MONO-INSTITUTIONAL EXPERIENCE IN THE TREATMENT OF NASOPHARYNGEAL CARCINOMA (NPC) WITH INTENSITY-MODULATED RADIOTHERAPY (IMRT)

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BACKGROUND

- ✓ Radiation therapy is considered as the mainstay of treatment in NPC management
- ✓ IMRT is a major breakthrough in the treatment of NPC
- ✓ The shift of RT technique from 2DRT to IMRT widens the therapeutic window by improving target coverage and normal organ sparing, and provides capacity for dose escalation
- ✓ The dosimetric advantage has already translated into a better local control rate and less toxicity rates.

Results from series treating NPC with IMRT with or without chemotherapy.

Study	N	T3/4 (%)	Median follow-up (mo)	Total dose (Gy)	Dose/fraction (Gy)	Time point (y)	Local control (%)	Nodal control (%)	Distant control (%)	Overall survival (%)
Lee (USA) [1]	118	41	30	70	2.12	4	96	98	72	74
Kam (HK) [2]	63	51	29	66	2	3	92	98	79	90
Wolden (USA) [3]	74	53	35	70.2	2.34	3	91	93	78	83
Kwong (HK) [4]	50	0	14	70	2	3	100	92.3	100	100
Kwong (HK) [5]	50	100	25	76	2.17	2	96[a]	NR	94	92
Lin (China) [6]	326	61	33	62.6–69.75	2.2–2.25	3	95	98	90	90
Lee (Korea) [7]	20	40	27	72	2.4	2	88[a]	NR	90	NR
Woong (Korea) [8]	24	29	26	64.8	2.4	3	93	87	88	96
Fang (China) [9]	110	24.5	40	72	2.4	3	84.2[a]	NR	82.6	85.4
Tham (Singapore) [10]	195	NR	37	70	2.12	3	89.6[a]	NR	89.2	94.3
RTOG0225 [11]	68	34	31	70	2.12	2	92.6	90.8	84.7	80.2
Wong (HK) [12]	175	35	34	70	2.12	3	93.6	93.3	86.6	87.2
Ng (HK) [13]	193	61	30	70	2–2.12	2	95	96	90	92
Bakst (USA) [14]	25	28	33	70.2	2.34	3	91	91	91	89
Xiao (China) [15]	81	100	54	68	2.27	5	94.9	NR	NR	74.5
Lai (China) [16]	512	52	52.8	NR	2.27	5	93	97	84	NR

PURPOSE

- Between 2003 and 2013, 46 pts underwent IMRT for NPC at the Department of Radiation Oncology of IRCCS – ASMN Reggio Emilia

- 14 ♀ and 32 ♂ with a mean age of 49,8 years (range 17-87 years)

-The aim of our study was to evaluate retrospectively :

✓ Overall survival rates (OS)

✓ Loco-regional progression-free rates (LRPFR)

✓ Distant metastasis-free rates (DMFR).

✓Acute and late toxicity (CTCAE 4.02 morbidity scoring criteria).

METHODS AND MATERIALS

Pretreatment work-up

- Complete history and physical examination
- Direct flexible fibre-optic endoscopic examination
- CT or MRI of the nasopharynx including skull base and neck region
- Biopsy
- CT chest
- CT abdomen and bone scan optional (performed when clinically indicated)
- Routine blood work including liver function tests
- EBV

METHODS AND MATERIALS

Disease characteristics of 46 pts

7 TH EDITION TNM CLASSIFICATION

Tumor stage	n	%
T1	24	52%
T2	15	33%
T3	5	11%
T4	2	4%
Nodal stage	n	%
N0	10	22%
N1	7	15%
N2	24	52%
N3	5	11%

STAGE GROUP (AJCC)

Stage group	n	%
I	8	17,4%
II	8	17,4%
III	23	50,0%
IV	7	15,2%

HISTOLOGY

Histology	n	%
WHO I	7	15,2%
WHO IIA	14	31%
WHO IIB	23	50%
NAS	2	4%

METHODS AND MATERIALS

CHEMOTHERAPY

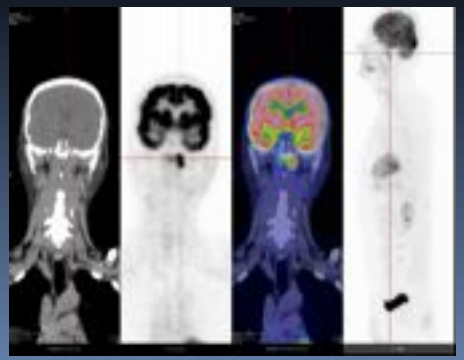
- ✓ 7 Patients (15,2%) received concomitant weekly cisplatinum
- ✓ 34 pts (73,9%) docetaxel, cisplatin, 5-fluorouracil (TPF) based induction chemotherapy and concomitant weekly cisplatinum
- ✓ 5 pts (10,9%) radiotherapy alone

