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A novel dynamic field-matching technique for treatment of patients with para-aortic node-positive cervical cancer: Clinical experience

*Craig Baden**, *Alexander Whitley*, *Javier López-Araujo*, *Richard Popple*, *Jun Duan*, *Robert Kim*

Department of Radiation Oncology, University of Alabama-Birmingham, Birmingham, AL, USA

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ABSTRACT

Aim: To report outcomes for patients with para-aortic lymph node positive cervical cancer treated with a dynamic field-matching technique.

Background: PET staging of cervical cancer has increased identification of patients with para-aortic lymph node metastasis. IMRT enables dose escalation in this area, but matching IMRT fields with traditional whole pelvis fields presents a challenge.

Materials and methods: From 2003 to 2012, 20 patients with cervical cancer and para-aortic lymph node metastasis were treated utilizing the dynamic field-matching technique. As opposed to single-isocenter half-beam junction techniques, this technique employs wedge-shaped dose junctions for the abutment of fields. We reviewed the records of all patients who completed treatment with the technique and abstracted treatment, toxicity, and disease-related outcome data for analysis.

Results: Median prescribed dose to the whole pelvis field was 45 Gy and para-aortic IMRT field 50.4 Gy. All but 3 patients underwent HDR (13 pts) or LDR (4 pts) brachytherapy. All patients developed lower GI toxicity; 10 grade 1, 9 grade 2, and 1 grade 4 (enterovaginal fistula). Median DFS was 12.4 months with 1 and 2-year DFS 60.0% and 38.1%. One-year OS was 83.7% and 2-year OS, 64.4%. A total of 10 patients developed recurrence; none occurred at the matched junction.

Conclusions: The dynamic field-matching technique provides a means for joining conventional whole pelvis fields and para-aortic IMRT fields that substantially reduces dose deviations at the junction due to field mismatch. Treatment with the dynamic matching technique is simple, effective, and tolerated with no apparent increase in toxicity.

* *Corresponding author at*: Hazelrig-Salter Radiation Oncology Center (176F), 1240B, 619 19th Street South, Birmingham, AL 35249-6832, USA. Tel.: +1 205 934 5670; fax: +1 205 975 0784.
E-mail address: craigbaden@gmail.com (C. Baden).

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1. Background

The development and increased utilization of FDG PET for cervical cancer staging has contributed to increased diagnosis of metastases to the para-aortic lymph nodes.[1–5] Intensity modulated radiation therapy (IMRT) enables definitive treatment of para-aortic target volumes with escalated doses of radiation while simultaneously sparing the adjacent organs at risk including the small bowel, spinal cord, and kidneys.[6–9] Though IMRT for postoperative pelvic radiation treatment for cervical cancer is well established, conventional 3-D conformal four-field pelvic RT remains a standard of care and is often preferred for intact cervical cancer.[10] Matching fields from both IMRT treatment for the para-aortic fields and conventional 4-field conformal treatment fields for the whole pelvis can prove challenging, often leading to significant dose inhomogeneities at the field junction.

2. Aim

Here we introduce a novel dynamic field matching technique to minimize inhomogeneities. We also report disease-related outcomes, toxicities, and patterns of failure from a series of 20 patients successfully treated with the technique.

3. Materials and methods

3.1. *Treatment planning for dynamic field matching*

Conventional field matching techniques, such as single isocenter half beams (SIHB), are prone to dose inhomogeneity due to imperfect mechanical accuracy of the linear accelerator. To minimize such inhomogeneities at the junction of para-aortic IMRT fields and static 3D conformal pelvic fields, we adopted the dynamic field matching technique that was initially developed for matching head-and-neck IMRT fields with the static supraclavicular field. The dynamic field match technique has been described in great detail in a previous publication, and we describe it only briefly here.[11]

Because dose inhomogeneity caused by the mismatch of abutting fields is proportional to the dose gradient at the field edges that constitute the match line, the dynamic field matching technique aims to reduce the dose gradient at these edges to minimize dose inhomogeneity. To achieve this, the superior borders of the pelvic fields are moved continuously (either open up or close down) over a 3 cm range (from 1.5 cm above to 1.5 cm below the conventional match line) during treatment, producing a 3 cm tapered dose junction. The para-aortic IMRT fields, which are purposely made to overlap with the pelvic fields by 3 cm, are optimized with consideration of the wedge-shaped dose contribution from the pelvic field to generate a complementary wedge at their inferior borders. The two sets of fields, which merge gradually, combine to deliver a homogeneous dose in the match zone. The two mutually complementing wedge shaped dose distributions at the field junctions effectively serve as a continuous match line feathering over a 3 cm range. Fig. 1 compares typical dose profiles of SIHB and dynamic field match techniques. The dose gradient for each component field is much less steep in the case of the dynamic field matching technique. These low gradient junctions help reduce dose heterogeneities resulting from patient setup error or imperfect mechanical calibration of the jaws. Fig. 2 demonstrates the dosimetric advantage of dynamic field match over the conventional SIHB method. For −3 mm to +3 mm overlap of the abutting fields, substantial dose heterogeneities are generated with the SIHB method (Fig. 2 left). These heterogeneities are greatly suppressed with the dynamic matching technique (Fig. 2 right).

