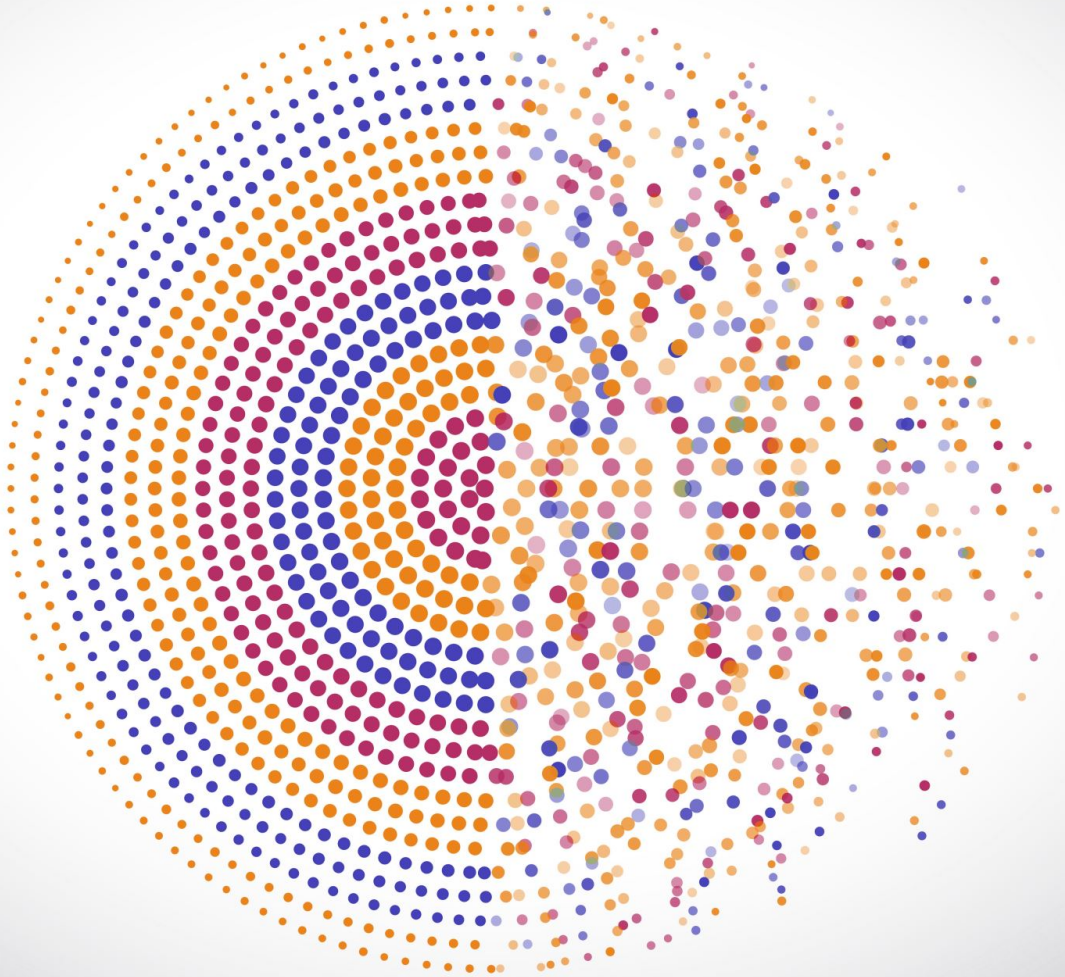
PROTON PLAN EVALUATION: HOW TO ‘BRAGG’ ABOUT A PERFECT PLAN

Dr Sapna Nangia



DOSE RESPONSE RELATIONSHIP

Established

- Medulloblastoma
- Nasopharynx
- Head neck cancer – dose intensity of chemotherapy , acceleration of treatment
- Adding a boost for breast cancer
- Liver
- Cervix
- Prostate

Controversial / Absent / Under investigation

- Lung
- Oesophagus
- Rectum
- Pancreas

Influence of Late Side-Effects Upon Daily Life After Radiotherapy for Laryngeal and Pharyngeal Cancer

Anders B. Jensen, Olfred Hansen, Karsten Jørgensen & Lars Bastholt

Pre IMRT era1994, Odense

All exerienced side-effects during the treatment period, spontaneously mentioned by the patient. Number of patients with percentages in parentheses

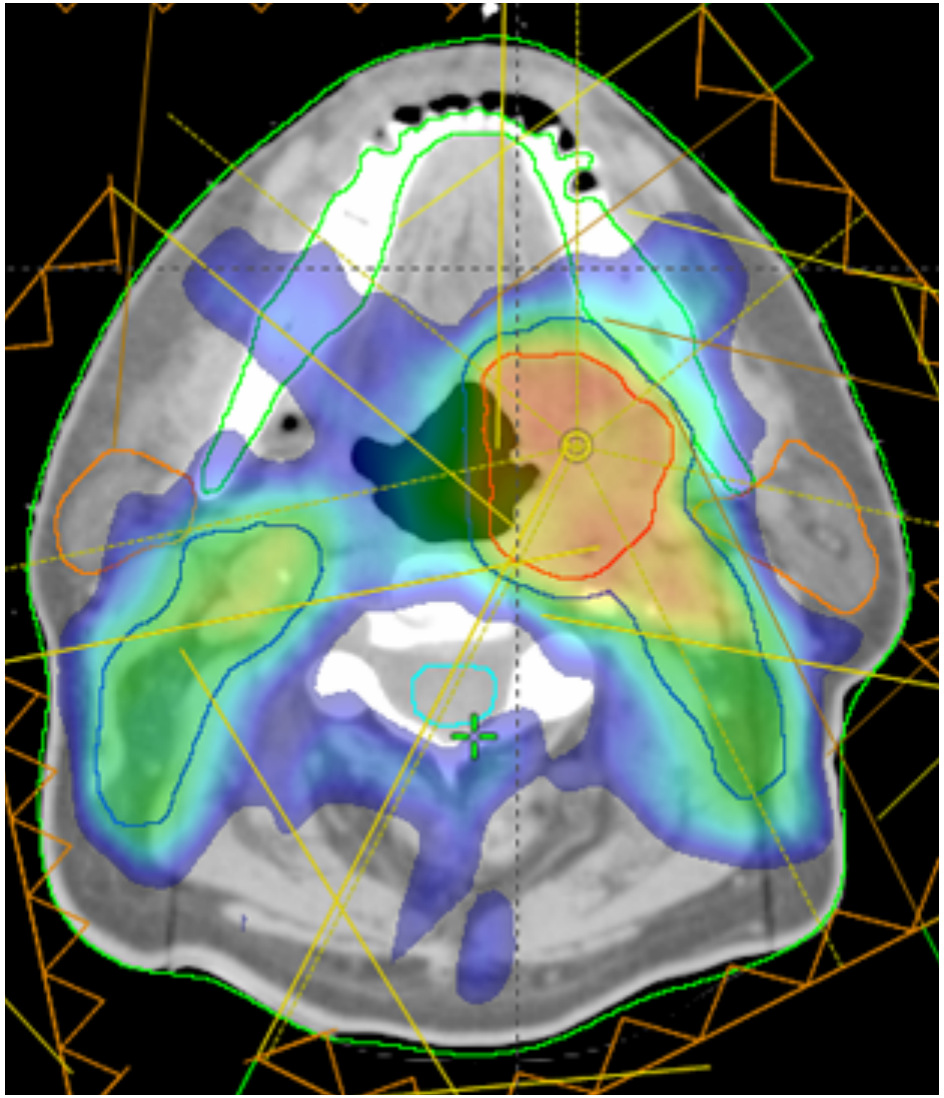
Problem	Laryngeal cancer	Pharyngeal cancer	Total %
Xerostomia	6(22)	12(75)	18(42)
Tiredness	6(22)	10(63)	16(37)
Taste change	2(7)	12(75)	14(33)
Psychological problems	6(22)	4(25)	10(24)
Pain	5(19)	5(31)	10(23)
Skin problems	1(4)	2(13)	10(23)
Weightloss	0	8(50)	8(19)
Voice problems	5(19)	2(13)	7(16)
Loathing for food	1(4)	4(25)	5(12)
Problems with swallowing	4(15)	1(6)	5(12)
Vomiting	0	3(19)	3(7)
Problems with teeth	1(4)	2(13)	3(7)
Hearing	0	3(7)	3(7)
Problems with swallowing the trial medicine	1(4)	2(13)	3(7)
Transport to hospital	2(7)	2(13)	4(9)
Other**	6(22)	8(50)	14(23)

* $p < 0.05$ for the group with laryngeal cancer vs pharyngeal cancer.
** Expectorations, eating problems, balance, hairloss, coughing.

