The effect of statistical noise on IMRT plan quality and convergence for MC-based and MC-correction—based optimized treatment plans

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Abstract. Monte Carlo (MC) is rarely used for IMRT plan optimization outside of research centres due to the extensive computational resources or long computation times required to complete the process. Time can be reduced by degrading the statistical precision of the MC dose calculation used within the optimization loop. However, this eventually introduces optimization convergence errors (OCEs). This study determines the statistical noise levels tolerated during MC-IMRT optimization under the condition that the optimized plan has OCEs <100 cGy (1.5% of the prescription dose) for MC-optimized IMRT treatment plans.

Seven-field prostate IMRT treatment plans for 10 prostate patients are used in this study. Pre-optimization is performed for deliverable beams with a pencil-beam (PB) dose algorithm. Further deliverable-based optimization proceeds using: (1) MC-based optimization, where dose is recomputed with MC after each intensity update or (2) a once-corrected (OC) MC-hybrid optimization, where a MC dose computation defines beam-by-beam dose correction matrices that are used during a PB-based optimization. Optimizations are performed with nominal per beam MC statistical precisions of 2, 5, 8, 10, 15, and 20%. Following optimizer convergence, beams are re-computed with MC using 2% per beam nominal statistical precision and the 2 PTV and 10 OAR dose indices used in the optimization objective function are tallied. For both the MC-optimization and OC-optimization methods, statistical equivalence tests found that OCEs are less than 1.5% of the prescription dose for plans optimized with nominal statistical uncertainties of up to 10% per beam. The achieved statistical uncertainty in the patient for the 10% per beam simulations from the combination of the 7 beams is ~3% with respect to maximum dose for voxels with $D>0.5D_{max}$. The MC dose computation time for the OC-optimization is only 6.2 minutes on a single 3 Ghz processor with results clinically equivalent to high precision MC computations.

1. Introduction

Although Monte Carlo (MC) dose calculation algorithms are recognized as the most accurate dose computation algorithms for treatment plan evaluation, they are rarely used for routine dose calculations or intensity modulated radiation therapy (IMRT) plan optimization outside of research centers due to the long computation times or extensive computational resources required to complete the process. To enable IMRT to benefit from the inherent accuracy of MC-based dose computations, this paper addresses methods to reduce the MC-dose computation time within the IMRT optimization processes, with an overall goal of creating optimized IMRT plans that are equivalent to those created with pure-high precision, MC based optimization in a clinically acceptable time frame. Specifically,
this paper investigates the maximum tolerable statistical uncertainty for MC dose calculations performed within an IMRT optimization loop such that the optimization convergence error (OCE) introduced by the statistical imprecision is less than 100 cGy, or ~1.5% of the PTV prescription dose. Both MC-based optimization and a MC-correction based optimization strategy are studied.

While literature exists on studies of the statistical precision required for MC-dose computations,[1-6] the question of what statistical precision is required for MC-based or MC-correction-based IMRT optimization remains un-answered. For 3D-CRT dose computations, Keall et al [2] found that an overall 1-sigma statistical precision of 2% was adequate for plan analysis based upon dose-volume histogram, iso-dose, and TCP/NTCP analysis. The effect of MC statistical noise on dose-volume histograms is to blur the dose volume histogram by a normal distribution with the achieved MC statistical precision.[2-4] Although Jiang et al [3] and Sempau and Bielajew [4] described methods which deconvolve the statistical noise and restore the “noiseless” DVH, such methods have not been taken advantage of for IMRT optimization systems, and the maximum permissible statistical noise has not been determined. Kawrakow [5] provided the theoretical framework for the effect of statistical noise on an IMRT objective functions and found that, near convergence, the IMRT cost function should converge as $1/N$, where $N$ is the number of particles simulated. Additionally, Kawrakow demonstrated that increased statistical uncertainty introduced systematic errors in the cost function that could be mathematically removed.

MC has been used for both bixel (beamlet)-based IMRT optimization [6-8] and full-field based [9-13] dose optimization. In bixel-based optimization, the incident fluence from each beam angle is subdivided into small rectangular elements (e.g. $1\times1$ cm$^2$ or $0.5\times0.5$ cm$^2$) and a one-time dose computation is performed to determine the dose contributions from each fluence element. The IMRT optimization then entails determining the bixel weights required to produce a given dose distribution. Following optimization, leaf sequences which will delivery the desired bixel fluence profile are determined, typically using the step-and-shoot IMRT delivery method. For bixel-based optimization, Ma et al [6] concluded that a 1-$\sigma$ statistical precisions of ~5% per beamlet (bixel) was adequate for optimization for a 5 field head-and-neck IMRT plan.