To generate a plan with the dynamic matching technique a commercial treatment planning system (Eclipse; Varian Medical Systems, Palo Alto, CA) was used. A conventional static 4-field 3DCRT plan is first generated using the MLC to shape the field apertures. The MLC is oriented such that the leaves move in the superoinferior direction. To generate the 3 cm wedge junction, the static MLC leaf sequences are converted to dynamic ones using in-house software, such that the leaves shaping the superior field borders move continuously from 1.5 cm below to 1.5 cm above the conventional match line during treatment. The pelvic plan is then recalculated with the dynamic MLC using fixed monitor units that have been calculated previously. For the para-aortic IMRT fields, the PTV is extended 1.5 cm inferior to the conventional match line. The IMRT plan is optimized to cover the extended PTV by inclusion of the dose contribution from the pelvic fields, producing another wedge junction to complement that of the pelvic fields. To avoid field overlap beyond the 3 cm match zone, the inferior borders of the IMRT fields, which were adjusted automatically by the treatment planning system to fit the dynamic MLC fields, are then manually closed to 1.5 cm inferior to the match line using collimator jaws and the plan is recalculated.

3.2. *Clinical data collection and analysis*

We retrospectively reviewed the records of all cervical cancer patients who completed treatment with the dynamic matching technique at our institution between 2003 and 2012. Data abstracted from the chart included patient demographic information, disease stage and features, radiation technique and doses, details of concurrent chemotherapy. Acute and late gastrointestinal and genitourinary toxicities were recorded from the medical record and graded using RTOG acute and late radiation morbidity scoring criteria.[12,13] For patterns-of-failure and actuarial disease related outcome analyses, we recorded first site of failure, date of disease failure, date of death, and date of last follow-up and calculated time to event or censorship from the date of diagnosis. Failure was considered local if recurrence occurred at the site of original disease, regional if elsewhere within the pelvis or PA lymph node chain, and distant if at another site. Locoregional control (LRC), disease-free survival (DFS), and overall survival (OS) estimates were determined by the Kaplan–Meier method utilizing SPSS Statistics 22.0 for Windows (IBM SPSS, Chicago, IL).

4. Results

From 2003 to 2012, 20 patients completed curative-intent treatment utilizing the dynamic matching technique after staging

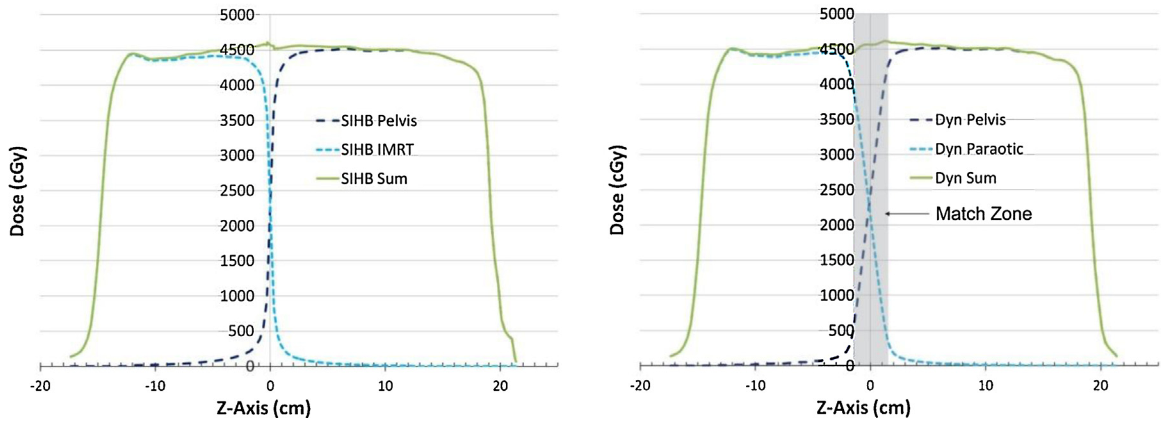

Fig. 1 – The graphs above demonstrate dose sum as well as dose contributions from whole pelvis and para-aortic fields for plans with single isocenter half beam (left) and dynamic field matching (right) techniques. The dose gradient at the pelvis and para-aortic junction is significantly less for each of the components in the dynamic field matching plan. The low dose gradient at the junction helps reduce dose inhomogeneity resulting from an imperfect match.

