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ORIGINAL ARTICLE

Conformal orbit sparing radiation therapy: a treatment option for advanced skin cancer of the parotid and ear region

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Abstract

Introduction: New surgical methods have enabled resection of previously in-operable tumours in the region of the parotid gland and ear. This has translated to deeper target volumes being treated with adjuvant radiotherapy. Due to the limitations of existing conformal techniques, alternative planning approaches are required to cover the target volume with appropriate sparing of adjacent critical structures. Although intensity modulated radiation therapy (IMRT) may be able to achieve these goals compared with the existing conformal method, a new orbital sparing radiation therapy (OSRaT) technique was evaluated as an alternative conformal planning process. The study objective was to evaluate the dosimetry of three planning methods: pre-existing conformal, IMRT and OSRaT techniques. **Methods:** Ten patients were planned retrospectively using the existing three-dimensional conformal radiotherapy (3DCRT), IMRT and OSRaT techniques. Dosimetry was analysed using the homogeneity index (HI), conformity index (CI), the volume of planning target volumes (PTV) under and over treated by the 95% isodose and dose to critical structures. **Results:** OSRaT achieved superior 95% coverage of the high-dose PTV while delivering HI similar to IMRT for intermediate and high-dose PTVs. The CI for the high-dose PTV was comparable between the three techniques, however IMRT was statistically better for the low- and intermediate dose PTVs. All three techniques showed adequate orbital sparing, however OSRaT and IMRT achieved this with less under dosing of the PTVs. **Conclusion:** For the treatment of patients with advanced skin cancer of the parotid and ear, both IMRT and the OSRaT techniques are viable options.

Introduction

The current treatment of choice for advanced skin cancer involving the parotid and/or the pinna/ear region is surgery and adjuvant radiation therapy.[1] The evolution of new surgical methods has allowed the deeper resection of previously in-operable tumours in this region. Extensive surgery and deep resections are necessary to achieve adequate resection margins in these tumours.[2] This can often include a lateral temporal bone dissection to obtain the desired clearance of the tumour. Consequently, this extensive surgery has resulted in the need for deeper clinical target volumes (CTV) for post-operative radiation therapy treatment.[3]

This increase in target volume depth inherently presented challenges for the existing radiation therapy techniques commonly used. Deeper planning target volume (PTV) coverage was required within close proximity to adjacent organs at risk (OAR) as depicted in Figure 1. The previous treatment method included three-dimensional conformal radiotherapy (3DCRT) with an electron junction to limit dose to the optic structures. The issue with this technique was its inability to provide adequate dose coverage to the increased depth of the PTV

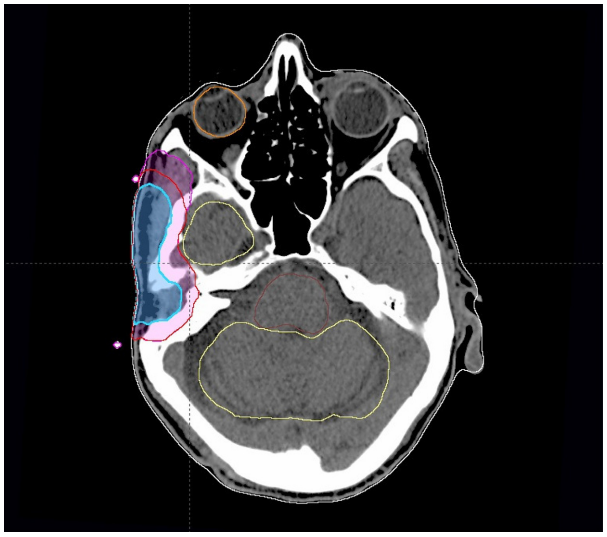

Figure 1. Transverse slice through skull base illustrating target volumes and their proximity to critical structures. Blue, clinical target volume; red, high target volume; purple, intermediate target volume; brown, brainstem; orange, ipsilateral orbit; yellow, brain structures.

in the temporal region. The electron field could not simply be replaced by extending the photon fields in this area due to the proximity to the surrounding optic structures, temporal lobe and cerebellum. As a result, PTV coverage was compromised or OAR dose was increased at the discretion of the consulting radiation oncologist. Intensity modulated radiation therapy (IMRT) may be able to achieve PTV coverage and organ sparing, however its use may be restricted to departmental resources. Hence, a new radiotherapy treatment technique needed to be developed to achieve adequate PTV coverage while minimising dose to surrounding OAR.

