Grid: A location dependent intensity modulated radiotherapy for bulky tumors

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ABSTRACT

Background: Grid radiation therapy, using the megavoltage X-ray beam, has been proven to be an effective method for management of large and bulky malignant tumors. This treatment modality is also known as Specially Fractionated Radiation Therapy (SFRT). In this treatment technique a grid block converted the open radiation field into a series of pencil beams. Dosimetric characteristics of an external beam grid radiation field have been investigated using experimental and Monte Carlo simulation technique.

Materials and Methods: Dose distributions (%DD as well as the beam profiles) of a grid radiation field have been determined using experimental and Monte Carlo simulation technique, for 6- and 18 MV X-ray beams from a Varian Clinics 2100C/D. The measurements were performed using LiF TLD and film in Solid Water phantom Material. Moreover, the MCNP Monte Carlo code was utilized to calculate the dose distribution in the grid radiation field in the same phantom material. The results of the experimental data were compared to the theoretical values, to validate this technique. Upon the agreement between the two techniques, dose distributions can be calculated for the grid field with different patterns and sizes of holes, in order to find an optimal design of the grid block.

Results: The results of dose profiles for 6 MV X-ray beams obtained with the Monte Carlo simulation technique was in good agreement with the measured data. In addition, the 3D dose distribution of the grid field generated by the Monte Carlo simulation gave more detailed information about the dose pattern of the grid.

Conclusion: The grid block can be used as a boost for treatment of bulky tumors. The Monte Carlo simulation technique can be utilized to optimize the pattern, size and spacing between the holes, for optimal clinical results. *Iran. J. Radiat. Res., 2005; 2 (4): 167-174*

Keywords: Grid, bulky tumors, specially fractionated radiation therapy.

INTRODUCTION

Treatment of large and bulky malignant tumors remains a challenge for oncologists. As tumor size increases the ability of most modalities including conventional external beam radiation to control the tumor decreases. The decrease in normal tissue tolerance with increasing volume of tissue irradiated restricts the escalation of total radiation dose by conventional external beam approaches. Altered fractionation such as hyperfractionation or accelerated fractionation has been utilized in an effort to increase the dose to the tumor and enhance local tumor control. However, for advanced and bulky tumors (>8 cm), local tumor control still remains dismal even with altered dose/time fractionation approaches (Dubben *et al.* 1998, Johnson *et al.* 1995). Therapeutic options are limited and palliative measures need to be tailored to the short life expectancy of these patients. "Spatially fractionated" radiation (grid

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therapy) is an adaptation of a concept in radiation therapy used in the past to deliver high cumulative doses of radiation to overcome the limitation of normal tissue tolerance. In the 1950s, this technique was routinely used with orthovoltage radiation to treat deeply seated tumors and avoid prohibitive skin and subcutaneous tissue toxicity (Liberson 1933, Marks 1950, 1952).

Adaptation of the old orthovoltage techniques of grid therapy to megavoltage radiation beams allows spatially fractionated high dose radiation to be delivered for palliation of selected massive and bulky tumors that have failed conventional approaches to management. A single large dose of spatially fractionated radiation can be delivered followed by a short course of conventional fractionated radiation to obtain rapid palliation of symptoms. In the Department of Radiation Medicine at the University of Kentucky, a modified spatially-fractionated technique for use with megavoltage radiation has been utilized for management of advanced tumors (Mohiuddin *et al.* 1999). In addition, Mohiuddin *et al.* 1996, reported the results of palliative treatment of sixty-one patients, treated for 72 symptomatic areas of disease, as shown in table 1. Figure 1 shows a sample of this treatment modality, before treatment and 6 months after radiation therapy. Pain was the predominant reason for treatment in 9 patients. Twenty-seven

Before   **After**

Figure 1. A sample clinical result of a patient with bulky tumor, before and 6 month after treatment with grid radiation therapy.

patients received treatment for symptoms associated with massive tumor bulk and five patients were treated for bleeding. Primary tumors were gastrointestinal in 18 patients of whom 12 had massive liver metastases. The others included 12 patients with sarcomas, 9 patients with urinary tract tumors, 9 with gynecologic tumors, 5 with melanoma, 4 with head and neck malignancy, 2 with breast cancer, 1 with lung and one with thyroid cancer. The following sections describe more detailed information for the results of this study (Mohiuddin *et al.* 1996).