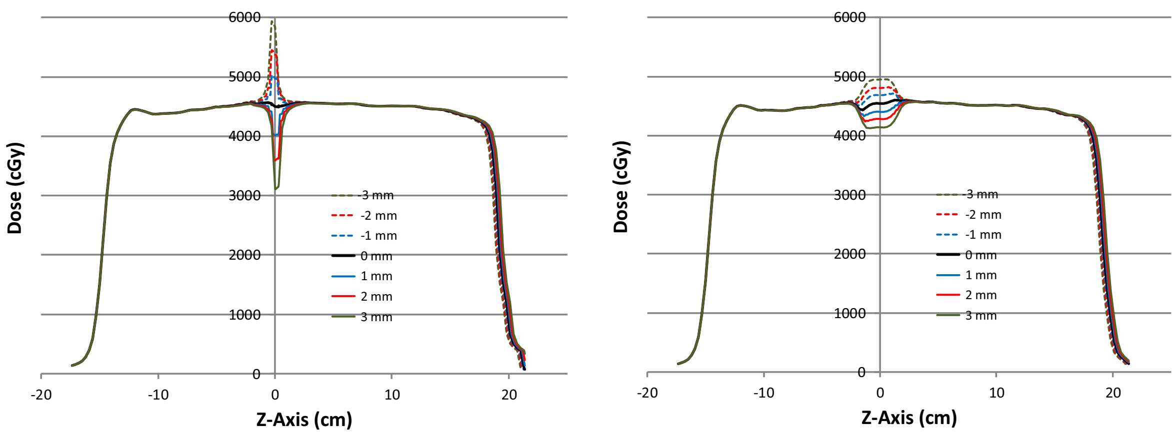

Fig. 2 – Sum doses at the field junction are depicted for single isocenter half beam (left) and dynamic field matching (right) techniques. A range of field mismatches from −3 mm (overlap) to +3 mm (gap) are displayed. Dynamic field matching substantially reduces the magnitude of dose inhomogeneity at the field junction.

work-up with CT or PET revealed evidence of PA lymph node involvement. Median age at diagnosis was 47 (range 36–70). Pathology revealed squamous cell carcinoma in 14 patients, adenocarcinoma in 5, and poorly differentiated carcinoma in 1.

Chemoradiation was completed with concurrent platinum-based chemotherapy (cisplatin alone in 17 patients, cisplatin and paclitaxel in 1 patient, and carboplatin and paclitaxel in 2 patients). Median prescribed dose to the whole pelvis field was 45 Gy (range 45–49.6) and para-aortic IMRT field 50.4 Gy (range 45–55.5). All but 2 patients received a parametrial boost with midline block (median boost dose 5.4 Gy) and 4 patients received additional IMRT boost to bulky PA nodal disease (total dose to PA boost volume 54–60 Gy). All but 3 patients underwent HDR (13 patients) or LDR (4 patients) brachytherapy, the majority receiving 8 Gy × 3 fractions.

All patients developed acute lower GI toxicity (11 grade 1 and 9 grade 2) and a minority developed acute GU toxicity (5 grade 1 and 2 grade 2). One late grade 4 toxicity was observed (enterovaginal fistula). The fistula was diagnosed 6 months after completion of radiation therapy with 45 Gy to the whole pelvis, 45 Gy to PA lymph node PTV, and LDR Syed needle brachytherapy (30 Gy). It developed within the whole pelvis 4-field box fields but well away from any dose contribution by IMRT fields.

Median follow-up for the cohort was 17.6 months (range 5.3–129.0). One and 2 year LRC were 89.5%. Median DFS was 12.4 months (95% CI 7.3–17.6) with 1 and 2-year DFS 60.0% and 38.1%. One-year OS was 83.7% and 2-year OS, 64.4%; median OS has not yet been reached. Of the 10 patients who developed recurrence, first site of recurrence was within the whole pelvis field for 1 patient, within the field and distant for 1 patient, and distant in 8 patients. There were no failures at the dynamic junction between IMRT and whole pelvis fields.

5. Discussion

The presence of para-aortic lymph node (PALN) metastases is the single most significant prognostic factor in patients with locally advanced cervical cancer. Detection of PALN disease involvement not only provides prognostic information but also determines the appropriate radiotherapy target volume. The utility of integrated PET/CT imaging is now well-established for the staging evaluation of patients with locally advanced cervical cancer, providing better sensitivity and specificity than either MRI or CT alone.[5,14] As utilization of PET/CT imaging in cervical cancer has increased, PALN metastases have been detected with greater frequency.

