Can Intensity-Modulated Radiation Therapy of the Paraaortic Region Overcome the Problems of Critical Organ Tolerance?

Johanne Hermesse, Magali Devillers, Jean-Marie Deneufbourg, Philippe Nickers[1]

Background and Purpose: The recent RTOG guidelines for future clinical developments in gynecologic malignancies included the investigation of dose escalation in the paraaortic (PO) region which is, however, very difficult to target due to the presence of critical organs such as kidneys, liver, spinal cord, and digestive structures. The aim of this study was to investigate intensity-modulated radiotherapy's (IMRT) possibilites of either increasing, in a safe way, the dose to 50–60 Gy in case of macroscopic disease or decreasing the dose to organs at risk (OR) when treatment is given in an adjuvant setting.
Material and Methods: The dosimetric charts of 14 patients irradiated to the PO region at the Department of Radiation Oncology, University Hospital of Liège, Belgium, in 2000 were analyzed in order to compare six-field conformal external-beam radiotherapy (CEBR) and five-beam IMRT approaches. Both CEBR and IMRT investigations were planned to theoretically deliver 60 Gy to the PO region in the safest way possible. Dose-volume histograms (DVHs) were calculated for clinical target volume (CTV), planning target volume (PTV), and OR. Student's t-test was used to compare the paired DVH data issued from CEBR and IMRT planning.
Results: The IMRT approach allowed to cover the PTV at a higher level as compared to CEBR. Using IMRT, the maximal dose to the spinal cord was reduced from 42.5 Gy to 26.2 Gy in comparison with CEBR ($p < 0.00001$). Doses to the kidneys were significantly reduced, with < 20% receiving ≥ 20 Gy in the IMRT approach ($p < 0.00001$). Irradiation of digestive structures was not different, with < 25% receiving 35 Gy. Doses to the liver remained low regardless of the method used.
Conclusion: At 60 Gy, IMRT is largely sparing the spinal cord and kidneys as compared to CEBR and represents an interesting approach not only for dose escalation up to 50–60 Gy (probably facilitating the radiochemotherapy approaches) but also in an adjuvant setting at lower doses. The dosimetric data of this study are in the same range as those published recently with a dynamic arc conformal approach.

Key Words: Paraaortic · Intensity-modulated · Radiotherapy

Strahlenther Onkol 2005;181:185–90
DOI 10.1007/s00066-005-1324-8

Kann intensitätsmodulierte Radiotherapie der paraaortalen Region Probleme der Strahlentoleranz gefährdeter Organe überwinden?

Hintergrund und Ziel: Die Erstellung der aktuellen RTOG-Leitlinien für klinische Entwicklungen in der gynäkologischen Onkologie erforderten auch Untersuchungen zur Strahlendosiseskalation in der paraaortalen (PO-) Region, die wegen der Nähe gefährdeter Organe wie Niere, Leber, Rückenmark und Gastrointestinaltrakt ein sehr problematisches Zielgebiet ist. Zweck dieser Studie war zu untersuchen, welche Möglichkeiten die intensitätsmodulierte Radiotherapie (IMRT) bietet, entweder auf sichere Weise die Strahlendosis auf 50–60 Gy im Fall ausgedehnter Malignome zu steigern oder die Strahlendosis gefährdeter „Risikoorgane" in der adjuvanten Situation zu vermindern.
Material und Methoden: Die Dosimetriekarten von 14 Patientinnen, bei denen im Jahr 2000 in der Abteilung für Radioonkologie am Universitätsklinikum Liège, Belgien, eine Radiotherapie der PO-Region durchgeführt worden war, wurden analysiert, um die konformale Sechs-Felder-Radiotherapie (KRT) mit Fünf-Felder-IMRT-Konzepten zu vergleichen. Für sowohl KRT als auch IMRT wurden Untersuchungen geplant, in denen in der PO-Region theoretisch 60 Gy auf sicherste Weise appliziert werden sollten. Dosis-Volumen-Histogramme (DVH) wurden berechnet für das klinische Zielvolumen (CTV), das Planungszielvolumen (PTV) und für die gefährdeten Organe. Mit dem Student-t-Test wurden gepaarte DVH-Daten der KRT- und IMRT-Planungen verglichen.
Ergebnisse: Das IMRT-Konzept erlaubte, im PTV eine im Vergleich zur KRT höhere Strahlendosis anzuwenden. Mittels IMRT wurde die maximale Rückenmarkdosis von 42,5 Gy zu 26,2 Gy im Vergleich zur KRT vermindert ($p < 0{,}00001$). Die Nierendosis wurde signifikant vermindert, indem im IMRT-Konzept < 20% des Organs ≥ 20 Gy erhielten ($p < 0{,}00001$). Die Strahlendosis im Gastrointestinaltrakt ergab mit 35 Gy in < 25% keine Unterschiede. Die Leberdosis blieb – unabhängig von der angewendeten Methode – niedrig.

