Chapter 4

Non-coplanar volumetric modulated arc therapy for irradiation of paranasal sinus tumors

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Abstract

Background: Sinonasal cancer (SNC) arises in the proximity of many critical organs at risk (OAR). Therefore, minimizing radiation doses to critical organs is a priority. We evaluated the use of a fast, non-coplanar volumetric arc therapy (VMAT) delivery technique for this purpose.

Materials/Methods: Planning CT scans of 10 patients who had previously postoperative radiotherapy for SNC to a dose of 66 Gray (Gy) were accessed. New coplanar RapidArc (RA) plans were generated using 2 complementary coplanar arcs of 358º, one counterclockwise (CCW), one clockwise (CW). Next, non-coplanar RA plans consisting of the same CCW arc combined with a cranio-caudal (CRCA) partial arc were generated. In optimizing the CRCA arc, attempts were made to lower doses to the optic structures, without compromising PTV coverage.

Results: Both RA plans achieved good PTV coverage, with 98.68% (coplanar) and 98.65% (non-coplanar) of the PTV receiving ≥ 95% of the prescription dose. Plan conformity index was 1.12 (coplanar plans) and 1.14 (non-coplanar), respectively. Non-coplanar plans generally resulted in lower doses to all optic structures, and in 5 patients, significant reductions in doses to optic nerves in the 55-60 Gy range were achieved. Mean differences for the $dose_{max}$ in organs at risk (OARs) were as follows: 7 (±5.6) Gy (left optic nerve), 9.5 (±5.0) Gy (right optic nerve) and 2.7 (±3.9) Gy (optic chiasm), all in favor of the non-coplanar plans.

Conclusions: In curative radiotherapy for SNC, use of a 2 arc non-coplanar technique achieved excellent PTV coverage, improved sparing of critical organs.

Introduction

Sinonasal cancers are uncommon tumors of the base of skull [1]. Treatment commonly consists of surgery followed by radiotherapy to a dose of 60-70 Gy. When 3-D conformal radiotherapy is used, suboptimal coverage of the target volume is occasionally accepted in order to minimize doses to critical organs, which in turn can lead to an increase in local failures [2-6].

The use of intensity-modulated radiotherapy (IMRT) enables more conformal target coverage in SNC and a better sparing of adjacent critical organs [7]. Single institution data suggests that IMRT reduces side effects and improves disease-free survival rates [8-11]. A potential drawback of static IMRT is the complex planning process and long delivery times, although class solutions have been developed to improve planning efficiency [12,13]. In comparison to conventional static IMRT, volumetric arc therapy enables faster delivery of highly modulated plans [14-16]. Many manufacturers offer variations of VMAT [17]. RapidArc ™ (Varian medical systems, Palo Alto) permits the use of non-coplanar arcs, which in turn enables an even more conformal dose distribution. As recent QUANTEC (Quantitative Analyses of

Normal Tissue Effects in the Clinic) guidelines on tolerance of the optic pathway recommend the ALARA (as low as reasonably achievable) principle [18], we performed a planning study using RapidArc in order to determine if further reductions of doses to critical in the organs at risk (OARs) was possible whilst maintaining adequate target coverage.

Materials and methods

Patients

In this retrospective planning study, the CT scans of 10 patients with SNC who had undergone postoperative radiotherapy to a dose of 66 Gy at our center, were used to evaluate the dose distributions of using non-coplanar arc delivery.

Patients were immobilized either with a 5 point thermoplastic mask (Civco medical solutions, Kalona, IA, USA) or a Brainlab mask (Munich, Germany). The target volume was defined by co-registration of the preoperative MRI or CT scans, and delineated on a contrast-enhanced planning CT scan acquired using 2.5mm slice thickness. The clinical target volume (CTV) comprised the preoperative tumor volume with a margin for possible microscopic spread, and included the surgical cavity. The CTV was expanded with 3 mm margin in order to derive a planning target volume (PTV). A planning organ at risk volume (PRV) of 0 to 2 mm around the OARs was used. Elective neck node planning was not performed.