All late side-effects related to treatment at follow-up, spontaneously mentioned by the patients. Number of patients with percentages in parentheses

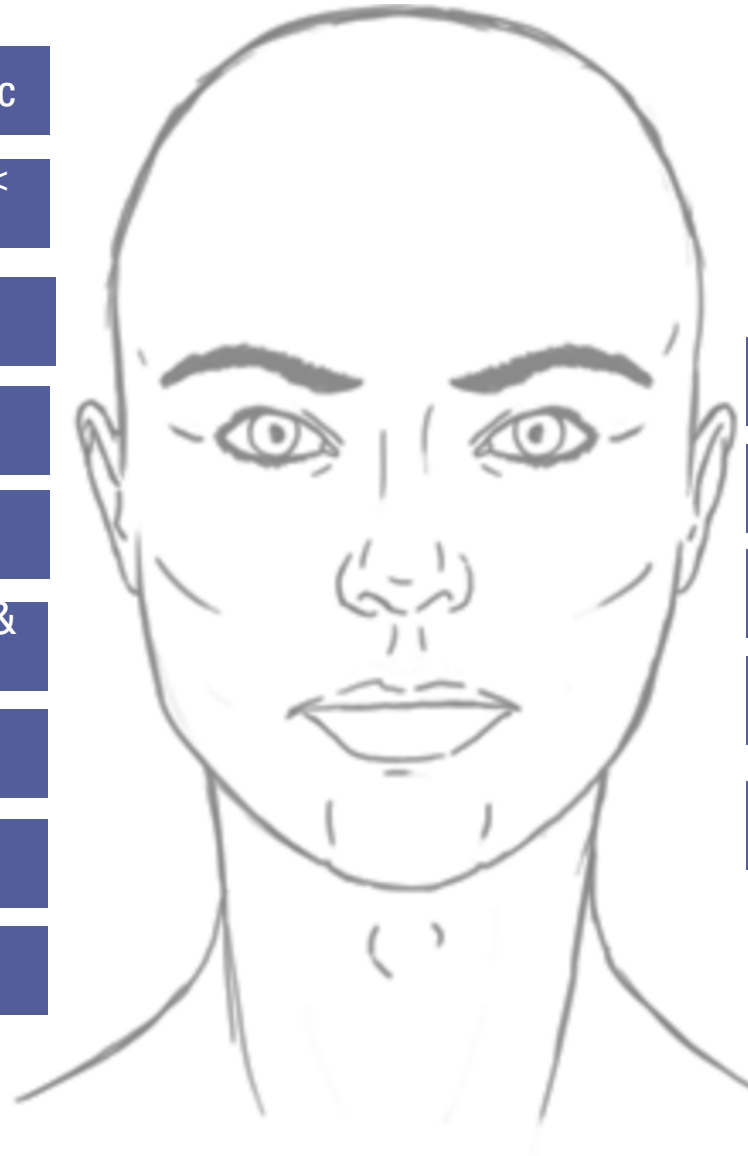
Problem	Langyngeal cancer	Pharyngeal cancer	Total %
Xerostomia	4(15)	15(94)	19(44)
Voice	10(37)	1(6)	11(26)
Taste change	1(4)	3(19)	4(9)
Teeth	0	4(25)	4(9)
Pain	2(7)	1(6)	3(7)
Eating problems	3(11)	0	3(7)
Others**	3(11)	2(13)	5(12)

* $p < 0.05$ for the group of patients with laryngeal vs pharyngeal cancer.
** Psychological problems, balance, coughing, skin problems, hairloss

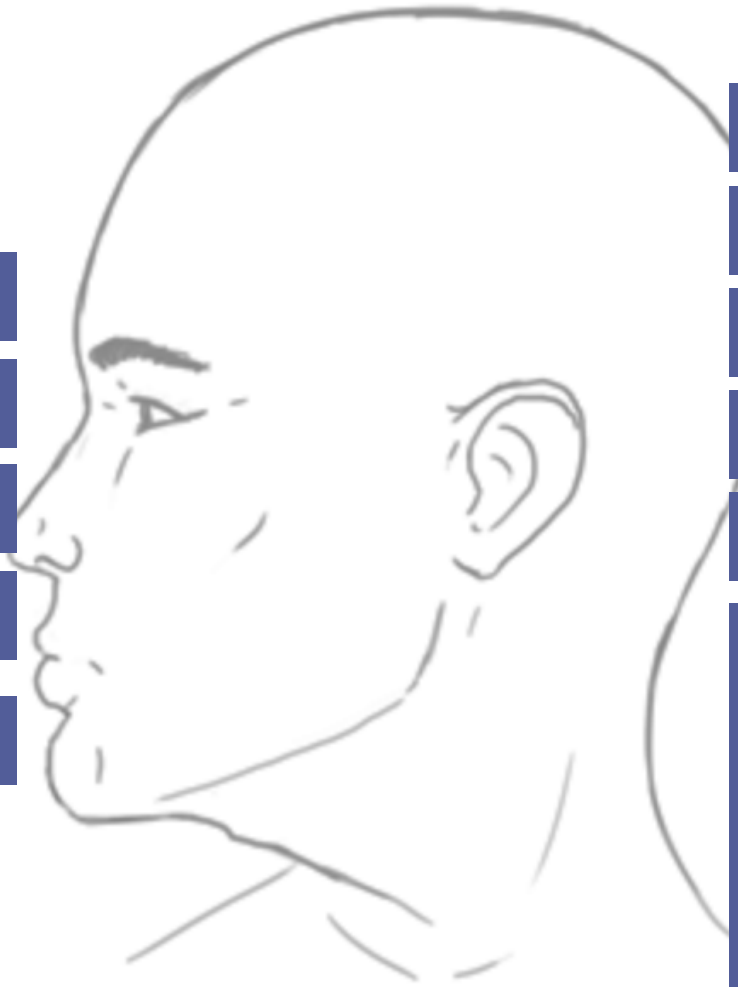


Apollo PROTON Cancer Centre

- Scalp 30 Gy < 1cc
- Eyebrow 30 Gy < 1cc
- Hippocampus D40% <,7.3Gy (EQD@)
- Temporal lobe
- Pterygoids and masseter
- Buccal mucosa & Lips
- Mandible
- Larynx
- Thyroid



- Optic neural structures
- Lacrimal Gland
- Lens
- Retina
- Skin & skin fold



- Whole Brain
- Pituitary
- Brainstem
- Cochlea
- Spinal Cord

DARS
Base of tongue
Sup constrictors
Mid constrictors
Inf Constrictors
Supraglottic
Larynx
Cricopharynx

Dose to tumour impacts control rates
Dose to OARs impacts physical functioning, and symptoms, cognitive, social and role function, and global QOL .

IMPACT OF DOSE TO OAR

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 77, No. 4, pp. 974–979, 2010

0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2009.06.025

CLINICAL INVESTIGATION Brain

FACTORS INFLUENCING NEUROCOGNITIVE OUTCOMES IN YOUNG PATIENTS WITH BENIGN AND LOW-GRADE BRAIN TUMORS TREATED WITH STEREOTACTIC CONFORMAL RADIOTHERAPY

ORIGINAL ARTICLE

Heart Dose Is an Independent Dosimetric Predictor of Overall Survival in Locally Advanced Non-Small Cell Lung Cancer

Christina K. Speirs, MD, PhD,[a] Todd A. DeWees, PhD,[a] Sana Rehman, MD,[a]

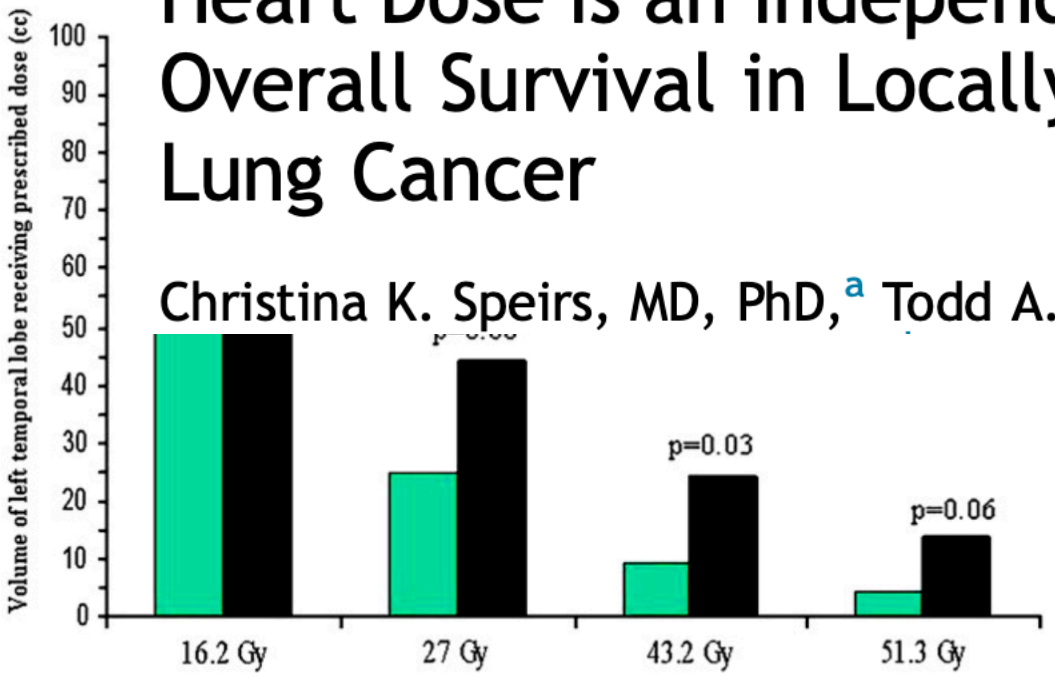


Fig. 1. Intelligence quotient (IQ) decline with respect to radiotherapy doses to left temporal lobe.