Traditionally, para-aortic nodal volumes have been irradiated either with an extended field that includes both the para-aortic nodes and the pelvis or with two sets of separate fields. With both of these techniques, a significant portion of small bowel is included in the irradiated volume. The decision to use either two or four fields for pelvic and para-aortic areas must be individualized, taking into account the patient's anatomy. The majority of patients are best treated with a four-field plan, since small bowel and portions of the rectum can be shielded on lateral fields. However, even utilizing the four-field technique, radiation treatment of both the pelvic and para-aortic target volumes is associated with significant toxicity, especially in the era of concurrent chemoradiation therapy. Prospective phase II cooperative group trials with chemoradiation and conventionally treated para-aortic volumes have reported unacceptably high rates of grade 3 and 4 acute and late toxicities.[15,16] Therefore, improvement upon conventional technique has been necessary to reduce associated toxicity.

Intensity modulated radiotherapy (IMRT) represents a major advance in the delivery of radiation therapy, allowing improved dose conformity, dose escalation, and sparing of adjacent normal structures compared with conventional RT.[17] In multiple series, IMRT treatment of para-aortic target volumes has been significantly superior to the conventional technique due to its improved toxicity profile.[18–20] Therefore, IMRT for treatment of para-aortic target volumes is a well-accepted approach. However, 3-D conformal pelvic radiation remains a standard technique for treatment of the whole pelvis due to uncertainties related to uterus, cervix, and vaginal motion.[21–23] Compared with conventional treatment, pelvic IMRT may allow for less radiation dose to organs at risk, but inadequate PTV margins increase the likelihood of a geometric miss of the tumor.[24] Therefore, standard treatment at our institution has included IMRT treatment for para-aortic volumes with the 3-D conformal 4-field technique for the whole pelvis.

Historically, we accomplished the field match between para-aortic and whole pelvis fields utilizing a common isocenter at the L4–L5 interspace.[9] The superior borders of each of the whole pelvis fields were placed on the central axis at the level of the isocenter. In the case of the IMRT para-aortic fields, optimization was completed with the target volume extrapolated 2 cm below the planned match line. After optimization, the jaw at the lower border of each IMRT field was then closed to the isocenter match line, allowing for steepening of the dose gradient in order to match the similarly steep dose contribution from the whole pelvis fields.

Recently, the novel dynamic field matching technique (described in the methods section above) was developed at our institution. This technique provides several advantages over the single isocenter half beam (SIHB) method which had been used previously. First and most importantly, by significantly reducing the dose gradient at the field edge (Fig. 1) the dynamic matching technique decreases the risk of dose inhomogeneity due to mismatch of abutting fields. In the case of larger mismatches between abutting fields the ability of the dynamically matched field junction to minimize inhomogeneity becomes increasingly important (Fig. 2). A second advantage of the dynamic field matching technique is the ability to treat larger para-aortic target volumes. In the case of SIHB, only half the beam is available to cover the para-aortic target, but with dynamic field matching the isocenter for IMRT fields may be shifted superiorly as needed in order to allow coverage of elongated para-aortic volumes. One minor disadvantage of the dynamic field matching technique relates to the requirement to orient the multileaf collimator so that the leaves move in the superoinferior direction. Occasionally, patient anatomy requires convex MLC blocking on lateral or AP-PA whole pelvis fields that may only be accomplished with MLCs oriented in the medial–lateral direction. Depending on the situation, the blocking convexity may be adjusted in order to permit treatment with dynamic matching if this is considered a higher priority.

Taken as a whole the 20 patients treated with the dynamic field matching technique in this series tolerated treatment very well. Though all patients did experience acute GI toxicity from treatment, this toxicity was considerably less severe than in previous chemoradiation series that employed conventional techniques to treat para-aortic volumes.[15,16] One- and 2-year disease free survival of 60.0% and 38.1% were similar to those reported in previous studies of extended field radiation and again demonstrated that a subset of women with para-aortic node positive cervical cancer may be cured.[15] Patterns of failure revealed that the majority of patients who failed had distant disease as a component of recurrent disease. Importantly, no patients developed recurrence or major side effects near the dynamic match junction. Limitations of this retrospective series include the relatively small number of patients as well as the short median follow-up. Extended follow-up will be required in order to assess more comprehensively late toxicities and patterns of failure.

6. Conclusions

Definitive chemoradiation to the pelvis and para-aortic target volumes provides potentially curative treatment for the increasingly diagnosed subset of patients with locally advanced cervical cancer and para-aortic involvement. The dynamic field matching technique presented here is a practical and clinically proven radiation technique for significantly minimizing dose inhomogeneities at the field junction.

Conflict of interest

None declared.

Financial disclosure

None declared.

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