General Principles of Radiotherapy In Head & Neck Cancers

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MUMBAI

The Silent Tsunami

HNSCC (Head & Neck Squamous Cell Carcinoma)

Accounts for about 4,50,000 cases worldwide

By 2020, incidence double

20% of cancer burden - 1,50,000 new cases in 2000 in India*

Oral Cancers

TMH - 12% of all new cases annually (1800)

> 75 % present with advanced disease

*GLOBOCAN-IARC, Lyon 2000

HNSCC CANCER

Patterns of failure

- Loco regional failure 75 - 90 %
- Distant Mets 05 -10 %
- Second Primary 10 - 20 %

HNSCC CANCER

Multidisciplinary Team

Surgical Oncologist
Radiation Oncologist
Medical Oncologist
Medical Physicists
Radiotherapy Technologist
Dentistry / Prosthodontics
Speech and Swallowing therapy
Physical Medicine & Rehabilitation
Social Services

Role of radiotherapy

- Radical: External beam
  Brachytherapy: Interstitial
  Intraluminal
- Concurrent chemo-radiotherapy
- Adjuvant
- Palliative

What is radiotherapy?

The use of ionising radiation in the treatment of malignant and benign conditions

Aim of radiotherapy

Deliver tumoricidal doses to the disease
limit dose to sorrounding normal structure to tolerance

General Management Guidelines: HNSCC Cancers

AIM

Highest loco-regional control

Anatomical with functional Preservation

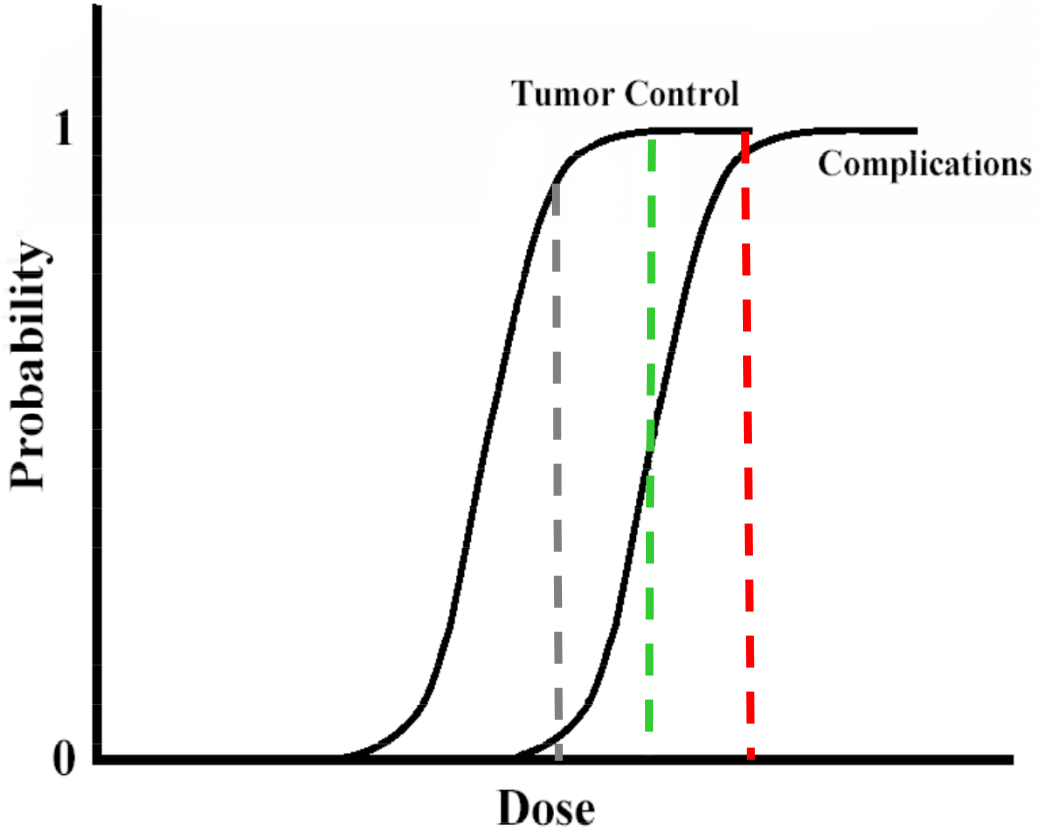
- **Stage I / II** disease - Single modality (Surgery or RT)
- **Stage III / IV** disease – Combined modality

*Surgery + RT (in most patients)
*Chemotherapy + RT in selected patients

Basis of fractionation in radiotherapy can be understood today in terms of the principles of

- Repair of sublethal damage
- Reassortment of cells within the cell cycle
- Repopulation
- Reoxygenation
- Inherent radiosensitivity

RADIOTHERAPY

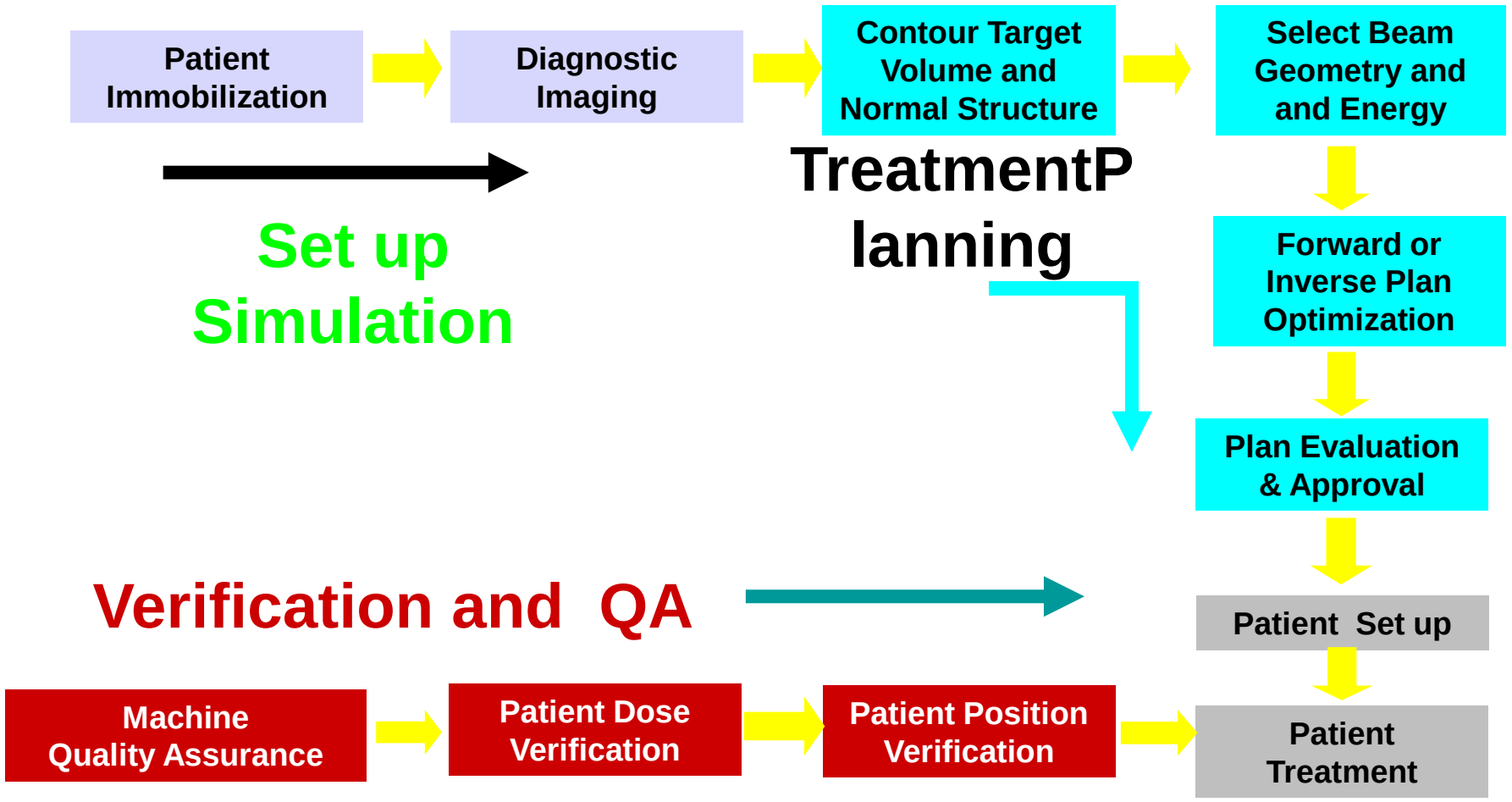


High tumour control,
high risk of complications

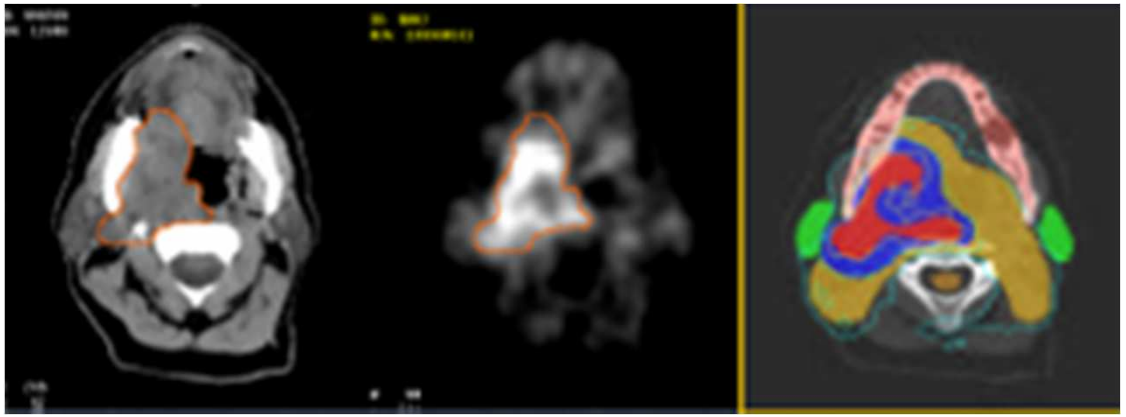
Low risk of complications,
low tumour control

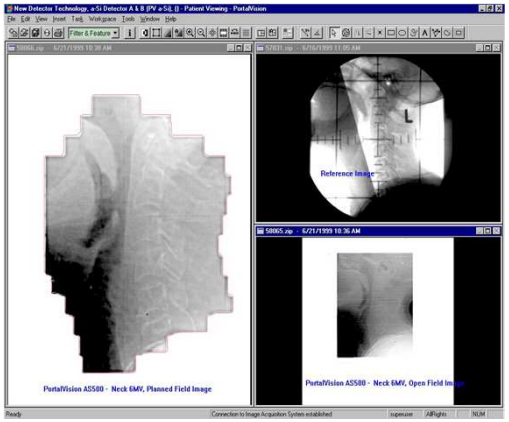
Medium tumour control,
medium risk of complications