[1] Department of Radiation Oncology, University Hospital of Liège, Belgium.

Received: May 25, 2004; accepted: November 30, 2004

Schlussfolgerung: Bei einer Dosis von 60 Gy schont die IMRT Rückenmark und Nieren im Vergleich zur KRT weitgehend und bietet ein interessantes Konzept nicht nur für die Dosiseskalation bis zu 50–60 Gy (was Radiochemotherapie-Planungen entgegenkommen dürfte), sondern auch für die niedriger dosierte adjuvante Strahlentherapie. Die Dosimetriewerte dieser Studie liegen in der gleichen Größenordnung wie die vor kurzem veröffentlichten Ergebnisse eines Konzeptes mit dynamischer Rotationsbestrahlung.

Schlüsselwörter: Paraaortal • Intensitätsmoduliert • Radiotherapie

Introduction

In 1988, the EORTC Radiotherapy Group investigated the place of prophylactic paraaortic (PO) lymph node irradiation in the treatment of patients with locally advanced cervical cancer [7]. The study randomized 441 patients in two treatment arms: pelvic irradiation alone or extended to PO nodes. No statistically significant difference was found between the two arms in terms of local control and overall survival. However, the incidence of secondary PO lymph nodes and distant metastases without primary recurrence was 2.8 times higher in patients irradiated to the pelvis only ($p < 0.01$).

The randomized RTOG 79-20 study included 367 IB or IIA cervical cancers, ≥ 4 cm in diameter, and stages IIB subjected to radiotherapy [12]. A prophylactic irradiation of the PO lymph nodes significantly improved 10-year overall survival from 44% to 55% ($p = 0.02$) in comparison with pelvic irradiation only. A lower incidence of distant failure in complete responders was observed at 5 years for the extended-field irradiation (12% vs. 21% for pelvic irradiation only; $p = 0.053$). Survival following first failure was significantly higher in the extended-field arm ($p = 0.007$).

On the other hand, the recently updated RTOG 90-01 study demonstrated, on 403 patients with locally advanced cervical cancers, that adjuvant combined pelvic radiotherapy and cisplatin-based chemotherapy significantly improved the 5-year survival rates to 72% as compared to 52% for extended-field radiotherapy to the PO region ($p < 0.0001$) [4]. Remained any place for PO irradiation in an adjuvant approach?

The RTOG 92-10 study tried to add chemotherapy to extended-field radiotherapy for cervical cancer with biopsy-proven positive PO nodes but was stopped prematurely for 24% of late grade 3 and 4 toxicity [6]. The GOG Protocol 8906, however, investigated extended-field radiation therapy with concomitant 5-fluorouracil and cisplatin for cervical carcinoma metastatic to the PO nodes. The results did not include any late toxicity to the small bowel ≥ grade 3 [14].