Follow-up ranged from 1-28 months. Of the 72 treatment sites, 64 were evaluable for palliative response. Analysis of all evaluable treatments revealed an overall response rate of 91% (58/64). Twenty-seven percent (17/64) of all treatments resulted in a complete palliative response (CR). Partial responses (PR) were obtained in 64% (41/64). Twenty-eight percent complete pain relief and 62% partial pain relief achieved with grid therapy. Symptoms related to large tumor masses were completely relieved in 19% and partially relieved in 71% (table 2).

Response was also assessed by cell type. Sarcomas and squamous cell carcinomas had an overall response rate (CR = PR) of 94% and 92% respectively. Melanomas responded in 83% and adenocarcinomas had an overall response rate of 69% (table 3).

The therapeutic response was analyzed

Table 1. Distribution of Patients by Primary Tumor, treated with grid Radiation Therapy. Reproduced from Mohiuddin *et al.* (1996) with Permission of the John Wiley and Sons, Inc and Wiley-Liss, Inc. Publishing.

Site	# of patients
Gastrointestinal	18
Sarcomas	12
Genitourinary	9
Gynecologic	9
Miscellaneous	
Melanoma	5
Lung	1
Breast	2
Thyroid	1
SCC- Head and Neck	4
Total	61

according to grid dose <1,500 cGy and ≥1,500 cGy. An overall palliative response of 100% was achieved with doses ≥1,500 cGy, while those <1,500 cGy achieved a response rate of 79%. Twenty-one percent of treatments <1,500 cGy resulted in no palliative response (table 4).

Response was also analyzed by concurrent external beam radiation dose. An overall palliative response was observed in 86% of patients treated with grid alone without external radiation (29% CR and 57% PR). Ninety-two percent of patients treated with grid therapy and concurrent external radiation responded (25% CR and 67% PR). However, the complete palliative response was higher for patients treated with external beam radiation doses of 4,000 cGy or greater (36% vs. 20% CR) (see table 4) although this was not statistically significant.

In this project, dosimetric characteristics of external beam grid therapy have been investigated using experimental and Monte Carlo simulation technique. The method of dosimetry and the results are presented here.

MATERIALS AND METHODS

Grid Block

The grid block was constructed from a 7 cm thick low melting alloy (cerroband) with divergent holes to produces a spatially fractionated radiation field (figure 2). This block was mounted on a lucite tray to fit into block tray holder of a Varian 2100C/D linear accelerator (Clinac 2100C/D, Varian Oncology Systems, Palo Alto, CA). The grid block was comprised of 256 holes in a 16 × 16 cm square lattice to provide 50% open and 50% blocked area. The holes on the blocks were projecting 1.0 cm FWHM (full-width-half-maximum) at the

Table 2. Palliative Response to grid Therapy. Reproduced from Mohiuddin *et al.* (1996) with Permission of the John Wiley and Sons, Inc and Wiley-Liss, Inc. Publishing.

Symptoms	# of TXs	# of PTs	CR	PR	CR+PR	NR	NE
Pain	32	29	8/29 (29%)	18/29 (62%)	26/29 (90%)	3/29 (10%)	3
Mass effect	35	27	6/31 (19%)	22/31 (71%)	28/31 (90%)	3/31 (10%)	4
Bleeding	5	5	3/4 (75%)	1/4 (25%)	4/4 (100%)	0	1
Overall	72	61	17/64 (27%)	41/64 (64%)	58/64 (91%)	6/64 (9%)	8

*CR = complete response; PR = partial response; NR = no response; NE = not evaluable

Table 3. Response Rate by Histology. Reproduced from Mohiuddin *et al.* (1996) with Permission of the John Wiley and Sons, Inc and Wiley-Liss, Inc. Publishing.

