

**IMRT TREATMENT DELIVERY EFFICIENCY - A MULTI-INSTITUTIONAL
RETROSPECTIVE STUDY**

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Running Title: Study of IMRT Treatment Efficiency

Acknowledgements:

The authors thank Mr. Larry Potter, Ms. Lydia Levinson and Mr. Christopher Waite-Jones for data collection at UNC, and Mr. Donald Sutton for data collection at ECU.

ABSTRACT

PURPOSE: To compare IMRT delivery efficiency in 6 institutions using different accelerators, IMRT delivery techniques, and treatment planning systems and to deduce key contributing factors for improvement.

METHODS AND MATERIALS: IMRT MUs, daily treatment delivery time, and other parameters from Record & Verify systems for 421 patients in 6 institutions using 4 different treatment planning systems are analyzed. IMRT treatments are delivered using compensator-IMRT on Siemens, segmental MLC-IMRT on Siemens, Elekta and Varian accelerators, and via TomoTherapy.

RESULTS: LINAC-based IMRT MUs increase with the number of fields per treatment and are 7 times less than TomoTherapy-IMRT MUs. The average MU ratio of LINAC-based IMRT to non-IMRT treatments is less than 2:1. The MLC-IMRT delivery time is proportional with the total number of segments per treatment. The shortest IMRT delivery times are associated with TomoTherapy (7.3 min.), plans using the least MLC segments (10.1 min.) and compensator-IMRT (11.3 min.) in average for 9-fld IMRT. Beam-ON time for all LINAC-based IMRT were < 2 min. or < 20% of IMRT delivery time.

CONCLUSION: LINAC-based MLC-IMRT delivery time largely depends on the number of segments per treatment. The influence of MU rate, number of fields, and MUs to the delivery time is small. Compensator-IMRT delivery time is comparable to the most efficient MLC-IMRT; TomoTherapy uses the shortest IMRT delivery time. MU rate has minor impact on LINAC-based IMRT delivery time; thus major improvement in the IMRT delivery efficiency requires significant reduction in MLC leaf motion and verification time.

Key Words: IMRT delivery, Treatment efficiency, Compensator-IMRT, MLC-IMRT, TomoTherapy.

Conflict of Interest: Thomas Mackie has financial interest in TomoTherapy Inc.

INTRODUCTION

Intensity-modulated radiotherapy (IMRT) commonly takes more time to deliver than conventional radiotherapy. Treatment delivery times impact both patient throughput and treatment quality because longer treatments are associated with more intra-fraction motion [1, 2]. IMRT treatment delivery *efficiency* can be characterized by its monitor unit (MU) usage and the time slot needed for schedule the patient treatment. There are several components in the patient treatment time and some of them, such as patient setup time using various forms of image guidance, are not directly related to the IMRT delivery technique used. However, one portion of the patient treatment time that is specifically dependent on the IMRT technique used and thus the efficiency to deliver IMRT treatment should be an important consideration in purchasing IMRT hardware and software. Generally, more MU usage leads to longer treatment delivery time but the exact relationship for IMRT treatments in different clinical situations has not been well understood. MU usage is also proportional to accelerator head leakage radiation and thus affects patient total body dose and secondary barrier radiation shielding design. The IMRT software component [3-7] is generally similar for all LINAC-based IMRT delivery hardware. Intensity-modulated treatment can be achieved using an MLC system on either the conventional LINAC-based systems, TomoTherapy [8], or compensators [9, 10]. MLC-IMRT forms the intensity modulation pattern by automatically changing MLC leaf configuration [11, 12] while compensator-IMRT provides static intensity modulation patterns [11] during treatment delivery. Although there are reported techniques that automatically exchange or form compensators during IMRT treatment [13, 14] most compensator-IMRT treatments today rely on manual compensator placement in the accelerator head. In recent years there has been a substantial increase in compensator-IMRT usage, largely due to the availability of commercial mail-in IMRT compensator fabrication services such as those offered by .decimalTM (121 Central Park Place, Sanford, FL 32771) and Oncology TechTM (5608 Business Park, San Antonio, Texas 78218). TomoTherapy is a special MLC-IMRT delivery approach [15,

16] that delivers radiation to a patient through 360 degrees of beam angle selection, one transverse slice at a time, using a rotating linear array binary collimator system of 64 MLC leaves. The rotation is considered as 51 arc segments. The modulation through any MLC leaf-pair is achieved by varying the time during an arc segment that the leaf is in the open state. TomoTherapy has the unique ability to form highly complex dose distributions but its delivery efficiency is perceived to be a concern.

