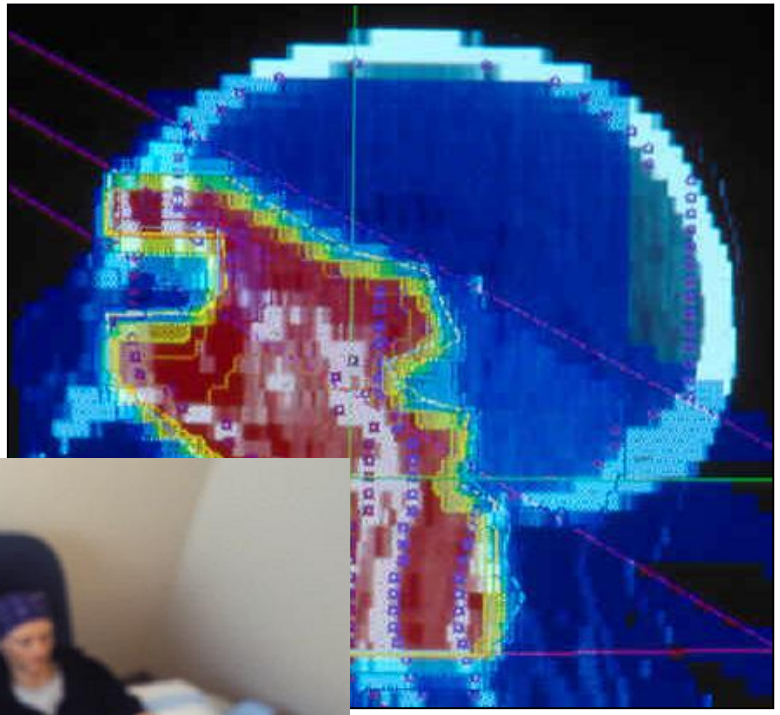
ONKOLOGICAL TREATMENT OF HEAD AND NECK TUMORS



Dr. Zoltán Takácsi-Nagy

SU, Department of Oncology, Budapest

550 000 NEW PATIENTS/YEAR WITH HEAD AND NECK CANCER ALL OVER THE WORLD (3-7 %)

TREATMENT:

- SURGERY
- RADIOTHERAPY (75 %)
- CHEMOTHERAPY

***60 % ARE STAGE III-IV. AT THE TIME OF THE DIAGNOSIS**

INCIDENCE OF ORAL CAVITY AND PHARYNGEAL TUMORS IN CENTRAL EUROPE (cases/100 000 inhabitants)

Year	Male	Female
1965–69	2,72	0,52
1970–74	3,57	0,58
1975–79	5,04	0,70
1980–84	8,09	0,91
1985–89	11,48	1,25
1990–94	16,32	1,82
1995–99	23,92	2,67
2000–04	35,17	3,85
2005–09	51,16	5,42

HEAD AND NECK CANCER

Oral cavity 35 %
Larynx 35 %
Pharynx 30 %

} cc.planocell.

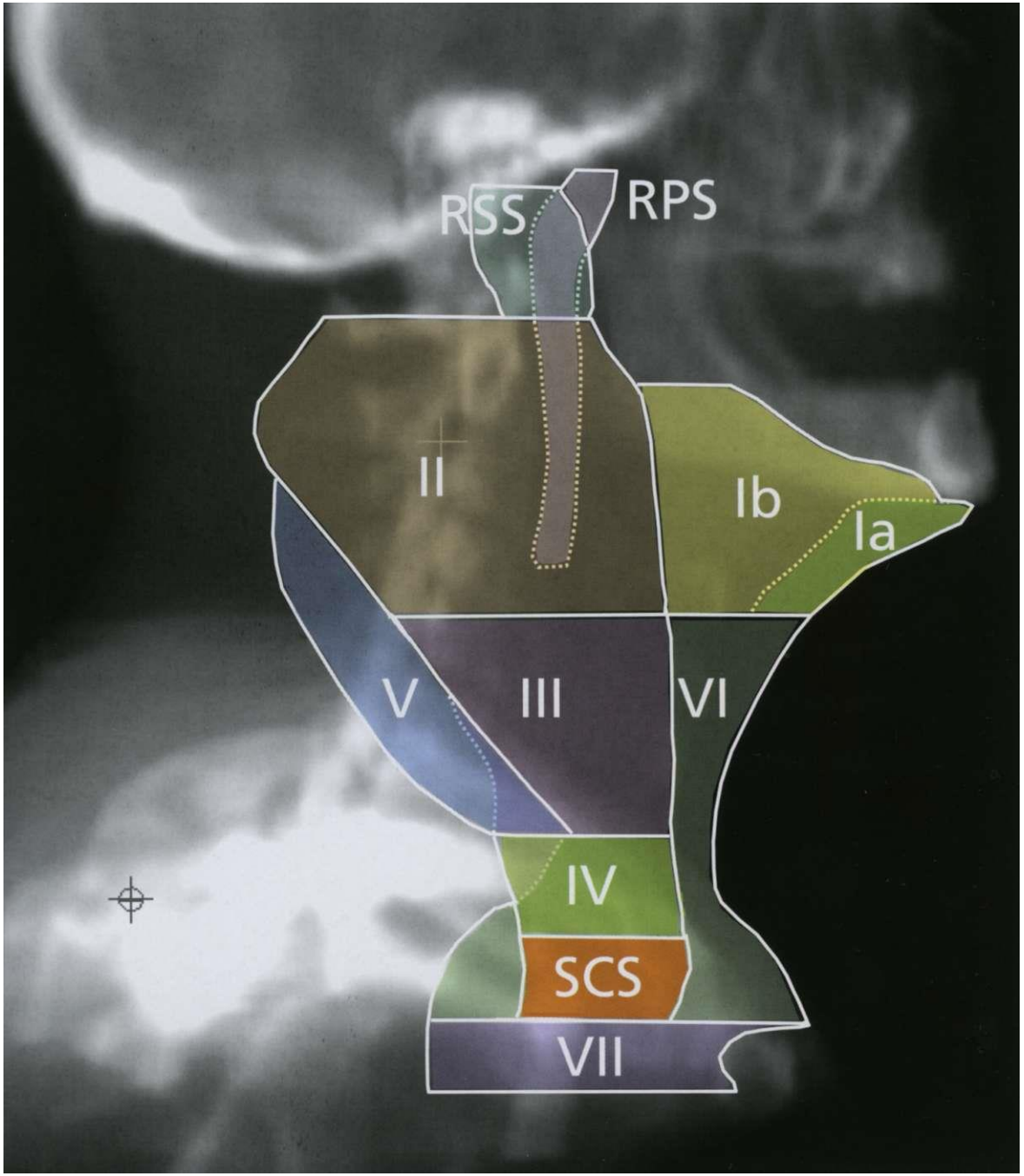
Etiology:

- Smoking
- Alkohol
- EBV
- HPV

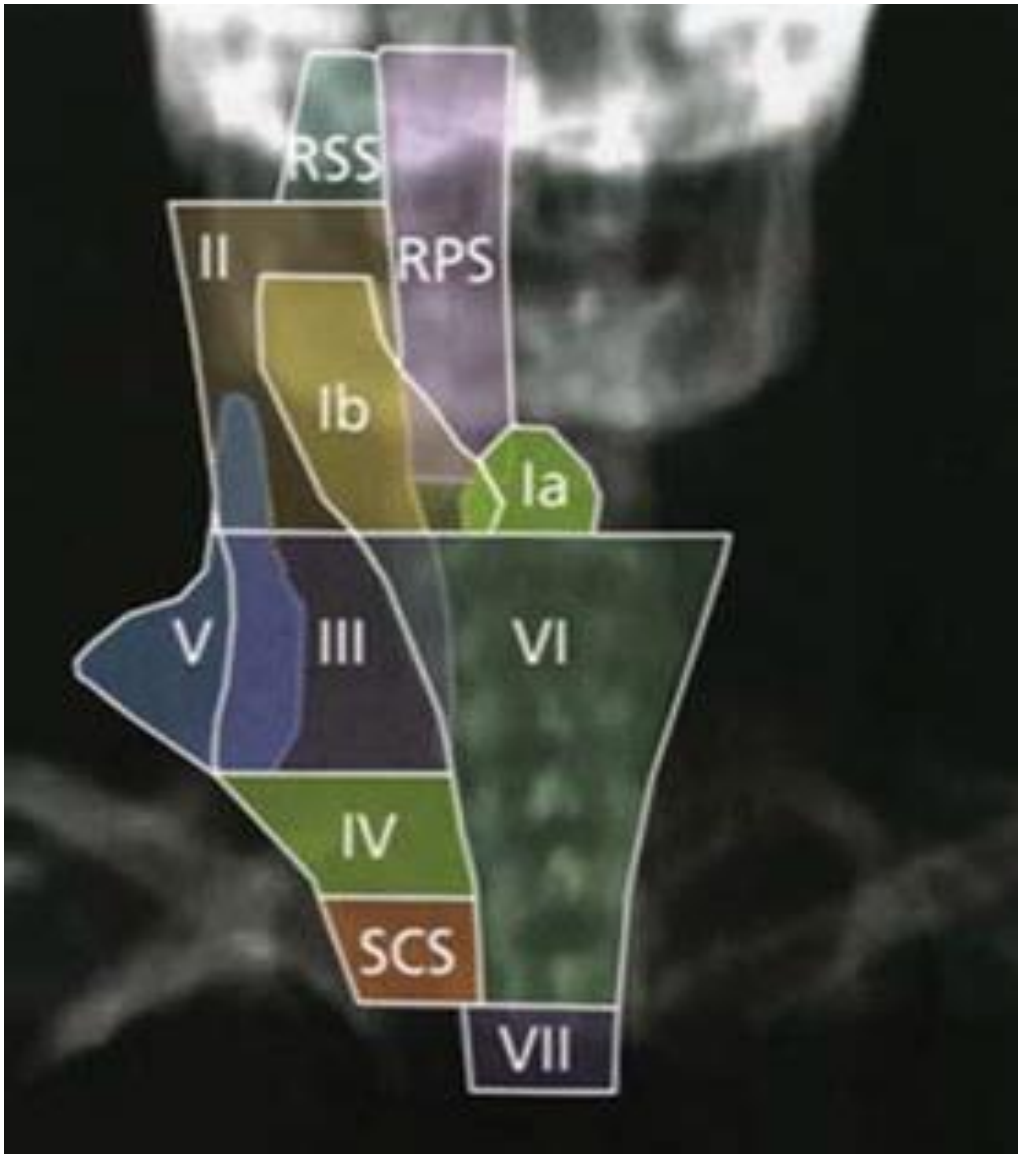
- The incidence of HPV caused oropharynx tumors increased with 200 %, but cancer caused by other factors decreased by 50 %
- They response very well to radiotherapy

Other tumors: Thyroid cancer (most frequent endocrine tumors), salivary gland tumors, sinus tumors (adenocc.), lymphomas, sarcomas etc.

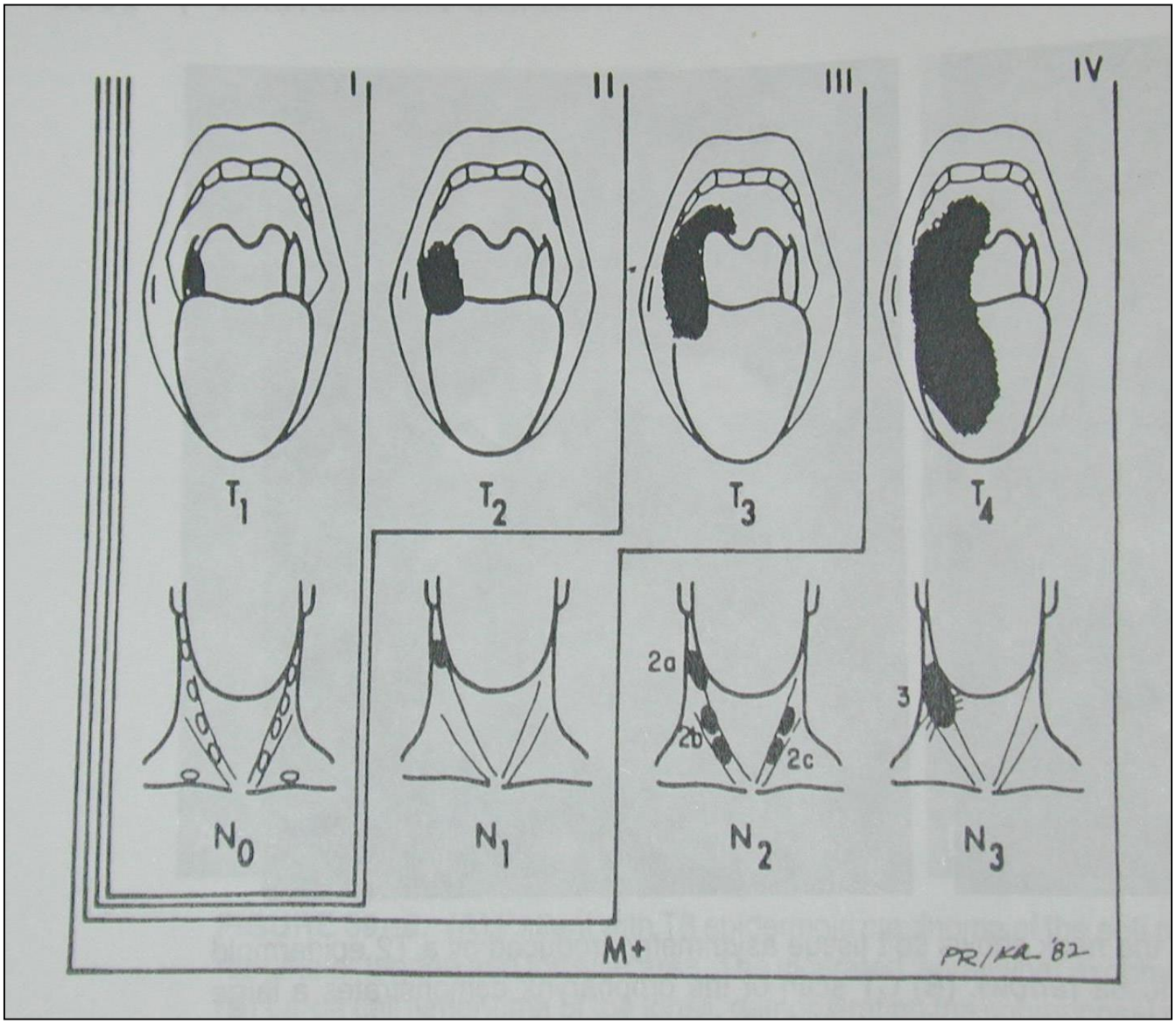
Lymph regions



Lymph regions



UICC TNM STAGES



TUMOR

Oral cavity and oropharynx

Tx Primary tumor is not detected
T0 No primary tumor
Tis Carcinoma in situ
T1 ≤ 2 cm (oral cavity: and depth of the invasion ≤ 5 mm)
T2 2 cm < T < 4 cm (oral cavity: and the depth of the invasion > 5 mm, but ≤ 10 mm)
T3 T > 4 cm (oral cavity: and/or the depth of the invasion > 10 mm)
T4 Tumor infiltrates the surrounding structures (bone, deep muscles of the tongue, other regions, stb.)

Nasopharynx

Tx Primary tumor is not detected
T0 No primary tumor
Tis Carcinoma in situ
T1 Tumor is located in the nasal cavity, perhaps spreads into the nasal cavity and/or oral cavity
T2 Infiltrates the surrounding soft tissues, parapharyngeal space
T3 Infiltrates the bone and sinuses
T4 Spreads to the surrounding tissues (brain, brain nerves, orbita, occlusal surface, etc.)

Hypopharynx

Tx Primary tumor is not detected
T0 No primary tumor
Tis Carcinoma in situ
T1 ≤ 2 cm
T2 2 cm < T < 4 cm
T3 > 4 cm or limits the movement of the larynx
T4 spreads to the surroundung (bone, cartilago, carotis, thyroid, oesephagus, other region, etc.) organs

Larynx

Tx Primry tumor is not detected
T0 No primary tumor
Tis Carcinoma in situ
T1 Tumor located only to one region (supraglottis, glottis, subglottis) (T1a one, T1b both vocal cords)
T2 Tumor infiltrates more than one region
T3 Tumor located to the larynx, but limits the movement of the vocal cord
T4 Spreads to the surrounding (cartilago, soft tissue, another region, etc.) tissues

LYMPHNODES

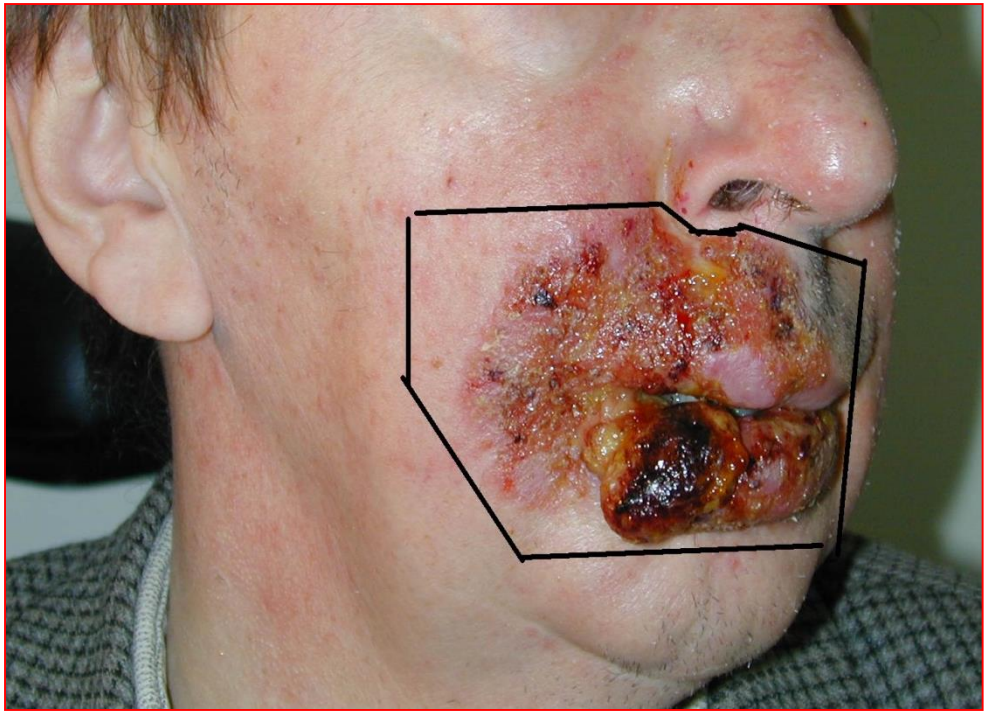
Nx Lymphnodes are not detected
N0 No lympnode metastasis
N1 one unilateral metastasis ≤ 3 cm (nasopharynx: unilateral and/or bilateral retropharyngeal metastasis over the caudal edge of the cartilago cricoidea ≤ 6 cm; by p-16 positive oropharongeal cancer one or more unilateral metastasis, but ≤ 6 cm)
N2 one (N2a) or more (N2b) unilateral, but 3 cm < N ≤ 6 cm;
or bilateral or contralateral metastasis (N2c); By nasopharynx bilateral metastasis over the caudal edge of the cartilago cricoidea ≤ 6 cm.
N3 N > 6 cm (by nasopharynx metastasis under the caudal edge of the cartilago cricoidea)

