# Brachytherapy in Oropharynx & Nasopharynx- Challenges

Dr Siddanna R Palled

Professor

Dept of Radiation Oncology

Kidwai Memorial Institute of Oncology

# Incidence of Cancer in India

- Systemic collection of all data from 28PBCRs and 58HBCRs
- 2012-2016 and projected for 2020.
- **N=667,666**
- Projeted number of patients with cancer in 2020- **1,392,197**.

  **M-679,421**

  **F-712,758.**
- There is increasing trend in all sites.
- NCD deaths in India -**63%.**
- Cancer one of the leading cause -**9%**

Mathur et al 2020

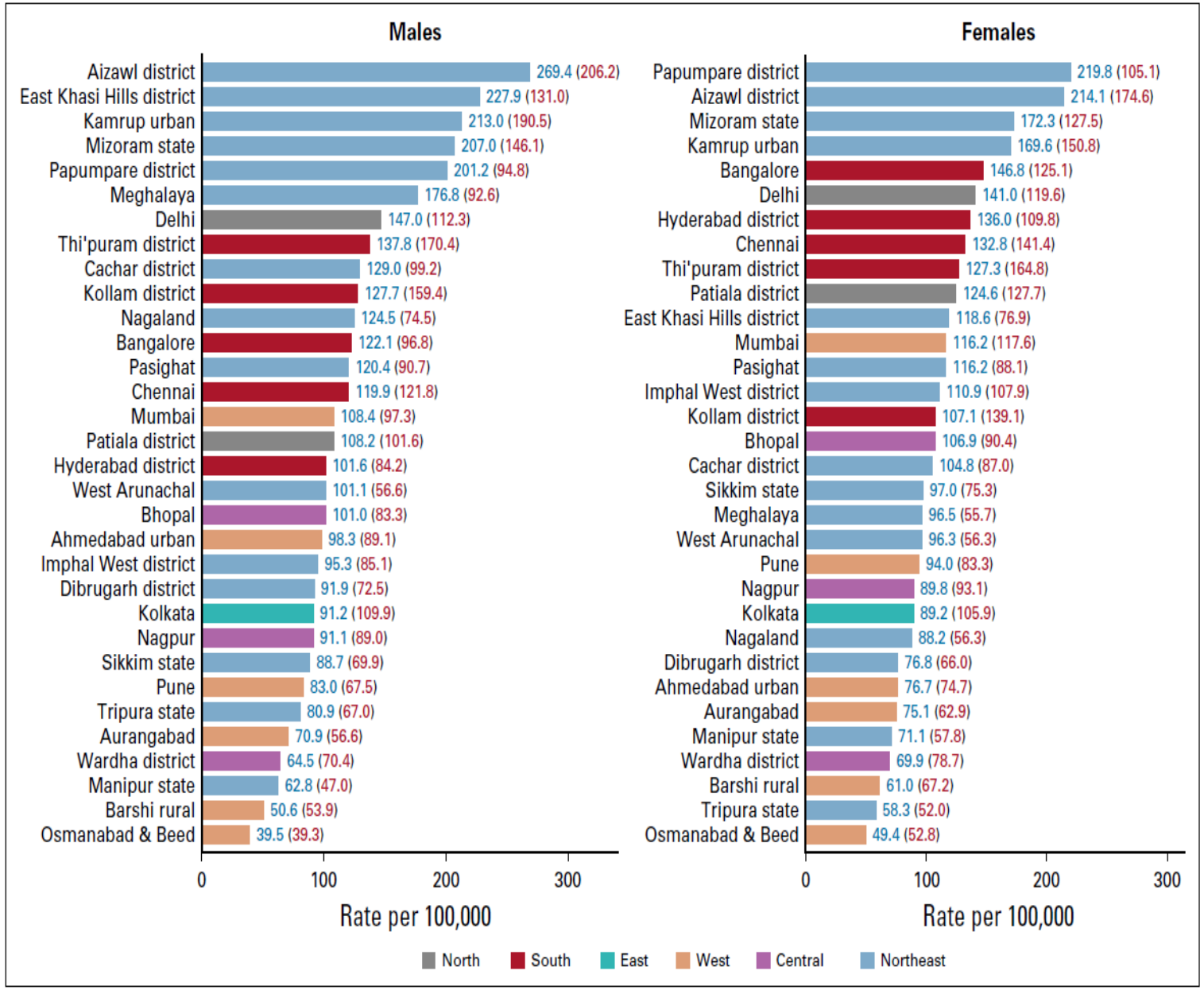
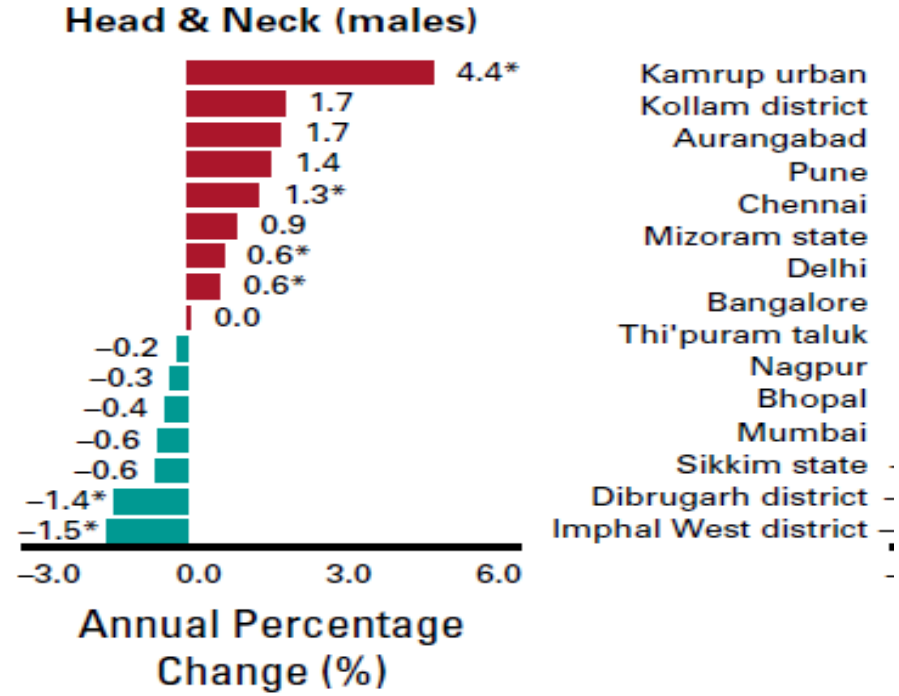



FIG 1. Comparison of all cancer sites' age-adjusted incidence rates (AARs) of all population-based cancer registries, 2012-2016 (International Statistical Classification of Diseases and Related Health Problems, 10th revision: C00-C97). AARs are in blue and crude rates are given in parentheses in red. Thi'puram district, Thiruvananthapuram district.