The purpose of this study was to compare three techniques employed in the treatment of these tumours: (1) the existing 3DCRT technique, (2) the IMRT and (3) the new conformal orbit sparing radiotherapy technique (OSRaT) to determine the best dosimetric method of treating these patients while taking into account departmental resources such as quality assurance on the treatment machine, staff training and planning calculation time.

Materials and Methods

Patient demographics

Institutional ethics approval was granted to conduct a retrospective dosimetric study involving 10 consecutive patients (Table 1) who had been previously treated with adjuvant radiation therapy for locally advanced skin cancer in the parotid and ear region. To be eligible, patients must have had a temporal bone resection and been treated with radical intent to a minimum prescription dose of 60 Gy in 30 fractions.

Table 1. Patient characteristics.

Characteristic	Number (N = 10)
Gender	
Male	10
Female	0
Age	Range (51–97 years)
Diagnosis	
SCC	8
BCC	1
Carcinoma of parotid	1
T stage	
Tx	1
T0	1
T2	2
T4	6
N stage	
N0	4
N1	2
N2	4

BCC, basal cell carcinoma; SCC, squamous cell carcinoma.

CT/simulation

All patients were planned using 3-mm slice thickness computed tomography (CT) scans and immobilised using Civco® (Civco Medical Solutions, Orange City, IA) thermoplastic shells. Each of the 10 CT data sets was used to create plans for the three different radiation therapy dosimetry methods evaluated, resulting in a total of 30 plans. All plans were generated using the Varian Eclipse Treatment Planning System version 8.6 (Varian Medical Systems, Palo Alto, CA) using an AAA algorithm with a 2-mm voxel calculation grid. The planning data were modelled on an Elekta Synergy® (Elekta AB, Stockholm, Sweden) linear accelerator which had a 1-cm multi-leaf collimator system. CT data sets were de-identified and PTV and OAR contoured by one radiation oncologist and one senior experienced radiation therapist. The same radiation therapist produced all plans and the same radiation oncologist reviewed all plans. Each plan was evaluated and checked according to the department's quality assurance process by the same quality assurance radiation therapist.

Target volume and dose levels

The high-dose CTV consisted of the resected disease area with a 1-cm margin cropped at defined anatomical boundaries that are barriers to tumour spread. The intermediate dose CTV included the whole of the operative bed including the high-dose CTV. The low-dose

CTV included both the high- and intermediate dose CTVs as well as covering elective areas at risk of recurrence. The low-dose CTV generally included the whole of the ipsilateral neck from above the zygoma to the supraclavicular region. All three CTV dose levels had a 5-mm geometric expansion to create the PTV. The three PTV dose levels were used for comparison. The prescription doses for the relative PTVs used in this study for 3DCRT and OSRaT were 60 Gy in 30 fractions for eight patients and 66 Gy in 33 fractions for two patients. The IMRT plans were generated using 60 Gy in 30 fractions for eight patients and 63 Gy in 30 fractions respectively (biologically equivalent to 66 Gy in 33#). This was done to match the prescription dose used in the corresponding 3DCRT and OSRaT plans.

The 3DCRT and OSRaT PTVs were characterised as low (50 Gy), intermediate (54 Gy) and high (60–66 Gy at 2 Gy per day). The IMRT plans were generated to be delivered concomitantly so the prescription doses were increased to give the same biological effect over 30 fractions. For the low PTV, 50 Gy was escalated to 54 Gy, while 54 Gy escalated to 56 Gy for the intermediate PTV. Where the high PTV was treated to 66 Gy in 33 fractions using the conformal techniques, the IMRT high PTVs were escalated to 63 Gy in 30 fractions. Otherwise all other high PTVs were planned to 60 Gy in 30 fractions.

3DCRT technique

The 3DCRT technique consisted of 4–5 static mono-isocentric photon fields per phase with a matching electron field at the level of the orbit (Fig. S1). This technique comprised a 6-MV anterior oblique photon field (motorised wedge thick to posterior), a 6-MV posterior oblique photon field (motorised wedge thick to anterior), lowly weighted 6 MV lateral photon field and an anterior neck field junctioned inferiorly to cover the elective neck nodal region. A lateral electron field was junctioned to the photon fields to facilitate orbital structure sparing. The electron energy was chosen to best suit the depth of PTV in this temporal region. A moving junction was used between the electron field and the photon fields to minimise the hot and cold spots. A total of three junctions were used between the photon fields and electron interface. The superior border of each of the photon fields was altered to junction with the inferior border of the electron field.