In the full-field dose optimization method, the dose is computed at each IMRT optimization iteration, thus allowing delivery effects (MLC leaf-scatter and leakage and leaf motion limitations) to be fully accounted for within the optimization. Repeated MC dose computation becomes time prohibitive with the full-field method. Even when plans are pre-optimized with a fast algorithm pencil-beam (PB) based dose computation algorithm, an average of 6.3 full field MC dose computation were required to optimize prostate treatment plans[11, 12].

To enhance the speed of full-field optimization, correction-based dose calculation methods, which utilize fast PB-algorithm with (MC-based) correction factors have been developed.[12, 14, 15] These methods reduce the required number of MC dose computations for prostate IMRT optimizations down to an average of 2.6 MC dose computations. Importantly, it has been shown that use of a single MC dose correction in the correction-based method is sufficient to produce clinically equivalent plans (all dose indices within 100 cGy or 1.5% of that for a full MC-IMRT optimized plan.), substantially reducing the MC dose computation time (factor of 6.3) compared to full MC-based optimization.

The studies of MC-optimization and MC-correction based optimization [12] used high-precision dose computations during the optimization to ensure that convergence errors due to statistical noise [1, 7, 16] could not negatively impact the results. Each beam was computed to a nominal statistical precision of 2% statistical uncertainty with respect to the maximum dose, resulting in an achieved statistical precision from the combination of the 7 beams of 0.9%. The time required for the optimizations were 700 CPU minutes$^1$ for the full MC-optimization, 326 CPU minutes for the full hybrid method, and 165 CPU minutes for the once-corrected (OC) optimization when patient doses were computed with the VMC++[17] MC algorithm. With only a single correction required for IMRT

$^1$ Time referenced to a single 3 Ghz Xeon processor running a 32-bit version of VMC++. Wall clock computation times were a factor of ~8 less due to the use of an 8 CPU computing cluster.
optimization, further time reductions for MC-based IMRT optimization are available through improved efficiency of the underlying MC codes or via the use of poorer statistical precision for the MC dose computations used within the IMRT optimization.

The objective of this work is to determine the maximum 1-σ combined statistical uncertainty that can be tolerated during MC-IMRT optimization under the condition that the OCEs in the optimized due to the MC statistical imprecision is less than 1.5% for MC- and OC-optimization strategies. The secondary objective is to determine the minimum time required to complete MC-based optimization strategies.

2. Materials and Methods

2.1. Test cases and evaluation metrics

Seven-field prostate IMRT treatment plans for 10 prostate patients are used in this study. Details of the plan generation and the objective function are given in references [12, 18]. The simultaneously integrated boost patient plans are optimized with a dose-volume based objective function for seven 18 MV beams at beam angles of 30°, 80°, 130°, 180°, 230°, 280°, and 330°. The two PTV and 10 OAR dose volume objective function metrics used in the optimization are given in the legend of Figure 3. The dose matrix resolution was 4×4×4 mm³ and covered the CT-scanned patient volume above the treatment table.

Plans are evaluated by comparison of isodose lines, dose-volume histograms, and evaluation of the dose-volume histogram metrics used by the optimization system. For the MC optimizations performed with statistical precision of N%, the optimization convergence error (OCE) for dose-volume metric x was evaluated by computing $OCE_{x}^{\text{MC}} = D_{x}^{\text{opt}} - D_{x}^{\text{MC}}$ where $D_{x}^{\text{MC}}$ is the dose from the N% MC optimization recomputed at a nominal statistical precision of 2% per beam. Similarly, the OCE for the once-corrected hybrid method is $OCE_{x}^{\text{OC}} = D_{x}^{\text{MC}} - D_{x}^{\text{OC}}$. An equivalence test is carried out by simultaneously using two one-tailed paired t-tests to determine the interval size consistent with the hypothesis that the method tested is equivalent to the $D_{x}^{\text{MC}}$ method. If the dose interval is less than 1 Gy (1.5% of the 65 Gy PTV dose), the methods are considered to be clinically equivalent.