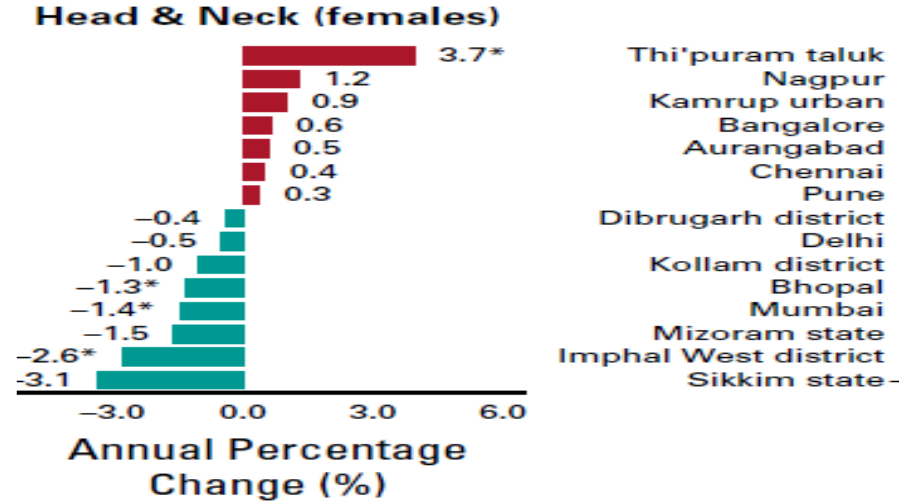
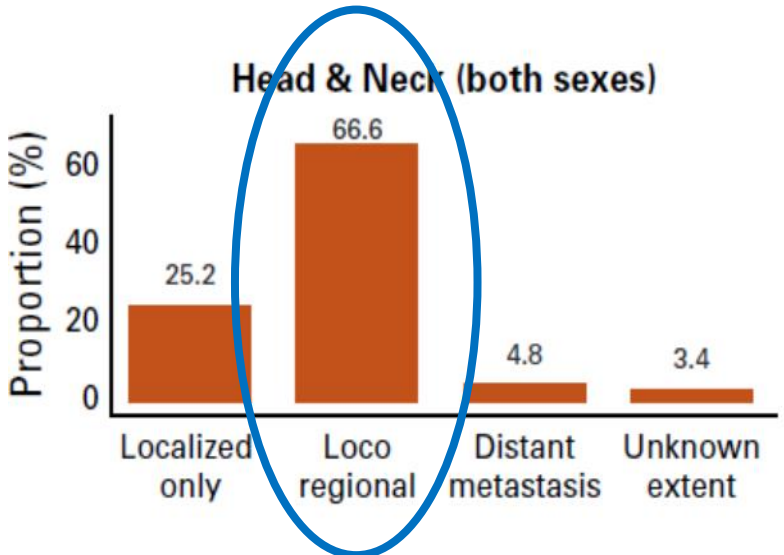



**TABLE 2.** Projected Incidence of Cancer Statistics in India, 2020

| Site | Male | | | Female | | | Both Sexes | | |
|---|---|---|---|---|---|---|---|---|---|
| | Patients | CR | Cum Risk | Patients | CR | Cum Risk | Patients | CR | Cum Risk |
| All sites | 679,421 | 94.1 | 1 in 9 | 712,758 | 103.6 | 1 in 9 | 1,392,179 | 98.7 | 1 in 9 |
| Oral cavity and pharynx | 139,018 | 19.2 | 1 in 41 | 49,951 | 7.3 | 1 in 112 | 188,969 | 13.4 | 1 in 60 |
| Tongue | 39,902 | 5.5 | 1 in 147 | 13,870 | 2.0 | 1 in 401 | 53,772 | 3.8 | 1 in 215 |
| Mouth | 57,380 | 7.9 | 1 in 103 | 22,483 | 3.3 | 1 in 241 | 79,863 | 5.7 | 1 in 144 |
| Pharynx | 3,029 | 0.4 | 1 in 1,793 | 1,102 | 0.2 | 1 in 5,475 | 4,131 | 0.3 | 1 in 2,701 |
| Other oral cavity | 38,707 | 5.4 | 1 in 137 | 12,496 | 1.8 | 1 in 476 | 51,203 | 3.6 | 1 in 213 |




Mathur et al 2020

# Head and Neck Cancer Management

Aim of the treatment

- Aim: Loco regional control with organ and function preservation.
- Stage I &II: Single modality Surgery or RT
- Stage III & IV: Combined modality Sx+ RT mainly and in select group CT +RT
- Selection of single modality: Which gives highest cure rates.
- With Organ, function and cosmesis leading-→ Good QOL

Brachytherapy: GEC-ESTRO, ABS , IBS Guidelines available in-general, for India ? **No Randomized Controlled trails**

Available Indian guidelines for the management of HNC are not updated regularly.

# Indications of Brachytherapy

- Radical In early stage.
- Boost in Locally advanced
- Adjuvant Post operatively (Intr-op, Periop)
- Recurrent Setting
- Reirradiation

## Why brachy:

Mainly to achieve good LRC by dose escalation with reduced toxicities by Step dose gradient.

# Types of Head and Neck Brachytherapy

- Mainly Interstitial
- Surface Mould and
- Intracavitary.

Interstitial:  Temporary or permanent .