For all these data, only 40–48 Gy were delivered to the whole PO region, mostly through anteroposterior-posteroanterior (AP-PA) fields. An alarmingly high toxicity could be observed particularly when concomitant chemotherapy was used. However, some pilot studies recently suggested that metastatic PO lymph nodes are better controlled when doses up to 45–60 Gy are delivered with optional concomitant chemotherapy. Disease-free survival (DFS) of at least 20% at 5 years has been reported without any prohibitive late toxicity resulting from small or large bowel side effects [1, 13, 14]. One of these studies investigated, on 29 patients, the role of dynamic arc conformal radiotherapy to increase the total dose up to 55–60 Gy with no late grade 3 side effect [1].

So techniques delivering higher doses to the PO region while sparing normal structures might be beneficial to the patients in selected situations. These developments were indeed recently encouraged by the RTOG [5]. Intensity-modulated radiotherapy (IMRT), as a very selective radiation treatment, seems to be a promising alternative to achieve this objective. Until now, no study reported, in detail, the dose volume histograms (DVHs) for the clinical target volume (CTV), planning target volume (PTV), and organs at risk (OR), neither for an IMRT approach nor with an inverse planning philosophy [1, 11]. From CT scan data of patients irradiated to the PO region, this study is investigating IMRT's possibilities of increasing the dose to 60 Gy in comparison with conformal external-beam radiotherapy (CEBR). The objective is to establish the safety levels of such approaches combined or not combined with chemotherapy.

Material and Methods

In 2000, 14 patients received adjuvant radiotherapy to the PO nodes at our department. After simulation they underwent a CT scan in supine position, covering the area (slices 1 cm apart) from the tenth thoracic vertebra (T10) to the lower border of the bony pelvis. These data were transferred in two different planning systems: ISIS® for CEBR analysis and the inverse planning CORVUS® for IMRT dosimetry. The PO region was delineated from the junction of T11–12 to the lower border of L5. Digestive structures including small and large bowel were regarded as a whole. Spinal cord and root were only contoured at the level of the CTV. Liver, left and right kidneys were delineated entirely and separately. For both treatment plans a theoretical dose was fixed to 60 Gy in 30 fractions.

For IMRT, a five-field technique (0°, 60°, 150°, 210°, 300°) with 6-MV photons was selected. Table 1 shows the constraints introduced in the inverse planning which intended to cover the PTV with the 95% isodose – an objective achieved with the CEBR technique. Spinal cord is a tissue with a "high relative seriality" implying that a dose above the tolerance limit, even to a small volume, can totally impair the function of the organ (myelitis). So it was considered as an OR for which preservation of the whole structure is primordial even at the expense of underdosing the target. By contrast, the liver has a "high relative parallelity", implying that the main parameter for impairing hepatic function is the proportion of the organ that receives a dose above the tolerance level. So it was regarded as a whole-unit structure due to a uniform biological function throughout the organ, which can tolerate hot spots focally without significantly impairing the whole function. The other organs are a combination of parallel and serial structures. So they were fixed as basic structures for which there are no special constraints except the normal values presented in Table 1. According to ICRU Report 62 [9], different factors were taken into account for delineating the PTV. At first, the internal margin, that is defined so as to take variations in size, shape, and position of the CTV in relation to the anatomic reference point into account, was considered nonexistent. The setup margins that are added to take uncertainties in patient-beam positioning into account were fixed to 3 mm for AP, 3 mm for left-right, and 5 mm for craniocaudal directions. All these different requirements determine the different weights of constraints the treatment planning had to take into account. Once the IMRT treatment planning had been completed, the constraints on the left kidney had to be modified to allow the 95% isodose covering the PTV better. The maximum tolerated dose to the left kidney indeed had to be increased to 40 Gy to avoid cold spots in the PTV at this level.

For CEBR planning, the PTV was obtained with an expansion of 3 mm of the CTV contours to conform to PTV volumes obtained from the IMRT inverse planning. The radiotherapy technique involved a 23-MV photon beam energy and six fields (30°, 90°, 150°, 210°, 270°, 330°). 30° wedges were placed on the posterior fields (150° and 210°) to spare the spinal cord. According to the ICRU 50 and 62 recommendations, the 95% isodose of the prescribed dose had to circumvent the PTV [8, 9].

