

Intensity-modulated radiotherapy in patients with head and neck cancer: a European single-centre experience

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Objective: The purpose of this study was to analyse retrospectively the intensity-modulated radiotherapy (IMRT) results in patients with head and neck cancer (HNC) treated between November 2003 and June 2007.

Methods: Patients with early and locoregionally advanced HNC were treated with inverse-planned step-and-shoot IMRT. The prescribed dose varied from 66 Gy to 70 Gy in those receiving IMRT as definitive treatment and from 60 Gy to 70 Gy in the post-operative setting. IMRT was given alone, after induction chemotherapy (ICT), with concomitant chemotherapy (CRT) or with both. Acute and late toxicities are reported; locoregional control (LRC), locoregional relapse-free survival (LRRFS) and overall survival (OS) were calculated from the start of radiation.

Results: IMRT was used in 78 patients (48 as definitive treatment, 30 post-operatively), of whom 20 also received ICT and 35 CRT. Three patients stopped IMRT early, one for toxicity (mucosa). Acute toxicity scoring revealed 5 cases (6%) of severe skin toxicity and 65 cases (83%) of severe mucosal toxicity. After a median follow-up of 18.7 months, late toxicities included xerostomia (44%), loss of taste (14%) and fibrosis of the neck (9%). 16 patients had died, of whom 10 due to tumour recurrence/progression and 2 due to treatment (but not IMRT related). The LRC, LRRFS and OS at 3 years are 66.1%, 48.5% and 60.3% in the definitive IMRT group and 85.4%, 82.5% and 85.9% in the post-operative setting, respectively.

Conclusion: We consider IMRT for locoregional HNC feasible not only as a single modality but also after surgery, after induction chemotherapy and concurrently with chemotherapy.

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Locoregional head and neck cancer (HNC) poses a major therapeutic and technological challenge. Different strategies have been applied to improve treatment outcome, such as altered fractionation radiotherapy [1, 2], concurrent chemoradiotherapy [3–8], brachytherapy (*i.e.* concurrent use of radiation and cetuximab [9]) and also, recently, the use of a more effective induction chemotherapy followed by (chemo-) radiation (*i.e.* sequential therapy) [10, 11].

Radiotherapy techniques have evolved strongly during the last decade with the implementation of intensity-modulated radiotherapy (IMRT). The sharp dose fall-off gradient of this technique permits the administration of a highly conformal and more homogeneous dose to the planning target volume (PTV) [12] than conventional and conformal radiotherapy. This allows better sparing of the organs at risk (*e.g.* parotid glands, submandibular and minor salivary glands, larynx and swallowing structures), leading to a decrease in acute and late side

effects [13–16]. This may open a window for treatment intensification of radiotherapy alone or combined with chemotherapy and/or targeted therapy. In addition, IMRT permits the administration of different doses to different adjacent risk zones at the same time, so-called “dose painting”.

For a long time, however, a major problem of IMRT was the lack of hard evidence of its superiority over the more classic irradiation techniques. Kam et al [17] showed in a prospective randomised study, without concurrent chemotherapy, significantly less observer-rated severe xerostomia and a significantly higher stimulated parotid and whole saliva flow rate after IMRT treatment for early stage nasopharyngeal carcinoma than two-dimensional radiotherapy. Interestingly, this was not in concordance with patient-reported outcome. Very recently, Nutting et al [18] reported the first phase III multicentre randomised controlled trial in patients with HNC showing significantly less Grade 2 or more xerostomia at 12 and at 18 months in the IMRT arm than the conventional radiotherapy arm, both without concurrent chemotherapy. No differences in acute mucositis or pain scores were found, although the IMRT group suffered from significantly more acute fatigue of Grade 2 or more.

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However, a clear survival benefit of IMRT over the more classic three-dimensional conformal radiation therapy has not been shown as yet [19, 20], and there are some concerns about the theoretically higher risk of induction of secondary cancers by IMRT because of the increased low-dose irradiated volume [21, 22]. IMRT might also lead to unexpected higher toxicity in areas that were not in the classic two-dimensional beam path but that are irradiated in the IMRT set-up, especially in combination with concurrent chemotherapy [23]. Therefore, experiences of IMRT, with and without induction and/or concurrent chemotherapy, should be reported and shared.

