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RESEARCH ARTICLE

Early Clinical Outcomes in Midline Sinonasal Cancers treated with Helical Tomotherapy-based Image-guided Intensity-modulated Radiation Therapy

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ABSTRACT

Introduction: Sinonasal cancers have variable biological behavior and outcomes. The physical proximity of several critical structures renders radiotherapy challenging for these cancers.

Purpose: To report our early experience of helical tomotherapy (HT)-based image-guided intensity-modulated radiation therapy (IMRT) in midline sinonasal cancers.

Materials and methods: Patients with midline sinonasal cancers were accrued on a prospective generic protocol of HT-based IMRT. HT plans were evaluated using standardized indices. All patients were followed up clinicoradiologically. Local control was defined as absence of failure (recurrence/progression) in the tumor bed, whereas distant disease control was defined as absence of distant metastases. All time-to-event data was analyzed using Kaplan-Meier methods.

Results: Ten patients with a median age of 42 years (range: 29-62 years) were included. HT was able to achieve excellent target volume coverage, good high-dose conformality with exquisite sparing of organs at risk. The acute toxicity of HT was generally mild and self-limiting. Seven patients experienced acute grade I-II ocular toxicity that responded to topical steroids, while one patient developed grade III conjunctivitis. The same patient later developed bilateral cataract necessitating extraction (late grade III ocular toxicity). No patient experienced dry-eye syndrome, corneal opacity or blindness. With a median follow-up of 27 months (interquartile range: 13-35 months), the 3-year Kaplan-Meier estimate of local progression-free survival, distant metastases-free survival, disease-free survival and overall survival was 59.3, 90, 53.3 and 90% respectively.

Conclusion: HT-based image-guided IMRT for midline sinonasal cancers achieves good high-dose conformality and is associated with mild, self-limiting acute ocular toxicity, minimal late morbidity with acceptable disease control.

Keywords: Image guidance, Intensity-modulated radiation therapy, Sinonasal, Tomotherapy.

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INTRODUCTION

Sinonasal cancers, although rare, are a highly heterogeneous group of malignant neoplasms with variable biological behavior and diverse clinical outcomes.[1] Maxillary sinus is the most common site of origin for paranasal sinus cancers, and is generally lateralized. Midline sinonasal cancers arise mostly from the nasal cavity followed by ethmoids, sphenoid sinus and rarely the frontal sinus. These cancers can arise from epithelial, glandular, neural or lymphoid tissues resulting in a spectrum of histopathological diagnosis.[1,2] Sinonasal cancers generally present in advanced stages as limited anatomical access makes early diagnosis difficult and the presence of air-filled cavities permits extensive tumor growth displacing adjacent organs or infiltrating surrounding tissues. The physical proximity of several critical structures (brain, eyes, lens, lacrimal glands, optic nerves, chiasma, pituitary and brainstem) renders the treatment of these tumors extremely challenging, regardless of modality. The selection and sequencing of treatment modalities is generally influenced by extent of disease, histology, patient or physician preferences and institutional biases based on available expertize and infrastructure. Endoscopic approaches[3,4] have largely replaced extensive craniofacial resections[5] and are being increasingly supplemented with postoperative radiation therapy with or without chemotherapy. Patients with postsurgical recurrences and inoperable tumors are often treated with concurrent chemoradiotherapy. Conventional radiotherapy for paranasal sinus cancers is typically delivered with a heavily weighted anterior field and two half-beam blocked lateral fields for midline lesions and anterolateral wedge pair portal for lateralized tumors without major emphasis on shielding normal tissues resulting in considerable morbidity.[6,7] It was commonplace to compromise on radiotherapy doses using conventional techniques to respect the tolerance of adjacent critical structures, resulting in suboptimal outcomes.[8]

The advent of intensity-modulated radiation therapy (IMRT) has ushered a new paradigm that has completely revolutionized contemporary radiotherapy practice and has vastly improved the outlook for head and neck cancers in general[9] and paranasal sinus cancers in particular. Since, high-precision techniques, such as IMRT, are relatively intolerant to setup errors, image guidance can improve dose delivery. Image-guided radiation therapy (IGRT) thus represents a logical advancement and is a natural corollary

to IMRT. Several dosimetric and clinical studies now support the use of IMRT and IGRT in sinonasal cancers for delivering tumoricidal doses to the tumor while sparing adjacent critical structures to optimize the therapeutic index (improvement in tumor control with reduction in acute and late toxicity). Helical tomotherapy (HT) has recently emerged as a promising and novel technology[10] for the planning and delivery of highly conformal doses to target volumes across various sites including the sinonasal region with excellent conformal avoidance of surrounding organs at risk (OAR). A 6 MV linear accelerator mounted on a ring gantry continuously rotates around the patient to deliver radiation in a helical mode as the patient translates through the ring. Herein, we review our preliminary experience of planning and delivery of image-guided IMRT on HT in midline sinonasal cancers and report on early clinical outcomes.