Planning objectives and techniques

A dose of 66 Gy in daily fractions of 2 Gy over 6.6 weeks was planned, aiming to achieve a dose coverage of 62.7 Gy (95% of the dose) to at least 98% of the PTV. In areas were the PTV reached the body surface, a local buildup was used for optimization purposes.

Maximum dose objectives for the OARS were set as follows: 60 Gy for optic nerves, 56 Gy for chiasm, 50 Gy for brainstem and 45 Gy for spinal cord. During optimization these constraints were pushed as far as possible towards the lower dose end, without compromising PTV coverage. The mean dose objective for the pituitary gland was <45 Gy. The dose constraints to the oral cavity, lenses and lachrymal glands were of lesser priority, aiming to keep the dose as low as possible without compromising PTV coverage. The mean dose to the Eclipse TPS version 8.9 (Varian, Palo Alto, CA, USA) was used for all treatment planning.

Coplanar RA plans were generated using 2 complementary coplanar arcs of 358° (one counterclockwise (CCW), one clockwise (CW)). A sequential approach was used, in which the CCW arc plan served as a base dose plan for the CW arc plan, which in turn compensated for any under- or overdosage arising from the CCW arc plan. The final result was a more homogeneous dose distribution, especially in air cavities. Equal priority ranking of 120-130 was used for both PTV and optic OARs in an attempt to achieve the best possible tradeoff between PTV coverage and OAR avoidance. If acceptable PTV coverage was unlikely due to the fact that the PTV overlapped one optic nerve, this structure was 'sacrificed'. In no case was the maximum dose to the chiasm exceeded.

Subsequently, non-coplanar RA plans were generated for each patient as follows. The same CCW arc plan was used as a base dose plan for the non-coplanar, cranio-caudal (CRCA) partial arc plan. This arc was planned for a couch rotation of 90º, starting at 160º to 320-340º (parallel to the position of the palate). During plan optimization for the CRCA arc, an attempt was made to further decrease doses to optic structures without compromising PTV coverage. All treatment planning and optimization was done by the same dosimetrist, minimizing the risk of interobserver variability.

Quantitative evaluation of plans was performed using Dose-Volume Histograms (DVH). According to ICRU 83, for plan comparisons the near minimum absorbed dose (D98%, minimum dose covering 98% of the PTV) and the near maximum absorbed dose (D2%, high dose covering 2% of the PTV) were registered, as were the target volume receiving at least 95% (V95) and more than 107% (V107) of the prescribed dose. In addition, a conformity index (CI, ratio between the V95 and the volume of the PTV) and a homogeneity index (HI, (D2% - D98%)/D50%, ideally approaching zero) were calculated. Statistical analysis was performed using the SPSS software package (version 15.0; SPSS, Inc., Chicago, IL).