IMRT technique

This technique comprised 6–7 intensity modulated 6 MV photon fields evenly spaced between 0° and 180° entering on the ipsilateral side (Fig. S2). The plan was optimised with planning objectives of 2 mm expansions for all dose levels and 5 mm ring structures were created to inhibit dose spread. A brain avoid structure was added when required to limit brain dose and conform the dose in the temporal region. The OARs were optimised to meet constraints as per department protocols.

OSRaT technique

This new technique comprised 5–6 mono-isocentric static 6 MV photon fields to encompass the PTV and avoid the use of an electron–photon junction. Like the previously described 3DCRT technique, the OSRaT technique comprised a 6-MV anterior oblique photon field (motorised wedge thick to posterior), a 6-MV posterior oblique photon field (motorised wedge thick to anterior) and a lowly weighted 6 MV lateral photon field. The superior border of the ipsilateral posterior oblique field was positioned 0.75–1 cm inferior to lens by the radiation therapist to reduce dose to the lens and create a 'Pseudo' junction. In contrast to the 3DCRT technique where an electron field was utilised, a 6-MV photon posterior or contralateral posterior oblique field covering the superior portion of the PTV was used and junctioned with the ipsilateral posterior oblique field as shown in Figure 2. This allowed the reduction in optical and brain dose while increasing PTV coverage.

Dosimetry analysis

All plans were assessed using the following criteria: dose delivered to surrounding OAR, homogeneity index (HI), dose conformity index (CI) and PTV coverage. PTV coverage was assessed with respect to the volume of 95% isodose (cc), for the relative prescription. Each intermediate and high PTV for the three dosimetry techniques was measured to establish:

1 the amount of PTV (cc) not covered by the 95% isodose (PTV<95%) and
2 the amount of 95% isodose (cc) extending outside the relative PTV (PTV>95%). Dose reporting followed the recommendations published in International Commission on Radiation Units and Measurements (ICRU) Report no. 83 for prescribing and reporting IMRT.[4]

The OAR doses recorded were spinal cord, brainstem, contralateral and ipsilateral lens and contralateral and ipsilateral orbit maximums, lacrimal gland mean, whole brain maximum and mean, volume of whole brain receiving 60 Gy or higher, cerebellum maximum and mean and the temporal lobe maximum and mean. The whole brain volume over 60 Gy was seen as clinically important due to the incidence of necrosis increases with higher dose levels.[5]