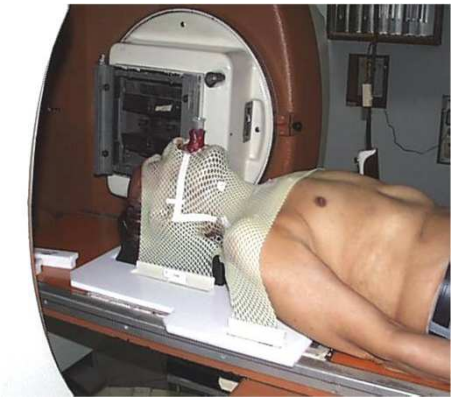
RADIOTHERAPY PROCESS



RADIOTHERAPY PROCESS







Radical Radiotherapy

Indications

Early stage disease

Inoperable (medical contra-indications)

Surgery is morbid

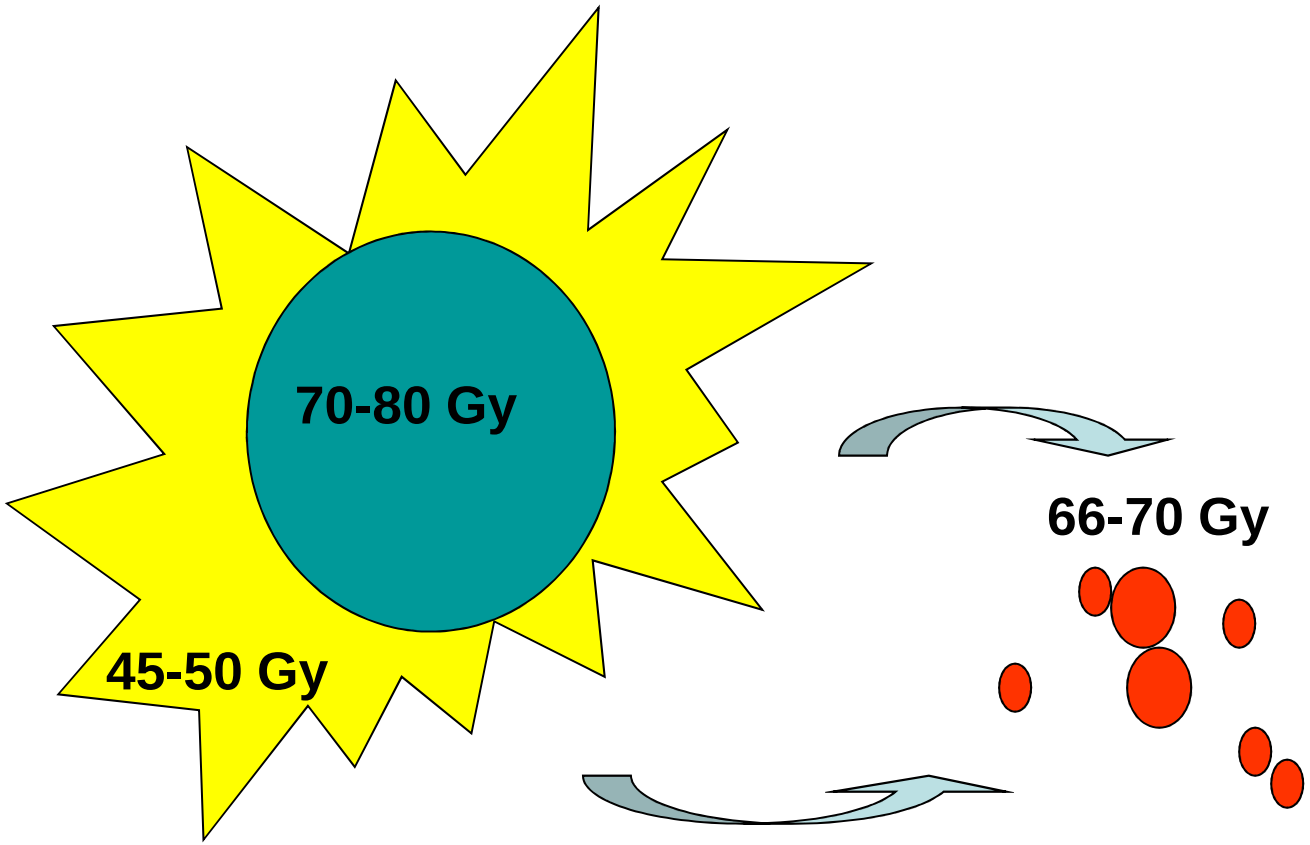
Combination of EBRT+ Brachytherapy

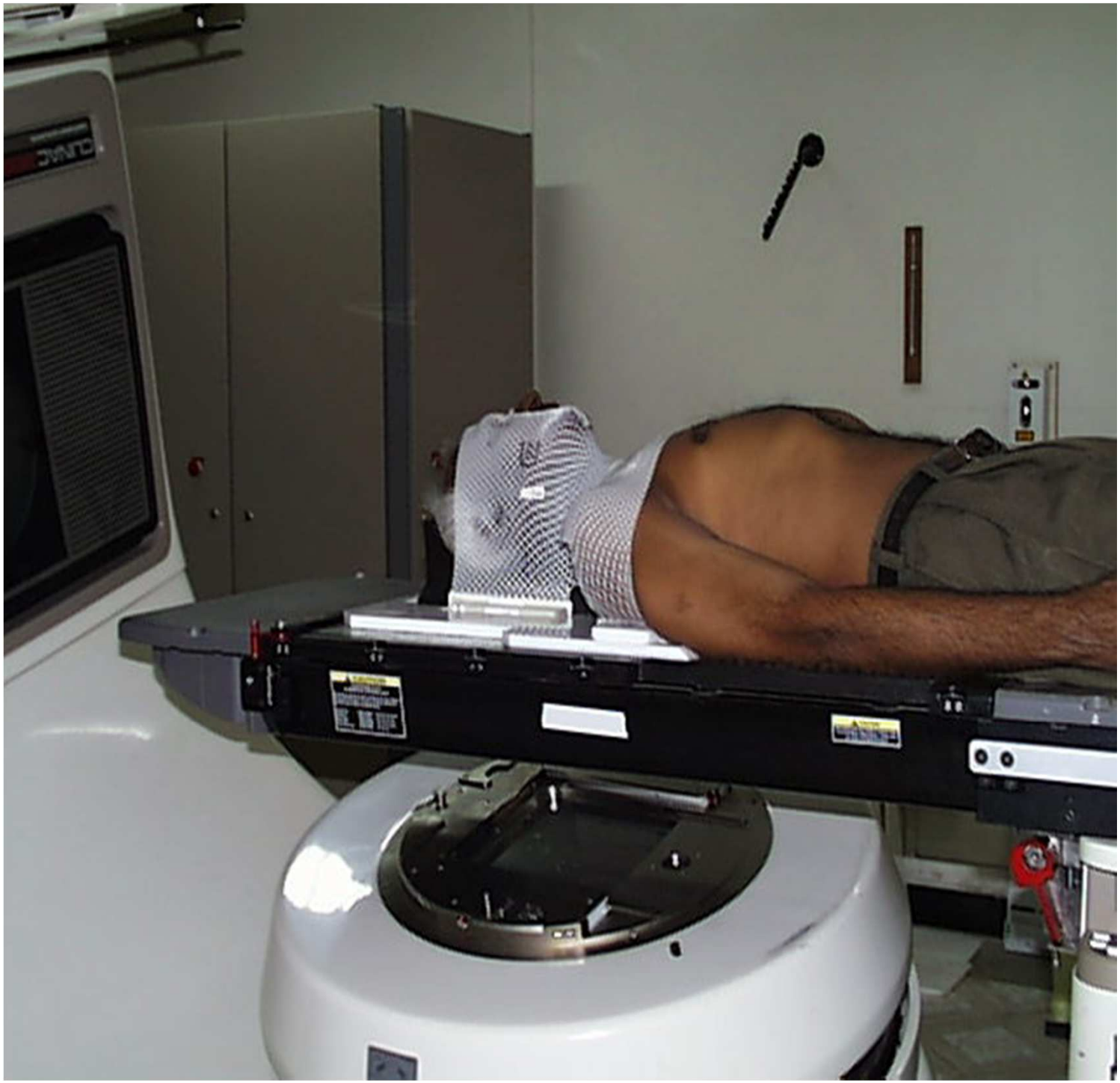
EBRT alone

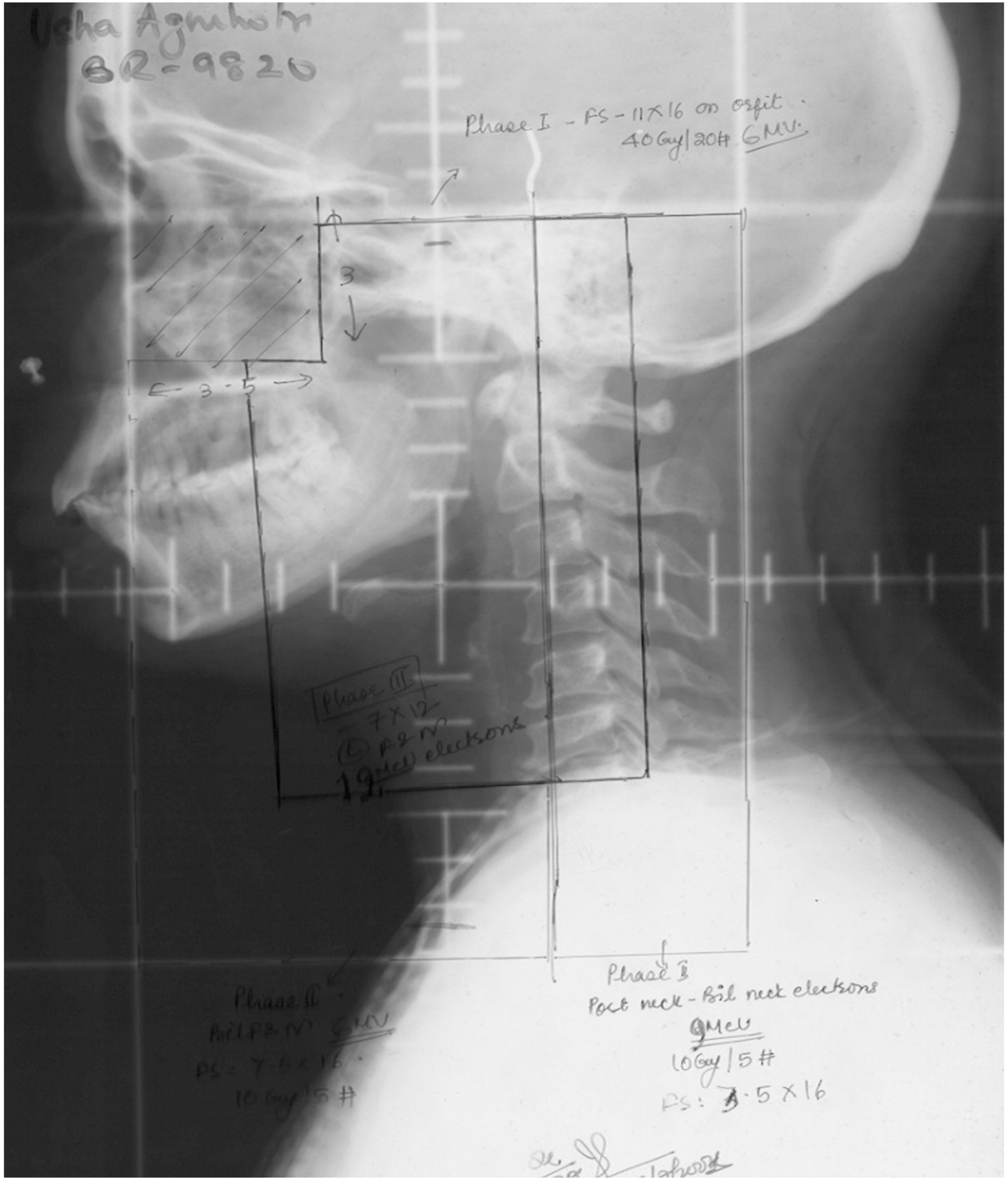