Independent of the specific delivery software and hardware used, IMRT is generally regarded as time-consuming. The impact of prolonged treatment on patient throughput, patient motion, and even radiobiology has been areas of concern for IMRT treatment[17-21]. Vendors have made significant efforts such as increasing monitor unit (MU) rate in an attempt to shorten IMRT delivery time. There is a general belief that IMRT treatments use considerably more monitor units and thus need a higher accelerator workload compare to conventional treatments, leading to an increase in secondary barrier radiation shielding of accelerator vaults [22, 23].

The aim of this multi-institutional study is to better understand and quantify the impact of various clinical/treatment factors on IMRT treatment delivery efficiency in *multiple clinics* using *different* technologies. Clinical IMRT delivery efficiency depends on multiple factors and not all of them are studied in this work. Attempts to draw quick one-to-one correlation between IMRT delivery efficiency and any single aspect of the technology can be erroneous. Nonetheless, we hope this study can shed some light on this issue.

MATERIALS AND METHODS

Multi-institutional Study

Daily IMRT treatment data from 421 randomly selected patients treated in six institutions were studied. The six institutions included three academic institutions- University of North Carolina Medical School (UNC), East Carolina University Brody School of Medicine (ECU), and University

of Wisconsin (UW) and three community hospitals - Rex/UNC Hospital (Rex), Christiana Care Health System (CC), and Moses Cone Regional Cancer Center (MCR). Table 1 summarizes institutional information. The patients were all treated with curative intent at an average dose of 2 Gy per fraction with 97% of the patients treated at 1.8-2.5 Gy per fraction. The most common treatment sites and the number of patients enrolled per treatment site per institution are listed in Table 2.

Multi-system study

A variety of IMRT treatment hardware, software, and approaches are used in the six institutions. The accelerators are Siemens (Siemens Medical Solutions USA, Inc. 51 Valley Stream Parkway, Malvern, PA 19355 USA), Elekta (Elekta AB (Publ), Box 7593 SE-103 93 Stockholm Sweden), Varian (Varian Medical Systems, Inc. 3100 Hansen Way, Palo Alto, CA 94304-1038 United States), and TomoTherapy (TomoTherapy Incorporated, 1240 Deming Way, Madison, WI 53717-1954 United States). The treatment planning systems are PPlanUNC from UNC, ADAC Pinnacle (540 Alder Drive, Milpitas, CA 95035-7443, United States), CMS XiO (CMS, Inc. 13723 Riverport Drive, Suite 100 Maryland Heights, MO 63043 United States), and TomoTherapy Planning Station. The treatment record and verify systems are MOSAIQ and Multi-ACCESS (IMPAC Medical Systems, Inc. 100 Mathilda Place, Fifth Floor, Sunnyvale, CA 94086 United States), LANTIS (Siemens Medical Solutions USA, Inc. 51 Valley Stream Parkway, Malvern, PA 19355 United States), and the TomoTherapy integrated record and verify system. Five institutions provided data on LINAC-based MLC-IMRT, two institutions on compensator-IMRT, and one institution on TomoTherapy IMRT. For Siemens accelerators, the MLC-IMRT data are from both the older (58-leaf MLC) and newer (82-leaf MLC) generations of delivery hardware and control software. One dataset of non-IMRT treatment using the same accelerators as the IMRT treatments is also collected at one institution (UNC). Because non-IMRT conformal treatment delivery

techniques are relatively uniform among institutions, we expect that the dataset is representative of non-IMRT treatment from other institutions. Basic information on accelerator maker/model, IMRT delivery technique(s), treatment planning system, and other relevant factors including the version/model of IMRT delivery technology used in each cancer center are summarized in Table 1. All time-related data is averaged over 5 fractional treatments.

- a. Treatment monitor units (MUs)
- b. Treatment site
- c. MU rate
- d. Fractional dose
- e. IMRT delivery time
- f. IMRT Beam-ON time
- g. Time elapsed between fields

The IMRT delivery time is defined as time elapsed between beam-ON of the first field/segment and beam-OFF of the last field/segment. This definition is used as it excludes time that is unrelated to the specific IMRT delivery technique, i.e. it excludes time for patient setup and pre-treatment imaging. Any time spent *within* the IMRT delivery time, e.g. therapists going into the treatment room to exchange compensators between fields, is included. For TomoTherapy (radiation is ON throughout the treatment), IMRT delivery time can be calculated as the total number of MUs divided by the MU rate after an initial offset correction.

