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Treatment planning for MLC based robotic radiosurgery for brain metastases: plan comparison with circular fields and suggestions for planning strategies

Abstract: To evaluate the possible range of application of the new InCise2 MLC for the CyberKnife M6 system in brain radiosurgery, a plan comparison was made for 10 brain metastases sized between 1.5 and 9cm^3 in 10 patients treated in a single fraction each. The target volumes consist of a PTV derived by expanding the GTV by 1mm and were chosen to have diversity in the cohort regarding regularity of shape, location and the structures needed to be blocked for beam transmission in the vicinity. For each case, two treatment plans were optimized: one using the MLC and one using the IRIS-collimator providing variable circular fields. Plan requirements were: dose prescription to the 70% isodose line (18 or 20Gy), 100% GTV coverage, ≥98% PTV coverage, undisturbed central high dose region (95% of maximum dose) and a conformity index as low as possible. Plan comparison parameters were: conformity index (CI), high-dose gradient index (GI_H), low-dose gradient index (GI_L), total number of monitor units (MU) and expected treatment time (TT). For all cases, clinically acceptable plans could be generated with the following results (mean±SD) for CI, GI_H, GI_L, MU and TT, respectively for the MLC plans: 1.09±0.03, 2.77±0.26, 2.61±0.08, 4514±830MU and 27±5min and for the IRIS plans: 1.05±0.01, 3.00±0.35, 2.46±0.08, 8557±1335MU and 42±7min. In summary, the MLC plans were on average less conformal and had a shallower dose gradient in the low dose region, but a steeper dose gradient in the high dose region. This is accompanied by a smaller volume receiving 10Gy. A plan by plan comparison shows that usage of the MLC can spare about one half of the MUs and one third of treatment time. From these experiences and results suggestions for MLC planning strategy can be deduced.

Keywords: Treatment planning, stereotactic radiotherapy, radiosurgery, robotic guided radiation therapy, multi leaf collimator, plan comparison

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1 Introduction

Single fraction stereotactic radiosurgery is one main treatment option for patients with single or multiple brain metastases [1]. The CyberKnife® (Accuray, Sunnyvale, US) is a dedicated treatment system for these high precision treatments due to intrafractional compensation of patient position deviations and the usage of many non-coplanar beams leading to a steep dose gradient around the lesions and sparing of healthy brain tissue. Conventional CyberKnife treatments are performed with circular beam apertures formed either by fixed tungsten cones or the adjustable IRIS™ collimator [2]. A new development for the CyberKnife M6™ is the InCise™ 2 [3] multi leaf collimator (MLC) with a leaf width of 3.85mm and a maximum field size of 11.5x10.1cm^2 in 80cm SAD. Besides broadening of treatment indications due to larger field sizes, the MLC potentially gives the opportunity to deliver treatment plans of equal dosimetric

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quality in a shorter treatment time for the classical indications.

The aim of this study is the evaluation of MLC plan quality and delivery efficiency for single brain metastasis plans in comparison to IRIS plans. The IRIS was used for comparison instead of fixed cones, because of shorter treatment times through the adjustable field size.

Additionally, treatment planning suggestions for the InCise 2 MLC are provided to create high conformal plans for single targets.

2 Material and methods

2.1 Patient data

From our first 125 patients with one or more brain metastases treated with the CyberKnife, 10 patients were chosen for this evaluation. For each patient, one treatment plan was optimized covering only one selected metastasis. In case of more metastases present, these were defined as critical structures to mimic a situation with more than one treatment plan per patient e.g. due to different fractionation schemes or re-irradiation after a short time. The patients were picked to represent a variety of cases in lesion size, location, shape and the number of necessary blocks because of additional metastases. The size varied between 1.5 and 9cm^3, while 5 had a volume of less than 3cm^3 and 5 had a larger volume, leading to 5 patients with a prescription dose of 20Gy and 5 patients with 18Gy. The lower limit in size was determined from a minimum segment size of the MLC of 56.25mm^2 and our institutional guide lines of using the IRIS collimator field sizes of at least 10mm, only. The metastases locations include the frontal, parietal, occipital and temporal lobes as well as the cerebellum. Lesion shape was classified as ratio of the largest and the smallest representative diameter of the lesion d_L/d_S, varying from 1.12 to 1.94. The number of blocked additional brain metastases ranged between 0 and 5.

2.2 Treatment planning

For each patient a structure set was delineated based on a treatment planning CT with 1mm slice thickness co-registered with a T1 weighted distortion corrected MRI with 1mm slice thickness. The GTV was expanded by a margin of 1mm to define the PTV. Each patient got a block structure in the most caudal CT slice to prevent beams along the cranio-caudal axis leading to avoidable dose in the body. If other metastases were present, they were expanded by a margin of 1cm and defined as additional block structure.

For each case two treatment plans were optimized using MultiPlan® 5.3 (Accuray, Sunnyvale, US), one for the MLC and one for the IRIS. Planning constraints were dose prescription (either 18 or 20 Gy) to the 70% isodose line, 100% GTV coverage, ≥98% PTV coverage and an undisturbed high dose region in the center of the metastasis (95% isodose line). The aim was a plan as conformal as possible, while ensuring a low skin/entrance dose through setting the maximum MU per treatment node to 250-300. To shape the dose fall-off around the metastases four tuning structures per plan were defined as spherical shells with 1mm thickness as usual in MultiPlan. The shells were placed in 3, 6, 10 and 20mm (MLC) and 2, 6, 10 and 20mm (IRIS) distance from the PTV.