METHODS AND MATERIALS

RADIATION THERAPY TECHNIQUES

IMMOBILIZATION AND SIMULATION

- ✓ Supine position
- ✓ Thermoplastic HN and shoulder mask
- ✓ A CT scan (3-mm cuts) with IV contrast was performed from the top of the head to the upper mediastinum
- ✓ A planning PET/CT in treatment position was done in 37 pts



METHODS AND MATERIALS

RADIATION THERAPY TECHNIQUES

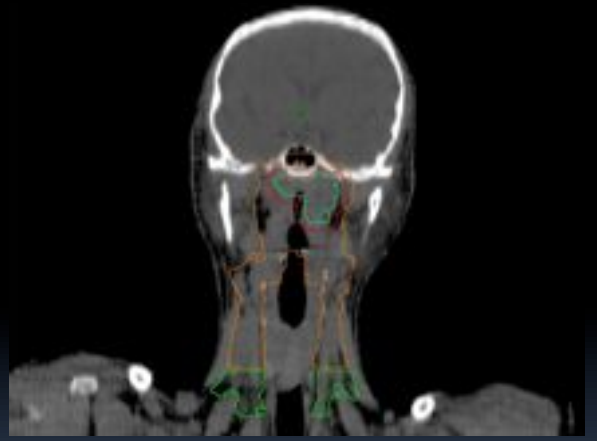
DELINEATION OF TARGET VOLUME

✓ GTV= macroscopic primary cancer (GTV- P) and nodes (GTV-N) > 1cm or nodes with necrotic centres;

✓ CTV HD = GTV(GTV-P and GTV-N) + a isotropic margin of ≥ 5 mm ((bones, muscles, air);

✓ CTV-P HR = an isotropic margin of ≥ 5 mm around CTV P (HD) + the entire nasopharynx, anterior 1/2 to 2/3 of the clivus (entire clivus, if involved),skull base (foramen ovale and rotundum bilaterally must be included for all cases), pterygoid fossae, parapharyngeal space, inferior sphenoid sinus (in T3-T4 disease, the entire sphenoid sinus) and posterior fourth to third of the nasal cavity and maxillary sinuses (to ensure pterygopalatine fossae coverage). The cavernous sinus was included in high risk patients (T3, T4, bulky disease involving the roof of the nasopharynx);

✓ CTV-N HR = an isotropic margin of ≥ 5 mm around CTV-N (HD) +
- Upper deep jugular (junctional, parapharyngeal): bilaterally;
- Subdigastric (jugulodigastric) [level II]: bilaterally;
- Midjugular (level III): bilaterally;
- Level Va bilaterally;
- Retropharyngeal: bilaterally;



✓ CTV-N LR =
- Low jugular and supraclavicular (level IV): bilaterally;
- Vb: bilaterally;
- Submandibular (level Ib): bilaterally;

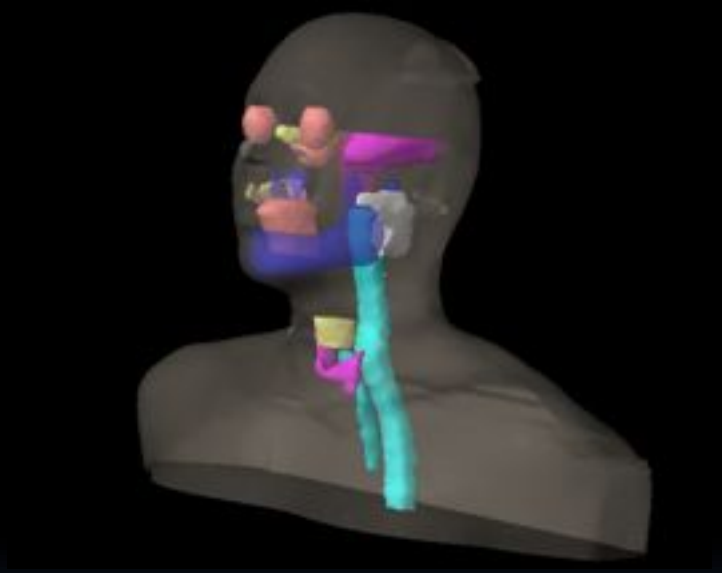
✓ PTVs = 3-5 mm margin around the CTV's to compensate for the variabilities of treatment set up and internal organ motion;