METASTASIS

Mx Distant metastasis is not detected
M0 No distant metastasis
M1 Distant metastasis is detected

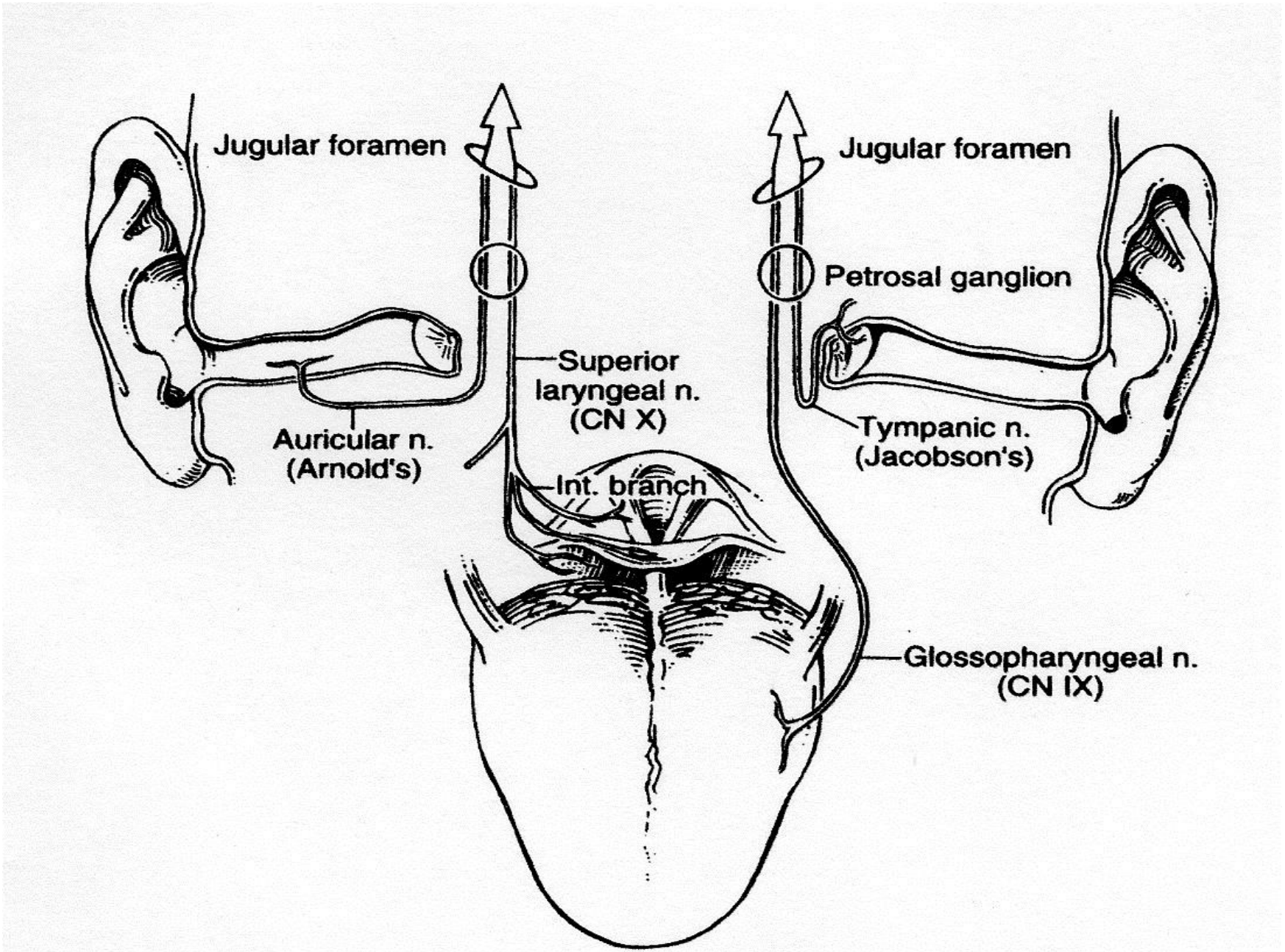
TUMORS OF THE HEAD AND NECK REGION CAN CAUSE A HIGH VARIETY OF SYMPTOMS – BECAUSE OF THEIR LOCATION – WHICH ARE OFTEN NOT SPECIFIC

OPERATION OF A NECK DISEASE (LYMPH NODE) WITHOUT DETAILED HEAD AND NECK EXAMINATION IS FORBIDDEN



SYMPTOMS

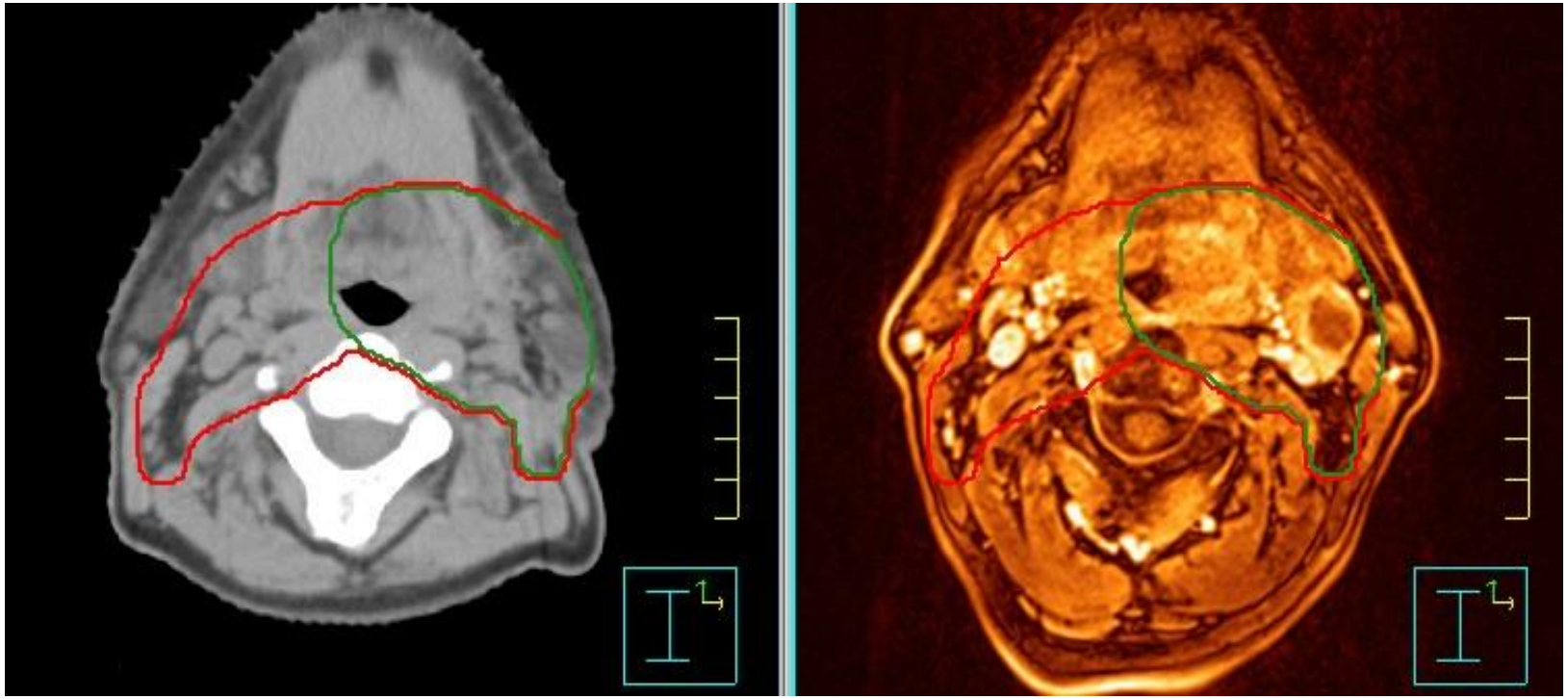
- **ULCERATIVE OR EXOPHYTIC LESIONS**
- **PAIN**
- **HOARSENESS**
- **NASAL SOUND**
- **SWALLOING DIFFICULTIES**
- **SPEACH DIFFICULTIES**
- **BLEEDING**
- **BRAINNERVES SYMPTOMS** (III, IV, V, VI, XII) – nasopharynx tumors


Jugular foramen
Jugular foramen
Petrosal ganglion
Superior
laryngeal n.
(CN X)
Auricular n.
(Arnold's)
Int. branch
Tympanic n.
(Jacobson's)
Glossopharyngeal n.
(CN IX)

EXAMINATION

- HISTORY
- PHYSICAL EXAMINATION
- INSPECTION WITH HEADLIGHT OR HEADMIRROR
- ENDOSCOPE
- PALPATION
- CT, MRI, PET-CT
- HISTOLOGY, ASPIRATION CYTOLOGY
- CHEST X-RAY
- ETC. (HPV, EBV)