2.2. Optimization strategies

Details of the two IMRT optimization methods used in this study which incorporate MC dose calculations are given by Siebers et al.[12]. Briefly, the optimizations are initialized with intensities and leaf sequences obtained from a pre-optimization which used a PB dose calculation algorithm and deliverable-based IMRT optimization[19]. In general, pre-optimization reduces the number of MC-based optimization iterations required. The first method (MC) utilizes MC dose computations throughout the optimization process, that is, after each intensity update; the dose is recomputed using the MC dose calculation algorithm for the objective function evaluation. The second method (once-corrected or OC) utilizes only a single MC dose calculation during the optimization. After the PB-based pre-optimization, the beams are recomputed with MC. The difference between the MC and PB doses are used to compute voxel-by-voxel correction factors for each beam. (The voxel-by-voxel correction factors for each beam are $C = D_{\text{MC}}^{\text{pre}} - D_{\text{FB}}^{\text{pre}}$, where the pre indicates these computations are performed using the leaf sequences resulting from the PB-based pre-optimization) During the optimization iterations, the second method use $D_{\text{FB}} + C$ for dose and objective function evaluation. The interested reader is referred to {Siebers, 2007, 2007Hybrid} for details on the second (correction-based) method and justification for using only a single MC-based correction. For each method, after optimization convergence, a high-precision MC dose computation is performed to enable OCE analysis.
Per beam nominal statistical precisions of 2, 5, 8, 10, 15, and 20% are used for the MC and OC optimization methods. These values are chosen since the 2% per beam corresponds with the statistical precision that was used in previous studies [11, 12] and the 20% extends beyond the range where significant OCEs (>1.5% of the prescription dose) are observed.

2.3. MC simulation run details
MC dose computations were performed using the VMC++ MC code[20]. Source particles are obtained as follows: For each treatment beam, particles are sampled from a previously commissioned phase-space data file (PHSP1) [21-23] which contains sample particles immediately upstream of the treatment jaws. The number of source particles required for a given statistical precision is pre-selected using values from phantom-based commissioning simulations to give a statistical precision close to the desired nominal value. The BEAMnrc MC code[24] is used to transport particles through the treatment head jaws, and surviving particles are written to an exit phase space (PHSP2). Since the optimization does not change the treatment jaws settings, the PHSP2 simulation is not repeated within the optimization loop. The per-iteration dose computations begin with sampling particles from the PHSP2 file and transporting them through the moving multi-leaf collimator (MLC) using an in-house algorithm [25]. To reduce stochastic fluence deviations, the MLC particle transport module was configured so that a given source particle will see the same random number sequence each iteration that the MLC module is run, (independent of the MLC control file). This results in the source particle being sampled at the same fractional MU instances of the dMLC delivery, and the same Compton scattering angle being selected for the scattered photons. (Note, the exiting primary and scattered particle weights will change since the MLC leaf sequence changes). Primary and scattered particles exiting the MLC are used as the VMC++ source. Following completion of the per beam dose computations, dose results are directly imported into the Pinnacle3 treatment planning system (Philips Medical Systems, Fitchburg, WI) for evaluation and use in our in-house IMRT program. [26].

3. Results
For each patient, the isodose lines and the DVHs produced by the MC-based and OC-based optimizations are clinically equivalent. Figure 1 compares the DVHs produced at the end of the optimization with each statistical precision before the high-precision re-computation of the fields for a typical patient. For both the MC and OC-based optimizations, the DVHs at the end of the optimization are characteristic of DVHs that result from the addition of statistical noise to MC dose calculations, effectively a convolution of the DVH with the combined statistical uncertainty [2, 4, 6]. DVHs for the same plans, recomputed at high precision, are given in Figure 2. The dose to the targets and critical structures increases with the statistical uncertainty used during the optimization, apparently to compensate for the “under dosing” of target voxels due to statistical noise during the optimization step.

The root-mean-square OCE for each structure (averaged over all ten patients) as a function of the per beam statistical precision is given in Figure 3 for the MC-optimized and OC-optimized plans. Results of the equivalence tests are summarized in Table 1. For both the MC-based and the OC-based optimization, the nominal statistical precision must be 10% per beam or less to introduce less than a 100 cGy dose error.
Figure 1: Dose volume histograms at the end of the optimization (before the high-precision recalculation) for the a) MC-based optimization and b) OC-based optimization. The statistical uncertainties given in the legend are the nominal per beam values. See the text and Table 2 for the combined statistical uncertainties for each nominal per beam value.

Figure 2: Final dose-volume histograms recomputed with nominal 2% statistics per-beam for the (a) MC-optimized and (b) OC optimization method with the nominal per beam statistical precisions as listed in the legend. Also given, for reference, is the MC optimization preformed with a nominal 2% per beam statistical precision which was used as the OCE reference. See the text and Table 2 for the combined statistical uncertainties for each nominal per beam value.

