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**PHYSICS CONTRIBUTION**

# VOLUMETRIC INTENSITY-MODULATED ARC THERAPY VS. CONVENTIONAL IMRT IN HEAD-AND-NECK CANCER: A COMPARATIVE PLANNING AND DOSIMETRIC STUDY

WILKO F. A. R. VERBAKEL, PH.D.,* JOHAN P. CUIJPERS, PH.D.,* DAAN HOFFMANS, B.SC.,* MICHAEL BIEKER, M.D., PH.D.,* BEN J. SLOTMAN, M.D., PH.D.,* AND SURESH SENAN, M.R.C.P., F.R.C.R., PH.D.*

*Department of Radiation Oncology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

**Purpose:** Volumetric intensity-modulated arc therapy (RA) allows for rapid delivery of highly conformal dose distributions. In this study, planning and dosimetry of RA were compared with conventional intensity-modulated radiation therapy (IMRT) plans of head-and-neck cancer patients.

**Materials and Methods:** Computed tomography scans of 12 patients who had completed IMRT for advanced tumors of the naso-, oro- and hypopharynx were replanned using RA using either one or two arcs. Calculated doses to planning target volume (PTV) and organs at risk (OAR) were compared between IMRT and RA plans. Dose distributions for single arc ($n$ = 8) and double arc ($n$ = 4) plans were verified using film dosimetry in three to five coronal planes using a quality assurance phantom.

**Results:** RA plans allowed for a mean reduction in number of monitor units (MU) by nearly 60%, relative to seven field sliding window IMRT plans. RA plans achieved similar sparing of all OAR as IMRT. Double arc RA provided the best dose homogeneity to PTV with a lower standard deviation of PTV dose (1.4 Gy), vs. single arc plans (2.0 Gy) and IMRT (1.7 Gy). Film measurements showed good correspondence with calculated doses; the mean gamma value was 0.30 (double arc) and area of the film with a gamma exceeding 1 was 0.82%.

**Conclusions:** RA is a fast, safe, and accurate technique that uses lower MUs than conventional IMRT. Double arc plans provided at least similar sparing of OAR and better PTV dose homogeneity than single arc or IMRT. 

**Arc therapy, RapidArc, Film dosimetry, Planning study, Head-and-neck cancer.**

## INTRODUCTION

Radiotherapy for advanced head-and-neck carcinomas has shifted away from three-dimensional conformal radiotherapy (3D-CRT) to intensity-modulated radiotherapy (IMRT). The clinical benefits of sparing of the parotid glands have been demonstrated (1–4) with resulting reduction of xerostomia for patients treated with IMRT compared with CRT. The main drawbacks of IMRT are the more complex and time-consuming treatment planning process and the need for more extensive physics quality assurance. In addition, IMRT uses a larger number of static beams and monitor units (MUs) (5), which increases radiation delivery times up to 20 min and also patient exposure to low-dose irradiation.

In general, an increase in the number of IMRT beams increases the degrees of freedom (6), making intensity modulated arc therapy a logical next step in IMRT delivery. Several optimization methods for arc therapy based on direct aperture optimization have been described (7–9). A recently described novel approach for volumetric modulated arc therapy enables IMRT-like dose distributions to be delivered using a single rotation of the gantry (10). This concept has been clinically implemented in the Eclipse treatment planning software (Varian Medical Systems, Palo Alto, CA) under the name RapidArc (RA). In RA, the gantry speed and dose rate vary continuously during delivery. In addition, there is full leaf interdigitation, allowing multiple small islands of dose to be delivered to the planning target volume (PTV) at each gantry position. Clinical introduction of such new treatment techniques should be preceded by detailed validation of a range of plans (11, 12). Extensive studies on treatment planning or dosimetric validation and comparison of RA dose distribution with those obtained by existing IMRT techniques have not yet been reported. Because IMRT plans for head-and-neck cancer are demanding and

Reprint requests to: W.F.A.R. Verbakel, PhD, Department of Radiation Oncology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands. Tel: +31-20-4440442; Fax:+31-20-4440410; E-mail: w.verbakel@vumc.nl

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Table 1. Patient characteristics

| | | UICC | $V_{boost}$ ($cm^3$) | $V_{total}$ ($cm^3$) |
|---|---|---|---|---|
| P1 | Nasopharynx | III | 375 | 615 |
| P2 | Nasopharynx | IIb | 195 | 477 |
| P3 | Nasopharynx | III | 221 | 837 |
| P4 | Nasopharynx | III | 470 | 797 |
| P5 | Oropharynx | IVb | 267 | 605 |
| P6 | Oropharynx + oral cavity | III | 126 | 341 |
| P7 | Oropharynx | III | 155 | 324 |
| P8 | Oropharynx | II | 193 | 459 |
| P9 | Oropharynx | IVb | 182 | 543 |
| P10 | Oropharynx | IVb | 144 | 543 |
| P11 | Oropharynx | IVb | 372 | 689 |
| P12 | Hypopharynx | IVa | 160 | 447 |

*Abbreviations:* UICC = International Union Against Cancer; PTV = planning target volume.