In this article we review the results of IMRT in patients with early and locoregionally advanced HNC treated at our hospital between November 2003 and June 2007.

Methods and materials

Patients

Since 2003 selected patients with newly diagnosed early and locoregionally advanced HNC according to the 2002 American Joint Committee on Cancer staging system [24] have been treated with IMRT. All patients were treated with IMRT either after surgery or as definitive treatment modality, with or without sequential and/or concurrent chemotherapy.

The pre-treatment evaluation included a complete history and physical examination, pan-endoscopy, chest X-ray, complete blood count, liver and renal biochemistry, CT scan of the head and neck region and for most patients also a baseline MRI scan of this region.

Treatment planning and delivery

For each patient a contrast-enhanced CT scan with 3 mm slice thickness was made in the treatment position with an immobilisation mask.

Volumes

The gross tumour volume (GTV), the clinical target volume (CTV) and the nearby organs at risk (OAR) were delineated on the Pinnacle 6.2b and 7.6c planning system (Philips Medical Systems, Eindhoven, the Netherlands). OAR contoured routinely were the spinal cord, brain stem, brain, parotid glands, larynx (when not involved) and the mucosa of the mouth outside the PTV. In cases of paranasal sinus tumours and nasopharyngeal tumours, we also delineated the optical nerves, optical chiasm and lacrimal glands. Lymph nodes were delineated according to the Danish Head and Neck Cancer Group (DAHANCA), European Organisation for Research and Treatment of Cancer (EORTC), Oncology and Radiotherapy Group for Head and Neck Cancer (GORTEC), National Cancer Institute of Canada (NCIC), Radiation Therapy Oncology Group (RTOG) consensus guidelines as described by Gregoire et al [25]. The PTV was defined as the CTV plus a 3 mm margin. A planning risk volume (PRV) was created 3 mm around the critical OAR (spinal cord, brain stem, optical nerves and optical chiasm).

Neck region

Most patients had bilateral lymph node irradiation while lymph node regions were irradiated unilaterally in case of tumours of the oral cavity or oropharynx located more than 2 cm from the midline. No lymph node irradiation was done in case of paranasal sinus tumours and after neck dissection without lymph node involvement.

Irradiation techniques

IMRT plans were made with the inverse step-and-shoot treatment planning module of Pinnacle 6.2b at the beginning and 7.6c afterwards. The dose to the PTV was prescribed according to the International Commission on Radiation Units and Measurements (ICRU) report 62 [26]. The prescribed dose to the non-involved lymph node levels was 50 Gy in 25 fractions in 5 weeks. The PTV of the tumour and of the high-risk lymph node levels was planned to receive 60–66 Gy in 6–6.5 weeks in the post-operative setting [8] and 70 Gy in 7 weeks in case of incomplete resection and in patients who received definitive IMRT, all in fractions of 2 Gy. For some non-operated patients in poor condition or with a rapidly proliferating tumour a simultaneous integrated boost technique was planned, 54 Gy (1.8 Gy/fraction) to the non-involved lymph node levels and 66 Gy (2.2 Gy/fraction) to the high-risk zone, in 30 fractions over 6 weeks.

The dose to the PRV of the spinal cord was limited to 50 Gy and a maximum of 59 Gy with 50% of the volume (D50) under 55 Gy was tolerated to the PRVs of the brain stem, the optical nerves and the optical chiasm. The dose to the other OAR was kept as low as possible, respecting the prescription to the PTV.

For unilateral neck irradiation we used 4 beams (340°–30°–100°–170° for the left side and 40°–330°–260°–190° for the right side), whereas for bilateral neck irradiation and paranasal sinus irradiation 5 (220°–290°–0°–70°–140°) or 7 (206°–258°–309°–0°–51°–102°–154°) equidistant beams were calculated.

For the overall treatment planning the number of segments varied from 50 to 80 in patients without cervical lymph node irradiation or with only unilateral neck irradiation, and from 80 to 115 segments in case of bilateral neck irradiation. The latter was reduced to 60–100 segments after dosimetric verifications on a humanoid phantom showing important dose differences above 100 segments [27].

IMRT treatment was delivered with 6 MV photons by an Electa SLi accelerator (Electa, Stockholm, Sweden) with electronic portal imaging device (EPID). Patients were treated on five consecutive days per week.