The IMRT beam-ON time is defined as the total amount of time when radiation is *actually* delivered. The time is estimated as the ratio of total monitor units (MUs) per IMRT treatment to monitor unit rate (MU/min). Although the actual IMRT beam-ON time can be somewhat different due to the delay of the accelerator control system, MU end effect, and MU rate fluctuation, these effects are thought to be insignificant. IMRT beam-ON time as a percentage of the IMRT delivery time is a strong indicator of the treatment efficiency. For instance, an IMRT treatment is not

efficient if it spends only 10% of the IMRT delivery time in actual radiation delivery; efficiency can be improved by shortening the IMRT delivery time when no radiation is given. For TomoTherapy, the IMRT beam-ON time equals IMRT delivery time.

The time between consecutive IMRT fields is defined as the time elapsed between beam-OFF of one field (not MLC segment) and beam-ON of the next field for conventional LINAC-based IMRT treatments. Data was either extracted from the record & verify system database or directly measured during actual patient treatments using a stopwatch. One institution (UNC) compared from the record & verify system with direct measurement for 10 patient treatments and found them to be similar (i.e. within 10 sec). The time between consecutive IMRT fields is a *portion* of the IMRT Delivery Time, and is very different between the automated MLC-IMRT and the manual compensator-IMRT treatment. TomoTherapy has nearly zero time between fields.

We hypothesize that TomoTherapy IMRT treatment efficiency has a different dependence compared to conventional LINAC-based systems. In this study we analyzed TomoTherapy IMRT delivery efficiency as a function of the volume and length of the planned treatment target (PTV), and of the complexity of the dose optimization. The complexity level is divided into simple (1), intermediate (2), and complex (3) based on complexity of the dose optimization goal, as judged by the planner. t UNC, non-IMRT patient treatment data as described above is also gathered for comparison to IMRT treatment on the same accelerator.

Correlation between two measurement variables, such as IMRT delivery time and MUs, is computed using CORREL correlation coefficient. The value of the CORREL coefficient varies between -1.0 and 1.0 where a negative value represents a reverse correlation, a positive value a proportional correlation, and a null value no correlation.

RESULTS

IMRT treatment MUs

Conventional LINAC-based delivery systems

Figure 1 shows the total number of MUs per IMRT treatment as a function of the number of fields per treatment for nine datasets (see Table 1) including the TomoTherapy IMRT and non-IMRT treatment datasets. Treatments with more fields (gantry angles) generally use more MUs but there is a lack of consistent correlation between MU usage and the number of fields per treatment in the datasets. Figure 1 shows that the compensator-IMRT tends to require fewer MUs than MLC-based techniques. Figure 2 shows the average ratio of IMRT MUs to non-IMRT MUs as a function of the number of fields per treatment. The IMRT MU data is averaged over all seven IMRT datasets using conventional LINACs; the non-IMRT data is from UNC only. The data shows that on average the IMRT treatments use at most twice as many MUs as corresponding conventional treatments.

Figure 3 shows the correlation between MLC-IMRT treatment MUs and the total number of MLC segments for three datasets (CCH-Siemens, UNC-Siemens, and Rex-Varian); segment data were not included in other datasets. IMRT MUs have a general trend to increase with the number of MLC segments however the data is variable. The data shown are from individual patients except for the Rex-Varian dataset, which are statistical data from a number of patients that received 5-, 7-, or 9-field IMRT treatments. The data is based on Rex's IMRT planning protocol (5-8 segments per field for 5 field IMRT, 8-10 segments per field for 6 and 7 field IMRT, 8-12 segments for 9 field IMRT).

TomoTherapy IMRT

Figure 1 shows that TomoTherapy IMRT treatment uses significantly more MUs than conventional LINAC based IMRT treatment. We found no correlation between TomoTherapy IMRT treatment MUs and the planning treatment volume or the level of treatment complexity was the average TomoTherapy IMRT MUs as well as the IMRT delivery time and the planning treatment volume (PTV) length as shown by the trend line in Figure 4. Such dependence is consistent with the nature of TomoTherapy's fan beam treatment delivery.

IMRT Delivery Time

Figure 5 illustrates IMRT delivery Time and non-IMRT delivery time as a function of the number of fields for all nine datasets. Generally, IMRT delivery time increases with the number of fields but there are significant variations among the datasets. Data from two institutions demonstrated that the *manual* compensator-IMRT techniques require significantly less IMRT delivery time compared to *automated* MLC-IMRT treatments using the same accelerator and treatment planning system. The large compensator-IMRT dataset (UNC-comp) represents the second fastest IMRT delivery time for LINAC-based IMRT delivery techniques.

Figure 6 reveals that IMRT delivery time on average has a linear correlation with the total number of MLC segment for the three datasets (UNC-Siemens, CCH-Siemens, Rex-Varian) for prostate and head and neck patients. Other sites comprised a very small portion of data for certain datasets and were not analyzed. Two types of accelerators and three different treatment planning systems were used, yet IMRT delivery time exhibited statistically very similar linear dependence on the total number of segment fields.

