

HEAD AND NECK

Post-operative intensity-modulated vs 3D conformal radiotherapy after conservative surgery for laryngeal tumours of the supraglottic region: a dosimetric analysis on 20 patients

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SUMMARY

Objective. To perform a dosimetric comparison between intensity modulated radiotherapy (IMRT) and 3D conformal radiotherapy in patients with locally advanced (stage III and IV) tumours of the supraglottic region treated with conservative surgery and post-operative radiotherapy.

Methods. An in-silico plan using a 3D conformal shrinking field technique was retrospectively produced for 20 patients and compared with actually delivered IMRT plans. Eighteen structures (arytenoids, constrictor muscles, base of tongue, floor of mouth, pharyngeal axis, oral cavity, submandibular glands and muscles of the swallowing functional units [SFU]) were considered.

Results. IMRT allowed a reduction of maximum and mean doses to 9 and 14 structures, respectively ($p < .05$).

Conclusions. IMRT achieved a reduction of unnecessary dose to the remnant larynx and the majority of surrounding SFUs. Further prospective analyses and correlations with functional clinical outcomes are required to confirm these dosimetric findings.

KEY WORDS: adjuvant treatment, IMRT, 3D-conformal radiotherapy, conservative surgery, laryngeal tumors

Introduction

Compared to traditional 3D-conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT) has been associated with an overall improvement in the cost/benefit ratio of radiation treatments for several cancers of the head and neck (HN) region ^{1,2}. Indeed, thanks to its more favourable dosimetric profile, IMRT has allowed for ameliorations in oncologic outcomes (e.g. advanced nasopharyngeal tumours) along with a lower prevalence of long-term side effects (e.g. xerostomia and dysphagia) ³⁻⁶. Therefore, IMRT is currently considered the gold standard for several HN subsites ⁷.

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In the context of organ preservation strategies for laryngeal cancers, conservative surgery followed by post-operative radiotherapy (PORT) represents the standard of care for locally advanced tumours as an alternative to concurrent chemoradiation⁸⁻¹⁰. Nevertheless, functional outcomes of patients treated with this combined approach (surgery and PORT) may not be fully satisfactory. In particular, treatment of the supraglottic (SG) region is burdened by a higher rate of dysphagia and respiratory dysfunction, due to the crucial role of this area in swallowing and breathing¹¹. Consistently, up to one-third of patients treated with PORT following conservative surgery may require enteral nutrition and/or permanent tracheostomy, or experience chondronecrosis¹²⁻¹⁴. This unfavourable long-term toxicity profile could be explained by the combination of surgical and radiation-related scarring and fibrosis which may impair the functionality of the remnant larynx.

Whether the use of IMRT can impact the toxicity profile in this clinical setting has not been extensively studied. Moreover, although IMRT is the standard technique to treat patients with HN cancer patients, it is still not extensively applied to all patients in many middle and low-income countries (MLIC). Therefore, the aim of the present analysis is to perform a dosimetric comparison investigating whether IMRT can minimize irradiation of healthy tissues compared to 3D-CRT in the setting of patients treated with PORT for tumours of the SG region after a conservative surgical approach.

Materials and methods

Data from 20 patients treated at our institution with conservative surgery for tumours of the SG area followed by post-operative IMRT were retrospectively reviewed and included in this study. The availability of written informed consent for the anonymised use of data for clinical research purposes was verified for each patient meeting inclusion criteria.

As per international and institutional guidelines, indication to PORT was given for patients with pT3/pT4 and/or close/positive surgical margins and/or ≥ 2 positive lymph nodes and/or lymph node > 3 cm and/or extracapsular extension (ECE) and/or adverse biological characteristics (perineural invasion, lympho-vascular infiltration and grading).

All patients were treated with Simultaneous Integrated Boost (SIB) - Volumetric Modulated Arc Therapy (VMAT) IMRT technique. Total prescription doses were: 66 Gy (2 Gy/fr) for lymph node(s) with ECE (High-Dose [HD]-volume); 59.4 Gy (1.8 Gy/fr) for the primary tumour bed (pT3, pT4) or pathologic lymph nodes without ECE (High-Risk [HR]-volume); 56.1 Gy (1.7 Gy/fr) for prophylactic irradiation of neck lymph nodes (Low-Risk [LR]-volume). In case of positive surgical margins to the primary surgical bed, prescription doses ranged from 60 to 66 Gy. In absence of positive surgical margins and

ECE, two dose levels (60 Gy 2Gy/fr and 54 Gy 1.8 Gy/fr for 30 total fractions) were prescribed. The whole remnant larynx was contoured as Clinical Target Volume (CTV) for the primary tumour (CTV T), while the entire neck level was included for the lymph node echelon irradiation (CTV N). A margin of 0.5 cm was given to CTV to obtain Planning Target Volumes (PTV). In all patients, the remnant larynx was contoured and dose distribution was optimised to avoid hotspots in this area ($> 107\%$ of the prescribed dose).