Histology	# of TXs	CR	PR	CR+PR	NR	NE
Sarcoma	18	8/18 (44%)	9/18 (50%)	17/18 (94%)	0	1
Squamous cell CA	13	4/13 (31%)	8/13 (61%)	12/13 (92%)	1/13 (8%)	0
Melanoma	6	3/60 (50%)	2/6 (33%)	5/6 (83%)	0	1
Adenocarcinoma	35	2/35 (6%)	22/35 (63%)	24/35 (69%)	5/35 (14%)	6

*CR = complete response; PR = partial response; NR = no response; NE = not evaluable

Table 4. Response Rate by Radiation Dose*. Reproduced from Mohiuddin *et al.* (1996) with Permission of the John Wiley and Sons, Inc and Wiley-Liss, Inc. Publishing.

Dose	# of TXs	CR	PR	CR+PR	NR	NE
GRID						
<1,500 cGy	32	9/29 (31%)	14/29 (48%)	23/29 (79%)	6/29 (21%)	3
≥1,500 cGy	40	8/35 (23%)	27/35 (77%)	35/35 (100%)	0	5
EXTERNAL BEAM						
0 cGy	32	8/28 (29%)	16/28 (57%)	24/28 (86%)	4/28 (14%)	4
<4,000 cGy	29	5/25 (20%)	18/25 (72%)	23/25 (92%)	2/25 (8%)	4
≥4,000 cGy	11	4/11 (36%)	6/11 (55%)	11/11 (100%)		

*CR = complete response; PR = partial response; NR = no response; NE = not evaluable.
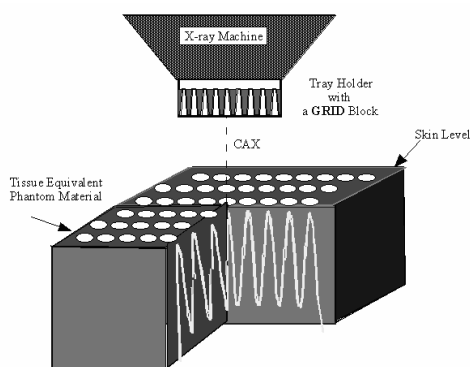
Figure 2. Schematic diagram of the beam profile from a grid block in a tissue equivalent phantom material.

isocenter of the beam with 1.8 cm center-to-center spacing. Various field sizes up to a maximum of 20×20 cm^2 at the level of the isocenter can be treated with this block.

The initial prototype of the grid block, used at university of Kentucky, was constructed by placing copper tubes between two lucite tray and filling the spaces between the tubes by cerroband (figure 3). The directions of the copper tubes were selected to match the beam angle for a particular X-ray machine, with the block in the block-tray of the linear accelerator. Since, the target to tray distance is not the same for different types of linear accelerators, one should construct a grid block for each machine type. Presently, these grid block are commercially available through Radiation Products Design Inc. (Albertville, MN). These blocks are designed and fabricated for different models of linear accelerators, with their specific geometric characteristics. Moreover, the blocks are mounted on
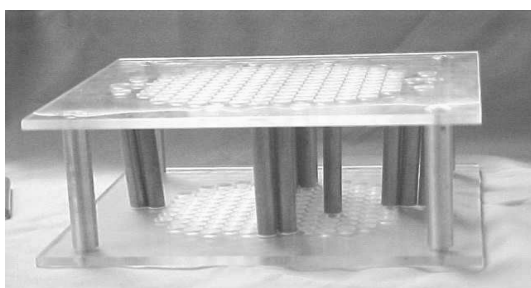

Figure 3. Schematic diagram of the main structure of the prototype GRID block, designed and fabricated at University of Kentucky.

rigid metal frames, for a better stability and reproducibility of the treatment field.