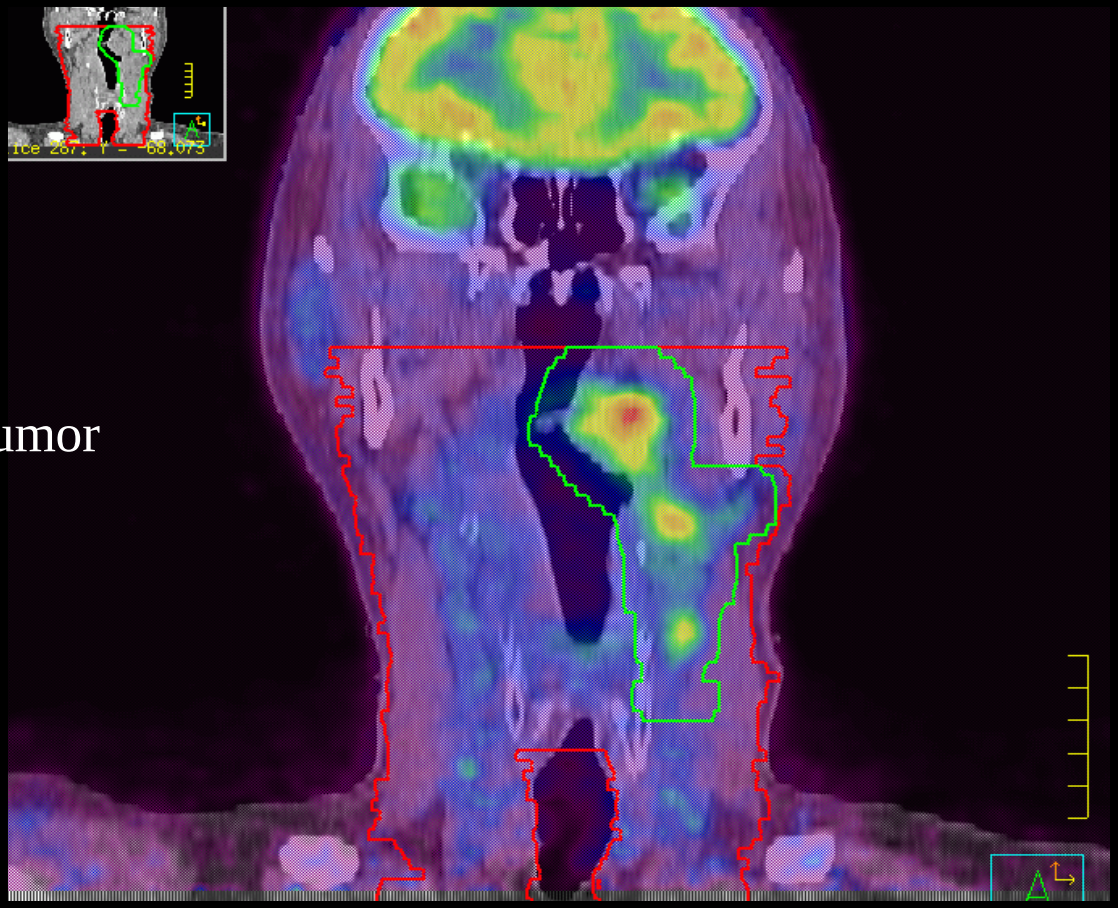
CT or MRI

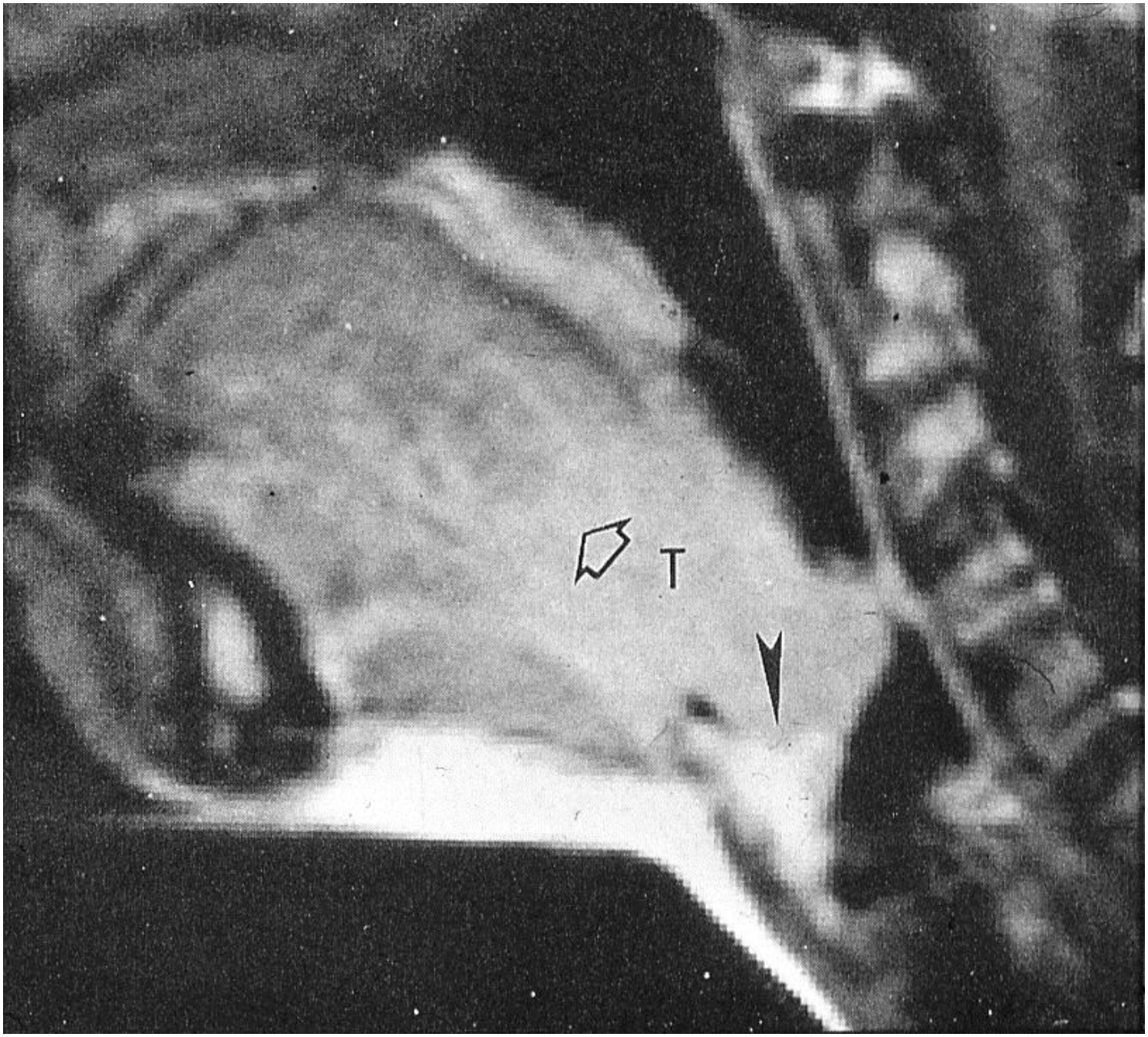


PET CT

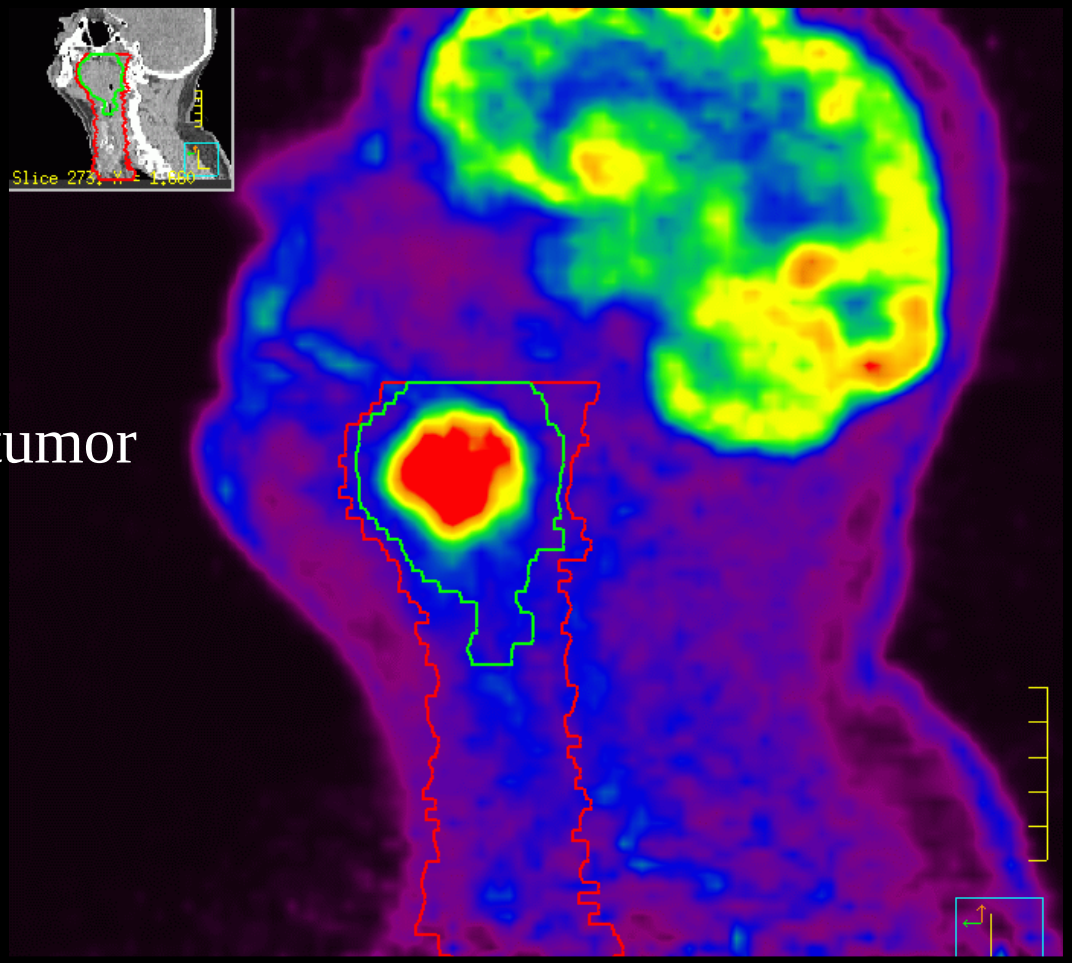
T2N2B Base of tongue tumor

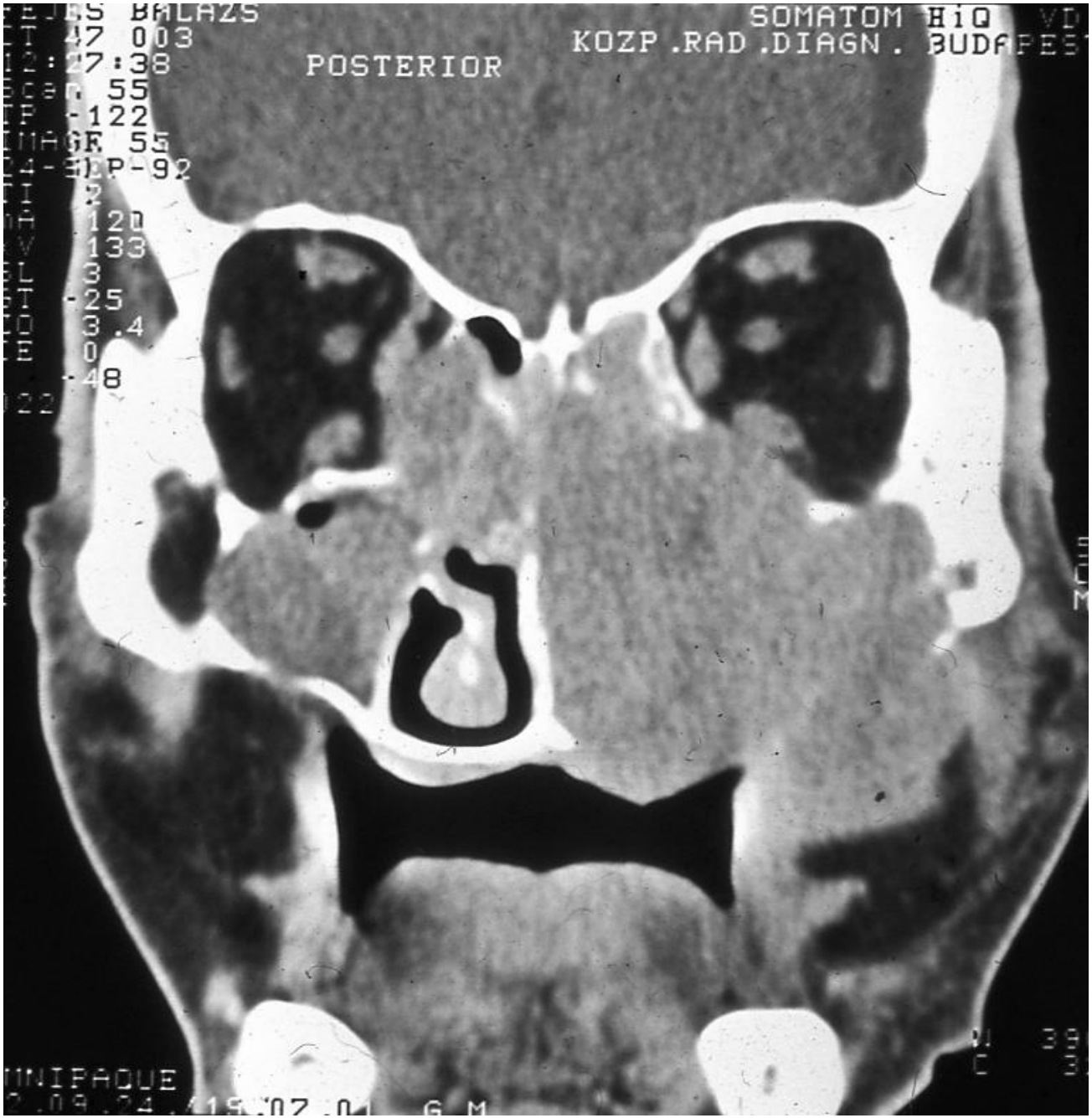
(Targetvolumes)

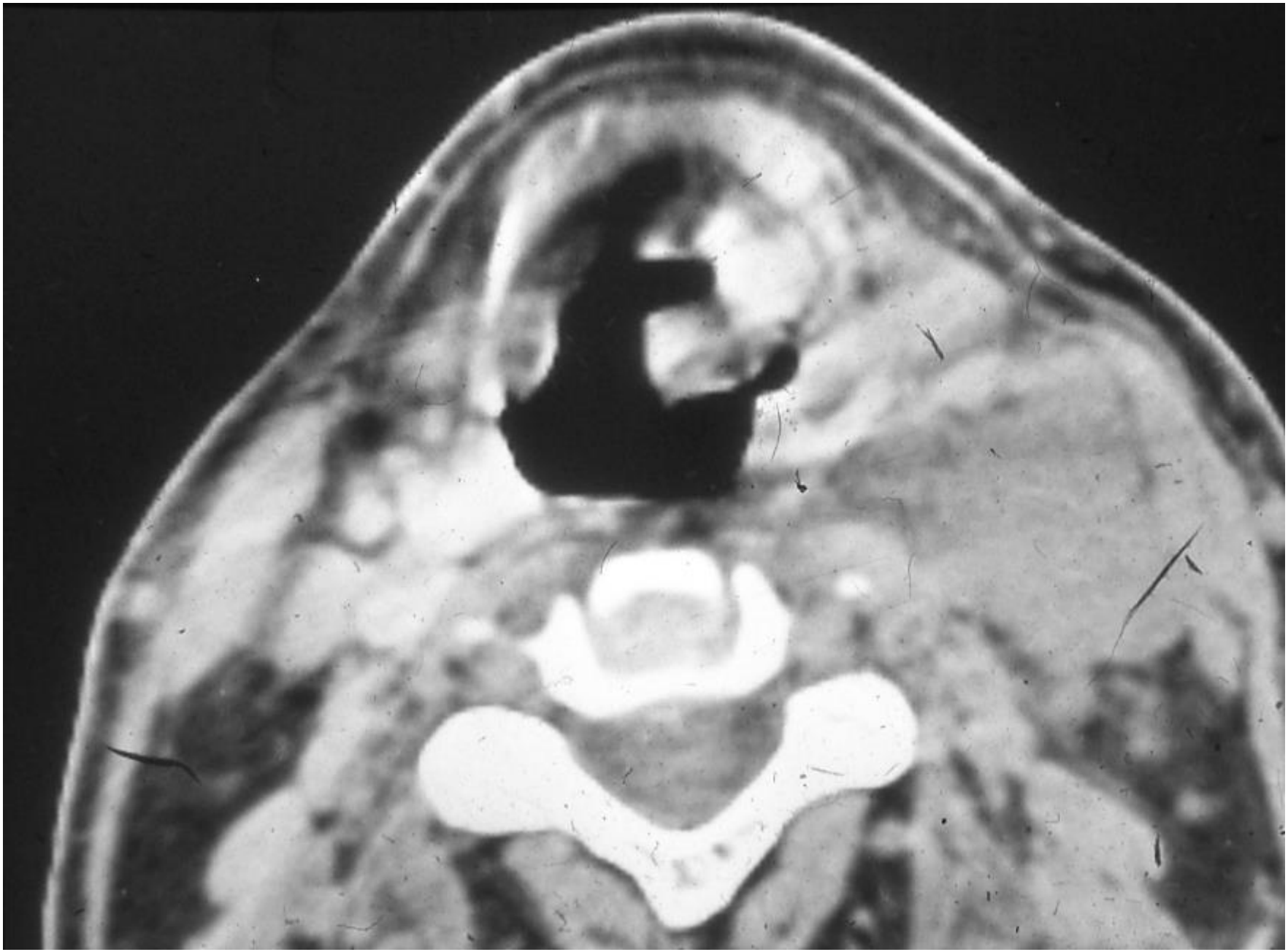



T

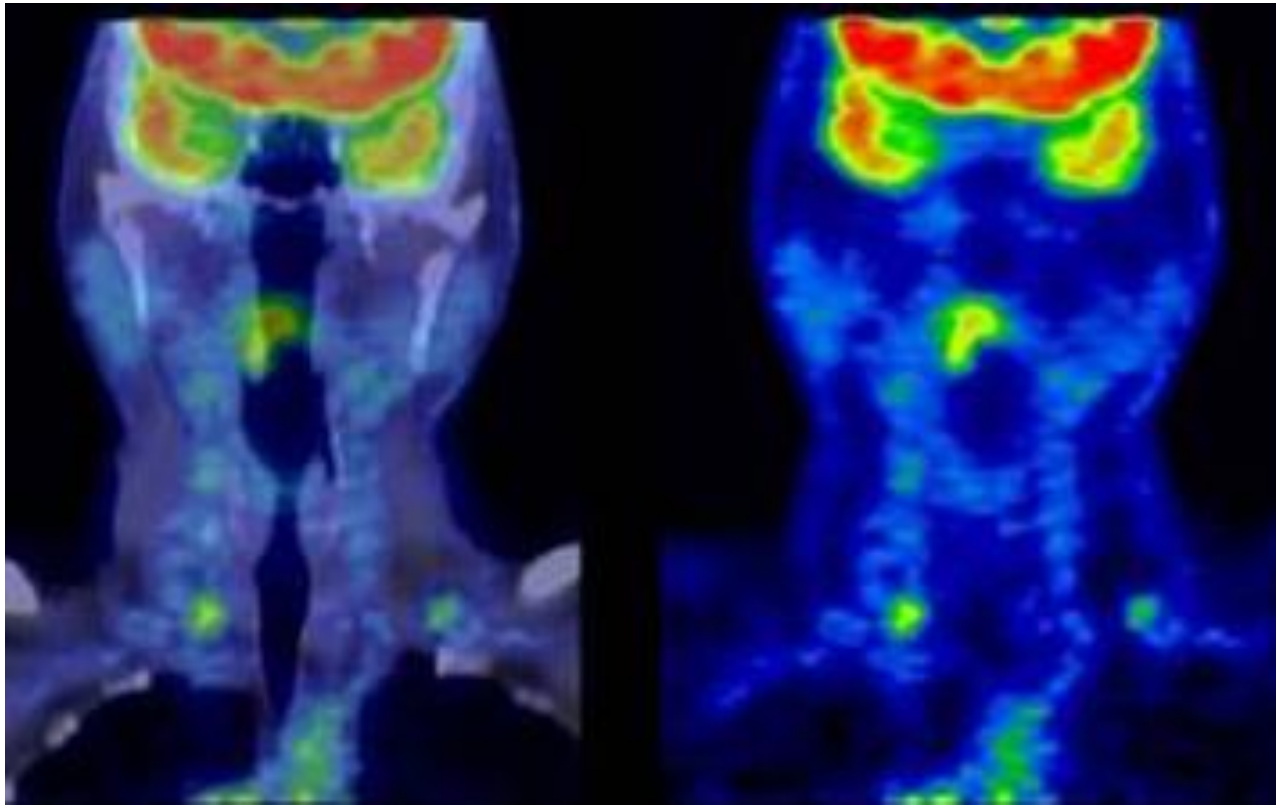
T3N0 Base of tongue tumor




BALAZS
SOMATOM HiQ
KOZP .RAD .DIAGN .
POSTERIOR
UNIPAQUE



POSITRON EMISSION TOMOGRAPHY (PET)



Palate tumor with supraclavicular metastasis on both side of the neck (N2c)

AIM OF RADIATION THERAPY

- Curative (total dose: 50-80,5 Gy)
- Palliative (total dose: 20-60 Gy)

- Postoperative (perishing the microscopical residual tumorcells)
- Definitive or primary (exclusively)

- Radiotherapy alone
- Combinated radio-chemotherapy

Thyroid cancers

Hystology:

- Papillar
- Follicular

90 %

- Medullar
- Anaplastic

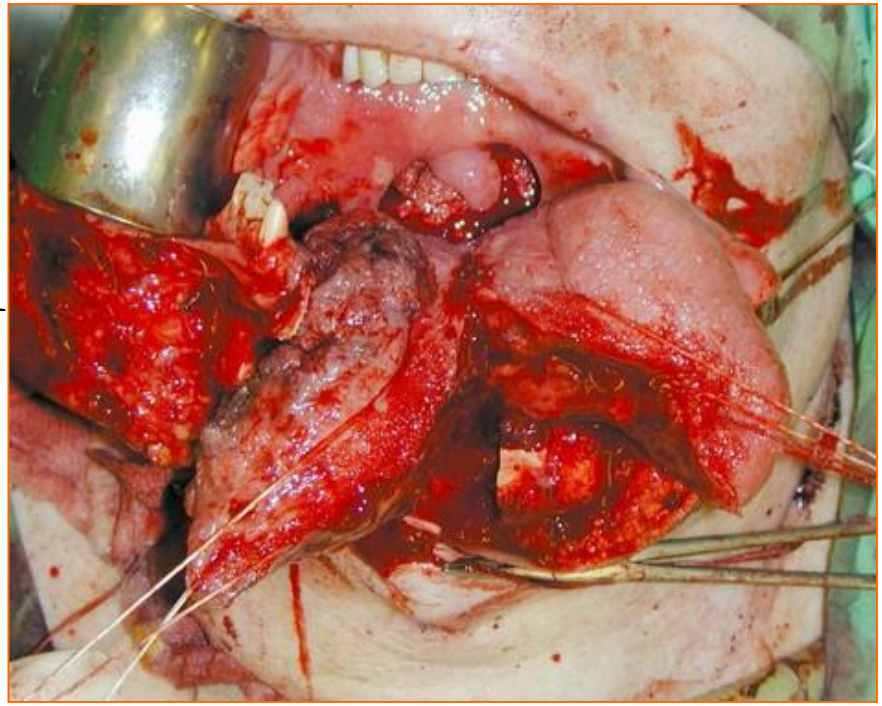
10 %

Examination:

- MR
- US operated cytology
- 99m Tc-pertechnetat scintigraphy
- 131/123 I scintigraphy
- 131/123 I-MIBG (meta-iodo benzylguanidin) scintigraphy
- Thyreoglobulin, antithyreoglobulin level - papillar, follicular recurrence or residual tumor
- Calcitonin, CEA, urine catecholamine level - medullar recurrence or residual tumor

MULTIDISCIPLINARY TREATMENT OF HEAD AND NECK TUMORS

- Surgery
- Radiotherapy (RT)
- chemotherapy/Biological therapy/Immuntherapy



- Combinated teratment:
  - surgery+ postop. RT
  - surgery + radio-chemotherapy
  - primary radiochemotherapy or bioradiotherapy

ONCOTEAM

MULTIMODAL TREATMENT

T1-2 N0-1

SURGERY

RADIOTHERAPY

Oral cavity: operation
Nasopharyx: radiotherapy

T3-4 N0-1 VAGY T1-4 N2-3

OPERATION +/- POSTOPERATIVE RADIOTHERAPY[1] OR RADIOCHEMOTHERAPY[2]

RADIOCHEMOTHERAPY – organ preservation

CETUXIMAB + RADIOTHERAPY

INDUCTION CHEMOTHERAPY + SURGERY or RADIOCHEMOTHERAPY

[1]**Indication: pT3-4, pN2, extracapsular extension, R1/R2 resection, vessel-, perineurál invasion**

[2]**Indikációja: extracapsular extension, positive surgical margin**

SURGERY

- Functional approach (remove as many tissues as needed)
- Monoblock principle (primary tumor and cervical metastasis, if it is possible, must be removed in one block)
- Tissue replacement procedures (Reconstructive Plastic Surgery)
- Multiple Team Operations: There are several surgical teams at the same time operating the patient (primary surgery, tissue preparation to replace resecatum)
- Special Instrument Requirements (endoscopes / laryngoscopes / laser devices; operating microscopes; microsurgical instruments / tissue transplantation; robotics /TORS: Transoral Robotic Surgery /)

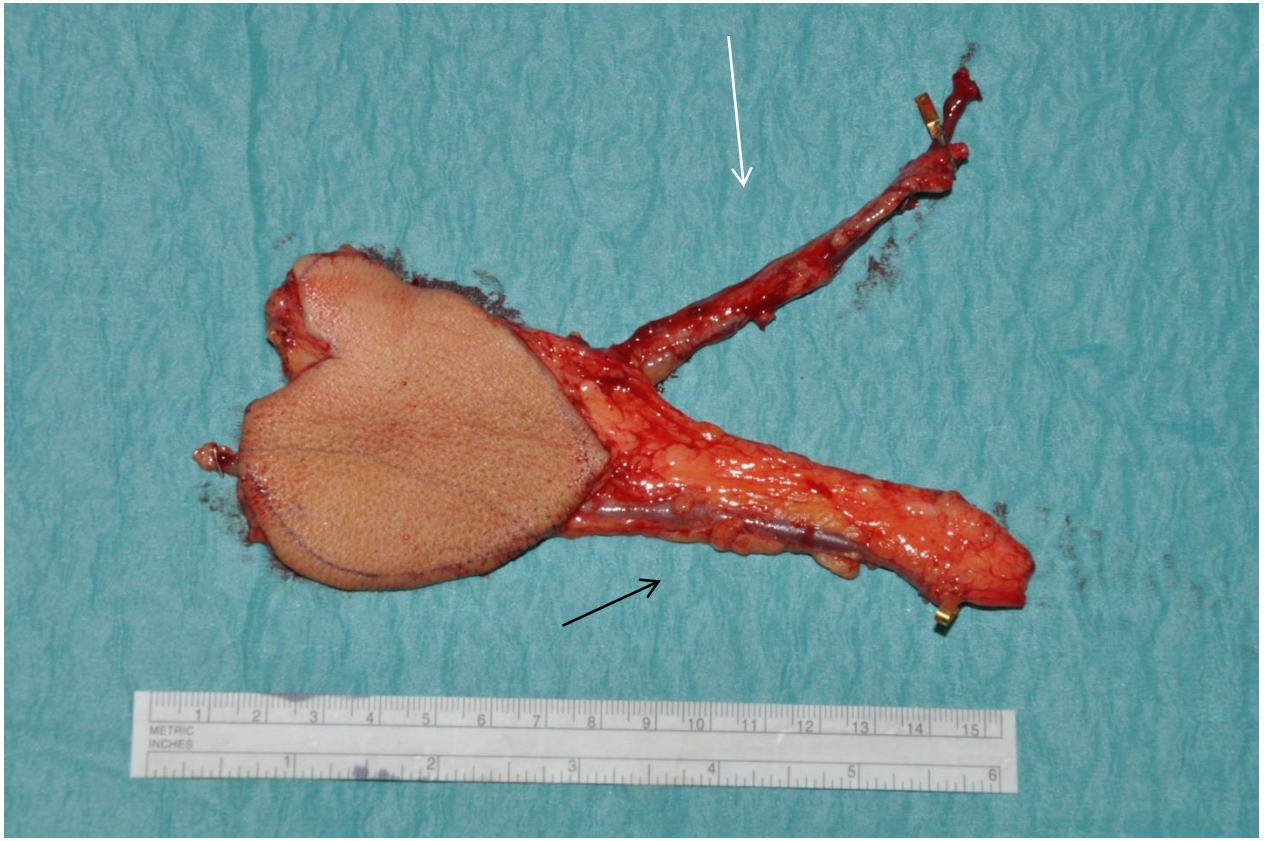
NECK DISSECTIONS

Therapeutic (N+) and elective (N0) neck dissection

- Radical (conventional: levels I-V, internal jugular vein, accessory nerves, and sternocleideomastoid muscle)
- Modified radical (levels I-V, but with functional features retained, most commonly nerve XI is the preserved feature)
- Extended radical (levels I-V + resection includes other regions or non-lymphatic structures)
- Selective cervical dissections (most commonly levels I-III, I-IV, and II-IV) - this procedure is performed only with negative cervical lymph node status.

