

# Dosimetric evaluation of parallel opposed spatially fractionated radiation therapy of deep-seated bulky tumors

Ali S. Meigooni,<sup>a)</sup> Michael Gnaster, Kai Dou, Ellis L. Johnson, Navid J. Meigooni, and Mahesh Kudrimoti

Department of Radiation Medicine, University of Kentucky Medical Center, Lexington, Kentucky 40536

(Received 18 October 2006; revised 13 December 2006; accepted for publication 13 December 2006; published 24 January 2007)

Application of a single fraction of parallel opposed GRID beams as a means of increasing the efficiency of radiation delivery to deep-seated tumors has been investigated. This evaluation was performed by measurement of dosimetric characteristics of the GRID radiation field in parallel opposed and single beam geometry. The limitations of the parallel opposed technique in terms of field size and tumor thickness have been evaluated for the conditions of acceptable spatial modulation. The results of this investigation have demonstrated an increase in therapeutic advantage for the parallel opposed technique over the single beam method when treating a deep seated tumor. © 2007 American Association of Physicists in Medicine. [DOI: 10.1118/1.2431423]

Key words: GRID radiation, SFR, dosimetry, parallel opposed

## I. INTRODUCTION

While many recent technological advances in radiation therapy have resulted in improved outcomes for treatment of patients with early stage disease, the management of advanced cancers remains a challenging clinical problem. These patients may have very large tumors or the disease may be located in areas that are difficult to target with conventional external beam methods. Procedures with more precise targeting and intensity modulation capabilities, such as TomoTherapy<sup>®</sup> or Cyberknife<sup>®</sup>, have the potential to improve many of these difficult treatment situations. However, these devices are expensive and their availability is still somewhat limited. As a result, options may be limited for some of these patients.

Spatially fractionated radiation therapy (SFR), also known as GRID therapy, is a promising alternative treatment modality for patients with advanced bulky tumors.<sup>1</sup> In this technique, an open radiation field from a linear accelerator is converted into a matrix of pencil beams using a specially designed Cerrobend<sup>®</sup> block (called hereafter as GRID block).<sup>1-4</sup> Dosimetric characteristics of the single GRID radiation fields for both photon and electron beams have been studied by several investigators.<sup>2,5,6</sup> GRID radiotherapy is currently given as a precursor to conventional palliative or curative fractionation schemes and consists of a single oppositional portal. Presently, the GRID dose is not counted as part of the standard therapy dose. In addition, the GRID radiation fields are designed to cover the gross tumor volume without additional margins. The field geometry is chosen to minimize the dose to the most critical organs. Mohiuddin *et al.* have noted higher pathological response rates and improved outcomes by delivering GRID doses of 12–20 Gy prior to conventional external radiation dose >40 Gy.<sup>1,2</sup> Some advantages of GRID therapy include ease of setup and delivery, simplified treatment planning, and a relatively inexpensive apparatus.

Early studies by Marks<sup>7</sup> have proven that when small areas of irradiated skin and subcutaneous tissue were shielded (with a grid), these protected areas served as centers for regrowth of the normal tissue that overlays the tumor volume. In *invitro* studies, Urano *et al.*<sup>8</sup> assessed the therapeutic advantage of GRID radiation using orthovoltage x-ray beams. They found that compared to open field radiation, they needed approximately 25% greater dose to achieve the same tumor control in the GRID field while the skin and soft-tissue tolerances were increased by about 80%. These results suggest a therapeutic advantage for sparing normal tissues with GRID radiation. In a retrospective analysis of orthovoltage GRID data from 1953 to 1989, Maruyama *et al.*<sup>9</sup> have introduced some guidelines for application of GRID therapy. More recently, Zwicker *et al.*<sup>10</sup> evaluated the radiobiological properties of megavoltage GRID irradiation, using the linear quadratic model. They have calculated the therapeutic advantage of GRID therapy as a function of dose as well as the radiosensitivity of the tissue.

Presently, the prescription point for all single portal GRID fields is the depth of  $d_{\max}$ , regardless of tumor depth. This results in a decreasing tumor dose for increasing tumor depth. Therefore, a single GRID radiation field prescribed to the depth of  $d_{\max}$  for these deep-seated tumors may result in less than optimal dose delivery for these lesions at depth. Methods that may be used to increase the dose at depth for these deep-seated tumors include shifting the prescription point to deeper depths, increasing the number of beams used to deliver the treatment, and increasing the photon energy.