METHODS AND MATERIALS

RADIATION THERAPY TECHNIQUES

DELINEATION OF OARS

- Spinal cord (PRV = 5 mm 3D margin)
- Brainstem (PRV = 1 mm 3D margin)
- Optic nerves (PRV = 1 mm 3D margin)
- Chiasm (PRV = 1 mm 3D margin)
- Parotid glands
- IAC
- Oral cavity
- Mandible
- Eyes
- Lens
- Temporal lobes
- Esophagus (including postcricoid pharynx)
- Glottic larynx
- Thiroid
- Brachial plexus
- PSCM

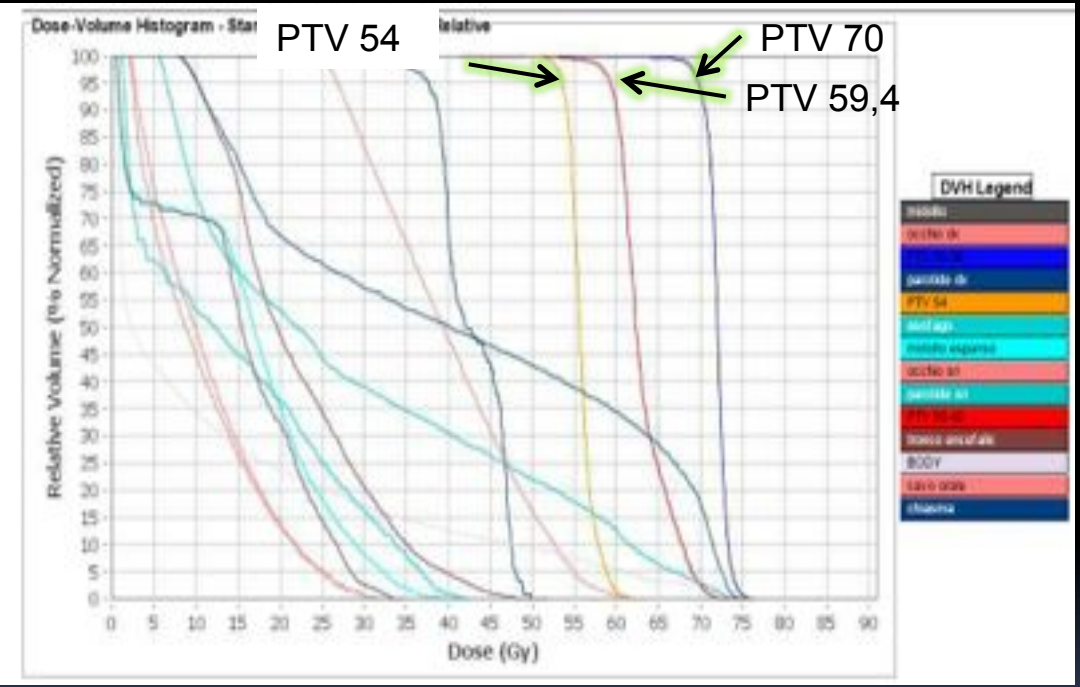


METHODS AND MATERIALS

RADIATION THERAPY TECHNIQUES

PRESCRIPTION DOSE

- ✓ RT was delivered by using a SIB IMRT technique in 30-33 fractions;
- ✓ 66–70 Gy to the PTV HD (P-N);
- ✓ 59,4-60 Gy to the PTV HR (P-N);
- ✓ 54-54,12 Gy to the PTV LR;
- ✓ Doses to OARS: RTOG 0225/0615;



- ✓ Radiation planning goals was to encompass at least 95 % of the PTVs with the prescription isodose surface;