MATERIALS AND METHODS

HT was installed and clinically commissioned at our institute toward end of 2007. Initially, suitable patients across all sites were accrued and treated on a prospective institutional review board—approved generic protocol of tomotherapy-based IMRT. Patients with midline sinonasal cancers deemed suitable for high-precision radiotherapy were also accrued on this prospective protocol after obtaining written informed consent.

Staging evaluation: The pretreatment evaluation included a complete history and physical examination, direct flexible fiberoptic endoscopic examination, complete blood count, liver function tests, chest X-ray, computerized tomography (CT) and/or magnetic resonance imaging (MRI) scan of the face/neck as appropriate. Radionuclide bone scan, positron emission tomography scan and CT scan of the abdomen or chest were obtained only when clinically indicated. Staging was done according to the Kadish system[11] for esthesioneuroblastoma and tumor node metastases (TNM) staging classification system[12] for all other cancers. Orbital infiltration was not documented in any patient, although four (40%) patients presented with intracranial extension. None of the patients had clinicoradiological evidence of lymph node involvement or distant metastases at referral for HT.

Surgery: Definitive debulking surgery (either gross total or near total resection) was done in nine patients, while one patient underwent only biopsy for an unresectable skull-base tumor eroding the clivus and involving the sphenoid and cavernous sinus. Six patients underwent open resection (including three craniofacial resections), while endoscopic only approach was used in three patients. One patient had a combined open and endoscopic resection. None of the patients underwent elective neck dissection.

Chemotherapy: Neoadjuvant chemotherapy (three cycles of docetaxel and cisplatin given at 3-weekly intervals) was used in one patient with intracranial extension prior to debulking surgery. The patient with unresectable skull-base tumor received cisplatin-based concurrent chemoradiation, while the patient with recurrent esthesioneuroblastoma received consolidation adjuvant chemotherapy (ifosfamide, cisplatin and etoposide).

Radiotherapy (immobilization, planning, imaging and contouring): All patients were immobilized in the supine position in a 3-clamp thermoplastic head mask in neutral neck position on a semicustomized neck support. Axial planning CT images were acquired from vertex to upper neck with 2 mm contiguous slice thickness using intravenous contrast. For five patients, planning axial MRI scans (postcontrast 3D-FSPGR sequence, square matrix, 2 mm slice thickness, zero gap) were also acquired in the treatment position in a dedicated head coil on a diagnostic scanner for fusion with the planning CT data set. Target volume delineation was done only after comprehensive evaluation of all available imaging (preoperative as well as postoperative) and relevant intraoperative details. OARs that were contoured typically included the eyes, lens, lacrimal glands, optic nerves, optic chiasm, pituitary, brainstem, temporal lobes and whole brain. The clinical target volume (CTV) was defined as the preoperative gross disease plus a margin to account for possible spread of microscopic disease consisting of the tumor bed (entire resection cavity plus all paranasal sinuses involved preoperatively). An automated isotropic margin of 3 mm was applied uniformly to the CTV to generate the planning target volume (PTV) to account for setup uncertainties. Gross residual disease due to presumed incomplete surgical resection (either on imaging or surgical details) was treated to a higher dose using either simultaneous integrated boost (n = 5) or sequential boost (n = 1). Elective neck nodal irradiation was not performed in any patient.