**Successful brachytherapy requires meticulous placement of radioactive sources (dwell positions) in the planned tumor volume**

# Head and Neck treatment challenges: Per se brachytherapy challenges

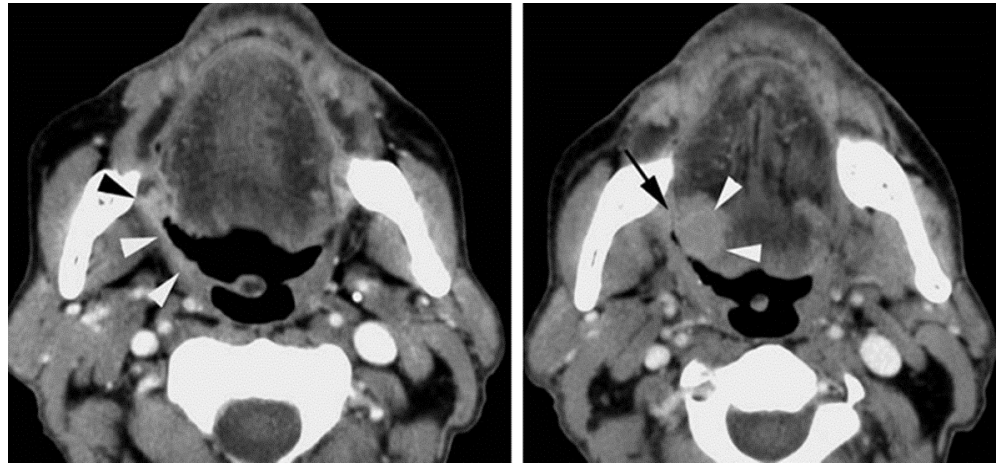
## Patient-related factors:

which affect overall prognosis and influence the treatment decisions.

These factors include:

- the age of the patient,
- performance status,
- nutritional status, Swallowing status
- associated comorbidities,
- active smoking,
- HPV-associated oropharyngeal cancers, and
- tumor programmed death-ligand 1 expression status, which is a predictive marker for response to anti-programmed cell death protein 1 therapy

# Head and Neck treatment challenges……..



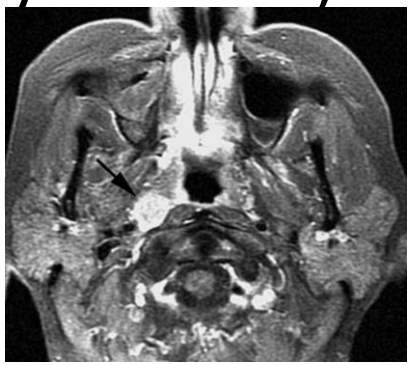
## Tumour factors:

Anatomical situation: Oropharnyx , Nasopharynx,

Critical structure proximity-→ dose escalation not possible.

Contour inhomogeneity, Bone, air , soft tissue.—Dose inhomogenity

- Stage: Early vs Advanced, Single modality vs Multi modality (brachy as Boost)
- Histology: Poorly differentiated.
- Adaptive treatment : depending on the response to initial treatme
- Tumour volume assessment: imaging CT, MRI, PET-CT.
- HPV-RTOG0522 trial conducted in United States of America -HPV-positive rate of 73%, Vs Indian 7.4–10.5% of total oropharyngeal carcinoma.



# Facility at treating Center: Major challenge

- Cost Effectiveness In comparison with EBRT with photon or Proton.
- HDR machine with source replacement regularly- cost is major factor
- Ir-192 source or Co-60 source.
- LDR Sources.
- CT simulator dedicated or from radiology department.
- Applicators: Needles single or multi use,
- Catheters single use, single leader or double leader. Multiple vendors , Machine compatibility.
- Inpatient facility
- OT facility: Minor OT,  supported by Major OT

# Cost of treatment for head and neck cancer in India

- A total of INR 40,993,017 (USD 0.67 million) was spent on radiotherapy care for treating HNC during 1 year.

(Salaries (42.6%) equipment/furniture (29%), space rent (20.7%), overheads and consumables (7.7%).

In terms of package rates: Cobalt radiotherapy -cheapest (INR 38,714, USD 634),

IMRT- most expensive (INR 192,914, USD 3161).

For Brachytherapy it varies from Public sector to Private sector.

**Peter Levandag et al: Costs for cancer in the nasopharynx**

14,528 Euros (US$16,509) /brachytherapy to

15,316 Euros (US$17,405) /stereotactic radiotherapy,

The treatment cost for other head and neck sites-21,858 Euros (US$24,126).

**DFS -48% to 74% ( p 0.002), OS- 35% to 72% ( p 0.005).**

# Expertise:

- Good Brachytherapy exposure
- Number of brachytherapy procedure carried out every year.
- **Training** of Radiation Oncologist, Physicist and Rad Technologist is a must
- Confidence of covering CTV for oncologist, dose distribution for Physicist

Dose Delivery for technologist.

## No replacement for bad implant geometry

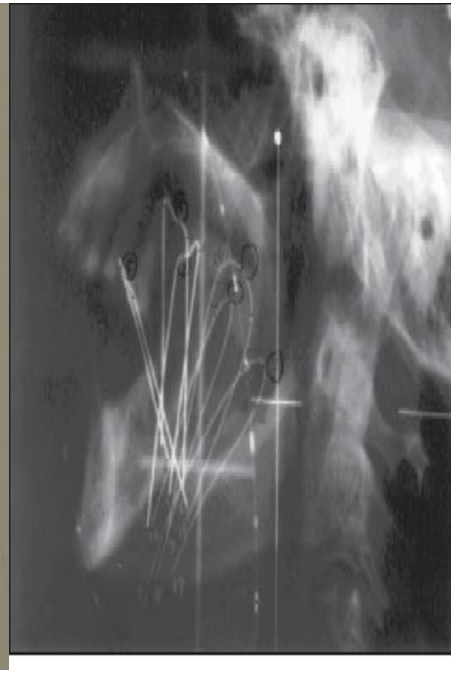
- Supporting faculty: Head and Neck Surgeon, Anesthetist and Dentist
- Supporting Staff good nursing care-critical to ensure avoidance of wound complications, and for patient education with regard to self-care. rehabilitation care

# Procedural challenges:

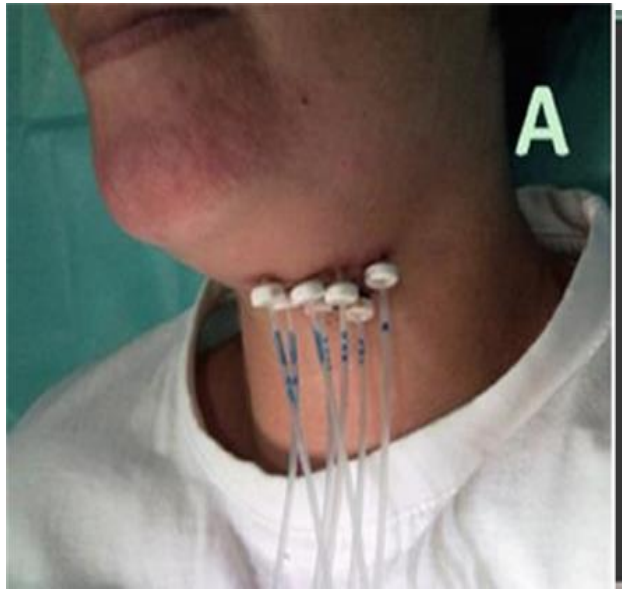
- Major worry is bleeding, more of blind insertion of needles with palpation
- Proper selection of needles and insertion into the target volume with maintaining parallelism. Single or multi planar volume implant.