Results

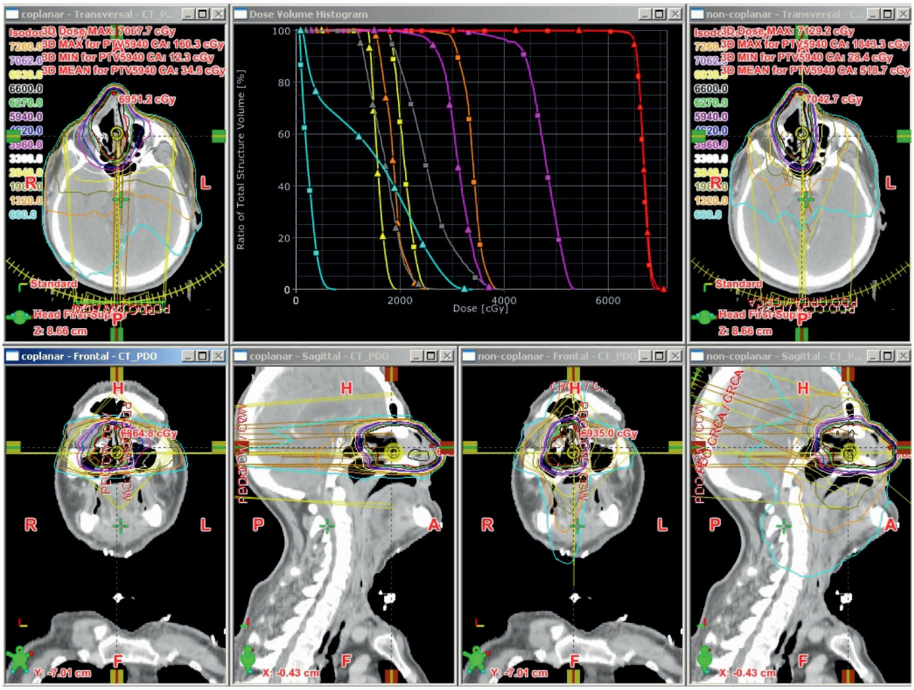
The mean PTV was 89 cc (range 50-162 cc). D98% and D2% of the PTV are depicted in Table 1. Despite the presence of air cavities, both coplanar and the non-coplanar RA plans achieved excellent PTV coverage, with 98.68% (coplanar) and 98.65% (non-coplanar) of the PTV receiving ≥ 95% of the prescription dose. Only 0.4% of PTV in the coplanar plans and 1.3% of PTV in the non-coplanar plans received doses >107% of the prescription dose. Plan CI was 1.12 for coplanar plans, and 1.14 for non-coplanar plans (Wilcoxon signed-rank test p=0,6). The HI was 0.09 for coplanar plans and 0.1 for non-coplanar plans (Wilcoxon signed-rank test p=0.4). A typical plan and DVH of one patient are depicted in Figure 1.

Table 1: D98% and D2% (Gy) to PTV , CI and HI

patient	D98% co	D98% non-co	D2% co	D2% non-co	CI co	CI non-co	HI co	HI non-co
1	62.2	64	70.2	69.5	1.16	1.32	0.12	0.08
2	63.4	63.4	70.6	70.4	1.11	1.11	0.11	0.1
3	63.4	62.6	68.7	69.6	1.2	1.17	0.08	0.1
4	64.5	64.5	68.5	69	1.29	1.23	0.06	0.07
5	62.7	62.7	69.6	69.8	1.04	1.08	0.1	0.11
6	62.7	62.4	68.8	70.8	1.11	1.14	0.09	0.13
7	63	63.1	69.6	70.2	1.01	1.01	0.1	0.1
8	63.4	62.7	70.4	71.7	1.08	1.1	0.1	0.13
9	63.7	63.6	69.8	70	1.08	1.08	0.09	0.09
10	64	64.3	70.3	70.2	1.16	1.16	0.09	0.09
average	63.3	63.3	69.7	70.1	1.12	1.12	0.094	0.1
st dev	0.68	0.75	0.76	0.75	0.086	0.063	0.016	0.019

Abbreviations: Doses in Gray, CI: Conformity Index, HI: Homogeneity Index, co: coplanar plan, non-co: non-coplanar plan, st dev: standard deviation

Figure 1



Dose distributions and DVH for a typical patient. Comparison of non-coplanar plan (pictures right) with coplanar plan (pictures left). DVH (■ = coplanar plan, ▲= non-coplanar plan) of PTV in red, chiasm in grey, left optic nerve in orange, right optic nerve in purple, oral cavity in blue, pituitary gland in yellow