HT planning and evaluation: The planning CT images and structure set was transferred to tomotherapy Hi-Art II version 3.1 (TomoTherapy Inc, Madison, WI, USA) via network. The 6 MV beam in HT is collimated and modulated by 64 pairs of pneumatically driven binary multileaf collimators having 0.625 cm projected leaf width at isocenter. It uses an inverse treatment planning process based on iterative least squares minimization of an objective function with the dose being calculated using a superposition-convolution algorithm. Typical planning parameters used for optimization and dose computation were

a fan beam thickness of 1 or 2.5 cm, pitch of 0.3 and a modulation factor between 2 and 3.5. HT allows directional blocking (entry doses) as well as complete blocking (entry and exit doses) during planning to prevent beamlets from entering and exiting through critical OARs. HT plans were evaluated qualitatively and quantitatively using standardized dose-volume indices in terms of target volume coverage, dose homogeneity, dose conformity and OAR sparing. For reporting purposes, maximum doses were specified as maximum dose (D_{max}) to a minimum yet clinically significant volume (1%). Similarly minimum doses were specified as the minimum dose (D_{min}) received by 99% of the volume. This eliminates isolated dose peaks and troughs within clinically insignificant volumes (single or few voxels). Target volume coverage and dose homogeneity were assessed as the volume of PTV receiving at least 95% ($V_{95\%}$) and 107% ($V_{107\%}$) of the prescribed dose in accordance with published recommendations. Dose homogeneity was evaluated quantitatively using the dose homogeneity index (DHI) defined as a ratio of the difference between dose to 5% volume ($D_{5\%}$) and 95% volume ($D_{95\%}$) by the mean dose (D_{mean}) to the PTV expressed as a percentage [$DHI = (D_{5\%} - D_{95\%})/D_{mean} \times 100\%$]. The conformation of therapeutic dose volume to the target volume was estimated using the conformity index (CI) as defined by Paddick [$CI = (V_{T,Pi} \times V_{T,Pi})/(V_T \times V_{Pi})$], where $V_{T,Pi}$ is the volume of target enclosed by the prescription dose; V_{Pi} is the volume of tissues including target covered by the prescription dose and V_T is the volume of target.[13] Maximum and mean dose (D_{max} and D_{mean}) was recorded for estimation of OAR sparing.

Verification and delivery: Patient-specific delivery quality assurance was carried out using film dosimetry and ion-chamber measurements. Initial setup was based on fiducial markers (pasted on the thermoplastic mask) aligned with a room laser system prior to treatment. Megavoltage CT (MVCT) scans were acquired prior to every fraction through the region of interest using the normal acquisition mode (slice thickness of 4 mm, image reconstruction matrix of 512 × 512, and field of view of 40 cm in diameter) to reduce scanning dose and time. The MVCT images were coregistered automatically with the planning CT images using bone matching. Coronal, axial and sagittal views were used with the chequerboard and balance set to partial transparency to verify coregistration and fine-tune the autofusion manually. The couch height was acquired and updated for all subsequent fractions to eliminate the couch sag, a systematic error inherent to HT. Translational (lateral, longitudinal and vertical) and rotational errors (roll, pitch and yaw) was documented for every treatment. A no-action level protocol where every error is corrected regardless of the magnitude (however small it may be) was followed and online corrections were applied for all translational errors and roll as necessary after image coregistration.

Follow-up and statistical analysis: All patients were seen on first follow-up 6 to 8 weeks after completion of HT-based IMRT and a post-treatment imaging done to document disease status. Subsequent follow-up were scheduled at 3 to 4 monthly intervals till 2 years and 6-monthly intervals thereafter till 5 years. At each follow-up visit, physical examination including fiberoptic sinonasal endoscopy was also done. Follow-up imaging was done at the discretion of the treating physician or on suspicious endoscopic findings. Acute and late normal tissue toxicities were graded according to the radiation therapy oncology group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) radiation morbidity criteria. Local control was defined as absence of failure (recurrence/progression) in the tumor bed, whereas distant disease control was defined as absence of distant metastases. Any failure (local or distant) or death was considered an event for disease-free survival (DFS). Local progression-free survival (LPFS), distant metastases-free survival (DMFS), DFS and overall survival were analyzed using the product-limit method of Kaplan-Meier and calculated from the date of surgery till the defined event or last follow-up whichever occurred earlier. All analyses were done on SPSS version 17.0.

RESULTS

Between September 2008 and March 2011, 10 patients with midline sinonasal tumors were treated on HT with image-guided IMRT and constitute the cohort study. Table 1 describes the patient characteristics of the study population.

