

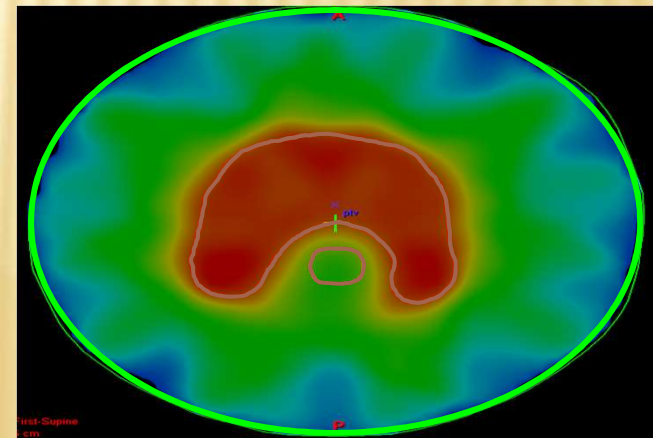
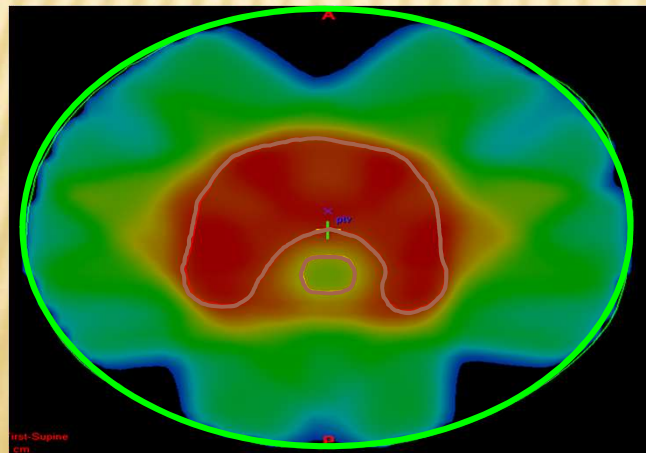
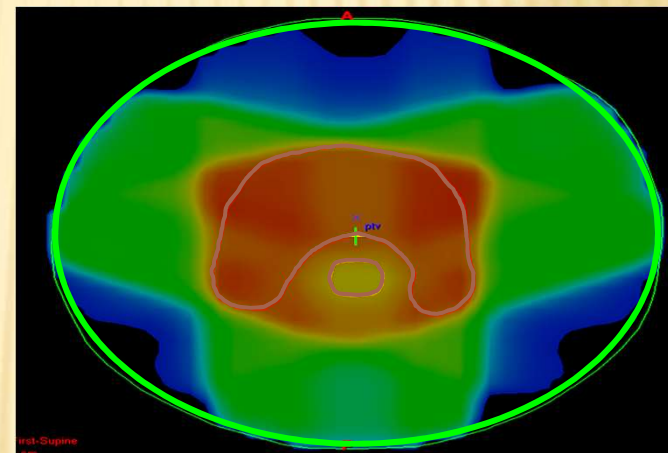
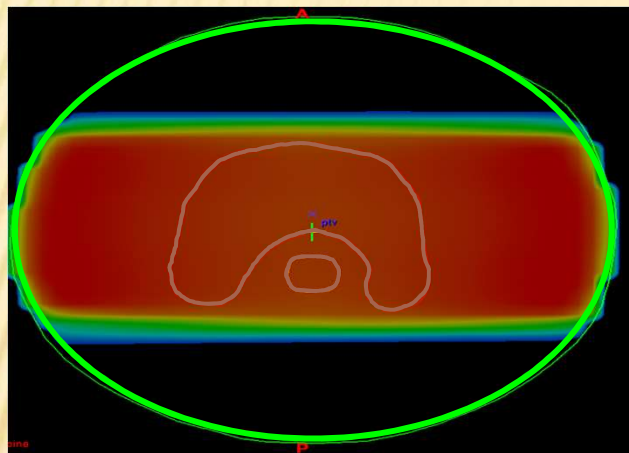
IMRT IN HEAD NECK CANCER

Dr Jyotirup Goswami

Consultant Radiation Oncologist

Narayana Superspeciality Hospital, Howrah

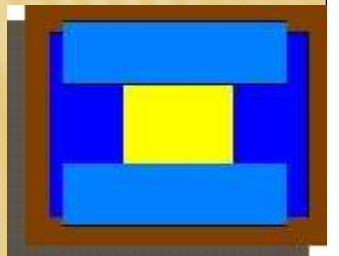
THE SEARCH FOR CONFORMALITY





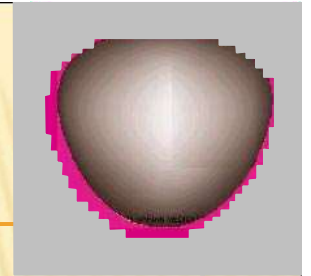
CONVENTIONAL RT

- ✗ Simple field arrangements
- ✗ Uniformly radiate both the target and the surrounding normal tissues.
- ✗ Includes the use of rectangular blocks to shield normal structures.

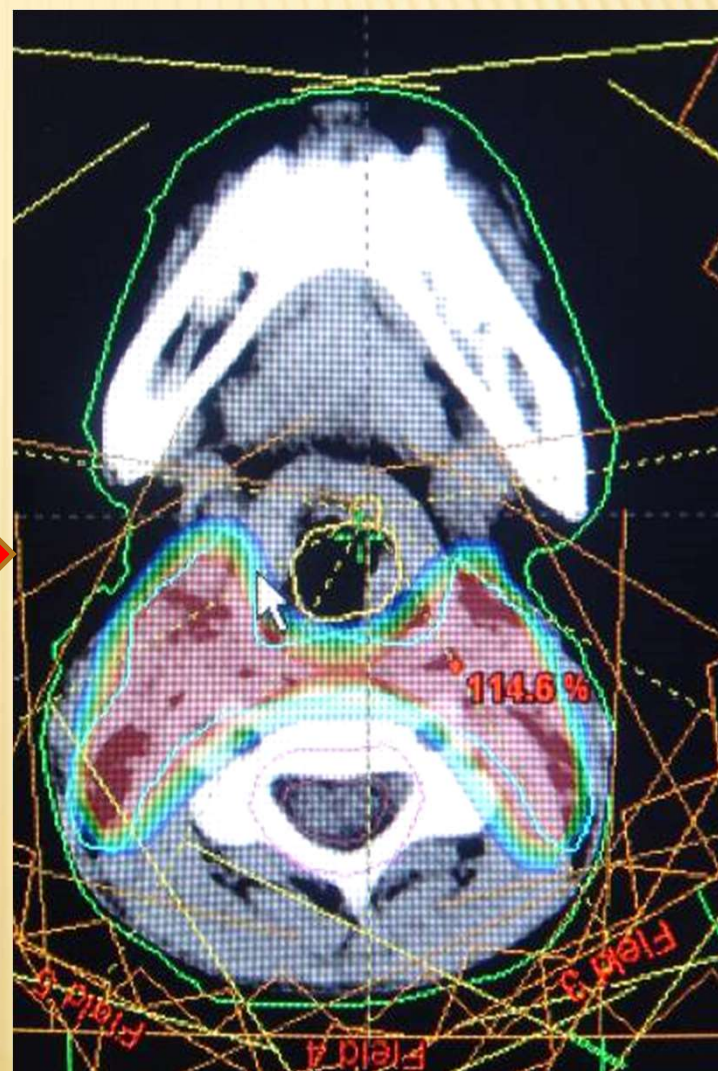
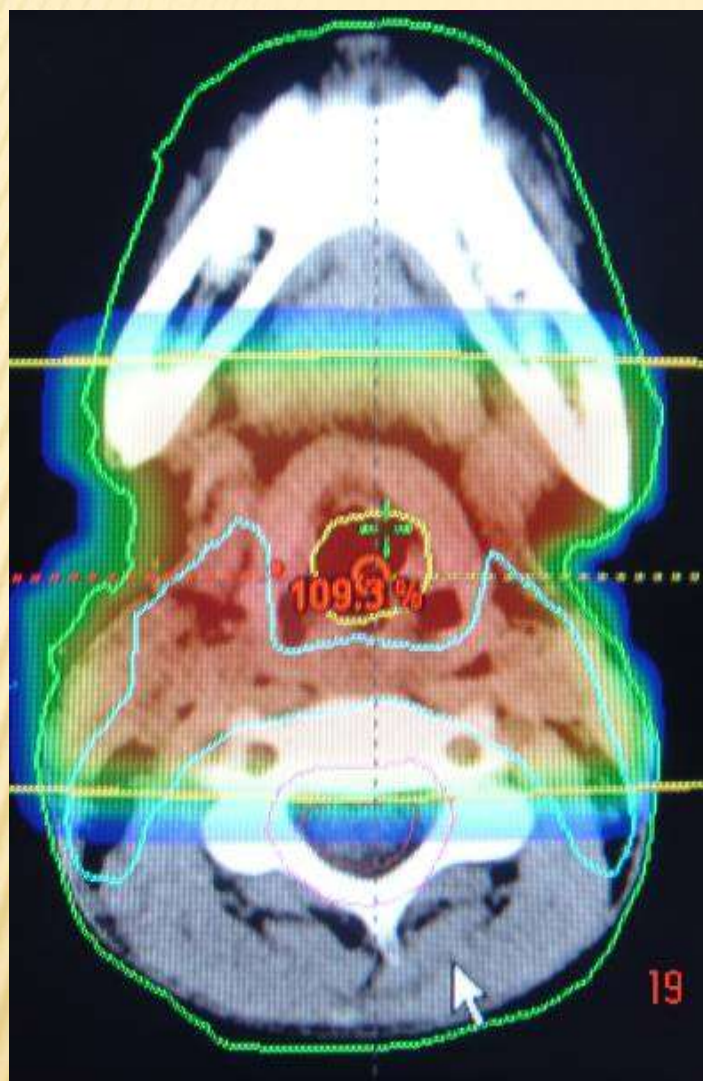