Table 1. Constraints introduced in the inverse treatment planning. CTV: clinical target volume.

Tabelle 1. In der inversen Strahlungsplanung festgelegte Grenzwerte. CTV: klinisches Zielvolumen.

	Limit dose (Gy)	Volume below (%)	Minimal dose (Gy)	Maximal dose (Gy)
CTV	60	5	57	66
Spinal cord	30	50	15	42
Liver	20	15	5	60
Left kidney	20	20	15	40
Right kidney	20	20	15	35
Digestive structures	40	10	5	60

Finally, we analyzed the CEBR and IMRT DVH data for the CTV, PTV, and OR.

Student's t-test was used to compare the paired DVH data issued from both irradiation modalities.

Results

The CTV and PTV volumes for both CEBR and IMRT techniques were identical and no significant difference was detected.

Figures 1a to 1c show the CTV and PTV of an IMRT planning in sagittal, axial, and coronal planes. In these slices the 100% isodose is surrounding the CTV and PTV.

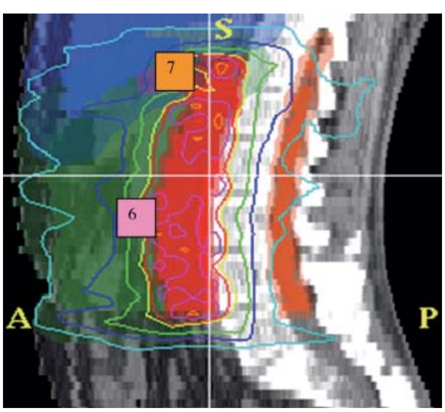


Figure 1a – Abbildung 1a

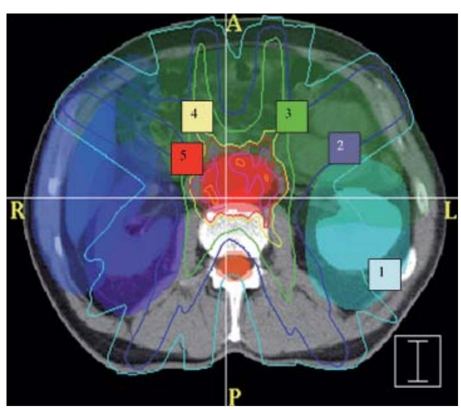


Figure 1b – Abbildung 1b

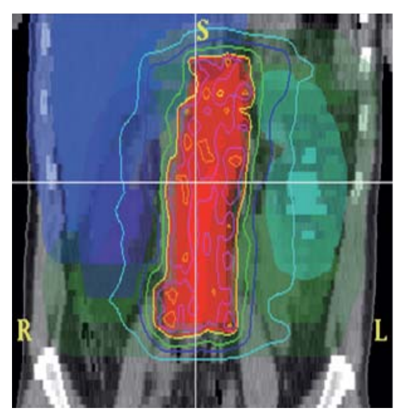


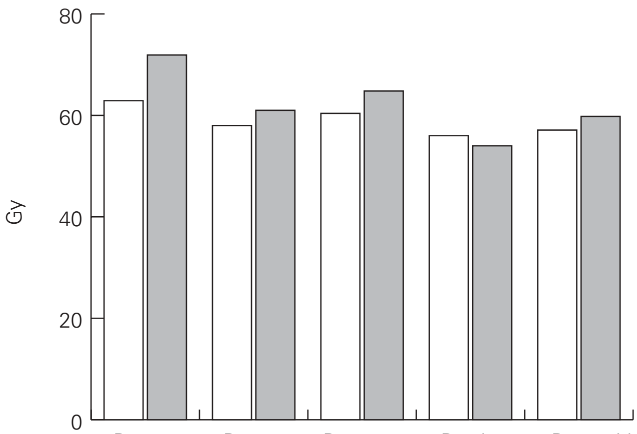
Figure 1c – Abbildung 1c

Figures 1a to 1c. Different views of the CTV and PTV. For 60 Gy prescribed, the 95% isodose is surrounding the PTV except the cranial level where small cold spots are visualized. Some hot spots of 68 Gy are observed only inside the PTV. The isodose 20 Gy is sparing the kidneys and spinal cord, respectively. The volume of digestive structures receiving > 40 Gy is small. 1: isodose 10 Gy; 2: isodose 20 Gy; 3: isodose 40 Gy; 4: isodose 57 Gy, 95% of the prescribed dose; 5: isodose 60 Gy; 6: isodose 64.2 Gy, 107% of the prescribed dose; 7: isodose 68 Gy; small hot spot inside the PTV which is the shadow of the CTV. a) Sagittal view. b) Axial view. c) Coronal view.