All patients except for P7 had the bilateral lymph nodes included in the PTV.

require strong dose modulation, we selected these tumors for a comparative study of RapidArc plans with IMRT.

## MATERIALS AND METHODS

### *Patient selection and contouring*

Twelve patients with head-and-neck tumors were selected for the planning study (Table 1). These patients were randomly selected from the list of patients with head-and-neck cancer that have received IMRT treatment between 2007 and 2008 at our department. All cases were difficult to plan using conventional IMRT because of large, irregular tumor volumes. They were treated to two dose levels by means of a simultaneously integrated boost, delivering in 35 equal treatment fractions 70 Gy to the boost volume (PTVboost) and 57.7 Gy to the elective PTV (PTVelective). PTVboost consisted of the gross tumor volume and lymph nodes containing visible macroscopic tumor or biopsy-proven positive lymph nodes, to which a margin of 10 mm for CTV and 3 mm margin for PTV was added. PTVelective consisted of elective nodal regions (13,14) with a margin of 3 mm for setup errors. Segmented organs at risk (OAR) were the parotid glands, spinal canal, brainstem, oral cavity, and larynx region. The laryngeal region and oral cavity were arbitrarily delineated by a single clinician and they were restricted to a minimum distance of 5 mm from the PTV.

### *Conventional IMRT planning*

The clinical (sliding window) IMRT plans were generated with seven coplanar equidistant fields of 6 MV. Optimizations and dose calculations were done with Helios/Eclipse versions 7.2.34 or 8.1.14 (Varian Medical Systems). For the optimization, the PTVs were reduced to 5 mm under the skin surface to prevent optimization problems in the build-up region. After optimization, the skin flash tool was used to extend the fluence of each field where necessary to cover the original PTV. PTVelective was reduced by a ring of 5 mm around PTVboost where a transient dose between 57.7 and 70 Gy was allowed. All IMRT optimizations were done by interactively adapting the objectives and their priorities. In the final plan, the objectives were to achieve PTV volumes receiving less than 95% of the prescribed dose ($V_{<95}$) smaller than 1% and $V_{>107}$ close to zero, although this was not followed strictly for PTVelective. For the OAR, the most important objective was to keep the maximum doses to the spinal cord and brainstem below 48 Gy and 55 Gy, respectively. The second main priority for OAR was to reduce the average dose to the parotid glands, where possible to below 26 Gy. Only after these objectives were met, reduction of the high-dose volume to the oral cavity and larynx region was attempted. To avoid hot spots of dose in the body of the patient, not delineated as one of the previously mentioned OAR, the rest of the body was subdivided in two to three extra OAR with objectives for the maximum dose. After optimization, the dose calculation was performed in Eclipse with the AAA algorithm (15,16) using a calculation grid of 2.5 mm. All the patients have been treated according to these IMRT plans using Varian Clinac 2300CD linear accelerators.

### *RA planning*

RA is based on a stepwise optimization of leaf positions for a single arc, which is divided into 177 angles, named control points. Instead of trying to optimize all control points of the RA planning at once, which would be extremely time consuming, Otto showed that a progressively increase of control points can converge the optimization in a short time period to an optimal solution (10).

Table 2. Plan comparison between conventional IMRT and RapidArc (average of 12 patients)

| | IMRT | Single Arc RA | Double Arc RA | Wilcoxon Matched-Pair Signed Rank Test ($p$) |
|---|---|---|---|---|
| V(boost)/$cm^3$ | 238 (126–470) | | | |
| V(elective)/$cm^3$ | 550 (324–837) | | | |
| MU | 1108 | 439 | 459 | 0.000000 |
| $V_{<95\%}$(boost)/% | 1.2 | 1.6 | 0.6 | 0.097 |
| $V_{>107\%}$(boost)/% | 0.8 | 1.8 | 0.2 | 0.270 |
| SD(boost)/Gy | 1.7 | 2.0 | 1.4 | 0.014 |
| $V_{<95\%}$(elective)/% | 1.0 | 2.3 | 0.9 | 0.912 |
| $V_{>107\%}$(elective)/% | 6.8 | 13.7 | 3.0 | 0.043 |
| SD(elective)/Gy | 1.7 | 2.1 | 1.5 | 0.097 |
| CI(boost) | 1.14 | 1.21 | 1.24 | 0.014 |
| CI(elective) | 1.54 | 1.60 | 1.59 | 0.638 |
| $D_{mean}$(left par)/Gy | 35 | 37 | 34 | 0.347 |
| $D_{mean}$(right par)/Gy | 38 | 36 | 34 | 0.384 |
| $D_{mean}$(larynx)/Gy | 45 | 47 | 47 | 0.136 |
| $D_{mean}$(oral cavity)/Gy | 35 | 35 | 36 | 0.238 |

The Wilcoxon matched-pair signed rank test is listed for intensity-modulated radiation therapy (IMRT) vs. double arc RapidArc (RA).