HT plans were evaluated qualitatively and quantitatively using standardized dose-volume indices on the dedicated HT workstation. Table 2 summarizes the dosimetric parameters of the target volumes as well as OARs. HT was able to achieve excellent PTV coverage, good dose conformality and homogeneity, with exquisite sparing of OARs (Figs 1A to D). Two (20%) patients underwent reirradiation on HT. The first patient was a diagnosed case of esthesioneuroblastoma who was observed after radical craniofacial resection, but developed local recurrence in the ethmoid sinus and scar recurrence in the scalp 2 years after initial surgery. At first recurrence, he underwent re-excision of recurrent tumor followed by postoperative image-guided IMRT to the local recurrence in the sinus with simultaneous irradiation of scarline in the scalp on using HT (60 Gy/30 fractions). Twenty-two months later, he developed subdural recurrence in the basifrontal region with another noncontiguous subdural meningeal deposit in the right

Table 1: Patient characteristics of the cohort study (N = 10)

Parameter	*Number of patients*
Age (range)	42 years (29-62 years)
Gender	
Male	04 (40%)
Female	06 (60%)
Site (anatomic)	
Nasal cavity	04 (40%)
Sphenoid sinus	02 (20%)
Ethmoid sinus	02 (20%)
Frontal sinus	02 (20%)
Histology	
Squamous cell carcinoma	01 (10%)
Adenoid cystic carcinoma	02 (20%)
Esthesioneuroblastoma	02 (20%)
Adenocarcinoma	02 (20%)
Mesenchymal chondrosarcoma	01 (10%)
Neuroendocrine tumor	01 (10%)
Carcinosarcoma	01 (10%)
Laterality (epicenter)	
Right	03 (30%)
Left	05 (50%)
Midline	02 (20%)
Presentation	
Primary (at initial diagnosis)	04 (40%)
Recurrent/progressive (after prior therapy)	06 (60%)
Stage grouping*	
I/II	02 (20%)
III	02 (20%)
IV	04 (40%)

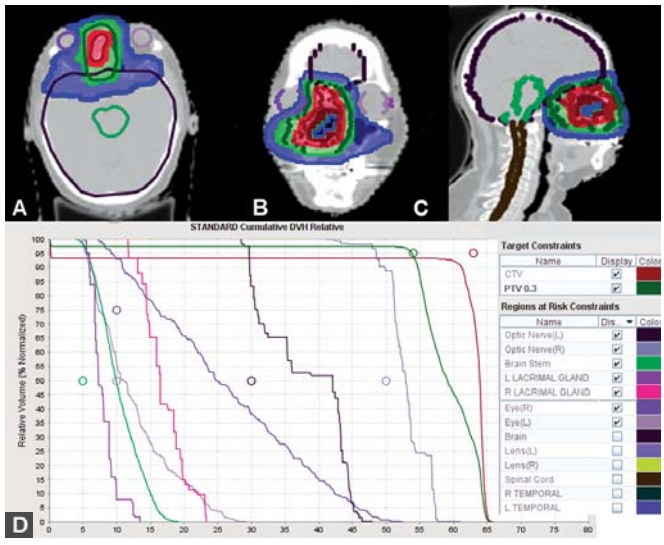
*The two esthesioneuroblastoma patients were Kadish stage B and C

Table 2: Radiotherapy dose-volume parameters of the cohort study

Parameter	*Value*
Planning target volume (PTV)	
Median PTV volume (range)	100.5 (74.9-317.4) cc
Median prescription dose (range)	57 Gy (50-63 Gy)
Median number of fractions (range)	30 fractions (25-30)
Mean V95% (SD)	99.7% (0.38)
Mean V107% (SD)	6.7% (14.0)
Dose homogeneity index (SD)	0.08 (0.05)
Conformity index (SD)	0.70 (0.18)
Organ at risk (OARs)	D_{mean} (SD)/D_{max}
Brain stem	17.6 Gy (06.3)/30.8 Gy
Optic chiasm	42.9 Gy (14.1)/50.3 Gy
Ipsilateral optic nerve	46.0 Gy (08.0)/56.8 Gy
Contralateral optic nerve	41.0 Gy (07.1)/52.9 Gy
Ipsilateral eye	24.7 Gy (13.8)/48.8 Gy
Contralateral eye	17.8 Gy (12.9)/45.1 Gy
Pituitary	44.9 Gy (14.5)/50.9 Gy
Whole brain	16.2 Gy (18.0)/53.4 Gy

SD: Standard deviation; D_{mean}: Mean dose; D_{max}: Maximum dose

occipital region, for which reirradiation was performed on HT (45 Gy to the basifrontal region and 60 Gy to the occipital region). The second patient was an elderly lady of sinonasal adenocarcinoma who had been treated earlier with surgery and postoperative radiotherapy (56 Gy/28 fractions).