Variable	Odds ratio	confidence interval)
Age <15 y	13.58	0.041 (1.1–166.42)
13% temporal lobe receiving >43.2 Gy (80% of the prescribed dose)	7.57	0.048 (1.02–56.16)

<23% left temporal lobe to receive 27 Gy

IMPACT OF DOSE TO OAR

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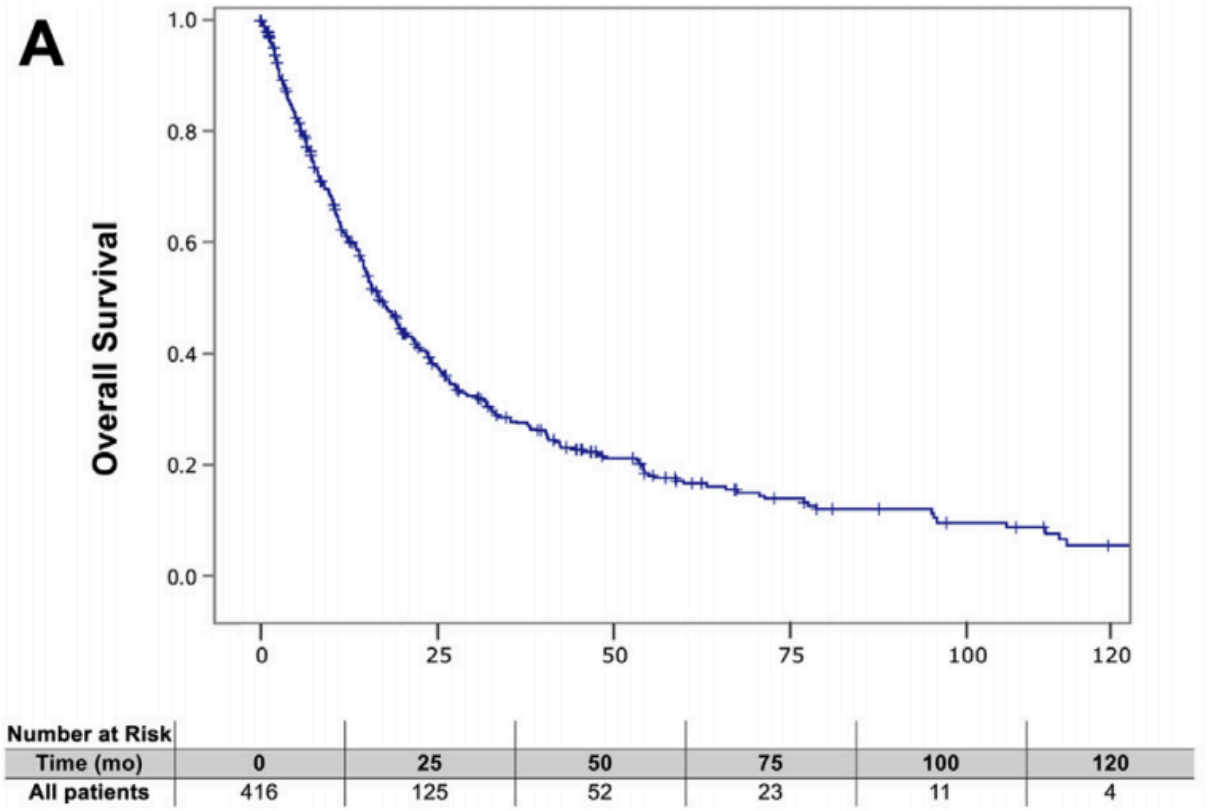
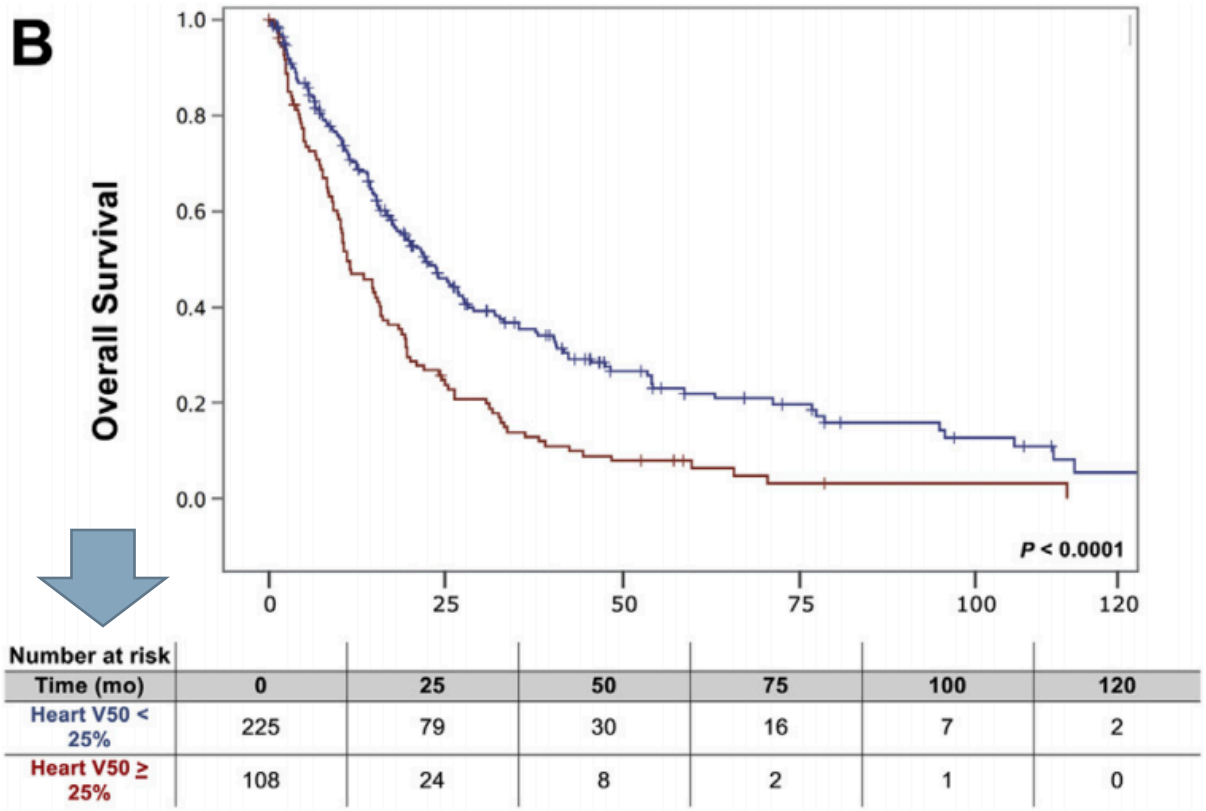
Journal of Thoracic Oncology *Vol. 12 No. 2: 293-301*