For the present analysis, arytenoids, constrictor muscles, base of tongue, floor of mouth (FOM), pharyngeal axis and submandibular glands were retrospectively contoured, as well as Swallowing Functional Units (SFU) (genioglossus muscle, hyoglossus/styloglossus muscle complex, intrinsic tongue muscles, longitudinal pharyngeal muscles, thyrohyoid muscle) as described by Gawryszuk et al.¹⁵.

Using the same volumes (both for target and organs at risk) and similar dose prescription (66, 60 and 54 Gy) as the IMRT plan, an in-silico RT treatment plan with 3D conformal shrinking field technique was retrospectively planned for each patient. A conventionally fractionated schedule (1 daily fraction of 2 Gy for 5 days/week) was prescribed. The surgical bed and upper and middle neck lymph nodes were irradiated with two opposing latero-lateral fields. Conversely, an anterior-posterior field was used to irradiate the lower neck echelons. The Planning Risk Volume (PRV) of spinal cord (spinal cord + 0.5 cm) received up to 40-42 Gy. The primary goal of the 3D treatment plan was dosimetric coverage of the CTVs.

Maximum (Dmax) and mean (Dmean) doses to the above-defined structures were retrieved from the IMRT plans and compared to the corresponding absorbed dose of the 3D conformal technique plans. When the remnant larynx was considered as target volume, IMRT and 3D-CRT techniques were compared in terms of difference between the prescribed dose and the maximum absorbed dose. In patients with the highest dose prescription (66 Gy) to lymph node echelon volume (10 patients), the absorbed dose to the remnant larynx was also quantified in order to explore the potential role of IMRT in reducing the unnecessary dose to the primary tumor surgical bed. Non-parametric Wilcoxon signed-rank tests were used to assess the statistical significance of the dose differences between the two treatments. A detailed description of dose prescriptions for the target volumes is reported in the Supplementary Materials (Tab. I).

Results

Clinical and tumour characteristics of enrolled patients, as well as long-term toxicity in terms of enteral nutrition and tracheostomy, are reported in Table I. Eighteen structures

were contoured in 20 patients by an expert radiation oncologist (DA) for a total of 360 contours.

Organs at risk

The dosimetric comparison showed that the average absorbed dose, in terms of both Dmax and Dmean, was higher ($p < 0.05$) in case of 3D-CRT for the majority of the structures analysed (Tab. II).

For 11%, 33% and 39% of structures, IMRT improved the absorbed dose for only Dmax, only Dmean and both, respectively. Only the pharyngeal axis received an average lower dose when treated with 3D-CRT compared to IMRT. For the oral cavity and oesophagus, no differences were found considering maximum and mean doses between the two technical approaches.

Among 7 patients for which one arytenoid had been surgically removed, the dosimetric comparison on the remnant arytenoid showed that the average Dmax and Dmean to the

remnant arytenoid was 65.6 Gy and 64.8 Gy for 3D-CRT versus 61.5 Gy and 60.7 Gy for IMRT. Details on data distribution of all structures analysed for both 3D-CRT and IMRT techniques are provided through violin plots (Figs. 1-3).

Remnant larynx

The remnant larynx received a lower average dose both for Dmax (67.95 vs 67.27 $p = 0.0026$ for 3D-CRT and IMRT, respectively) and Dmean (63.39 vs 60.06 $p < 0.001$ for 3D-CRT and IMRT, respectively) when treated with IMRT compared to 3D-CRT.

If we consider only the 10 patients with ECE lymph nodes, the average Dmax to the remnant larynx was lower in the IMRT plans compared to 3D-CRT plans: 65.74 Gy (median 65.27 Gy, IQR: 63.16-67.84) vs 69.27 (median 70.26 Gy, IQR: 66.89-71.59), respectively; the average Dmean was lower as well: 58.18 Gy (median 61.05 Gy, IQR: 59.83-

Table I. Summary of clinical and tumour characteristics of enrolled patients and long-term toxicity (enteral nutrition and tracheostomy).