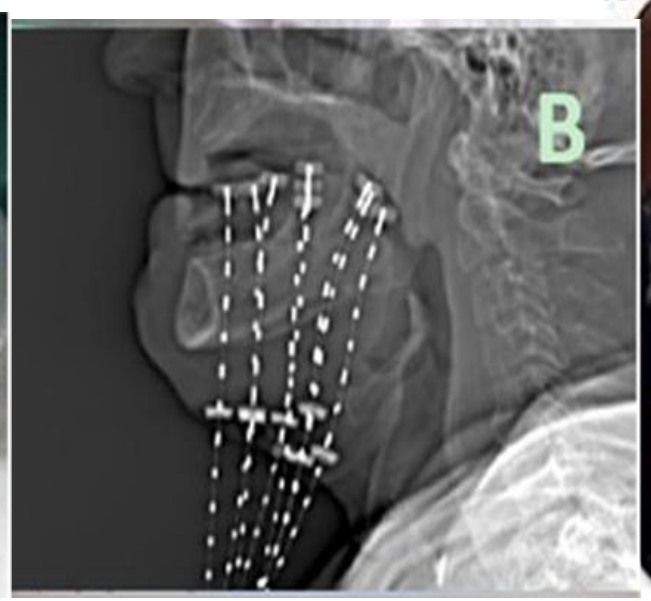
Types:

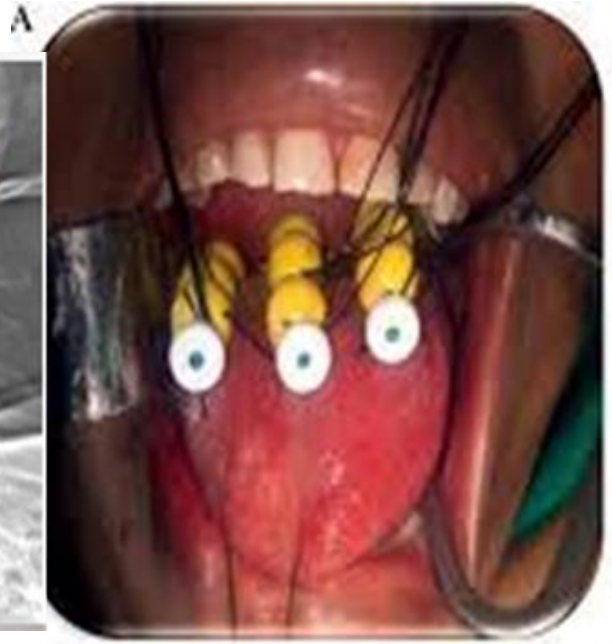
- Rigid Pierquin and Chassagne Guide-Gutter or Hairpin Technique
- Flexible:Plastic Tube Technique of Henschke,
- Through-and-Through Technique
- Loop Technique
- Sealed End Technique
- Hypodermic Needle Technique of Pierquin
- Thread Technique
- Direct Implantation Method.



- Replacement of needle with catheters –single leader with single button or double button or double leader for surface dose.
- Surface dose coverage.
- Numbering the catheters with flags and securing them with inner solid guide.
- In the OT: Check for any catheter kink or narrow lumen- replace them then and there only



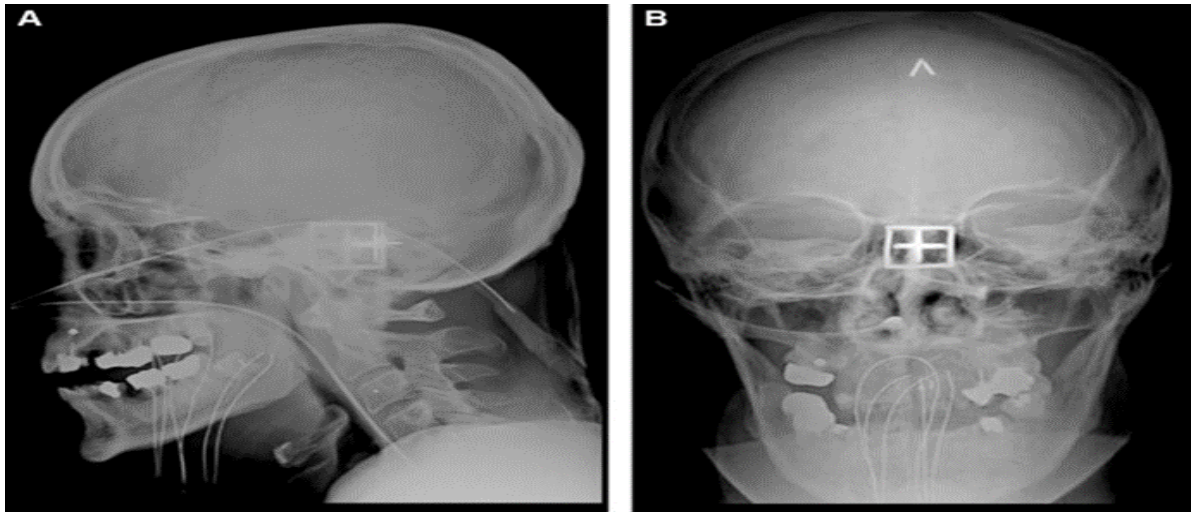

In the wards:

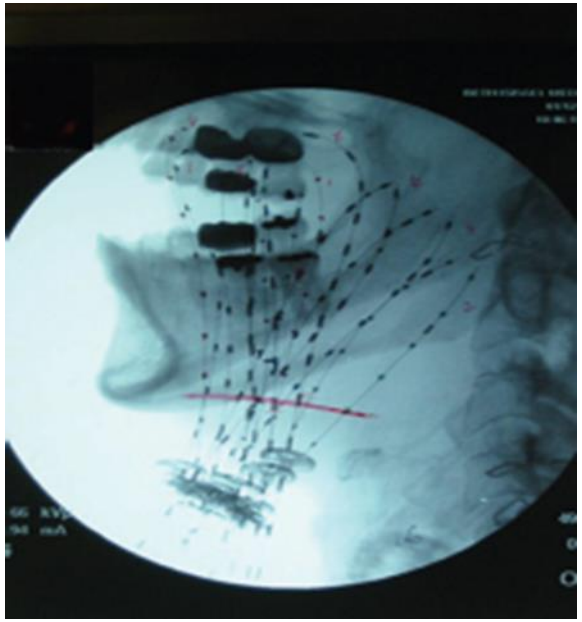
- Patient monitoring Round the clock
- Nutritional care: NGT or Peg tube
- Secure Airway: Elective tracheostomy.
- Antibiotic coverage
- Aseptic precautions in OT, wards and treatment console.

- Completion Brachytherapy: removal of the catheters should be done with the coordination of the head and neck surgical team.
- must have intravenous access. Suction, dressing materials, and adequate analgesics are also needed.
- Arterial hemorrhage: bidigital compression
- Care after discharge:

# Physics Challenges……

- TPS is one of the Major challenges
- Various vendors: Varian, Elekta, Bebig- Which to choose
- Planning :  2D- orthogonal X-ray / 3D-CT based.
- Training of Physicists
- Catheter reconstruction: difficult in multiplane Catheter recognition and numbering (with dummy or without).
- Dose Prescription: Different dose/fraction prescriptions.



- Optimization : BDR based or Inverse volume based.
- CTV Volume coverage:
- LDR brachytherapy, variations in the activity, number of 192Ir sources, and loading duration will allow for optimization of the implant dosimetry.
- For HDR brachytherapy, optimization is similarly achieved through variations in the dwell time and position of the high-activity 192Ir source, which is fixed to the end of a computer-controlled sliding guidewire.
- It is important to note that even the best optimization cannot overcome poor implant geometry.
- OAR constraints : Mandible(ORN), DARS, Skin dose (STN)

# LDR, HDR, PDR

Historically, LDR brachytherapy was utilized for head and neck brachytherapy, and considerable clinical data demonstrating its safety and efficacy established LDR as the "gold standard."

LDR, a dose rate between 0.3 and 0.6 Gy/hr is recommended to reduce the risk of late complications.

HDR brachytherapy: Now mature data to support the use for several head and neck subsites,

Generally doses between 3 - 4 Gy/fraction, Twice-daily fractions, 6 hours inter-fraction interval, recommended

PDR: Long-term results have been published for the fractionation schedule - mirrors LDR brachytherapy,

PDR, a pulses of 0.4 to 0.7 Gy every hour, 24 hours per day or slightly higher dose every three hour. However, there are no prospective long-term data.

J.J. Mazeron et al. / Cancer/Radiothérapie 7 (2003) 62–72

# THREE-DIMENSIONAL DOSE ADDITION OF EXTERNAL BEAM RADIOTHERAPY AND BRACHYTHERAPY FOR OROPHARYNGEAL PATIENTS USING NONRIGID REGISTRATION

Two computed tomography (CT) scans N=5 patients: 1-EBBRT_CT 2. BT_CT

The salivary glands and the chewing and swallowing muscles were contoured, and a dose distribution was calculated.

A nonrigid transformation -by registering the organs' surfaces.
BT dose distribution was mapped onto the EBRT dose distribution.
the physical doses were converted to in 2 Gy (EQD2), and the total dose was found by adding dose voxel by voxel.

The effect of the perturbations was quantified using DVH and gamma analyses (distance-to-agreement/dose-difference = 1 mm/1 Gy).

- The variations in input parameters and delineations caused only small perturbations in the DVH of the added dose distributions.
- For most organs the gamma index was low, and it was moderately elevated for organs lying in areas with a steep gradient (median gamma index #2.3 for constrictor muscles, #0.7 for all other organs).
- Conclusions: Allows adding dose distributions of combined EBRT and BT for oropharyngeal patients. In general, the method is reliable and robust with respect to uncertainties in organ delineation, perturbations in input parameters of the method, and a/b values

# ICRU -58

Dose prescription and reporting :based on the Paris System.

In addition to reporting the GTV and CTV, the “Treated Volume” is encompassed by the isodose corresponding to the minimal peripheral dose to the CTV.

Additionally, a description of the sources,

techniques, time pattern, and

prescription dose should be documented.

Common quality parameters:

The dose nonuniformity ratio (DNR),

homogeneity index (HI), and uniformity index (UI), should also be recorded. The goal DNR (defined as V150/V100) at the authors’ institution is generally less than 25%

# What is the Role of Brachytherapy in the IMRT Era?

Decline of brachytherapy utilisation in the US, reasons included:

1) an increase in the use of robotic
2) increase in the sophistication of EBRT

    (IMRT and image guided radiotherapy (IGRT)), stereotactic ablative body radiotherapy (SABR) and proton therapy

3) increase in the reimbursement for IMRT
4) negative press as the result of poor quality implants
5) limited opportunities for training due to the reduced number of facilities offering brachytherapy
6) few physicians have brachytherapy experience and are therefore less likely to refer patients.

# What Is the Role of Brachytherapy in the IMRT Era?

- In the current era of IMRT-based (chemo)radiation for oropharynx cancer, the role of an interstitial implant has been questioned .
- There are emerging data supporting the use of reduced-dose IMRT-→ interstitial implant ⇩ reduce the dose to surrounding normal structures.
- Teguh et al of 85 oropharynx patients: brachytherapy ⇩ the dose to the pharyngeal constrictors to beyond the sparing that is achievable with IMRT, resulting in less dysphagia.
- 46 Gy EBRT (using IMRT or 3D-CRT) -> boost using either IMRT, interstitial brachytherapy, or stereotactic radiation.
- For oropharynx patients, more dysphagia: boosting with IMRT Vs boosting with brachytherapy or stereotactic radiation.