Abbildungen 1a bis 1c. CTV und PTV in verschiedenen Ebenen. Bei Anwendung von 60 Gy umfasst die 95%-Isodose das PTV mit Ausnahme der kranialen Abschnitte, wo kleine „cold spots" zu sehen sind. Einige „hot spots" mit 68 Gy sind nur innerhalb des PTV festzustellen. Die 20-Gy-Isodose schont Nieren und Rückenmark. Das Volumen des Gastrointestinaltrakts, auf das > 40 Gy treffen, ist klein. 1: 10-Gy-Isodose; 2: 20-Gy-Isodose; 3: 40-Gy-Isodose; 4: 57-Gy-Isodose, 95% der vorgesehenen Dosis; 5: 60-Gy-Isodose; 6: 64,2-Gy-Isodose, 107% der vorgesehenen Dosis; 7: 68-Gy-Isodose; kleiner „hot spot" innerhalb des PTV, der den Schatten des CTV bildet. a) Sagittal. b) Axial. c) Coronal.

Figure 2 illustrates the doses delivered to the CTV with both techniques. 95% of the CTV is receiving 61 ± 0.8 Gy with IMRT as compared to 58 ± 1.4 Gy with CEBR ($p = 0.003$). The mean dose to the CTV is 64.8 ± 2.8 Gy with IMRT in comparison to 60.4 ± 1.9 Gy with CEBR ($p < 0.0001$). The dose distribution inside the CTV is, however, more heterogeneous with IMRT. Mean cold spots of 54 ± 4.2 Gy are indeed observed inside the CTV as compared to 56 ± 3.8 Gy for CEBR ($p < 0.00001$). The volume of CTV receiving less than the prescribed dose 60 Gy is only 1.4% ± 0.5% with IMRT versus 6.5% ± 3.2% with CEBR ($p < 0.00001$).

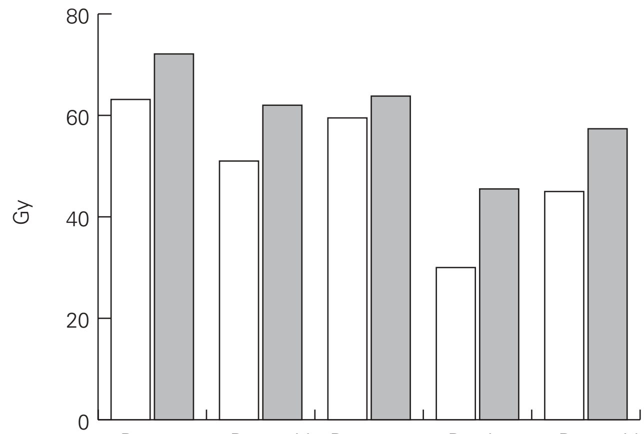
Figure 3 represents the doses received by the PTV with both methods. 95% of the PTV is receiving 62 ± 1.8 Gy with IMRT as compared to 51 ± 2.6 Gy with CEBR ($p < 0.00001$). The mean dose to the PTV is 63.8 ± 1.4 Gy with IMRT in comparison with 59.5 ± 1.1 Gy for CEBR ($p < 0.00001$). Unlike the



	D max	D 95%	D mean	D min	D 99%V
CEBR	62.9	58	60.4	56	57.1
IMRT	71.9	61	64.8	54	59.8

Figure 2. Doses delivered to the CTV with both techniques. p < 0.05 for all comparisons.