OS @ 1 yr 61%, @ 2 yrs 38%

OS @ 1 yr if V50Gy< 25% - 70.2% vs 46.8% if V50 Gy > 25%

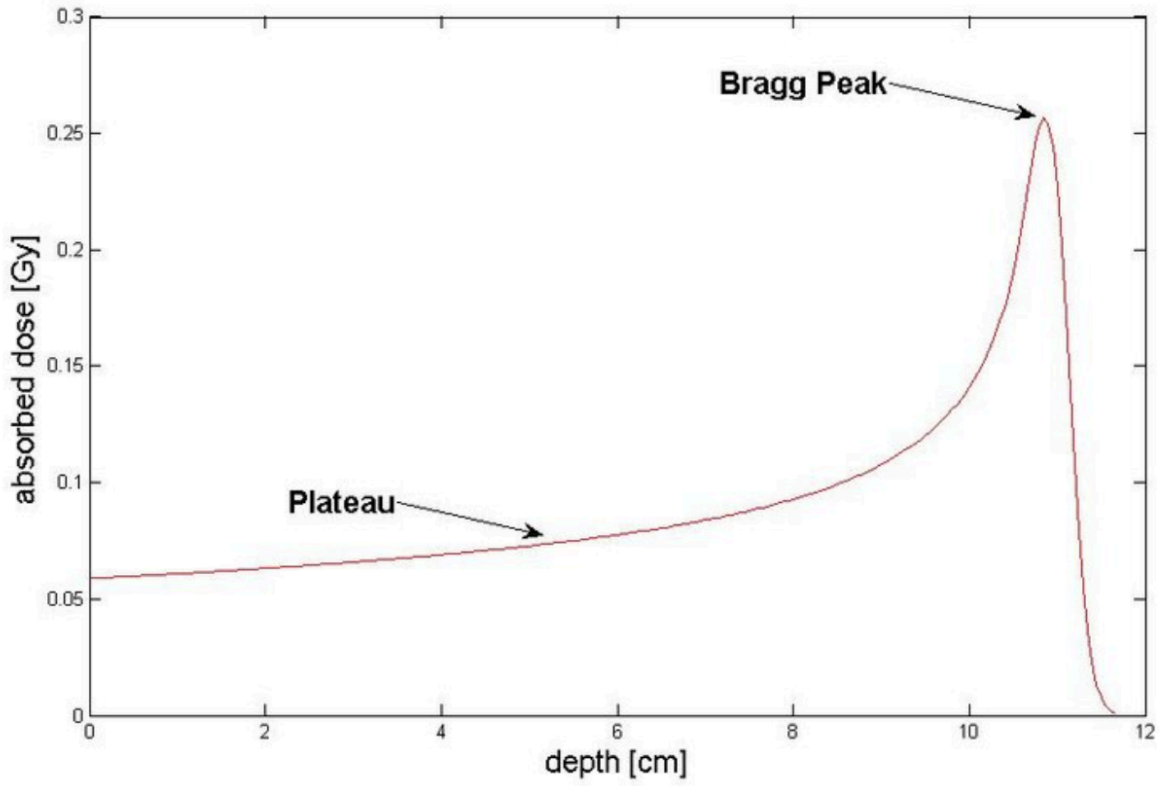


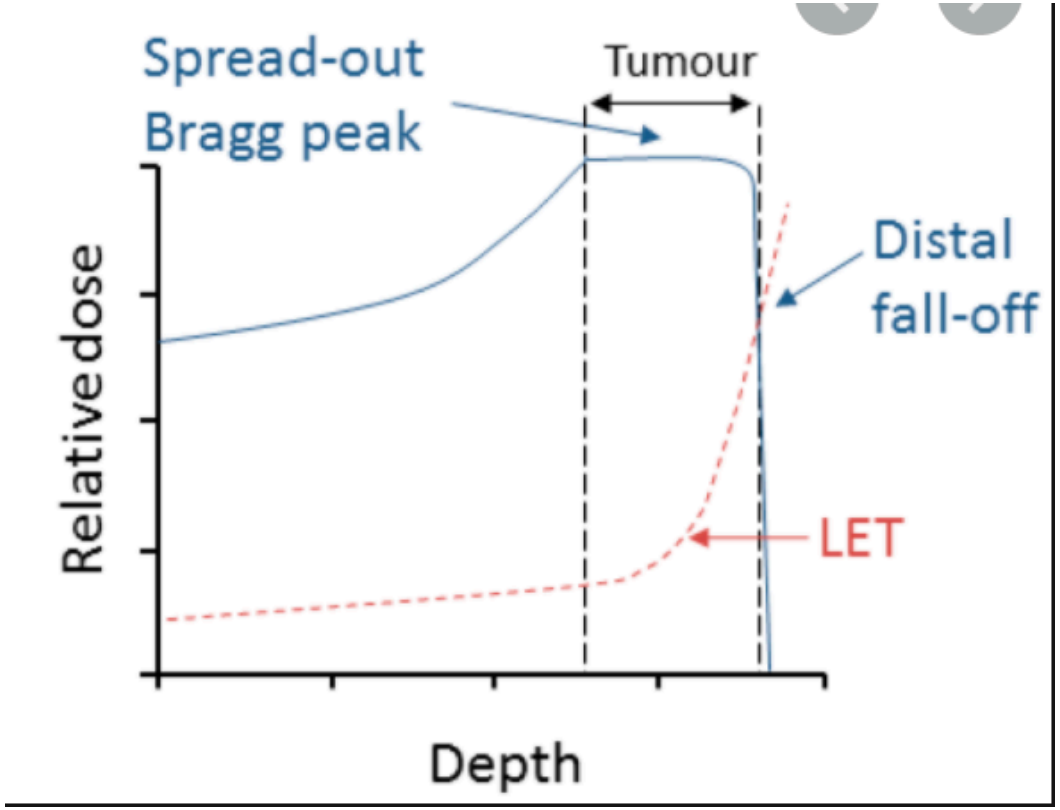
Number at Risk						
Time (mo)	0	25	50	75	100	120
All patients	416	125	52	23	11	4



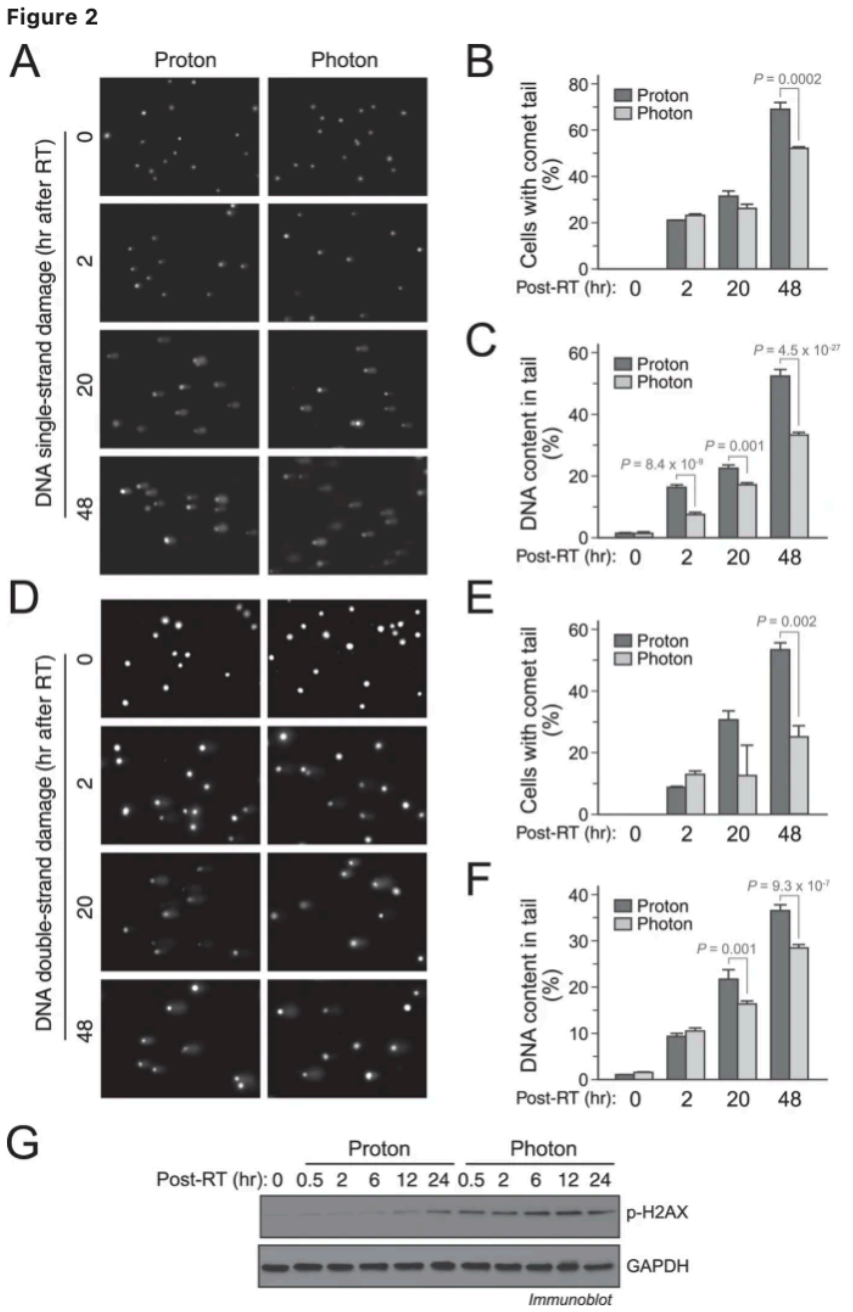
Number at risk						
Time (mo)	0	25	50	75	100	120
Heart V50 < 25%	225	79	30	16	7	2
Heart V50 ≥ 25%	108	24	8	2	1	0

The Bragg peak





DNA damage & repair,



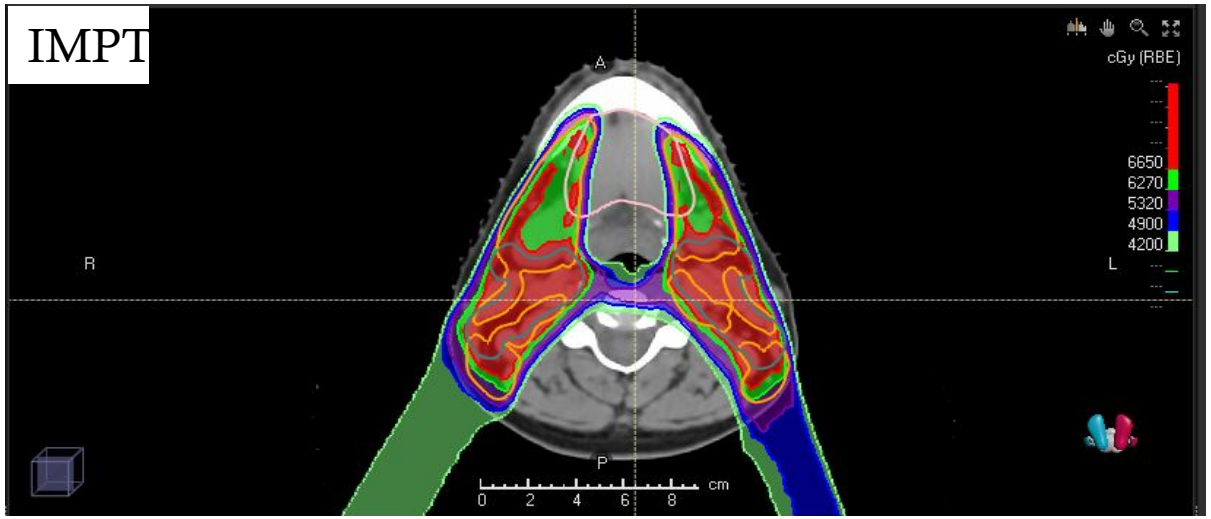
Mitteer et al *Sci Rep* **5**, 13961 (2015).