The same group recently published their results:

- N= 167 oropharyngeal patients (99 tonsillar fossa, 30 soft palate, 38 base of tongue)
- 46 Gy IMRT + brachytherapy boost ( PDR technique , mean dose of 22 Gy. Only 17% of patients received chemotherapy for T3 or N3 disease.
- In patients with node-positive disease, neck dissection was performed.
- Local and regional control at 5 years was excellent at 94% and 97%, respectively, with very low rates of late grade 3 toxicity: 3% mucosal ulceration, 2% xerostomia, and 1% dysphagia.

# Dose volume histogram constraints in patients with head and neck cancer treated with surgery and adjuvant HDR brachytherapy: A proposal of the head and neck and skin GEC ESTRO Working group

Acknowledges the lack of widely accepted DVH constraints in adjuvant head and neck brachytherapy and issues recommendations to minimize mandibular ORN and Soft Tissue Necrosis (STN).

- N=227 patients of head and neck cancer ->Sx-> adjuvant HDR brachytherapy alone or combined with other treatment modalities(2000–2018).

**STN** --28 out of 227 cases (12.3%) with an avg time to appearance of 4.0 months. positive correlation between CTV size and STN ($p = 0.017$) .

- Total EQD2-DVH TV100 dose <87Gy and STN ($p = 0.06$).
- The risk of STN in the absence of both factors- 2%, with one factor -15.7% and with both factors -66.7% ($p = 0.001$).

**ORN**: 13 out of 227 cases (5.7%) -avg time to appearance of 26.2 months. Dose to Mandible 2cm3 (p = 0.027). Pts Total Physical Doses greater than 61 Gy had a 20-fold increased risk.

In Unirradiated pts the panel recommends to avoid implantation of postoperative CTVs exceeding 15 cm3 at Total EQD2-DVH TV100 doses in excess of 87 Gy as well as to limit the irradiation of the Mandible2cm3 to 61 Gy.

In previously irradiated patients the panel cannot make a recommendation.

## Is Brachytherapy Feasible After Head and Neck Cancer Reconstructive Surgery? Preliminary Report-----> yes

Pulsed dose-rate brachytherapy seems to be a safe option that can be performed at the site of reconstruction in immediate postoperative

- period with minimal wound complications and with no impact on flap survival. Further clinical study based on larger patient
- series is needed to present statistically proven results.

# Local control in advanced cancer of the nasopharynx: Is a boost dose by endocavitary brachytherapy of prognostic significance?

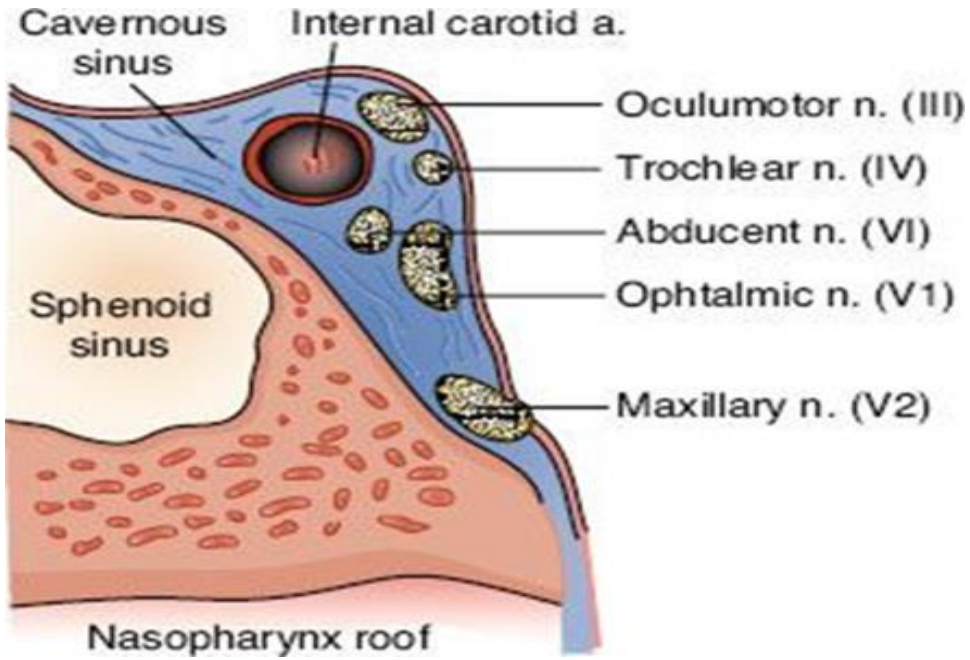
Peter V Levendag
T1,2, N0 tumors, **Local boost** :the local relapse rate (LRR) was significantly smaller- 0% (0/34, EBT boost) vs. 14% (14/102, no EBT boost) ( $p<0.023$).
T3,4 tumors: LRR of 10% (4/38, EBT or stereotactic radiation boost) vs. 15% (17/111, no boost) was found ( $p<0.463$).

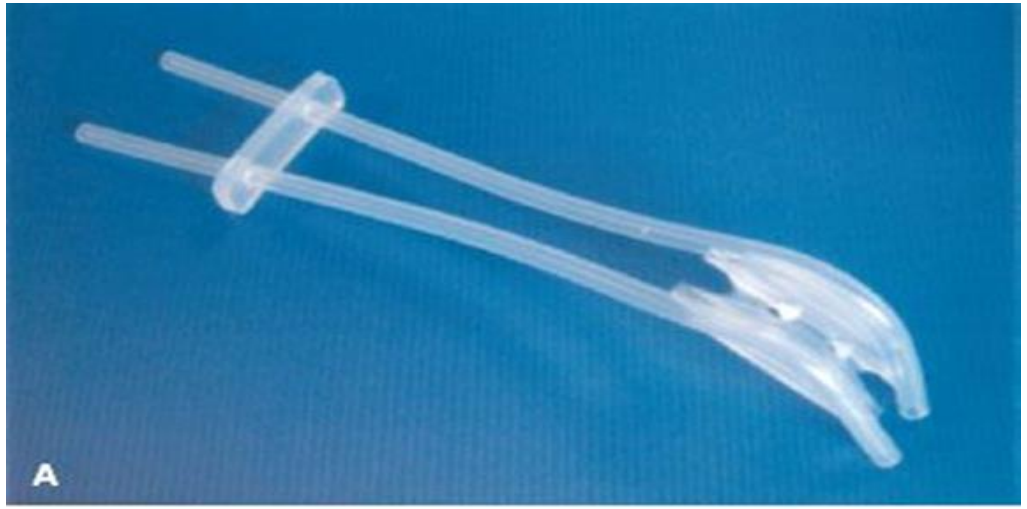
Brachytherapy in **reirradiation** of locally recurrent nasopharyngeal cancer: case report of 5 cases
The total radiation dose EQD2 was between 60 and 70. The median follow-up after reirradiation was 42months. Local control was observed in all cases. All patients are still alive.