Radical Brachytherapy

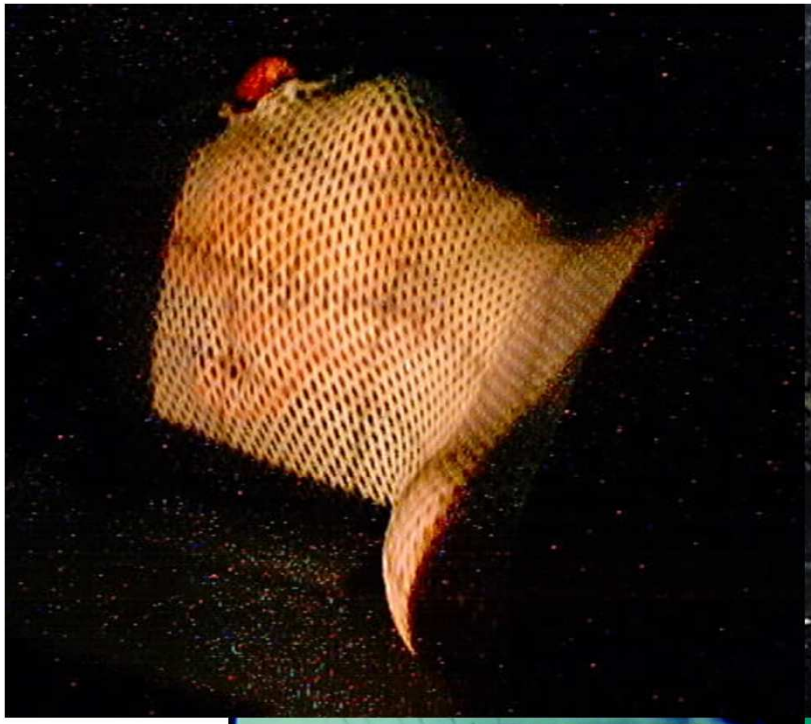
Radical Radiotherapy

Volume:

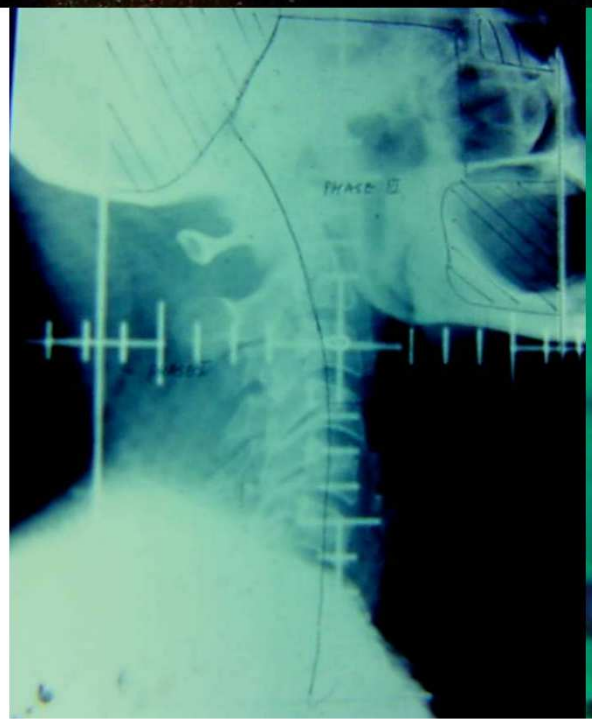


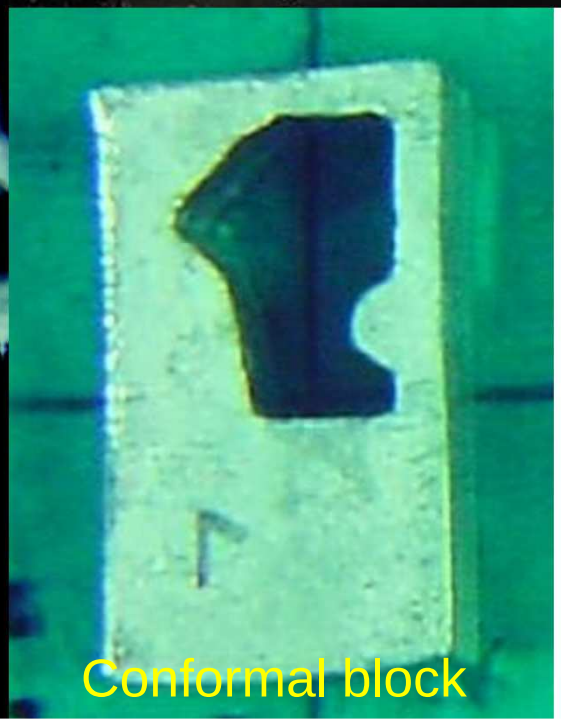



Usha Agnihotri
BR-9820
Phase I - FS - 11×16 on osfit.
40Gy/20# 6MV.
3
3.5
Phase III
7×12
(L) P&N
12MeV electrons
Phase II
Bil P&N 6MV
FS = 7.5×16
10 Gy/5#
Phase II
Post neck - Bil neck electrons
9MeV
10Gy/5#
FS: 3.5×16