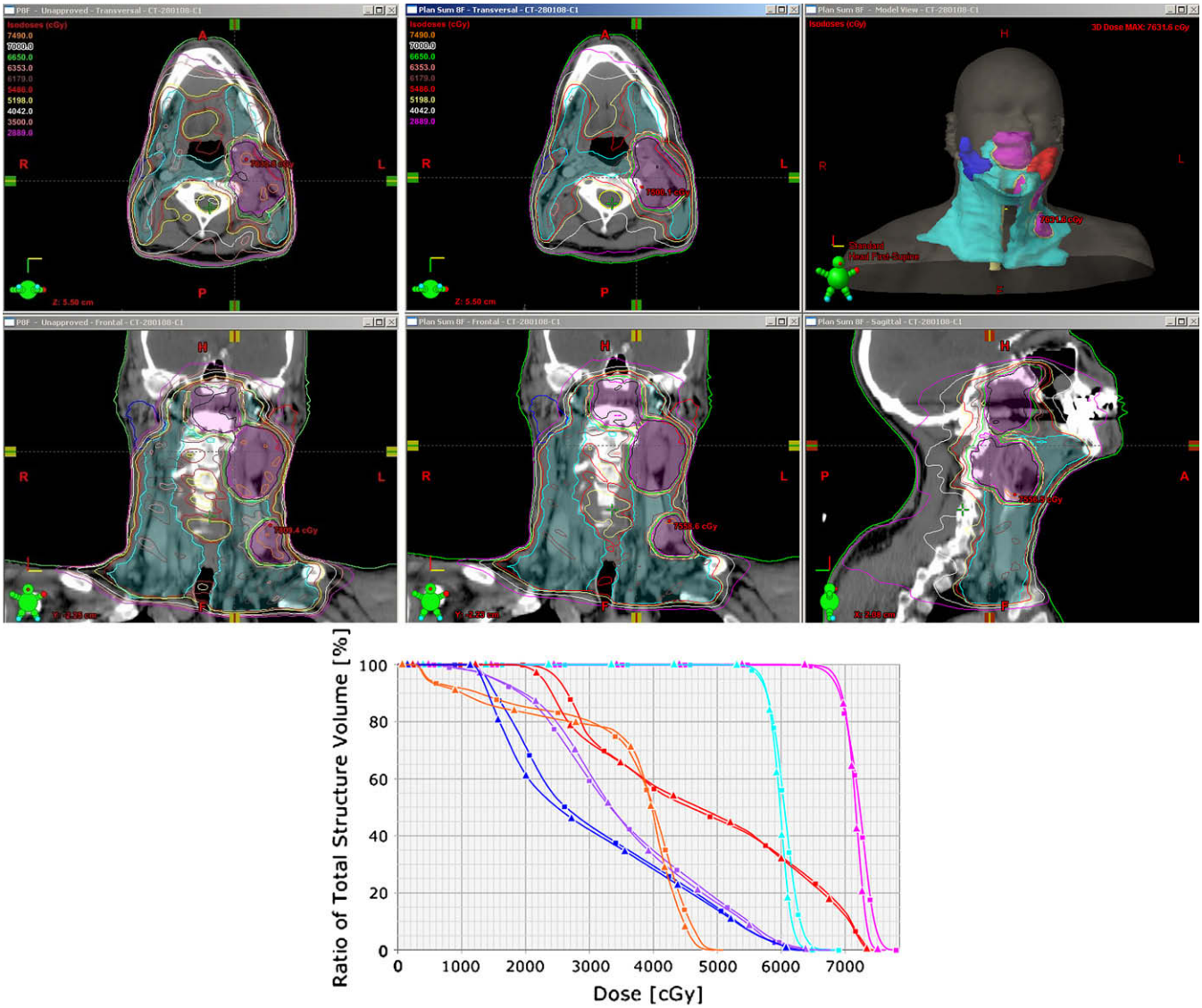


Fig. 1. Comparison of dose distributions and dose-volume histograms (DVHs) for a typical patient for a single arc (left) vs. double arcs (middle and right). Isodose lines show fewer hot spots in the planning target volume (PTV) for double arc plans, and the DVHs of double arc plans (triangles) show the steepest PTV DVH and lowest organs at risk (OAR) DVH compared with single arc plans (squares). The PTVs are in magenta and light blue, the parotid glands in red and blue, spinal cord in orange, and oral cavity in purple.

For 4 patients, plans were optimized with preclinical version 8.2.16 of RA, and for the other 8 patients with the clinical version 8.2.22. After optimization, the dose was calculated with Eclipse using the AAA algorithm, with a calculation grid of 2.5 mm. Both RA and Eclipse versions have incorporated the tongue-and-groove effect (17) in their dose calculation. The RA plan consists of a single counterclockwise full arc from gantry angles 179° to 181°. The collimator angle was chosen between 35° and 45°, allowing us to cover large PTVs up to almost 30 cm in length.

The same dose objectives as in the IMRT plan were used for PTVs, spinal cord, brainstem, and parotid glands. However, a ring structure measuring 1 cm wide and starting 5 mm outside the PTV, enforcing rapid dose falloff, was used for optimization instead of all other OAR used in IMRT. Furthermore, the ''normal tissue objective'' feature of RA was used to prevent the optimizer creating hot spots in non delineated parts of the body.