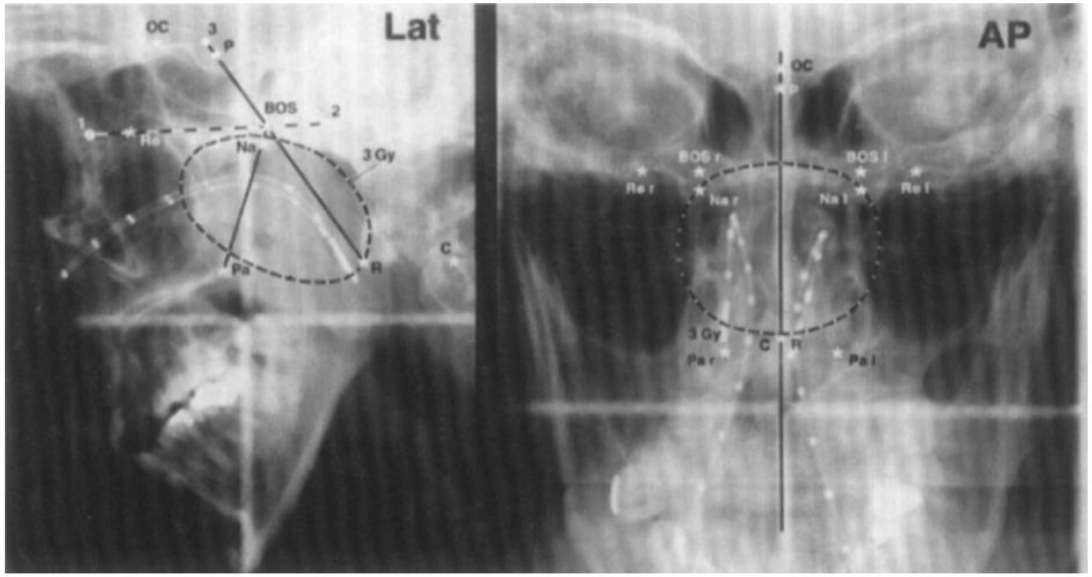
# A new applicator design for endocavitary brachytherapy of cancer in the nasopharynx

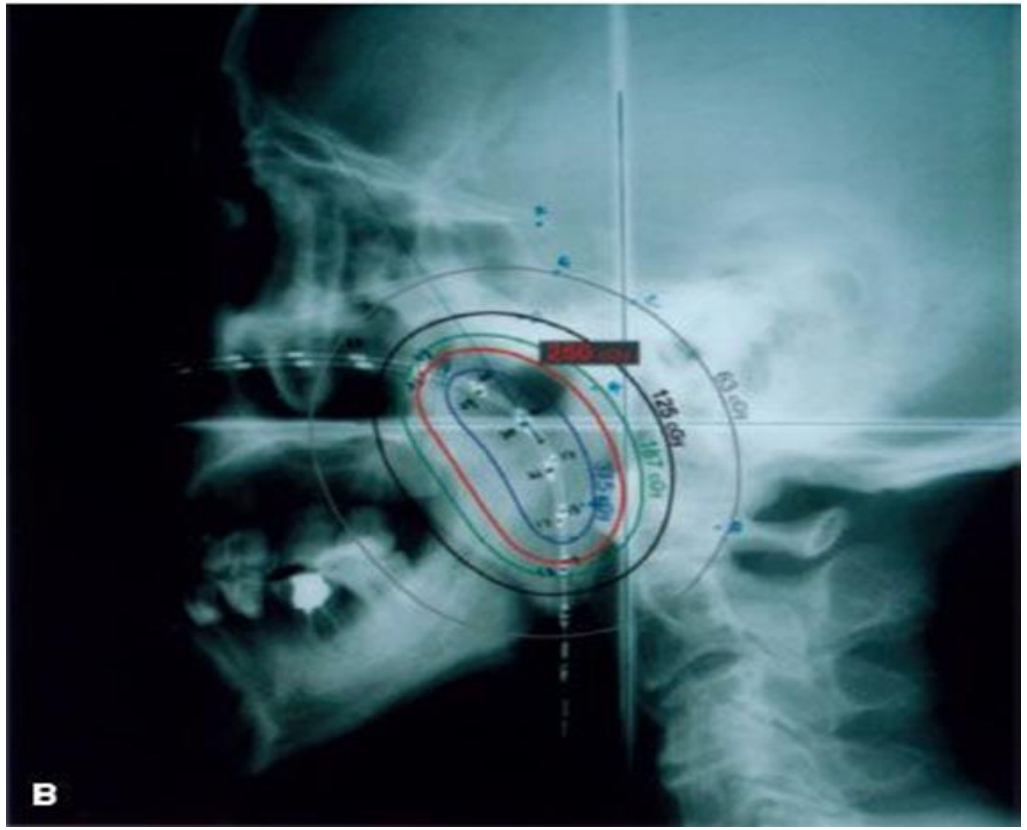
- inexpensive, reusable and flexible silicone applicator,
- tailored to the shape of the soft tissues of the nasophaqmx,
- which can be used with either low-dose-rate brachytherapy or high (pulsed)-dose-rate remote controlled afterloader
- This Rotterdam nasopharynx applicator proved to be easy to introduce, patient friendly and can remain in situ for the duration of the treatment (2-6 days).
- The design, technique of application and the first consecutive 5 years of clinical experience in using this applicator are presented.