B. Dosimetry Technique
1- Experimental Procedures

Dosimetric characteristics of the grid irradiation field were determined by measuring the relative dose distribution in a plane perpendicular to the beam (i.e. beam profile) and also along the beam direction (i.e. percent depth dose). Beam profile of 6- and 18-MV X-rays were measured along two orthogonal directions (i.e., cross-plane and in-plane) in a tissue equivalent material (Solid Water, Radiation Measurements Inc., Middleton, WI) using Kodak radiographic film (Kodak, Kodak X-Omat V Film, Eastman Kodak Co., Rochester, New York, N.Y.). These measurements were performed at the depth of 5 cm for field sizes of 5×5, 10×10, and 20×20. In these measurements a 10 cm backscattering material were used to provide full scattering condition.

Absolute doses were measured at the center of the grid holes and also in the blocked areas of the grid (figure 4). These measurements were performed at the depth of maximum dose (dmax) using Thermoluminescent Dosimeter (LiFTLD-100, Harshaw Chemical Co, now Solon Technologies, Solon,

Figure 4. Schematic Diagram of TLD dosimetry. Points A and B represent the points inside the hole and in the shadow of the grid block.

OH) in Solid water phantom material. The irradiated TLDs were read using Harshaw TLD reader (Atlas 2000 A-B) and the film responses were converted to dose following the procedures described by Meigooni *et al.* (Meigooni *et al.* 1995). Each measurement consisted of at least four TLDs at each region. After reading the TLDs, they were annealed using the procedure recommended by Cameron *et al.* (Cameron *et al.* 1967).
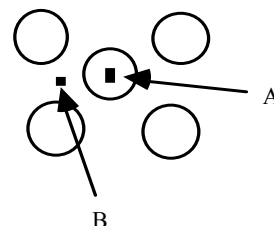
2- *Monte Carlo Simulations*

Monte Carlo simulations were carefully modeled to determine the dose profile n a grid radiation field similar to the experimental set-up, using MCNP Monte Carlo code. The simulations were performed, in water phantom material, for 6MV photon beam from EX21 machine was taken from the published paper (Sheikh-Bagheri and Rogers 2002). Figure 5 shows the grid pattern that was used in the Monte Carlo simulation. A history number of $5 \times x10^8$ was used in each simulation, which resulted in the statistical uncertainty better than 10%.

Figure 6. A radiographic image of the grid block field.

Figure 5. Schematic Diagram of grid block pattern used for Monte Carlo simulations.

RESULTS

Figure 6 shows the pattern of the grid holes at University of Kentucky that were obtained using a film dosimetry technique, at 5 cm depth in water equivalent material. Using this radiograph, the beam profile in two orthogonal directions of in-plane and cross-plane were measured. Figure 7 shows the beam profiles of 6 MV X-ray beam. This figure indicates that dose under the blocked regions of the grid was about 25- 30% of the dose at the center of the grid. Moreover, the variations of the FWHM of the absorbed dose under each grid hole were insignificant (within 0.2 mm). The differences between in-plane and cross-plane profiles are due to the pattern of grid holes. The small peaks in the in-plane profile represent the area between two grid holes. Similar results are seen
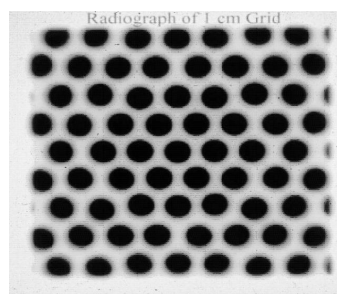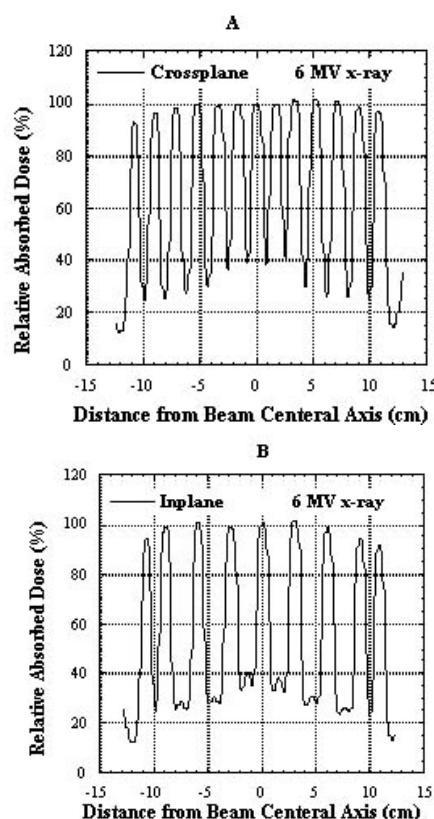