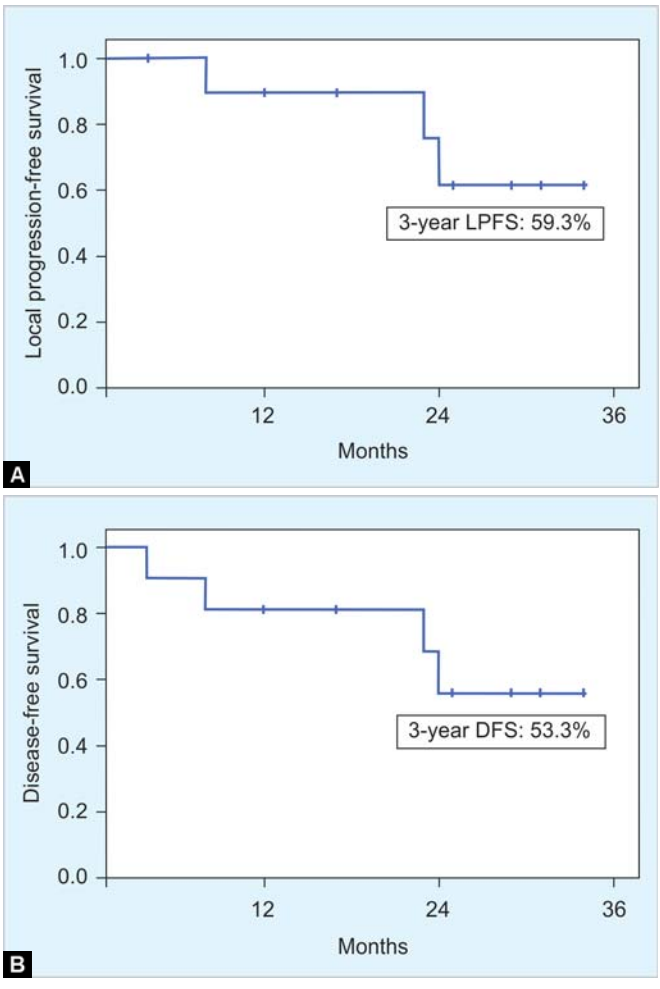
Figs 1A to D: Dose wash in axial (A), coronal (B) and sagittal (C) planes showing excellent coverage of the PTV (green line) by the prescription dose (54 Gy—green) with simultaneous integrated boost (63 Gy—red) to the residual disease (red line). The 50% dose wash (blue) is also displayed to show conformal avoidance of both eyes. Corresponding dose-volume histogram (D) of the same patient

She recurred 4 years later for which she received salvage chemotherapy followed by subtotal resection. She was subsequently treated with reirradiation on HT.

Toxicity outcomes: All patients were reviewed weekly during the course of radiotherapy. All patients tolerated the treatment well and completed the planned course of irradiation without any interruption attributable to HT-induced toxicity. The acute toxicity of HT was generally mild, transient and self-limiting. The most frequent nonocular toxicities were mild (grade I-II) dermatitis (90%) and mucositis (20%). Mild (grade I-II) acute ocular toxicity in the form of conjunctival congestion, itching and watering was noted in seven (70%) patients that responded to topical steroids. It generally subsided by the time patients reported for first follow-up at 6 to 8 weeks. One patient (10%) had moderate to severe (grade III) bilateral conjunctivitis and photophobia during radiotherapy which resolved slowly with conservative management over the subsequent 1 year. No patients experienced any significant late skin, mucosal or salivary gland toxicity. Three patients (30%) complained of decreased olfaction on follow-up. The patient who suffered from acute grade III conjunctivitis developed cataract in both eyes 1 year later resulting in visual impairment necessitating extraction and intraocular lens implantation (late grade III ocular toxicity). No patient experienced radiation-induced dry-eye syndrome, corneal opacity or blindness.