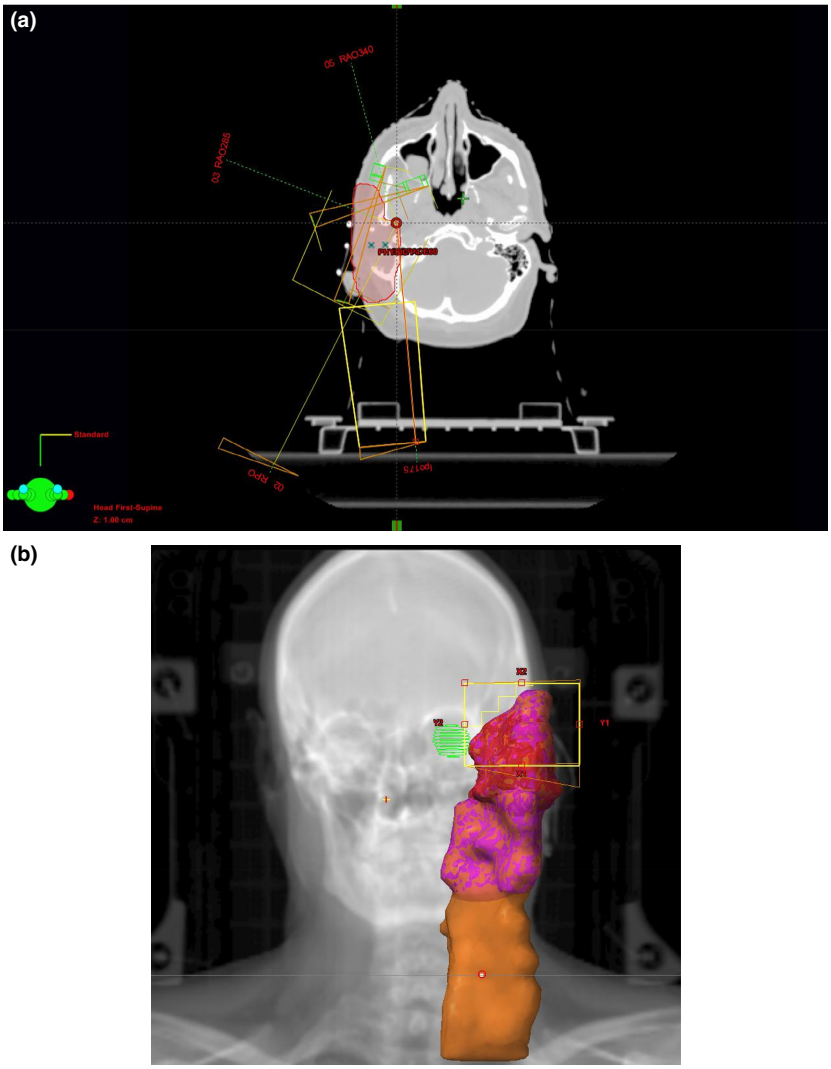

Figure 2. (A) OSRaT – orbital sparing contralateral post-oblique field and (B) beams eye view.

The HI was calculated by the difference between the near-maximum and near-minimum dose normalised to the median dose and measures the dose homogeneity across the PTV. A HI value approaching zero indicates a more homogenous dose distribution within the PTV.[4]

$$\mathrm{HI} = \frac{D2\% - D98\%}{D50\%},$$

where D2% is the dose covered by 2% of the target volume (TV), D98% is the dose covered by 98% of the TV and D50% is the dose covered by 50% of the TV.

CI was measured by using the formula below:

$$\mathrm{CI} = (\mathrm{TV95}/\mathrm{TV}) \times (\mathrm{TV95}/\mathrm{V95}),$$

where TV95 is the volume of target covered by 95% isodose line, TV is the total target volume and V95 is the volume of tissue covered by the 95% isodose line. A (CI) value approaching 1 indicates a more conformal dose distribution within the PTV.[4]

Statistical analysis

A linear mixed model (LMM) was used to compare the three plans created for the 10 patients to take into account random effects with the paired data for OAR and dosimetry descriptors. Specifically, the dosimetric differences were analysed with the three techniques. A value of $P < 0.05$ was defined as having statistical significance. To investigate the differences between techniques for statistical significance, a post hoc Tukey test was performed for individual comparison.

All statistical analyses was performed using R statistical software version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria). The LMM was performed using R Package 'nlme' function 'lme' and the Tukey test for multiple comparisons used R package 'multicomp' function 'glht'.

Results

TV coverage

The HI and CI were calculated for the low, intermediate and high PTV for each technique (Table 2). 3DCRT HI was found to be inferior when compared to IMRT and OSRaT for the intermediate and high PTV. OSRaT and IMRT had similar HI for the intermediate and high PTV, while IMRT was superior in the low PTV HI with a median value of 0.26 compared to 0.33.

The CI for IMRT was better for the low and intermediate TV when compared to the other two techniques. This was complemented by a reduction in intermediate PTV over treated for IMRT in comparison to 3DCRT and OSRaT. The CI for the high PTV was not statistically different between the three techniques (Fig. 3). The identified outliers were a result of variation demonstrated in the depth of the corresponding target volumes.

In terms of volumes measured, the intermediate and high PTV over and under treated by the 95% dose are displayed in Figure 4. There was no significant difference found between IMRT and OSRaT for the high PTV under treated. OSRaT provided the best coverage of the high PTV in the superficial region. The majority of the high TV under treated by IMRT was found to be located superficially (not under bolus). Conversely, significant deficiencies in the deeper margins of the high PTV were found with the 3DCRT technique when compared to OSRaT and IMRT.

OAR dose comparison

All three techniques provided clinically adequate optical sparing, however differences were seen between the brain doses between the three techniques as displayed in Figure 5.

Similarities in dose delivered were found between the IMRT and OSRaT techniques for the mean whole brain and mean temporal lobe doses, whereas the 3DCRT technique delivered significantly lower doses to these OAR. The mean cerebellum doses were statistically similar between the IMRT and OSRaT techniques. However, a significant difference was noted between the OSRaT and 3DCRT technique with the 3DCRT technique delivering a lower dose. Significant differences were also noted between the IMRT and OSRaT techniques for the mean contralateral lens and maximum ipsilateral orbit doses with IMRT delivering a higher dose. However, these differences were not considered to be clinically significant (Table 3).

The volume of whole brain receiving 60 Gy or greater was not statistically different between the three techniques ($P = 0.088$), however IMRT showed an obvious reduction in volume when compared to OSRaT and 3DCRT when a dose of 63 Gy (as opposed to 66 Gy) was prescribed.

