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Dose planning

Radiotherapy for unresectable sinonasal cancers: Dosimetric comparison of intensity modulated radiation therapy with coplanar and non-coplanar volumetric modulated arc therapy

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ABSTRACT

Background and purpose: To compare volumetric modulated arc therapy (VMAT) and intensity modulated radiation therapy (IMRT) plans for treatment of unresectable paranasal sinuses cancers (PNSCs) with different clinical presentations.

Material and methods: Four patients treated for primary target volume only (group 1), four requiring elective nodal irradiation (group 2) and four with positive nodes in macroscopic disease (group 3) were selected. For each patient were generated 7 fields IMRT, coplanar VMAT (c-VMAT) and non-coplanar VMAT (nc-VMAT) treatment plans. Total doses were 70 Gy and 54 Gy to high dose planning target volume (HD-PTV) and low-dose-PTV, respectively. Dose–volume histogram, conformity and homogeneity index (CI and HI), and monitor units (MUs) per Gy were evaluated.

Results: VMAT provided significantly better target coverage, in terms of $V_{100\%}$ (Volume encompassed by the isodose 100%), than IMRT, in particular when nc-VMAT was used. In general, organ at risk sparing is similar with the three approaches, although nc-VMAT can allow a statistically significant reduction of dose to contralateral parotid gland and cochlea for all three groups.

Conclusions: VMAT can offer significant improvement of treatment for all unresectable PNSCs over existing IMRT techniques. In particular, nc-VMAT may be a further advantage for those patients with sinonasal cancers and involvement of the nodes in whom large volumes and complex/irregular shape have to be irradiated, even if clinical benefits should be established in the future.

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Paranasal sinuses cancers (PNSCs) represents 3–5% of all head and neck (H&N) carcinomas and less than 1% of all tumors [1,2]. The majority of sinonasal tumors have epithelial origin, like squamous cell carcinoma (SCC), intestinal-type adenocarcinoma (ITAC), undifferentiated (SNUC) and neuroendocrine carcinoma (SNEC) [2], generally diagnosed at advanced stages [1]. Outcomes for unresectable stages are poor and radiotherapy (RT) is recommended as standard treatment, possibly combined with chemotherapy (CHT), even if the evidence supporting this association is limited in this specific head and neck subsite [1,3].

Due to the horseshoe-shaped target volume and the proximity or involvement of several critical structures (dura, brain, middle cranial fossa, orbital apex and clivus), these tumors are good candidates for intensity modulated radiation therapy (IMRT) although often outcomes for patients with unresectable Stage IVB PNSC are not duly reported [3–6]. A total dose of at least 65 Gy was a significant positive prognostic factor for tumor local control and overall survival, prompting to further dose escalation [3]. Unfortunately, despite IMRT benefits, potential treatment-related toxicity, in particular visual impairment, has so far limited the investigation of dose escalation.

Volumetric modulated arc therapy (VMAT) is based on modulated rotational delivery, as opposed to IMRT with static gantry. A volumetric dose distribution is achieved through one or more gantry rotations, with continuous variation of gantry speed, dose rate and multileaf collimator (MLC) leaf positions.

VMAT improves not only target coverage and/or critical structure sparing, but also delivery efficiency compared to conventional IMRT in several H&N cancers [7–17]. Few data are available on VMAT efficacy for locally advanced or unresectable PNSC. In one

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report on 4 patients staged T4, postoperative VMAT provided no significant dosimetric improvements compared to IMRT, even if authors concluded that "the findings may change with a larger sample of patients in this rare condition" [18]. A comparison of conventional IMRT with single arc and multiple arc VMAT in 5 PNSC patients (only one submitted to definitive RT) revealed increasing spread of low doses to lenses and decreased target coverage in inter-orbital region with the technique [10].

Our comparative study evaluated the potential benefits of VMAT compared to conventional IMRT in patients with unresectable PNSC and the impact of a more complex VMAT setup, including non coplanar arcs, on different clinical presentations.

Patients and methods

Patients

Twelve patients with epithelial PNSC, staged IVB and treated with induction-CHT and concomitant RT-CHT, were selected as follows: 4 cases receiving RT on the primary target volume only (group 1), 4 cases without nodal involvement but needing elective nodal irradiation (group 2) and 4 cases with nodal involvement (group 3). The original treatments were IMRT for 5 patients, c-VMAT for 4 patients and nc-VMAT for 3 patients. Disease characteristics, staging and tumor volumes are summarized in Table 1.

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Volume definition

All patients, with an immobilization thermoplastic mask with 5 fixation points underwent a planning computed tomography scan with 3 mm slices, from skull apex to the mid-sternum. The gross tumor volume (GTV) included primary tumor and positive lymph nodes, determined by clinical information, endoscopic and magnetic resonance imaging (MRI).