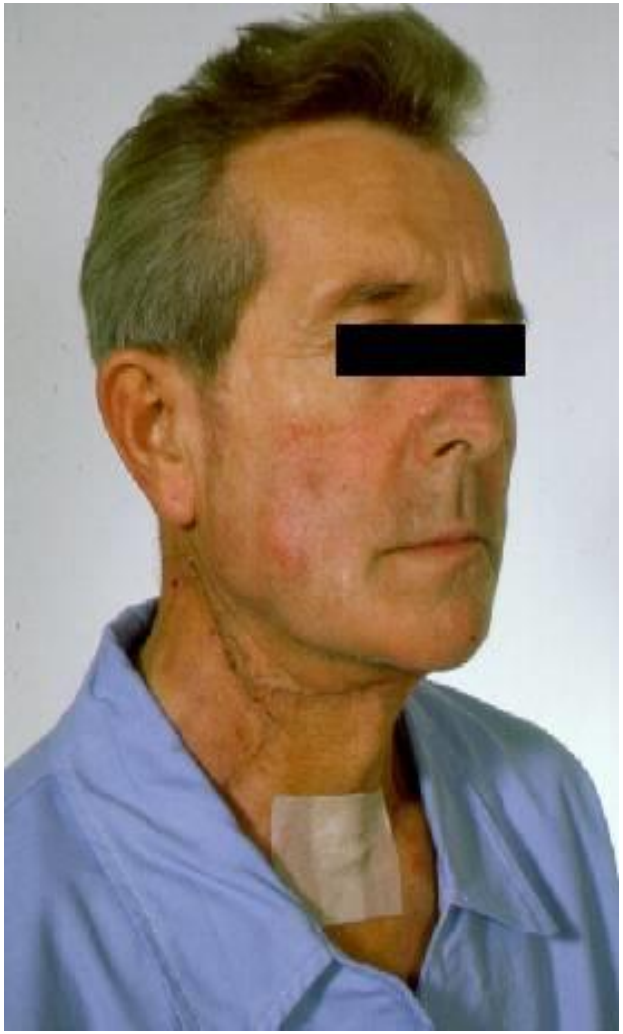
POSTOPERATIVE REPLACEMENT OR RECONSTRUCTION OF RESECTED TISSUES

- Local
- Locoregional (face or neck)
- Free flap (tissue is taken from outside the head and neck area /pectoralis major, latissimus dorsi skin-muscle flap/)
- Microvascular flap (a block of tissue taken from any area of the body with the supplying microvessel /forearm flap, upper arm flap, latissimus dorsi flap, anterolateral thigh flap, iliac crest flap, fibula bone, etc.)



Forearm flap with skin island shaped to substitute tongue and floor of mouth (black arrow: cephalic vein, white arrow: radial artery and vein)

Microvascular free forearm flap was used to replace tongue; implants and fixtures rehabilitate masticatory function



Contour of the face after the same resection A: reconstructed with vascularised fibula skin-muscle-bone flap B: without reconstruction

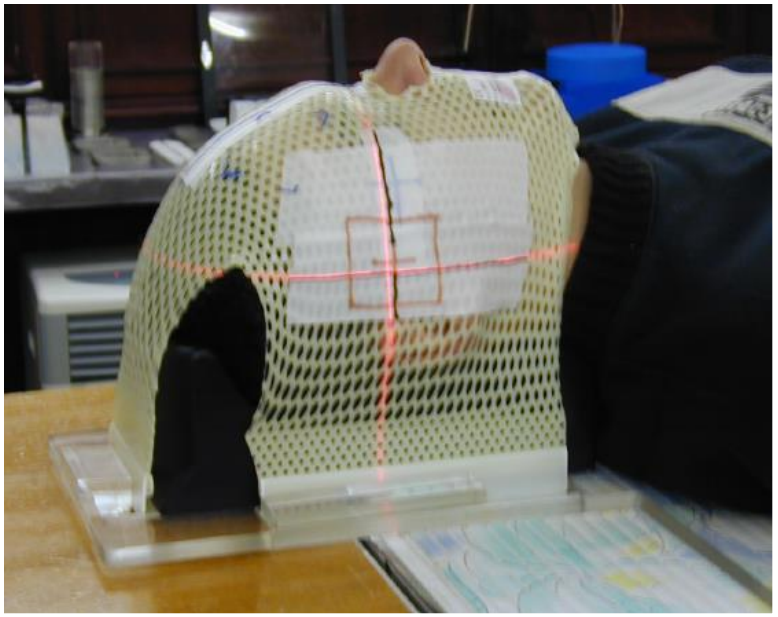
EXTERNAL RADIOTHERAPY

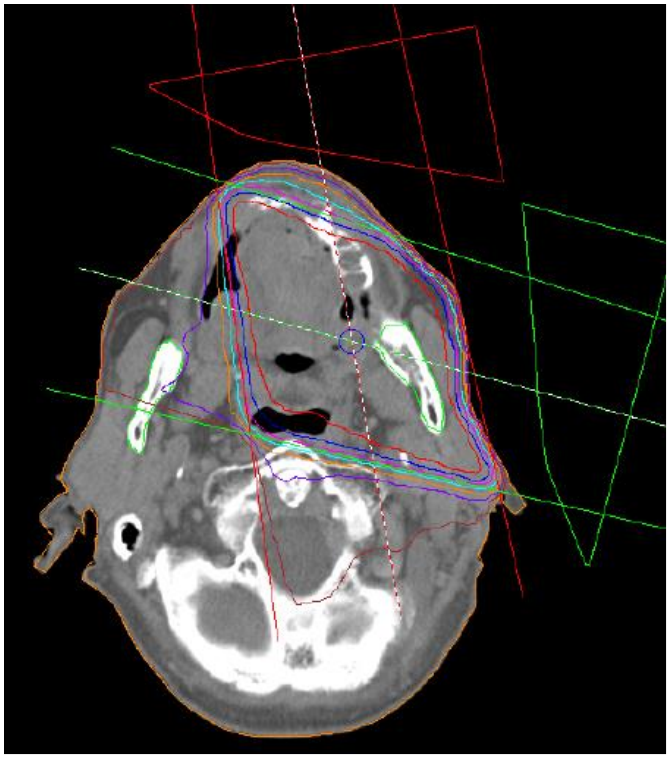
Megavoltage equipment:

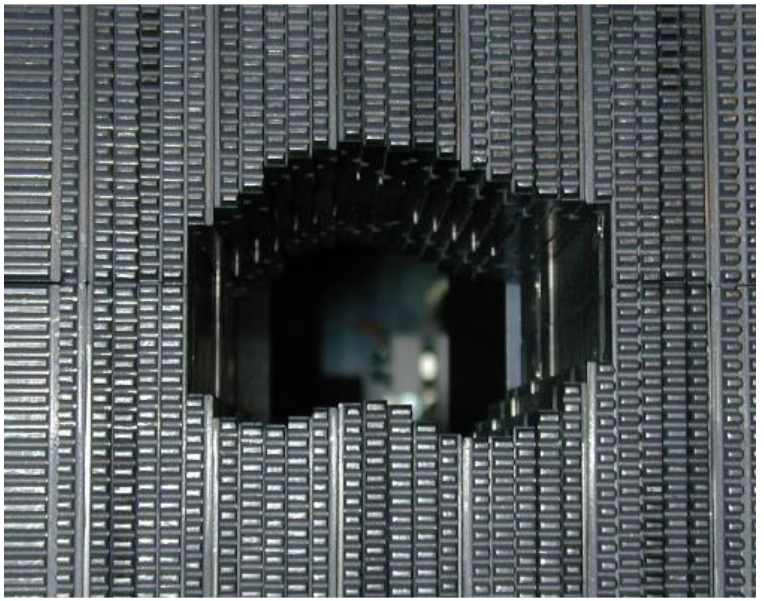
LINear ACcelerator - 6-18 MV photon or elektron

LINAC

TREATMENT PLANNING







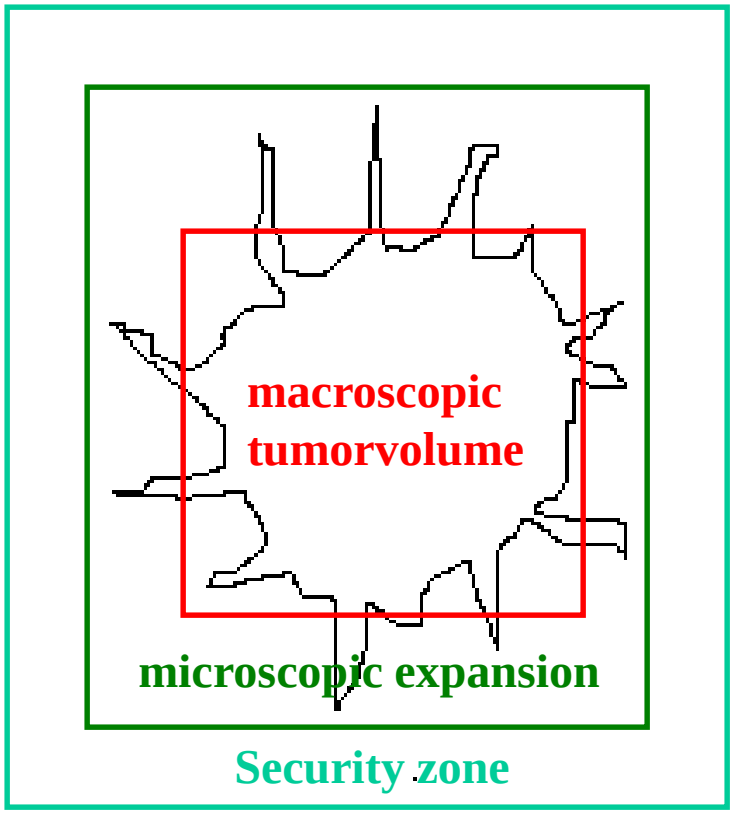
- Conformal 3D radiotherapy
- Irregular, individually shaped fields using “multi-leaf collimator”
- IMRT, IGRT

TARGETVOLUMES

GTV = Gross Tumor Volume ⟸ CT, MRI, PET, UH

CTV = Clinical Target Volume

PTV = Planning Target Volume



CONTOURING OF TARGET VOLUMES AND CRITICAL ORGANS

CTV1: GTV (primary tumor + involved lymphnodes), or preoperative GTV + 0,5 cm

PTV1 = CTV1 + 0,5 cm

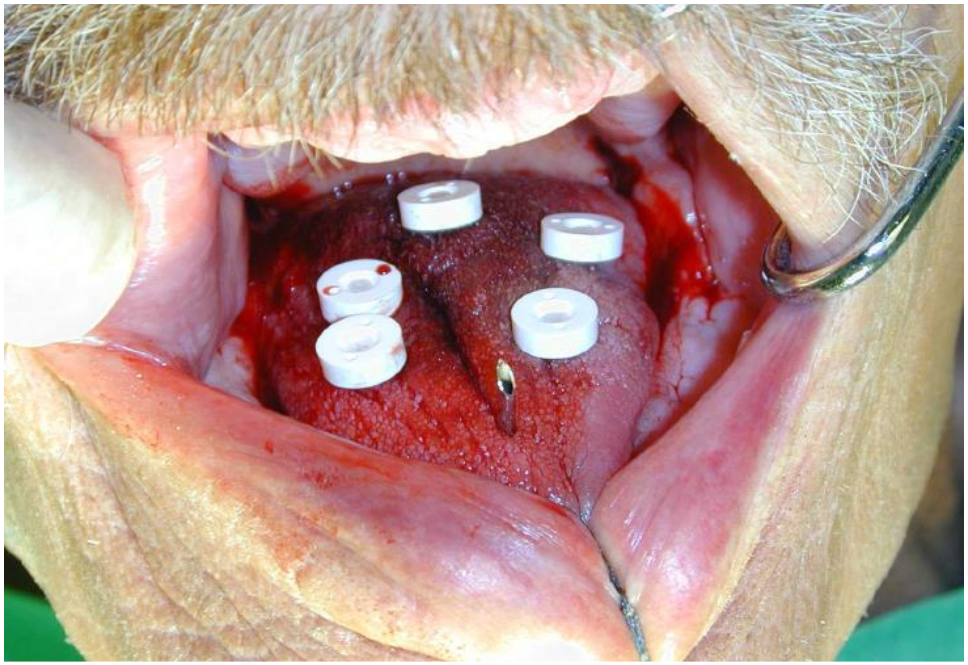
CTV2: Elektive neck region

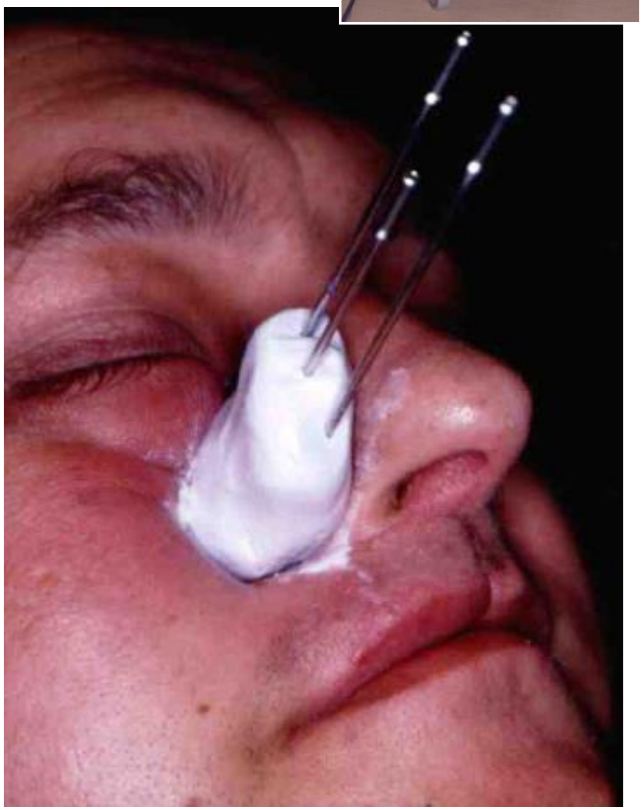
PTV2 = CTV2 + 0,5 cm

PRV (Planning Organ at risk Volume) = organs et risk volume + 3-5 mm

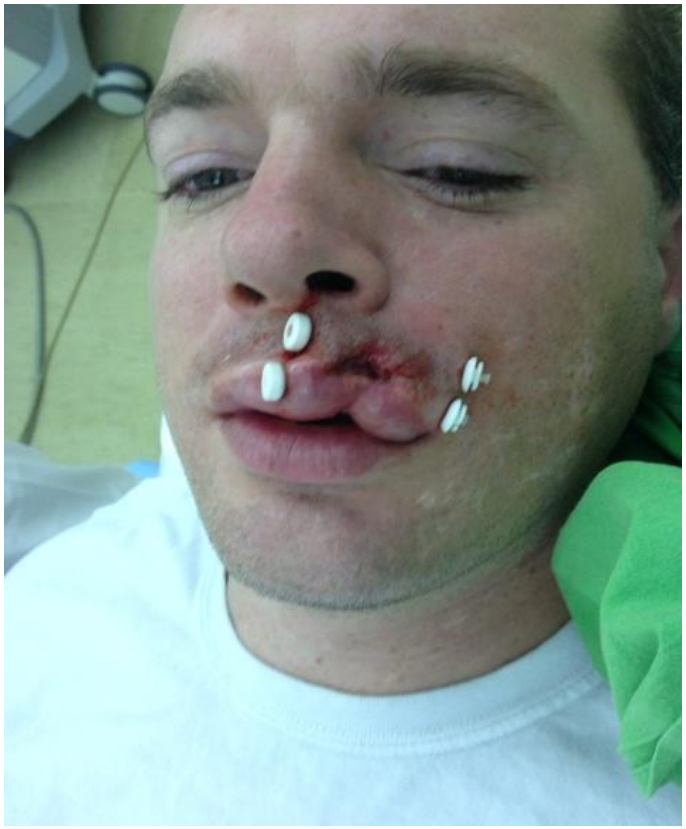
BRACHYTHERAPY (BT)

- interstitial BT (oral cavity, base of tongue)
- intracavital BT (epipharynx, maxilla)
- intraluminal BT (oesophagus, bronchus)
- superficial „moulage” BT (palatum, tonsilla)