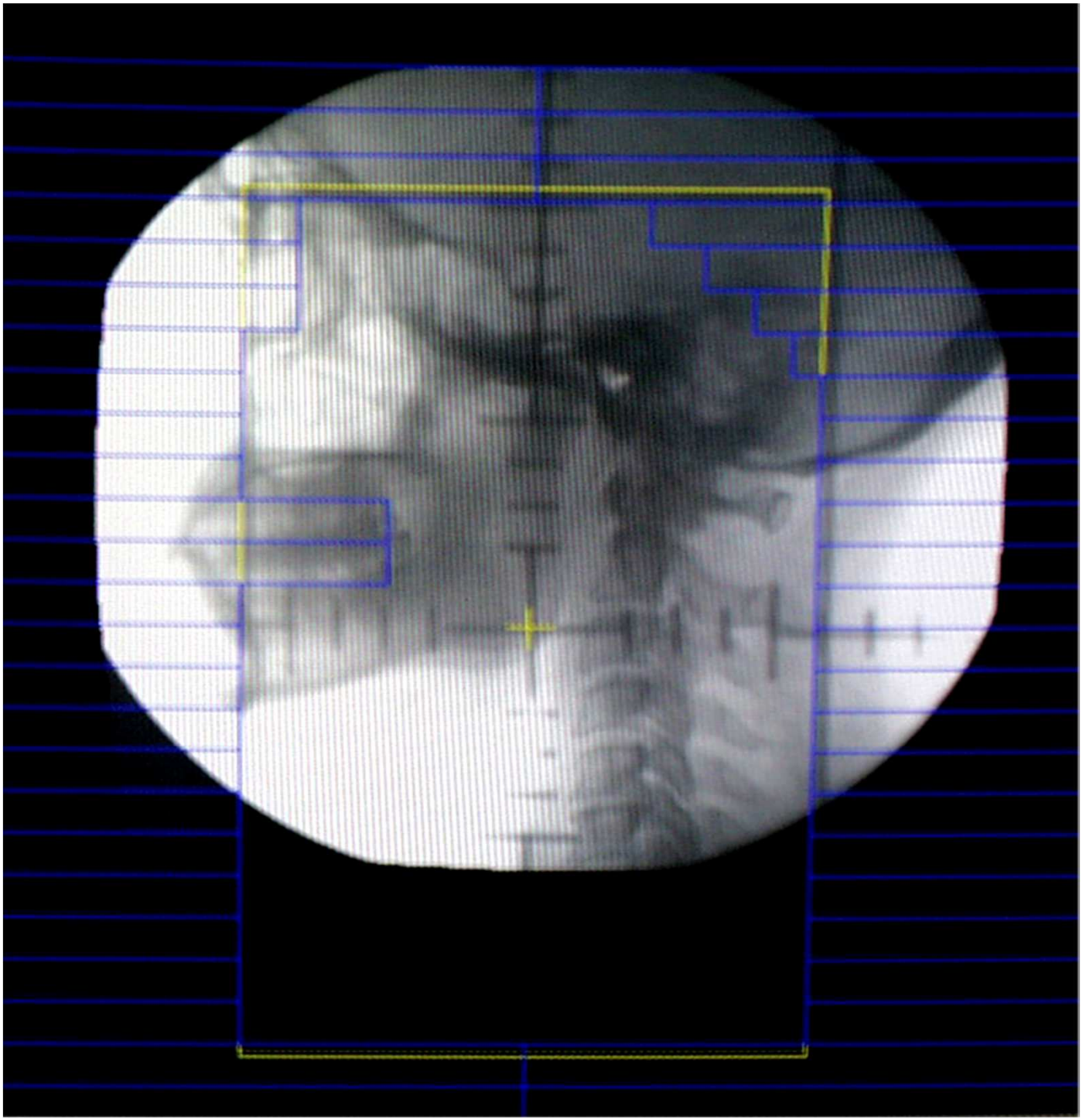


Tissue compensator

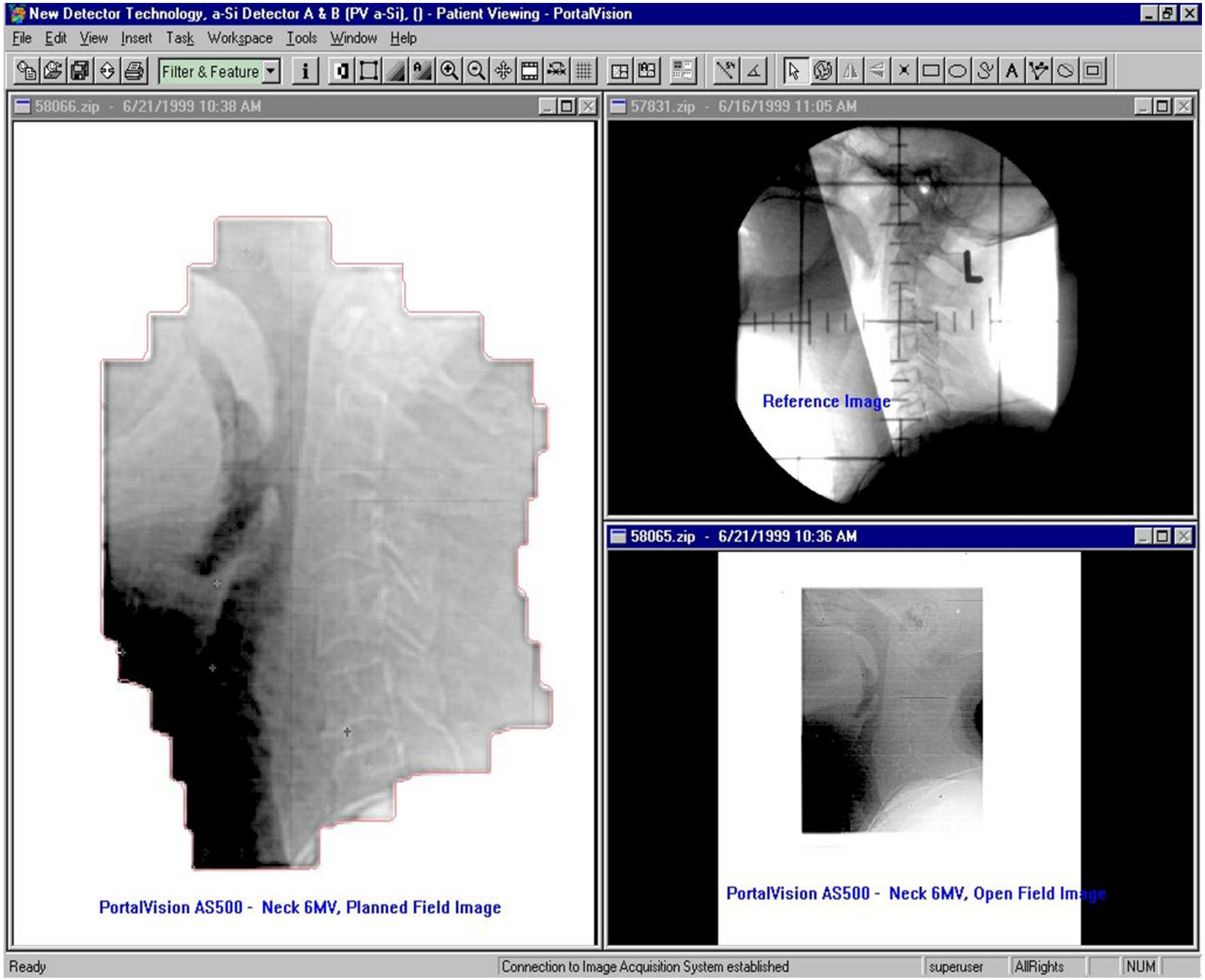


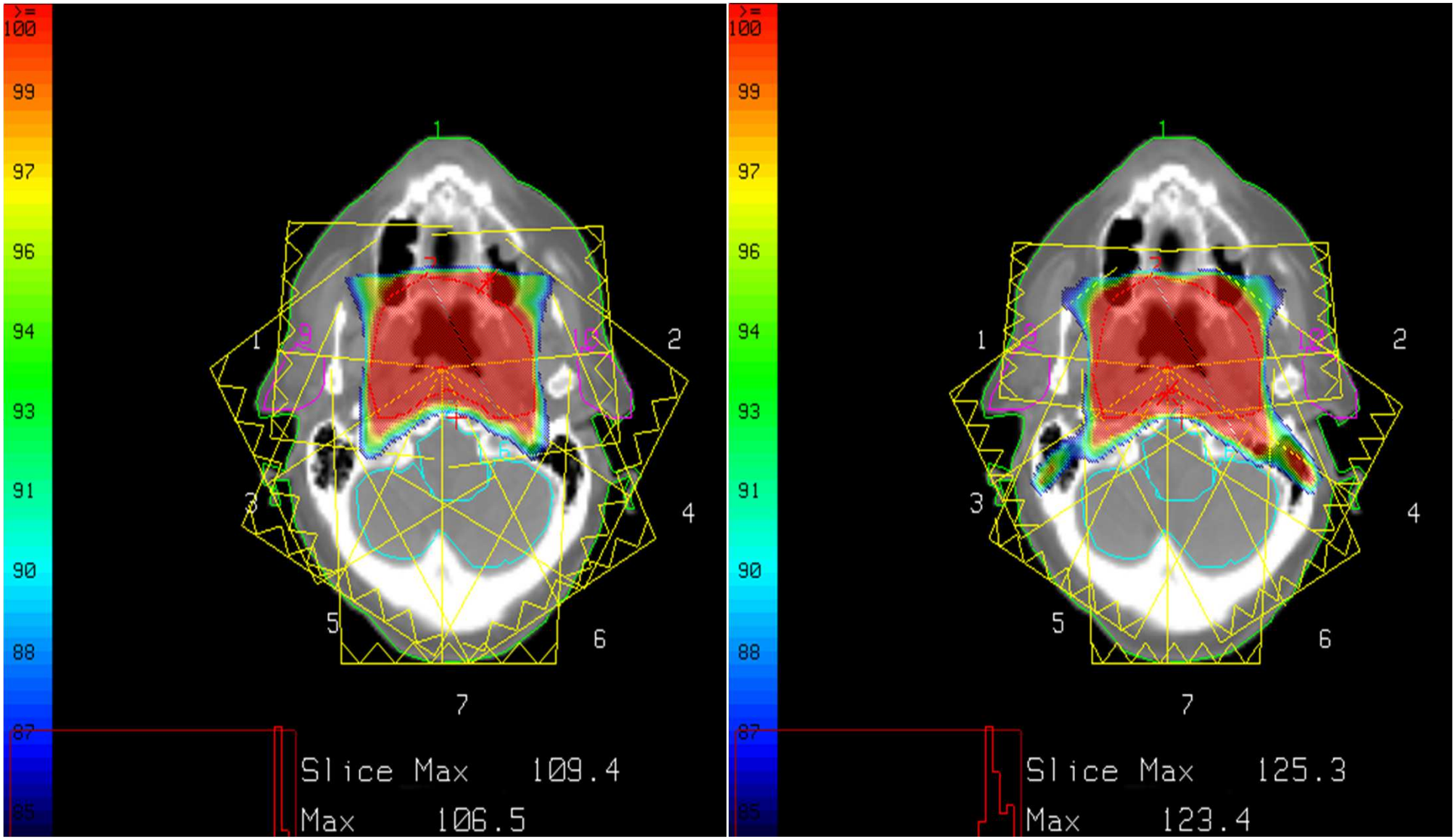


Conformal block



ELECTRONIC PORTAL IMAGING

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Slice Max 109.4
Max 106.5
>=
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4
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6
7
Slice Max 125.3
Max 123.4

Conventional fractionation

1.8 - 2 Gy/ fr
One fraction per day
5 days a week

Altered Fractionation Schedules

Biologic Rationale:

a) the fraction size is the dominant factor in determining late effects, and the overall time has little influence

b) by contrast, the fraction size and overall treatment time both determine the response of acutely responding tissues

Accelerated treatment

- approx. conventional total dose
- conventional fraction number
- overall time is approx. halved (since two fractions are given)
- Intent- to reduce repopulation in rapidly proliferating tumours.

Hyperfractionation

- to further separate the early and late effects
- overall treatment time 6-8 wks
- two fractions / per day
- number of fractions are doubled to 60-80
- dose per fraction - decreased
- Intent - further reduce late effects while achieving the same or better tumour control and the same or slightly increased early effects.