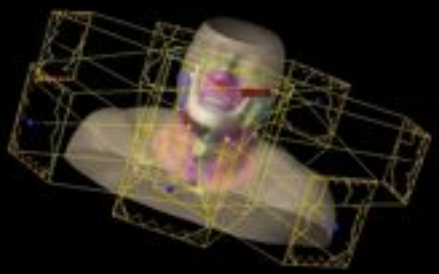
METHODS AND MATERIALS

RADIATION THERAPY TECHNIQUES

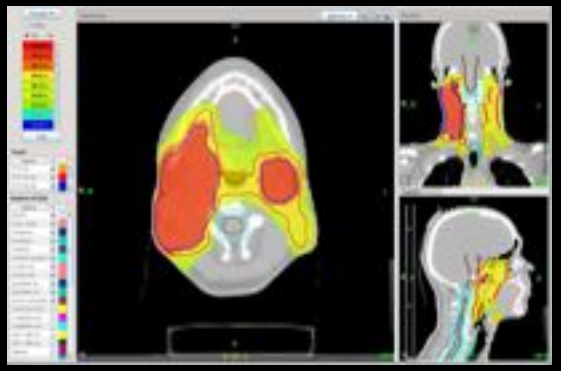
TREATMENT DELIVERY

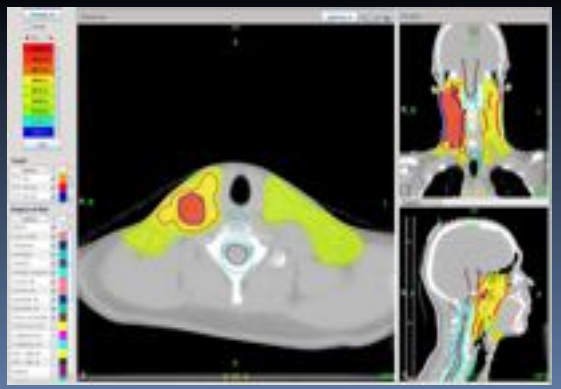
The IMRT was delivered using two different techniques

-dMLC-IMRT technique for 22 patients (48%)



-Helical Tomotherapy for 24 patients (52%)





METHODS AND MATERIALS

FOLLOW-UP

✓Patients were evaluated:

- Weekly during radiation therapy;
- First FU was at 40 days after the completion of their treatment;
- Every 2-3 months in the first 2 years;
- Every 6 months from year 2 through year 5;
- Annualy thereafter;

✓Each FU included a complete history/physical examination and fiberoptic endoscopy

✓Generally CT/PET was performed after 3 months after the completion of treatment;

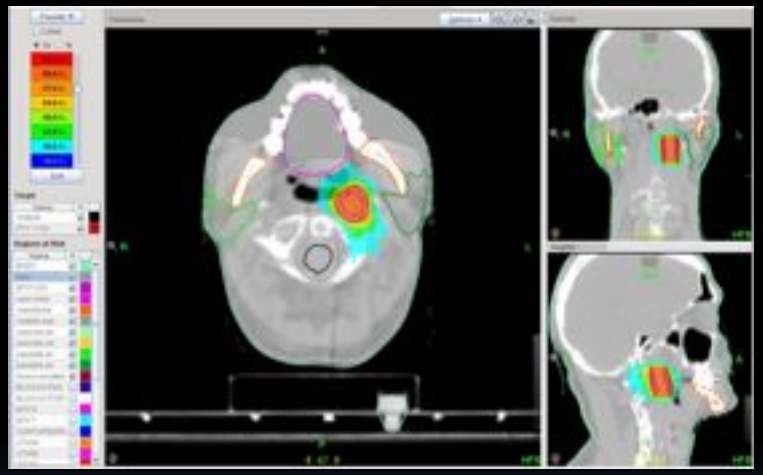
✓CT scan or MRI of the nasopharynx and neck, chest radiography and liver sonography were performed annually;

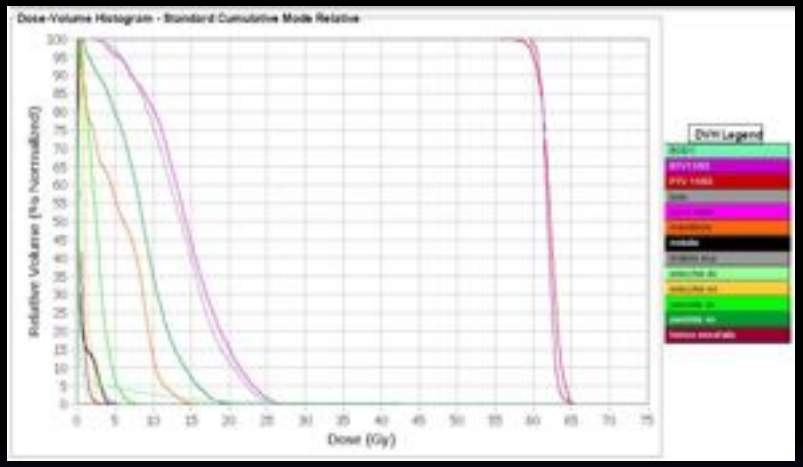
RESULTS

With a median follow-up of 55,7 months (range 3,6-136,5 months)

✓7 patients (15,2%) had locoregional failures (all were in-field HD), 1 with syncronous DM:

-2 patients were reirradiated with a total dose of 60 Gy (1 after surgery)
-2 patients were treated with chemotherapy
-3 patients were treated with only surgery