Figure 3: Root mean square optimization convergence error with the (a) MC-optimized and (b) once-corrected optimization method for different per beam nominal statistical precisions. The pure MC-optimization with a nominal 2% per beam statistical precision was used as the reference standard for the OCE computation. See the text and Table 2 for the combined statistical uncertainties for each nominal per beam value.
Table 1: Dose window size (in cGy) required to state optimization results are equivalent to the MC nominal 2% per beam statistical optimization result for each nominal per beam statistical precision studied. The shaded boxes are above the 100 cGy threshold. See the text and Table 2 to convert the nominal per beam statistical uncertainties to the combined statistical uncertainties for the plan.

|       | 2%  | 5%  | 8%  | 10% | 12% | 15% | 20% |
|-------|-----|-----|-----|-----|-----|-----|-----|
| MC    | --  | 77  | 47  | 88  | 131 | 214 | 180 |
| OC    | 40  | 63  | 51  | 67  | 130 | 195 | 181 |

The statistical uncertainty achieved from the combination of the multiple beams in the patient are listed in Table 2. Values are given with respect to the local dose and with respect to the maximum dose. These values are computed via

$$\sigma_{D_{\text{local}}} = \sqrt{\frac{1}{N_{D>0.5D_{\text{max}}}} \sum_{D_{i}>0.5D_{\text{max}}} \left( \frac{D_{i}}{D_{\text{max}}} \right)^2}$$

and

$$\sigma_{D_{\text{max}}} = \sqrt{\frac{1}{N_{D>0.5D_{\text{max}}}} \sum_{D_{i}>0.5D_{\text{max}}} \left( \frac{\sigma_{D_{i}}}{D_{\text{max}}} \right)^2},$$

where the summation runs over the voxels with $D > 0.5D_{\text{max}}$ and $D_{\text{max}}, \sigma_{D_{i}}$ are due to the sum (quadrature sum for $\sigma_{D_{i}}$) over the 7 beams for each patient. These definitions follow directly from the recommends of the ICCR 2000 meeting [27]. The nominal 10% per beam statistical precision required to introduce less than a 100 cGy dose error (above) corresponds with an achieved statistical precision of ~3% with respect to $D_{\text{max}}$. This is in general agreement with ~2% precision with respect to $D_{\text{max}}$ recommended for 3D clinical plan evaluation. {Keall, 2000, 0010757600}

Also listed in Table 2 is the CPU time required to complete the MC-optimization, the complete hybrid optimization (described in reference [12]) and the OC-optimization. The times are scaled to a single 3 Ghz CPU running 32 bit versions of the MC codes. The times tallied for each method include the MC transport though the treatment jaws only once (creation of PHSP2), as this calculation does not need to be repeated for further optimization iterations at the same statistical precision. For the OC method, this single BEAMnrc simulation utilizes ~40% of the total CPU time, with the transport through the MLC and patient requiring 6% and 54% respectively. This indicates that a major speed improvement for the OC method will come from reducing the time required to source particles for the VMC++ MC algorithm.

Table 2: Achieved statistical precision and dose computation times for MC-based IMRT optimization with 4×4×4 mm³ voxels (averaged over all patients). Times are scaled to a single 3 Ghz processor running 32 bit versions of the MC transport codes. For each calculation type, the time includes the time to run particles through the jaws using the BEAMnrc Monte Carlo user code once. The Hybrid method is described in reference [12].

| Statistical Precision (%) | Dose Calculation Time Required for Optimization (min) |
|---------------------------|---------------------------------|
| Nominal Per Beam          | $\sigma_{D_{\text{local}}}$ | $\sigma_{D_{\text{max}}}$ | MCopt | Hybrid | One Correction |
| 2                         | 0.9                            | 0.6                           | 700    | 326    | 164           |
| 5                         | 2.4                            | 1.5                           | 102    | 48     | 25            |
| 8                         | 3.7                            | 2.4                           | 40     | 18.6   | 9.6           |
| 10                        | 4.7                            | 3                             | 25.7   | 12.1   | 6.2           |
| 12                        | 5.6                            | 3.5                           | 17.6   | 8.3    | 4.3           |
4. Conclusions
The MC statistical precision required for full-field based IMRT optimization for 7 field prostate IMRT plans was determined. For both full MC optimization and OC optimization, if the nominal statistical precision is 10% per beam or better (achieved combined statistical precision of $\overline{\sigma}_{D_{\text{ref}}} \leq 4.7\%$ and $\overline{\sigma}_{D_{\text{max}}} \leq 3\%$ for voxels with $D > 0.5D_{\text{max}}$) then the OCE introduced by MC statistical uncertainties is less than 100 cGy, or 1.5% of the prescription dose. Using the OC method, plans with this statistical precision can be optimized with only 6.2 CPU minutes required for the MC dose computation. However, clinical use of the MC dose calculation will require the overall statistical precision in the dose that is reviewed and approved by the physician to have a ~2% statistical precision.[2] To achieve this, a ~5% per beam statistical precision dose calculation would have to be run following optimization, requiring an additional 25 CPU minutes on the present hardware.

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