CONFORMAL RT



- ✖ Multiple fields, including oblique and non-coplanar fields
- ✖ Varying weightage and wedges.
- ✖ Shaped blocks :Blocks may be Cerrobend blocks, or motor-driven Multi Leaf Collimators (MLC).
- ✖ CT-based 3D planning



INTENSITY MODULATED RADIOTHERAPY

- ✗ IMRT is a higher form of 3DCRT.
- ✗ Two forms:
- ✗ Forward planned IMRT : basically a form of complex 3DCRT using field-in-field technique.
- ✗ Inverse planned IMRT : requires Inverse Treatment Planning (ITP) software.

Forward Planning

Inverse Planning

Beam parameters (beam orientation, shape, modifier, beam weights, etc.)



3D dose distribution.

If not satisfactory, then modify the beam parameters

3D dose distribution



Beams Fluence Profile

If objective criteria is not satisfied, Then, changes the beam parameters and/ or objective criteria

INVERSE PLANNING

- ✗ The user specifies the dose and dose-volume constraints for the PTV and OARs, using a system of priorities and weights.
- ✗ Normally the beam arrangement is predefined also.
- ✗ The system performs iterative calculations with a quadratic function, to achieve the best possible dose distribution based on the given dose constraints.
- ✗ After this, the accurate dose distribution is recalculated after considering the machine (jaw & MLC) parameters.

DOSE CONSTRAINTS

1. Based on physical parameters.

Dose based

Dose volume based

2. Biological model

Tumor control probability.

Normal tissue complication probability.

EUD.

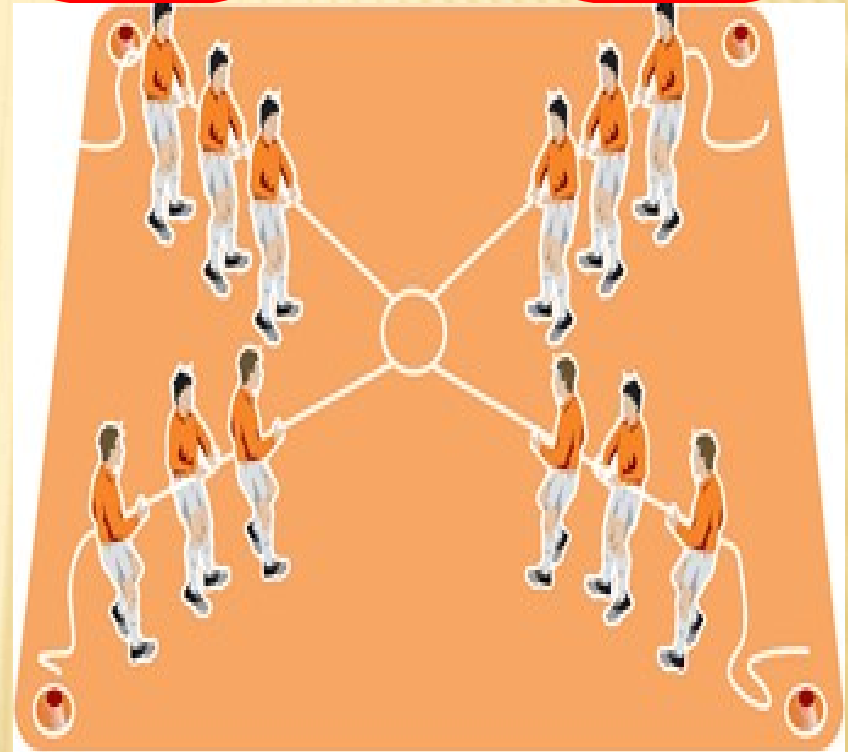
Effective volume.

OPTIMISATION

- ✗ The process by which the optimum beam weight or intensity distribution is determined that can best satisfy the **objective function/ cost function/ score** as specified by planner.

Conformality

OAR sparing



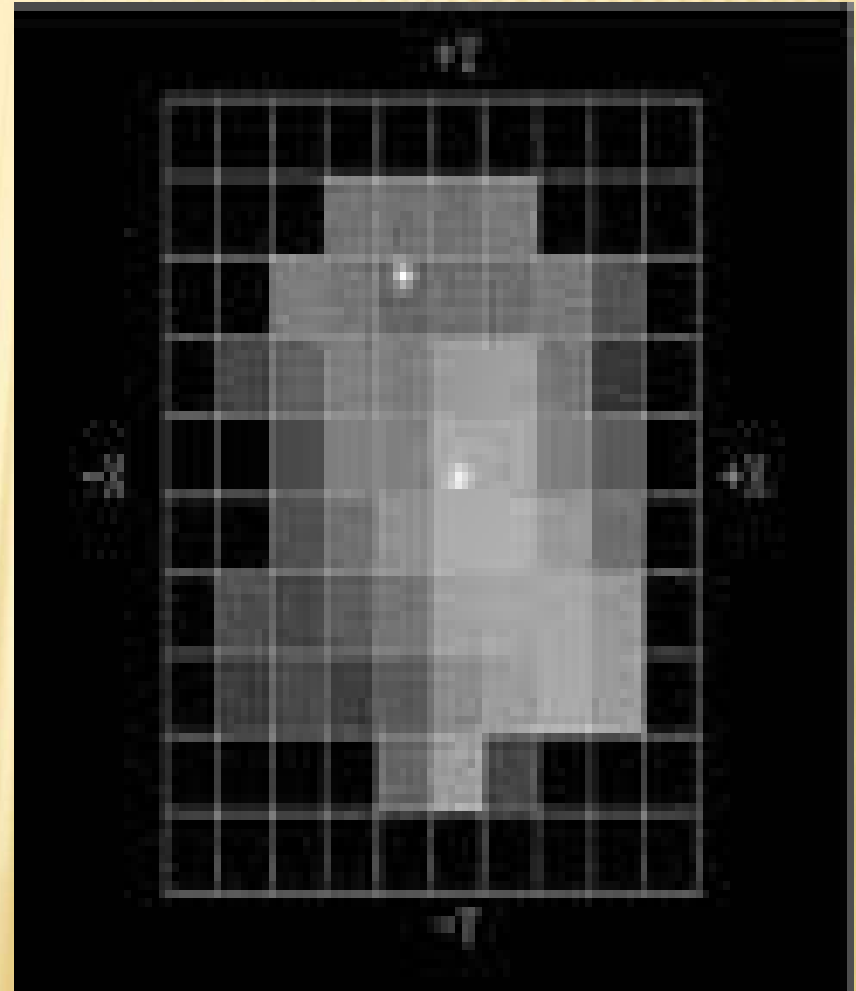
Target coverage

Homogeneity

OPTIMISATION ALGORITHMS

- Essential for speeding up the optimisation process.
- The algorithms are almost entirely **iterative** ones.
- This means that they start with an initial guess for the beam profiles and modify the profiles step by step, until the optimum is found.