Figure 7 displays the correlation coefficients of IMRT delivery time and 1) total number of MLC segments per treatment for MLC-IMRT datasets, 2) total MUs for all datasets, and 3) total number of fields per treatment for all datasets.

Time between consecutive IMRT fields

Table 3 shows the average time between consecutive IMRT fields in five of the datasets. For MLC-IMRT treatments, the average time between fields varies from 35 to 75 seconds and 70 seconds for compensator-IMRT. Manual compensator-IMRT took 30 seconds more between fields than MLC-IMRT treatment on the same accelerator.

Beam-ON time

IMRT beam-ON time is the total time that radiation is *actually* being delivered during treatment. The time is calculated as the ratio of accelerator MU rate to the total MUs of the IMRT treatment. The IMRT beam-ON time is also expressed as the fraction of the IMRT delivery time and it is calculated as the ratio of the IMRT beam-ON time to the IMRT delivery time. For TomoTherapy, the ratio is one as radiation is on continuously. Figure 8a shows the beam-ON time as a function of the number of fields per IMRT treatment for all LINAC datasets. The non-IMRT treatment data represents the basic limitation of the treatment delivery speed using the current IMRT technology, which is less than one minute. All LINAC-based IMRT treatments studied used ≤ 2 minutes of average irradiation time.

Figure 8b illustrates IMRT Beam-ON time as a fraction of the Treatment Delivery Time. It shows that IMRT delivery time decreases as the number of fields per IMRT treatment increases. On average, the fraction of IMRT delivery time when radiation is on is very low – from 20% to 7% for IMRT treatments with 6 or more fields for all LINAC based IMRT technologies studied. This suggests that increasing MU rate (MU/min) alone is likely not an effective means to improve IMRT delivery time. Major IMRT delivery time efficiency improvement must come from reduction of the 80% of IMRT delivery time when radiation is actually off.

DISCUSSION**IMRT MU Usage**

This study suggests that MU usage is similar across 5 institutions using different accelerators, IMRT delivery techniques, treatment planning systems, and means of intensity modulation (i.e. fixed compensators, MLCs). The average IMRT to non-IMRT treatment MU ratio, also referred as the IMRT factor, is no more than 2 - a value that is significantly lower than some calculated values for accelerator vault secondary shielding [22]. TomoTherapy IMRT uses the most MUs - about 8

times more compared to the LINAC-based IMRT treatments as the fan-beam irradiates one slice of treatment volume at a time. To remedy the increased leakage radiation from the large MU usage TomoTherapy accelerator uses a primary collimator that is 1 TVL thicker than that of the conventional LINAC.

IMRT Delivery Time

Despite the large MU usage TomoTherapy IMRT has the shortest treatment time (average 7.3min.) among the IMRT datasets studied for the same fractional dose. The high treatment delivery time efficiency is largely due to the continuous radiation delivery with TomoTherapy. For LINAC-based treatments, our limited data suggest that IMRT delivery time differences among datasets seen in Figure 4 is largely due to the difference in the total number of MLC segments per treatment, which is determined mainly by the IMRT treatment planning approach, and not the difference in accelerator and MLC system (Fig. 6).

The manual compensator-IMRT is the second fastest LINAC-based IMRT treatment (average 11.3 min for 9-fld IMRT). The time between fields data show that compensator-IMRT uses only 30s more time per field than the corresponding MLC-IMRT treatment on the same accelerator. The time lost due to manual operation in the compensator-IMRT is an order of magnitude smaller than the time the MLC-IMRT treatment use for segment formation and position verification in the automated segmental MLC-IMRT treatment. The manual operation time also depends on the layout of the accelerator control console relative to the accelerator entrance, the size and design of the treatment room, and the type of the door to accelerator room. At UNC, the accelerator room has a maze but an unshielded door that is manually operated. Had an automatic shielded door been used instead, the time between fields for the compensator-IMRT would be longer.

IMRT beam-ON time

Our study reveals that less than 2 minutes of the LINAC-based IMRT delivery time is actually used for radiation delivery, which is 20% or less of the IMRT delivery time for average IMRT treatments (≥ 6 fields per treatment). The majority of IMRT delivery time (80%) is spent on preparation of radiation delivery – such as MLC segment field formation and verification for the MLC-IMRT, compensator exchange for compensator-IMRT, and gantry and collimator angle change and verification for all IMRT treatments. Thus accelerator MU rate does not have major impact on IMRT treatment delivery time in LINAC-based IMRT treatments. For instance, a doubling in MU rate (from 500 to 1000 MU/min) will only improve the IMRT delivery time by 10%.

