Influence of multiple brain metastases’ size and number on the quality of SRS – VMAT dose delivery

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Abstract. Stereotactic radiosurgery with volumetric modulated arc therapy (SRS-VMAT) has recently been introduced for treatment of multiple brain metastases with a single isocenter. The technique’s high efficiency is nevertheless dependent of metastatic tumors’ characteristics such as size and number. In this work the impact of the metastases’ size and number on the plan quality indices clinically used for plan evaluation and acceptance is investigated. Fifteen targets with a diameter of 1 cm and average volume of 0.7 cm³ and ten targets with a diameter of 2 cm and average volume of 6.5 cm³ were contoured on an anonymized patient CT dataset, in Monaco (Elekta) treatment planning system. VMAT plans for different target volumes (1 and 2 cm in diameter) and various target numbers (1–15) were generated using four non-coplanar arcs and the Agility (Elekta) linear accelerator (5 mm MLC width) using a Monte Carlo dose calculation algorithm and 1mm dose calculation grid resolution. Conformity index (CI), gradient index (GI) and heterogeneity index (HI) were determined for each target. High quality plans were created for both 1 cm and 2 cm in diameter targets for limited (<6) number of targets per plan. For increased number of irradiated targets (>6) both CI and GI, clinically used for plan evaluation and acceptance, were found to deteriorate.

Keywords: multiple brain metastases, stereotactic radiotherapy, radiosurgery, vmat

1. Introduction
Metastases to the brain are the most common brain tumor and over the past decade, fundamental treatment approaches such as surgery and/or stereotactic radiosurgery (SRS) have been exploited in order to deal with the metastatic tumors [1]. Multi-isocenter Volumetric Modulated Arc Therapy (VMAT) has been introduced as a beneficial SRS treatment technique since it delivers a precisely-sculpted 3D dose distribution with a 360-degree rotation of the gantry in a single or multi-arc treatment using a dynamic multileaf collimator (MLC), variable dose rate and variable gantry speed. Therefore, SRS VMAT offers reduced treatment time as compared with other techniques [2], [3], [4] and high dose conformity while sparing the surrounding healthy tissue. Recent in-depth investigations featured that multi-arc non-coplanar VMAT with a single isocenter equally provides high quality treatment plans [2], [4], [5], [6], [7], [8], [9], [10]. According to those investigations, single-isocenter VMAT technique further shortens the treatment time of SRS for
multiple metastases (multi-meta), while preserving its high efficiency. However, the technique’s high efficiency can be limited because of its correlation with metastatic tumors’ characteristics such as size and number. Warnick et al. [1] reported that patients with six or fewer recurrent tumors are usually treated by SRS to all progressive lesions that are smaller than 3.5 cm since at larger volumes, the radiation fall-off into the adjacent normal brain is not as steep and the risk of radiation injury increases exponentially.

In this study, the impact of the metastases’ size and number on the plan quality indices clinically used for plan evaluation and acceptance is investigated for single-isocenter multi-arc non-coplanar VMAT technique.

2. Materials and Methods

2.1. Target Contouring
Elekta’s Monaco, version 5.10, treatment planning system (TPS) was used for target volume delineation and plan preparation. Taking into consideration that the typical metastatic tumor is spherical, discrete, and contrast enhancing [1], fifteen spherical targets with a diameter of 1 cm and average volume of 0.7 cm³ and ten spherical targets with a diameter of 2 cm and average volume of 6.5 cm³ were contoured on an anonymized patient CT/MR dataset.

2.2. Treatment Planning
The treatment planning is performed using Monaco optimization process which is carried out in two stages. In the first stage, the optimizer produces the preliminary result - an ideal fluence distribution - in order to evaluate how accurately the cost functions achieve the planning goals. The second stage performs the segmentation, which includes optimization of the segment shapes and weights, so that deliverable fields are obtained. Eight multi-meta VMAT plans were generated for various target numbers (1-15) and target diameter equal to 1 cm. Similarly, six multi-meta VMAT plans were generated for various target numbers (1-10) and target diameter equal to 2 cm. Single-isocenter non-coplanar SRS VMAT plans were prepared with a 360º arc (couch angle: 0º), three half arcs (couch angles: 45º, 90º, 315º) and the Agility (Elekta) linear accelerator with 5 mm MLC width with a dose prescription of 20 Gy in a single fraction for all the irradiated targets.