Disease outcomes: Three patients had local recurrence/progression in the tumor bed at 7, 22 and 24 months from

irradiation respectively. The first of these, a patient of recurrent adenocarcinoma, who had been reirradiated on HT was started on metronomic chemotherapy based on radiological progression. The second patient, a diagnosed case of recurrent esthesioneuroblastoma, was salvaged with reirradiation on HT and systemic chemotherapy. The third patient with recurrent mesenchymal chondrosarcoma underwent salvage debulking surgery and is presently under observation with stable residual disease, reirradiation being reserved for future symptomatic progression. One patient with adenocarcinoma developed multiple bony metastases 4 months after HT, for which he received palliative RT to the cervicodorsal spine but succumbed 5 months later due to progressive disease. With a median follow-up of 27 months (interquartile range: 13-35 months), the 3-year Kaplan-Meier estimate (±standard error) of LPFS, DMFS and DFS was 59.3 (±18.5%), 90 (±9.5%) and 53.3% (±17.6%) respectively (Fig. 2). Nine patients were alive at the time of this analysis for a 3-year overall survival of 90% (±9.5%).



Figs 2A and B: Kaplan-Meier estimates of local progression-free survival (A) and disease-free survival (B) for the cohort study treated on helical tomotherapy

DISCUSSION

Sinonasal cancers pose unique challenges to the oncologic fraternity[1] as they have traditionally been associated with suboptimal disease outcomes yet significant tumor and treatment-related morbidity. In view of their relatively rarity, diverse histology, advanced stage at presentation, intricate anatomic relationship with critical structures and variable biological behavior, considerable uncertainty exists regarding the choice and sequencing of optimum treatment modality, with treatment recommendations being based largely on patient and physician preferences. Nonetheless, radiotherapy is being increasingly used in the multimodality management of these cancers either in the adjuvant setting following surgical resection (endoscopic piece-meal resection, close or involved margins) or less frequently as primary definitive treatment in surgically unresectable disease. Conventional radiotherapy is associated with unacceptably high ocular morbidity (conjunctivitis, optic neuropathy, retinopathy, xerophthalmia, corneal opacity, cataract and even blindness) in a significant proportion (35-50%) of patients, even at lower doses.[6,7,14-16] Radiotherapy planning and delivery has significantly improved in sinonasal cancers with the advent of IMRT,[17,18] due to its potential to produce highly conformal dose distributions with significant sparing of surrounding OARs.

Table 3: Outcomes in sinonasal cancers treated with IMRT

Author	*No. of pts (N)*	*Median RT dose (Gy)*	*Median follow -up (months)*	*Local control*	*Overall survival*	*≥Grade III late ocular toxicity*
Claus[19]	32	70	15	Not reported	80% (1-year)	None
Duthoy[20]	39	70	31	68% (4-year)	59% (4-year)	2 patients
Combs[21]	46	64	16	81% (2-year)	90% (3-year)	None
Daly[22]	36	70	39	58% (5-year)	45% (5-year)	None
Dirix[23]	25	60	27	81% (2-year)	88% (2-year)	None
Madani[24]	84	70	40	74.9% (3-year) 70.7% (5-year)	70.2% (3-year) 58.5% (5-year)	1 patient
Dirix[25]	40	63	30	76% (2-year)	89% (2-year)	None
Duprez[26]	130	70	52	59% (5-year)	52% (5-year)	11 patients

Many of these reports are updates of previous studies with more number of patients and mature follow-up

Several planning studies have demonstrated the dosimetric superiority of linear accelerator (linac)-based IMRT over conventional as well as three-dimensional conformal radiotherapy. The most robust evidence in favor of IMRT for sinonasal cancers comes from several retrospective and prospective clinical outcome studies[19-26] reporting excellent local control (60-90%) and overall survival (50-70%) with significantly reduced severe late ocular toxicity (Table 3).

The most common linac-based approach employs 7 to 9 non-coplanar beams[17,22] and provides excellent PTV coverage, high-dose conformality and OAR sparing. HT has recently emerged as a novel platform for image-guided IMRT across various sites, including the sinonasal region and is generally considered to be superior to linac-based IMRT. However, non-coplanar beams are not possible in HT due to ring gantry design which may be considered a disadvantage for sinonasal malignancies. In a dosimetric comparison in five patients with unresectable sinonasal cancer, HT provided comparable PTV coverage, equivalent or slightly better OAR avoidance with significantly improved uniformity compared to noncoplanar linac-based IMRT, leading the authors to conclude that the perceived disadvantage of coplanar geometry in HT is counterbalanced by the large number of field projections.[27] In another such dosimetric study in 10 patients with unresectable sinonasal cancer, HT significantly reduced doses to the optic apparatus (chiasma, ipsilateral optic nerve and retina) and ipsilateral lacrimal gland.[28] The dose distribution was more homogeneous with HT, though the conformality and coverage was comparable between the two techniques.