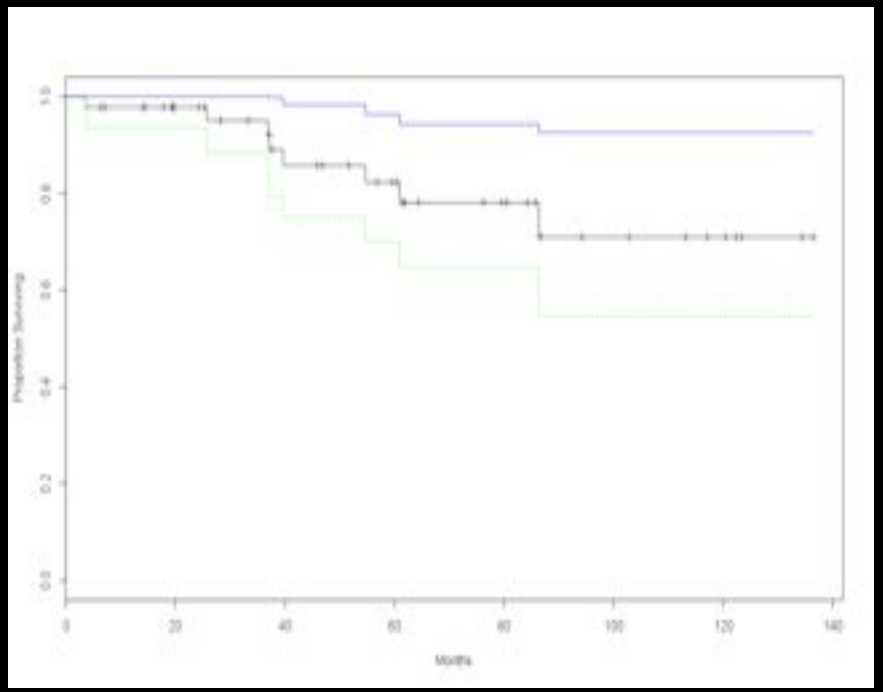


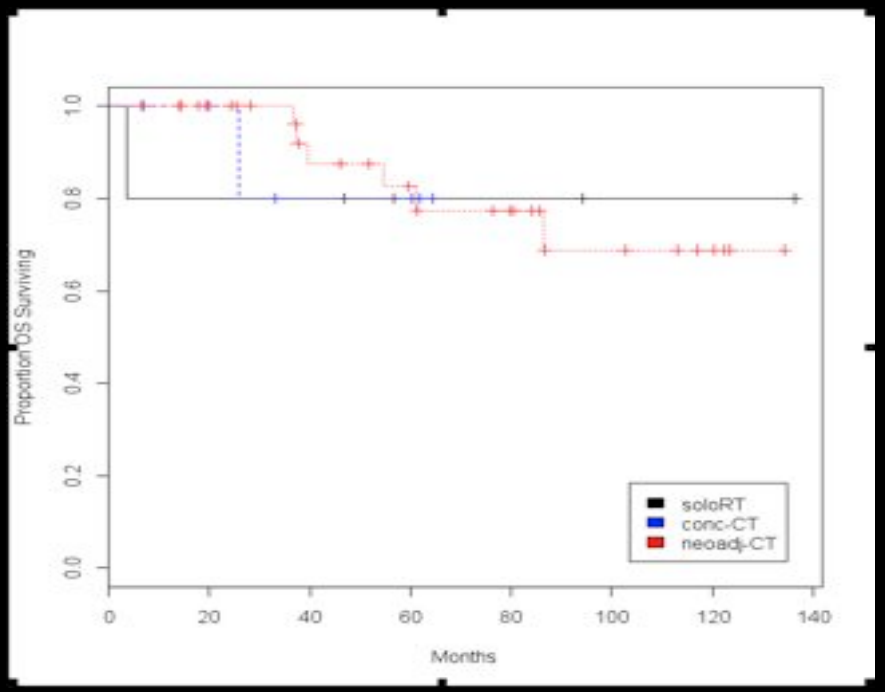
✓3 patients (6,5%) developed DM and 2 patients (4,3%) had DM as first site of failure;

✓8 patients (17,3%) died:
- 4 from nasopharyngeal carcinoma;
- 1 from toxicity related to radiation therapy (dysphagia G5);
- 3 from other causes without having patterns of loco-regional relapse and/or DM reported;