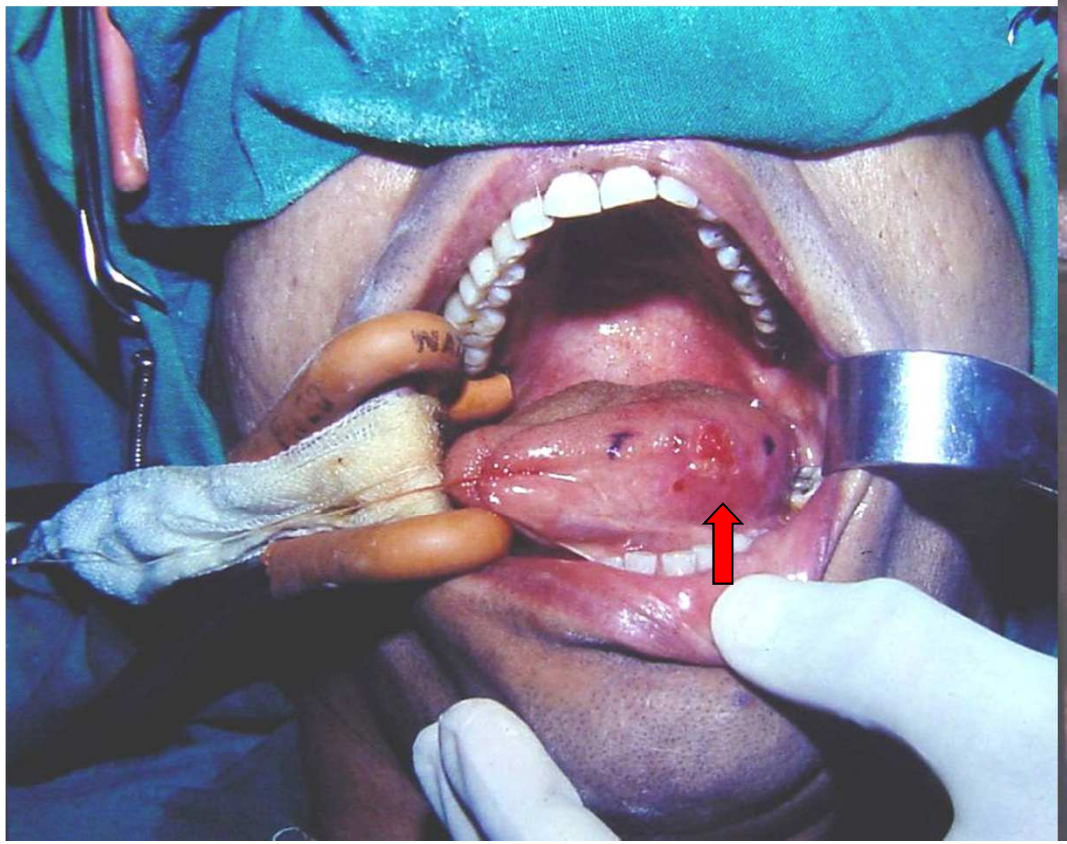
Altered Fractionation- In conclusion

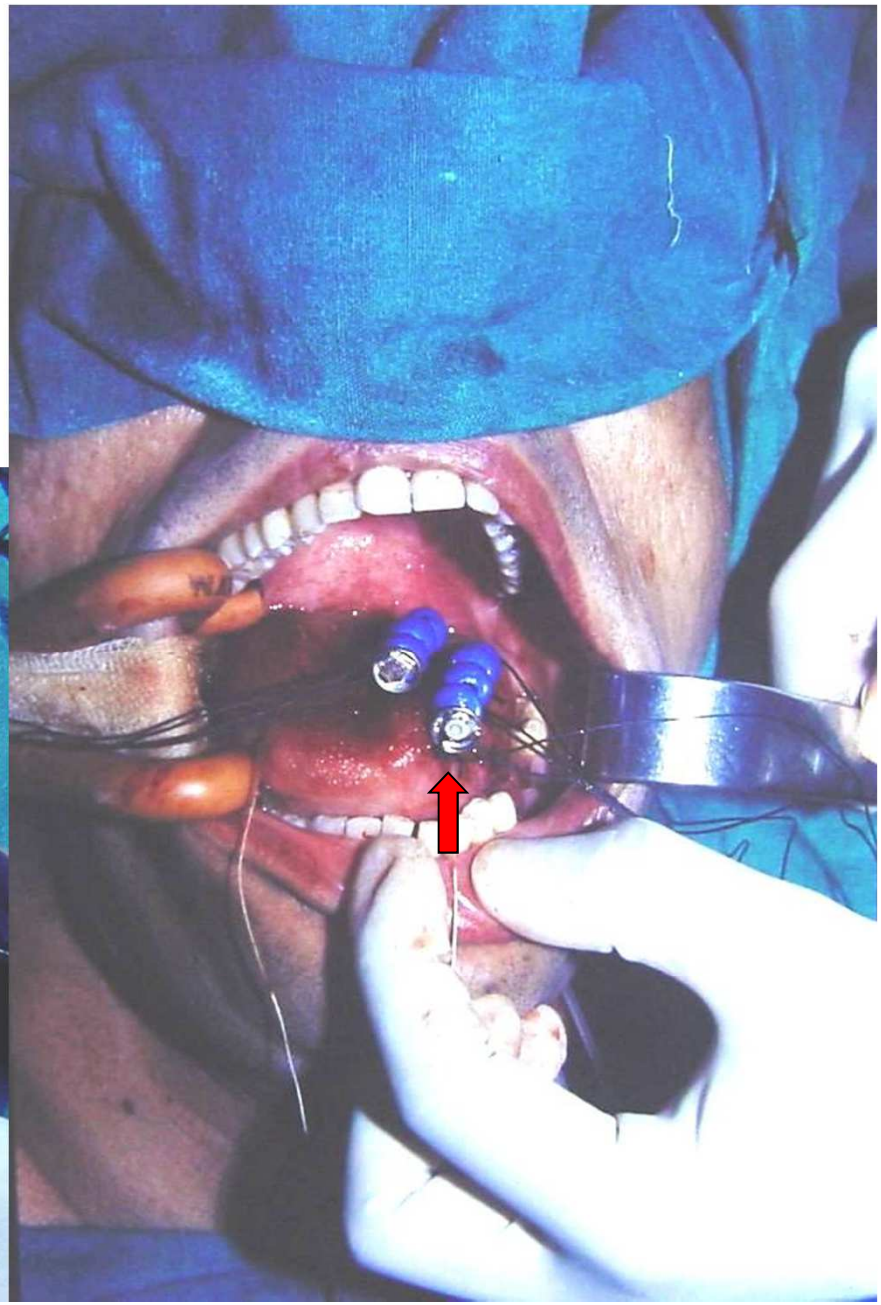
Modification of dose per fraction, total dose based on tumor kinetics in an attempt to increase therapeutic ratio

Criteria for brachytherapy

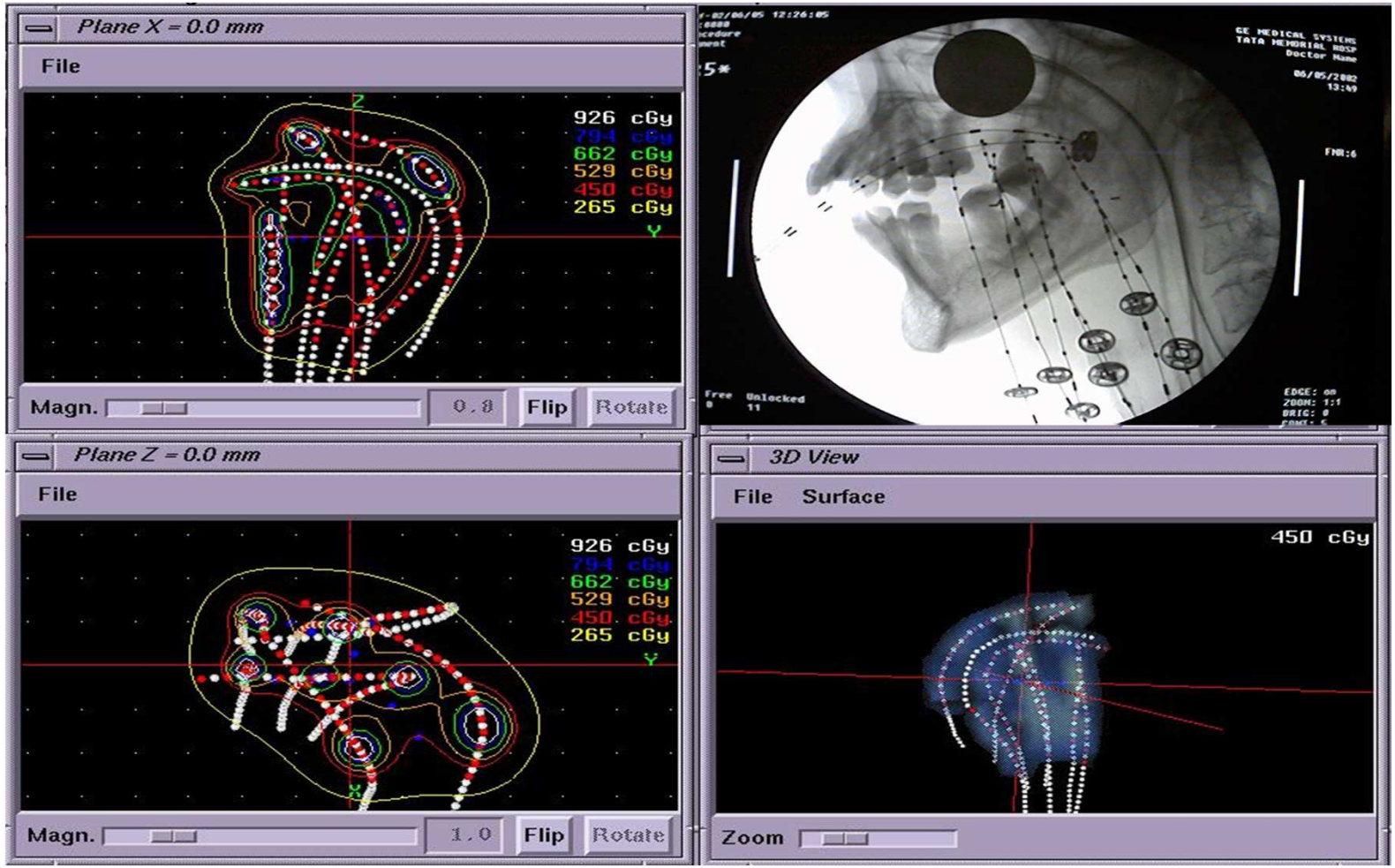
- Accessible
- <3 cm in size
- Away from bone
- No nodal disease