IMRT delivery time and its correlation to other delivery parameters

Our data shows that the influence of different MLC/accelerator systems on the IMRT delivery time is small (Fig.6). In average a faster MLC system from Varian uses a slightly less IMRT delivery time than a slower MLC system from Siemens for IMRT treatment of a given number of segments. Based on our data (Fig. 6 -7) MLC-IMRT delivery time is best correlated with the total number of MLC segments per treatment. This correlation can be translated as such: MLC-IMRT delivery time has the best correlation with the total amount of time spent in MLC segment formation and verification because the actual beam-ON time is short. Total MUs and total number of fields per treatment have small impacts on IMRT delivery time are small although they have good correlations with IMRT delivery time (Fig. 8 and Table 3).

We did not attempt to study IMRT dosimetric quality, as this is an enormous task beyond the scope of this work. A recent multi-institutional attempt to correlate IMRT planning and treatment dosimetry among existing treatment planning systems including all systems used in this study failed to find a conclusive correlation [24]. It is reasonable to assume that the LINAC-based IMRT delivery comparison is performed under similar dosimetry quality in this study.

Dynamic MLC-IMRT technique is not studied in this work, as it is not used in any of the

participating institutions. It is reasonable to assume the corresponding dynamic MLC-IMRT treatment using the same number of MUs will have a lower IMRT delivery time. Direct aperture optimization based IMRT [25], which is able to significantly reduce the number of IMRT segment fields, is also not studied.

6. CONCLUSION

Different LINAC-based IMRT techniques applied to different accelerators use similar MUs for treatments of a given number of treatment fields while TomoTherapy IMRT use eight times more MUs. There is a wide spread among the 6 institutions in IMRT delivery time (time between the first beam-ON and the last beam-OFF) for treatments of a given number of treatment fields. Our data suggest that IMRT delivery time is linearly proportional to the total number of MLC segments per treatment. The three datasets with the fastest IMRT delivery times are associated with TomoTherapy unit, MLC-IMRT with the least number of MLC segments, and compensator-IMRT. Conventional LINACs are not efficient in the fixed-beam geometry IMRT delivery – generally only <20% of the IMRT delivery time is actually spent on radiation delivery. Thus significant reduction of the MLC-IMRT treatment delivery time requires a major reduction in time required for MLC leaf motion and position verification.

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Table Legends

Table 1. List of basic information on the nine datasets used in this study. The list includes the abbreviated name of each dataset, the associated institution, accelerator maker, IMRT delivery technique, and the treatment planning system used.

Table 2. List of number patients and the distribution common IMRT treatment sites for the 6 institutions participated in this study.

Table 3. List of the average time spent between two successive IMRT fields in five datasets. The time is defined as the average time elapsed between the beam-OFF of the previous field and beam-ON of the next field in clinical application.

Figure Legends

Figure 1. Total MUs as a function of the number of fields per treatment. The data point represents statistical data (average and standard deviation) from a number of patients treated with the same number of fields. Note: the horizontal axis is inaccurate for the TomoTherapy dataset as its treatment effectively has more than 50 fields.

Figure 2. Ratio of IMRT MUs and the non-IMRT MUs as a function of the number of fields per treatment. The IMRT MUs are averaged over all seven LINAC-based IMRT datasets (see Figure 1); the non-IMRT data is from one dataset (UNC-non-IMRT).

Figure 3. Total MUs per treatment as a function of the total number of segment fields per MLC-IMRT treatment (data from three institutions). The UNC-Siemens and CCH-Siemens datasets are per patient data. The Rex-Varian dataset is based on their IMRT treatment planning protocol for 5, 7, and 9 fields IMRT treatments. The error bars represent the minimum and maximum values in the x-axis and the standard deviation value in the y-axis.

Figure 4. Tomotherapy IMRT MUs vs. length of the planning treatment volume (PTV). The two linear fit lines are offset and due to a "warm up" time inherent in Tomotherapy treatments, where the beam is on for approximately 10 seconds with all MLC leaves closed at the beginning of treatment to allow the beam output to stabilize before treatment begins.

Figure 5. IMRT (non-IMRT) treatment delivery time as a function of the total number of fields per treatment. Data with no standard deviation means data is from a single patient.

Figure 6. MLC-IMRT delivery time vs. the total number of segments per IMRT. All data points are per patient data, except for one dataset where statistical data is given for patients received 5, 7, and 9 field IMRT. The error bars represent the minimum and maximum values in the x-axis and the standard deviation value in the y-axis.

Figure 7. Correlation coefficients of IMRT delivery time and 1) total number of segments per MLC-IMRT treatment, 2) total number of MUs, and 3) number of fields per treatment for all LINAC-based IMRT datasets. The non-IMRT dataset, which exhibits similar correlation as compensator-IMRT, is also included for comparison.