Table 1. Patient characteristics (n=78)

Age (years)	Median 60 (range 34–82)
Gender	54 male / 24 female
Performance stage	0 in 34, 1 in 43, unknown in 1
Primary tumour stage	I 7
	II 20
	III 16
	IV 34
	Unknown 1

Table 2. Tumour and lymph node staging [24]

	T1	T2	T3	T4	Tx	All
N0	7	20	9	8	0	44
N1	2	3	2	2	0	9
N2	5	4	4	3	1	17
N3	0	3	0	1	2	6
Nx	0	0	0	1	1	2
All	14	30	15	15	4	78

Quality assurance

We performed a patient-specific dosimetric verification on a humanoid phantom for the first 50 patients in addition to the standard machine-specific quality control [28, 29]. Analysis of these phantom verifications showed high reliability of dose calculations and delivery. Based on these data the verifications on a humanoid phantom were continued randomly.

Verification of patient positioning was done by EPID for the first three fractions, after which the systematic error was calculated and corrected on the mask. Online corrections were made for errors of more than 3 mm in any direction. The electronic portal imaging (EPI) was performed daily until three consecutive days with random errors of less than 3 mm. Afterwards EPI was repeated once a week with the same evaluation criteria.

Concomitant treatment

Patients with an operable HNC received IMRT after surgery with or without concomitant chemotherapy depending on prognostic factors; patients with inoperable disease were often treated in a study protocol [10, 30] with platinum-based induction chemotherapy followed

by IMRT with or without concomitant chemotherapy (cisplatin, carboplatin or gemcitabine).

Follow-up and assessment

Patients were seen weekly during radiotherapy. Acute radiation toxicity was graded according to the RTOG radiation morbidity scoring criteria [31].

After the completion of their treatment, patients were seen every month during the first year, every 2 months in the second year and every 3–6 months thereafter. Late toxicity was always mentioned but not properly graded.

The first post-treatment CT scan was obtained 2–6 months after the completion of radiotherapy; thereafter, regular CT or MRI studies were obtained every 6 months or earlier on indication.

Statistics

Locoregional control (LRC) and survival rates (locoregional relapse-free survival (LRRFS) and overall survival (OS)) at 3 years have been calculated separately for those receiving IMRT as definitive treatment and those in the post-operative setting by using the Kaplan–Meier method [32]. The duration of LRC is defined as the time from the start of radiotherapy until the first documented progression or recurrence of locoregional disease or until death by any cause. LRRFS is calculated from the start of IMRT until the first documented locoregional recurrence or until death of any cause. OS is calculated from the start of IMRT until death of any cause.

All statistical analyses were performed with SPSS 15.0.0 for Windows (September 2006; SPSS Inc., Chicago, IL).

Table 3. Treatment options and radiotherapy dose in relation to stage and primary tumour site

n	Primary site	St I	St II	St III	St IV	St X	n × radiation dose (Gy)/n of fractions (reason of protocol violation)
Definitive IMRT (48 patients)							
6	Oral cavity	1	3	2			6 × 70/35
15	Oropharynx	2	6	3	4		1 × 44/22 (toxic megacolon), 4 × 66/30, 2 × 66/33 (T1N0), 8 × 70/35
12	Nasopharynx	1		1	10		1 × 62/31 (patient refusal), 1 × 66/33 (T1N0), 2 × 68/34, 8 × 70/35
3	Hypopharynx				3		1 × 66/30, 2 × 70/35
6	Larynx	1	4		1		1 × 50/25 (prior supraclavicular RT), 3 × 66/33, 2 × 70/35
4	Sinus			1	3		1 × 50/25 (pre-operative), 1 × 60/30, 2 × 70/35
2	1 nose, 1 CUP				1	1	2 × 70/35
Post-operative IMRT (30 patients)							
13	Oral cavity	2	3	3	5		2 × 60/30, 11 × 66/33
6	Oropharynx		2	2	2		1 × 60/30, 1 × 66/33, 1 × 68/34 (pos SM), 3 × 70/35 (pos SM)
1	Nasopharynx				1		1 × 70/35 (after adenoidectomy)
1	Larynx				1		1 × 56/28 (prior RT for lymphoma)
1	Sinus			3			3 × 66/33
6	Salivary gland	2	2	2			1 × 18/9 (intercurrent death), 3 × 66/33, 1 × 68/34 (pos SM), 1 × 70/35 (pos SM)
2	1 CUP, 1 EAC			1	1		1 × 60/30, 1 × 66/33

St, stage; CUP, carcinoma of unknown primary; EAC, external auditory canal; IMRT, intensity-modulated radiotherapy; pos SM, positive resection margins; RT, radiotherapy.