Although, high-precision photon irradiation techniques have dramatically improved the therapeutic ratio, the application of proton beam or carbon ion therapy in sinonasal cancers can be particularly rewarding. The physical characteristics of protons or carbon ions (Bragg peak, narrow lateral penumbra, no exit dose) are extremely suited for treatment of head and neck cancers[29] including sinonasal malignancies. The German experience[30] of carbon ion boost of 24 GyE in combination with 50 Gy of photon IMRT is also encouraging as acute reactions were not increased, despite dose escalation and reasonable early tumor response was achieved.

The limitations of the present study include small patient numbers, relatively short follow-up, and lack of objective serial visual assessment. Notwithstanding the limitations, to the best of our knowledge, this is the first clinical outcome report of HT-based image-guided IMRT in sinonasal cancers. At median follow-up of 27 months, HT resulted in 3-year LPFS and overall survival of 59.3 and 90% respectively, with markedly low incidence of severe (grade III-IV) acute or delayed ocular toxicity, that compares favorably with conventional radiotherapy and is comparable to linac-based IMRT.

CONCLUSION

HT-based image-guided IMRT for midline sinonasal cancers achieves excellent target volume coverage, good high-dose conformality and OAR sparing, and is associated with mild, self-limiting acute ocular toxicity, minimal late morbidity and acceptable disease control and survival.

REFERENCES

1. Turner JH, Reh DD. Incidence and survival in patients with sinonasal cancer: A historical analysis of population-based data. Head Neck 2012 Jun;34(6):877-85.
2. Wang X, Shi G, Liu Y, Ji H, He M, Li J, et al. Analysis of the clinical and pathological characteristics of sinonasal neoplasms (article in Chinese). J Clin Otolaryngol Head Neck Surg 2011;25: 1071-75.
3. Nicolai P, Castelnuovo P, Villaret AB. Endoscopic resection of sinonasal malignancies. Curr Oncol Rep 2011;13:138-44.
4. Hanna E, DeMonte F, Ibrahim S, Roberts D, Levine N, Kupferman M. Endoscopic resection of sinonasal cancers with and without craniotomy: Oncologic results. Arch Otolaryngol Head Neck Surg 2009;135:1219-24.
5. Ganly I, Patel SG, Singh B, Kraus DH, Bridger PG, Cantu G, et al. Carniofacial resection for malignant paranasal sinus tumors: Report of an International Collaborative Study. Head Neck 2005;27:575-84.
6. Shukovsky LJ, Fletcher GH. Retinal and optic nerve complications in a high dose irradiation technique of ethmoid sinus and nasal cavity. Radiology 1972;104:629-34.
7. Martel MK, Sandler HM, Cornblath WT, Marsh LH, Hazuka MB, Roa WH, et al. Dose-volume complication analysis for visual pathway structures of patients with advanced paranasal sinus tumors. Int J Radiat Oncol Biol Phys 1997;38: 273-84.
8. Dirix P, Nuyts S, Geussens Y, Jorissen M, Vander Poorten V, Fossion E, et al. Malignancies of the nasal cavity and paranasal sinuses: Long-term outcome with conventional or three-dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 2007;69:1042-50.
9. Bernier J, Hall EJ, Giaccia A. Radiation oncology: A century of achievements. Nat Rev Cancer 2004;4:737-47.
10. Mackie TR, Holmes T, Swerdloff S, Reckwerdt P, Deasy JO, Yang J, et al. Tomotherapy: A new concept for the delivery of dynamic conformal radiotherapy. Med Phys 1993;20: 1709-19.
11. Kadish S, Goodman M, Wang CC. Olfactory neuroblastoma: A clinical analysis of 17 cases. Cancer 1976;3:71571-76.
12. Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC cancer staging manual (7th ed). New York: Springer 2009.
13. Paddick I. A simple scoring ratio to index the conformity of radiosurgical treatment plans. Technical note. J Neurosurg 2000;93(Suppl 3):219-22.
14. Jiang GL, Tucker SL, Guttenberger R, Peters LJ, Morrison WH, Garden AS, et al. Radiation-induced injury to the visual pathway. Radiother Oncol 1994;30:17-25.