Discussion

This study demonstrated that the existing 3DCRT technique, with its use of electrons, has sub-optimal coverage at depth due to the more extensive surgery requirements and the associated limitations of electrons. This technique has inherent dosimetric uncertainties,

Table 2. Mean dosimetric indices (±SD) comparison for the three techniques using linear mixed model.

Target volumes	3DCRT	IMRT	OSRaT	*P*-value
Homo index Low	0.36 (±0.04)	0.26 (±0.04)	0.33 (±0.07)	**<0.0001**
Conformity index Low	0.55 (±0.04)	0.62 (±0.03)	0.54 (±0.03)	**<0.0001**
Homo index Med	0.31 (±0.07)	0.2 (±0.09)	0.23 (±0.08)	**<0.0001**
Conformity index Med	0.49 (±0.09)	0.52 (±0.11)	0.48 (±0.09)	**0.01**
Homo index High	0.26 (±0.09)	0.13 (±0.07)	0.15 (±0.08)	**<0.0001**
Conformity index High	0.36 (±0.13)	0.43 (±0.19)	0.41 (±0.12)	0.196
Over cc Med	310.33 (±86.94)	264.35 (±82.86)	319.74 (±82.52)	**0.014**
Under cc Med	13.57 (±10.16)	17.57 (±22.76)	10.42 (±10.43)	0.457
Over cc High	213.97 (±100.47)	187.9 (±104.1)	196.34 (±105.66)	0.826
Under cc High	10.53 (±10.33)	5.91 (±6.38)	3.84 (±4.01)	**0.047**

P-values less than 0.05 in bold were statistically significant. 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity modulated radiation therapy; OSRaT, orbital sparing radiation therapy; cc, cubic centimetres; Homo, homogeneity; Med, intermediate; Over, volume over treated by 95% isodose line; Under, volume under treated by the 95% isodose line.