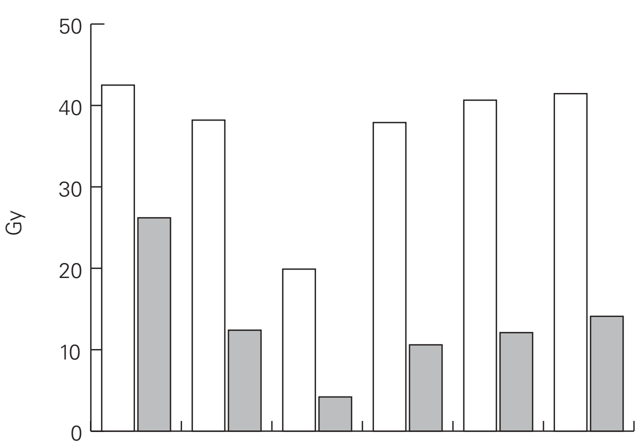
Abbildung 2. Strahlendosen, die bei beiden Techniken das CTV erreichen. p < 0,05 für alle Wertepaare.



	D max	D 95%V	D mean	D min	D 99%V
CEBR	63.14	51	59.5	30	44.99
IMRT	72.11	62	63.8	45.5	57.36

Figure 3. Doses delivered to the PTV with both techniques. p < 0.05 for all comparisons.

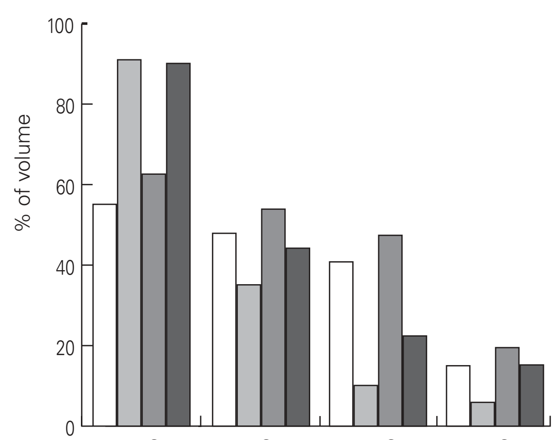
Abbildung 3. Strahlendosen, die bei beiden Techniken das PTV erreichen. p < 0,05 für alle Wertepaare.



	D max	D mean	D min	D 75%V	D 50%V	D25%V
CEBR	42.5	38.2	19.9	37.9	40.65	41.45
IMRT	26.2	12.4	4.2	10.6	12.1	14.1

Figure 4. Doses delivered to the spinal cord. p < 0.00001 for all comparisons.

Abbildung 4. Strahlendosen, die auf das Rückenmark treffen. p < 0,00001 für alle Wertepaare.



	10 Gy	15 Gy	20 Gy	24 Gy
R kidney CEBR	55.1	47.9	40.8	15
R kidney IMRT	91	35.1	10.1	5.9
L kidney CEBR	62.6	53.9	47.4	19.5
L kidney IMRT	90.1	44.2	22.4	15.2

Figure 5. Volume of each kidney receiving 10, 15, 20, and 24 Gy. p < 0.00001 for all comparisons.

Abbildung 5. Volumen jeder Niere, auf das 10, 15, 20 bzw. 24 Gy treffen. p < 0,00001 für alle Wertepaare.