Tables 2 A and B summarize the doses in both optic nerves and the chiasm. Except for patient 5 (optic nerve L) and patient 10 (optic chiasm), non-coplanar plans achieved lower doses in all optic structures. In 5 patients, a significant reduction of the maximum dose in the 55-60 Gy interval in the left (patients 7,8) and right (patients 1,3,9) optic nerve was achieved. The mean differences for the maximum doses in the organs at risk were as follows: 7 (±5.6) Gy (left optic nerve), 9.5 (±5.0) Gy (right optic nerve) and 2.7 (±3.9) Gy (chiasm), all in favor of the non-coplanar plans. All values are statistically significant according to the Wilcoxon signed-rank test with $p=0.008$ for the left optic nerve, $p=0.002$ for the right optic nerve and $p=0.037$ for the chiasm.

Table 2A: Dmax (Gy) to optic structures

patient	L opt n co	L opt n non-co	R opt n co	R opt n non-co	chiasm co	chiasm non-co
1	38.4	23.9	57.8	42.8	20	17
2	35.2	26.6	46.9	43.5	33.5	32.4
3	61.6	61.6	60	57.5	53.4	51.4
4	38.7	24.8	53.9	38.2	40.4	27.9
5	63.9	64.7	48.4	40.5	52	49.8
6	19.8	16.6	23.1	15.5	20.3	16.8
7	59	55.4	37.9	25.1	37.8	36.4
8	57.9	52.4	32.4	22.8	48.3	47
9	32.3	19.8	56.2	51.1	36.6	33.2
10	51	42.1	39.7	24.1	38.1	41.2
average	45.8	38.8	45.6	36.1	38	35.3
st dev	14.9	18.5	12.1	13.6	11.6	12.4

Abbreviations: Doses in Gray, L: left, R; right, opt n: optic nerve, co: coplanar plan, non-co: non-coplanar plan, st dev: standard deviation

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Table 2B: D2% (Gy) to optic structures

patient	L opt n co	L opt n non-co	R opt n co	R opt n non-co	chiasm co	chiasm non-co
1	37.2	22.8	57.3	40	15.7	15.8
2	33.6	24.1	45	41.4	31.1	31
3	59.5	59.4	56.9	53.4	47.2	47.8
4	37.6	23	52.7	36.3	36.2	23.6
5	61.5	62.3	44.3	36.6	47.6	45.6
6	19.1	12.6	21.7	14.2	19.9	15.1
7	56.5	52.2	35.4	21.2	34.5	32.2
8	55.5	50.1	30.9	20.5	42.2	43.3
9	28.8	17.2	53.7	48.4	34.6	29.4
10	47.8	39.7	37.9	22.8	35.4	38.5
average	43.7	36.3	43.6	33.5	34.4	32.2
st dev	14.5	18.6	12	13.1	10.4	11.7

Abbreviations: Doses in Gray, L: left, R; right, opt n: optic nerve, co: coplanar plan, non-co: non-coplanar plan, st dev: standard deviation

The average difference in mean doses of the pituitary gland was 2.4 (± 2.9) Gy, also in favor of the non-coplanar plans (25.6 Gy versus 30.0 Gy) ($p = 0.08$). As expected, mean doses in the oral cavity were higher with non-coplanar plans, with a mean difference of 6.0 Gy (± 3.0 Gy) ($p = 0.001$), going from 4.9 Gy in the coplanar plans to 10.9 Gy in the non-coplanar plans.

Creating a constraint set for planning requires less than 10 minutes, the optimization process approximately 0.5 hour, followed by 15 minutes of dose calculation, which allows for a total planning time of about 1 hour. Typical beam-on times are 90 seconds for the CW and CCW arcs and 60 seconds for the CRCA arc. A time slot of 15 minutes per patient is programmed on the accelerator, leaving enough time for set-up, daily imaging for setup using kV/images verification and the actual treatment.