In this work, it is our aim to investigate the use of a single fraction of a parallel opposed arrangement of GRID fields as a means of increasing the dose to deep-seated tumors. Clinical and dosimetric aspects of parallel opposed irradiation have been extensively discussed in conventional radiotherapy and the advantages are well known.<sup>11</sup> However, the extrapolation of this beam arrangement to GRID fields in the context of maintaining a minimum level of spatial intensity

modulation is not necessarily straightforward. Considering the geometry of GRID fields in a parallel opposed arrangement, corresponding pencil beams from opposing fields will precisely align only in the plane of isocenter. In other planes, dephasing of corresponding pencil beams may lead to a degradation of spatial modulation. In this project, film and ionization chamber dosimetry methods have been utilized to evaluate the dose distribution obtained from parallel opposed GRID fields. We have evaluated the applicability of this technique in terms of the limitations in field size and tumor thickness where adequate spatial intensity modulation may be maintained. In addition, we demonstrate an increased therapeutic advantage in deep-seated tumors for parallel opposed GRID fields over that obtained from a single GRID field due to the increased dose that can be delivered using the opposed beam approach.

## II. MATERIALS AND METHODS

A commercially available GRID block (Radiation Products Design, Inc., Albertville, MN) was utilized for all measurements in this study. This device was constructed by casting divergent apertures arranged in a symmetric, hexagonal pattern in a 7.5 cm thick Cerrobend<sup>®</sup> block using a stereotactic method. The aperture diameter and center-to-center spacing are 13 and 21 mm, respectively, projected onto the plane of isocenter. This block design allows for a greater proportion of the irradiated field to receive the therapeutic dose of greater than 85% of the maximum as compared to a previous nondivergent block design.<sup>12</sup> This block was designed for use in a Varian Clinac 2100EX linear accelerator (Varian Oncology Systems, Palo Alto, CA) having a block tray distance of 65.4 cm. This device was mounted onto a support plate having the same dimensions as a standard Varian Clinac 2100EX blocking tray, which can be installed into the accessory tray mount. GRID fields were evaluated for a 6 MV photon beam.

### A. Film dosimetry

For the film dosimetry, Kodak X-Omat V radiographic film (Eastman Kodak Co., Rochester, NY) was used in Solid Water<sup>™</sup> tissue equivalent phantom material (Radiation Measurements Inc., Middleton, WI) to measure absorbed dose and to determine beam profiles (inplane and crossplane) of single and parallel opposed 6 MV photon beams. Films were analyzed using a Lumiscan 50 laser scanner (Lumisys, Sunnyvale, CA) along with the corresponding film calibration curve. The film calibration curves were generated from multiple films exposed to the 6 MV photon beam at a depth of  $d_{\max}$  (100 cm SSD; 10 × 10 field size) for increasing dose settings (1, 5, 10, 20, 30, 50, 60, and 70 cGy).

The irradiation setup for parallel opposed GRID fields consists of a 23 cm thick slab Solid Water<sup>™</sup> phantom positioned such that midplane corresponds with isocenter. The resulting SSD for each beam is 88.5 cm. Films were positioned at the depths of  $d_{\max}$ , 6.5 cm, and 11.5 cm (midplane) relative to each of the two opposed beams. These films were kept in the same position for irradiation with opposite beams.

The tumor thickness in the direction of the beam central axis is assumed to be centered at midplane. The GRID doses were equally weighted for the two opposed beams. For the purposes of comparison, all beam profiles were normalized to the maximum value in the central hole.

Films were also obtained for the single beam technique currently in clinical use. A set of films for a single GRID field was obtained for the same geometry as the parallel opposed setup described above (i.e., 88.5 cm SSD, and depths of  $d_{\max}$ , 6.5 cm, and 11.5 cm). These films allow for direct comparison of beam profiles, in terms of the degree of spatial modulation, for both single beam and parallel opposed methods. One additional set of films was obtained for the setup used in the ion chamber measurements (100 cm SSD, depth of  $d_{\max}$ , 5 cm, and 10 cm). These were used for the purpose of validating the film dosimetry results against those obtained from ion chamber measurements.