CTV, the PTV is less covered with CEBR. Mean cold spots of 45.5 ± 4.8 Gy are observed inside the PTV in comparison to 30 ± 7.7 Gy for CEBR ($p < 0.00001$). The volume of PTV receiving less than the prescribed dose of 60 Gy is only 4.77% ± 1.6% with IMRT versus 27.5% ± 7.6% with CEBR ($p < 0.00001$).

Figure 4 shows the doses to the spinal cord. The maximal dose is reduced from 42.5 ± 0.7 Gy to 26.2 ± 3.9 Gy with IMRT ($p < 0.00001$). Doses to 75%, 50%, and 25% of this OR (D75%V, D50%V, D25%V) are also considerably lowered using IMRT.

Kidney irradiation is highly reduced with IMRT (Figure 5). The volume of the left kidney receiving 20 Gy is decreasing from 47.4% ± 8.5% with CEBR to 22.4% ± 4.9% ($p < 0.00001$). For the right kidney, the volume is reduced from 40.8% ± 4.9% to 10.1% ± 3.6% ($p < 0.00001$).

Doses to digestive structures are not different with < 25% receiving ≥ 35 Gy. Doses to the liver remain low with both techniques the mean dose being 9.15 ± 5.6 Gy for IMRT as compared to 9.5 ± 7.8 Gy for CEBR ($p = 0.6$). With IMRT, 75%, 50%, and 25% of the volume received 3.1 ± 0.7 Gy, 6.2 ± 0.9 Gy, and 13.7 ± 3.6 Gy, respectively.

Discussion

Recent RTOG guidelines for future clinical trials included investigation of dose escalation in the PO region [5]. This approach, however, remains very difficult to achieve due to the presence of OR in close vicinity to the CTV like spinal cord, kidneys, and digestive structures. So, only techniques largely sparing the OR at the highest level offer a chance of safely achieving the minimum level of 54–60 Gy necessary to sterilize a macroscopic lesion. Moreover, at lower dose levels required in an adjuvant setting or for lymphomas, seminomas or other malignancies, the higher ballistic selectivity of a radiation treatment is always appreciated in a multidisciplinary treatment approach.

Recently, published pilot studies suggested that PO metastatic lymph nodes are better controlled when doses from 45 to 60 Gy are used even with concomitant chemotherapy, while DFS rates of 20% at 5 years have been published [13, 14]. A recent study on 29 patients with PO metastases investigated the role of dynamic arc conformal radiotherapy to increase the total dose up to 55–60 Gy. No late grade 3 side effects were observed at a short median follow-up of 11 months with some patients receiving concomitant chemotherapy.

At present, details on doses delivered to OR with a PO IMRT approach are scarce and incomplete in the literature [1–3, 10, 11, 15]. We suggest that it is possible to deliver ≥ 60 Gy to the PO region using IMRT based on an inverse planning approach, making combinations with chemotherapy probably safer. The heterogeneity of irradiation inside the CTV is higher with IMRT in comparison to CEBR. However, if the severity of cold spots is slightly higher with IMRT, the volume receiving less than the prescribed dose is smaller as compared to CEBR. On the other hand, when the PTV is analyzed, the heterogeneity of irradiation is higher with CEBR, mainly due to the presence of larger volumes irradiated at lower doses. The maximal dose to the spinal cord is reduced to 26.2 Gy, while 20 Gy are delivered to only 22% and 10% of the left and right kidneys. For both CEBR and IMRT, doses to liver and digestive structures remain low with < 25% of the organs receiving < 14 Gy and < 35 Gy, respectively.

When compared with the dynamic arc conformal technique [1], IMRT in this inverse planning approach seems to better protect the kidneys. For a similar prescribed dose, indeed 26% of the organ volume received 20 Gy versus 10% and 22% for the right and left kidneys in the present study. Similar doses to the liver are delivered with both techniques, as 50% and 25% of the organ are receiving < 10 Gy and < 20 Gy. No comparison can be made regarding the spinal cord, as data are not available for the dynamic arc conformal technique [1]. Whether or not these new technologies will provide a benefit to the patients in terms of survival has to be further investigated in clinical trials, but they will probably make concomitant chemoradiotherapy approaches to the PO region safer.