Table 4. Toxicities and overall treatment time in relation to different treatment approaches

Treatment Categories	No.	Acute toxicity								Late toxicity								OTT of CRT Median (range) in days
		Skin				Mucosa				Xerostomia	Fibrosis of the neck	Loss of taste	Bone problems	Dysphagia	Teeth problems			
		G0	G1	G2	G3	G4	G0	G1	G2							G3	G4	
RT	18	3	8	6	1	0	0	0	0	0	7	3	3	1	1	0	49 (40–53)	
CRT	10	1	6	3	0	0	0	0	0	0	6	1	3	0	0	1	51 (30–54)	
Surgery→RT	23	1	13	5	4	0	0	0	0	0	10	2	1	2	0	0	46 (13–53)	
Surgery→CRT	7	0	5	2	0	0	0	0	0	0	2	0	0	0	0	1	46 (37–51)	
ICT→RT	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	46 (46–46)	
ICT→CRT	18	2	10	6	0	0	0	0	0	0	9	1	4	0	1	1	50 (36–54)	
All	78	7	44	22	5	0	0	0	0	0	34	7	11	3	2	3	48 (13–54)	

IMRT, intensity-modulated radiotherapy; CRT, concurrent chemotherapy and IMRT; ICT, induction chemotherapy; OTT, overall treatment time; RT, radiotherapy.

Results

Between November 2003 and June 2007, 1099 patients with HNC were irradiated at our department. Of these 78 patients were treated with IMRT for their primary disease. 63 of the 78 patients had squamous cell carcinoma (SCC), 9 had adenocarcinoma and 6 had an undifferentiated carcinoma. Primary tumour site included the oral cavity in 19 patients, the oropharynx in 21, the nasopharynx in 13, the larynx in 7, the hypopharynx in 3, the maxillary sinus in 4, the ethmoidal sinus in 1, unknown (carcinoma of unknown primary; CUP) in 2, the nose in 1, the external auditory canal in 1 and the salivary glands in 6. Further information on patient and tumour characteristics is given in Tables 1 and 2.

Induction chemotherapy (all platinum based) was given to 20 patients and 35 patients received chemotherapy concurrently with IMRT (CRT). In those receiving CRT this was applied with cisplatin in 17 cases, with carboplatin in 12 cases and with gemcitabine in 6 cases. Further details on treatment and treatment delivery are given in Tables 3–6. 60 patients had bilateral neck irradiation, 13 had unilateral neck irradiation and in 5 patients the lymph nodes were not irradiated. Patients who were treated with definitive IMRT received a median dose to the PTV of 70 Gy (range 44–70 Gy), given in 35 fractions over 7 weeks. Five patients in this group were treated with a simultaneous integrated boost (54 Gy (1.8 Gy/fr.) to the non-involved lymph node areas and 66 Gy (2.2 Gy/fr.) to the high-risk zone in 30 fractions over 6 weeks). In the post-operative setting the median dose to the PTV was 66 Gy (range 18–70 Gy, the latter in case of macroscopic incomplete resection), given in fractions of 2 Gy. Details on radiotherapy doses in relation to tumour characteristics and treatment are given in Table 3.

The overall treatment time of the radiotherapy in all treatment categories is given in Table 4.

Three patients discontinued IMRT, one owing to development of a toxic megacolon, one patient developed a fatal pulmonary infection and one patient refused treatment after 31 fractions (62 Gy) because of mucosal toxicity.

Acute and late toxicities according to treatment are given in Table 4. One patient still had a feeding tube 2 years after the end of radiation. This patient had been treated with definitive IMRT (without additional chemotherapy) for a T2N0M0 tonsil carcinoma.

Of the 48 patients who received definitive IMRT, 35 (73%) developed a complete response (CR), 8 (17%) a partial response (PR) and 4 a disease stabilisation (SD). One patient died during treatment from a toxic megacolon. Five patients (four with PR and one with SD) underwent salvage surgery and became free of disease.