Figure 8. (a) Average IMRT radiation beam-ON time vs. number of fields per treatment; (b) Average beam-ON time as a fraction of IMRT delivery time for all LINAC-based IMRT and one non-IMRT dataset.

Table 1

Dataset	Institution	Accelerator Maker	IMRT Technique	TPS (Maker)
UNC- non-IMRT	University of North Carolina	Siemens Primus	Non-IMRT (MLC)	PLanUNC (UNC)
UNC- Siemens	University of North Carolina	Siemens Primus	Segmental MLC IMRT (82-leaf MLC)	PLanUNC (UNC)
UNC-comp	University of North Carolina	Siemens Primus	Compensator-IMRT (Block, MLC)	PLanUNC (UNC)
ECU- Siemens	East Carolina University	Siemens Primus	Segmental MLC-IMRT (58-leaf MLC)	XiO 4.33.02 (CMS)
ECU-comp	ECU	Siemens Primus	Compensator-IMRT (Block, MLC)	XiO 4.33.02 (CMS)
Rex-Varian	Rex Regional Hospital - UNC	Varian 2100	Segmental MLC-IMRT	ADAC (7.6)
MCR- Elekta	Moses Cone Reg. Cancer hospital	Elekta Precision	Segmental MLC-IMRT	XiO 4.33.02 (CMS)
CCH- Siemens	Christiana Care Hospital	Siemens Oncor	Segmental MLCIMRT (82 leaf MLC)	Pinnacle 8.0k (Varian)
UW-Tomo	University of Wisconsin (UW)	Tomotherapy Hi-Art	Fan beam IMRT (binary MLC)	Tomo planning station (Tomotherapy)

Table 2

Institution	H & N	Prostate	Breast	Brain	Pelvis	Lung	Other	Non-IMRT
Rex	7	42	0	0	0	0	1	0
ECU	7	10	17	4	6	4	7	0
MCR	10	27	0	1	0	0	2	0
CCH	10	30	1				13	0
UW	11	23	0	4	1	5	4	0
UNC	62	61	12	5	9	1	10	14
total pt /site	107	193	30	14	16	10	37	14
Total (%)	25%	46%	7%	3%	4%	2%	9%	3%
number of patients:	421							

Table 3

Dataset	Average time between fields
UNC-comp	70s
UNC-Siemens	45s
Rex-Varian	35s
MCR-Elekta	75s
ECU-Siemens	53s