RESULTS

OVERALL SURVIVAL

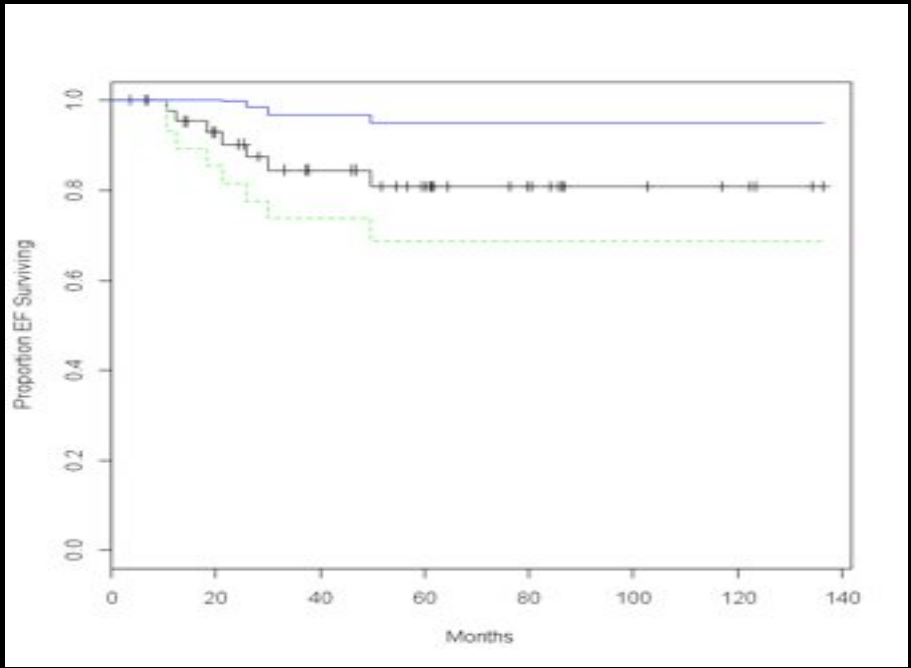


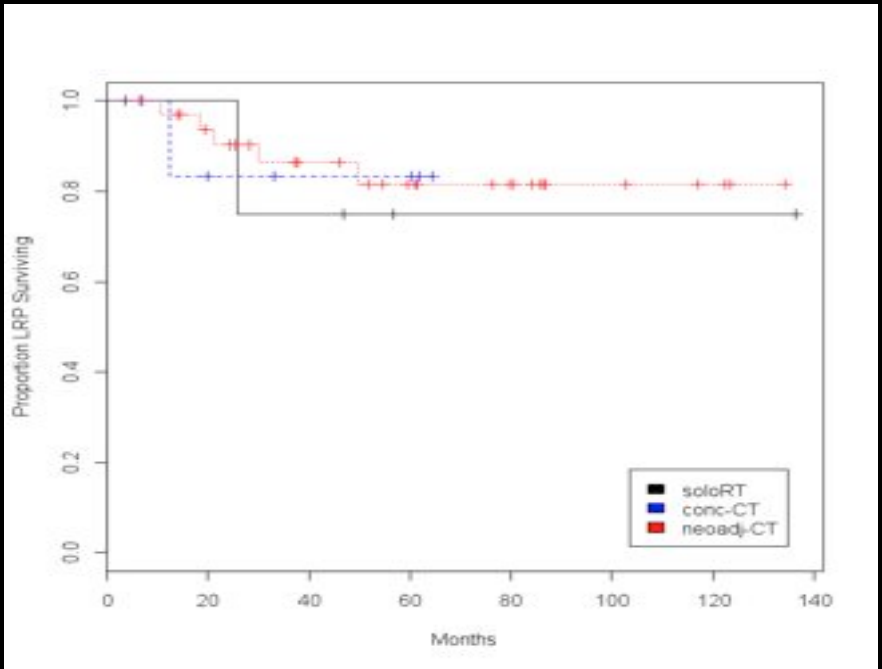


The 2-year and 5-year estimate overall survival rates was 97,8% and 82,2% respectively.