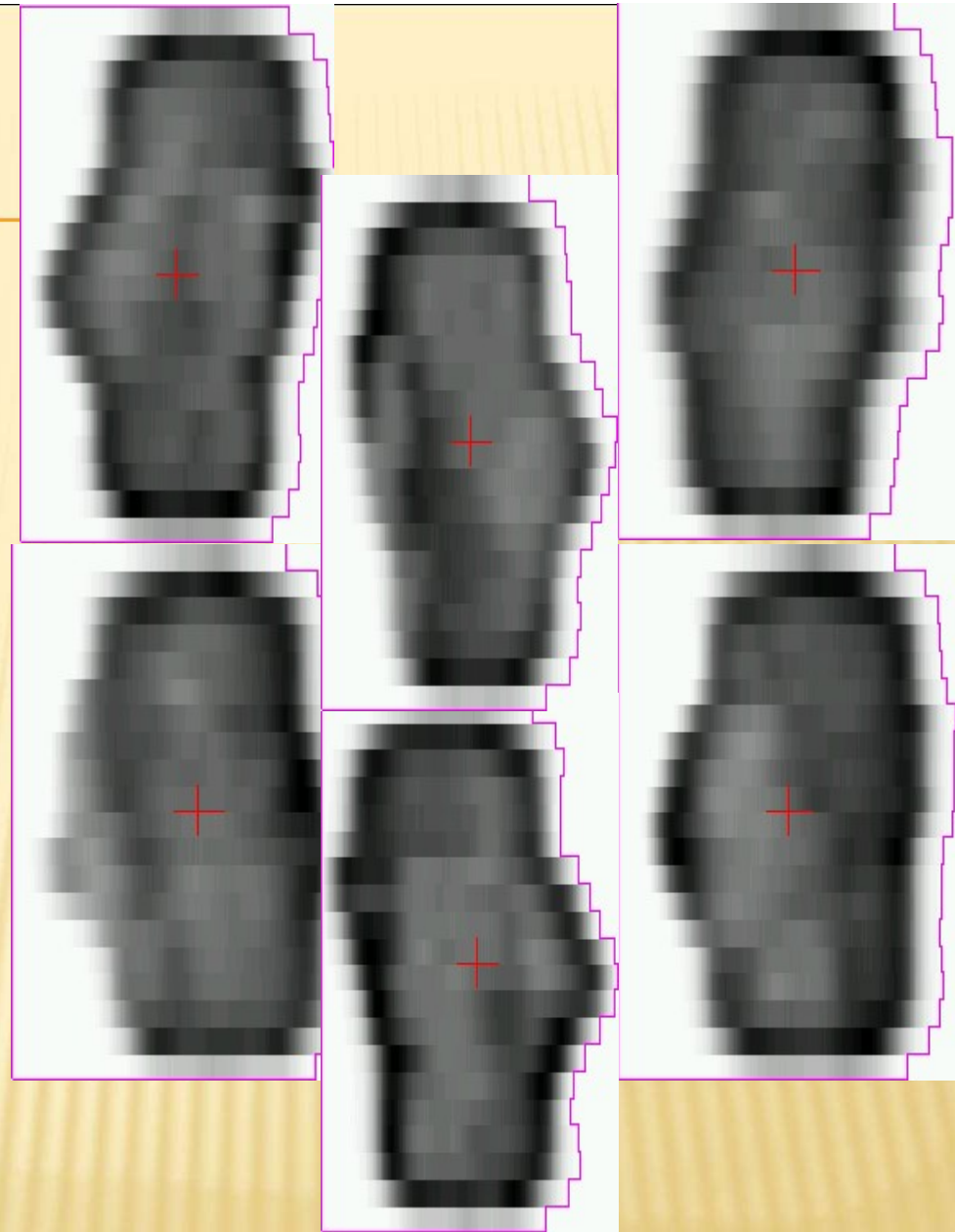
- ✗ The desired dose constraints are used to generate a fluence matrix.
- ✗ Fluence across the individual beams are modulated to create beamlets of different fluence.



Beamlets

DELIVERY TECHNIQUES

- ▶ **Step-and shoot:** done by superposing a number of **different beam shapes** with the same gantry orientation- these are called **segments**. Created by differing **MLC arrangements**, where the target is **differentially blocked**.
- ▶ **Dynamic/ sliding window:** the **MLCs sweep across the field** with different speeds and durations to create the same effect.



Segments

STEP & SHOOT VS SLIDING WINDOW IMRT

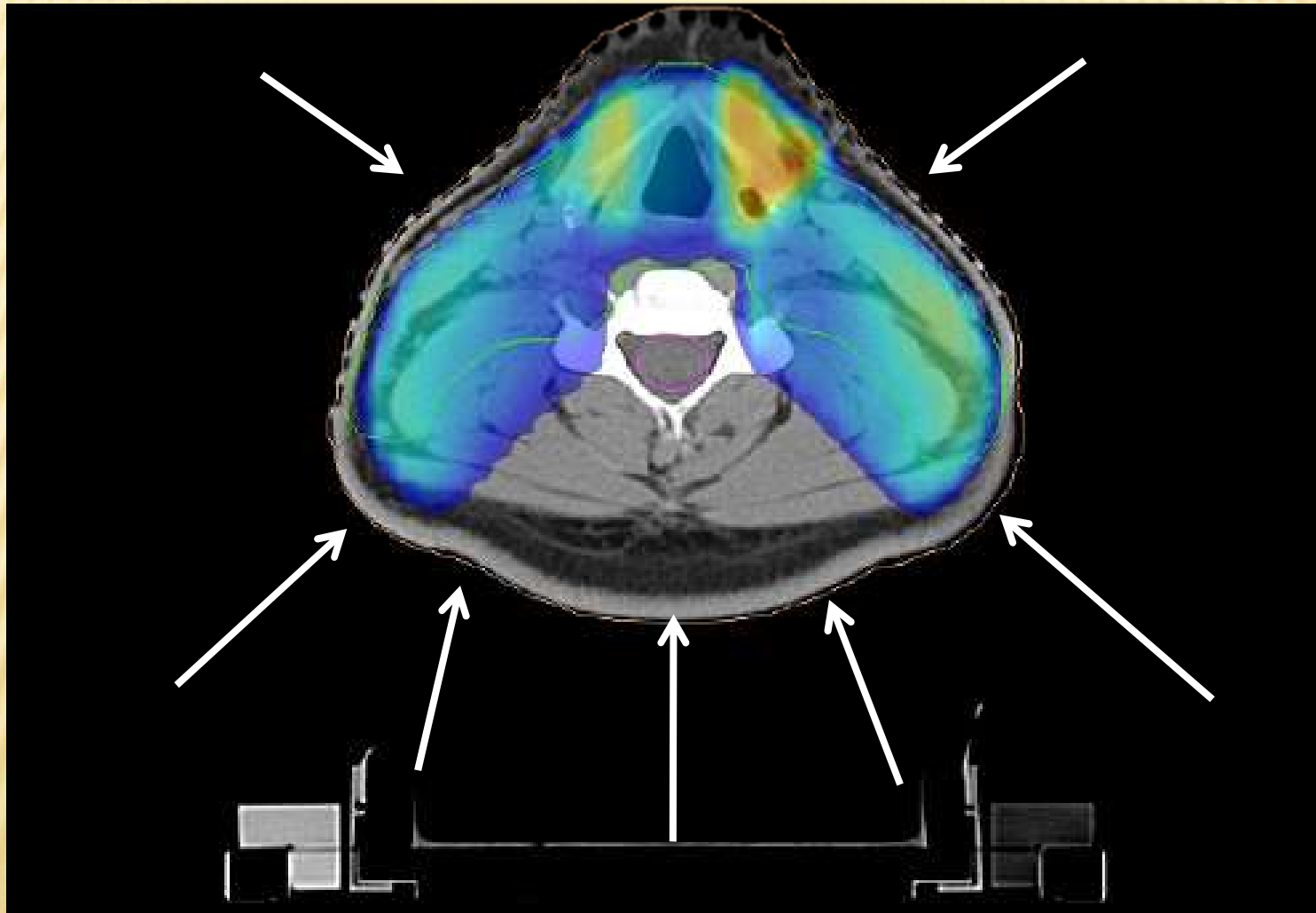
Comparing 3DCRT and inversely optimized IMRT planning for head and neck cancer: Equivalence between step-and-shoot and sliding window techniques

Barbara Longobardi^a, Elena De Martin^a, Claudio Fiorino^{a,*}, Italo Dell'oca^b, Sara Broggi^a, Giovanni Mauro Cattaneo^a, Riccardo Calandrino^a

Conclusions: With the Varian planning and delivery system, Step-and-shoot approximations of inversely optimised fluences in head-neck IMRT compare well with SW delivery, even with only five intensity levels. With a number of intensity level of 10 or more, no differences can be appreciated in PTV coverage/OAR sparing with respect to SW.