After a median follow-up of 18.7 months (range 4 days to 51.7 months) 16 patients had died: 10 from tumour recurrence/progression, 1 from a toxic megacolon, 1 as result of a post-operative complication after salvage surgery, 3 from a second primary and 1 from a pulmonary infection. Details of treatment and outcome in relation to treatment setting and tumour stage are given in Table 5 and 6.

Table 5. Treatment options and outcome in relation to tumour stage for all patients

n	TRT option	St I	St II	St III	St IV	St X	Recurrence (recurr)/ progression (progr)	n death/cause
Definitive IMRT (48 patients)								
18	RT	4	9	4**	0	1	2 Tu recurr, 1 LN recurr	1 postop complic, 1 LN recurr, 2nd primary
10	CRT	0	3*	2**	5	0	1 Tu recurr, 1 Tu & LN recurr, 1 Tu progr	1 Tu progr, 2 × 2nd primary, 1 toxic death
2	ICT→RT	1	0	0	1	0		
18	ICT→CRT	0	1	1	16	0	1 Tu recurr, 2 LN recurr, 1 Tu & LN recurr, 4 Tu progr, 1 LN progr	1 Tu recurr, 1 LN recurr & liver M+, 3 Tu progr, 1 Tu progr & skin/lung M+
Post-operative IMRT (30 patients)								
23	RT	2	6	8	7	0	1 Tu & LN recurr, 1 Tu progr	1 Tu progr & lung M+, 1 intercurrent death
7	CRT	0	1	1	5	0	1 Tu recurr	1 Tu recurr

TRT, treatment; postop, post-operative; CRT, concurrent chemotherapy and IMRT; ICT, induction chemotherapy; RT, radiotherapy; IMRT, intensity modulated radiotherapy; St, stage; M+, metastasis; Tu, primary tumour; LN, lymph node; complic, complication. *Salvage surgery in 1 patient; **salvage surgery in 2 patient.

After 3 years the LRC was 66.1% (standard error (SE) 7.7%) in those receiving definitive IMRT (Figure 1), and 85.4% (SE 6.8%) in those who received IMRT in the post-operative setting (Figure 2). The 3 year LRRFS and OS were 48.5% (SE 9.6%) and 60.3% (SE 9.8%) in the definitive IMRT group; these figures were 82.5% (SE 7.1%) and 85.9% (SE 8.1%) for those treated in the post-operative setting, respectively (Figures 1 and 2).

Further analysis of the patients in the definitive IMRT group showed for the 30 (62.5%) Stage 3/4 patients at 3 years an LRC of 64.7% (SE 9.9%), an LRRFS of 40.7% (SE 12.4%) and an OS of 45.3% (SE 12.8%).

A separate analysis was done for the patients ($n=48$) who had squamous cell cancer (SCC) in the four disease sites: oral cavity ($n=19$), oropharynx ($n=19$), larynx ($n=7$) and hypopharynx ($n=3$). Overall, toxicity data in this SCC subgroup were quite similar to those observed in the total population. RTOG Grade 3 dermatitis occurred in 2 patients (4%), RTOG Grade 3 mucositis was observed in 41 patients (85%), but there was no Grade 4 toxicity. None of the patients in this subgroup discontinued IMRT as result of intolerance. Of the 30 patients in this subgroup who were treated with

definitive IMRT, 21 (70%) developed a CR, 5 (17%) a PR and 2 an SD; the 3 year LRC was 66.8% (SE 10.0) and the 3 year LRRFS and OS were 42.6% (SE 14.3%) and 54.5% (SE 13.6%), respectively (Figure 3). For the 18 patients of this subgroup who were treated with IMRT in the post-operative setting, the 3 year LRC was 82.2% (SE 9.3%), the LRRFS was 82.2% (SE 9.3%) and the OS was 90.0% (SE 9.5%) (Figure 4).

Discussion

In our retrospective audit, IMRT could be delivered without important interruptions, even when given with concurrent chemotherapy and/or after induction chemotherapy. The overall treatment time for the radiotherapy part, which has been reported to be a major prognostic factor [33, 34], was maximally 54 days, although most patients could be irradiated within the foreseen timeframe (median 47 days; range 13–54).