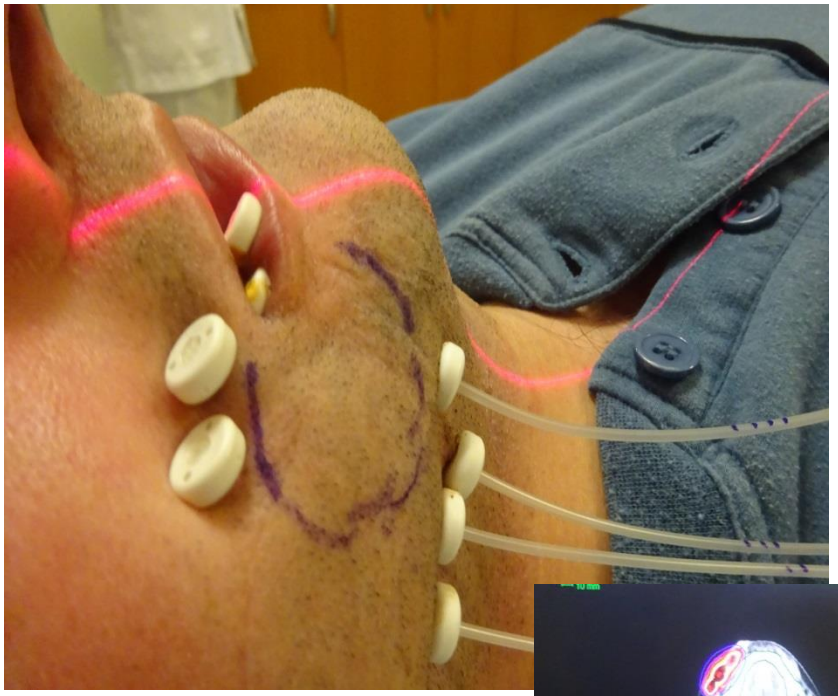


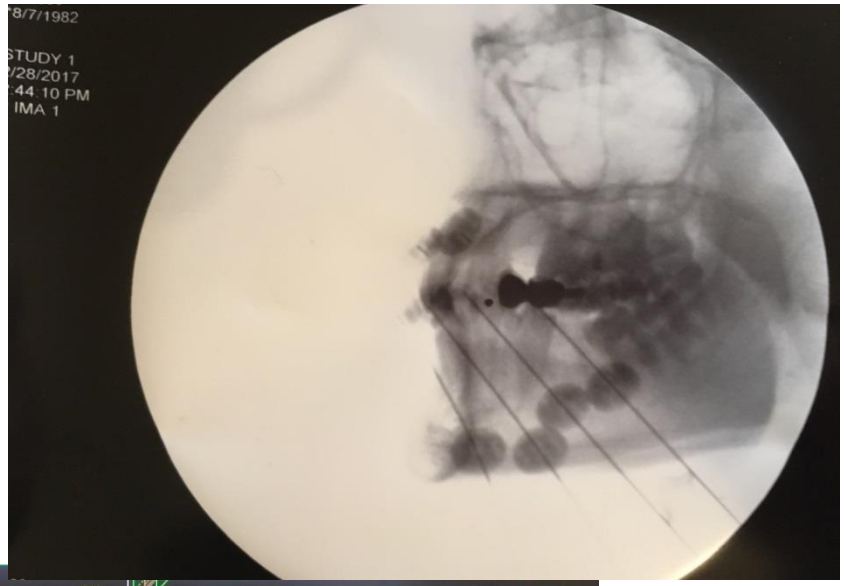
Interstitial treatment of lip cancer

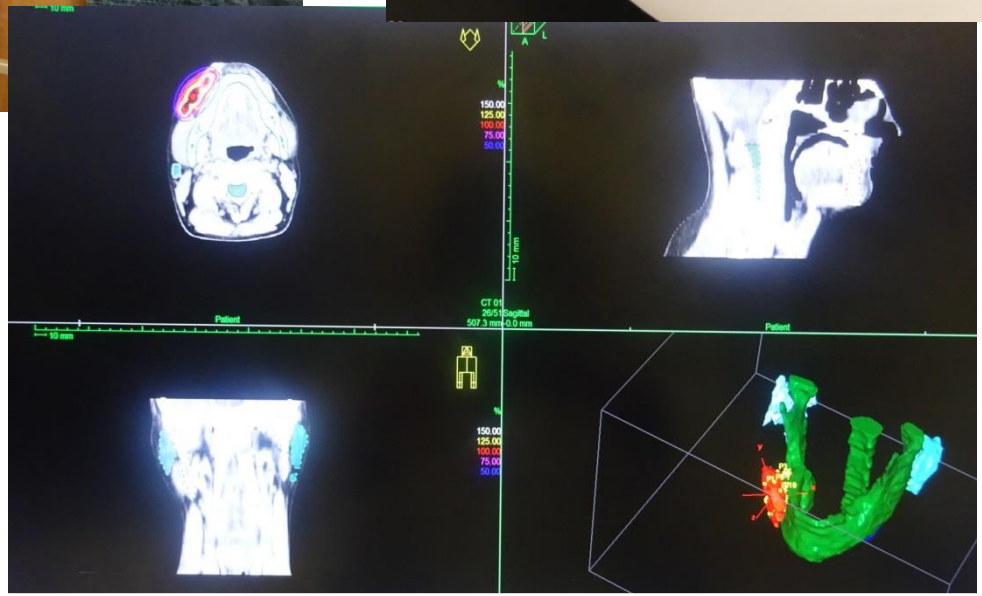


8 weeks after therapy

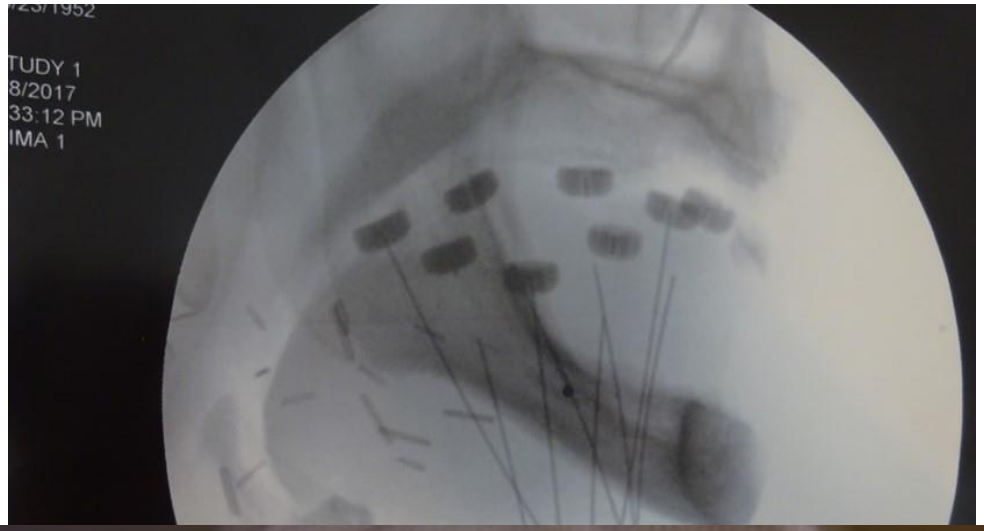
Interstitial brachytherapy of buccal tumor

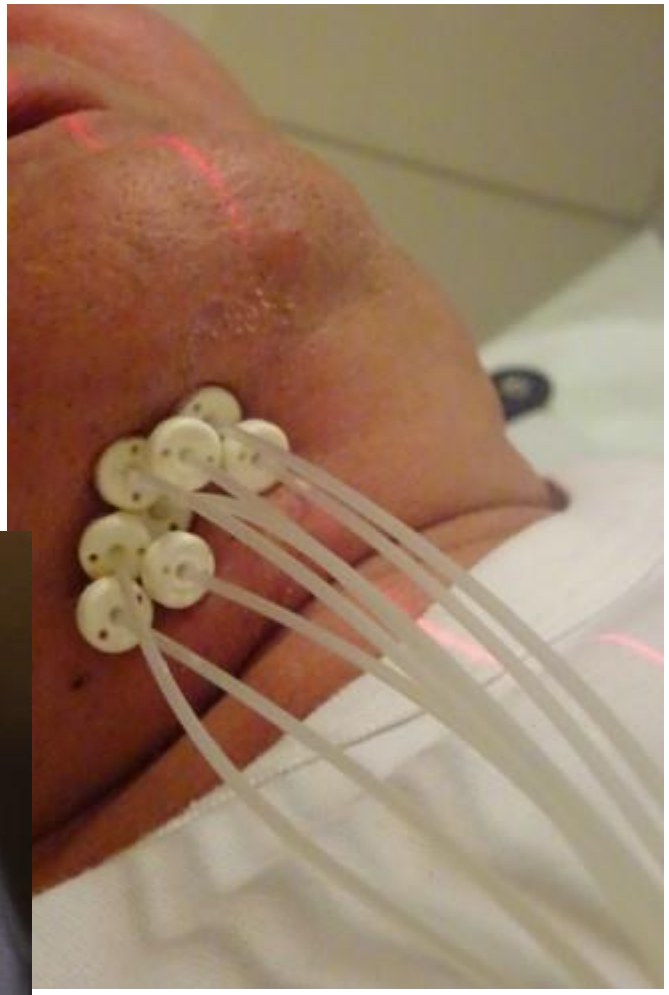






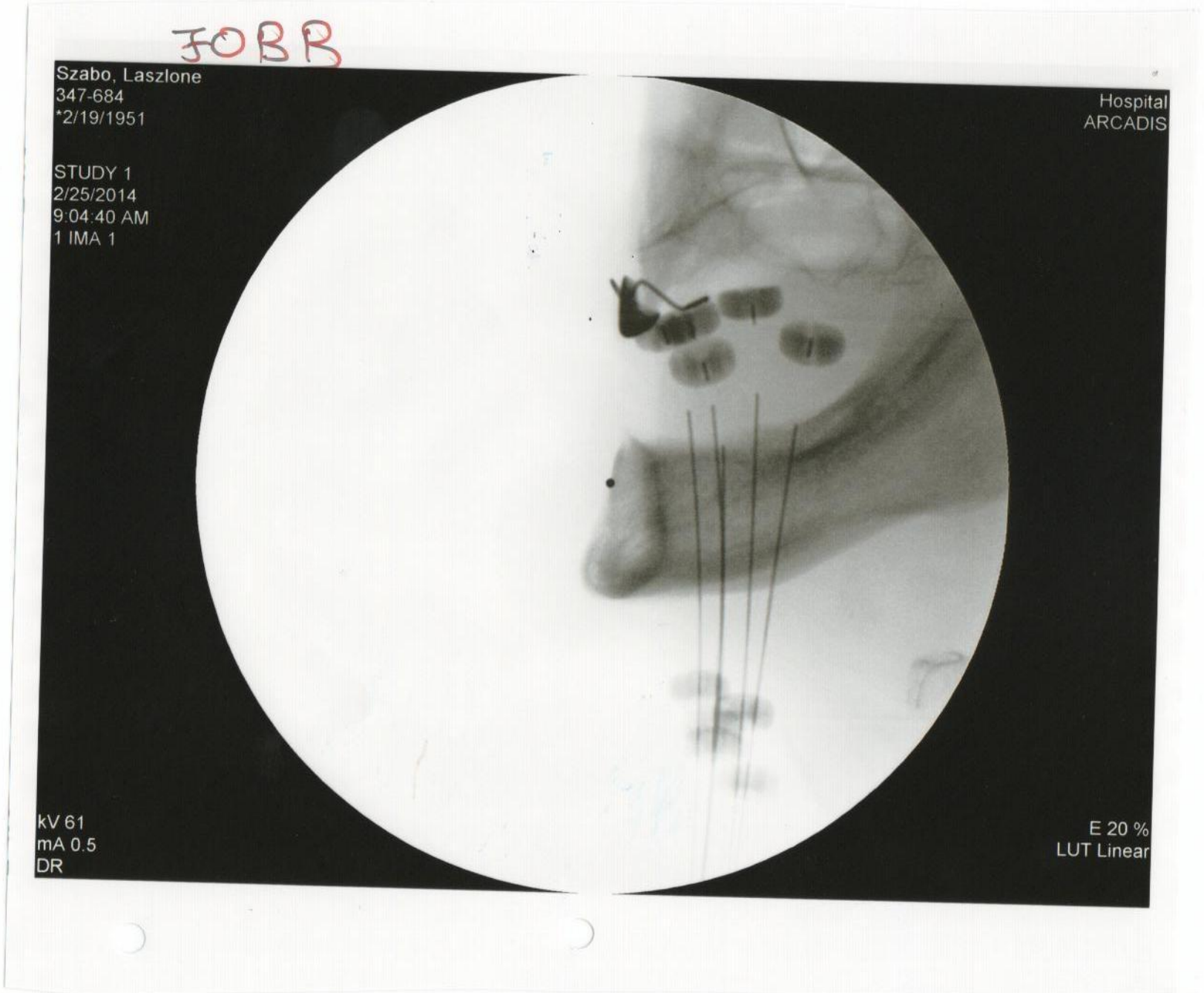
Sublingua and tongue

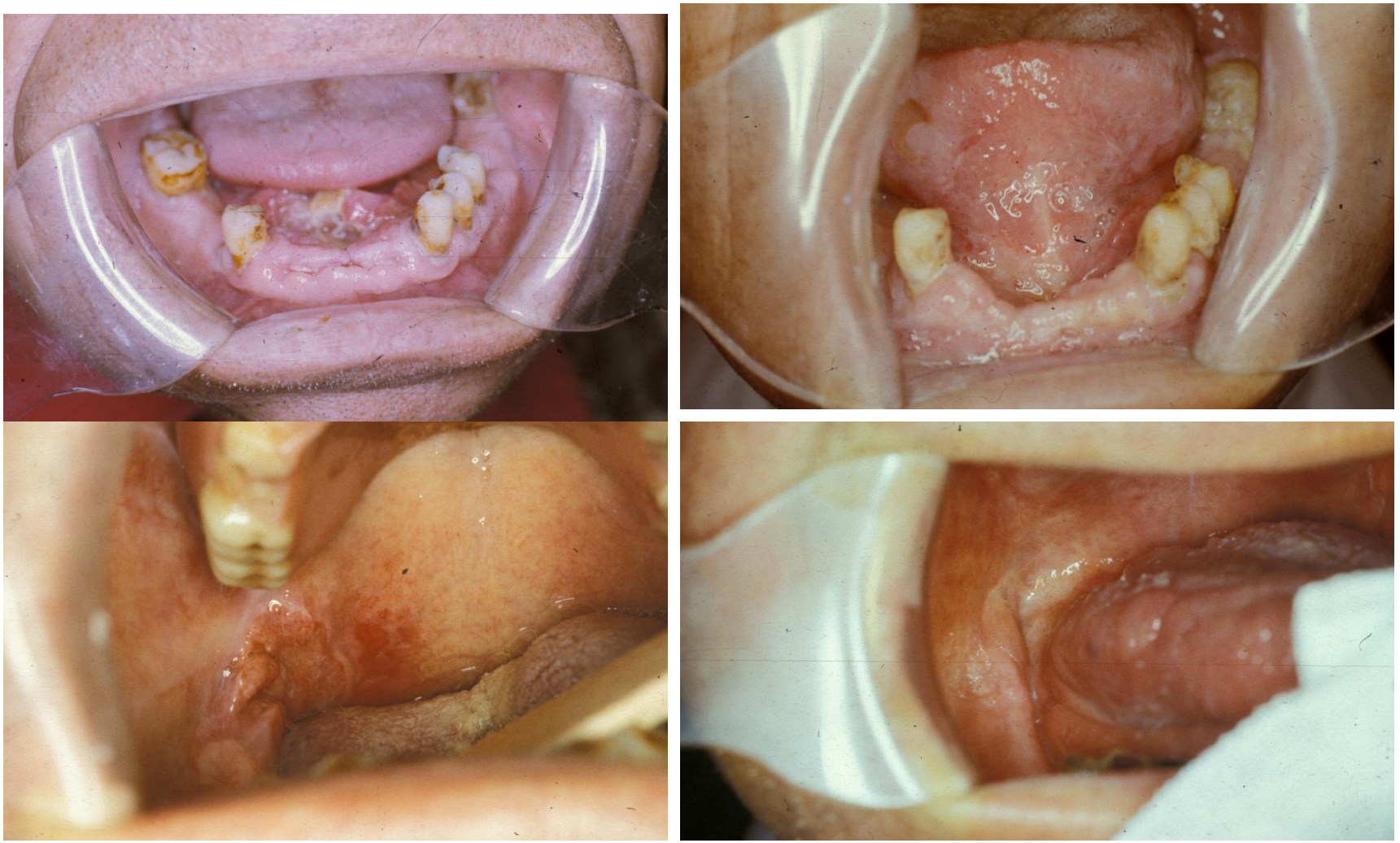




Flexible catheters

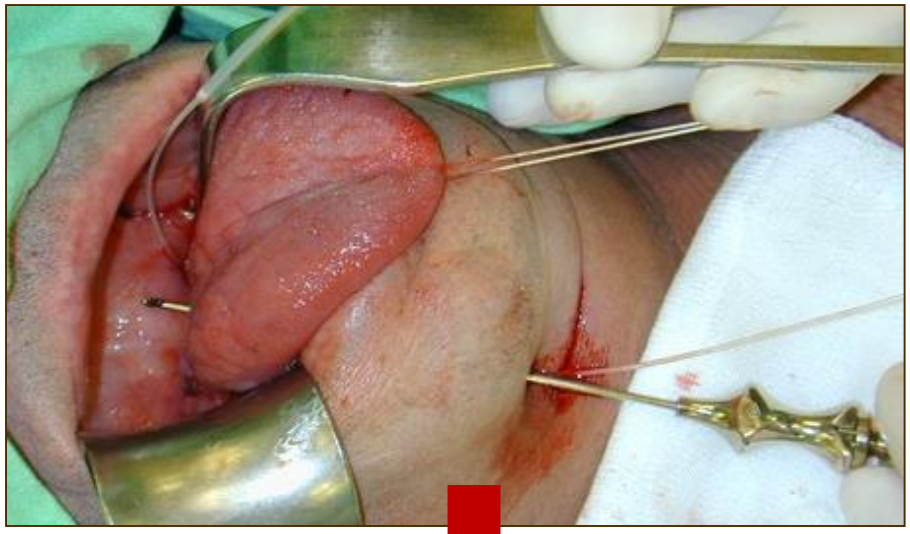
Interstitial treatment of sublingua tumors with flexible, plastic catheters (lateral view)