Because optimization results with an early version of RA software showed somewhat greater dose inhomogeneity within the PTV for single arc RA plans, compared with IMRT, we also evaluated RA plans consisting of two arcs. As the RA version used did not allow for simultaneous optimization of 2 RA arcs, arc optimization was performed sequentially, with the first single-arc RA plan scaled down to 1 Gy per fraction and defined as a base dose plan. The second arc, which rotated clockwise, was optimized to a full 2 Gy per fraction while making use of this base dose plan. The final plan consists of the sum of the two RA plans, each normalized to 1 Gy per fraction, with the first arc delivered during counterclockwise rotation and the second during the clockwise rotation back to gantry angle 179°. For the second arc, the collimator was rotated 5° extra to reduce overlapping tongue and groove effects with the first arc. To determine how the PTV dose homogeneity is influenced by the objectives for the OAR, additional single arc RA plans were made without any OAR objectives for 2 of the patients.

For all the plans, the mean dose, $V_{<95}$ and $V_{>107}$ was scored for each PTV. Another measure for the dose homogeneity was the standard deviation (SD) of the PTV dose, SD(boost or elective). For

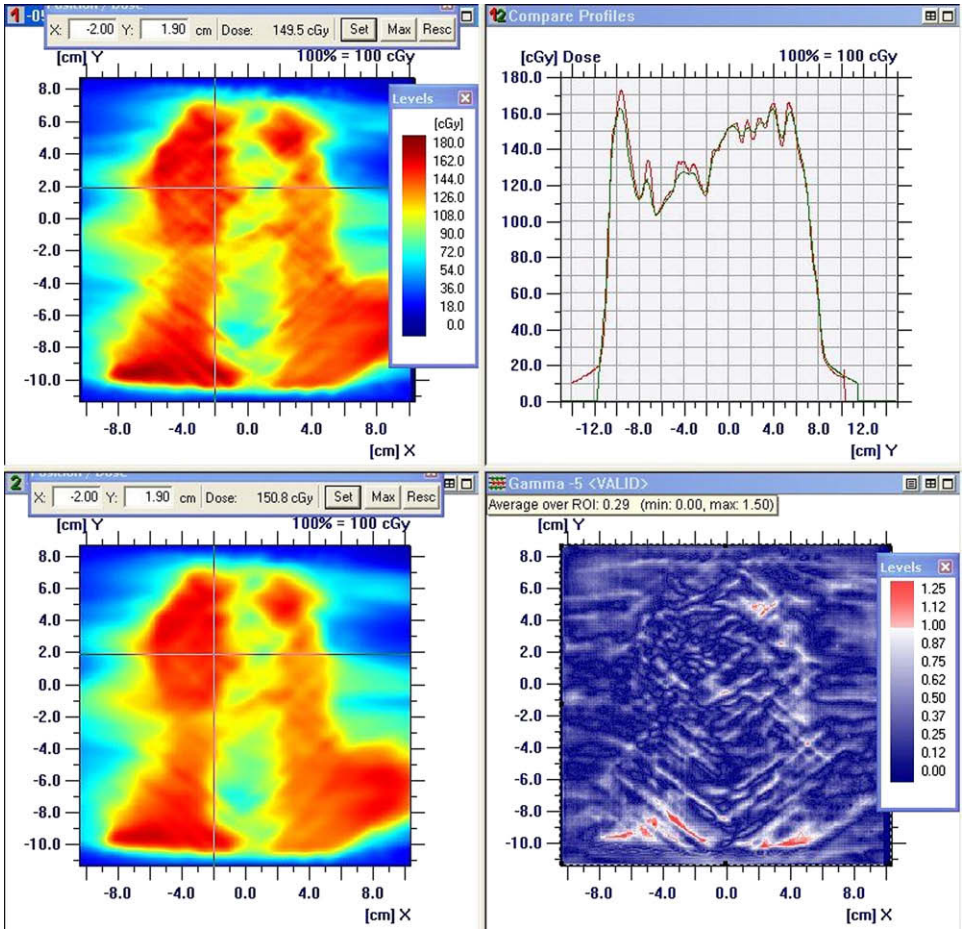


Fig. 2. Left upper: film measurement for a single arc RapidArc (RA) plan for a nasopharyngeal tumor, compared with calculation (left lower). Right upper is the dose profile comparison between the two (red line is measurement, green is calculation) along the y axis. For the gamma-evaluation, right lower, limits were 2 mm, 6 cGy.

a PTV with a very homogeneous dose, the DVH falloff is very steep and the SD very small. The conformity of the dose to the PTV is expressed by the conformity index (CI) being the volume of the body receiving more than 95% of the prescribed dose, divided by the volume of the PTV. Consequently, CI will be larger than one, and will increase with decreasing plan conformity. For the OAR, the mean dose ($D_{mean}$) to the parotid glands was scored, the maximum dose to the spinal cord and brain stem, and the mean dose to the oral cavity and the laryngeal area. The results of IMRT and double arc RA plans were compared with the two-sided Wilcoxon matched-pair signed-rank test. The threshold for statistical significance was $p \leq 0.05$.