**Peter C. Levendag**


Cavernous sinus
Internal carotid a.
Oculumotor n. (III)
Trochlear n. (IV)
Abducent n. (VI)
Ophtalmic n. (V1)
Maxillary n. (V2)
Sphenoid sinus
Nasopharynx roof


A


Lat
AP
OC
BOS
3 Gy
C
R


B

Example of brachytherapy dose distribution, non-optimized and optimized, in target and normal tissue patient points for a single patient treated by HDR endocavitary brachytherapy

| Patient points | Non-optimized dose (cGy) (%) | Optimized dose (cGy) (%) |
|---|---|---|
| NA (R) | 268 (89) | 292 (97) |
| NA (L) | 332 (111) | 308 (103) |
| BOS (R) | 146 (49) | 146 (49) |
| BOS (L) | 128 (43) | 128 (43) |
| R | 366 (122) | 303 (101) |
| OC | 45 (15) | 46 (15) |
| P | 69 (23) | 70 (23) |
| Re (R) | 48 (16) | 52 (17) |
| Re (L) | 60 (20) | 61 (20) |
| Pa (R) | 213 (71) | 238 (79) |
| Pa (L) | 253 (84) | 248 (83) |
| C | 90 (30) | 78 (26) |

# Single center excellent result

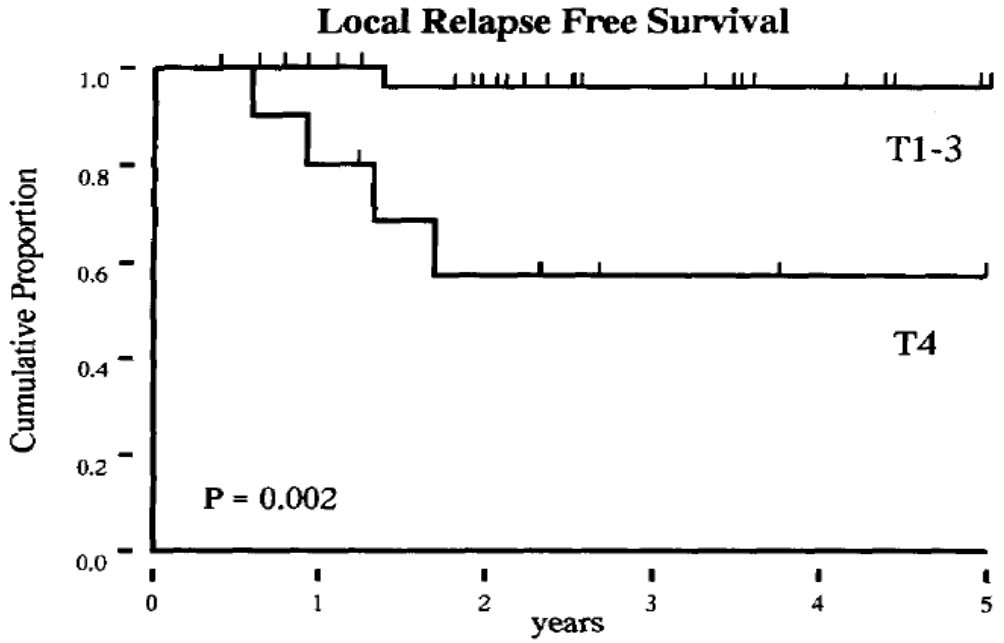
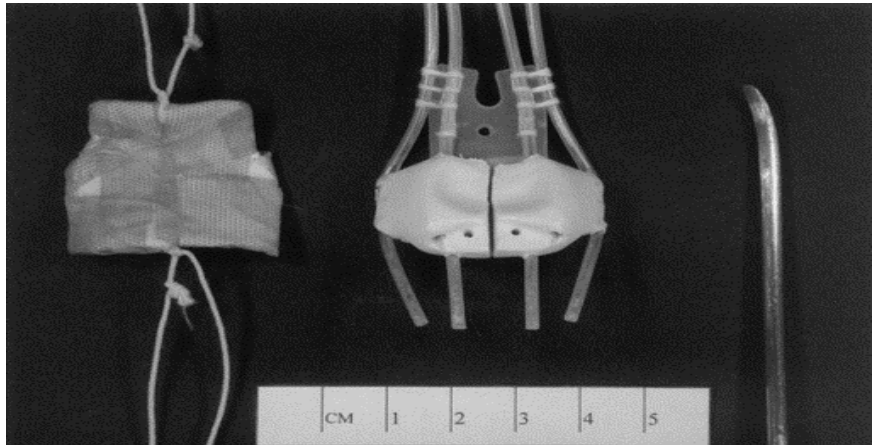



Fig. 3. Local relapse free survival for primary NPC patients treated from 1991 to 1995 in Rotterdam by a combination of ERT and HDR-BT.



87 pts - locally persistent NPC treated (1990–1998) - HDR intracavitary brachytherapy were retrospectively analyzed.
complete regression of local disease--> observation.
87 pts persistent viable disease at a median time of 6 weeks post-RT.
Ho's staging system : Stage I—8, II—33, III—41, IV—5; T1—19, T2—48, T3—20; N0—32, N1—22, N2—28, N3—5.

Rx-HDR intracavitary brachytherapy22.5–24 Gy in 3 weekly sessions (Co-60, Ir-192) in all but 4 patients.

The 5-year actuarial LFFS rates 85% and 76.6% (p 5 0.15), and DSS-72% and 67.8% (p 5 0.2) BT group Vs ERT.
The 5-year actuarial LFFS rates for T1, T2, and T3 disease were 94.7%, 88.2%, 67.4%, and 84.1%, 79.8%, 62.6%.
locally persistent NPC can be effectively salvaged by brachytherapy.

# Indian Experience, IBS, GEC-ESTRO, ABS Guidelines- commonly states

1) patient selection, the pre-treatment work up and patient care,
2) treatment strategy,
3) target definition,
4) implant techniques,
5) dose and dose rate prescription,
6) treatment planning and reporting,
7) treatment monitoring
8) catheter removal, and
9) post-treatment patient care and follow-up.

- The use of brachytherapy in combination with external beam radiotherapy and/or surgery was also covered as well as the use of brachytherapy in previously irradiated patients. Given the developments in the field,
- these recommendations needed to be updated to reflect up-to-date knowledge.
- Brachy definitely produces good DFS→ OS lesser toxicities.

- Rigorous training , workshops, good protocol developments at high volume centers.

## Conclusion:

Brachytherapy poses challenges:
Challenges are many,  for every step you perform.
From acquiring facility to performing good implant by learning from mistakes to training other faculty or registrars.
Conducting pooled clinical trails for producing good evidence with novel questions .

Brachytherapy: a dying art or missed opportunity ?
Brachytherapy rigorous training Courses is the answer


# Thank you