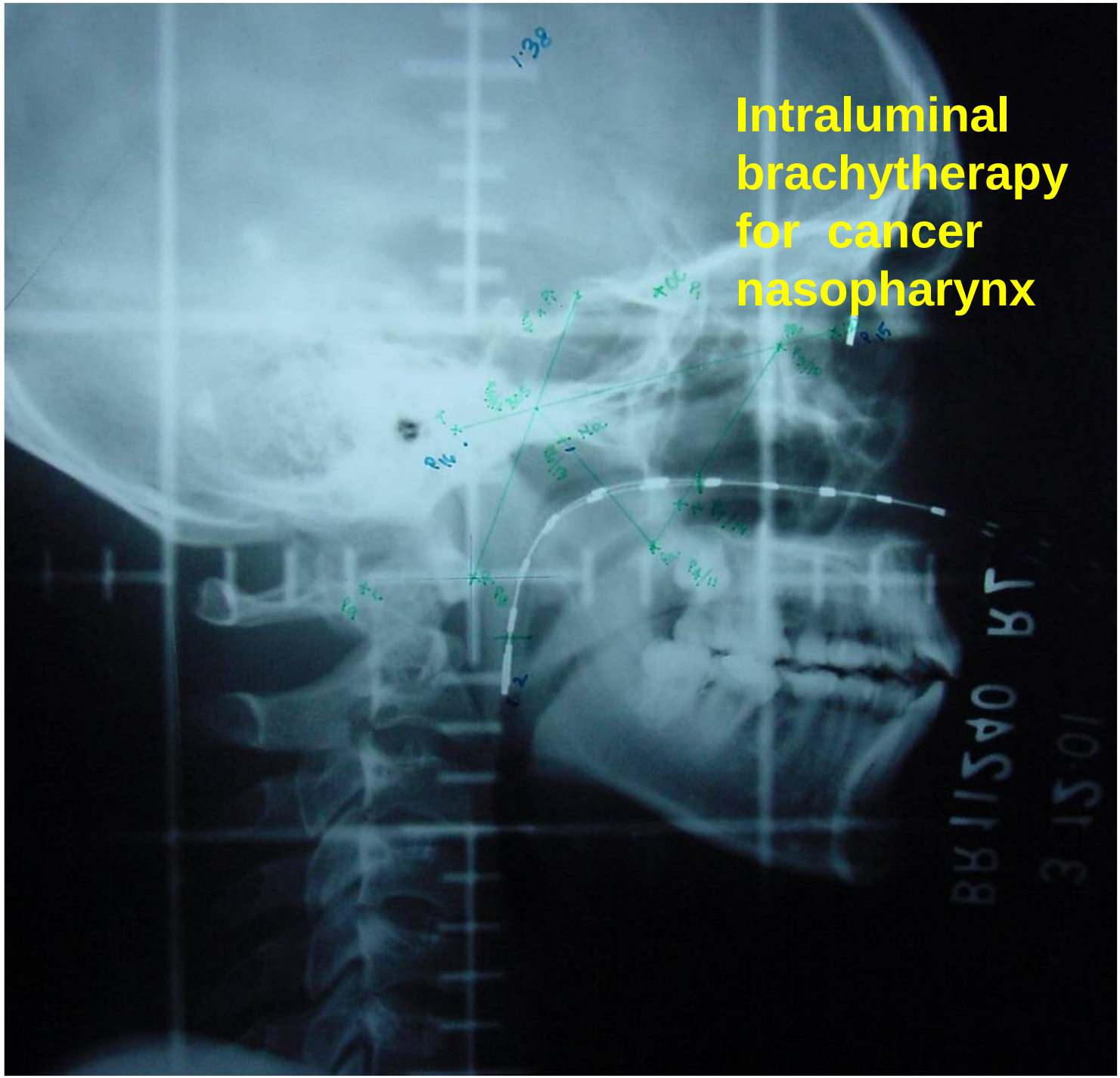
INTERSTITIAL BRACHYTHERAPY FOR CARCINOMA OF TONGUE





DISTRIBUTION OF TONGUE IMPLANT




Intraluminal
brachytherapy
for cancer
nasopharynx

Prophylaxis

Pre-treatment

- Dental prophylaxis:
  - Extraction
  - Scaling
- Application of fluoride gel

Adjuvant Radiotherapy

Indications

T3,T4 primary

High grade

Infiltration of soft tissues/ muscle/ bone

Perineural invasion

Lymphovascular emboli

Cut margin positive/ close

Thickness

Recurrent disease

Multiple nodes

Perinodal extension

Adjuvant Radiotherapy

Volume

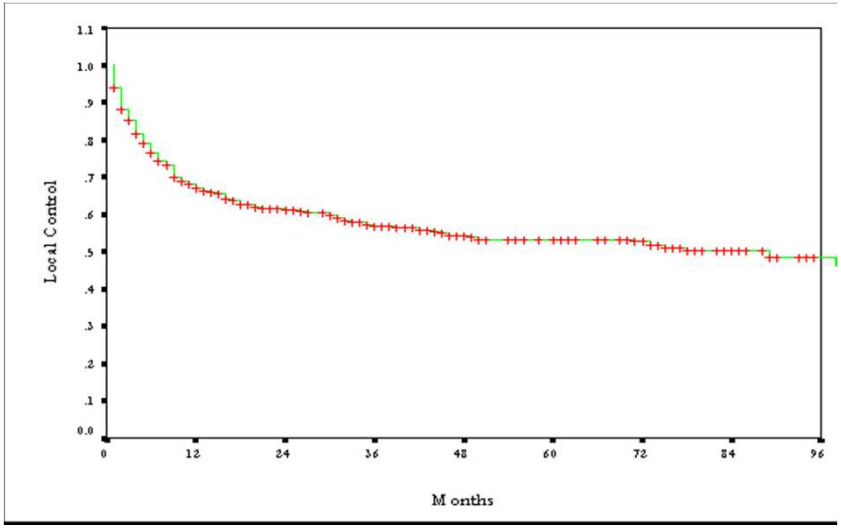
Primary + one station beyond involved nodes

Dose

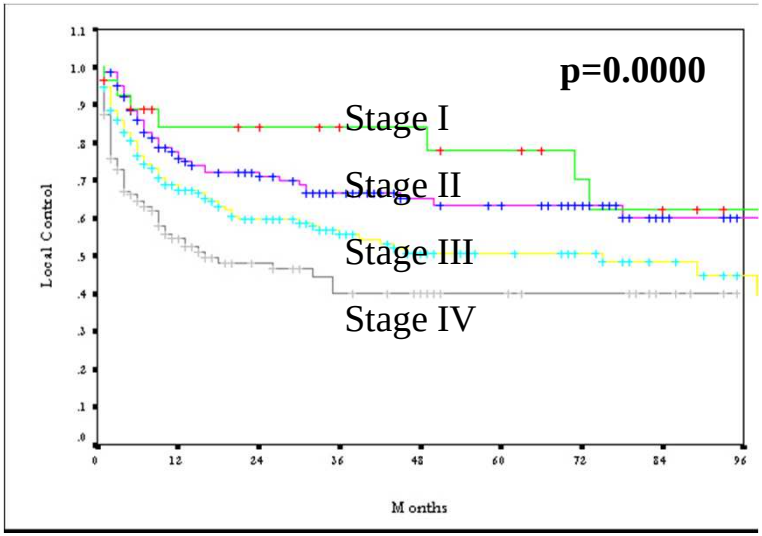
56 - 60 Gy/ 28 - 30 fr/ 5-6 weeks


2002
1 2
7 8 9
14 15 16
22 23
29 30

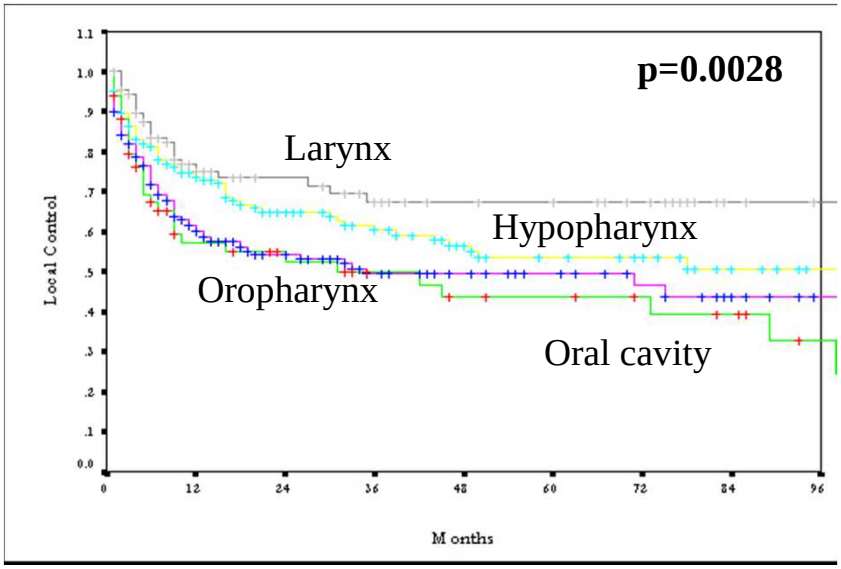
Radical RT (TMH): 568 PTS. *Clin Oncol 2006*



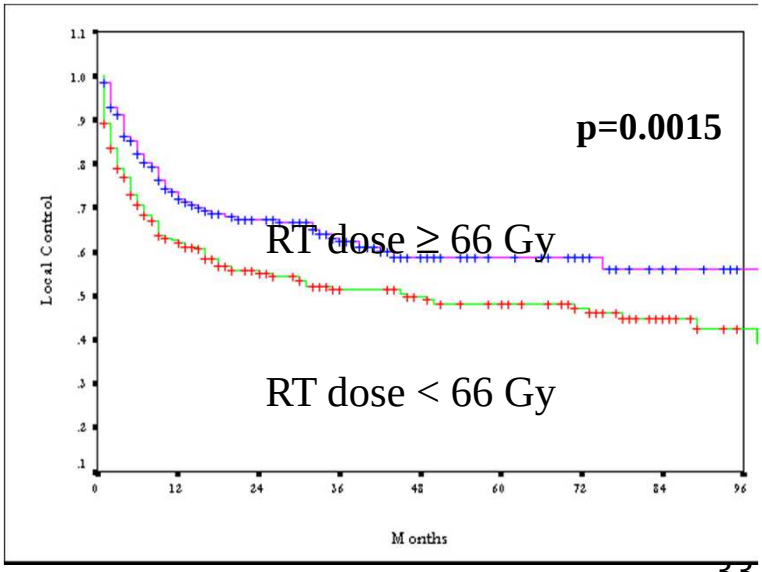
5-yr Local Control: 53%



Local Control vs stage

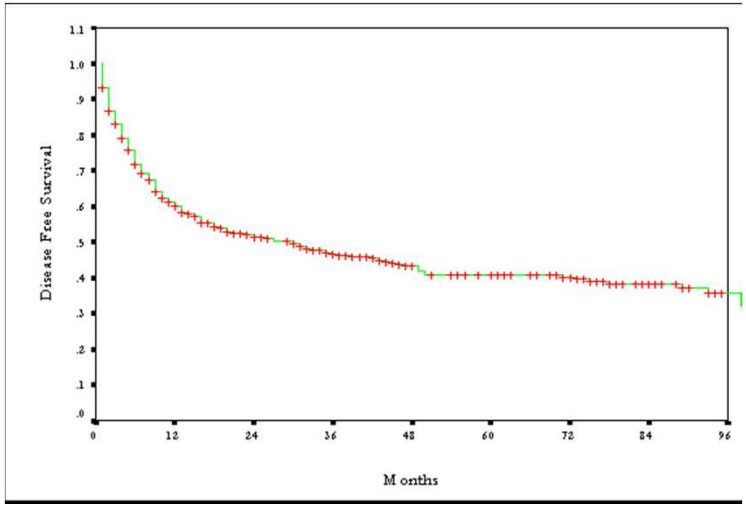


Local Control vs primary site

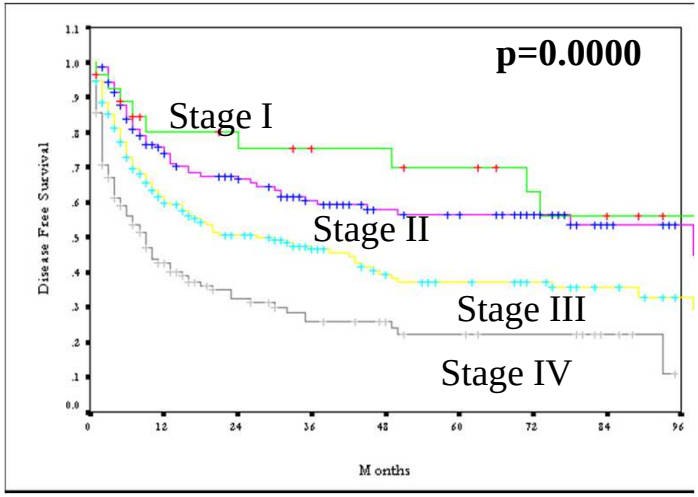


Local Control vs RT dose

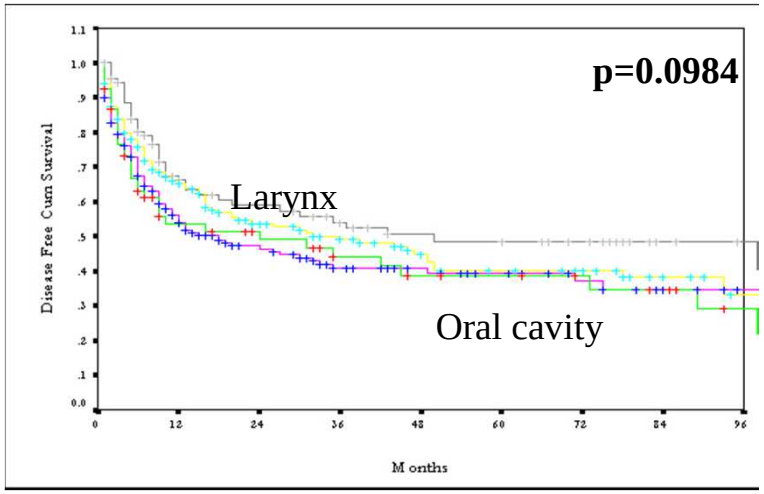
Radical RT (TMH): 568 PTS. *Clin Oncol 2006*