Patient ID	Gender	Age	Smoking habit	Comorbidities	Surgery	Enlarged surgery	Arytenoid removal	Tumour grading	Surgical margins	Perineural invasion	Lymphovascular invasion
1	M	74	ex	yes	E	no	no	G3	neg	no	no
2	M	58	ex	no	O	yes	no	G3	close	yes	yes
3	M	70	no	no	O	no	yes	G1	pos	no	no
4	M	54	ex	yes	O	no	no	G1	neg	no	no
5	M	64	ex	yes	O	yes	no	G3	pos	yes	no
6	M	67	ex	yes	E	yes	no	G3	neg	no	no
7	M	53	ex	no	O	yes	no	G3	close	no	no
8	M	60	yes	no	O	no	no	G2	neg	no	yes
9	F	62	ex	no	O	yes	no	G3	neg	no	no
10	M	57	ex	no	O	yes	no	G2	pos	no	no
11	M	59	ex	yes	O	no	yes	G1	neg	yes	no
12	M	58	ex	yes	O	no	yes	G2	neg	no	no
13	M	61	yes	yes	O	no	no	G2	neg	no	no
14	F	71	yes	yes	O	no	no	G3	close	no	no
15	F	62	yes	yes	O	no	yes	G2	neg	no	no
16	M	60	ex	yes	O	no	no	G2	neg	yes	no
17	M	41	yes	yes	O	no	yes	G3	neg	no	no
18	F	60	ex	no	E	no	no	G3	neg	no	no
19	M	75	yes	yes	O	no	yes	G2	neg	yes	no
20	M	56	ex	no	O	no	yes	G3	neg	no	no

E: endoscopic; F: female; G: grade; M: male; neg: negative; O: open; pos: positive.

62.02) vs 63.12 Gy (median 64.01 Gy, IQR: 62.80-68.10), respectively, for IMRT over 3D-CRT.

In 4 patients, the remnant larynx did not represent a target volume (pT1-pT2 with no adverse risk factors). Even if the dose received by this structure remained high, due to the proximity to neck lymph nodes areas (irradiated at different dose levels), the average absorbed dose resulted lower in IMRT plans compared to 3D-CRT plans: Dmax 65.11 Gy (median 64.84 Gy, IQR: 63.49-66.46) vs 67.27 Gy (median 67.95 Gy, IQR: 66.53-68.69), respectively; Dmean 53.47 Gy (median 53.86 Gy, IQR: 46.33-61.00) vs 58.77 Gy (median 59.20 Gy, IQR: 56.43-61.54), respectively.

Moreover, the average difference between the prescribed dose and absorbed dose (Δd) to the remnant larynx was significantly lower in the IMRT plans compared to 3D-CRT plans for both Dmax ($p = .00252$) and Dmean ($p = .00048$). Specifically average difference for Dmax was 18.01 Gy (median 7.01 Gy, IQR: 3.52-11.63) vs 20.39 Gy (median

9.71 Gy, IQR: 6.43-13.86) for IMRT and 3D-CRT, respectively while for Dmean was 10.69 Gy (median 1.68 Gy, IQR: 0.26-5.61) vs 15.18 Gy (median 5.29, IQR: 3.53-9.92) for IMRT and 3D-CRT, respectively.

Discussion

According to international guidelines, PORT for laryngeal tumours can be performed using either a 3D conformal technique or an IMRT⁷. Nevertheless, in patients treated with PORT after a mini-invasive surgical procedure, several studies recommend the use of modern RT techniques in order to better conform the dose distribution and reduce the absorbed dose to the healthy tissues, including but not limited to the remnant larynx¹⁶⁻¹⁹. The findings of the present study clearly show that IMRT can minimise the unnecessary dose to tumour surgical bed (remnant larynx) and reduce the absorbed dose to swallowing-related structures in this setting. To our knowledge, this is the first report that

Extracapsular extension	Pathologic tumour category	Pathologic lymph node category	Concurrent chemotherapy	Tracheostomy during radiotherapy	Temporary tracheostomy during follow-up	Tracheostomy at last follow-up	Enteral nutrition during follow-up	Enteral nutrition at last follow-up
yes	T1	N1	no	no	yes	yes	yes	yes
yes	T2	N3	yes	no	no	no	no	no
no	T3	N0	no	no	no	no	no	no
yes	T2	N1	no	no	yes	no	yes	no
yes	T3	N2c	yes	no	yes	no	no	no
no	T1	N2b	no	no	no	no	no	no
no	T3	N0	no	no	no	no	no	no
yes	T1	N3	no	no	no	no	no	no
no	T2	N2c	yes	no	no	no	no	no
no	T3	N2c	no	no	no	no	no	no
no	T3	N0	no	no	no	no	no	no
no	T3	N2a	no	yes	no	no	no	no
yes	T3	N1	yes	no	no	no	no	no
no	T3	N0	no	yes	yes	no	no	no
yes	T3	N2c	yes	yes	yes	no	no	no
no	T4a	N0	no	no	no	no	no	no
no	T3	N0	no	no	no	no	no	no
no	T2	N2a	no	no	no	no	no	no
yes	T3	N2b	no	no	yes	no	no	no
no	T4a	N0	no	no	yes	no	no	no