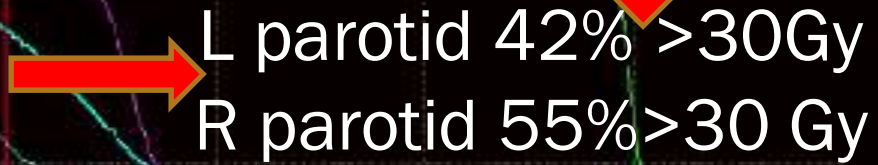
COMPLEX 3DCRT/ FORWARD PLANNED IMRT (WESTBANK EXPERIENCE)

95% DOSE COLOUR WASH



7 Beam arrangement

| Structure | Volume (mL) | Min. Dose (µg) | Max. Dose (µg) | Mean Dose (µg) | Cold Ref. (µg) | Volume -1 (%) | Hot Ref. (µg) | Volume | % in Volume | Is in Q2 |
|----------------------|-------------|----------------|----------------|----------------|----------------|---------------|---------------|--------|-------------|----------|
| paracet | 28.320 | 215.8 | 5880.7 | 2661.5 | | | 3000.0 | 42.45 | 10000 | yes |
| paracet | 31.888 | 125.6 | 5415.1 | 1005.0 | | | 3000.0 | 55.35 | 10000 | yes |
| patient Unsup. Tis.) | 5161.992 | 1.9 | 6020.6 | 270.3 | | | | | 10000 | no |
| city 00 | 600.544 | 3005.1 | 6047.0 | 5929.6 | | | | | 10000 | yes |



3DCRT VS IMRT

THREE-DIMENSIONAL CONFORMAL VS. INTENSITY-MODULATED RADIOTHERAPY IN HEAD-AND-NECK CANCER PATIENTS: COMPARATIVE ANALYSIS OF DOSIMETRIC AND TECHNICAL PARAMETERS

LUCA COZZI, PH.D.,* ANTONELLA FOGLIATA, DR.,* ALESSANDRA BOLSI, DR.,*[†]
GIORGIA NICOLINI, DR.,* AND JACQUES BERNIER, PH.D., M.D.[‡]

Materials and Methods: Twenty-six head-and-neck cancer patients were irradiated following a feasibility internal protocol with IMRT. Treatments were performed with either the static step-and-shoot (20) or the dynamic sliding window (6) techniques on a 6 MV Varian Clinac equipped with a multileaf collimator with 80 leaves. Dose plans were computed using commercial treatment planning systems: MDS-Nordion Helax-TMS for static cases and Varian Eclipse for dynamic cases. Dose plans were evaluated in terms of physical quantities based on dose-volume histograms and isodose distributions. Each IMRT plan was also compared to a reference 3D conformal therapy plan (3DCRT).

Results: Elective target volumes ranged from 530 to 1151 cm³ with a mean of 780 ± 141 cm³. Boost volumes ranged from 248 to 832 cm³ with a mean of 537 ± 165 cm³. Thirty-two dose plans were generated with static technique and 10 with dynamic. In the static mode, 6.8 ± 3.4 fields were applied on average with 12.5 ± 1.3 segments per field. In the static mode, 264 ± 56 MU per Gy were erogated, whereas in the dynamic mode, 387 ± 126 MU per Gy were erogated, to be compared to 147 ± 20 computed for reference 3DCRT plans. For all target volumes in general conformity was improved compared to 3DCRT (e.g. V_{95} increased from 85% to 93% with $p < 0.001$, or equivalent uniform dose normalized to prescribed dose increased from 0.86 to 0.96 with $p = 0.002$). Irradiation of parotid glands or spinal cord improved, as well: For parotids, $D_{7/3T}$ reduced from 59 Gy to 41 Gy ($p < 0.001$). For spinal cord, D_{max} reduced from about 40 Gy to about 30 Gy ($p < 0.001$).

IMRT vs Rapid Arc vs Tomotherapy

INTENSITY-MODULATED RADIATION THERAPY (IMRT) DOSIMETRY OF THE HEAD AND NECK: A COMPARISON OF TREATMENT PLANS USING LINEAR ACCELERATOR-BASED IMRT AND HELICAL TOMOTHERAPY

KE SHENG, PH.D.,* JANELLE A. MOLLOY, PH.D.,*[†] AND PAUL W. READ, PH.D., M.D.*

- ✗ Dosimetric study (N=10)
- ✗ All patients had oropharyngeal carcinoma (5 BOT, 5 tonsil)
- ✗ 2 sets of plans: IMRT vs Tomotherapy
- ✗ Improved dose homogeneity within the target volume with HT (SD within the PTV reduced by 71%)
- ✗ Improved critical structure sparing (EUD of surrounding normal tissue reduced by 17.4% for BOT and 27.1% for tonsil)
- ✗ 80% reduction in NTCP of parotid glands

Volumetric modulated arc radiotherapy for carcinomas of the oro-pharynx, hypo-pharynx and larynx: A treatment planning comparison with fixed field IMRT

Eugenio Vanetti^a, Alessandro Clivio^a, Giorgia Nicolini^a, Antonella Fogliata^a, Sarbani Ghosh-Laskar^b, Jai Prakash Agarwal^b, Ritu Raj Upreti^b, Ashwini Budrukkar^b, Vedang Murthy^b, Deepak Dattatray Deshpande^b, Shyam Kishore Shrivastava^b, Ketayun Ardeshtir Dinshaw^b, Luca Cozzi^{a,*}

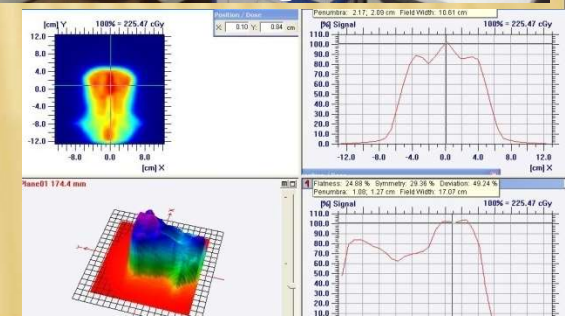
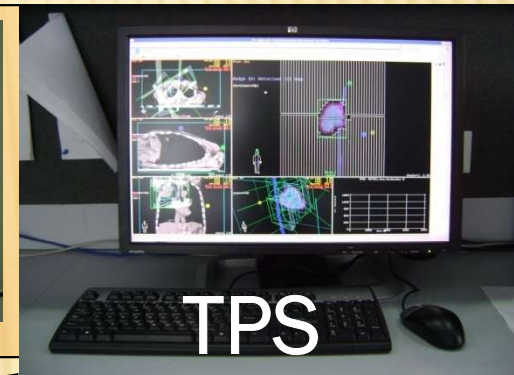
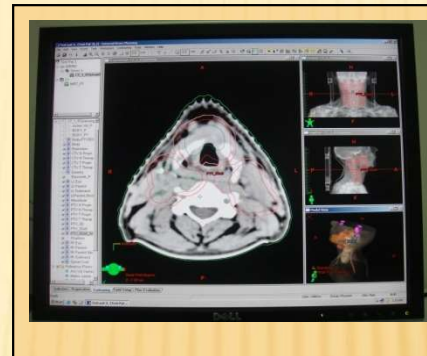
- ✗ Dosimetric study (N=29)
- ✗ Patients of carcinoma oropharynx, hypopharynx and larynx
- ✗ Conventional (Sliding Window) IMRT vs Rapid Arc(single arc) vs Rapid Arc (double arc)
- ✗ Both variants of rapid arc were significantly better in sparing normal tissue. Average doses to ipsilateral parotid were 40 Gy vs 36.2 Gy vs 34.4 Gy & to contralateral parotid were 32.6 Gy vs 30.9 Gy vs 28.2 Gy
- ✗ Rapid arc (double arc) also significantly improved target coverage & homogeneity with respect to conventional IMRT.

PRACTICALITIES OF IMRT

PROCESS OF IMRT PLANNING

- × Immobilization
- × Planning CT
- × Image transfer
- × Contouring of volumes
- × Margins
- × Treatment planning
- × Selection of optimum plan (dose distribution & DVH analysis)
- × Plan quality assurance
- × Plan implementation
- × Position verification (2D/3D)
- × Treatment execution