### B. Ionization chamber

Depth ionization and beam profiles (inplane and crossplane) were acquired for the single GRID field using a Wellhofer CC01 micro-ionization chamber along with a Wellhofer scanning system (Scanditronix Wellhofer North America, Bartlett, TN). The water phantom setup consisted of a 48 × 48 × 48 cm<sup>3</sup> water tank, a CU 500E electrometer, and WP700 v.3.4 data acquisition/processing software. The scanning system was carefully aligned to maintain centering the ion chamber active volume within the profile of the central GRID beam at all depths for a central axis depth scan. The ion chamber was oriented with its long axis parallel to the CAX of the beam for the purpose projecting the smallest dimension of the chamber (2 mm diameter) to the GRID beam during scanning. Cross beam scans were obtained along the two orthogonal directions perpendicular to the CAX of the beam passing through the central hole. These inplane and crossplane beam profiles were obtained at 100 cm SSD for the field sizes 10 × 10 cm<sup>2</sup>, 15 × 15 cm<sup>2</sup>, 20 × 20 cm<sup>2</sup>, and 25 × 25 cm<sup>2</sup> for the 6 MV photon beam. Percent depth dose (PDD) was measured at 100 cm SSD for single beam field sizes of 5 × 5 cm<sup>2</sup>, 10 × 10 cm<sup>2</sup>, 20 × 20 cm<sup>2</sup>, and 25 × 25 cm<sup>2</sup> for the 6 MV photon beam. These depth doses were obtained directly from the normalized depth ionization profiles without any further consideration for loss of electronic equilibrium or energy spectrum changes. These data were used to validate the film dosimetry methods described previously.

### C. Determination of therapeutic advantage

The methodology of Zwicker *et al.*<sup>10</sup> has been used to evaluate the potential therapeutic advantage for a tumor located at 11.5 cm depth for both the single GRID and parallel opposed GRID techniques for prescribed doses of 12 and 15 Gy. In the single GRID method, the dose prescription is assumed to be at the depth of  $d_{\max}$  while in the parallel opposed technique the prescription is assumed to be at the tumor depth (11.5 cm). The therapeutic advantage is defined as

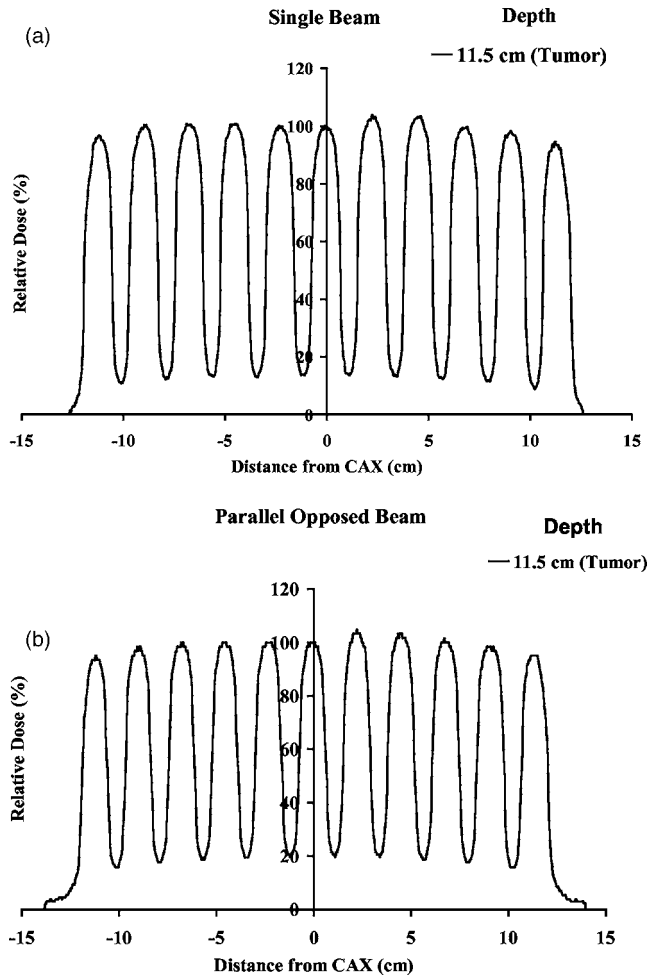


FIG. 1. Comparison of relative dose profiles at the tumor level, normalized to the maximum dose in the central hole, for a single field GRID therapy (a) versus parallel opposed fields GRID therapy (b).