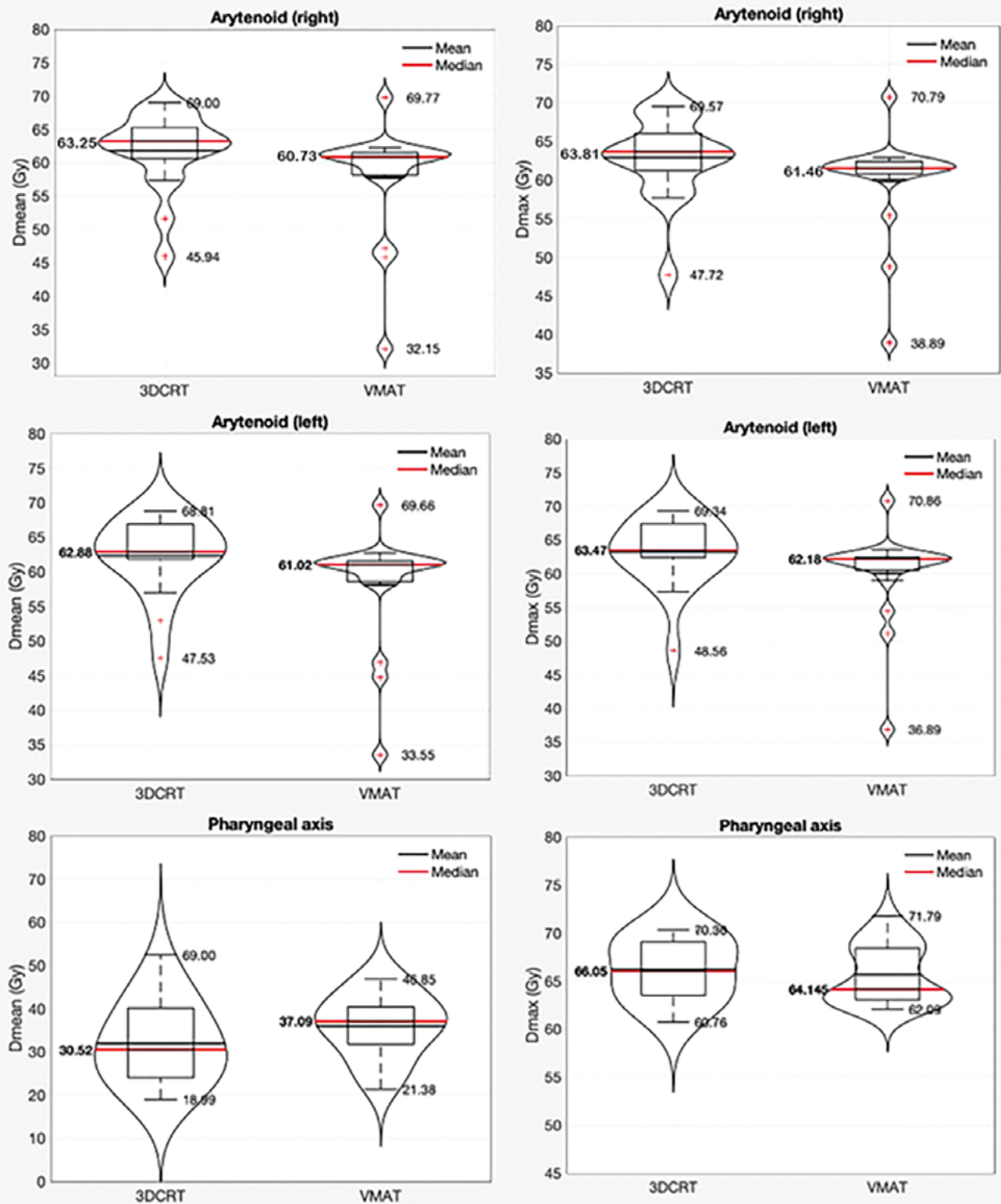
Table II. Dosimetric comparison of absorbed doses to swallowing-related structures and remnant larynx between 3D-conformal radiotherapy and volumetric arc modulated radiotherapy.

Organs at risk	Median Dmax (Gy)			Median Dmean (Gy)		
	3D-CRT	IMRT	p value	3D-CRT	IMRT	p value
Remnant larynx	67.95	65.27	0.0025	63.38	60.86	< 0.001
Floor of mouth	64.83	62.97	< 0.001	48.82	44.63	0.3898
Genioglossus muscles	62.10	60.64	< 0.001	42.77	42.32	0.6031
Hyoglossus/styloglossus muscles complex (right)	63.91	62.78	0.3125	58.44	56.14	0.0013
Hyoglossus/styloglossus muscles complex (left)	64.96	62.72	0.0226	58.31	55.36	0.0045
Intrinsic tongue muscles	59.88	60.46	0.1010	21.36	33.18	0.0332
Longitudinal pharyngeal muscles	62.40	62.86	0.2340	52.97	50.93	0.0015
Constrictor muscles	65.12	64.81	0.3320	57.87	55.82	< 0.001
Thyrohyoid muscle (right)	66.80	63.33	< 0.001	64.99	60.72	< 0.001
Thyrohyoid muscle (left)	68.26	63.07	< 0.001	65.13	61.18	< 0.001
Arytenoid (right)	63.81	61.46	0.0075	63.25	60.73	0.0037
Arytenoid (left)	63.47	62.18	0.0065	62.88	61.02	0.0032
Pharyngeal axis	66.05	64.14	0.2263	30.53	37.10	0.0151
Base of tongue	63.86	62.87	0.2627	57.88	55.02	< 0.001
Oral cavity	62.70	62.45	0.3524	26.57	34.37	0.0524
Oesophagus	62.75	62.08	0.2041	31.86	33.17	0.2627
Submandibular gland (right)	65.16	62.52	0.0010	62.44	56.02	< 0.001
Submandibular gland (left)	64.19	61.98	0.0139	62.30	56.81	< 0.001