### *Dose measurements*

A dosimetric validation was performed for all single arc ($n = 8$) and double arc ($n = 4$) plans. For this purpose, the dose distribution of each plan was recalculated on our standard verification phantom, a 23-cm cube of polystyrene slabs. This in-house phantom has multiple drawers for the simultaneous insertion of Gafchromic EBT films at different plane positions, thereby allowing dose verification in multiple coronal, sagittal, or transversal planes during a single treatment session. For verification of RA plans, the dose was measured in three to five coronal planes, at least 15 mm apart. The method used for dosimetry using Gafchromic EBT film has been described in detail previously (18). Because the dosimetric uncertainty of single Gafchromic EBT film measurements is about 1.8% (1 standard deviation), the use of double films was chosen to increase the accuracy for each measurement plane to 1.3% (1 standard deviation). For each measurement session, an independent dose calibration of the EBT films was performed. The plans were delivered on a Varian Trilogy linear accelerator. At least 12 hours after irradiation, the films were scanned on an Epson flatbed scanner with a resolution of 0.3 mm. The corresponding calculated dose distributions were exported from Eclipse with a resolution of 0.59 mm, using linear interpolation. Comparison of measured versus calculated dose distribution was done in OmniPro I'mRT software (IBA Dosimetry, Germany). To quantify the differences between measurements and calculations, gamma evaluations were calculated (19) with spatial and dosimetric limits of, respectively, 2 mm and 3% (of the dose in the boost volume).

## RESULTS

### *Dose calculations*

Clinically acceptable single arc RA and double arc RA plans were achieved in all 12 cases. Although the exact times for optimization and planning were not registered for each patient, RA optimizations were clearly faster than the average IMRT optimization as each RA plan required only a single optimization session and the same number of optimization steps, independent of the amount of interactive change of the optimization objectives. A typical single RA

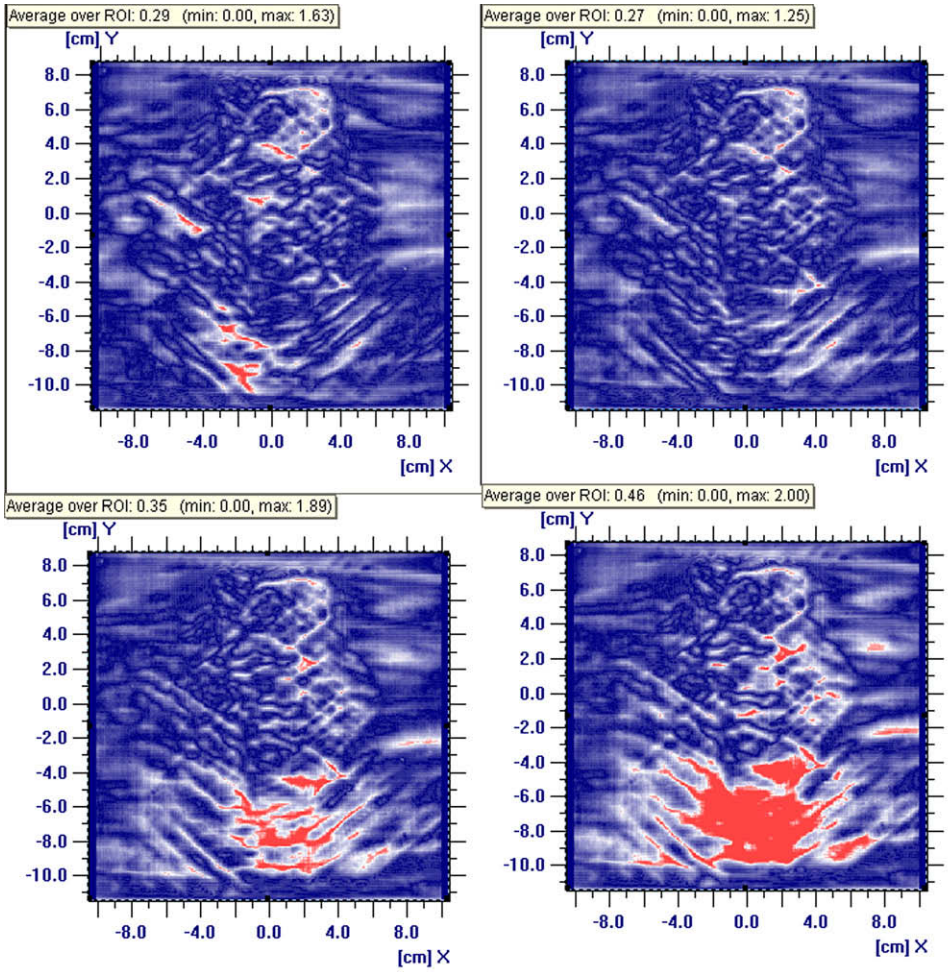


Fig. 3. Gamma evaluation of measured plane at 20 mm, compared with calculations at 18, 19, 20, and 21 mm, respectively. Best agreement is achieved for comparison with the calculated plane at 19 mm.

head-and-neck optimization required 20 min, followed by a 20 min of AAA forward dose calculation.