Figure 2

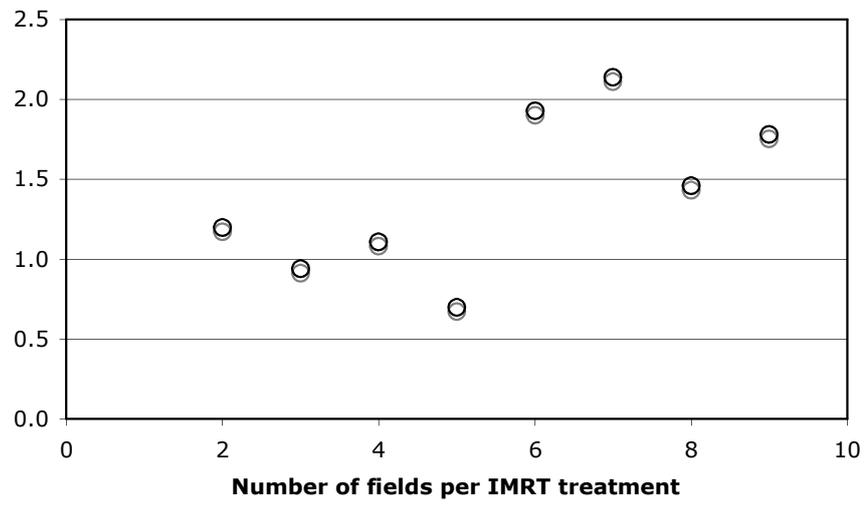


Figure 3

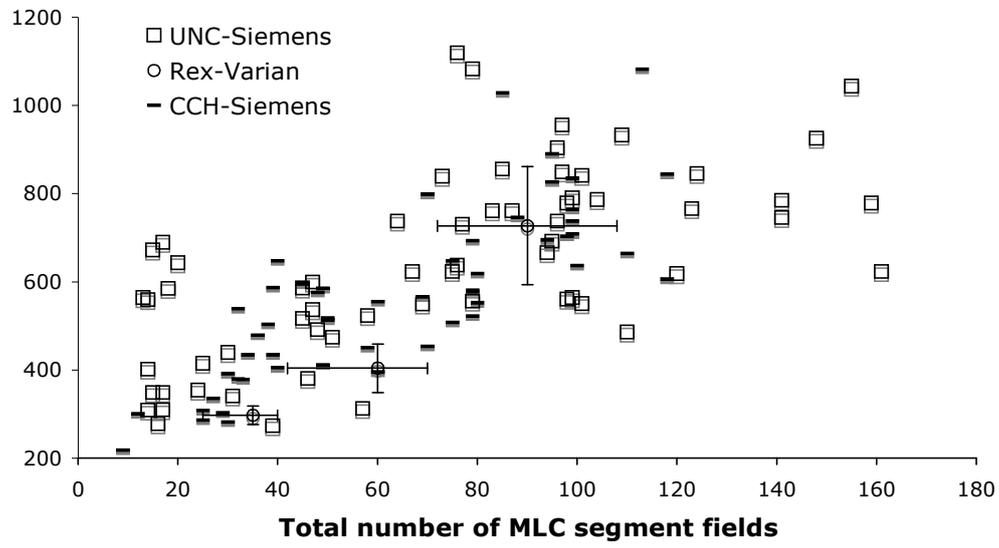


Figure 4

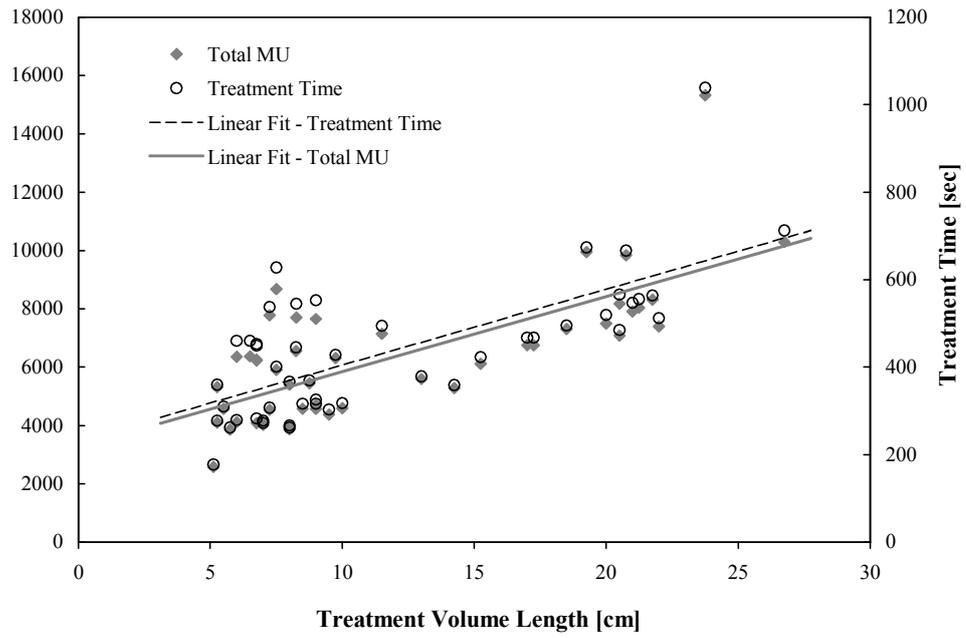


Figure 6