3D-CRT: 3D-conformal radiotherapy; Dmax: maximum dose; Dmean: mean dose; IMRT: intensity modulated radiotherapy; Gy: gray.

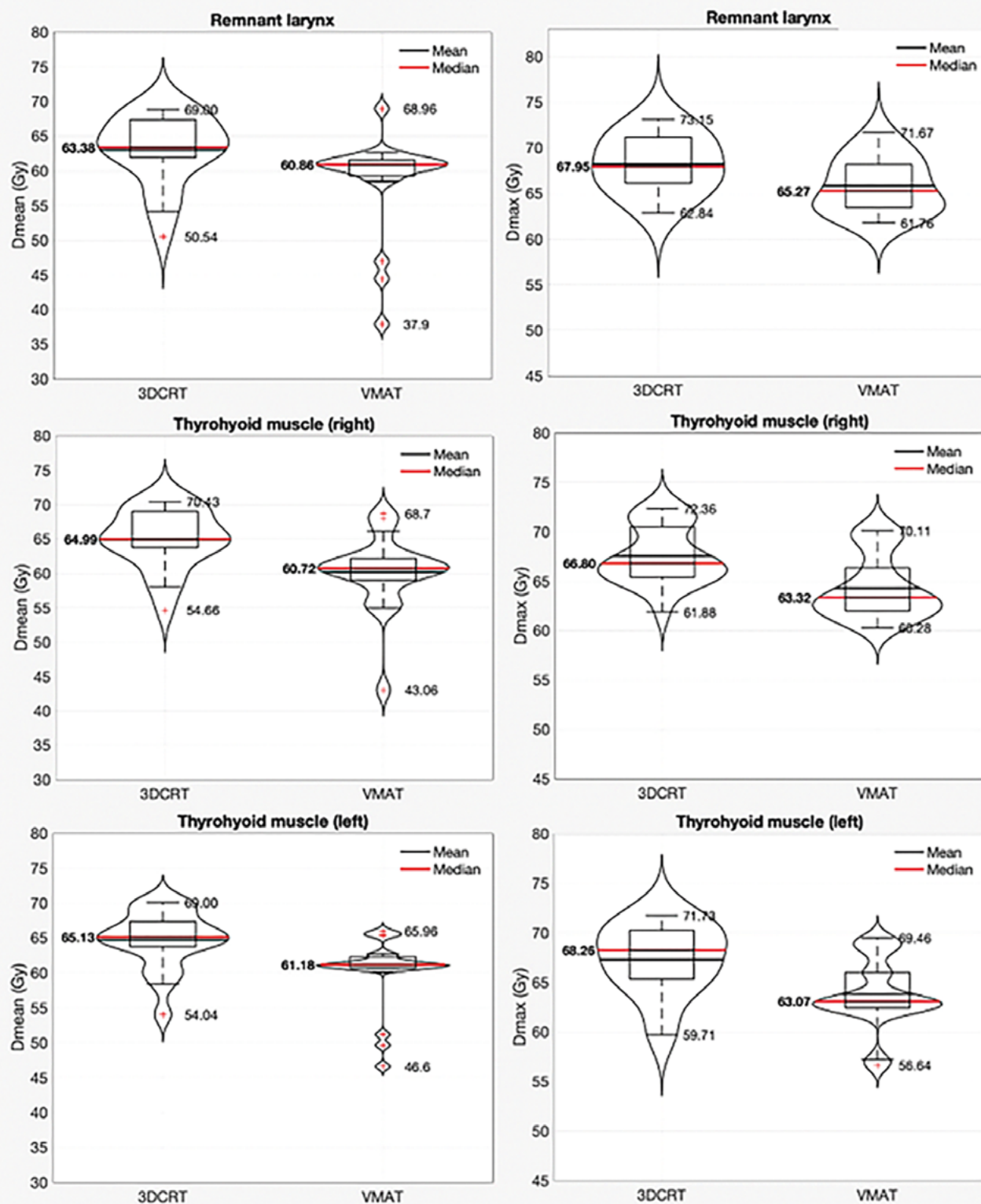
quantifies the dosimetric advantage of IMRT over 3D-CRT in the setting of PORT after laryngeal preservation surgery, providing the proof of concept that more conformed radiation techniques can improve laryngeal functional outcomes. In a previously published study by our group²⁰, the toxicity profile of 20 patients treated with IMRT was compared to that of 32 patients who received 3D-CRT. Compared to the 3D-CRT group, patients treated with IMRT experienced a lower rate of permanent aspiration/pneumonia (6% vs 0%, respectively), laryngeal stenosis requiring endoscopic dilatation (21% vs 15%, respectively), laryngeal necrosis (6% vs 0%, respectively), and permanent tracheostomy (12.5% vs 5%, respectively). Female gender was associated with an increased risk of temporary tracheotomy and chondronecrosis, while older age correlated with a higher risk of enteral nutrition. Unfortunately, due to the unavailability of the majority of 3D-CRT plans (no longer available due to the old version of the treatment planning system), it was not possible to carry out a dosimetric comparison between the two cohorts. We believe that the results of the present study provide strong support to those clinical findings. Indeed, in the comparative dosimetric analysis, the remnant larynx received a lower dose in the IMRT cohort compared to the 3D-CRT cohort not only as a group but also in all the sub-analyses performed. After a surgical organ preservation strategy, laryngeal func-