Discussion

Tumors arising in the paranasal sinuses remain a challenge in radiotherapy treatment planning due to the proximity of many critical OARs. In the present study, we evaluated a novel approach using non-coplanar arcs for treatment delivery, which allowed for further decreases in doses to the optic pathways in nearly 50% of cases, without compromising PTV coverage. QUANTEC data indicate that the incidence of radiation-induced optic neuropathy using fractions of ≤2Gy is near zero with a dose of 50 Gy, but increases to 3-7% in the 55-60 Gy region, and becomes substantial above 60 Gy [18]. Using our non-coplanar technique could therefore potentially lower the risk of optic neuropathy.

No statistical difference was observed between the CI and HI, and we were able to achieve a lower dose in nearly all optic structures, and in all patients. In 50% of patients, we were able to achieve a significant reduction of the dose in the clinically relevant 55-60 Gy interval in the left (patients 7,8) and right (patients 1,3,9) optic nerve.

Although non-coplanar static IMRT can create very conformal dose distributions in the sinonasal region [12,13,20], the major advantage of volumetric arc therapy is the use of unrestricted beam directions over the range of the arc. Two studies compared a non-coplanar IMRT technique with tomotherapy [14,16], both leading to a more conformal dose distribution and to a decreased dose in the OARs in 1 report favoring tomotherapy [16]. One disadvantage of tomotherapy is, however, the limited ability to use non-coplanar setups.

An additional advantage of our 2-arc technique is the fast planning and delivery time. The choice of beam directions of (non-coplanar) static IMRT fields to create an optimal plan can be very time consuming, so class solution approaches have been proposed [12,13]. Although it reduces planning time from a few days to 2 hours [12], beam set-up is no longer individualized. With a planning time of about 1 hour and beam-on time of less than 3 minutes, our non-coplanar arc technique compares favorably to both static IMRT and tomotherapy.

One drawback of our technique is a somewhat higher dose to the oral cavity. Next to using a soft constraint, we attempted to reduce the dose by ending the CRCA arc parallel to the hard palate, such that only exit doses at the start of the arc passed through the oral cavity, resulting in a mean dose below 15 Gy in all but 1 patient. This was considered acceptable, since Ruo Redda et al observed no (acute) taste loss at doses below 20 Gy [19]. Mean doses to the pituitary gland were below 30 Gy for both RA delivery approaches. We did not use hard constraints for the lens or lachrymal gland, but given that non-coplanar plans are more box-shaped, mean doses in both OARs are lower using this technique. Another drawback is the fact that this technique can only be used in cases where no elective neck irradiation is required.

In view of the close proximity of optic pathways to the PTV, a significant dose reduction in OARs using proton therapy is unlikely in many cases. A systematic review and meta-analysis comparing photon, carbon-ion and proton therapy was recently published [21]. One study reported a 5 year local control of 84% in a series of 14 patients with esthesioneuroblastoma who were treated using proton therapy [22]. In the sinonasal area, only 2 comparative planning studies are available. Mock et al, comparing proton and photon treatment planning, reported on differences in mean (of 5 patients) total doses to the OARs but did not state maximum doses [23]. A study comparing carbon-ion therapy and photon therapy showed a decrease in the mean (of 7 patients) of maximum doses in the ipsilateral optic nerve from 57.5 Gy to 54.4 Gy [24]. Alternatively, an advantage of photon therapy compared to proton therapy is that the dose distribution is almost invariant for small changes in presence of soft tissue or other material in the sinuses.

Conclusion

Based on the results of this planning study, our current policy is to treat SNC patients not requiring elective neck treatment with a 2 arc non-coplanar technique, using a Brainlab mask and daily online setup protocol. This is a fast and highly conformal technique, leading to the best possible tradeoff between adequate PTV coverage and OAR sparing.