WORKFLOW



ITP SOFTWARE INTERFACE: SETTING PRIORITIES & CONSTRAINTS

Structures and Constraints

| Structure | Volume [cc] | Points | Resolution [mm] |
|--|-------------------|-----------------|-----------------|
| <input checked="" type="checkbox"/> L EYE | 7 | 2000 | 1.49 |
| <input checked="" type="checkbox"/> L PAROTID | 21 | 2000 | 2.12 |
| Line | Volume [%]: 96.9 | Dose [Gy]: 0.0 | Priority: 50 |
| | 85.7 | 0.0 | |
| | 67.1 | 1.5 | |
| | 47.2 | 6.9 | |
| | 32.7 | 13.6 | |
| | 21.1 | 20.4 | |
| | 10.7 | 28.9 | |
| | 3.6 | 41.3 | |
| | 0.0 | 57.2 | |
| <input checked="" type="checkbox"/> L optic nerve | 0 | 216 | 1.00 |
| <input checked="" type="checkbox"/> PTV 54 low risk | 79 | 2634 | 3.00 |
| Upper | Volume [%]: 0.0 | Dose [Gy]: 58.0 | Priority: 50 |
| Lower | Volume [%]: 100.0 | Dose [Gy]: 55.0 | Priority: 60 |
| <input checked="" type="checkbox"/> PTV high risk/70 | 520 | 17332 | 3.00 |
| Upper | Volume [%]: 0.0 | Dose [Gy]: 68.4 | Priority: 50 |
| Lower | Volume [%]: 100.0 | Dose [Gy]: 66.5 | Priority: 60 |
| <input checked="" type="checkbox"/> R Eye, NOS | 8 | 2000 | 1.52 |
| <input checked="" type="checkbox"/> R OPTIC Nerve | 0 | 139 | 1.00 |
| <input checked="" type="checkbox"/> R PAROTID | 21 | 2000 | 2.10 |
| <input checked="" type="checkbox"/> Spinal Cord | 14 | 2000 | 1.83 |
| <input checked="" type="checkbox"/> hot1 | 4 | 2000 | 1.19 |
| <input checked="" type="checkbox"/> prv cord | 34 | 2000 | 2.48 |
| Upper | Volume [%]: 0.0 | Dose [Gy]: 40.0 | Priority: 50 |
| <input checked="" type="checkbox"/> ptv 54 | 593 | 19761 | 3.00 |

Dose Volume Histogram

DVH

Add Upper Constraint
Add Lower Constraint
Delete

Base dose plan:
Select...

| Field | MLC | Method | X Smooth | Y Smooth | Minimize Dose | Fixed Jaws | Field Weight |
|---------|-----------------|---------|----------|----------|---------------|--------------------------|--------------|
| Field 1 | Millenniu... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |
| Field 2 | Millennium_1... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |
| Field 3 | Millennium_1... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |
| Field 4 | Millennium_1... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |
| Field 5 | Millennium_1... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |
| Field 6 | Millennium_1... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |
| Field 7 | Millennium_1... | Beamlet | 40 | 30 | 0 | <input type="checkbox"/> | 1.000 |

Fluence Map

Max time (min): 100
Max iterations: 1000

Optimize

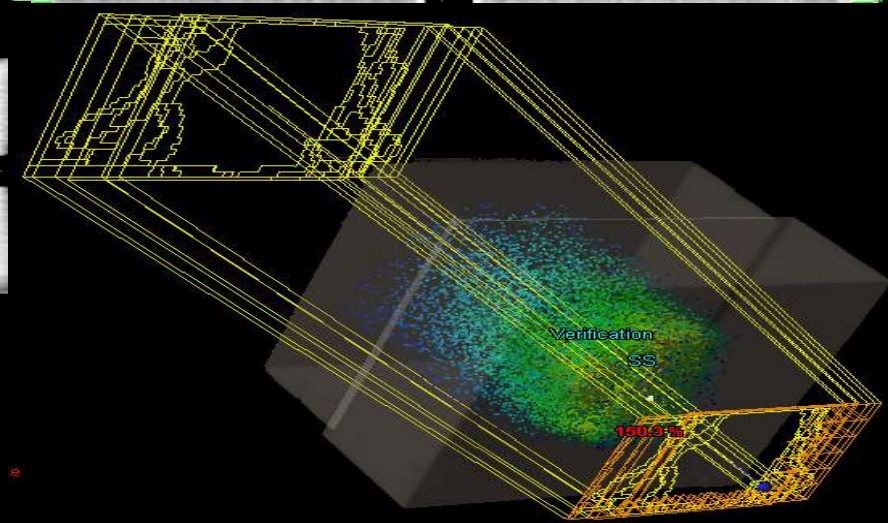
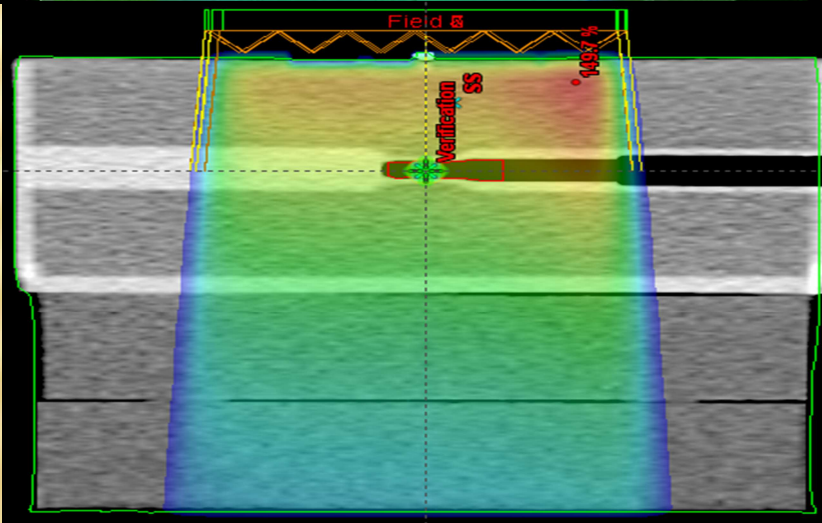
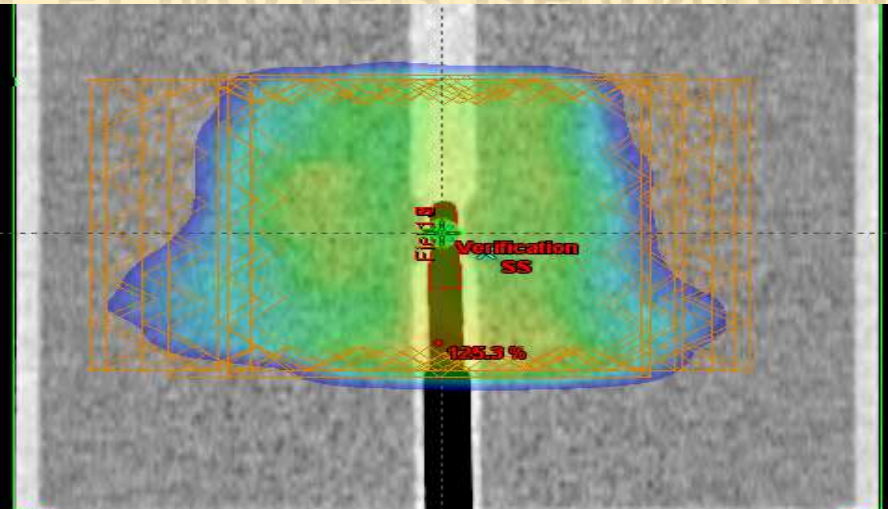
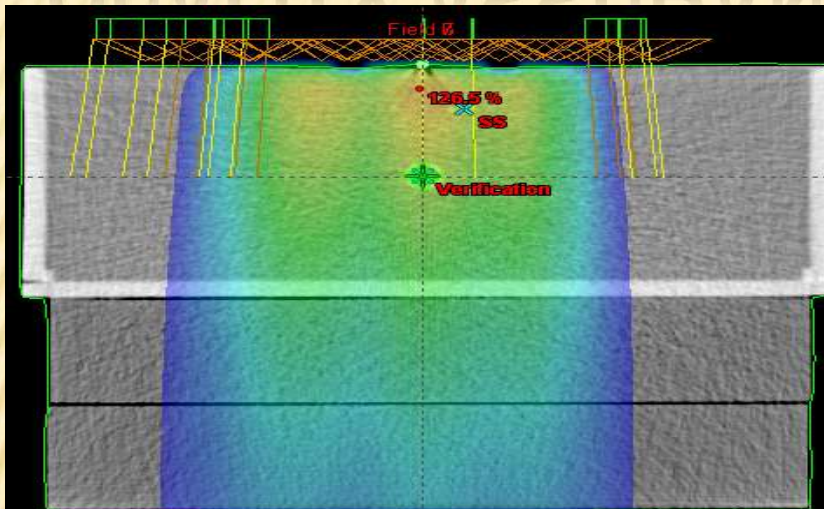
☐ View with interpolation
☐ Use color