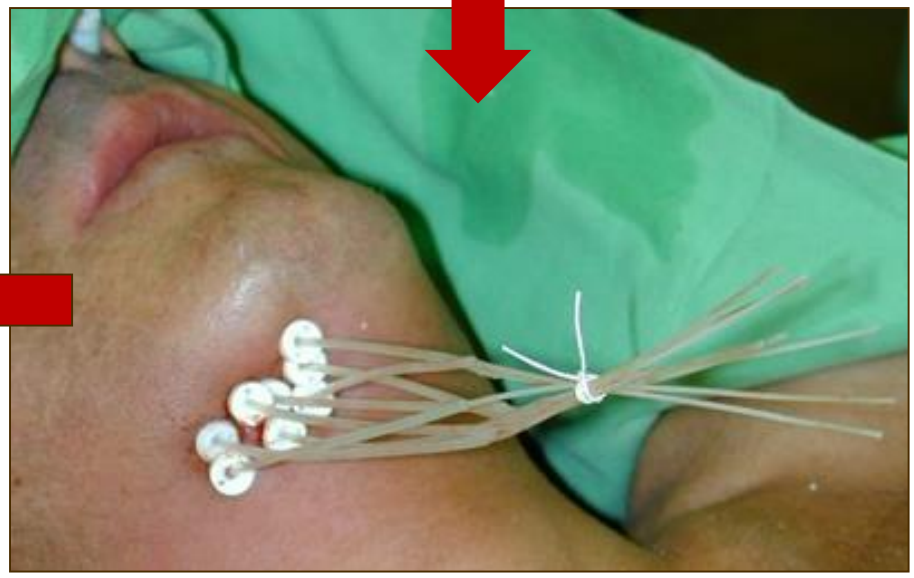


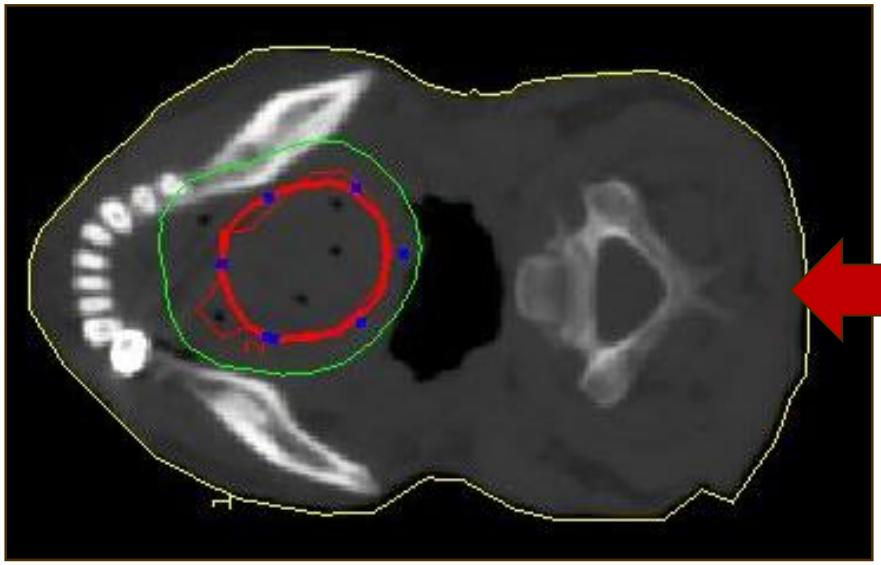


Sublingua, trigonum retromolare tumor before and after BT

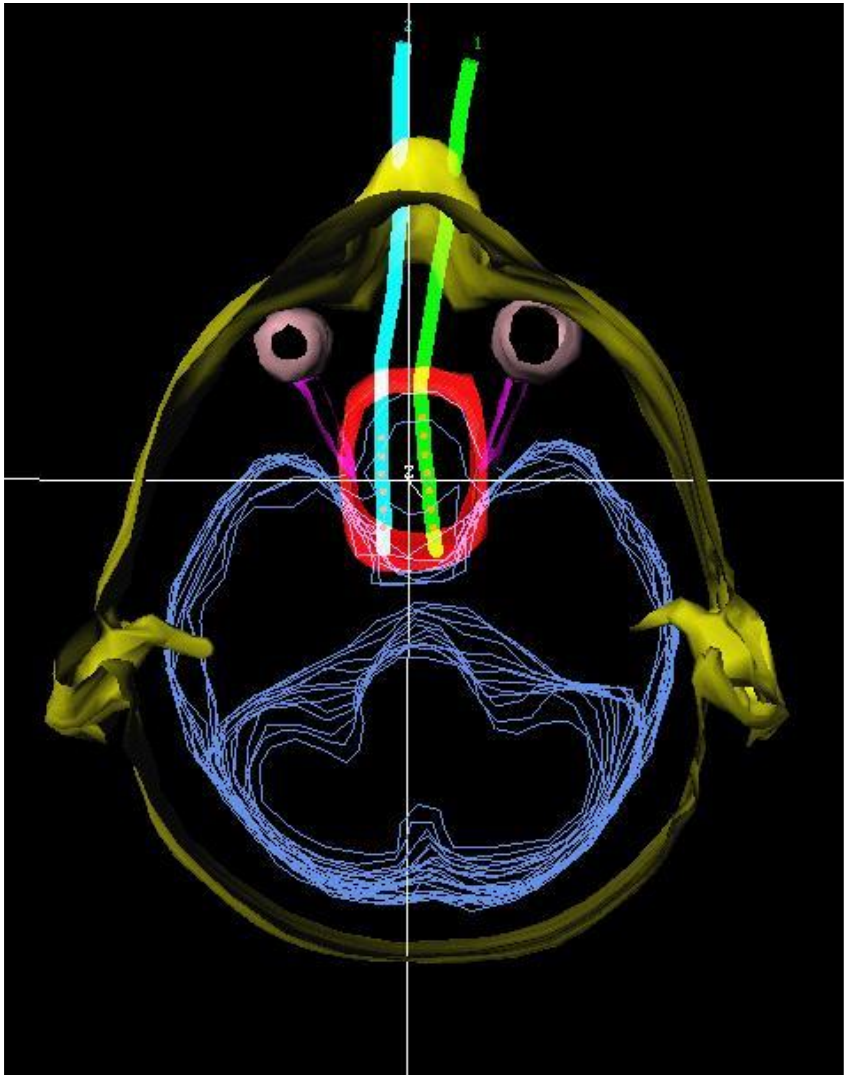
Interstitial brachytherapy of base of tongue tumor







Brachytherapy of the nasopharynx



INCREASING THE EFFECTIVITY OF RADIOTHERAPY

- **ALTERED FRACTIONATION (hyperfractionation - with 8 % better survival)**
- **RADIOCHEMOTHERAPY**
- **BIOLOGICAL THERAPY**

RADIOCHEMOTHERAPY (RCT) IN THE THERAPY OF LOCOREGIONAL ADVANCED (T3-4 and/or N2-3) PHARYNGEAL AND LARYNGEAL TUMOR

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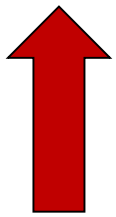
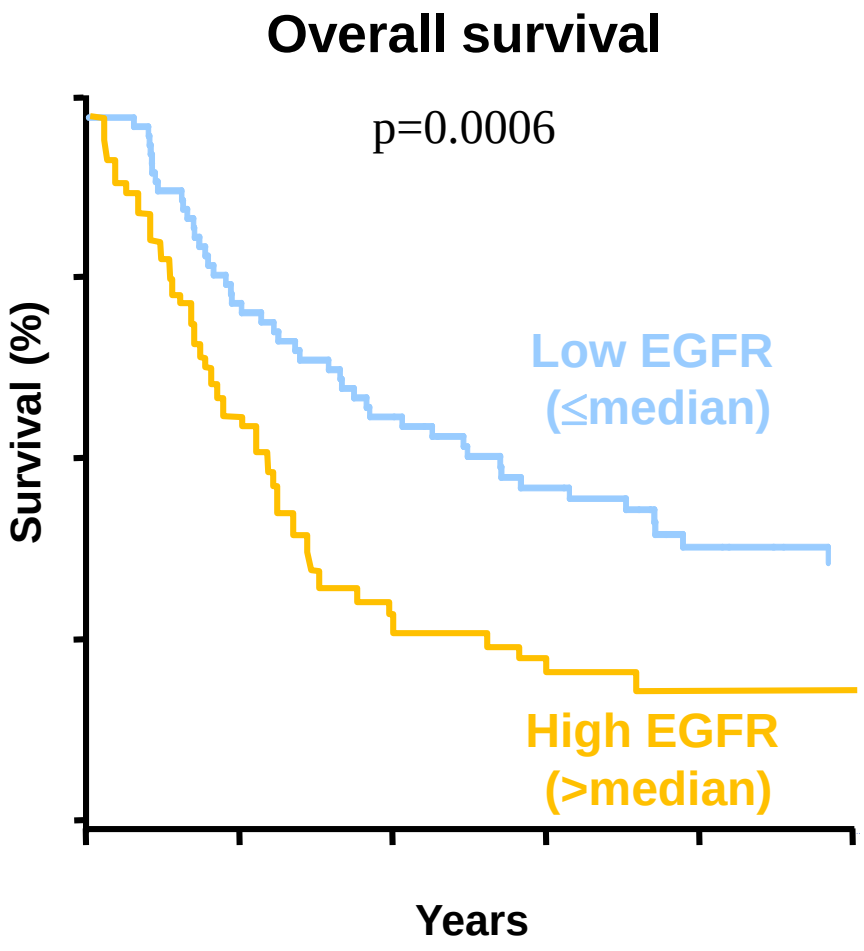
100 mg/m^2 Cisplatin (days: 1, 22 & 43) - STANDARD

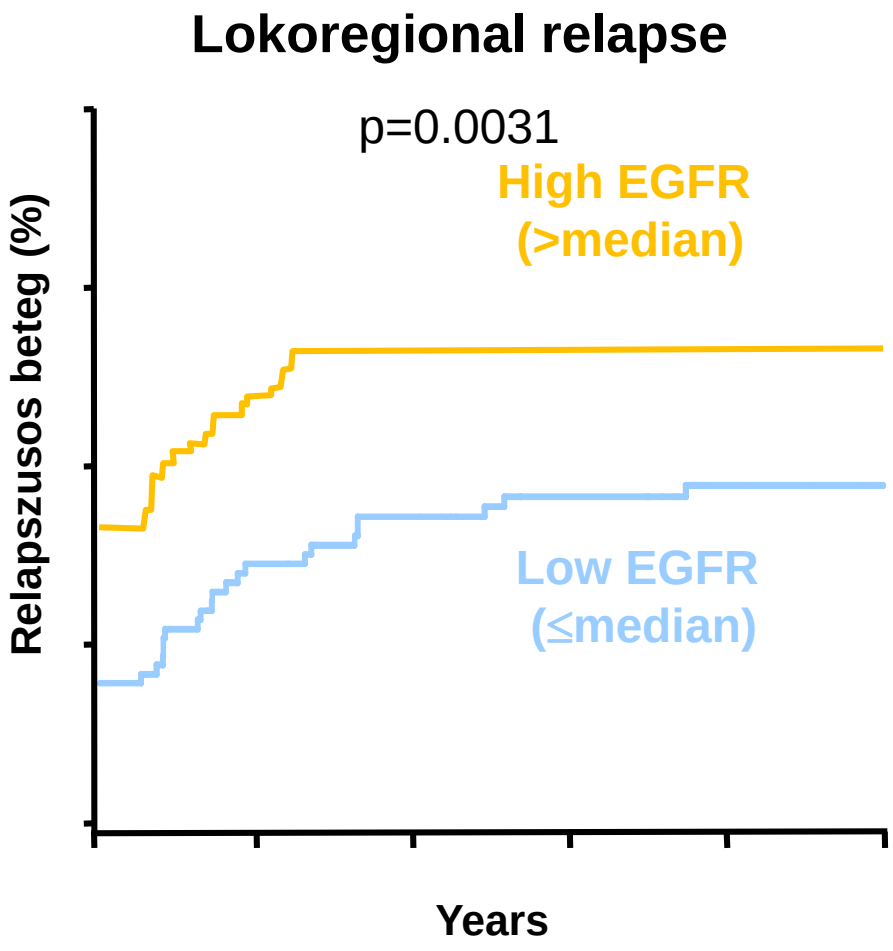
Local tumorkontroll: 18-26%

Ovearall survival: 6,5 %



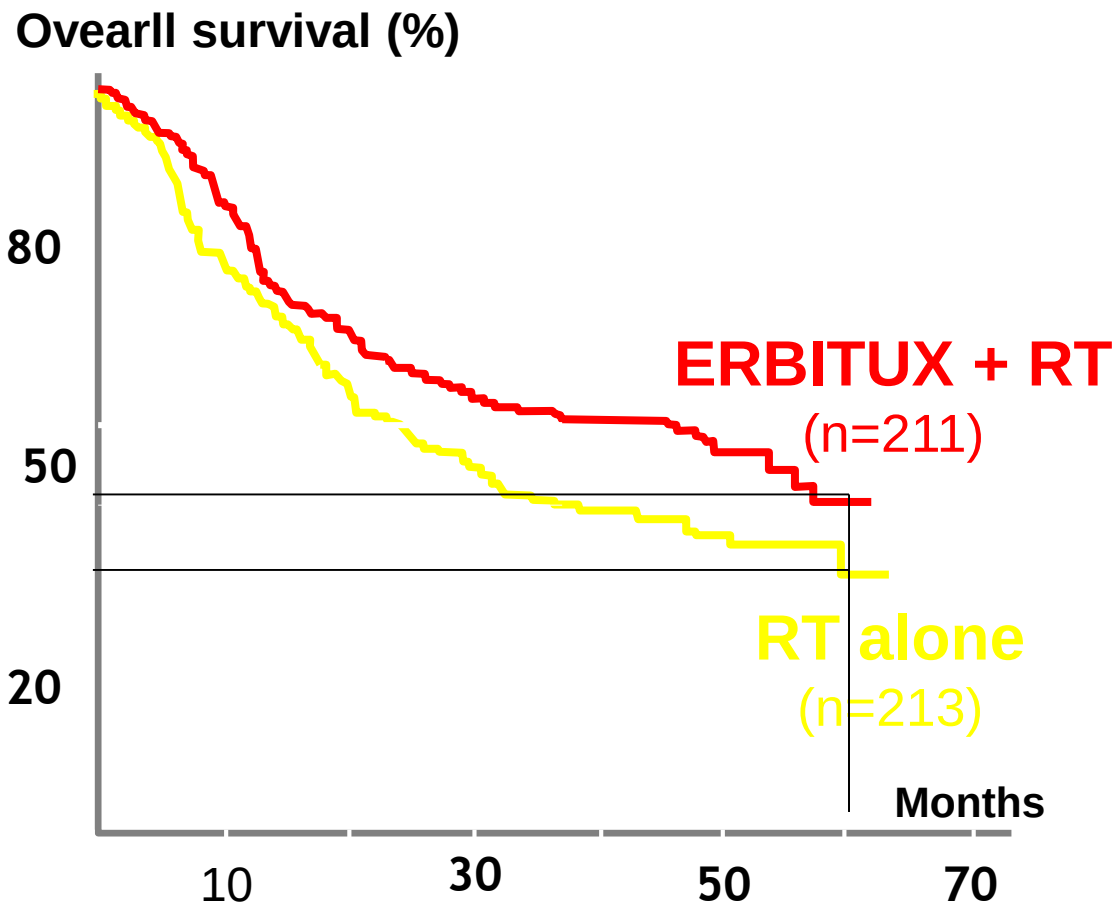
CONNECTION BETWEEN EGFR EXPRESSION AND PROGNOSIS IN HEAD AND NECK CANCER





Ang KK, et al. Cancer Res 2002;62:7350–7356

ERBITUX (E) + RADIOTHERAPY (RT) vs. RT



5-year survival:

➔ **RT: 36,4 %**

➔ **E + RT:45,6 %**

(p = 0,018)

3-year lokoregional kontroll:

➔ **RT: 34 %**

➔ **E + RT: 47 %**

(p = 0,005)

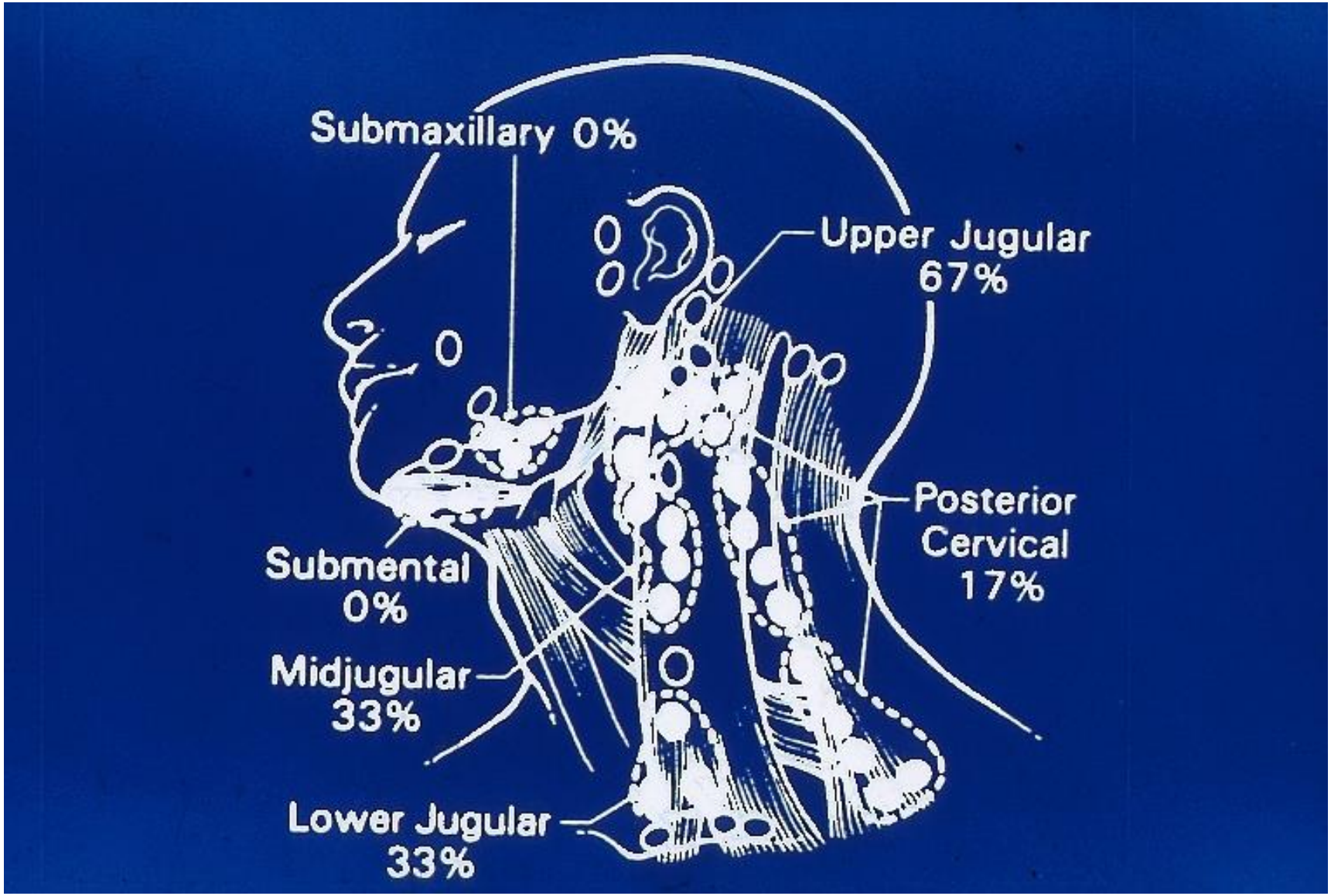
Side effects: rashes

Bonner J.A. et al. Lancet, 11:21-28, 2010.