$$\text{Therapeutic Advantage} = \frac{\text{SF}_{\text{GRID field}}^{\text{Normal tissue}}}{\text{SF}_{\text{Open field}}^{\text{Normal tissue}}}, \quad (1)$$

where the tumor SF is equal for both uniform and GRID fields. The  $\alpha/\beta$  ratios used for these calculations, 10 Gy for tumor cells and 2.5 Gy for normal cells, represent typical values for these tissue types.

### III. RESULTS

The PDD and dose profiles were measured at 100 cm SSD for a single beam GRID field using an ion-chamber in water and compared to film dosimetry measured at 100 cm SSD in Solid Water™ at depths of  $d_{\text{max}}$ , 5 cm, and 10 cm. The results have indicated that the PDD obtained from the ionization chamber is in excellent agreement (within  $\pm 3\%$ ) with the film dosimetry for the 6 MV photon beam. Moreover, there is a good agreement between the film and ion-chamber measured profiles at the depth of 1.5 cm for a field size of  $25 \times 25 \text{ cm}^2$ . Based on these analyses, film dosimetry was validated as an acceptable technique for analyzing the parallel opposed GRID radiation fields.

Figure 1 shows the comparison between the measured

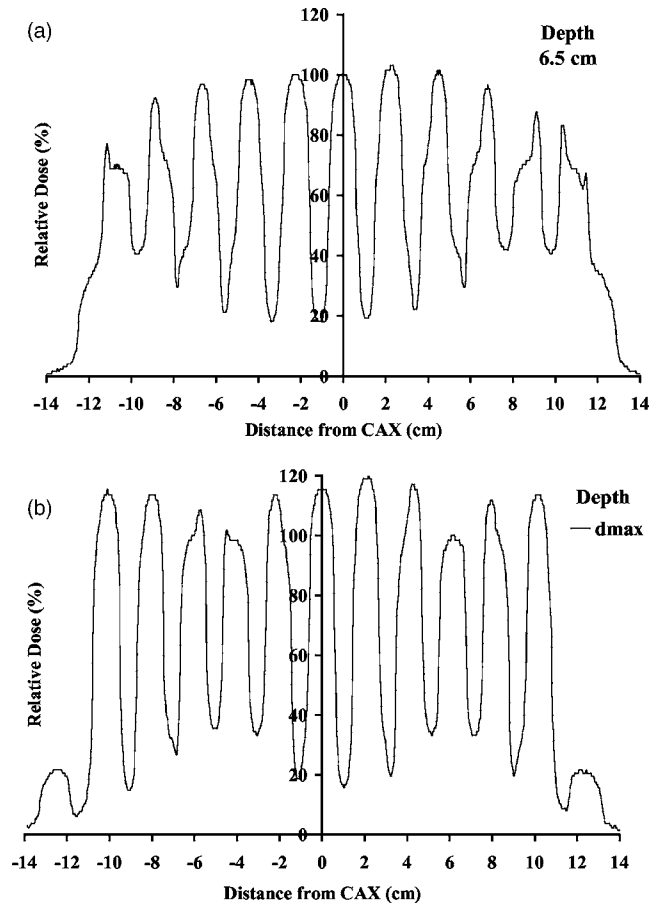


FIG. 2. Comparison of the crossplane beam profiles measured at the depths of 6.5 cm (a) and  $d_{\text{max}}$  (b) for parallel opposed GRID fields using 6 MV x rays.

dose profiles at the depth of 11.5 cm for both single and parallel opposed GRID field irradiation. These profiles represent the dose distribution delivered to the center of a tumor at this depth. In terms of spatial intensity modulation, the parallel opposed irradiation GRID profile is quite similar to that of single field GRID irradiation. Figure 2 shows the comparison between the dose profiles of the parallel opposed GRID fields at the depths of 6.5 cm (5 cm offset from midplane) and  $d_{\text{max}}$  (10 cm offset from midplane). These profiles indicate that a reasonable degree of spatial modulation is maintained throughout the region of interest.