OK Cancel Apply

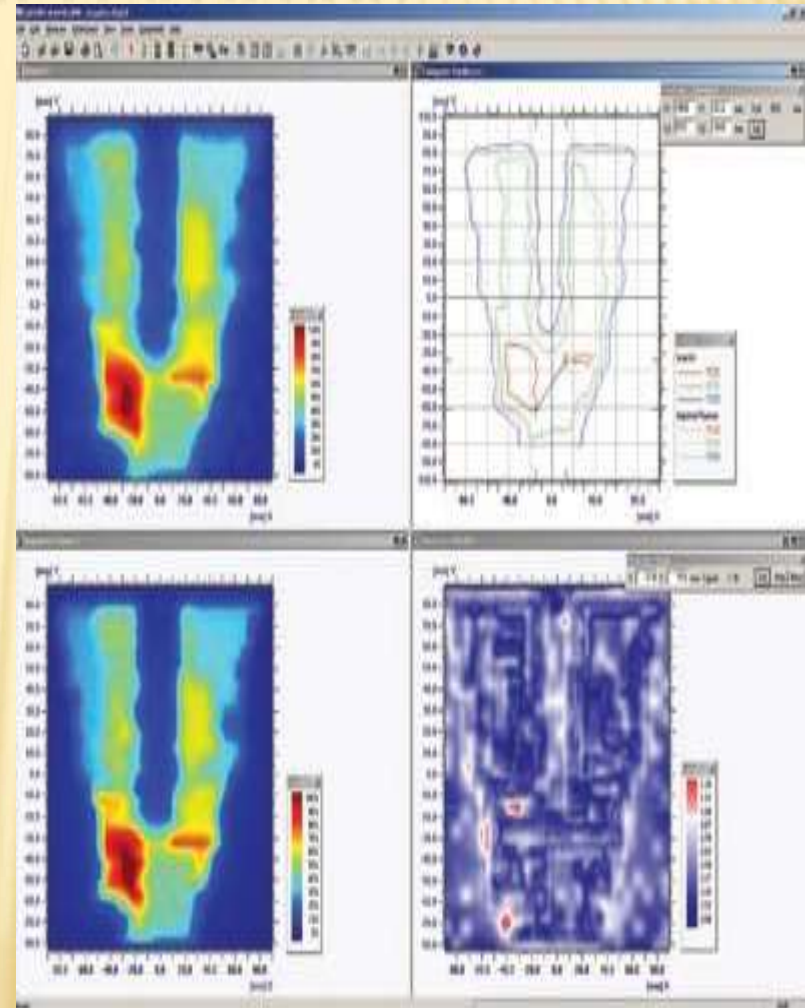
WHAT HAPPENS IN IMRT QA?

- ✗ The patient's plan is opened on the CT dataset of the phantom.
- ✗ Gantry angles are set to zero.
- ✗ The plan is recalculated.
- ✗ The new plan is executed with the phantom in place.
- ✗ Point doses (measured & calculated) are compared to ensure accurate dose calculation by the TPS has been done.

QUALITY ASSURANCE: WATER PHANTOM



QUALITY ASSURANCE: IMATRIXX (ION CHAMBER ARRAY)



IMRT DOSE & FRACTIONATION

EUD

- ✗ Standard dose constraints assume that the whole organ is being uniformly irradiated at 1.8-2Gy/#.
- ✗ In IMRT, aside from use of higher dose/# (in SIB), most OARs are only partially irradiated. There is also a steep dose gradient within a given OAR.
- ✗ Equivalent Uniform Dose (EUD) is that dose, which had the organ been wholly and uniformly irradiated, would have produced the same biological effect.
- ✗ Complex voxel-based calculation.

SIB-IMRT/SMART VS SEQUENTIAL IMRT

- ✗ Dosimetric advantage: Superior PTV conformality & superior parotid gland sparing. Dogan et al (2003)
- ✗ Logistical advantage : lesser number of treatment days required.
- ✗ Radiobiological advantage: Due to higher dose/# (to the target) and lesser duration of treatment, the NTD (Normalised Total Dose=EQD2) is actually higher than the Nominal Dose.

| Treatment Strategy | Anatomic structure | Prescribed | | | Actual | |
|--------------------|--------------------|------------|-----------------------------------|---------------------------------------|--|-----------------------------|
| | | NTD (Gy) | Nominal dose in 30 fractions (Gy) | Nominal dose/fx (Gy) for 30 fractions | Nominal equivalent uniform dose in 30 fractions (Gy) | Equivalent uniform NTD (Gy) |
| SIB-IMRT1 | GTV | 70.0 | 65.9 | 2.20 | 67.3 | 73.5 |
| | Elective | 50.0 | 54.0 | 1.80 | 51.4 | 46.2 |

SIB-IMRT VS CONCOMITANT BOOST RT (CBRT) (MSKCC, 2006)

- ✗ Study period Sep 1998- Jun 2004
- ✗ N=293
- ✗ All were patients of Ca oropharynx (112 were stage III/IV).
- ✗ 41 received SIB-IMRT with concurrent chemotherapy
- ✗ 71 received conventional 2DRT with late concomitant boost (CBRT) along with concurrent chemotherapy
- ✗ RT dose was 70 Gy. Parotid dose constraint for IMRT was mean dose ≤ 26 Gy.
- ✗ Significant advantage in terms of PEG-dependancy & severe xerostomia at 2 years, in favour of IMRT.

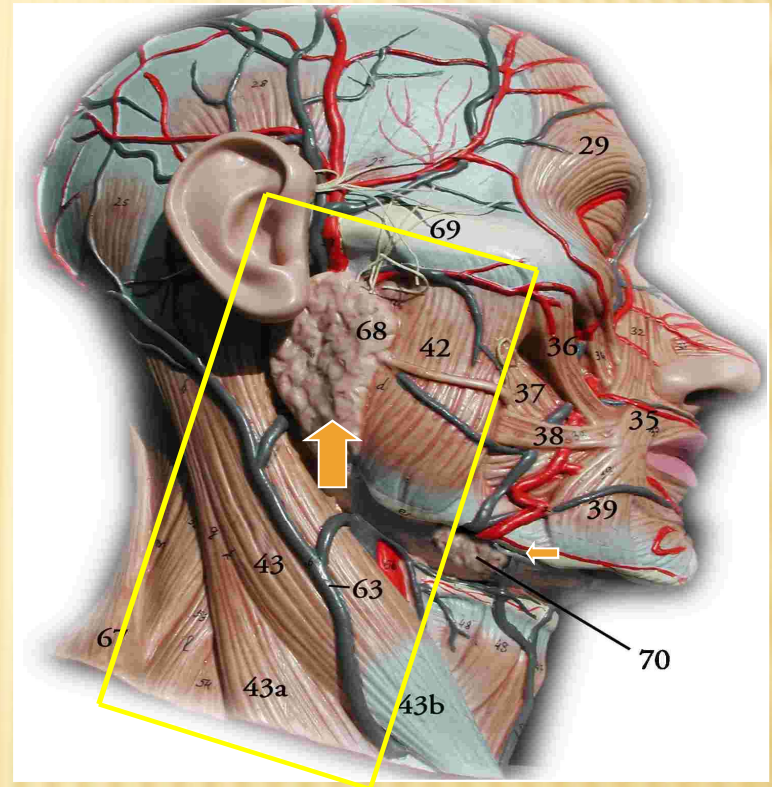
COMMON SIB DOSE SCHEDULES

- ✖ (1) 70 Gy/35# to PTV (GTV)
 - 63 Gy/35# to PTV (CTV1:high risk microscopic ds)
 - 54 Gy/35# to PTV (CTV2: low risk microscopic ds)

- ✖ (2) 66 Gy/30# to PTV (GTV)
 - 60 Gy/30# to PTV (CTV1:high risk microscopic ds)
 - 54 Gy/30# to PTV (CTV2: low risk microscopic ds)

CLINICAL IMPACT OF IMRT

✖ What happens to the parotid glands in Conventional RT?



PAROTID DOSE & XEROSTOMIA

- ✖ Eisbruch et al (1999): A mean parotid dose of < 26 Gy should be planning goal.
- ✖ Eisbruch et al (2007): Substantial parotid flow recovery (upto 86% of pretreatment levels) at 2 years if mean doses are between 25-30Gy.
- ✖ Eisbruch et al (2010): Severe xerostomia ($<25\%$ of baseline) avoided if mean parotid dose kept to <20 Gy (if one parotid is to be spared) or <25 Gy (if both are to be spared)

DOES PAROTID-SPARING IMRT HAVE A NEGATIVE IMPACT ON LOCAL CONTROL?

- ✗ Cannon & Lee (2008): (N=3) All patient had recurrence near a spared parotid gland.
- ✗ Eisbruch et al (2005): (N=158, all stage III/IV) 19/23 failures occurred in-field, within the high-dose volume. Suggest that clinical rather than dosimetric factors predicted outcome & suggested treatment intensification in these advanced cases.

SUBMANDIBULAR GLAND DOSE & XEROSTOMIA

- ✗ Xerostomia does not correlate with parotid doses alone.
- ✗ If submandibular gland doses are kept to $\leq 39\text{Gy}$, then also there is good recovery of salivary flow rates at 2 years.