Table 2 summarizes the results of PTV coverage and OAR doses averaged for the 12 cases. The average number of monitor units was reduced by 59% for the RA plans, and a two-arc plan required only 5% more monitor units than a single-arc plan. Sparing of OAR was not significantly different between IMRT and RA, though the dose to the parotid glands was on average 2 Gy lower with double arc RA plans compared with single arc RA and IMRT (Table 2). The dose homogeneity to PTVboost was largely improved by the double arc RA technique compared with the single RA plan as appears from the standard deviations of the PTVboost dose, and from the $V_{<95}$ and $V_{>107}$ though these last two do not show the same significance. The improved PTV homogeneity for a double arc vs. a single arc appears also from Fig. 1 that shows the comparison of dose distributions and DVHs for a specific patient for a single arc vs. double arcs.

For 2 patients, a single arc RA optimization was performed without any OAR objectives. Although the resulting PTV dose homogeneity improved in comparison to the optimization where OAR objectives were used, it was still not possible to achieve the dose homogeneity seen for double arc or IMRT.

*Dosimetric verification*

*Single arc RA plans.* Film measurements of 12 single arc RA plans in 8 patients, which consisted of a total of 47 coronal planes, showed high agreement with calculated values, with a mean gamma of 0.34 and on average 2.14% (maximum 6.1%) of the film surface exceeding a gamma of 1.0. Film measurements, as in the example in Fig. 2, exhibited relatively strong spatial dose modulations, which were not completely predicted by the calculations.

Compared with standard IMRT, calculated RA plans show a greater spatial dose modulation within the PTV. The strong modulation of dose in a RA plan can lead to dose differences larger than 3% when changing a plane by 2 mm in the direction perpendicular to this plane. This can easily lead to a gamma value > 1. In some cases, a comparison of film measurements with calculations in planes at 1 mm distance (Fig. 3) result in a much better gamma value statistics. This indicates that a ''2.5D'' gamma evaluation based on comparison of a two-dimensional measurement with multiple two-dimensional dose distributions would give better agreement, whereas a full 3D gamma evaluation of the two-dimensional measurements with a 3D dose distribution would be preferred.

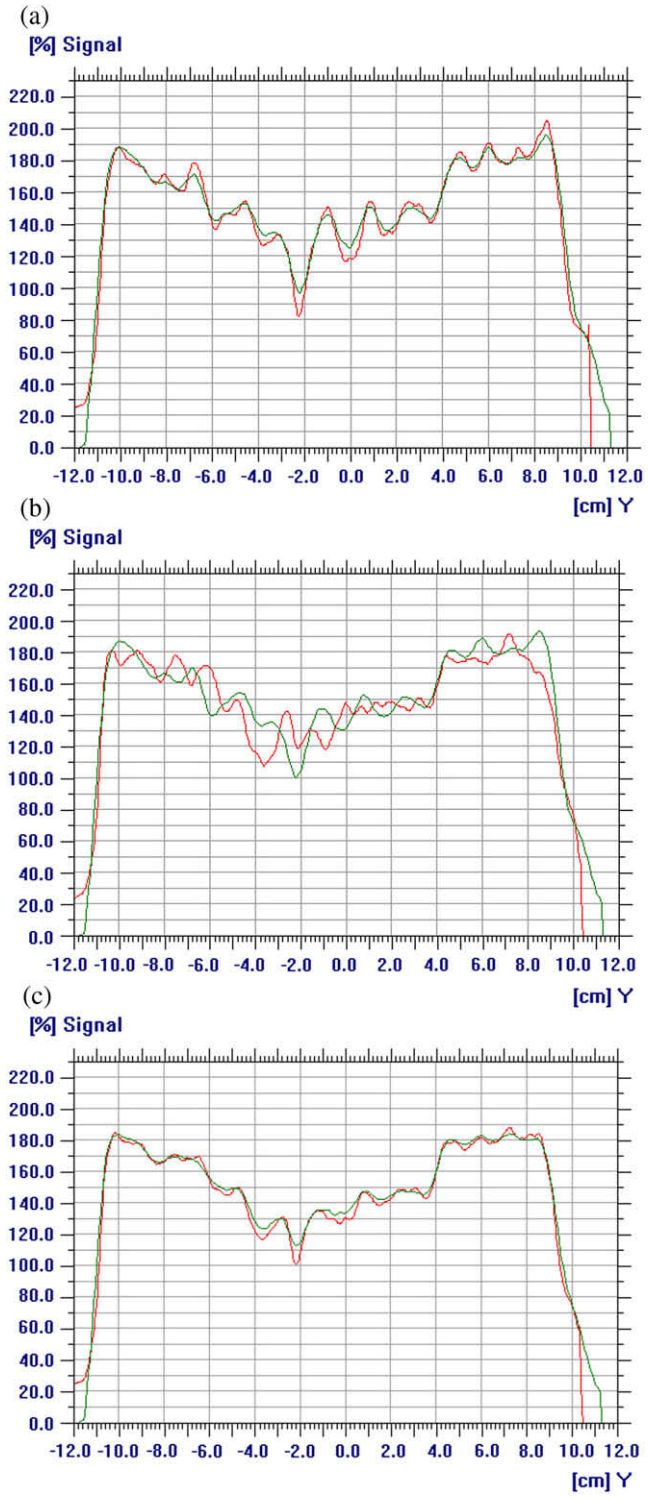


Fig. 4. Dose profile along a longitudinal line for a nasopharynx case. (a) Single RapidArc (RA), film measurement (red) vs. calculated dose (green). (b) Measurement of second RA (red) vs. calculation of first RA (green). (c) Sum of 2 RA, measurement (red) vs. calculation (green).