Figure 7. Crossplane (A) and inplane (B) dose profiles for 1 cm grid using 6 MV X-ray beam. Reproduced from Mohiuddin *et al.* (1999) with Permission of the

for 18 MV X-ray beam. Figure 8 shows a comparison between the 6 MV and 18 MV beam profile.

Figure 9 shows a comparison between the Monte Carlo simulated and measured dose profiles, for 6 MV X-ray beams. These results indicate that the Monte Carlo simulation method is capable to reproduce the measured data. One may use this capability to optimize the grid
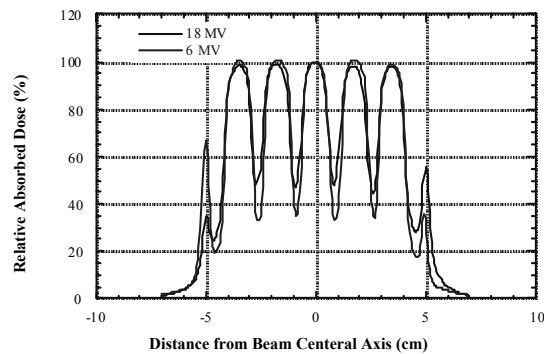
Figure 8. Crossplane dose profiles for 1 cm grid using 6 MV and 18 MV X-ray beams.
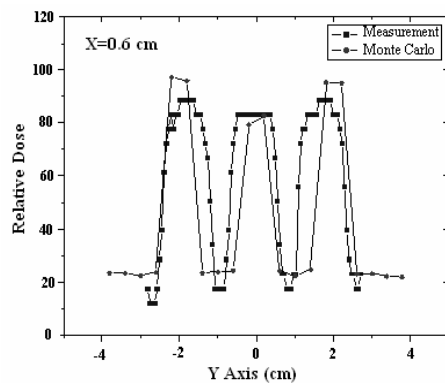

Figure 9. Comparison of the Monte Carlo simulated and measured Crossplane dose profiles for 1 cm grid using 6 MV X-ray beam.

whole size and pattern for the clinical applications. Figure 10 shows the 3D view of the grid dose distribution calculated using Monte Carlo simulations.

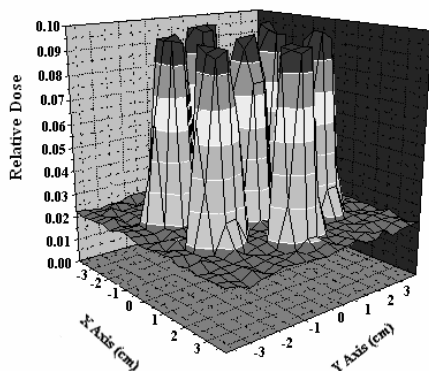The results of TLD measurements indicate a dose rate of 0.983 cGy/MU at the center of the

Figure 10. The Monte Carlo calculated 3D dose distribution of the grid field, using 6 MV X-ray beam.

grid holes, using the 6MV X-ray beam (table 5). However, doses in the blocked region of the grid, between the grid holes, were 25% and 44% of the dose in the center of the grid hole, for 6MV and 18 MV X-ray, respectively. The TLD data are in good agreement with the film dosimetry shown in figure 7.

Table 5. TLD measured dose rate at the center of grid hole (A) and under the shadow (B).