CONSTRUCTOR DOSE & DYSPHAGIA

- ✗ Levendag et al (2007): Significant correlation between doses to superior and middle constrictors and incidence of severe dysphagia. Steep dose response curve, with 19% increase in probability with every 10Gy dose.
- ✗ Bhide et al (2009): No statistically significant correlation between radiation dose to the pharyngeal constrictors and observer-assessed/ patient-reported severe dysphagia at 1 year

IMRT : IMPACT ON QOL

- ✗ Evidence-based review by Nutting et al (2010):
- ✗ Significant heterogeneity in data.
- ✗ Conflicting results.

IS CONC CHEMO NECESSARY WITH SIB-IMRT?
IF REQUIRED, IS IT TOLERATED?

CHEMO: BED

HOW MUCH RADIATION IS THE CHEMOTHERAPY WORTH IN ADVANCED HEAD AND NECK CANCER?

MOHIT KASIBHATLA, M.D., JOHN P. KIRKPATRICK, M.D., PH.D., AND DAVID M. BRIZEL, M.D.

Department of Radiation Oncology, Duke University Medical Center, Durham, NC

Conclusions: Chemotherapy increases BED by approximately 10 Gy₁₀ in standard and modified fractionated radiotherapy, equivalent to a dose escalation of 12 Gy in 2 Gy daily or 1.2 Gy twice daily. Such an escalation could not be safely achieved by increasing radiation dose alone. © 2007 Elsevier Inc.

between increase in locoregional control (LRC) and increase in BED with modified vs. standard fractionated radiotherapy. The increase in LRC with chemoradiotherapy vs. radiotherapy alone, the BED of the radiotherapy-alone arms, and the “S” value were used to calculate the BED contribution from chemotherapy and the total BED of chemoradiotherapy from each study.

RTOG 00-22 (2010)

- ✗ N=69 (14 institutions)
- ✗ All patients of Ca oropharynx, stage T1-T2,N0-N1,M0
- ✗ No chemo was permitted
- ✗ RT dose was 66Gy/30# to PTV(gross disease) and 54-60Gy/30# to PTV (subclinical)
- ✗ Median FU=2.8 years
- ✗ 2-yr LRF was only 9%.
- ✗ Very low rate of severe (>grade 2) late toxicities: skin (12%), mucosa(24%). Xerostomia (grade 2) was seen in 55% patients at 6 months but reduced to 16% at 2 years
- ✗ Moderately hypofractionated IMRT without chemotherapy in early oropharyngeal carcinomas, is safe & well-tolerated.

**INTENSITY MODULATED RADIOTHERAPY IN THE TREATMENT
OF OROPHARYNGEAL CANCER: AN UPDATE OF THE MEMORIAL
SLOAN-KETTERING CANCER CENTER EXPERIENCE**

JEREMY SETTON, B.A.,*¹ NICOLA CARIA, M.D.,*¹ JONATHAN ROMANYSHYN, M.D.,*
LAWRENCE KOUTCHER, M.D.,* SUZANNE L. WOLDEN, M.D.,* MICHAEL J. ZELEFSKY, M.D.,*
NICHOLAS ROWAN, B.A.,* ERIC J. SHERMAN, M.D.,[†] MATTHEW G. FURY, M.D., PH.D.,[†]
DAVID G. PFISTER, M.D.,[†] RICHARD J. WONG, M.D.,[‡] JATIN P. SHAH, M.D.,[‡] DENNIS H. KRAUS, M.D.,[‡]
WEIJI SHI, M.S.,[§] ZHIGANG ZHANG, PH.D.,[§] KAREN D. SCHUPAK, M.D.,* DAPHNA Y. GELBLUM, M.D.,*
SHYAM D. RAO, M.D., PH.D.,* AND NANCY Y. LEE, M.D.*

**CONCURRENT CHEMOTHERAPY AND INTENSITY-MODULATED
RADIOTHERAPY FOR LOCOREGIONALLY ADVANCED LARYNGEAL AND
HYPOPHARYNGEAL CANCERS**

NANCY Y. LEE, M.D.,* WILLIAM O'MEARA, M.D.,* KELVIN CHAN, B.A.,*
CESAR DELLA-BIANCA, PH.D.,[†] JAMES G. MECHALAKOS, PH.D.,[†] JOANNE ZHUNG, B.A.,*
SUZANNE L. WOLDEN, M.D.,* ASHWATHA NARAYANA, M.D.,* DENNIS KRAUS, M.D.,[‡]
JATIN P. SHAH, M.D.,[‡] AND DAVID G. PFISTER, M.D.[§]

**INTENSITY-MODULATED RADIOTHERAPY IN POSTOPERATIVE TREATMENT OF
ORAL CAVITY CANCERS**

DANIEL R. GOMEZ, M.D.,* JOANNE E. ZHUNG, B.A.,* JENNIFER GOMEZ, B.A.,* KELVIN CHAN, B.A.,*
ABRAHAM J. WU, M.D.,* SUZANNE L. WOLDEN, M.D.,* DAVID G. PFISTER, M.D.,[†] ASHOK SHAHA, M.D.,[‡]
JATIN P. SHAH, M.D.,[‡] DENNIS H. KRAUS, M.D.,[‡] RICHARD J. WONG, M.D.,[‡] AND NANCY Y. LEE, M.D.*

-
- ✖ SIB-IMRT with conc chemotherapy is well-tolerated and effective for all common head-neck sites.
 - ✖ Trials included mostly locally advanced cases.
 - ✖ Locoregional failure rates are around 5-20%.
 - ✖ Overall survival rates are around 60-85%.
 - ✖ 2-yr severe xerostomia rates are around 0-30%.

IMRT IN HNC: THE EVIDENCE SO FAR

Lancet Oncol 2008; 9: 367–375

Evidence behind use of intensity-modulated radiotherapy: a systematic review of comparative clinical studies

Liv Veldeman, Indira Madani, Frank Hulstaert, Gert De Meerleer, Marc Mareel, Wilfried De Neve

2 Meta-analyses

Clinical Oncology 22 (2010) 643–657



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journal homepage: www.elsevier.com/locate/clon



Overview

A Review of the Clinical Evidence for Intensity-modulated Radiotherapy

J. Staffurth on behalf of the Radiotherapy Development Board¹

Cardiff University, Velindre Hospital, Whitchurch, Cardiff, UK

-
- ✘ 30 studies, including 3 RCTs so far comparing IMRT with conventional RT/3DCRT
 - ✘ Of the 3 RCTs, 2 are small studies on Nasopharyngeal cancer, from China.
 - ✘ The 3rd is the PARSPORT study from UK on oro-hypopharyngeal and laryngeal cancers.

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- ✖ Pow et al (n=51) : Stage II NPX: 2DRT vs IMRT: IMRT significantly increased xerostomia-related but not overall HRQoL.
 - ✖ Kam et al (n=60): Stage I & II NPX: 2DRT vs IMRT: IMRT significantly reduced the clinician-assessed (but not the patient reported!!) grade 2-4 xerostomia at both 6 weeks and 12 months.

PARSPORT

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

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Methods—We undertook a randomised controlled trial between Jan 21, 2003, and Dec 7, 2007, that compared conventional radiotherapy (control) with parotid-sparing IMRT. We randomly assigned patients with histologically confirmed pharyngeal squamous-cell carcinoma (T1–4, N0–3, M0) at six UK radiotherapy centres between the two radiotherapy techniques (1:1 ratio). A dose of 60 or 65 Gy was prescribed in 30 daily fractions given Monday to Friday. Treatment was not masked. Randomisation was by computer-generated permuted blocks and was stratified by centre and tumour site. Our primary endpoint was the proportion of patients with grade 2 or worse xerostomia at 12 months, as assessed by the Late Effects of Normal Tissue (LENT SOMA) scale. Analyses were done on an intention-to-treat basis, with all patients who had assessments included. Long-term follow-up of patients is ongoing. This study is registered with the International Standard Randomised Controlled Trial register, number ISRCTN48243537.

Lancet Oncol. 2011 February ; 12(2): 127–136.

Findings—47 patients were assigned to each treatment arm. Median follow-up was 44.0 months (IQR 30.0–59.7). Six patients from each group died before 12 months and seven patients from the conventional radiotherapy and two from the IMRT group were not assessed at 12 months. At 12 months xerostomia side-effects were reported in 73 of 82 alive patients; grade 2 or worse xerostomia at 12 months was significantly lower in the IMRT group than in the conventional radiotherapy group (25 [74%; 95% CI 56–87] of 34 patients given conventional radiotherapy vs 15 [38%; 23–55] of 39 given IMRT, $p=0.0027$). The only recorded acute adverse event of grade 2 or worse that differed significantly between the treatment groups was fatigue, which was more prevalent in the IMRT group (18 [41%; 99% CI 23–61] of 44 patients given conventional radiotherapy vs 35 [74%; 55–89] of 47 given IMRT, $p=0.0015$). At 24 months, grade 2 or worse xerostomia was significantly less common with IMRT than with conventional radiotherapy (20 [83%; 95% CI 63–95] of 24 patients given conventional radiotherapy vs nine [29%; 14–48] of 31 given IMRT; $p<0.0001$). At 12 and 24 months, significant benefits were seen in recovery of saliva secretion with IMRT compared with conventional radiotherapy, as were clinically significant improvements in dry-mouth-specific and global quality of life scores. At 24 months, no significant differences were seen between randomised groups in non-xerostomia late toxicities, locoregional control, or overall survival.