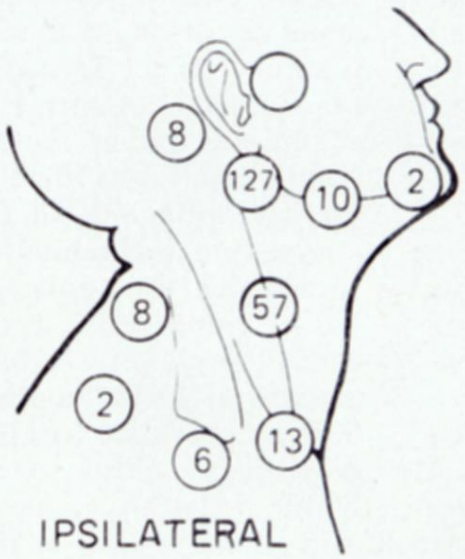
MUCOSITIS (Grade 3)

Skinreactions (Erbitux)

IN THE TREATMENT OF HEAD AND NECK TUMORS LOCOREGIONAL TREATMENT IS A BASIC REQUIREMENT

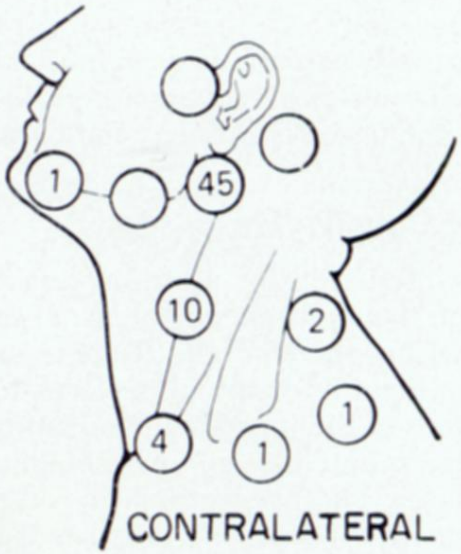


Stage III-IV. base of tongue tumor. Examination of clinical negative neck after dissection histology



IPSILATERAL

Base of Tongue

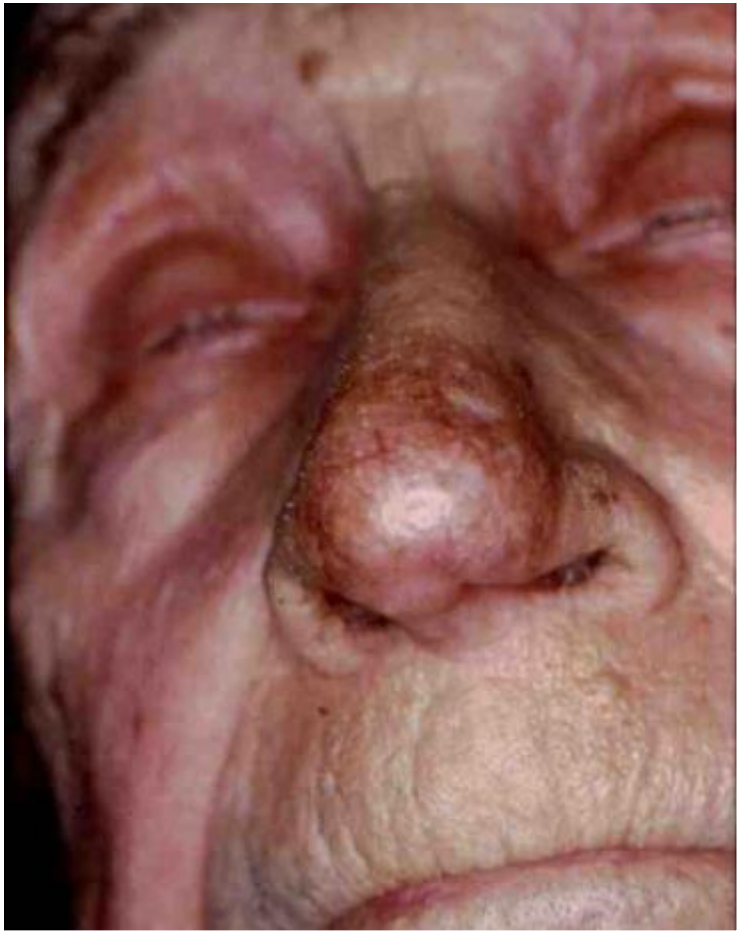


CONTRALATERAL

N_0	N_1	N_{2A}	N_{2B}	N_{3A}	N_{3B}	$N_1 - N_3$ / Total
41	30	21	26	14	53	144 / 185 = 78%

SKIN TUMOR - RT

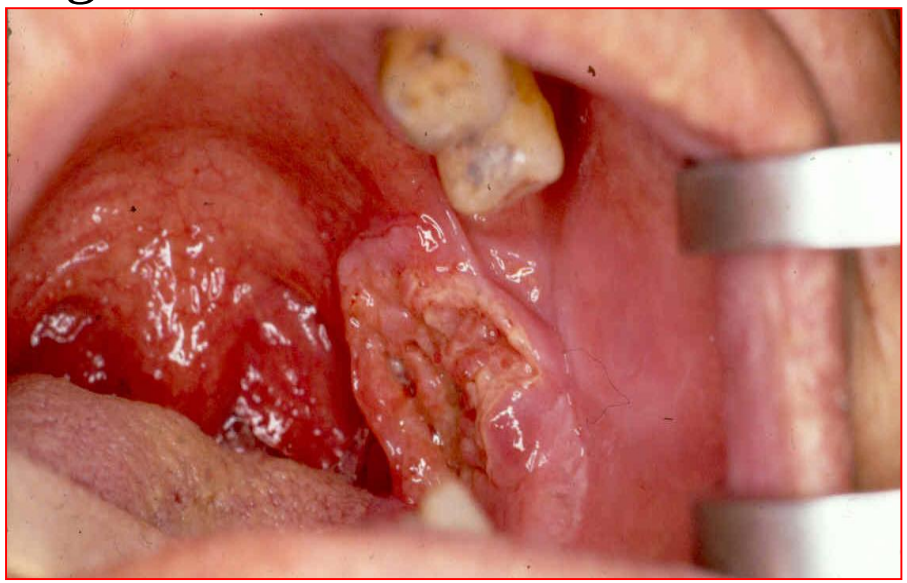
Before RT

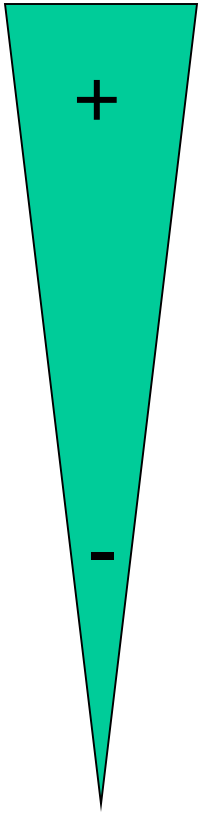


After RT

RADIOTHERAPY OF PHARYNGEAL TUMORS

- Nasopharynx
- Mesopharynx
  - Tonsilla, facila arch, palatum molle, uvula, lateral and posterior pharyngeal wall, base of tongue
- Hypopharynx
  - sinus piriformis, postrior pharyngeal wall, postcricoid region





Radiosensitivity

DOSE

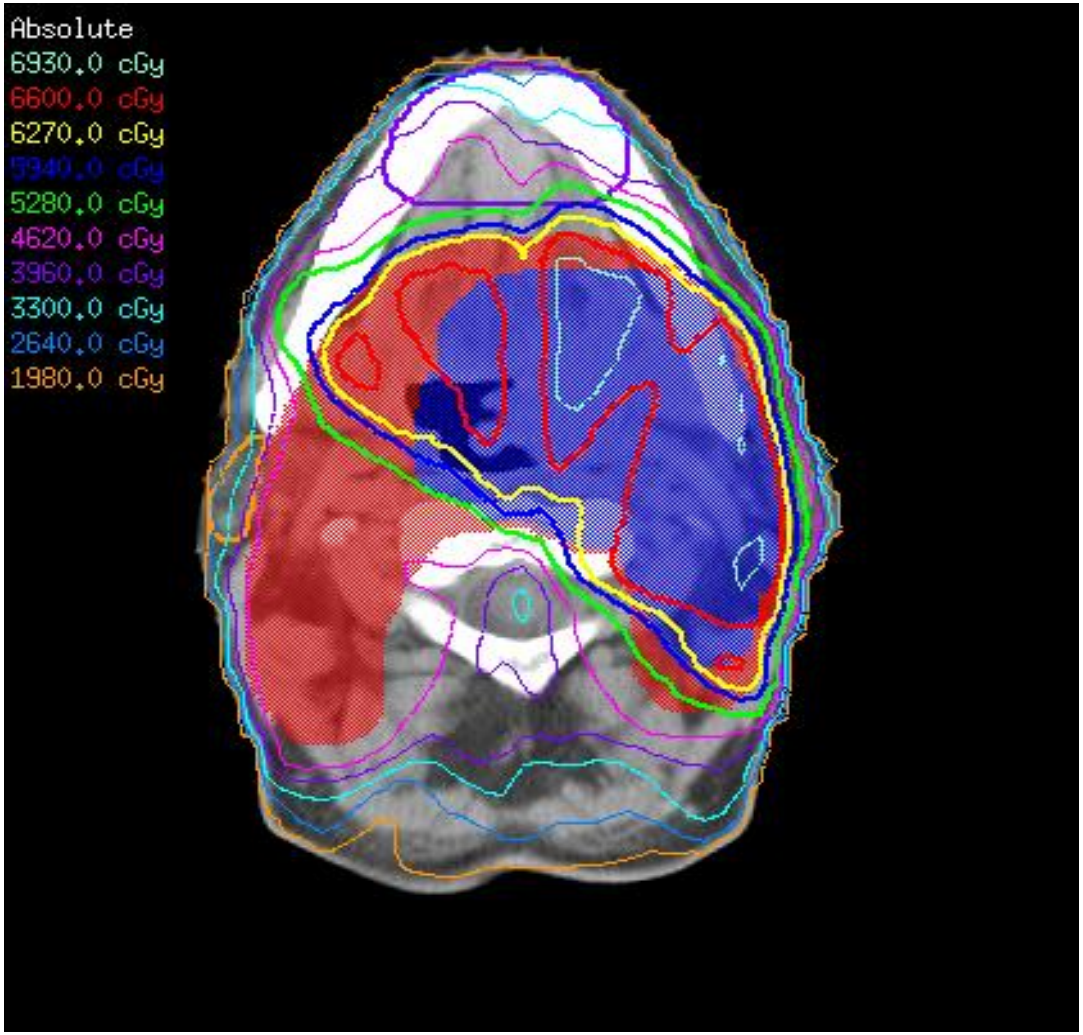
Radio/chemo-bioradiotherapy alone: 66-70 Gy

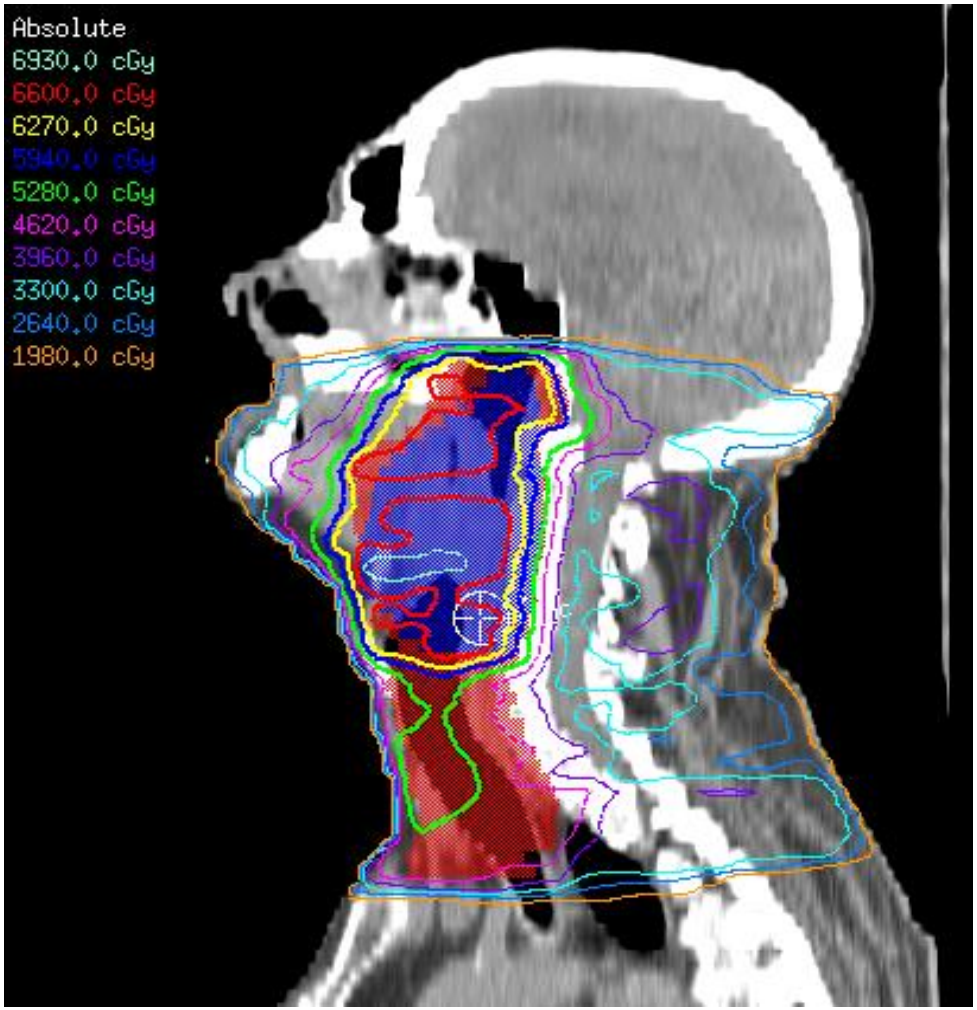
Postoperative radiotherapy: 60-66 Gy

Elective dose (not tumor or metastatic lymphnode): 50 Gy

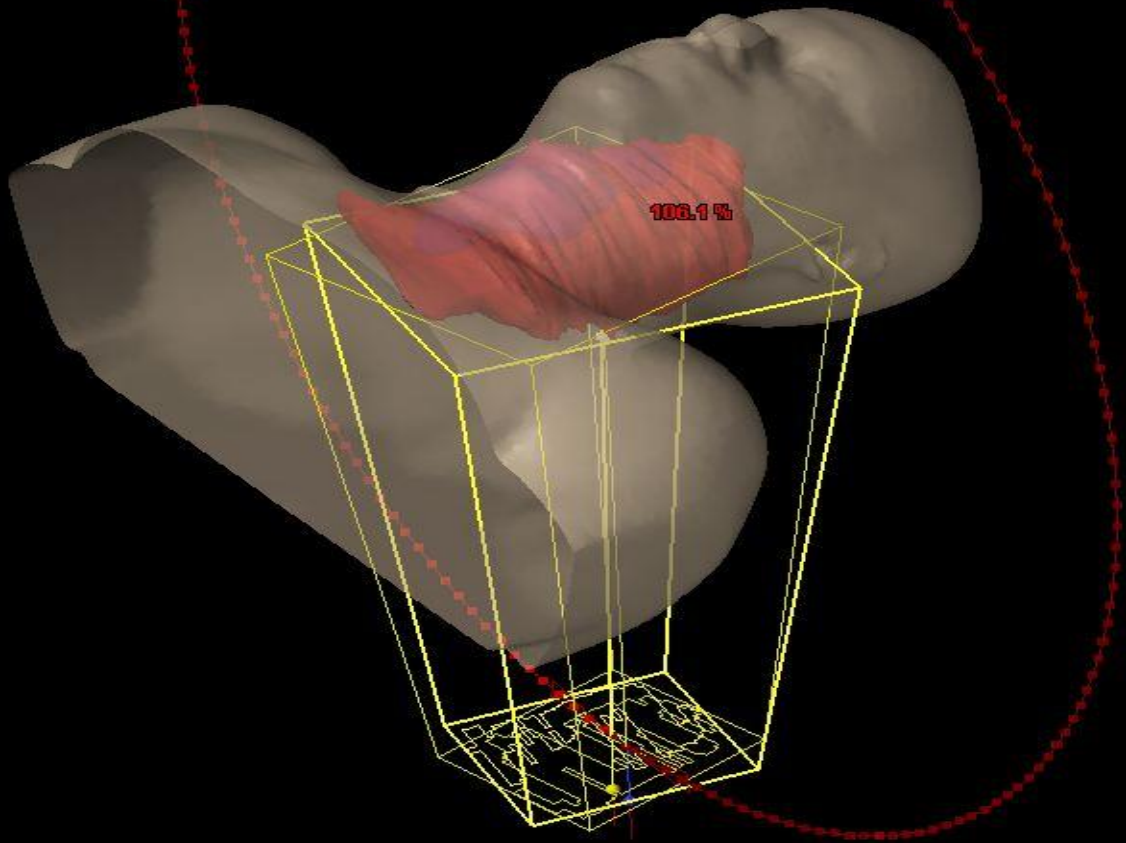
Tolerance dose:
Medulla: 45-48 Gy
Lens: 6 Gy
Parotis: 20-30 Gy