Table I shows the absolute doses calculated for depths of  $d_{\text{max}}$ , 6.5 cm, and 11.5 cm, for doses of 12 and 15 Gy prescribed to  $d_{\text{max}}$  using a single beam GRID therapy and prescribed to tumor using the parallel opposed GRID therapy. With a parallel opposed GRID technique, a tumor located at 11.5 cm depth will receive about 90% more dose than it receives in the single field GRID method. Also shown in Table I is the calculated therapeutic advantage for both single and parallel opposed beams. These results indicate a significant increase in the therapeutic advantage for the parallel opposed GRID method as compared to the single beam therapy.

TABLE I. Comparison of the absorbed dose and the corresponding therapeutic advantage (TA) of parallel opposed GRID therapy and single field GRID therapy, for a prescribed dose of 15 Gy, and 12 Gy as a function of depth. The prescription point for the single beam is  $d_{\max}$  and for the parallel opposed beam is isocenter (i.e., tumor).

Depth	Single beam GRID therapy		Parallel opposed beam (POB) GRID therapy		Ratio (POB to single)	
	Dose (Gy)	TA <sup>a</sup>	Dose (Gy)	TA <sup>a</sup>	Dose	TA <sup>a</sup>
$d_{\max}$	<b>15.00</b>	1.88	18.30	2.04	1.22	1.09
6.5 cm	10.79	1.60	15.00	1.88	1.39	1.18
Tumor	8.06	1.39	<b>15.00</b>	1.88	1.86	1.35
$d_{\max}$	<b>12.00</b>	1.72	13.80	1.8	1.15	1.05
6.5 cm	8.63	1.39	12.36	1.72	1.43	1.24
Tumor	6.45	1.00	<b>12.00</b>	1.72	1.86	1.72

<sup>a</sup>Reference 12.

#### IV. DISCUSSION AND CONCLUSION

Presently, SFR GRID therapy utilizes either 6 or 18 MV photon beams with the dose prescribed at a depth of maximum dose ( $d_{\max}$ ), regardless of the tumor depth. However, the use of a single GRID field in treatment of a deep-seated tumor with a 12–15 Gy dose prescription to  $d_{\max}$  may result in insufficient dose delivery to the tumor. As a result, the therapeutic advantage achieved with a single GRID field may be unnecessarily reduced for deeper lying lesions. Increasing the single beam prescription depth for the purpose of achieving better therapeutic advantage in the tumor would increase the dose to the overlying normal tissues and hence might increase complications. An alternative solution to this problem is the use of a single fraction of multi-beam therapy, such as parallel opposed beams. Two major questions that arise in the clinical application of parallel opposed GRID therapies are (1) would the SFR modulation remain intact with the use of two opposed beams and (2) would inherent accelerator beam setup tolerances and intrafraction patient motion have a detrimental impact on the efficacy of this technique?

Dose profiles in the tumor measured with parallel opposed GRID fields illustrate that two opposed beams preserve the SFR modulation at isocenter and create a profile very similar to that of a single GRID beam (Fig. 1). In addition, the degree of spatial fractionation remains relatively intact for fields  $15 \times 15 \text{ cm}^2$  or less and for tumor thicknesses of up to 10 cm (Fig. 2). Moreover, the parallel opposed GRID therapy provides much higher dose to the tumor and hence increases the therapeutic advantage of the GRID therapy for treatment of deep seated tumors.

To investigate the impact of the uncertainties involved in machine/beam setup, several films were exposed using various field sizes, gantry orientations, and collimator settings. The results of these films confirmed that parallel opposed GRID therapy can be performed with the standard tolerances of the linear accelerators. The question of intrafraction

patient motion is an important one, but was not within the scope of this investigation. Single GRID field treatments typically require 3 to 4 min to deliver. While the possibility of significant patient motion exists under these conditions, present clinical experience obtained with single GRID techniques necessarily includes the possible influence of patient motion. Patient motion has not, as yet, been specifically addressed in single GRID treatments. The use of parallel opposed GRID fields will surely increase the amount of time required for treatment, maybe by as much as 50%. The extra beam-on and setup time involved in treating parallel opposed GRID fields and their influence on patient motion artifacts are not known. While the effects of patient motion should be the topic for future investigation, the possibility of such motion should not preclude the use of parallel opposed GRID fields in the limited conditions we have described.