The different treatment strategies within each stage group (Table 4) can be explained by the diversity of tumour sites and by the specific treatment protocols in the different referring hospitals.

Table 6. Treatment options and outcome in relation to tumour stage for patients with a squamous cell carcinoma of oral cavity, oropharynx, hypopharynx and larynx

n	TRT option	St I	St II	St III	St IV	Recurrence (recurr)/progression (progr)	n death/cause
Definitive IMRT (30 patients)							
17	RT	4 ^a	9 ^b	4 ^{cde}	0	2 Tu recurr ^{ab} , 1 LN recurr ^c	1 LN recurr ^c , 1 postop complication ^d
8	CRT	0	3 ^{fgh}	1 ⁱ	4 ^{ijkl}	1 Tu recurr ^f , 1 Tu and LN recurr ^g , 1 Tu progr ^j	1 Tu progr ⁱ , 2 × 2 nd primary ^{hk} , 1 toxic death ^l
5	ICT→CRT	0	1 ^m	0	4 ^{no}	1 Tu recurr ^m , 2 Tu progr ^{no}	1 Tu recurr ^m , 1 Tu progr ⁿ , 1 Tu progr & M+ ^o
Post-operative IMRT (18 patients)							
13	RT	2	4	4 ^p	3 ^q	1 LN recurr ^p , 1 Tu & LN recurr ^q	
5	CRT	0	1	0	4 ^r	1 Tu recurr ^r	1 Tu recurr ^r

TRT, treatment; postop, post-operative; CRT, concurrent chemotherapy and IMRT; ICT, induction chemotherapy; RT, radiotherapy; IMRT, intensity modulated radiotherapy; St, stage; M+, metastasis; d,e,f,i, salvage surgery; Tu, primary tumour; LN, lymph node.

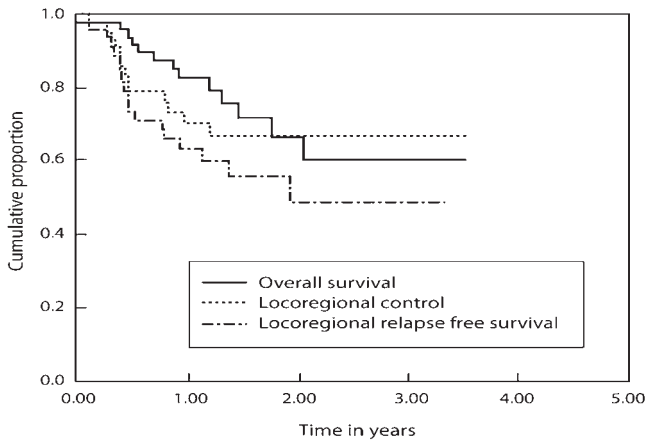


Figure 1. Treatment results in patients receiving intensity-modulated radiotherapy as a definitive non-surgical approach.

We considered the acute toxicity acceptable: skin toxicity was mild with RTOG grade 3 dermatitis in only five patients (7%) and no grade 4; mucosal toxicity was more pronounced with an RTOG Grade 3 mucositis in 64 patients (82%) and only 1 RTOG Grade 4 toxicity. Only one (1.3%) patient refused to continue IMRT after 62 Gy of the planned 70 Gy owing to mucositis. Similar acute toxicity data were reported by Seung et al [35].

After a median follow-up of 18.7 months we observed xerostomia, although not properly graded, in 34 patients (44%), loss of taste in 11 patients (14%), fibrosis of the neck in 7 (9%), dysphagia in 2 patients (of whom 1 needed a permanent feeding tube) and bone and teeth problems in less than 5%.

16 patients (21%) had died, 10 (13%) as a result of treatment failure.