In addition, X-Ray Voxel Monte Carlo (XVMC) dose calculation algorithm [11] and 1mm dose calculation grid resolution were used. Monte Carlo (MC) method is considered as the most accurate method for dose calculation in radiotherapy. However, MC simulations are time consuming and need high performance computing to be time efficient and practical in use. XVMC is a fast MC algorithm for photon beams that dramatically reduces computational times. Compared to full MC simulations, in XVMC various approximations on the particle transport are made. At first a fast electron transport algorithm is used. Second, a fast ray tracing method is used to calculate the number of electrons created in each voxel by the primary photon beam. To reduce the calculation time even further several variance reduction techniques are used while the accuracy of the calculated dose is maintained. In the final stage a pre-calculated virtual energy fluence model, based on measurements of the linear accelerator and MC calculations is utilized.

2.3. Plan evaluation tools
Paddick’s conformity index (PCI) and gradient index (PGI) were calculated for all the generated plans [12], [13]. Moreover, heterogeneity index (HI) and target coverage V_{20Gy} (%) were exported from Monaco TPS. The values of the indices will be compared for different target volumes (1 and 2 cm in diameter) and various target numbers (1-15), in order to evaluate the clinical feasibility of the plans.

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\text{PCI} = \frac{TV_{\text{PIV}}^2}{TV \times \text{PIV}} \quad (1), \quad \text{PGI} = \frac{\text{PIV}_{50\%}}{\text{PIV}} = \frac{V_{10}}{V_{20}} \quad (2), \quad \text{HI} = \frac{D_{5\%} \text{ of target receiving } D_{\text{max}}}{D_{95\%} \text{ of target receiving } D_{\text{min}}} \quad (3)
\]
3. Results & Discussion
The results of the calculated indices clinically used for plan evaluation and acceptance for the different plans with different size and number of targets are presented in the Tables 1 and 2 as follows.

Table 1. The effect of varying number of targets on plan evaluation parameters is presented in parts (a), (b) and (c), for targets with diameter equal to 1 cm and average volume of 0.7 cm³.

| targets no. | V_{20Gy} (%) | PCI | PGI | HI |
|-------------|---------------|-----|-----|----|
| (a)         |               |     |     |    |
| 2           | 99% 0.70      | 3.50| 1.47|    |
|             | 96% 0.77      | 3.65| 1.56|    |
| 4           | 93% 0.36      | 3.79| 1.52|    |
|             | 97% 0.72      | 3.87| 1.49|    |
|             | 97% 0.75      | 3.71| 1.52|    |
|             | 96% 0.37      | 3.80| 1.48|    |
| 6           | 89% 0.79      | 3.97| 1.60|    |
|             | 85% 0.76      | 4.30| 1.55|    |
|             | 84% 0.80      | 5.37| 1.45|    |
|             | 82% 0.75      | 4.77| 1.46|    |
|             | 81% 0.78      | 5.14| 1.43|    |
|             | 85% 0.79      | 4.67| 1.47|    |
| 8           | 90% 0.77      | 4.93| 1.62|    |
|             | 88% 0.79      | 4.25| 1.55|    |
|             | 80% 0.77      | 5.68| 1.41|    |
|             | 82% 0.75      | 5.17| 1.50|    |
|             | 82% 0.71      | 5.19| 1.53|    |
|             | 81% 0.80      | 5.54| 1.45|    |
|             | 83% 0.76      | 5.71| 1.41|    |
|             | 84% 0.79      | 5.36| 1.46|    |