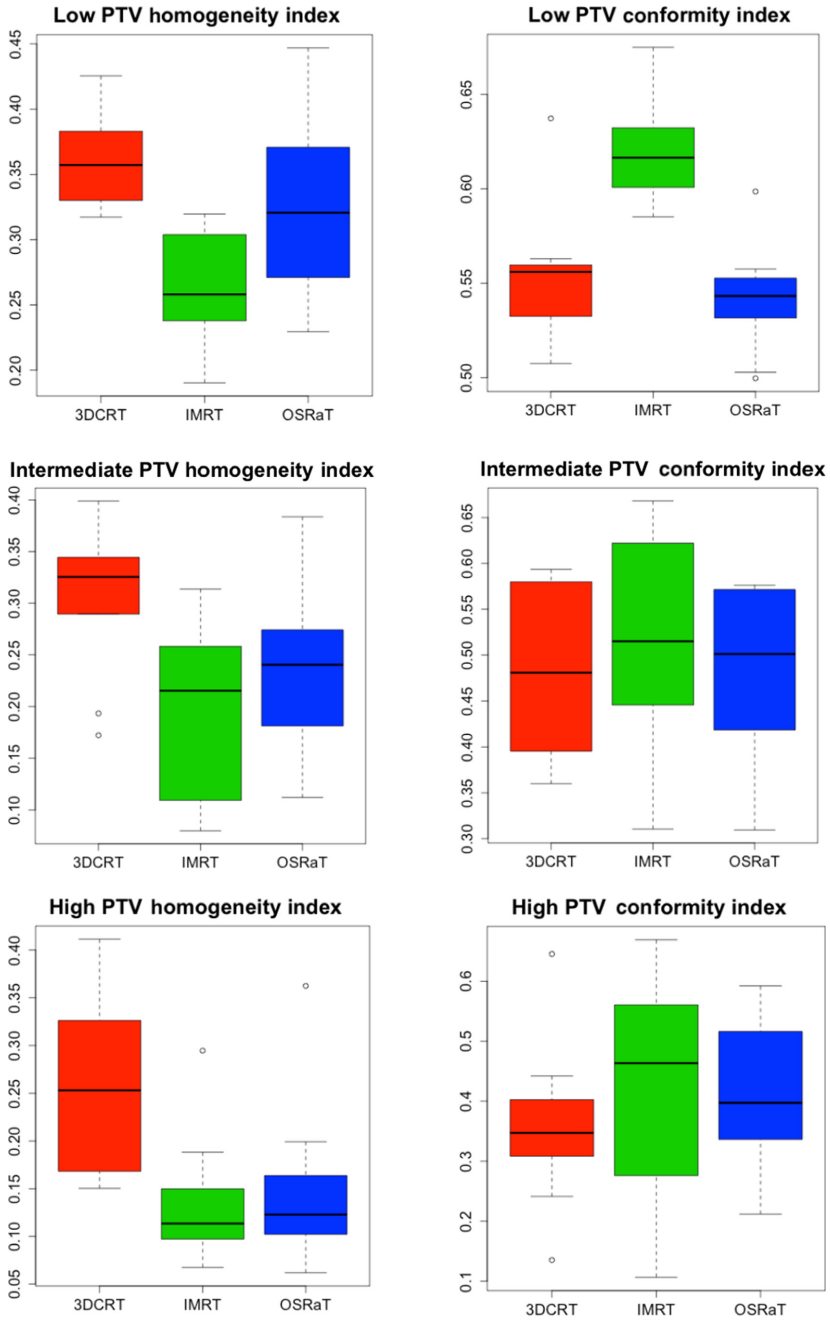

Figure 3. Box and whisker plots depicting dosimetric indices of reported PTVs for each technique. PTV, planning target volumes; 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity modulated radiation therapy; OSRaT, orbital sparing radiation therapy.

which is commonly seen with photon–electron junction regions,[6] which affects both deep margin coverage and homogeneity and leads to significant over and under dosing.

Logically, IMRT appears the way to overcome these dosimetric issues. IMRT step and shoot methods involving several fields could deliver adequate coverage and homogenous plans.[7] However, IMRT may not be a viable option for all departments as it requires extensive physics measurement resources, treatment machine time for quality assurance and staff training.[8] OSRaT was developed to provide a viable alternative for treating advanced skin cancer in the region of the parotid gland and ear when IMRT resources are limited. In this

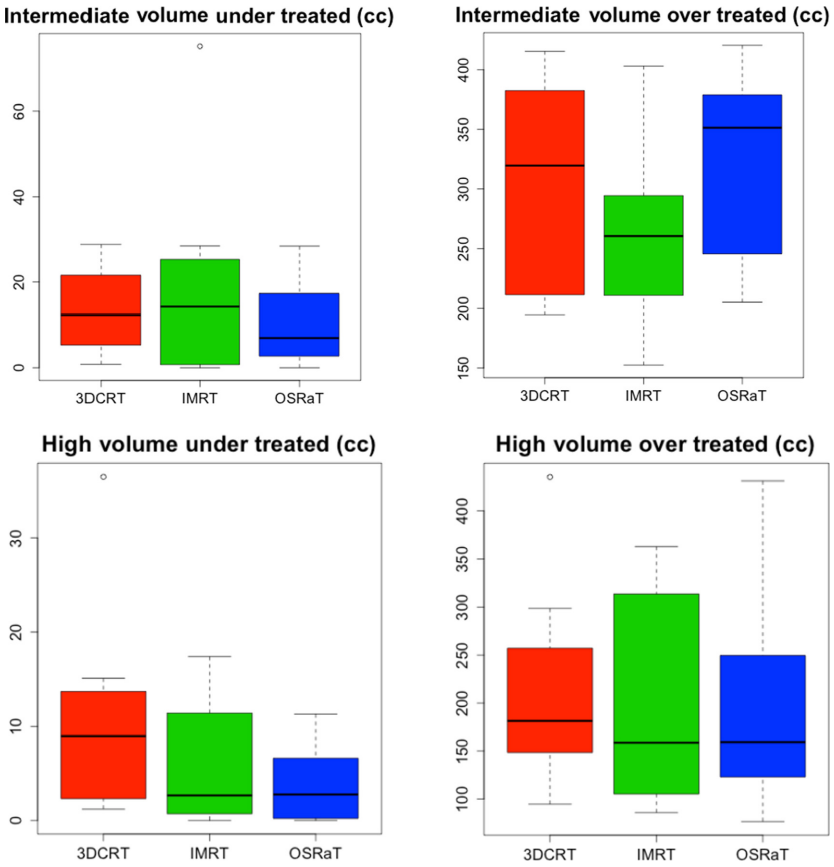

Figure 4. Box and whisker plots depicting dosimetric volumes of the planning target volumes over and under treated in cubic centimetres (cc) by the 95% prescribed isodose line for each technique. 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity modulated radiation therapy; OSRaT, orbital sparing radiation therapy.

dosimetric comparison, IMRT demonstrated the best dosimetric solution overall, but comparable results were found using the OSRaT technique in terms of PTV coverage and OAR dose sparing when compared with IMRT.