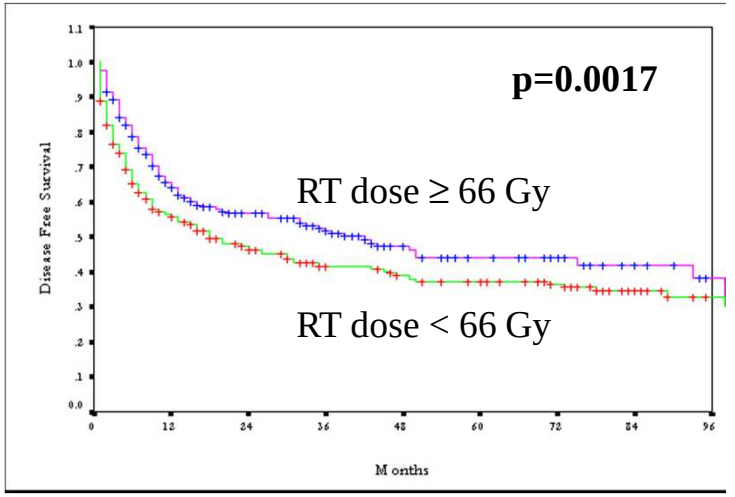
5-yr DFS: 41%



DFS vs stage



DFS vs primary site



DFS vs RT dose

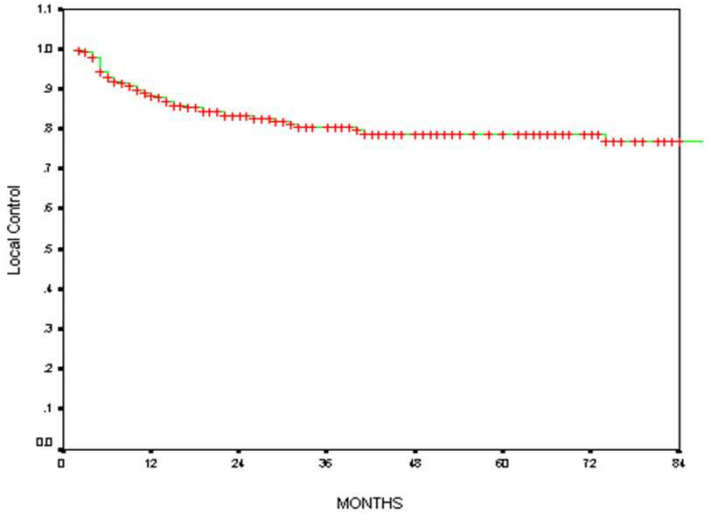
Post-operative Radiotherapy

Indications:

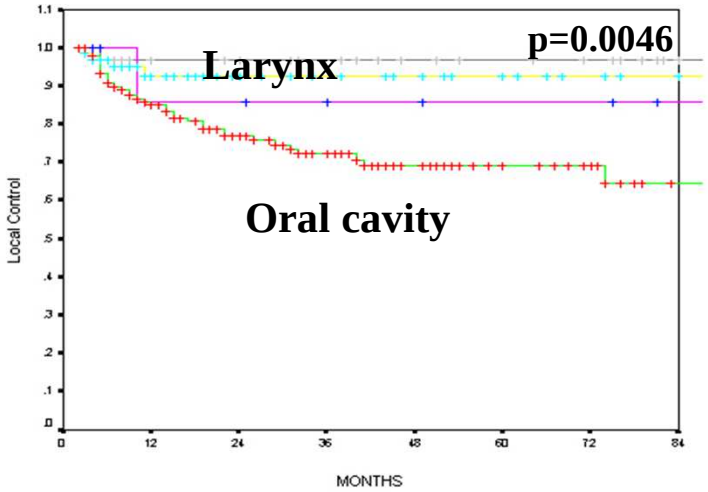
- T3/4 STAGE
- HIGH GR HISTOLOGY
- CUT MARGIN + OR CLOSE
- LVI/PNI

- NODE POSITIVE
- PNE

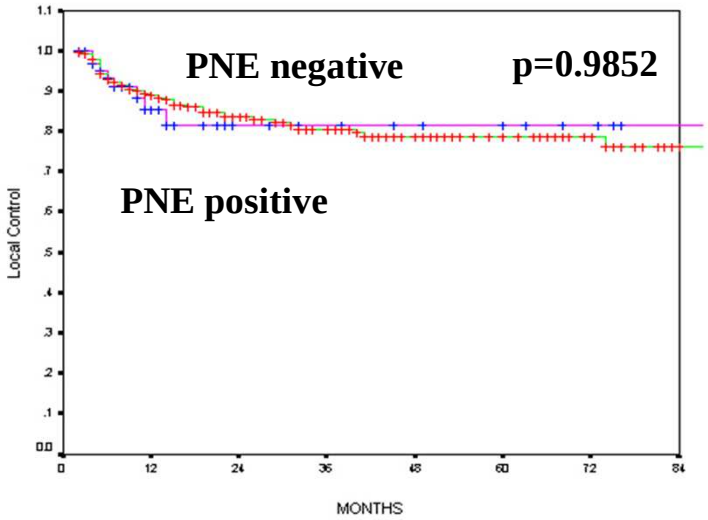
Post-op RT (TMH) 368 Pts.: *J. Surg Oncol 2005*



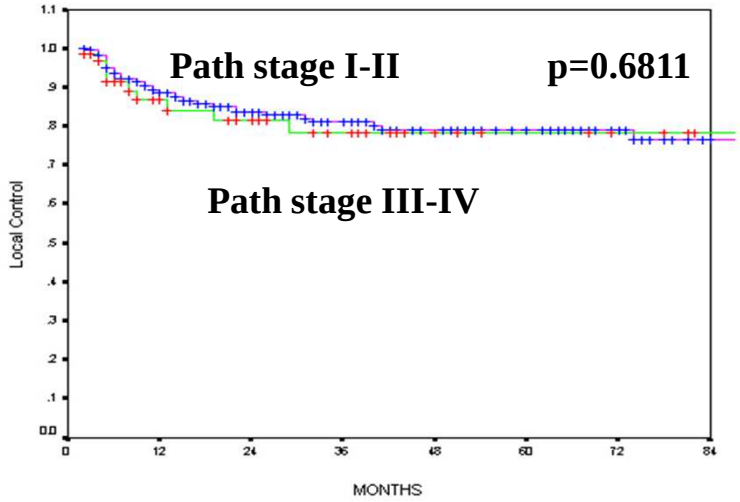
5-yr Local control: 79%



Local control vs Primary site

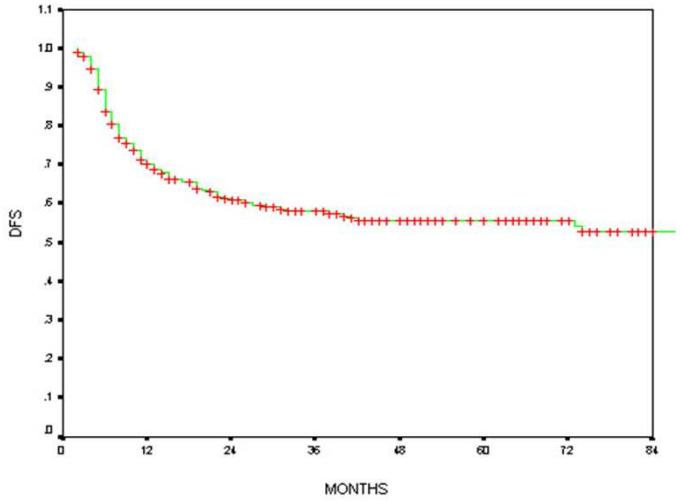


Local control vs PNE

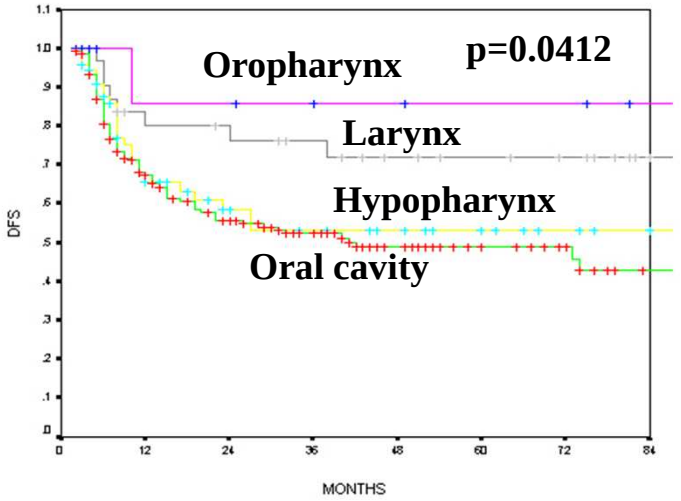


Local control vs stage

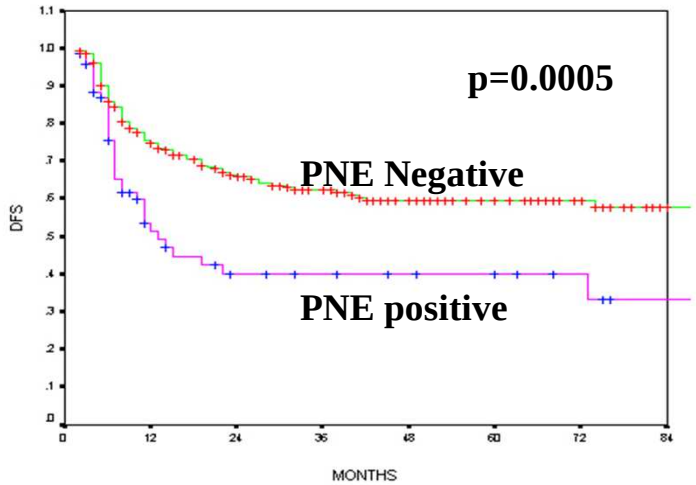
Post-op RT (TMH) 368 Pts. *J. Surg Oncol 2005*