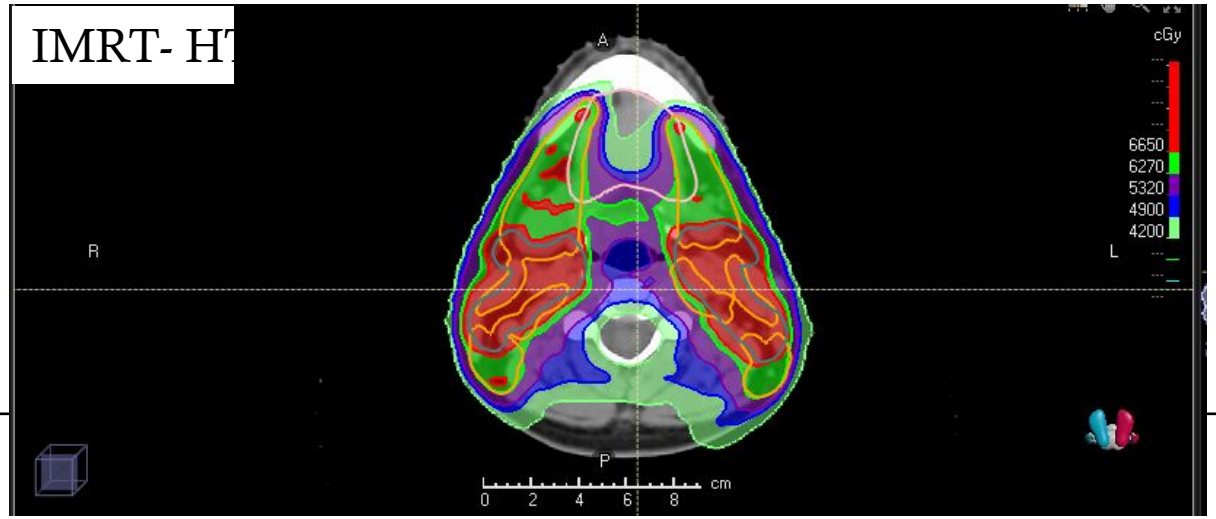
NASOPHARYNGEAL CANCER

- 41 years/ Male,
- No co-morbidities, No addictions, No significant family history
- Decreased hearing in the right year since last 6 months, insidious in onset and gradually progressive.
- Heaviness in the right eye gradually progressing and hindering in movement of the eye and causing diplopia since last 2 months.
- History of occasional nasal bleeding

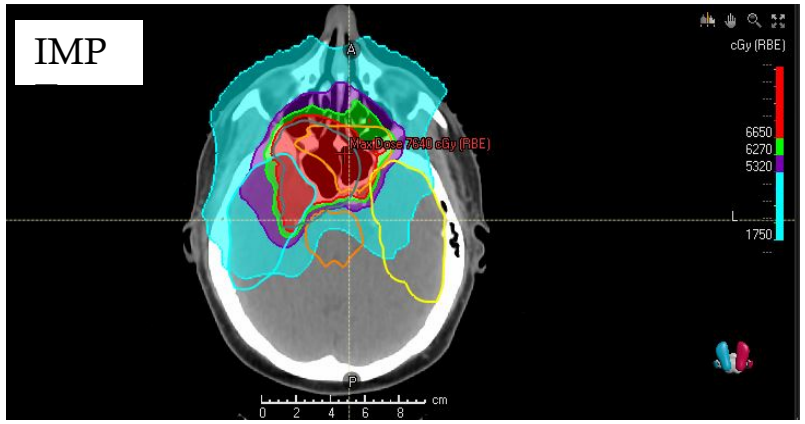
- MRI Brain (19.02.20) – Moderately enhancing altered signal intensity in the right cavernous sinus and meckel's cave with infratemporal extension via foramen ovale / lacerum and into pteryo-palatine fossa, right parapharyngeal space and nasopharynx.
- Biopsy from the cavernous sinus lesion (27.02.20) - Nasopharyngeal carcinoma, Raygaud pattern.
- PET CT scan (28.02.20) – FDG avid thickening in the posterior and right lateral wall of the nasopharynx effacing the fossa of rosenmuller with extension into the right medial pterygoid muscle.extension into the carotid canal and right cavernous sinus region encasing the intrapetrous and the intracavernosal segments of the right ICA. Prominent right retropharyngeal LN. enlarged bilateral cervical level II LN
- Visual Peripheral field analysis revealed constriction of vision on the right temporal side.
- Started on neoadjuvant chemotherapy (NACT) (TPF based), received 3 cycles LD 22.04.20

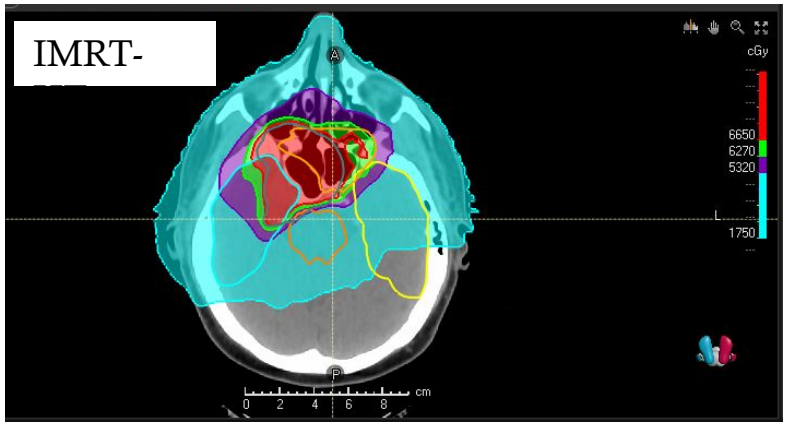
IMPT VS IMRT PLAN COMPARISON (HIGHER ISO-DOSE)

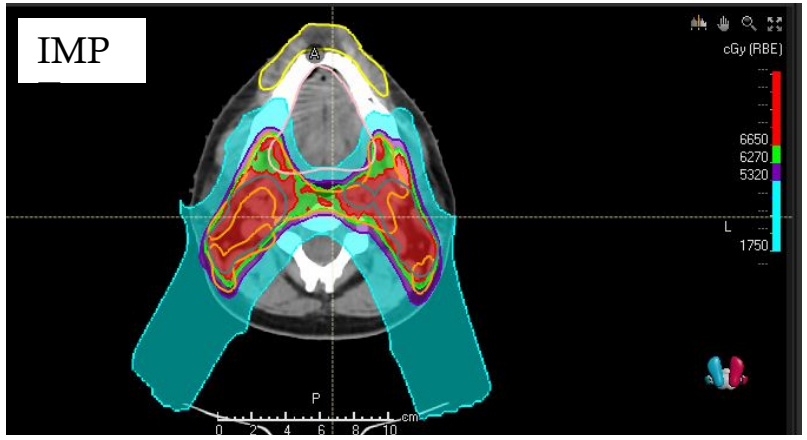


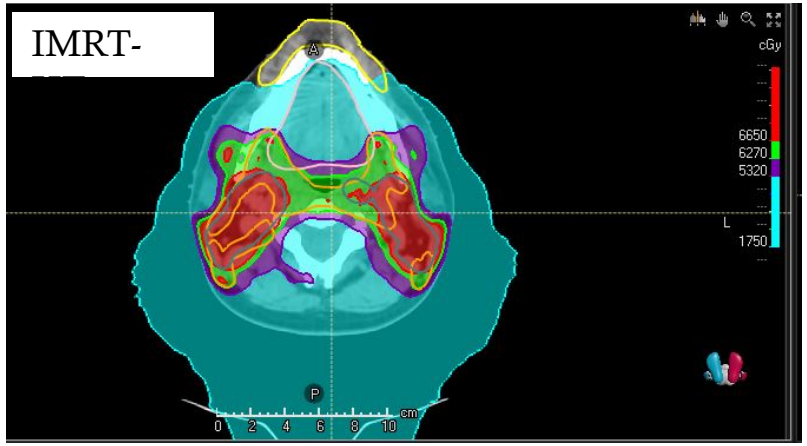


IMPT VS IMRT PLAN COMPARISON (LOWER ISO-DOSE)