OTHER STUDIES IN ORAL/OROHYPOPHARYNGEAL/LARYNGEAL CANCERS

- ✖ 15 non-randomised studies: IMRT (n=959) vs 2DRT/3DCRT (n=1455)
- ✖ All report reduced acute & late xerostomia, leading to better xerostomia- HR QoL
- ✖ 2 studies have reported statistically significant improvements in tumor control.

PROSPECTIVE ASSESSMENT OF PATTERNS OF FAILURE AFTER HIGH-PRECISION DEFINITIVE (CHEMO)RADIATION IN HEAD-AND-NECK SQUAMOUS CELL CARCINOMA

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- ✖ Siemens trial (3DCRT vs IMRT)
- ✖ N=60
- ✖ The aim was to analyse location of site of locoregional failure and their dose-volume correlation
- ✖ It was found that the majority of failures (75%) were within the high-dose volume & only 25% were marginal.

NASOPHARYNGEAL CARCINOMA IN CHILDREN: COMPARISON OF CONVENTIONAL AND INTENSITY-MODULATED RADIOTHERAPY

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- ✗ IMRT led to significant improvements in acute grade 3 toxicities of skin, mucous membrane & pharynx
- ✗ IMRT also led to significant delayed progress to grade 2 toxicity in the above sites
- ✗ Mean dose to the target also significantly improved with IMRT compared to conv RT

ONGOING/ UNPUBLISHED RCTS OF IMRT IN HNC

| Study name | Principle research question | Number of patients | Status | Trial sponsor | Code |
|---|---|--------------------|-----------------------|--|-----------------|
| Study of three-dimensional conformal radiotherapy vs intensity-modulated radiotherapy for squamous cell carcinoma of the head and neck | Phase II RCT of 3DCRT versus IMRT | 60 | Active not recruiting | Tata Memorial Hospital, India | NCT 00652613 |
| A multicentre randomised study of cochlear sparing intensity-modulated radiotherapy versus conventional radiotherapy in patients with parotid tumours (COSTAR) | Phase III RCT of 3DCRT versus IMRT | 84 | Recruiting | Institute of Cancer Research, UK | ISRCTN 81772291 |
| IMRT plus cisplatin versus conventional radiotherapy plus cisplatin in stage III–IV HNSCC | Phase III RCT of dose-escalated IMRT versus standard dose 3DCRT | Not stated | Recruiting | Group Oncologie Radiotherapie, France | NCT 00158678 |
| Radiation therapy and cisplatin with or without cetuximab in treating patients with stage III or stage IV head and neck cancer | Phase III RCT of concurrent accelerated chemoradiation with or without cetuximab, stratified for use of IMRT | 720 | Recruiting | RTOG; NCI, USA | NCT 00265941 |
| A phase III study of standard fractionation radiotherapy with concurrent high-dose cisplatin versus accelerated fractionation radiotherapy with panitumumab in patients with locally advanced stage III and IV squamous cell carcinoma of the head and neck | Phase III RCT of standardly fractionated chemoradiation versus accelerated panitumumab–radiotherapy, stratified for use of IMRT | Not stated | Recruiting | Princess Margaret Hospital; NCIC, Canada | NCT 00820248 |
| Late-course accelerated hyperfractionated IMRT for locoregionally advanced nasopharyngeal carcinoma | Phase II/III RCT of conventionally fractionated versus late-course accelerated hyperfractionated IMRT | Not stated | Recruiting | Guangxi Medical University, China | NCT 00778908 |

IMRT: VARIATIONS

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- ✖ IMRT is not a magic- box & there is no single right answer.
 - ✖ Hence, as before, the treatment methods and results remain very much dependant on the physician's approach.
 - ✖ Almost every area of IMRT planning sees significant variation in approach between any 2 clinicians.

- ✗ Dose levels: 2/3
- ✗ Dose prescription technique: to 2-3 different PTVs OR different levels to GTV, CTV, PTV
- ✗ Boost technique: SIB/sequential
- ✗ Dose to electively irradiated nodes : 50 & 60Gy/ uniformly 50 Gy/ uniformly 60 Gy
- ✗ Spinal cord constraint parameter: max/ 1%/2%/ 1cc/2cc
- ✗ (ICRU 83 recommends reporting all OARs on $D_{2\%}$)
- ✗ Spinal cord dose constraint : 45/47/48/50 Gy
- ✗ Parotid constraint parameter: whole parotid/ (parotid-PTV)

PATTERN OF CARE SURVEY IN HEAD & NECK CANCER

JYOTIRUP GOSWAMI & SUMAN MALLIK (AROICON 2011)

- ✦ **Aims & objectives:** As new paradigms and techniques emerge and older ones are eclipsed in the treatment of head and neck cancer, it is important to gauge attitudes and approaches in the Radiation Oncology community. This study was an attempt to objectively analyse a few subjective but highly crucial issues relating to practice in head and neck cancers.
- ✦ **Materials & methods:** Keeping constraints of time and convenience in mind, a brief questionnaire comprising 20 key questions was framed and circulated by email to radiation oncologists of Consultant rank across India, in both government and corporate sectors, between June 2011-August 2011. The questions related to diagnosis, radiotherapy planning, chemotherapy protocol, supportive care, follow up and management of post-radiotherapy recurrences. Responses were collated and analysed

- ✖ % of patients undergoing Triple scopy for staging: (a) 0-20 (b) 20-40 (c) 40-60 (d)>60
- ✖ % of patients undergoing PET-CT for staging: (a) 0-20 (b) 20-40 (c) 40-60 (d)>60
- ✖ Indication for Induction chemotherapy for oropharyngeal/hypopharyngeal/laryngeal cancers: (a) stage II onwards (b) stage III onwards (c) only stage IV (d) not considered
- ✖ Induction chemotherapy regime & no of cycles: (a) TPFx3 (b) PFX3 (c) TIPx3 (d) Others --
- ✖ **Spinal cord tolerance parameter:** (a) Max dose (b) 1% volume (c) 1cc volume (d) 2cc volume
- ✖ **Spinal cord tolerance dose (Gy):-**
- ✖ **Parotid dose constraints for IMRT:** (a) Average dose to whole parotid <26 Gy (b) Dose received by 50% of Whole parotid <30 Gy (c) Average dose to (Whole parotid-PTV) <26 Gy (d) Dose received by 50% of (Whole parotid-PTV) <30 Gy (e) Average dose to whole parotid <20 Gy
- ✖ % of patients on IMRT: (a) 0-30% (b) 30-50% (c) >50%
- ✖ **IMRT fractionation:** (a) Conventional (b) SIB
- ✖ **SIB-IMRT dose levels: ----**
- ✖ PET-CT based RT planning: (a) Yes (b) No
- ✖ Routine counselling for PEG tube insertion before RT: (a) Yes (b) No
- ✖ Routine Triple scopy for follow-up: (a) Yes (b) No
- ✖ Routine Imaging for follow-up: (a) Yes (b) No
- ✖ Imaging modality for follow-up: (a) CT (b) MR (c) PET-CT
- ✖ Preferred management of locoregional recurrence post-radiotherapy: (a) Surgery alone (b) Surgery + systemic therapy (c) Reirradiation
- ✖ Preferred chemotherapy regime for locoregional recurrence: (a) Platinum (b) Taxane-Platinum doublet (c) Others---
- ✖ Preferred biologically targeted agent for locoregional recurrence: (a) Cetuximab (b) Nimotuzumab (c) Others---
- ✖ Reirradiation safeguard: (a) >6 months (b) >2 years (c) Other---
- ✖ Reirradiation dose: (a) 40-50 Gy (b) 50-60 Gy (c) > 60 Gy

- ✘ **Results:** Out of 80 emails sent, only 25 (31.25%) responded.
- ✘ Most clinicians (68%) were still using maximum dose as spinal cord tolerance dose parameter and the preferred threshold, in 52% was 44-46Gy.
- ✘ Majority of clinicians (68%) were using intensity modulated radiotherapy (IMRT) in fewer than 30% of cases.
- ✘ Most (68%) were using simultaneous integrated boost as preferred IMRT schedule.

- ✘ **Conclusions:** While the study is a work in progress, it underlines the importance of good communication and evidence-based approaches.

THANK YOU