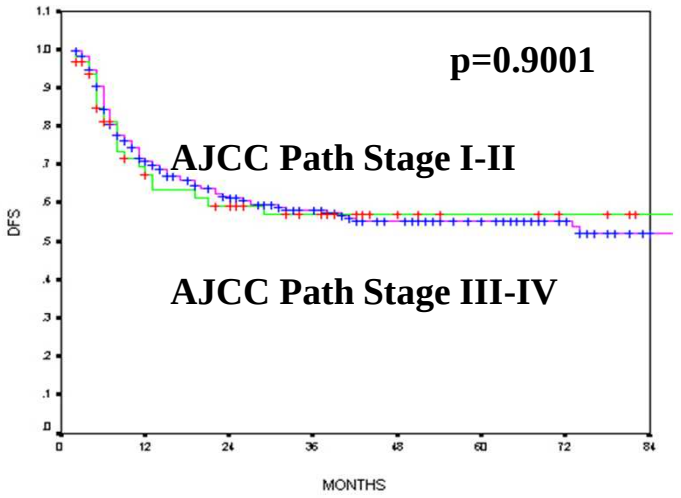
5-yr DFS: 56%



DFS vs primary site



DFS vs PNE



DFS vs Path stage

CONFORMAL RADIOTHERAPY

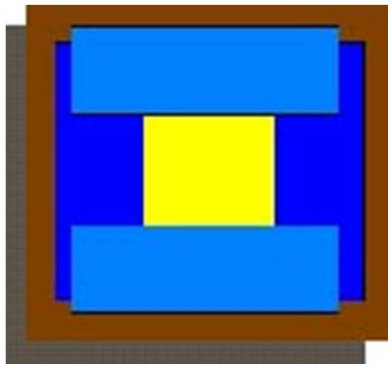
- **Enhanced conformation allows for greater dosages of radiation to reach the target volume (*conformal shaping*)**

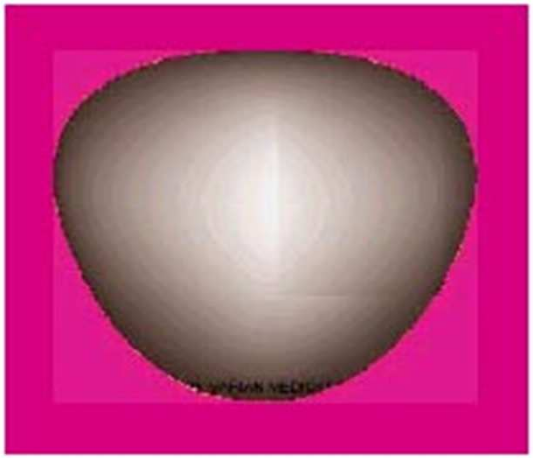
- **While minimizing the dose delivery to surrounding normal tissues (*conformal avoidance)***

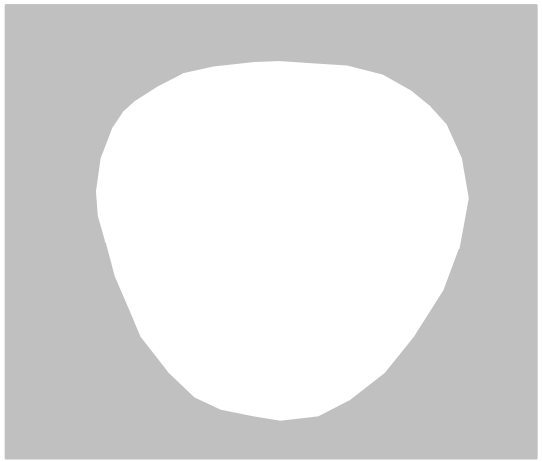
Improving Efficacy of Irradiation

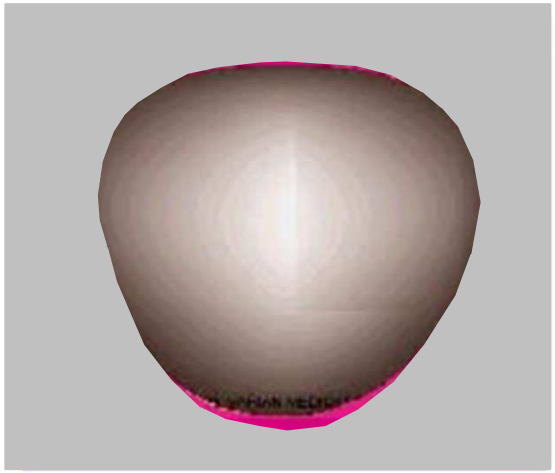
- **Physical Dose Escalation**
  - **Better target definition/delineation**
  - **Better radiation delivery**
- **Biological Dose Escalation**
  - **Altered Fractionation Schemes**
  - **Radiation and Chemotherapy**
  - **Selective Tumor Radiosensitization**
  - **Bio reductive drugs Tirapazamine**
  - **EGFR Inhibitors**

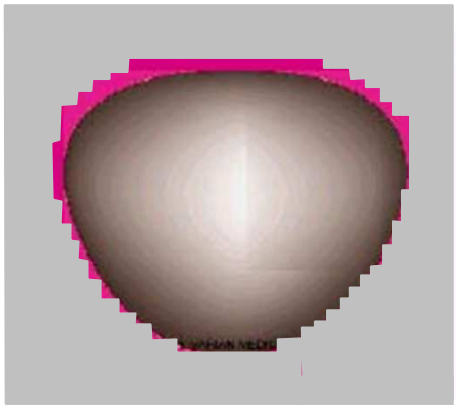
technology

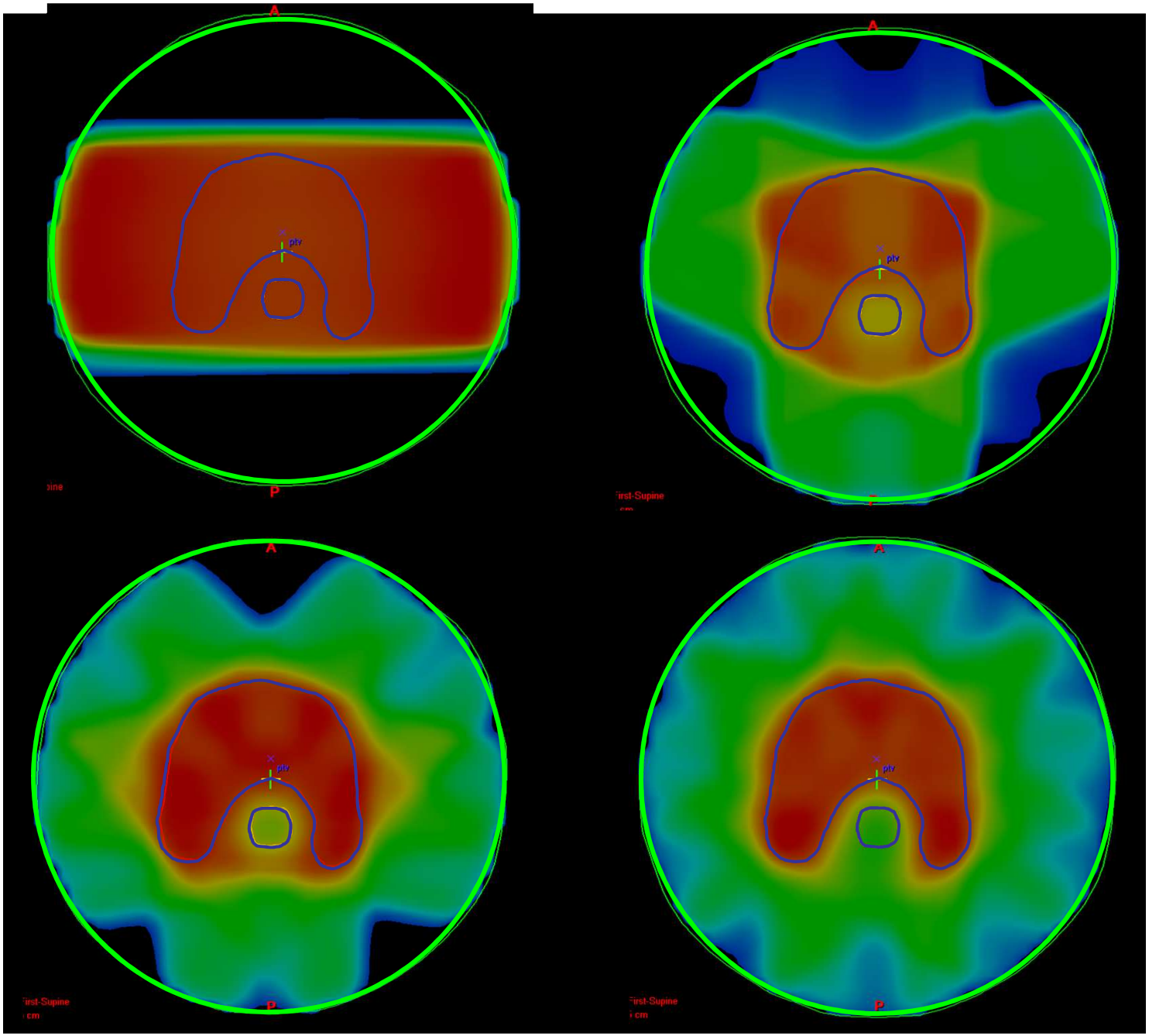








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META-ANALYSES OF CHEMORADIOTHERAPY

Investi-gators	No. of Trials Period	No. of pts.	Relative Risk of Death (RT / CT + RT)			Absolute Benefit	
			Neo	Con.	Overall	Conc.	Overall
Stell (1992)	28 (before 1991)	4292	1.09 (NS)	0.71 p=0.02	0.92 (NS)	7.0	2.8
Munro (1995)	54 (1963-1993)	7828	0.83 p=0.01	0.56 p<0.001	0.73 p<0.001	12.1	6.5
El Sayed (1996)	42 (1963-1993)	5079	0.95 (NS)	0.78 p<0.005	0.89 p<0.001	8.0	4.0
MACH NC (1998)	63 (1965-1993)	10741	0.95 (NS)	0.81 p<0.001	0.89 p<0.001	8.0	4.0
Browman (2001)	18 (1970-2000)	3192		0.83 p<0.0001		11	

Meta-analyses

- 6 Meta-analyses addressing the status of chemotherapy in HNC
- Only 1 is IPD based (MACH-NC)
- 5 favour the addition of chemotherapy
- Concomitant Platinum based chemotherapy appears most beneficial WHILE neo-adjuvant and adjuvant chemotherapy provide no advantage
- Concomitant chemoradiotherapy increases survival
- Morbidity not yet quantified

Head and Neck Intergroup Trial R91-11

- **Abstract ASCO 2002**
- **576 patients**
- **RT alone VS Three-weekly Platinum VS NACT (Platinum + 5FU)**
- **No Survival Difference =76% (5 yr)**
- **Larynx preserved in 66% of concurrent arm VS 58% in NACT arm VS 52% in RT arm**

Points to Ponder

- **Chemoradiotherapy and Altered fractionation (concomittant boost and hyperfractionation) may provide improvement in control and ?survival -**

- **Are they feasible?**
- **Which is better ?**
- **What is the optimum combination and sequencing?**

Factors

- Type of radiation
- Dose per fraction
- Time between fractions
- Total dose delivered
- Irradiated volume
- Anatomic structures exposed

Effects of Radiotherapy

- Skin
- Mucosa
- Salivary glands
- Spinal cord
- Teeth

Palliative radiotherapy

Symptoms:

Bleeding

Fungation

Pain

Volume:

Gross disease with min margins

Dose:

8Gy/1fr or 20Gy/5 fr or 40Gy/16 fr