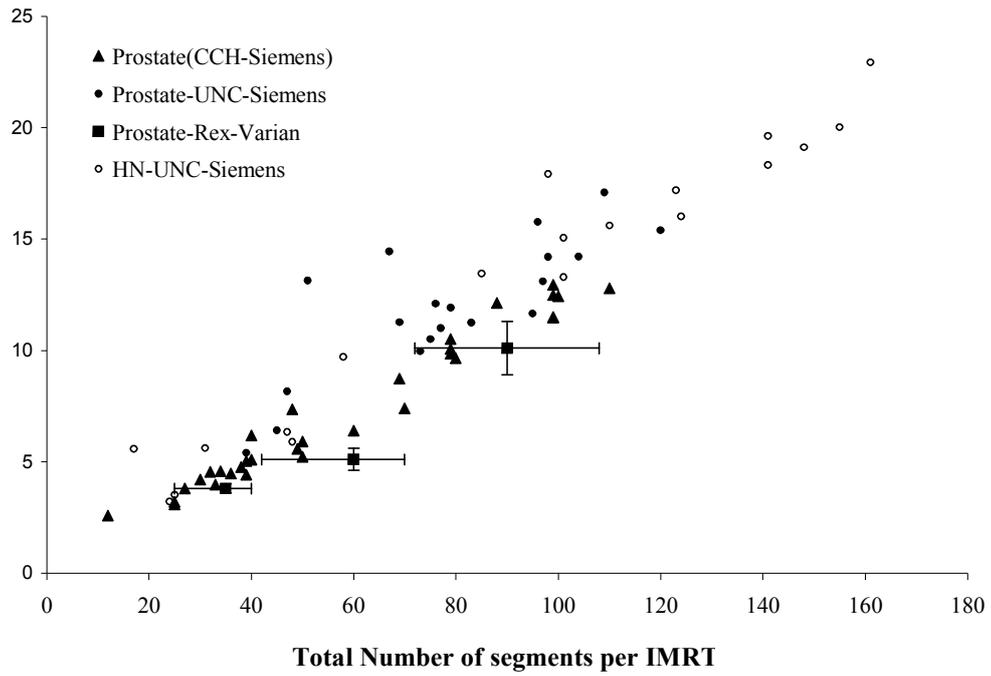


Figure 7

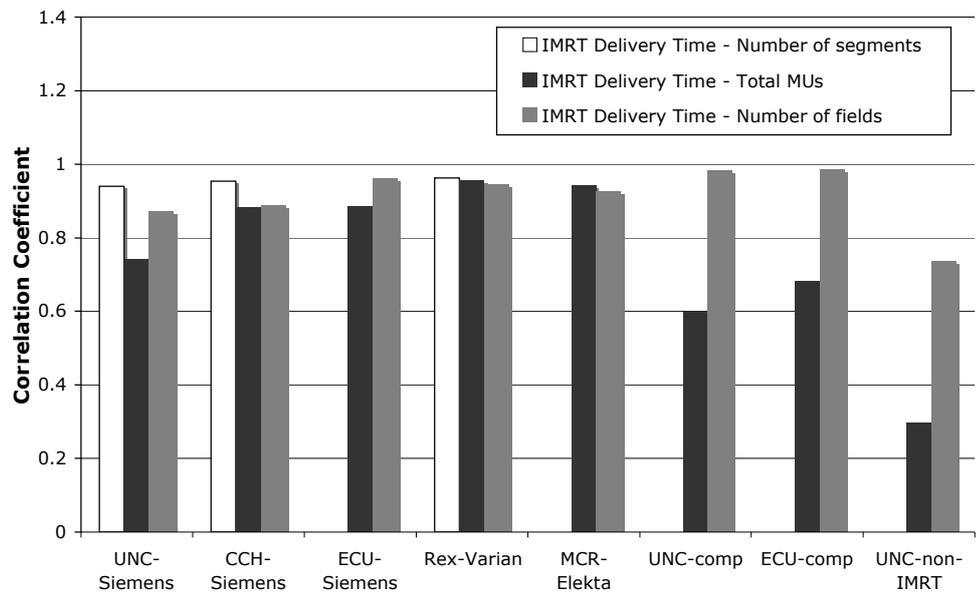


Figure 8a

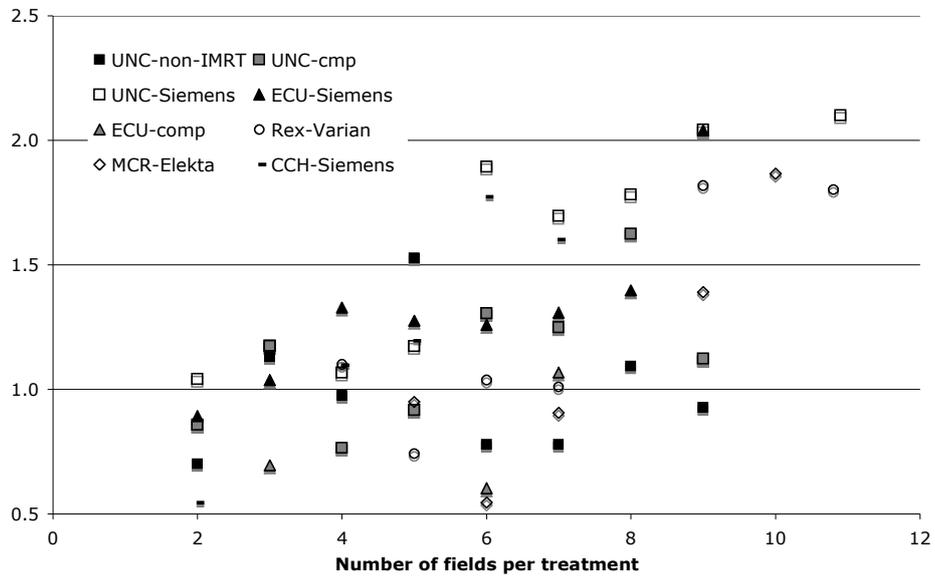


Figure 8b