15. Parsons JT, Bova FJ, Fitzgerald CR, Mendenhall WM, Million RR. Radiation optic neuropathy after megavoltage external-beam irradiation: Analysis of time-dose factors. Int J Radiat Oncol Biol Phys 1994;30:755-63.
16. Karim AB, Kralendonk JH, Njo KH, Tabak JM, Elsenaar WH, van Balen AT. Ethmoid and upper nasal cavity carcinoma: treatment, results and complications. Radiother Oncol 1990;19:109-20.
17. Claus F, De Gersaem W, De Wagter C, Van Severen R, Vanhoutte I, Duthoy W, et al. An implementation strategy for IMRT of ethmoid sinus cancer with bilateral sparing of the optic pathways. Int J Radiat Oncol Biol Phys 2001;51:318-31.
18. Chen AM, Daly AE, Bucci MK, Xia P, Akazawa C, Quivey JM, et al. Carcinomas of the paranasal sinuses and nasal cavity treated with radiotherapy at a single institution over five decades: Are we making improvement? Int J Radiat Oncol Biol Phys 2007;69:141-47.
19. Claus F, Boterberg T, Ost P, De Neve W. Short term toxicity profile for 32 sinonasal cancer patients treated with IMRT. Can we avoid dry eye syndrome? Radiother Oncol 2002;64:205-08.
20. Duthoy W, Boterberg T, Claus F, Ost P, Vakaet L, Bral S, et al. Postoperative intensity-modulated radiotherapy in sinonasal carcinoma: Clinical results in 39 patients. Cancer 2005;104:71-82.
21. Combs SE, Konkel S, Schulz-Ertner D, Münter MW, Debus J, Huber PE, et al. Intensity modulated radiotherapy (IMRT) in patients with carcinomas of the paranasal sinuses: Clinical benefit for complex shaped target volumes. Radiat Oncol 2006;1:23.
22. Daly ME, Chen AM, Bucci MK, El-Sayed I, Xia P, Kaplan MJ, et al. Intensity-modulated radiation therapy for malignancies of the nasal cavity and paranasal sinuses. Int J Radiat Oncol Biol Phys 2007;67:151-57.
23. Dirix P, Nuyts S, Vanstraelen B, Nulens A, Hermans R, Jorissen M, et al. Post-operative intensity-modulated radiotherapy for malignancies of the nasal cavity and paranasal sinuses. Radiother Oncol 2007;85:385-91.
24. Madani I, Bonte K, Vakaet L, Boterberg T, De Neve W. Intensity-modulated radiotherapy for sinonasal tumors: Ghent University Hospital update. Int J Radiat Oncol Biol Phys 2009;73:424-32.
25. Dirix P, Vanstraelen B, Jorissen M, Vander Poorten V, Nuyts S. Intensity-modulated radiotherapy for sinonasal cancer: Improved outcome compared to conventional radiotherapy. Int J Radiat Oncol Biol Phys 2010;78:998-1004.
26. Duprez F, Madani I, Morbee L, Bonte K, Deron P, Domján V, et al. IMRT for sinonasal tumors minimizes severe late ocular toxicity and preserves disease control and survival. Int J Radiat Oncol Biol Phys 2012 May 1;83(1):252-59.
27. Chen AM, Sreeraman R, Mathai M, Vijayakumar S, Purdy JA. Potential of helical tomotherapy to reduce dose to the ocular structures for patients treated for unresectable sinonasal cancer. Am J Clin Oncol 2010;33:595-98.
28. Sheng K, Molloy JA, Larner JM, Read PW. A dosimetric comparison of non-coplanar IMRT versus helical tomotherapy for nasal cavity and paranasal sinus cancer. Radiother Oncol 2007;82:174-78.
29. Mendenhall NP, Malyapa RS, Su Z, Yeung D, Mendenhall W, Li Z. Proton therapy for head and neck cancer: Rationale, potential indications, practical considerations, and current clinical evidence. Acta Oncol 2011;50:763-71.
30. Jensen AD, Nikoghosyan AV, Ecker S, Ellerbrock M, Debus J, Munter MW. Carbon ion therapy for advanced sinonasal malignancies: Feasibility and acute toxicity. Radiat Oncol 2011;6:30.

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