RESULTS

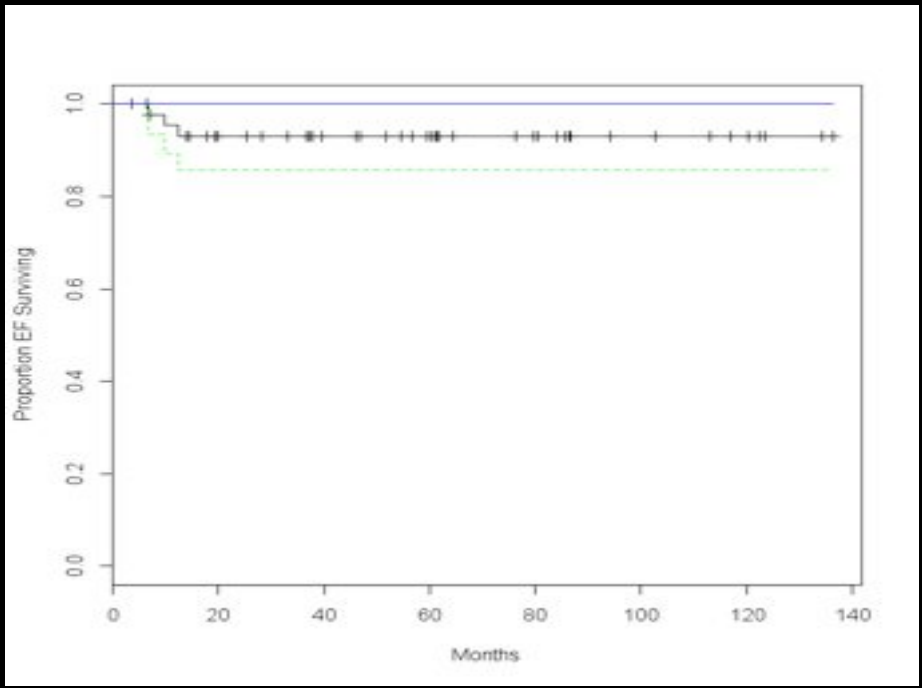
LOCAL-REGIONAL PROGRESSION-FREE RATES

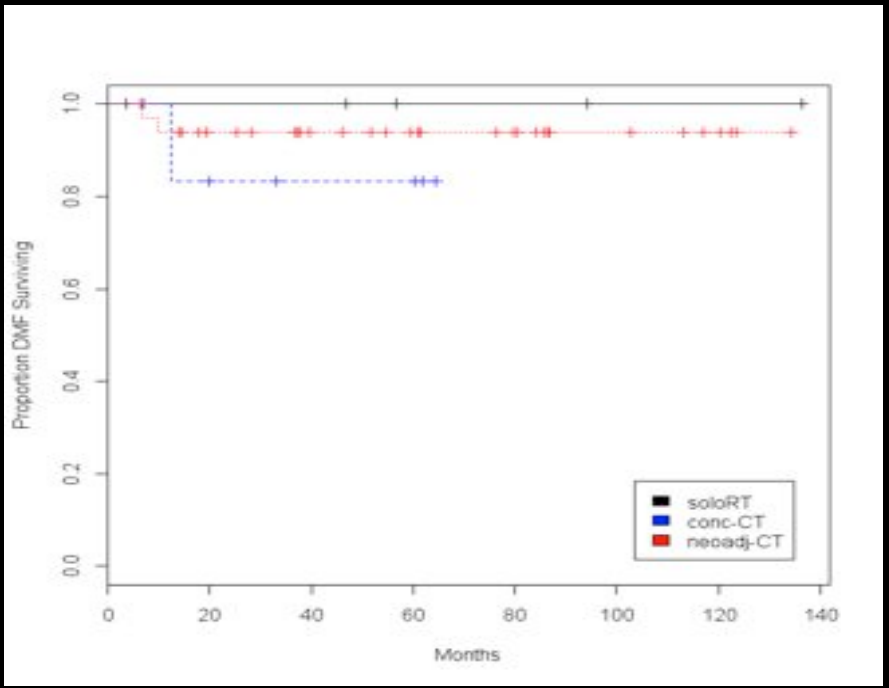




The 2/5-year local-regional progression-free rates
was 90,2% and 80,8% respectively

RESULTS
DISTANT METASTASES-FREE RATES

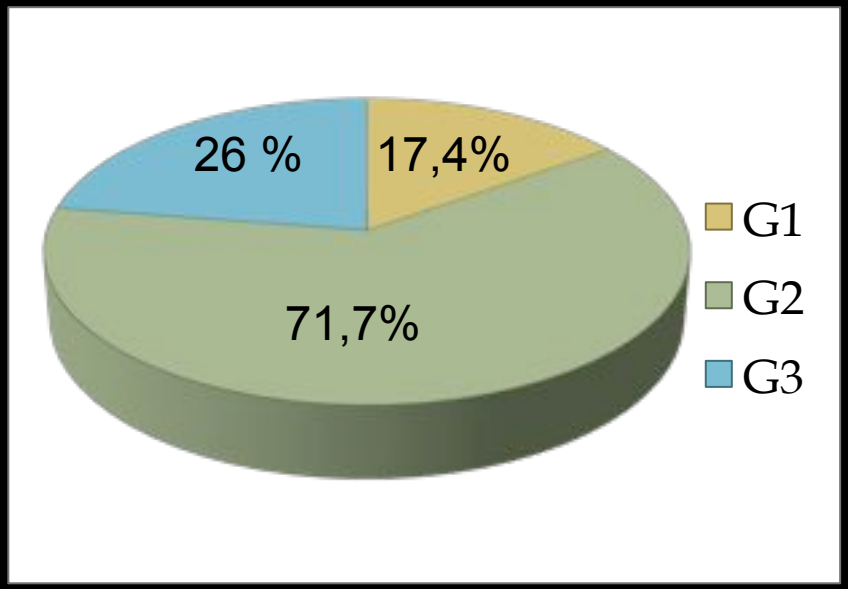




The 2/5-year distant metastases-free rates of 93,1%.

RESULTS

ACUTE TOXICITY



G1 in 8 pts (17,4%)
G2 in 33 pts (71,7%)
G3 in 12 pts (26 %)

G5 dysphagia in 1 pt !