In summary, parallel opposed beam setup for GRID radiation therapy is a viable option for treatment of deep-seated bulky tumors. With this treatment modality, the spatially fractionated modulation can be preserved while the absorbed dose to the tumor can be increased. This will enhance the therapeutic advantage of GRID therapy for deep seated tumors. This treatment modality can be implemented with any commercially available linear accelerator operating within standard mechanical tolerances.

#### ACKNOWLEDGMENTS

The authors would like to acknowledge Phillip Sawyer for providing assistance during the setup and calibration of the Wellhofer water phantom dosimetry scanning system. Also, the authors would like to thank David Pascoe for his valuable assistance during the preparation of the manuscript. The GRID blocks used in these investigations were provided by Radiation Products Design, Inc.

<sup>a</sup>Electronic mail: alimeig@uky.edu

<sup>1</sup>M. Mohiuddin, D. L. Curtis, W. T. Grizos, and L. Komarnicky, "Palliative treatment of advanced cancer using multiple nonconfluent pencil beam radiation," *Cancer* **66**, 114–118 (1990).

<sup>2</sup>M. Mohiuddin, M. Fujita, W. F. Regine, A. S. Meigooni, G. S. Ibbott, and M. M. Ahmed, "High-dose spatially fractionated radiation (GRID): A new paradigm in the management of advanced cancers," *Int. J. Radiat. Oncol., Biol., Phys.* **45**, 721–727 (1999).

<sup>3</sup>U. Malik, H. Zhang, S. A. Dini, A. S. Meigooni, N. J. Meigooni, K. Komanduri, and M. Mohiuddin, "Grid: A location dependent intensity modulated radiotherapy for bulky tumors," *Iran. J. Radiat. Res.* **2**, 167–174 (2005).

<sup>4</sup>W. Harris, "Recent clinical experience with the GRID in the X-Ray treatment of advanced cancer," *Radiology* **58**, 343–350 (1952).

<sup>5</sup>G. Mitev and N. Suntharalingam, "Semi-empirical calculation of dose distributions for high energy photon beam grid therapy," *Med. Phys.* **13**, 592 (1986) (Abstract).

<sup>6</sup>J. E. Reiff, M. S. Huq, M. Mohiuddin, and N. Suntharalingam, "Dosimetric properties of megavoltage grid therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **33**, 937–942 (1995).

<sup>7</sup>H. Marks, "Clinical experience with irradiation through a GRID," *Radiology* **58**, 338–342 (1952).

<sup>8</sup>M. Urano, G. Kaneda, S. Shimazaki, and S. Hayshi, "Radiation dose tumor-control assays for irradiation through a sieve," *Am. J. Roentgenol., Radium Ther. Nucl. Med.*, **102**, 38–42 (1968).

<sup>9</sup>Y. Maruyama, R. J. Yaes, M. Urano, P. Patel, and J. C. Hernandez, "Stem-cell deletion and GRID therapy," *Br. J. Radiol.*, **62**, 386–387 (1989).

<sup>10</sup>R. D. Zwicker, A. S. Meigooni, and M. Mohiuddin, "Therapeutic advan-

tage of GRID irradiation for large single fractions," *Int. J. Radiat. Oncol., Biol., Phys.* **58**, 1309–1315 (2004).

- <sup>11</sup>F. M. Khan, "Treatment planning I: Isodose distributions," in *The Physics of Radiation Therapy*, 3rd edition (Lippincott Williams and Wilkins, New York, 2003).
- <sup>12</sup>A. S. Meigooni, K. Dou, N. J. Soleimani-Meigooni, M. Gnaster, S. B. Awan, S. A. Dini, and E. L. Johnson, "Dosimetric characteristics of a newly designed GRID block for megavoltage radiation and its therapeutic advantage using a linear quadratic model," *Med. Phys.* **33**(9), 3165–3173 (2006).