinoma





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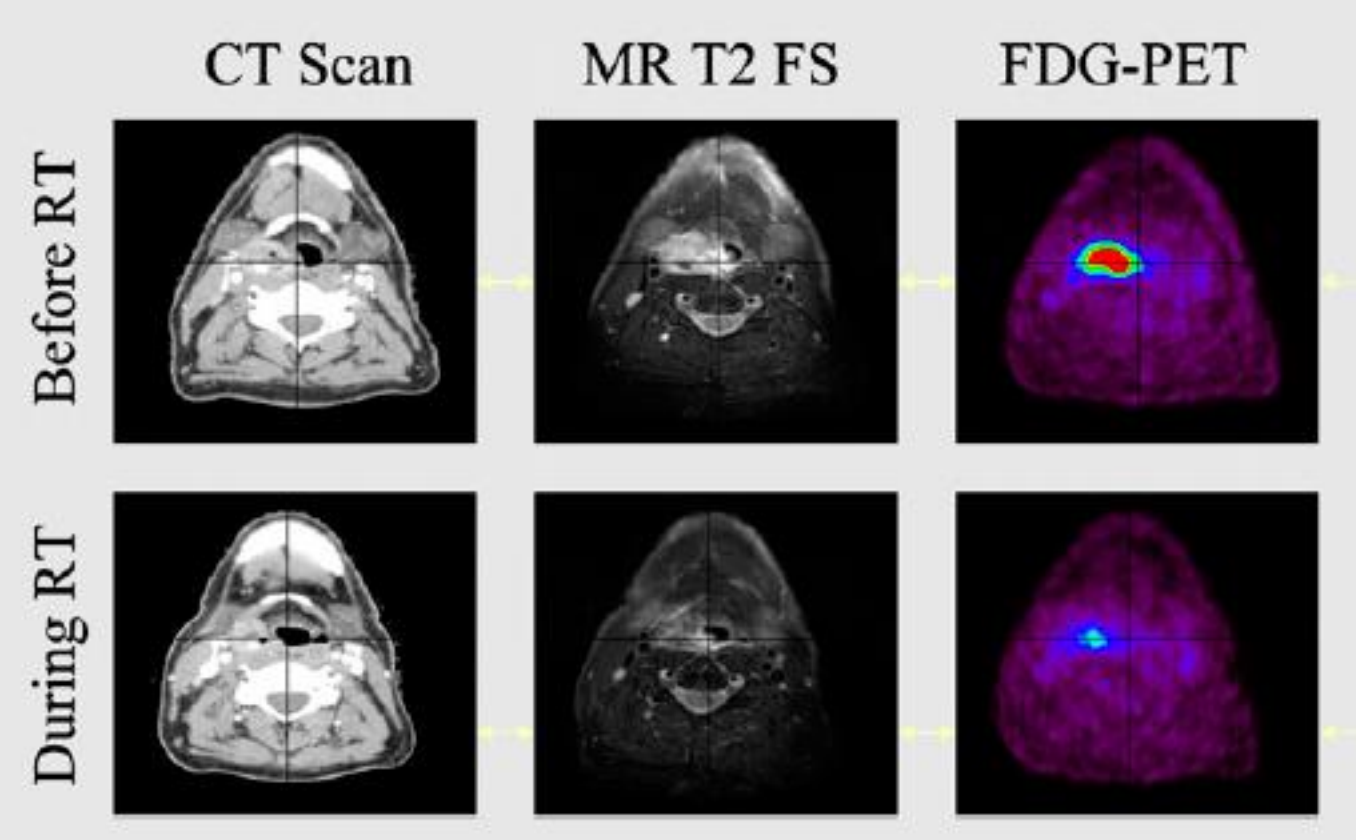
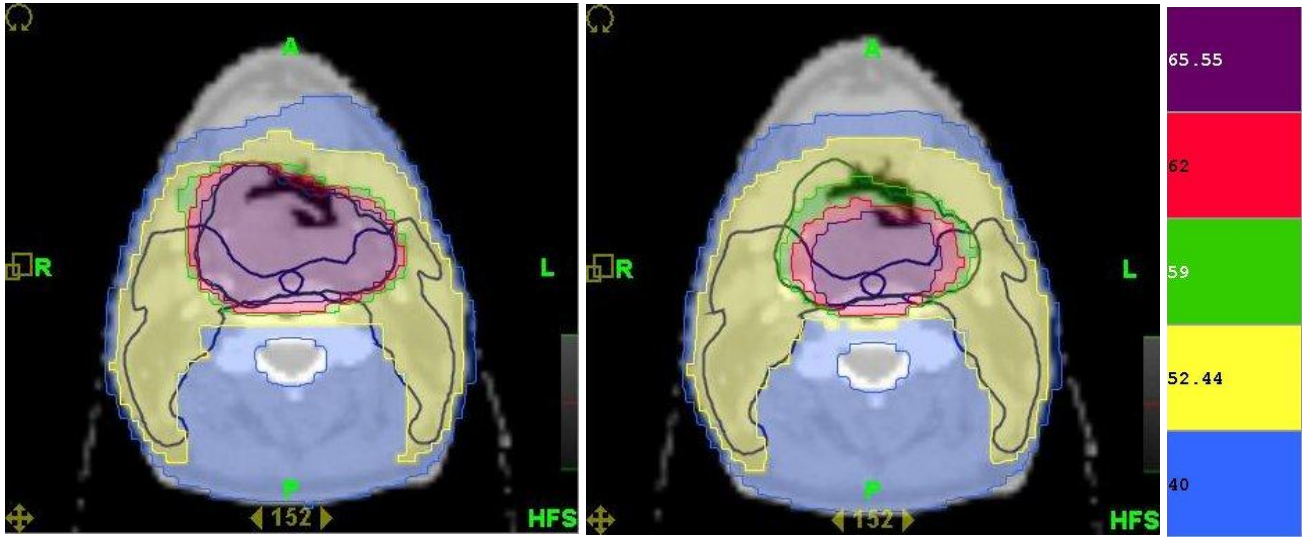
Adaptive treatment