RT alone

	G1	G2	G3	G4	G5
Mucositis		2-3-6	4		
Oral pain		3	4		
Dysphagia		3	4		4
Otitis		2			
Dysgeusia					
Xerostomia		3			

RT-CHT concomitant

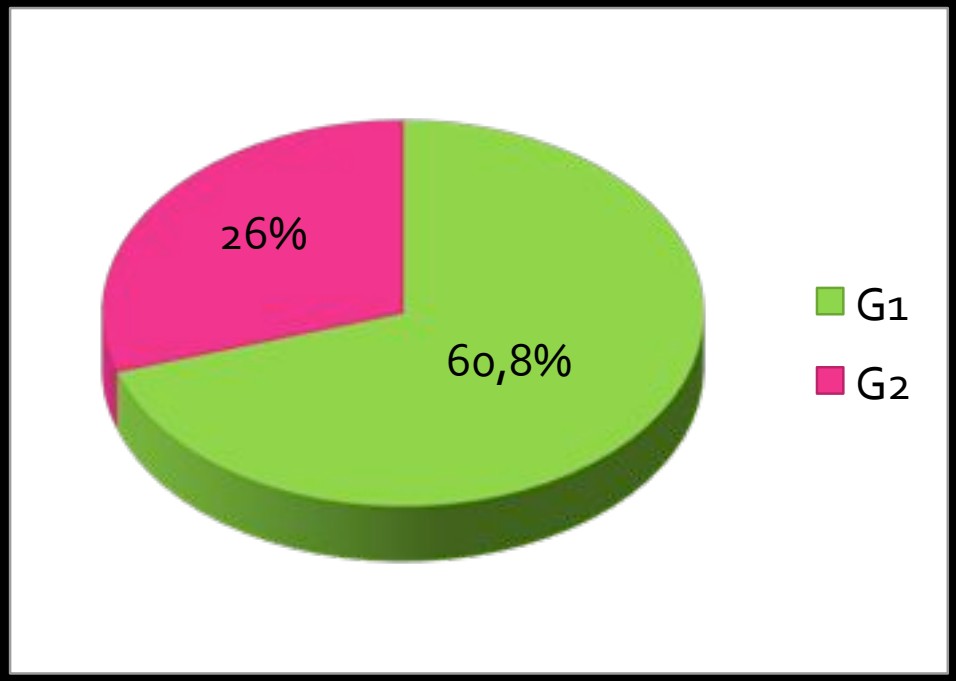
	G1	G2	G3	G4	G5
Mucositis	2	2-3-4-7-4-4			
Oral pain		4-4			
Dysphagia	3	3-4-4			
Otitis					
Dysgeusia					

CHT-RTCHT

	G1	G2	G3	G4	G5
Mucositis	31-34	3-32-33-8-11-25-27-19-29-21-14-30-23-2-15-6-10-16-17	26-20-4-35-22-5-24-18-28-13		
Oral pain	2	33-8-11-25-23-27-19-30-15-21-16-17	32-26-35-5-22--24-18-28		
Dysphagia		3-8-11-25-19-30-2-7-28-15-21-16-17-27	32-26--35-22-5-24-18-13		
Otitis	27-23				
Dysgeusia	22-6	23-16			
Xerostomia	22	9-33-35			

RESULTS

LATE TOXICITY



G1 in 28 pts (60,8%)

G2 in 12 pts (26%)

No patients experienced G3 or G4

RT alone

	G1	G2	G3	G4	G5
Xerostomia	2,3,6	5			
Hearing loss	7	8			
Neuropathy					
Trismus					
Dysphagia					
Subcutaneous fibrosis					
Soft tissue necrosis					
Chondronecrosis					
Voice alteration	1				

RT-CHT concomitant

	G1	G2	G3	G4	G5
Xerostomia	2,3,6	5,8,4			
Hearing loss	8				
Neuropathy					
Trismus					
Dysphagia	8,4				
Subcutaneous fibrosis					
Soft tissue necrosis					
Chondronecrosis					
Voice alteration					

CHT-RTCHT

	G1	G2	G3	G4	G5
Xerostomia	3-31-26-25-34-14-30-2-17-6-5-7-21-24-10-28	9-33-35-23-16			
Hearing loss	26-19	35			
Neuropathy		8			
Trismus	22				
Dysphagia	16				
Subcutaneous fibrosis	23-28	2			
Soft tissue necrosis					
Chondronecrosis					
Voice alteration					

CONCLUSION

Our experience of using IMRT treatment for a cohort of patients with early and advanced stage NPC showed:

- ✓A very high rate of overall survival and locoregional control at 2/5 years
- ✓The local failures were all in-field HD
- ✓Acute and late toxicities with IMRT were limited

THANKS FOR YOUR ATTENTION!