IMPT VS IMRT PLAN - DOSE STATISTICS

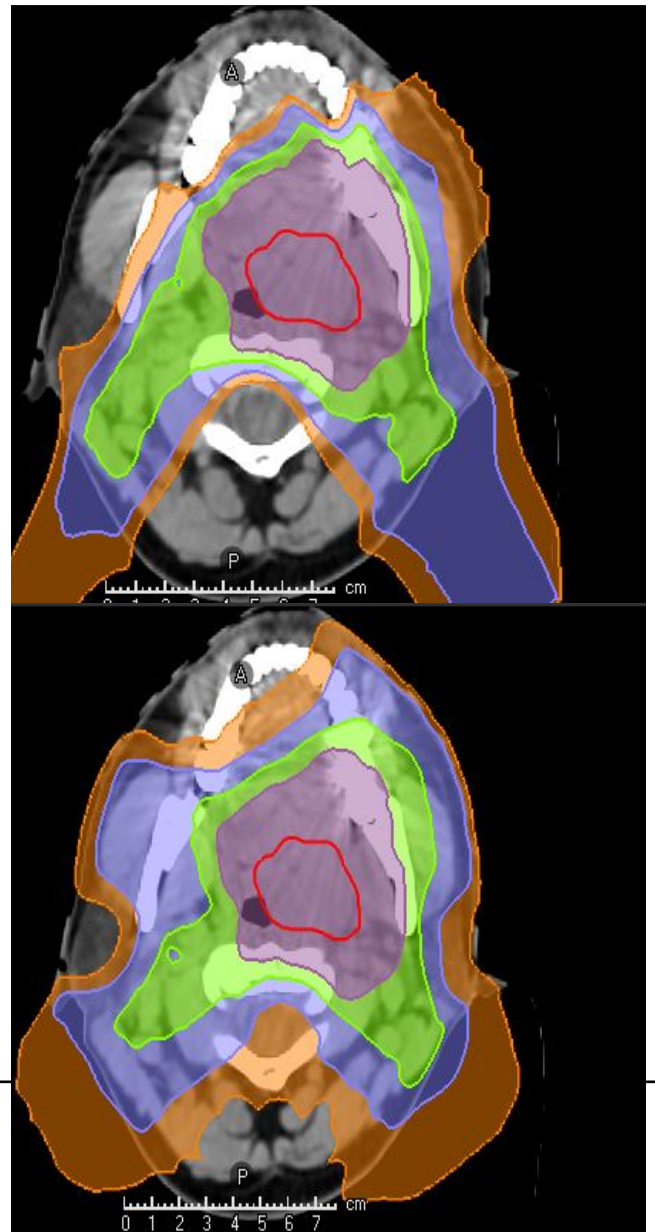
OAR doses	IMPT dose in GyE	IMRT dose in Gy	Comparison
Brainstem (Dmax)	51.77	55.30	6.3 % decrease in dose
Temporal Lobe (Dmean)	9.23(Left) 19.85 (Right)	15.68 (Left) 25.52 (Right)	41.1 % decrease in dose 22.2% decrease in dose
Hippocampus (Dmean)	3.20 (Left) 13.11 (Right)	8.45 (Left) 19.13 (Right)	62.1% decrease in dose 31.4% decrease in dose
Hippocampus (Dmax)	17.22 (Left) 48.75 (Right)	18.37 (Left) 55.71 Right)	6.2% decrease in dose 12.4% decrease in dose
Eye (Dmean)	7.20 (Left) 6.85 (Right)	7.45 (Left) 6.67 (Right)	3.3% decrease in dose 2.6 % increase in dose
Optic nerve Rt (Dmax)	44.91	52.58	14.5 % decrease in dose
Optic Chaism (Dmax)	48.27	48.09	0.3 % increase in dose

IMPT VS IMRT PLAN - DOSE STATISTICS

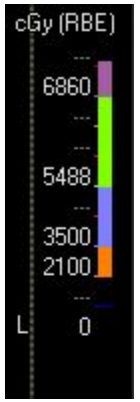
OAR doses	IMPT (GyE)	IMRT (Gy)	Comparison
Parotid (Dmean)	21.99 (Left) 21.40 (Right)	30.67 (Left) 31.45 (Right)	28.3 % decrease in dose 31.9 % decrease in dose
Oral cavity (Dmean)	33.14	47.15	29.7 % decrease in dose
Mandible (Dmean)	40.28	45.19	10.8 % decrease in dose
Larynx (Dmean)	27.73	43.89	36.8 % decrease in dose
Midline mucosa (Dmean)	35.23	46.24	23.8 % decrease in dose
Spinal Cord (Dmax)	23.36	37.56	37.8 % decrease in dose

PATIENT REPORTED OUTCOMES – BETTER IN OROPHARYNGEAL CANCER

- 39 years, Male complaints of foreign body sensation for 3 weeks and difficulty in swallowing & swelling over left upper neck of one week duration
- FNAC from left cervical lymph node-Atypical cells, suggestive of squamous cell carcinoma.
- Left tonsillar biopsy - Moderately differentiated Squamous cell carcinoma, keratinizing type (IHC for p16-Positive).
- PETCT done showed increased uptake in left tonsil and left lateral wall of oropharynx of size 3x2.8x4cm (SUV 13) with minimal extension into left parapharyngeal space. Left level II node seen 2.6x2.4cm (SUV 12)
- On examination-Proliferative growth seen over tonsillar bed, anterior tonsillar pillar and posterior tonsillar pillar and superiorly extending short of the base of uvula. Neck-Mobile left level II node 2x2 cm.



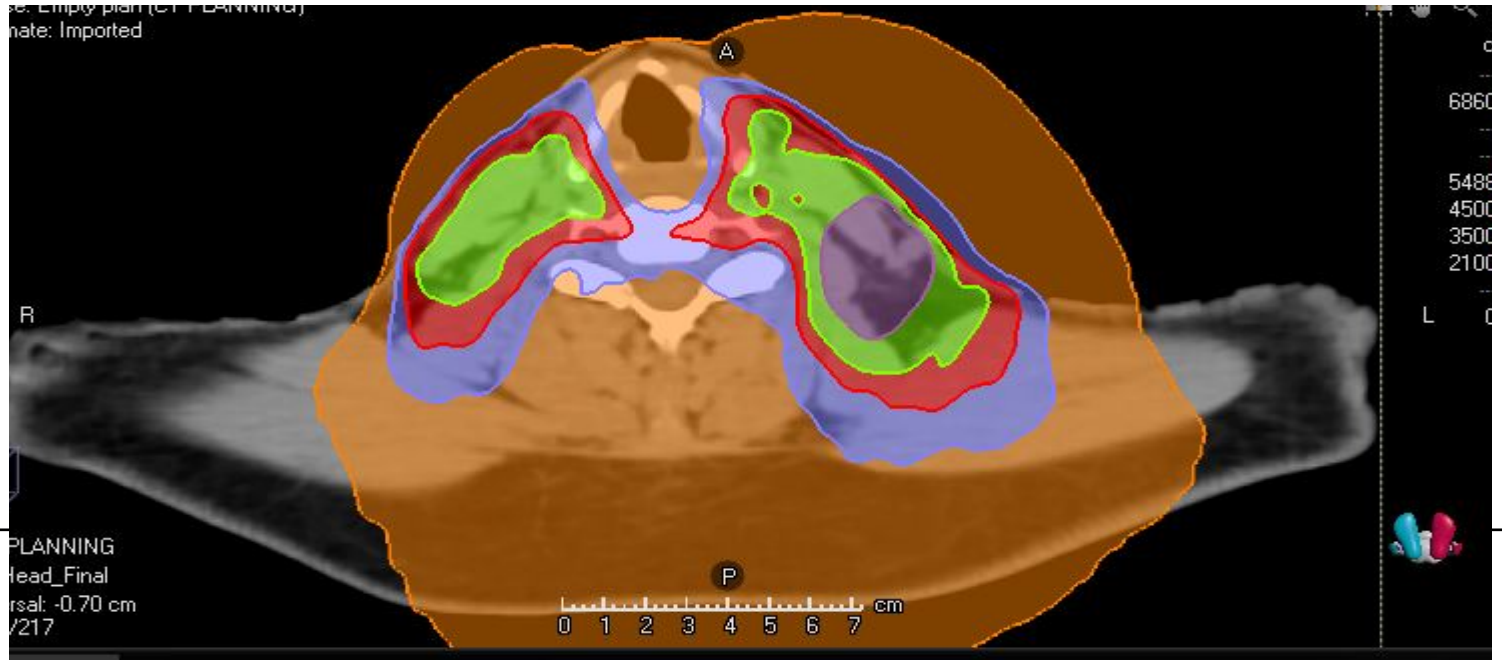
PROTON



TOMOx

PROTON

TOMOTHERAPY



OAR	Proton (GyE)	Tomo (Gy)	Difference (%)
Brain stem D1cc	39.1	45.2	13.5
Spinal cord D1cc	16.8	36.6	54.1
Lips Mean dose	21.8	43.2	49.5
Oral cavity Mean dose	40.1	49.0	18.2
Larynx Mean dose	41.2	46.6	13.1
Mandible mean dose	34.9	44.8	22.1
Midline mucosa mean dose	47.8	53.1	9.9
Constrictors mean dose (Outside PTV)	38.4	43.8	12.3
Prescription dose covering 98% of the volume (D98) in CTV 70	69.3	69.3	
Prescription dose covering 98% of the volume (D98) in CTV 56	55.8	55.5	

STEPS FOR PLANNING – SALIENT DIFFERENCES

- Account for uncertainties
- The concept of robust optimization
- Difference in motion management strategies
- Close monitoring

STEPS FOR PLANNING – WHAT IS DIFFERENT - I

- Immobilisation
  - Attention to beam path/length/number
  - Attention to replicability
  - Attention to CT stopping power of accessories
  - Attention to proximity of nozzle & range shifter
  - Requirement of respiratory management
  - Standard delineation of scars, drain sites etc.
- Imaging
  - Avoid contrast
  - Pay attention to artefacts
    - SEMAR (Single Energy Metal Artifact Reduction)
    - MVCT
    - OPG
  - Motion management
    - 4DCT
    - Abdominal compression
- Target delineation
  - No change in GTV/CTV delineation
  - Attention to skin
  - Contour metal/High HU material/variable tissue (gut, sinuses)

STEPS FOR PLANNING – WHAT IS DIFFERENT - II

- Preplanning audit
  - Motion
  - Beam path and length
  - Avoiding endranging on critical structure
- Dose Prescription
  - In GyE incorporating RBE.
  - Higher prescription?
  - Tighter constraints
  - Often in close proximity of critical structures
  - Often in reirradiation setting

STEPS FOR PLANNING – WHAT IS DIFFERENT - II

- Plan evaluation
  - Tighter prescription parameters
  - Avoid hot spots on OARs
  - Check for OAR doses
  - Check beam path
  - Assess End of Range
  - Ensure coverage of all targets by at least two beams
  - Identify location of hotspots.