To define High Risk–Clinical Target Volume (HR–CTV) around primary tumors we added to GTV an anatomic expansion to take into account subclinical extension. Thus, this margin can vary largely. We followed the definition used by Claus, who defined the compartment-related CTV as follows: in the nonoperated patient, the CTV was based on the MRI imaging of the GTV; in those regions where GTV was flanked by intact bone or by cranial nerves, no margin was added; in those regions where GTV invaded compartments enclosed by bone, like other paranasal sinuses, or extended up to their ostia, the whole compartment was included in the CTV contours; in those regions where GTV invaded radiologically defined spaces known to resist poorly invasion by malignant tumors (e.g., masticator or parapharyngeal spaces), and where GTV invaded the orbit or extended intracranially, either the entire space or a margin of 0.5–1.0 cm was added to the GTV edge [19].

A low-risk CTV (LR-CTV) was defined for group 2 patients including bilateral nodal levels Ib–III and retropharyngeal nodes, according to international guidelines [20]. Within group 3, for patients staged b $\geqslant$N2b, the LR-CTV included all ipsilateral neck or bilateral neck. Planning target volumes (HR-PTVs and LR-PTVs) were generated by adding a 3 mm margin to the corresponding CTVs.

Organs at risk (OARs) included optic chiasm, optic nerves, brainstem, spinal cord, temporal lobes, eyeballs, cochleae, lenses and lacrimal glands. Parotid glands, mandible, glottic larynx were also considered for patients needing elective or curative neck irradiation. Optic nerves were divided into ipsi-lateral and contra-lateral, according to tumor proximity. In absence of clearly established MRI images, visual field tests were analyzed to determine the more impaired, potentially expendable side of the ocular structures. Symmetric margins of 5 and 2 mm were added to spinal cord and brainstem, respectively, generating the corresponding planning organ at risk volumes (PRVs). No margins were added to optic pathways and others structures. Healthy tissue (HT) [16] was defined as the patient volume covered by the CT scan minus the larger delineated PTV. For each group of patients the HT caudal extension was limited to 5 cm below the PTVs to ensure a better intra-group comparison.

Dose prescription and planning objectives

Although in clinical practice a different dose prescription can be pursued on the basis of the disease stage and extension, for this study – in order to better compare different RT approaches – the same dose prescription for all techniques was used: a prescribed total dose (PTD) of 70 Gy for HR-PTVs and of 54 Gy for LR-PTVs. A single phase with 2 Gy/fraction was planned for group 1 patients and a modified simultaneous integrated boost approach (Sequential SIB, SEQ/SIB) was used for patients of groups 2 and 3. This approach was described in detail elsewhere [14]. Briefly, the SEQ/SIB consisted of a first phase with 2 Gy/fraction to the HR-PTV and 1.8 Gy/fraction to the LR-PTV, followed by a phase with 2 Gy/fraction to the HR-PTV only.

Plans were optimized by increasing as much as possible PTVs coverage without exceeding the neurological OARs (n-OAR) constraints. The highest priority was sparing brainstem and spinal cord, optic chiasm and contra-lateral optic nerve at least, to preserve mono-lateral vision. PTV coverage and sparing of the remaining structures were second and third priorities, respectively

Table 1
Selected patients and tumor characteristics.

Group	Histology	Site (sinus)	TNM (AJCC 2010) [31]	GTV (cm^3)	HR-PTV (cm^3)	LR-PTV (cm^3)
1	SNUC	Ethmoid	T4bN0	107	200	–
	SNUC	Ethmoid	T4bN0	127	240	–
	SCC	Ethmoid	T4bN0	74	126	–
	SNEC	Maxillary	T4bN0	62	170	–
2	SNUC	Ethmoid	T4bN0	58	140	325
	ITAC	Ethmoid	T4bN0	229	383	605
	SCC	Ethmoid	T4bN0	139	251	428
	SNUC	Ethmoid	T4bN0	114	169	436
3	SNUC	Ethmoid	T4bN2b	91	264	558
	SCC	Maxillary	T4bN2b	110	229	432
	SNEC	Ethmoid	T4bN2c	148	356	602
	SNUC	Ethmoid	T4bN3	201	483	804

Abbreviations: SNUC = sinonasal undifferentiated carcinoma; SCC = squamous cell carcinoma; SNEC = sinonasal neuroendocrine carcinoma; ITAC = intestinal-type adenocarcinoma; GTV = gross tumor volume; HR-PTV = high risk planning target volume; LR-PTV = low risk planning target volume.