The OSRaT technique displayed less tissue under dosing in the high PTV especially in the deeper surgical margins region when compared to 3DCRT. OSRaT also achieved a superior median HI of 0.15 compared to 0.26 for 3DCRT and was comparable to IMRT. The use of a contralateral photon posterior oblique or posterior field junctioned with the ipsilateral post-oblique field enables the OSRaT technique to achieve improved deep margin coverage when compared to 3DCRT.

A major clinical consideration for these advanced skin cancers was that OSRaT demonstrated improved superficial region coverage when compared to IMRT when bolus was not applied. IMRT has been documented to display dose uncertainty superficially and can be overestimated with larger voxel size calculation grids.[9] In addition, this study also demonstrated that the high PTV was under treated by the IMRT technique, with a median value of 2.01 cc more than the OSRaT technique.

An important consideration for clinicians when choosing an appropriate technique is the potential increase of whole brain tissue volume receiving greater than 60 Gy due to the deeper surgical margins and temporal bone resections. Higher dose levels have been evidenced to lead to greater incidences of necrosis.[5] The median volume of whole brain receiving 60 Gy or greater was 1.75, 0.88 and 2.48 cc for 3DCRT, IMRT and OSRaT techniques respectively ($P = <0.088$). Although this was not statistically significant, there could be clinical benefits for the use of IMRT, as opposed to OSRaT, when a dose of 66 Gy is prescribed, as IMRT reduced the volume of whole brain tissue exposed to more than 60 Gy. However, this must be balanced with the improved superficial coverage achieved when using OSRaT, in comparison to IMRT, when deciding on an appropriate technique for these advanced skin cancers.

Although 3DCRT demonstrated significantly lower mean doses in the whole brain compared to both OSRaT

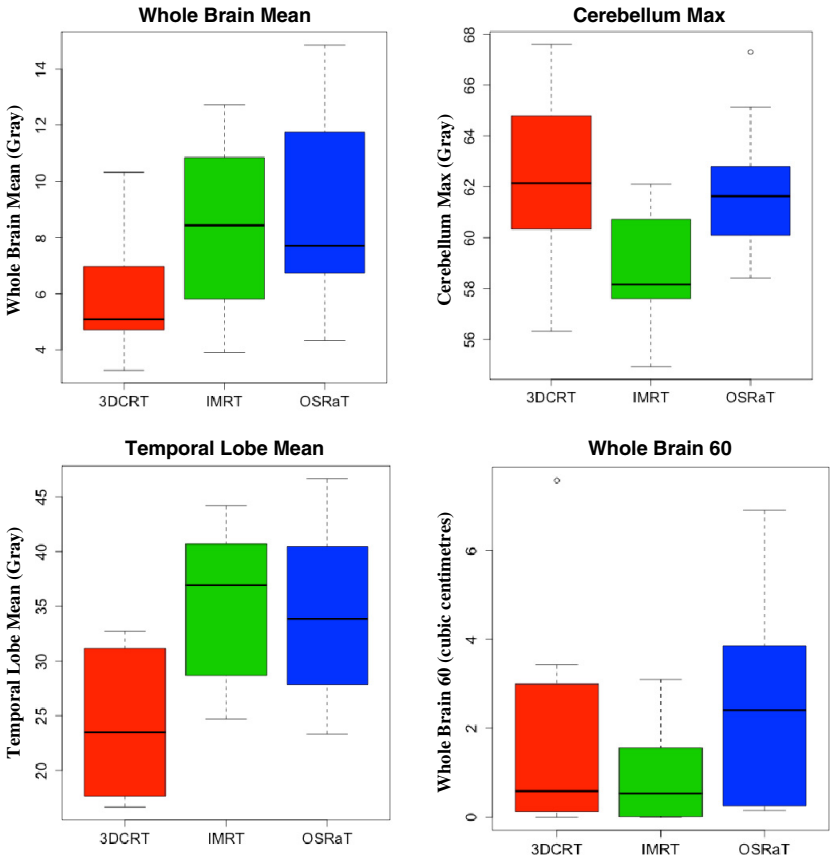

Figure 5. Box and whisker plots depicting dosimetric indices of reported organs at risk doses for each technique. 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity modulated radiation therapy; OSRaT, orbital sparing radiation therapy.

and IMRT, it was mostly attributed to the suboptimal depth coverage of the deeper surgical margins with electrons which could translate to high a risk of recurrence.[1] This significant under dosing with 3DCRT is clearly shown by the under dose of the high TV with median values of 10.5 cc compared to 3.84 and 5.91 cc for OSRaT and IMRT respectively (*P*-value of 0.047).