Radiotherapy of oropharyngeal tumor

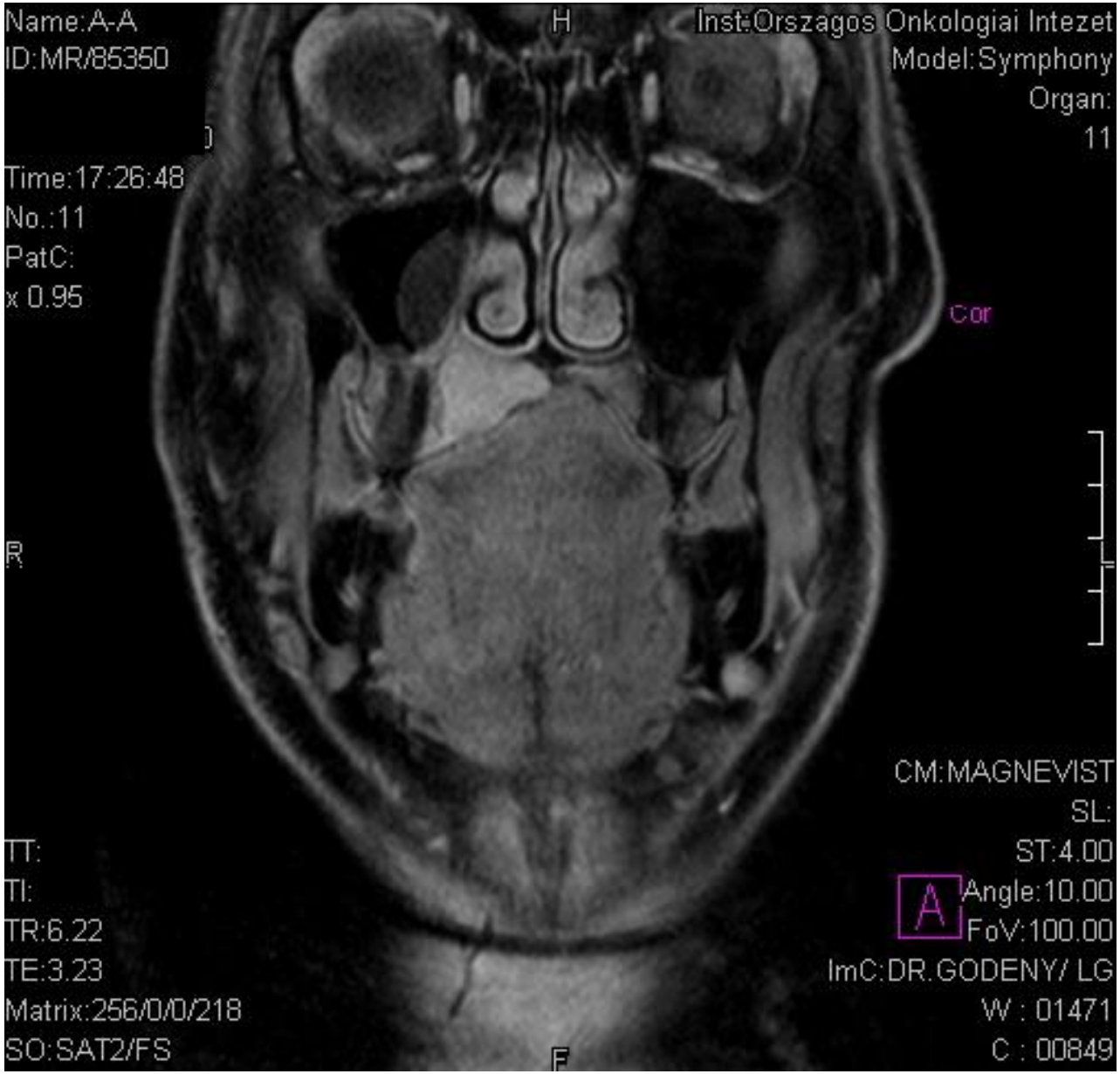



Absolute
6930.0 cGy
6600.0 cGy
6270.0 cGy
5940.0 cGy
5280.0 cGy
4620.0 cGy
3960.0 cGy
3300.0 cGy
2640.0 cGy
1980.0 cGy

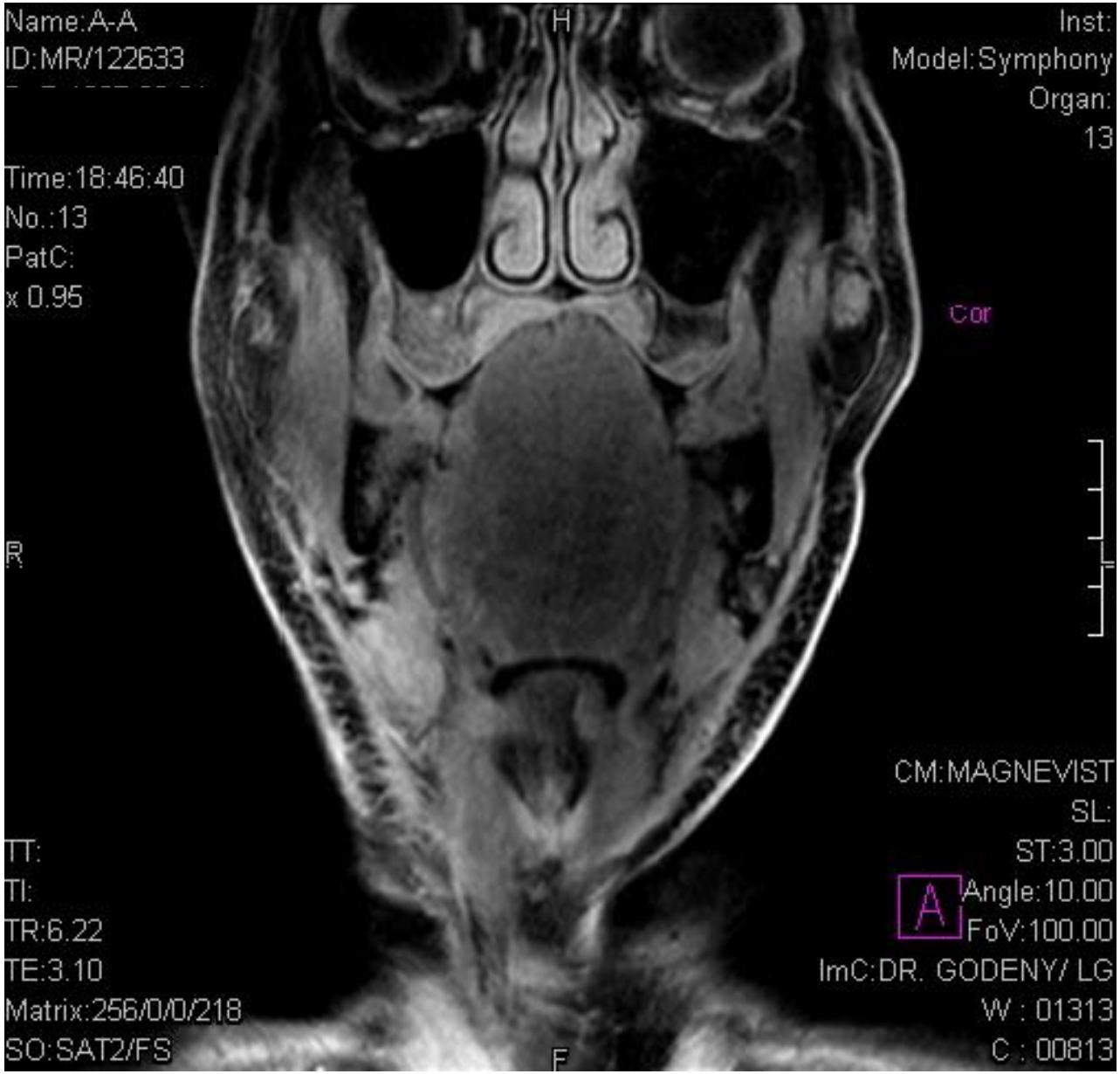
IMRT RapidArc technique



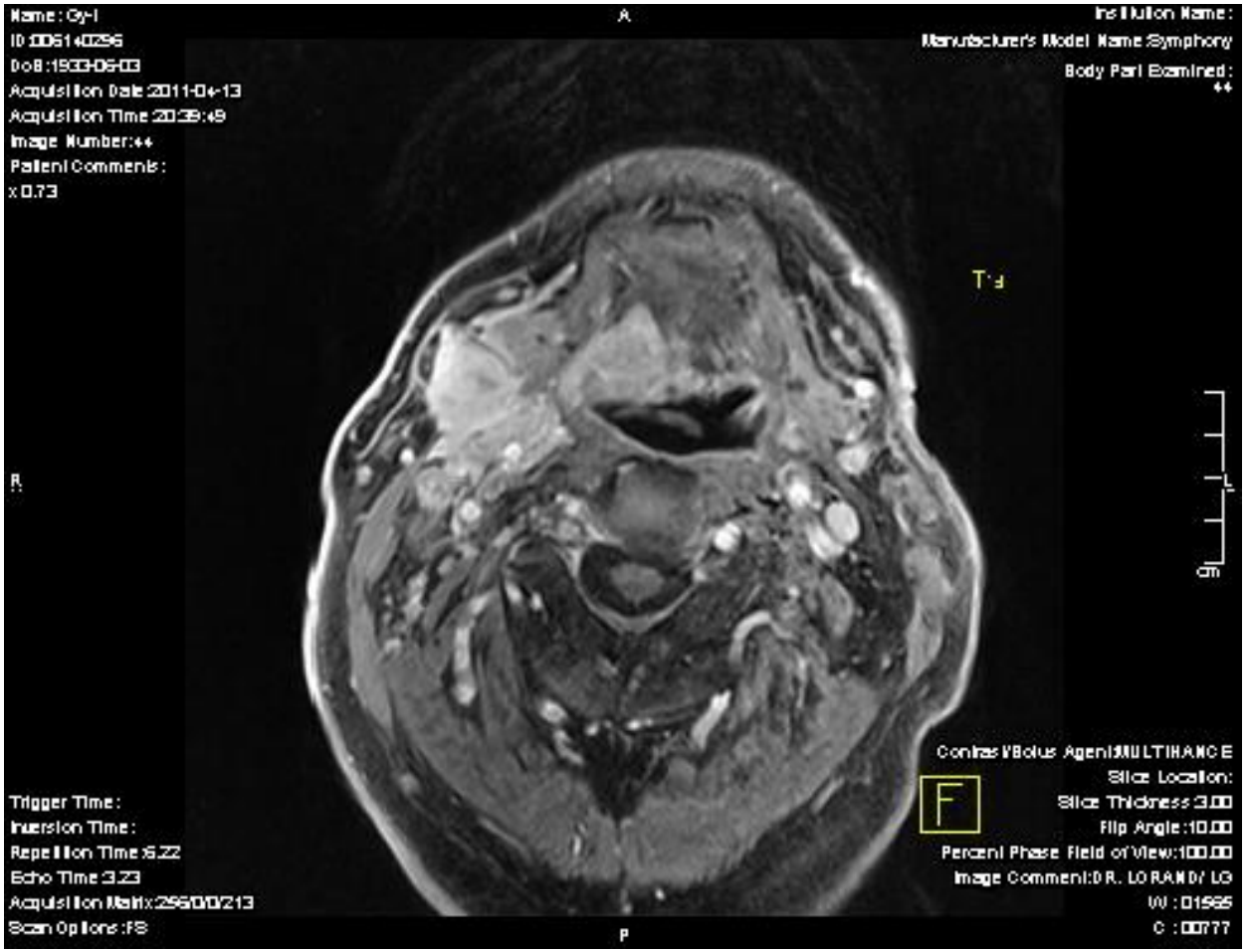
•Radiotherapy of T1N0 vocal cord tumour from opposing fields, with immobilising mask)



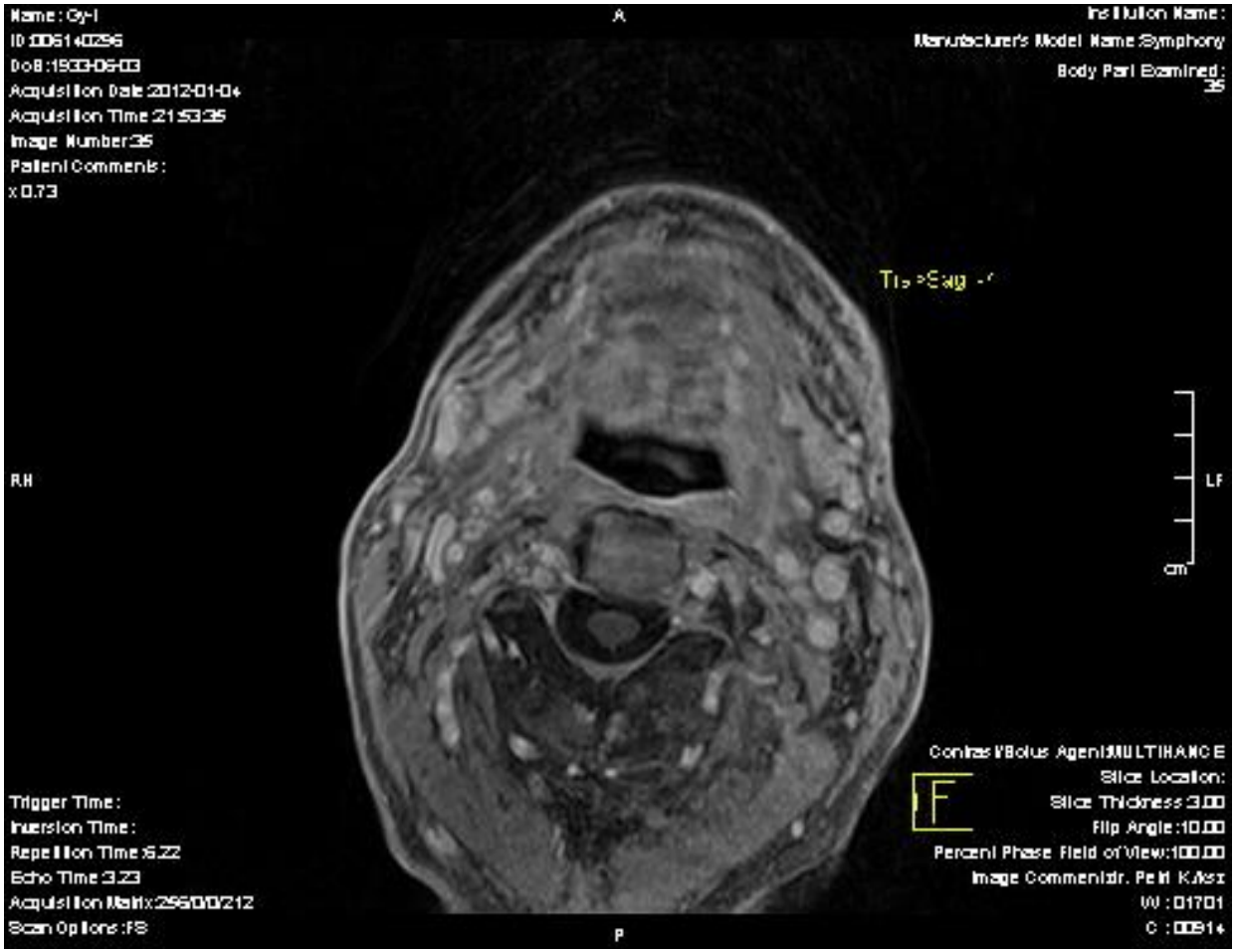
Before bioradiotherapy



After bioradiotherapy



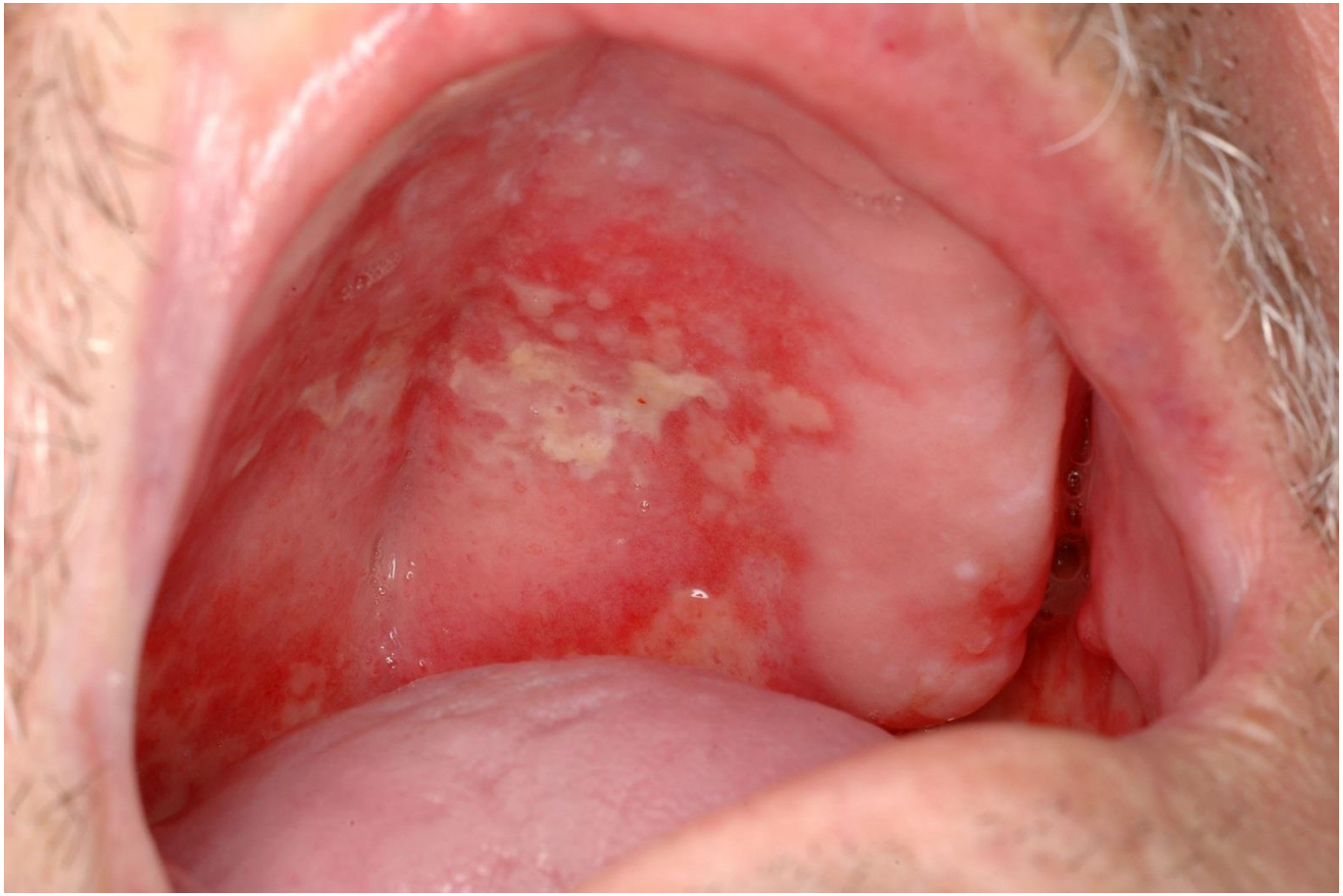
Before radiochemotherapy



After radiochemotherapy

SIDE EFFECTS OF RADIOTHERAPY

- MUCOSITIS/EPITHELITIS
- XEROSTOMY (IMRT)
- DECREASED Ig-A LEVEL (CARIES)
- DETERIORATION OF SENSE OF TASTE
- SOFT TISSUE/OSTEORADIONECROSIS
- INJURY OF THE SPINAL CORD



CHEMOTHERAPY

- Concomitant
- Induction: 2-4 cycles Taxotere-Platina-5-Fu
  - remission: Radiotherapy (RChT or BRT)
  - no remission: Operation
- Palliative: Erbitux-Platina-5 Fu (6 cycles)

Immuntherapy – Improving T-cell answer reactions

Side effects of chemotherapy: blood picture, renal function deterioration
Side effects of immuntherapy: inflammation

TREATMENT OF SALIVARY GLAND, THYROID, SINONASAL TUMORS

- **Operation**
- **Postoperative radiotherapy**

Salivary gland:

- T3-4, GII-III, lymphnode metastasis, recurrence, closer or positive surgical margin, vascular, perineural invasion
- Irradiation of the neck is necessary without dissection: T3-4, GIII, lymphnode metastasis, recurrence

Sinus:

- postoperative radiochemotherapy is necessary by positive resection margin, extracapsular invasion, or without surgery

Thyroid gland:

- papillar and follicular carcinoma (without Iodine uptake), medullar tumor with R1 resection, anaplastic tumor, recurrence
- I131 therapy indicated by tumors with Iodine uptake

Thank for your attention!