J Nucl Med 2011; 52:331–334

Impact on dose distribution

Classic CT-based planning Adaptive PET-based planning



SIB-IMRT
30x2.3 Gy
30x1.85 Gy

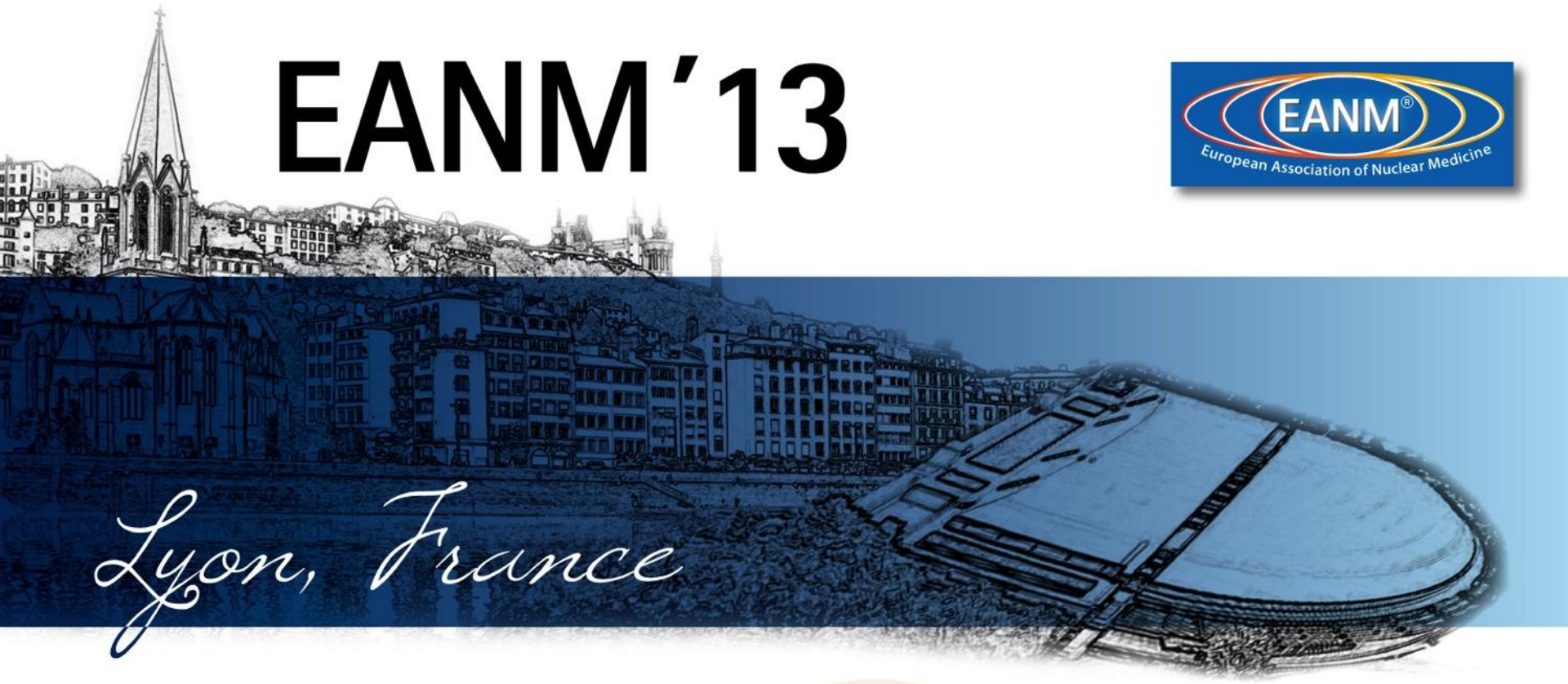
P<0.001

Planning	V_{10}	V_{50}	V_{80}	V_{90}	V_{95}	V_{100}
Classic CT-based	100%	100%	100%	100%	100%	100%
Adaptive CT-based	99%	100%	100%	85%	80%	66%
Classic PET-based	99%	99%	98%	83%	82%	81%
Adaptive PET-based	99%	100%	98%	73%	67%	58%

Courtesy of V. Gregoire

Geets, 2007

EANM'13



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October 19–23, 2013
Lyon, France

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