The LRC, LRRFS and OS at 3 years for the whole population in this retrospective audit are difficult to interpret because of the variable patient population, the different disease sites and the different treatment protocols. However, when we focus on the SCCs in the four disease sites, oral cavity, oropharynx, larynx and hypopharynx, then the results do not differ much from those observed in total patient cohort, *i.e.* LRC, LRRFS

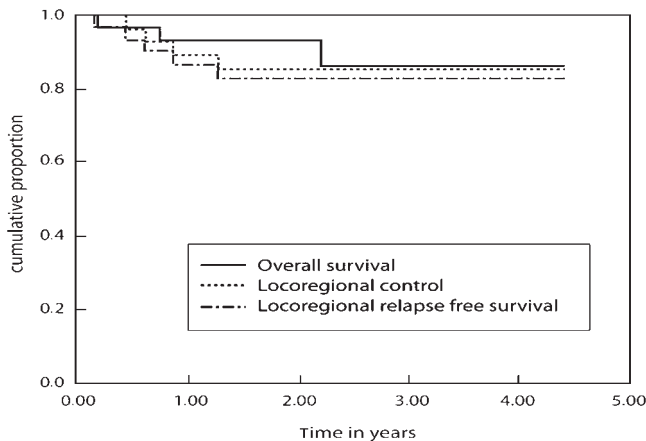


Figure 2. Treatment results in patients treated with intensity-modulated radiotherapy in the post-operative setting.

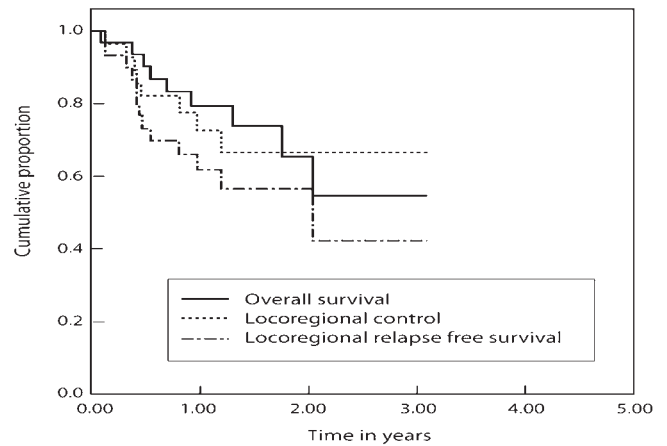


Figure 3. Treatment results with intensity-modulated radiotherapy in primarily non-operated patients with a squamous cell carcinoma of oral cavity, oropharynx, hypopharynx and larynx.

and OS were 66.8%, 42.6% and 54.5%, respectively, for those who received definitive IMRT, and 82.2%, 82.2% and 90.0%, respectively, for those receiving IMRT in the post-operative setting.

Our results are clearly inferior to those reported by several American groups [35–42] but are in line with those reported from institutions in Europe [43–45]. The causes of these differences are merely speculative, but most likely they are both patient and tumour related. In a subset analysis of the international Phase III trial in which patients were treated with radiotherapy alone or with radiation plus cetuximab, survival curves for those patients treated outside the USA were clearly inferior to those treated in the USA, with an absolute difference in 3 year survival of more than 30% [9, 46]. Of interest in this analysis was the fact that only about 50% of the non-USA patients participating in the trial had a performance status more than 80%, while in the USA patients this percentage was much higher (± 75 –80%). It is well known that cross-trial comparisons are notoriously difficult. This may be even more so in case of trials performed in different continents.

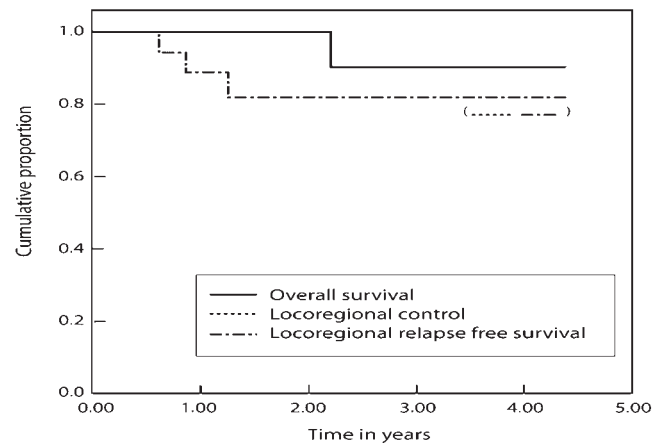


Figure 4. Treatment results with intensity-modulated radiotherapy in patients with a squamous cell carcinoma of oral cavity, oropharynx, hypopharynx and larynx in the post-operative setting.

Conclusion

We consider IMRT feasible and safe in our patient population not only as single modality for locoregional HNC but also after surgery, induction chemotherapy and when given concurrently with chemotherapy. Acute and late toxicity were considered acceptable.

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