tion depends on several other factors, including age, gender, comorbidities, and extension of the surgical approach, as well as the availability of a rehabilitation service^{12,13,19}. Moreover, several healthy structures are involved in the swallowing and breathing processes. Specifically, irradiation of the pharyngeal constrictor muscles has been demonstrated to be associated with long-term swallowing defects. Moreover, the so-called dysphagia-aspiration-at-risk structures (DARS – constrictor muscles, glottic and SG larynx), as well as muscle-based SFU can also have an impact on reducing radiation-related dysphagia^{6,15,22,23}. Accordingly, minimising the absorbed dose to the above-mentioned structures may theoretically reduce long-term dysphagia and aspiration. The present analysis showed that both mean and maximum doses to swallowing-related structures were significantly lower in the IMRT plans compared to the 3D-CRT for the majority of the analyzed structures. Hence, the results of this study provide the proof of concept that a more conformal radiation technique can allow improvement of long-term swallowing defects, although a dose/volume constraint threshold is not yet available. PORT is indicated in the case of advanced tumour stage, positive surgical margins, pathologic nodal involvement, and aggressive biological behaviour⁷. The prescribed dose varies according to the pathologic characteristics of the tumour



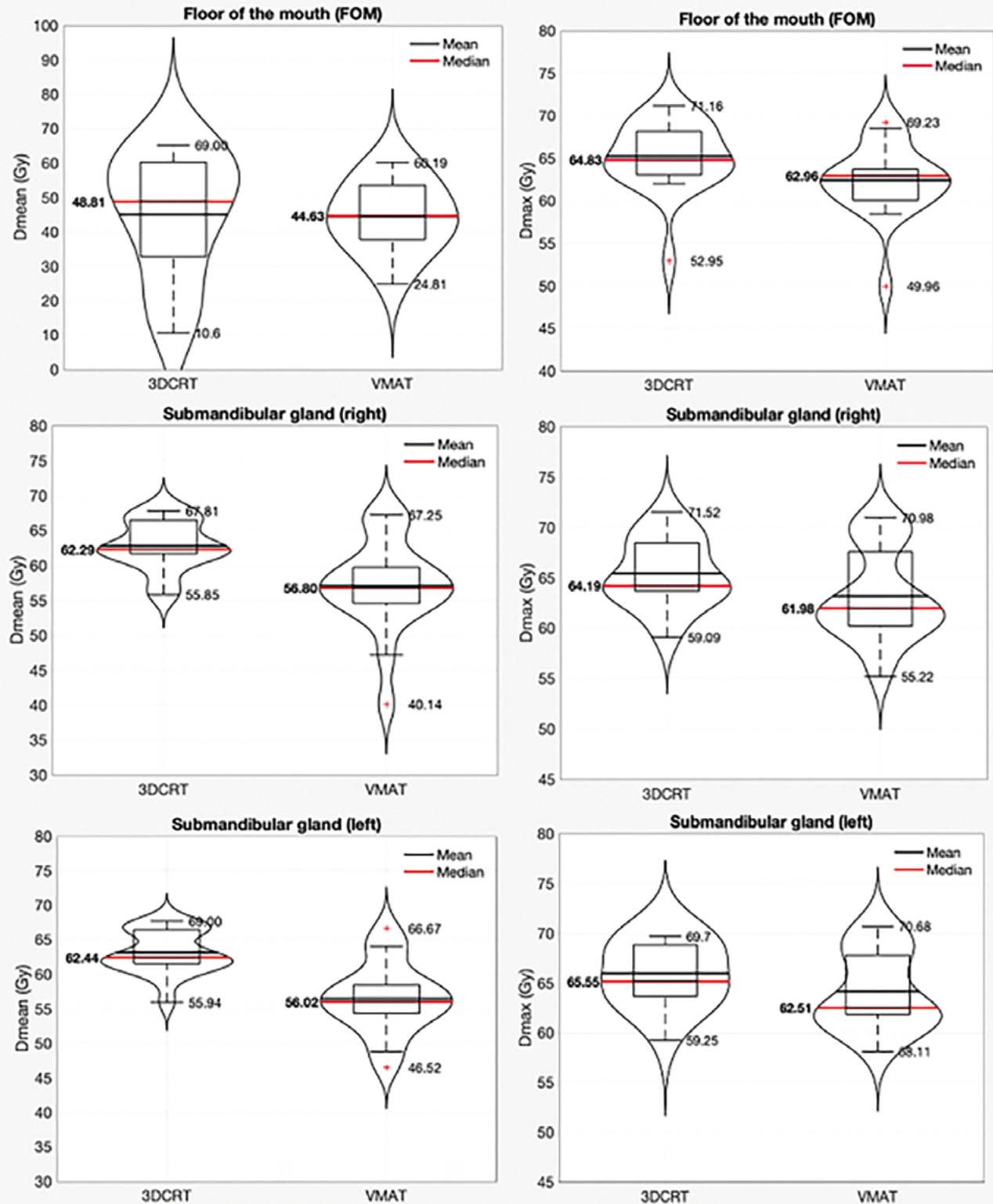
3DCRT: 3D conformal radiotherapy; VMAT: volumetric modulated Arc therapy; Dmean: Mean dose; Dmax: maximum dose.