- Robust optimisation

STEPS FOR PLANNING – EVAUATION OF QACT

- Change in beam path
- Change in target
- Change in OAR
- Impact on target coverage
- Impact on OAR doses
- Impact of unspecified tissue

COMPARATIVE EVALUATION- THE MODEL BASED APPROACH

Another for of evaluation:The model based approach for selection of patients for proton therapy

- **Patient rated moderate to severe xerostomia**
- **Physician rated ≥ Grade II dysphagia**
- **Tube feeding dependance**

Standard coverage requirements
Sparing of bilat parotids, swallowing structures (SPC, IPC, CP)
Oral cavity

Target Δ NTCP thresholds

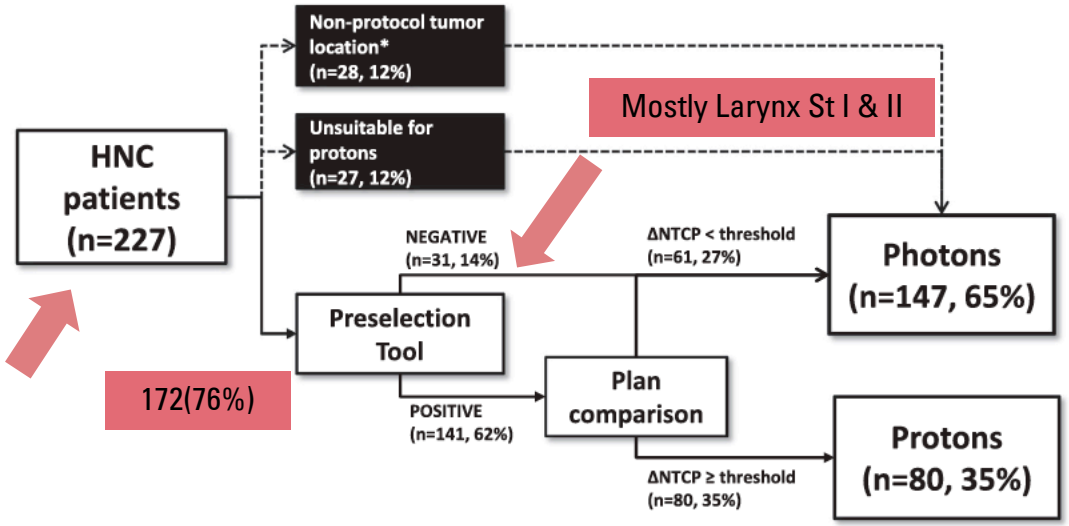
Patient rated moderate to severe xerostomia ≥ **10%**

Physician rated ≥ Grade II dysphagia ≥ **10%**

Tube feeding dependance ≥ **5%**

Σ Δ NTCP ≥ 15%

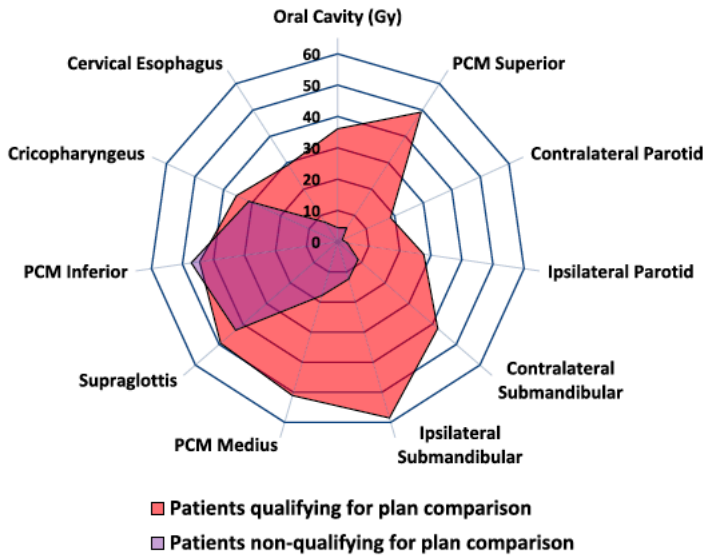
Preselection tool. Compare clinically prepared VMAT plan with IMPT plan assuming 0 dose to all OARs.
Put patient through the IMPT process if one threshold is reached.



Create SIB based IMPT plan. Robustness earlier 5mm later 3mm

The model based approach for selection of patients for proton therapy

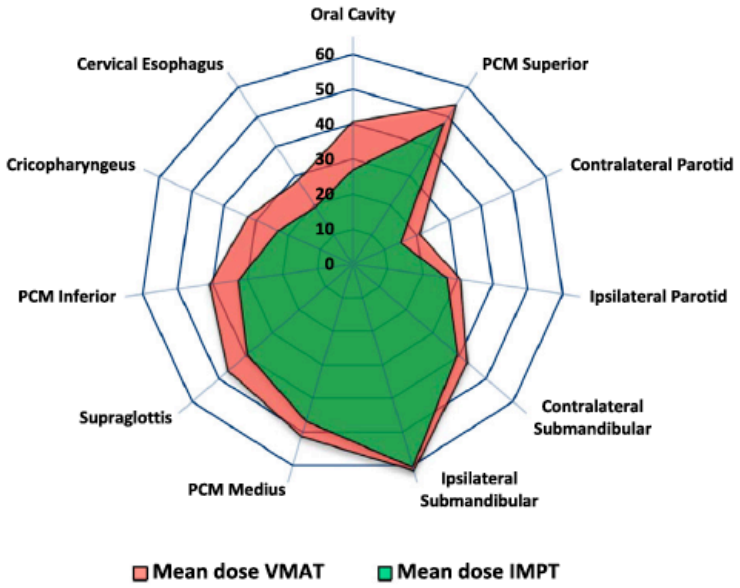
Who did not get preselected



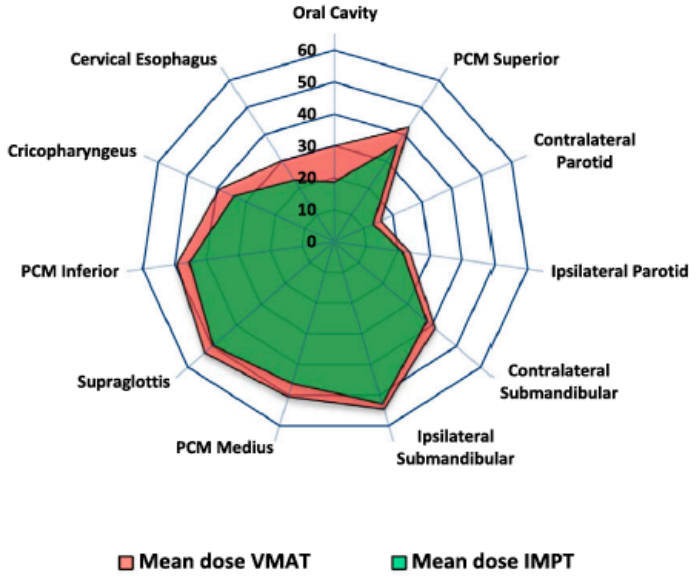
Synchronous tumour
Rapid progression
Psychologically
Metal implants
Unsuitable immobilisation