Photon Energy	Location	Measured Relative Absorbed Dose (at dmax)	
		cGy / M.U.	%
6 MV	A	0.983 ± 5%	100 ± 5%
------	B	0.25 ± 5%	25 ± 5%
18 MV	A	0.890 ± 5%	100 ± 5%
------	B	0.335 ± 5%	44 ± 5%

Figure 11 shows the radiochromic film measured percentage depth dose of the grid radiation field, along the CAX of a 6 MV X-ray beam, as compared to a 3×3 cm^2 open field data. Similar data has bean measured for 18 MV X-ray beams.
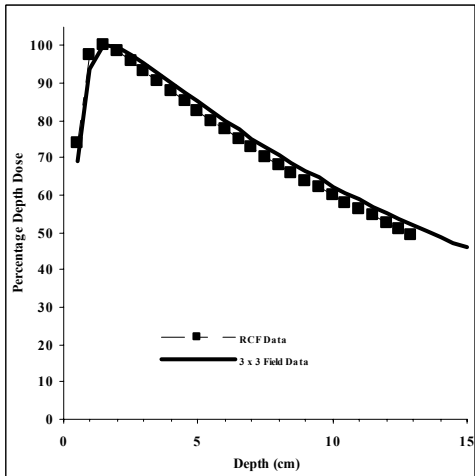

Figure 11. Comparison of the Percentage depth dose of a 6 MV grid field with the percentage depth dose of a 3×3 cm^2 open field.

DISCUSSION

The efficacy of grid therapy was determined in the 1950s through the use of orthovoltage X-ray radiation (Becker *et al.* 1956, Kaneda *et al.* 1965). Recently, there has

been renewed interest in the delivery of palliative treatment using megavoltage grid therapy (Mohiuddin *et al.* 1990, Maruyama 1989, Reiff *et al.* 1995, Urano *et al.* 1968). Beneficial treatment of large malignant tumors requires delivery of large doses of radiation through increased field sizes. However, the tolerance doses for normal tissues and stroma may be exceeded by such high doses of radiation. Grid therapy provides an alternative modality of treatment that can be used to compensate for these limitations. The success of grid therapy was based on the fact that small volumes of tissue could tolerate high doses of radiation. Since the development of megavoltage radiation and the concomitant skin sparing, grid therapy has been discontinued due to technological challenges caused by the higher beam energies. However, patients with massive or bulky tumors that produce complex symptoms pose a challenging problem for the oncologist. Urano *et al.* (1968) studied the grid (also known as sieve) method for tumor therapy in animal models and found that 1.23 times greater dose was required for tumor control but the skin and soft-tissue tolerance increased by a factor of 1.8. Therefore grid therapy gave rise to a gain factor of about 1.5. Maruyama *et al.* (1989) summarized the orthovoltage data from 1953 to 1989 and concluded that grid therapy may be a useful method for many radiation therapy situations if certain prescribed guidelines were followed. Some of his guidelines were based on the assumption that all of the tissues beneath the open area of the grid would get the full dose while the tissues under the blocked area would receive about 15% of the dose. The results of over 400 patients at University of Kentucky indicate the success of this treatment modality (Mohiuddin *et al.* 2002, 1999).

Dosimetric characteristics of grid radiation therapy have been investigated using experimental and theoretical techniques. The outputs of the X-ray beam were measured at the center of the grid holes and under the shadow of the block using the TLD chips and film dosimetry techniques. Dose rate of 6 MV and 18 MV X-ray beams from a Varian 2100 linear accelerator were found to be 0.983 cGy/MU and 0.89 cGy/MU, respectively. In addition, the dose rates in the shadow of the block were found to be 25% and 44% of the dose rates measured at the open portion of the grid (i.e. center of the holes), for the 6MV and 18 MV X-ray beams, respectively. Beam profile in orthogonal directions indicated a uniform pattern of dose distribution within the grid radiation field (i.e. dose rate at the center of the holes and underneath the blocked shadows were the same from one side of the field to the other).

The results of dose profiles for 6 MV X-ray beams obtained with from the Monte Carlo simulation technique was in good agreement with the measured data. In addition, the 3D dose distribution of the grid field generated by the Monte Carlo simulation gave more detailed information about the dose pattern of the grid. The Monte Carlo simulation technique can be utilized to optimize the pattern, size and spacing between the holes, for optimal clinical results.

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