Table 2. The effect of varying number of targets on plan evaluation parameters is presented in parts (a) and (b), for targets with diameter equal to 2 cm and average volume of 6.5 cm³.

| targets no. | V_{20Gy} (%) | PCI | PGI | HI |
|-------------|---------------|-----|-----|----|
| (a)         |               |     |     |    |
| 2           | 98% 0.95      | 2.82| 1.54|    |
|             | 96% 0.93      | 2.88| 1.40|    |
| 4           | 97% 0.90      | 3.28| 1.37|    |
|             | 97% 0.91      | 3.57| 1.30|    |
|             | 97% 0.92      | 3.15| 1.32|    |
| 6           | 96% 0.91      | 4.47| 1.22|    |
|             | 93% 0.88      | 4.44| 1.21|    |
|             | 97% 0.92      | 5.22| 1.19|    |
|             | 96% 0.87      | 4.37| 1.22|    |
|             | 95% 0.90      | 5.11| 1.20|    |
|             | 95% 0.90      | 4.75| 1.20|    |
| 8           | 65% 0.27      | 6.24| 1.24|    |
|             | 90% 0.88      | 5.11| 1.25|    |
|             | 74% 0.45      | 5.83| 1.30|    |
|             | 68% 0.40      | 5.90| 1.23|    |
|             | 82% 0.42      | 5.28| 1.24|    |
|             | 86% 0.57      | 5.74| 1.25|    |
|             | 86% 0.84      | 5.28| 1.23|    |
|             | 89% 0.88      | 4.93| 1.25|    |

| targets no. | V_{20Gy} (%) | PCI | PGI | HI |
|-------------|---------------|-----|-----|----|
| (b)         |               |     |     |    |
| 2           | 68% 0.29      | 7.55| 1.28|    |
|             | 62% 0.43      | 8.20| 1.32|    |
|             | 61% 0.38      | 7.97| 1.29|    |
|             | 80% 0.50      | 5.69| 1.32|    |
| 10          | 63% 0.36      | 7.35| 1.25|    |
|             | 47% 0.25      | 7.33| 1.33|    |
|             | 59% 0.35      | 6.68| 1.30|    |
|             | 87% 0.58      | 6.01| 1.29|    |
|             | 81% 0.79      | 5.82| 1.31|    |
|             | 83% 0.54      | 5.26| 1.29|    |
Results reveal that conformity index (PCI) strongly depends on the size and number of multiple metastases. For less than 6 targets, an excellent PCI value is observed and highly conformal plans are achieved independent of target size. For more than eight multiple targets of 1 cm in diameter and more than six targets of 2 cm in diameter, PCI deteriorates resulting in poor plan quality. Gradient index (PGI) depends significantly on the number of the irradiated targets and deteriorates (i.e. dose to normal tissues increases) as this number increases. For limited number of targets (<8) both indices are superior for the larger target size (2 cm) and deteriorate for the smaller target size mainly due to the limited MLC width (5 mm) of the linear accelerator used (Elekta, Agility).

For each arc, during successive segments, the MLC leaves adjust dynamically in order to deliver dose sequentially to a certain number of targets. During the leaf travel, low dose spillage is delivered through the MLC openings to parts of the healthy brain leading to PGI deterioration. McDonald et al. showed a noticeable low dose spillage and also reported that increasing the number of metastases and increasing the target dispersion this effect is exacerbated [3], which is also confirmed in this study. The increase in low dose spillage may be the result of the island blocking problem which occurs when two or more targets share the same MLC leaf pair, resulting in an area of normal brain tissue that is not blocked by the MLCs [14].

4. Conclusion
For limited number of targets (≤ 6), high quality plans are achieved with single-isocenter VMAT technique. For six or less in number targets (1-2 cm in diameter) the dose distribution conforms very well to the shape and size of each target, and also the dose fall-off outside the target is steep, providing the optimal dose delivery to the lesions and the optimal radioprotection of healthy brain. For increased number of irradiated targets (>6) both conformity and normal tissue sparing were found to deteriorate.

5. References
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