References

1. Aoki T, Nagata Y, Mizowaki T, et al. Clinical evaluation of dynamic arc conformal radiotherapy for paraaortic lymph node metastasis. Radiother Oncol 2003;67:113–8.
2. Bogner L, Scherer J, Treutwein M, et al. Verification of IMRT: techniques and problems. Strahlenther Onkol 2004;180:340–50.
3. De Meerleer G, Vakaet L, De Gersem W, et al. Direct segment aperture and weight optimization for intensity-modulated radiotherapy of prostate cancer. Strahlenther Onkol 2004;180:136–43.
4. Eifel PJ, Winter K, Morris M, et al. Pelvic radiation with concurrent chemotherapy versus pelvic and para-aortic radiation for high-risk cervical cancer: an update of RTOG 90-01. Int J Radiat Oncol Biol Phys 2002;54:Suppl:1.
5. Greven M, Levenback C, Chao CKS, et al. Gynecology Cancer Working Group. Research Plan 2002–2006. Int J Radiat Oncol Biol Phys 2001;51:Suppl 2:58–9.
6. Grisby PW, Heydon K, Mutch DG, et al. Long-term follow-up of RTOG 92-10: Cervical cancer with positive para-aortic lymph nodes. Int J Radiat Oncol Biol Phys 2001;51:982–7.
7. Haie C, Pejovic MH, Gerbaulet A, et al. Is prophylactic para-aortic irradiation worthwhile in the treatment of advanced cervical carcinoma? Results of a controlled clinical trial of the EORTC Radiotherapy Group. Radiother Oncol 1988;11:101–12.
8. ICRU, International Commission on Radiation Units and Measurements, Report 50. Prescribing, recording, and reporting photon beam therapy. Washington: ICRU, 1993.
9. ICRU Report 62. Prescribing, recording and reporting photon beam therapy (Supplement to ICRU Report 50). Washington: ICRU, 1999.
10. Lohr F, Dobler B, Mai S, et al. Optimization of dose distributions for adjuvant locoregional radiotherapy of gastric cancer by IMRT. Strahlenther Onkol 2003;179:557–63.
11. Portelance L, Chao KSC, Grisby PW, et al. Intensity-modulated radiation therapy reduces small bowel, rectum, and bladder doses in patients with cervical cancer receiving pelvic and para-aortic irradiation. Int J Radiat Oncol Biol Phys 2001;51:261–6.
12. Rotman M, Pajak T, Choi K, et al. Prophylactic extended-field irradiation of para-aortic lymph nodes in stages IIB and bulky IB and IIa cervical carcinoma, ten-year treatment results of RTOG 79-20. JAMA 1995;274:387–93.

13. Saad AA, Lo SS, Han I, et al. Radiation therapy with or without chemotherapy for cervical cancer with periaortic lymph node metastasis. Int J Radiat Oncol Biol Phys 2002;54:Suppl:40.
14. Varia MA, Bundy BN, Deppe G, et al. Cervical carcinoma metastatic to para-aortic nodes: extended field radiation therapy with concomitant 5-fluorouracil and cisplatin chemotherapy: a Gynaecologic Oncology Group study. Int J Radiat Oncol Biol Phys 1998;42:1015–23.
15. Willner J, Jost A, Baier K, et al. A little to a lot or a lot to a little? An analysis of pneumonitis risk from dose-volume histogram parameters of the lung in patients with lung cancer treated with 3-D conformal radiotherapy. Strahlenther Onkol 2003;179:548–56.

Address for Correspondence
Philippe Nickers
Department of Radiation Oncology
University Hospital of Liège
Domaine Universitaire du Sart Tilman B35
4000 Liège
Belgium
Phone (+32/4) 366-7596, Fax -7952
e-mail: philippe.nickers@skynet.be