All three techniques achieved acceptable OAR doses but the results from this study showed that IMRT was superior with its ability to limit brain volume receiving doses greater than 60 Gy. Higher IMRT mean values were noted when compared to 3DCRT for cerebellum and temporal lobe. This was indicative of the lack of surgical margin coverage at depth with the 3DCRT electron plan rather than a better result for the 3DCRT target coverage. Additionally, slightly higher OAR doses are noted for IMRT and 3DCRT to the contralateral orbit and ipsilateral lens in comparison to OSRaT.

An additional consideration is that OSRaT not only achieved comparable PTV coverage when compared to IMRT, but was also found to be more efficient to deliver than the conventional 3DCRT. This was primarily a result of it being a mono-isocentric technique without the need to re-enter the room to position the junctioning electron field. This suggests that improved patient throughput can be achieved with this technique and reduces the potential of intra-fraction movement. It also eliminates electron insert manufacturing. The conformal OSRaT technique also has a potential cost benefit for a department when compared to IMRT[8] as it requires no extra quality assurance physical measurements on the treatment machines.

The authors' accept there may be some limitations that could have bearing on the results for this study. The first limitation is the small cohort of 10 patients used in the study. A larger cohort could improve the power to detect statistically significant results. Another consideration is the introduction of different radiation oncologists for target delineation and different radiation therapists for dosimetry planning. Additionally, the authors recognise the potential for bias as the radiation therapists for planning and quality assurance were not blinded to the relative dosimetric techniques. However, the effect of this bias was minimised by each plan being generated using the same clinical minimum dose coverage requirements and organ at risk dose constraints which had to be met for the plan to be clinically acceptable.

Table 3. Dosimetric comparison of the three techniques for organs at risk.

OAR	3DCRT (GY)	IMRT(GY)	OSRaT(GY)	*P*-value
SCMAX	36.31 (±5.45)	35.69 (±3.1)	36.18 (±5.73)	0.866
Brainstem	30.83 (±10.12)	33.71 (±6.83)	32.66 (±10.62)	0.21
Lacrimal Gland Mean	6.61 (±3.84)	6.83 (±2.45)	6.47 (±3.09)	0.936
Lens Ipsi Max	5.82 (±1.86)	6.25 (±0.87)	5.61 (±1.62)	0.557
Lens Contra Max	3.08 (±2.21)	4.43 (±1.21)	2.15 (±0.49)	**0.003**
Orbit Ipsi Max	15.02 (±8.44)	17.58 (±8.99)	13.96 (±7.27)	0.146
Orbit Contra Max	5.38 (±3.86)	9.80 (±2.79)	4.72 (±3.26)	**<0.0001**
Whole Brain Max	63.77 (±4.8)	62.39 (±2.53)	63.40 (±2.69)	0.481
Whole Brain Mean	5.83 (±2.03)	8.39 (±2.97)	9.06 (±3.29)	**<0.0001**
Cerebellum Max	62.37 (±3.36)	58.77 (±2.27)	61.82 (±2.82)	**<0.0001**
Cerebellum Mean	22.00 (±5.8)	23.17 (±4.13)	25.91 (±6.42)	**0.047**
Temporal Lobe Mean	24.08 (±6.04)	35.58 (±6.93)	34.42 (±8.12)	**<0.0001**
Temporal Lobe Max	61.34 (±5.36)	61.1 (±2.71)	61.91 (±3.31)	0.834

P-values less than 0.05 in bold indicate statistical significance. OAR, organs at risk; 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity modulated radiation therapy; OSRaT, orbital sparing radiation therapy; Gy, gray.

Conclusion

This study demonstrated that the OSRaT technique is a clinically viable option in radiation therapy centres with limited IMRT resources available. This method, when compared to IMRT, was capable of achieving comparable deep margin coverage, improved superficial coverage while still limiting dose to optical structures and other OAR.

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Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Transverse, coronal, sagittal and three-dimensional view depicting the field arrangement for the 3DCRT dosimetry technique; orange, elective PTV; purple, intermediate PTV; red, high-dose PTV.
Figure S2. Transverse, coronal, sagittal and three-dimensional view depicting the field arrangement for the IMRT dosimetry technique; orange, elective PTV; purple, intermediate PTV; red, high-dose PTV.