References

1. Silverberg E, Grant RN. Cancer statistics, 1970. CA Cancer J Clin. 1970;20:11-23
2. Blanco AI, Chao KS, Ozyigit G, Adli M, Thorstad WL, Simpson JR, et al. Carcinoma of paranasal sinuses: long-term outcomes with radiotherapy. Int J Radiat Oncol Biol Phys 2004;59:51-8
3. Dulguerov P, Jacobsen MS, Allal AS, Lehman W, Calcaterra T. Nasal and paranasal sinus carcinoma: are we making progress? A series of 220 patients and a systematic review. Cancer 2001;92:3012-29
4. Jakobsen MH, Larsen SK, Kirkegaard J, Hansen HS. Cancer of the nasal cavity and paranasal sinuses. Prognosis and outcome of treatment. Acta Oncol 1997;36:27-31
5. Spiro JD, Soo KC, Spiro RH. Squamous carcinoma of the nasal cavity and paranasal sinuses. Am J Surg 1989;158:328-32
6. Waldron JN, O'Sullivan B, Warde P, Gullane P, Lui FF, Payne D, et al. Ethmoid sinus cancer: twenty-nine cases managed with primary radiation therapy. Int J Radiat Oncol Biol Phys 1998;41:361-9
7. Veldeman L, Madani I, Hulstaert F, De Meerleer G, Mareel M, De Neve W. Evidence behind use of intensity-modulated radiotherapy: a systematic review of comparative clinical studies. Lancet Oncol 2008;9:367-75
8. 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
9. 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;67:151-7
10. Combs SE, Konkel S, Schulz-Ertner D, Munter 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
11. Chen AM, Daly ME, 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;69:141-7
12. Claus F, De Gersem 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
13. Wang X, Zhang X, Dong L, Liu H, Gillin M, Ahamad A, et al. Effectiveness of noncoplanar IMRT planning using a parallelized multiresolution beam angle optimization method for paranasal sinus carcinoma. Int J Radiat Oncol Biol Phys 2005;63:594-601
14. 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;82:174-8
15. Doornaert P, Verbakel WF, Bieker M, Slotman BJ, Senan S. RapidArc planning and delivery in patients with locally advanced head-and-neck cancer undergoing chemoradiotherapy. Int J Radiat Oncol Biol Phys 2011;79:429-35
16. 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;33:595-8
17. Palma DA, Verbakel WF, Otto K, Senan S. New developments in arc radiation therapy: a review. Cancer Treat Rev 2010;36:393-9
18. Mayo C, Martel MK, Marks LB, Flickinger J, Nam J, Kirkpatrick J. Radiation dose-volume effects of optic nerves and chiasm. Int J Radiat Oncol Biol Phys 2010;76(Suppl 3):28-35
19. Ruo Redda MG, Allis S. Radiotherapy-induced taste impairment. Cancer Treat Rev 2006;32:541-7
20. Serre A, Idri K, Fenoglietto P, Ailleres N, Santoro L, Lemanski C, et al. Dosimetric comparison between coplanar and non coplanar field radiotherapy for ethmoid sinus cancer. Radiat Oncol 2007;2: 35

21. Ramaekers BL, Pijls-Johannesma M, Joore MA, van den Ende P, Langendijk JA, Lambin P, et al. Systematic review and meta-analysis of radiotherapy in various head and neck cancers: Comparing photons, carbon-ions and protons. Cancer Treat Rev 2010;37:185-201

22. Nishimura H, Ogino T, Kawashima M, Nihei K, Arahira S, Onozawa M, et al. Proton-beam therapy for olfactory neuroblastoma. Int J Radiat Oncol Biol Phys 2007;68:758-62

23. Mock U, Georg D, Bogner J, Auberger T, Potter R. Treatment planning comparison of conventional, 3D conformal, and intensity-modulated photon (IMRT) and proton therapy for paranasal sinus carcinoma. Int J Radiat Oncol Biol Phys 2004;58:147-4

24. Amirul IM, Yanagi T, Mizoe JE, Mizuno H, Tsujii H. Comparative study of dose distribution between carbon ion radiotherapy and photon radiotherapy for head and neck tumor. Radiat Med 2008;26:415-21