*Double-arc RA plans*. For 4 patients, 14 film measurements of double arc RA plans were analyzed. The mean gamma was reduced to 0.30 and the area of the film with a gamma exceeding 1 was only 0.82%, with the comparable values for single arc plans being 0.34 and 2.14%, respectively. Figure 4 shows a typical dose profile comparison for a single arc and double arc plan. In the measurements, spatial dose modulations were more pronounced than in the calculations. In the double arc RA plans, the dose distribution of the second arc compensates the dose modulation of the first arc (Fig. 4b). Consequently, PTV dose homogeneity improves with the summed dose distribution of the double arc plan and measurements of the resulting sum plan (Fig. 4c) agree much better with the calculations.

The agreement between film measurements and calculations were compared between IMRT plans, single arc RA, and double arc RA plans for 2 patients. In Fig. 5, an example of this comparison is shown for one plane. Averaged over these 2 patients, four planes per patient, the average gamma-values for IMRT, single RA, and double RA, were 0.37, 0.35, and 0.29, respectively. The film surface with a gamma larger than 1 was 3.6%, 2.5%, and 0.9%, respectively.

## DISCUSSION

A recent planning study has shown that a precursor of RA software could achieve conformal dose distributions for a prostate tumor (20). The current planning and dosimetric studies reveal that RA is an excellent technique to treat head-and-neck cancer as well, where PTVs are much larger and more irregular in shape than in prostate cancer. Treatment is delivered rapidly, with a single arc delivery of 2 Gy requiring less than 80 s, and double arc plans in less than 3 min. This contrasts with a typical IMRT sliding window delivery for seven fields that requires 8–12 min. Speed of delivery is a major advantage of RA as it reduces the risk of intrafraction movements. In addition, the shorter time needed for delivery is more patient-friendly and will enable the treatment of more patients per machine.

RA plans spared the studied OAR at least as well as IMRT, and for these complex locally advanced head-and-neck tumors, only the plan CI for PTVboost was statistically significantly different from IMRT. This may be the price to pay for a more homogeneous PTV dose. For the PTVelective, no difference in conformity index was observed. It should be noted that fewer objectives for OAR were used for the RA optimizations in comparison to IMRT. No objectives were used for oral cavity, larynx region, upper back of the neck, lower back of the neck, brain, or lungs; these were all replaced by a simple ring structure around the PTV and the normal tissue objective in the optimizer. Another key advantage of RA is the efficient use of monitor units (MU), because RA needed only 40% of the number of MU compared with seven field sliding window IMRT plans. Dose to healthy organs not in the proximity of the PTV arises largely from collimator transmission and scatter radiation from the linac, and this dose is proportional to the number of MU. Such scattered doses can increase the risk of for secondary tumors (21). These chances are now largely reduced by the use of RA without concessions to the dose distributions.

A recent report highlighted the fact that wide interinstitutional variability in PTV dose homogeneity exists for