Figure 1. Comparison between mean doses (left) and maximum doses (right) of right arytenoid (top), left arytenoid (center), pharyngeal axis (bottom) between the two techniques; whiskers represent the minimum and the maximum values (outliers are excluded and represented with red crosses).



3DCRT: 3D conformal radiotherapy; VMAT: volumetric modulated Arc therapy; Dmean: Mean dose; Dmax: maximum dose.

Figure 2. Comparison between mean doses (left) and maximum doses (right) of remnant larynx (top), right thyrohyoid muscle (center), left thyrohyoid muscle (bottom) between the two techniques; whiskers represent the minimum and the maximum values (outliers are excluded and represented with red crosses).



3DCRT: 3D conformal radiotherapy; VMAT: volumetric modulated Arc therapy; Dmean: Mean dose; Dmax: maximum dose.

Figure 3. Comparison between mean doses (left) and maximum doses (right) of floor of the mouth (top), right submandibular gland (center), left submandibular gland (bottom) between the two techniques; whiskers represent the minimum and the maximum values (outliers are excluded and represented with red crosses).

and the region considered, with areas at higher or lower risk of local recurrence requiring different doses⁷. The majority of patients in the present cohort had a diagnosis of advanced primary tumour (pT3-pT4) and only three patients had positive surgical margins, and thus a median dose of 60 Gy was prescribed to the primary tumour surgical bed. However, a statistically significant difference was found between 3D-CRT and IMRT, both in terms of maximum and mean dose to the remnant larynx. Moreover, a lower difference between the prescribed and absorbed dose was found in IMRT compared to 3D-CRT plans. These findings suggest that IMRT allows to reduce the unwanted dose to the remnant larynx thanks to the more conformity dose distribution.

Of note, in patients with early category primary tumours (pT1, pT2) the prescribed dose to the remnant larynx could be further reduced or even avoided in selected cases. An exploratory study on 4 patients for which the remnant larynx did not represent a target volume was also performed, which confirmed that IMRT allowed reduction of the absorbed dose to this structure compared to 3D-CRT. Nevertheless, due to the number of patients in the present cohort, whether IMRT can gain a dosimetric improvement in this setting needs to be investigated further.

Both quality of life and overall survival of patients treated with a laryngeal organ preservation strategy for locally advanced tumours can be worsened by long-term treatment-related side effects. Indeed, swallowing and breathing dysfunctions might cause recurrent ab-ingestis pneumonitis, respiratory distress and dysphagia. Results of the Radiation Therapy Oncology Group 91-11 trial showed that deaths not attributed to larynx cancer or treatment were higher in patients treated with concurrent chemoradiation compared to those treated with induction chemotherapy followed by radiation alone (69.8% vs 52.8%, respectively, at 10 years; $p=0.03$)²⁴. It was hypothesised that fatal treatment-related episodes not identified with the system for monitoring and grading late effects could have occurred. Overall, they suggested that new strategies aiming to improve the rate of functional organ preservation and, as a consequence, reduce long-term morbidity, are needed in these patients. Therefore, achieving a functional larynx as a result of an organ preservation strategy (performed either with conservative surgery or chemoradiation) should represent the primary goal not only to maintain a good quality of life, but also to not compromise long-term survival.

In addition to dosimetric comparison, more complex radiobiological models are currently used to quantify the clinical benefit (if any) of modern radiation treatment techniques over “traditional” approaches. Normal Tissue Complication Probability (NTCP) models aim to assess a patient’s risk of developing a given radiation-associated toxicity.