Outcome after selection

Patients qualifying for proton



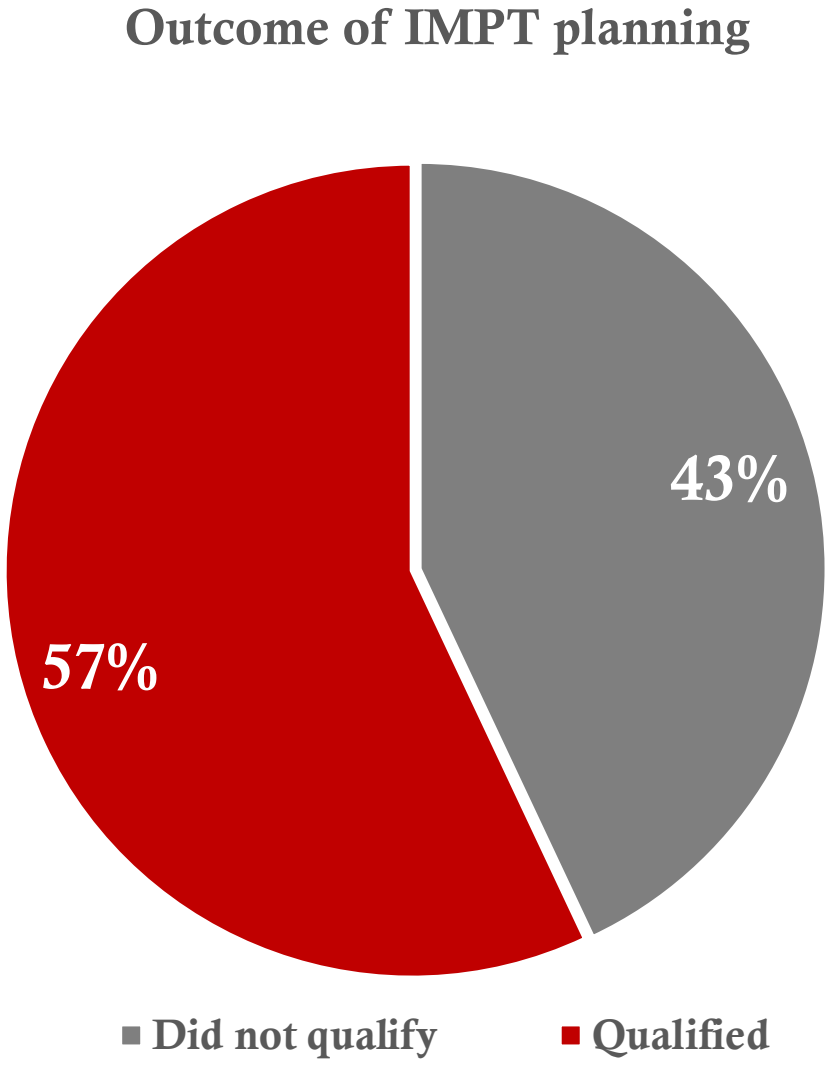
Patients non-qualifying for proton

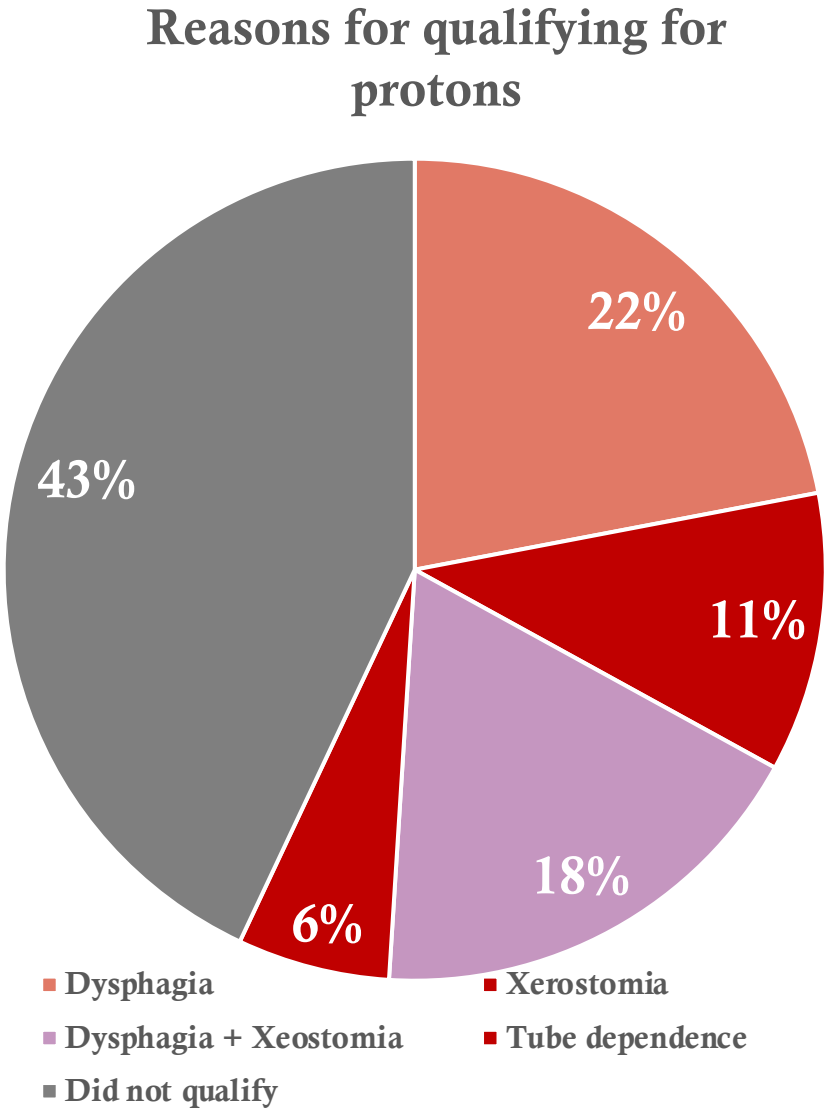


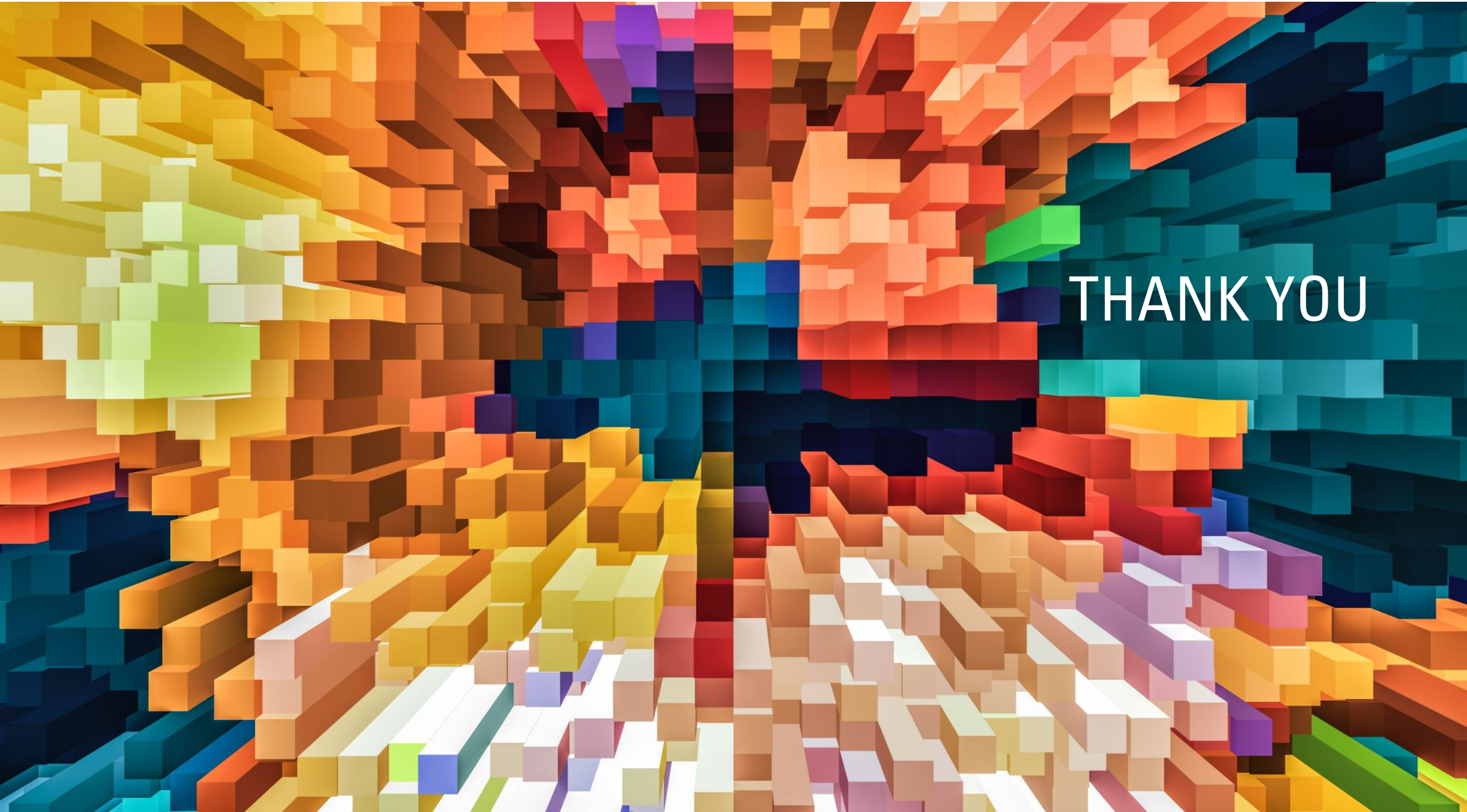
Patients qualifying for proton significantly related to

- Higher T stage
- Higher N stage
- Tumour location (OP vs others)
- Baseline xerstomia
- Baseline dysphagia
- Baseline weight loss > 10%
- Treatment modality
- Overlap of OAR with PTV

The model based approach for selection of patients for proton therapy



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