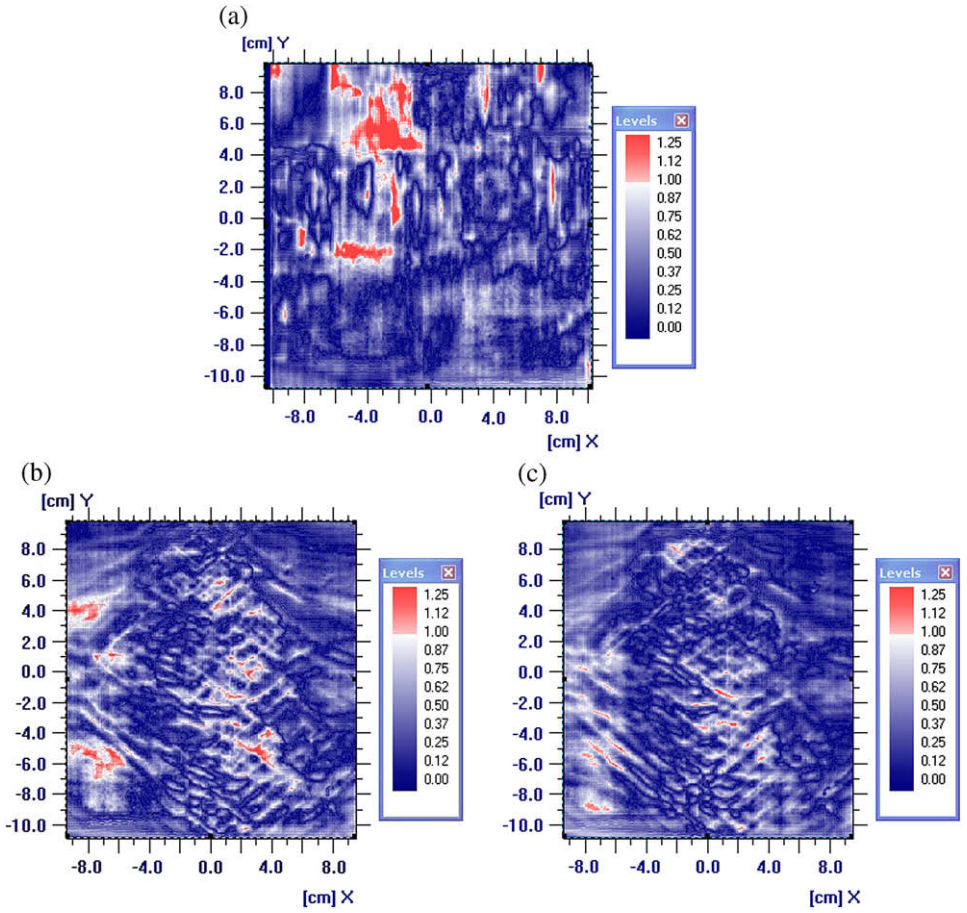


Fig. 5. Gamma evaluation of coronal planes of a nasopharynx case. (a) Intensity-modulated radiation therapy, (b) single arc RA, (c) double arc RA.

IMRT plans (11), and a PTV dose homogeneity which is often much worse than for 3D conformal irradiation techniques. It is recognized that tumor control probability can be substantially reduced by an inhomogeneous dose in the PTV (22). With the current version of RA, all plans with a single RA arc show a larger dose inhomogeneity in the PTV than the IMRT plans but plans based on two arcs resulted in excellent PTV homogeneity which surpassed that achieved using IMRT. The sum of two arc reduces hot spots in the PTV when the first RA plan is used as a base dose plan, after which the second arc compensates for areas of suboptimal dose. The resulting sum of both plans shows dose modulation amplitudes that are approximately half as large as those seen in plans with a single arc. A second possible explanation for the advantage of using two arcs is a physical limit to the dose homogeneity for a single arc arising from limited leaf speed and the limited number of control points. With use of a single arc, the leaves can move with a maximum speed of 0.5 cm per degree of gantry rotation, whereas optimal coverage of the PTV at specific gantry positions could require dose delivery at two or more separated parts of the PTV along one leaf pair. Because the head-and-neck plans studies contained large PTVs, the span of the entire PTV over a leaf pair can easily be 15 cm. If a part of the PTV has to be blocked at one gantry position, it can take 20° of gantry rotation or more before the leaf has traveled to the other side of the PTV. Testing of single arc RA optimization without OAR objectives confirms that, with only PTV objectives in the plan, the dose homogeneity in the PTV is still worse than for a plan consisting of a double arc where all OAR objectives are taken into account. A second arc adds more degrees of freedom for possible leaf positions and can thus be a solution for this problem. If this explanation plays a key role, our approach using a base dose plan is not the most optimal approach, and an optimization where both arcs are simultaneously taken into account could be better. Preliminary tests using a newer version of RA (8.6.10), which allows simultaneous optimization of multiple arcs, has shown that this approach further improves PTV dose homogeneity, while allowing slightly further sparing of the OAR (unpublished data).

The use of a new technology for planning and delivery of highly conformal dose distributions requires not only planning studies, but also independent dosimetric verification to ensure that the calculated dose distributions can be delivered as planned (12). For IMRT, an independent monitor unit verification by a different program or by means of dose measurements in a phantom is considered as clinical standard. Our measurements provide the first report of a dosimetric validation of RA plans. Treatment plans with a double RA arc showed a better agreement between measurements and

calculations. For the single arc plans, the deviations between measurements and calculations occur mostly at local ''peaks'' and ''valleys'' of the dose distributions as appears from Fig. 4a. The second arc optimization plans these ''peaks'' mostly at the ''valleys'' of the first arc (Fig. 4b), so that deviations between measurements and calculations are compensated this way.

GafChromic EBT films were scanned with a resolution of 0.3 mm, providing excellent spatial resolution of the dose measurements. It should be noted that for the gamma evaluation, a dose limit of 3% of the PTVboost dose was used. This limit includes also the inaccuracy of the film dosimetry and is thus a tight limit for dosimetric evaluation. A standard deviation of 1.3% for the measured dose means that on average 5% of the film surface can exhibit a deviation larger than 2.6%, leaving only a small margin for possible uncertainties of the plan itself. An alternative for film dosimetry would be to measure the dose with an ionization chamber array. This would provide a more accurate, stable, and fast way of dosimetry, but it would lack the spatial accuracy because of the limited number of detectors and the finite size of the ionization chambers (23). Work to evaluate protocols for RA verification using a variety of approaches is currently in progress (24).

## CONCLUSIONS

Film dosimetry has shown that RA accurately delivers the calculated dose distribution. Single arc RA plans give dose distributions that are similar to that achieved for a seven-field sliding window IMRT, with the exception of a reduced dose homogeneity in PTV. Double arc RA plans provide a better PTV homogeneity than IMRT and achieve similar OAR sparing as is seen with IMRT. Because the delivery of RA is fast and allows for large reductions in MU, we have now replaced IMRT with RapidArc for all indications at our department.

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