Several NTCP models have been developed and validated for patients with HN cancers^{25,26}. Unfortunately, due to both the strict patient selection criteria and the retrospective nature of the current study, our cohort could not be used either to validate NTCP models already available in the literature or to build new models for swallowing and /or respiratory dysfunction.

Even if IMRT is considered worldwide to be the standard of care for the treatment of HN patients, less conformal techniques are still used in daily clinical practice in several MLICs. HN cancer is a global health issue and IMRT may not be offered routinely in many MLICs, offering only two-dimensional RT or 3D-CRT. Indeed, of a total of nearly 15,000 megavoltage machines in operation worldwide, only 37% are in MLICs, even though they account for more than 80% of the global population^{27,28}. Therefore, we strongly believe that our study may have a wider implementation, helping the future evaluation of health economics and the prioritisation of the introduction of IMRT for HN patients. We are aware that the main flaw of the study is the small sample size. While the majority of dosimetric parameters favour IMRT, the results of statistical analysis should be considered with caution due to the limited number of patients analysed. Moreover, it is yet to be determined whether the dosimetric advantage of IMRT over 3D-CRT could translate into a lower incidence of radiation-related toxicity. Therefore, further analysis including patients treated with PORT after a laryngeal surgical preservation approach is required to investigate the correlation (if any) between dosimetric and clinical findings. In addition, the majority of patients in the present cohort had a locally advanced tumour stage, which prevented exploring the existence of dosimetric differences between early- and late-stage groups. However, we believe that the findings provided by this analysis can lead to further studies with the aim of investigating the role of the IMRT technique in reducing treatment-related swallowing and breathing impairments in the setting of laryngeal organ preservation strategies.

Conclusions

Compared to 3D-CRT, the present dosimetric analysis showed that adjuvant IMRT achieved a significant reduction in the unnecessary dose to both remnant larynx and surrounding swallowing-related structures in patients with locally advanced SG tumours treated after conservative surgery. Further studies with a larger number of patients providing a correlation between laryngeal functional outcomes and absorbed dose to swallowing-related structures are needed to assess the clinical impact of such a dosimetric advantage.

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Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

DA, SM, BAJF: conceptualisation; DA, SM, SV, CA: methodology; SV, VZ, AF, SVo, FB, MGv, SG: data curation; SM, CIF, AC: data collection; DA, SM, MGv, MZ: writing - original draft; all authors: writing: editing & review; MGv: visualisation; MA, CA, BAJF, AS: supervision.

Ethical consideration

The study was approved by the Institutional Ethics Committee (RTP R044).

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

Written informed consent was obtained from each participant/patient for study participation and data publication.

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Supplementary Table I. Dose prescription and mean and maximum doses to the remnant larynx.

Patient ID	Prescription dose to "High dose area" (Gy)	Prescription dose to "High risk area" (Gy)	Prescription dose to "Low risk area" (Gy)	Prescription dose to remnant larynx (Gy)	Mean IMRT dose to the remnant larynx (Gy)	Maximum IMRT dose to the remnant larynx (Gy)	Mean 3D-CRT dose to the remnant larynx (Gy)	Maximum 3D-CRT dose to the remnant larynx (Gy)
1	63	60	54	0	60.77	67.29	62.58	67.60
2	66	59.4	56.1	59.4	62.59	64.35	63.11	66.81
3	-	59.4	56.1	59.4	61.42	63.95	63.66	66.08
4	66	59.4	56.1	59.4	61.11	62.96	62.74	65.23
5	66	59.4	56.1	59.4	62.32	69.33	66.96	71.37
6	-	60	54	0	61.71	63.46	61.19	68.30
7	-	60	54	60	60.14	70.22	65.07	68.42
8	66	59.4	56.1	56.1	68.96	71.67	68.54	73.15
9	66	59.4	56.1	0	46.95	66.19	54.12	69.86
10	66	59.4	56.1	66	61.06	68.28	68.84	70.66
11	-	60	54	60	60.96	63.38	62.99	66.52
12	66	59.4	56.1	59.4	60.20	62.58	63	67.11
13	66	59.4	56.1	59.4	37.90	61.76	50.54	64.87
14	-	60	54	60	58.40	68.12	56.13	62.84
15	66	59.4	56.1	59.4	59.71	63.74	64.91	71.96
16	-	60	54	60	60.33	63.04	63.72	66.17
17	-	59.4	56.1	59.4	61.69	69.72	67.80	71.62
18	-	60	54	0	44.45	63.50	57.20	63.33
19	66	59.4	56.1	59.4	61.04	66.51	68.48	71.66
20	-	60	54	60	58.81	66.90	68.65	71

3D-CRT: 3D-conformal radiotherapy; IMRT: intensity modulated radiotherapy; Gy: gray.