For all plans the full head path was used and the opportunity to reduce the maximum number of nodes for the MLC (171) was not taken, giving most options for the optimizer. For the same reason the "conformal avoidance" segment shape generation method was used with all sub-options. In the larger metastases "isocentric conformal" segments for a tuning structure e.g. "PTV minus 4mm" were additionally used. For the IRIS plans 1 to 3 collimator sizes were chosen according to target size and shape.

For all treatment plans a fraction time reduction optimization was performed in the end, followed by a segment/beam reduction step to remove all segments/beams with less than 3MUs for dose-to-monitor linearity reasons.

2.3 Plan comparison

To compare the derived treatment plans several parameters were used. First of all, the conformity index CI as calculated by MultiPlan from the tissue volume V_{Dp} receiving at least the prescription dose Dp and the PTV volume receiving at least the prescription dose $V_{PTV,Dp}$ (see eq. 1), was compared

$$\boldsymbol{CI} = \frac{V_{Dp}}{V_{PTV,Dp}}. \qquad (1)$$

Additionally the new conformity index nCI from MultiPlan, which weights the CI with the inverse target coverage, using the volume of the PTV V_{PTV} (see eq. 2) was compared, as this is often used for plan comparison in clinical routine

$$\boldsymbol{nCI} = \frac{V_{Dp}}{V_{PTV,Dp}} \times \frac{V_{PTV}}{V_{PTV,Dp}}. \qquad (2)$$

To quantify the dose gradient around the target, two gradient indices were used. First, the high-dose gradient GI_H [4], comparing the tissue volume getting at least half of the prescription dose $V_{0.5Dp}$ with V_{Dp}:

$$GI_H = \frac{V_{0.5Dp}}{V_{Dp}}. \quad (3)$$

Second, the low-dose gradient GI_L [5] with the additional use of the volume receiving at least one fourth of the prescription dose $V_{0.25Dp}$:

$$GI_L = \frac{V_{0.25Dp}}{V_{0.5Dp}}. \quad (4)$$

As it is of clinical relevance regarding therapy toxicity [6], the volume receiving at least 10Gy V_{10} was determined, also. To compare the delivery efficiency, four values were evaluated, the treatment time TT containing 5min of patient setup and intrafractional X-ray imaging every 30s, as calculated by MultiPlan, the number of monitor units MU in the plans, the number of used treatment nodes and the number of segments (MLC) and beams (IRIS).

To evaluate if the differences found between the MLC and the IRIS plans are statistically significant ($p<0.05$), a paired samples student's t-test was performed for all mentioned comparison parameters using MatLab® R2015a (The Mathworks Inc., Nattick, US). Additionally, for all comparison parameters and their relative differences, the Pearson's linear correlation coefficient was calculated relative to lesion size and lesion shape d_L/d_S.

3 Results

For all cases clinically acceptable MLC and IRIS plans could be generated. Comparison of plan parameters can be found in table 1 with the corresponding p-values. All differences except of the V_{10} are significant. On average the MLC plans have a worse conformity index, worse new conformity index and worse low-dose gradient, but a better high-dose gradient, leading to a smaller V_{10}. MLC plans consist of less nodes and segments in comparison to IRIS beams, use less MU and are deliverable in a shorter treatment time. A conformity index below 1.1 could be reached for all IRIS plans. For the MLC this was not possible for the two smallest metastases and two irregular shaped ones. No effect from the number of additional blocked structures could be seen, not even in the number of used nodes. Correlation analysis between size and shape and all comparison parameters and their relative differences shows strong correlation (Pearson's correlation coefficient $|r| \geq 0.8$) only for the following pairs: MLC plans: size and V_{10} and size and GI_H, IRIS plans: size and V_{10}, size and treatment time and size and number of beams.

In figure 1 an example of a transversal plan slice can be seen. It is visible, that the IRIS plan is more conformal, while the V_{10} is a bit larger. To show the low dose area, the 2Gy isodose is displayed, containing less volume in the IRIS plan.

Table 1: Results for all compared plan parameters (mean±SD) as well as the absolute difference between MLC and IRIS plans. The p-values from the t-tests are bold for significant differences.

Parameter	MLC	IRIS	Diff	p
CI	1.09±0.03	1.05±0.01	0.04±0.03	**1.4E-3**
nCI	1.11±0.03	1.07±0.01	0.04±0.03	**3.5E-4**
V_{10} [cm³]	10.7±5.5	11.4±6.2	-0.7±1.1	7.7E-2
GI_H	2.77±0.26	3.00±0.35	-0.24±0.22	**8.1E-3**
GI_L	2.61±0.08	2.46±0.08	0.15±0.06	**3.9E-5**
Nodes	51±15	67±15	-16±15	**9.3E-3**
Segments/ Beams	60±24	179±48	-119±38	**4.0E-6**
MU	4514±830	8557±1335	-4042±991	**4.2E-7**
TT [min]	27±5	42±7	-15±5	**4.0E-6**

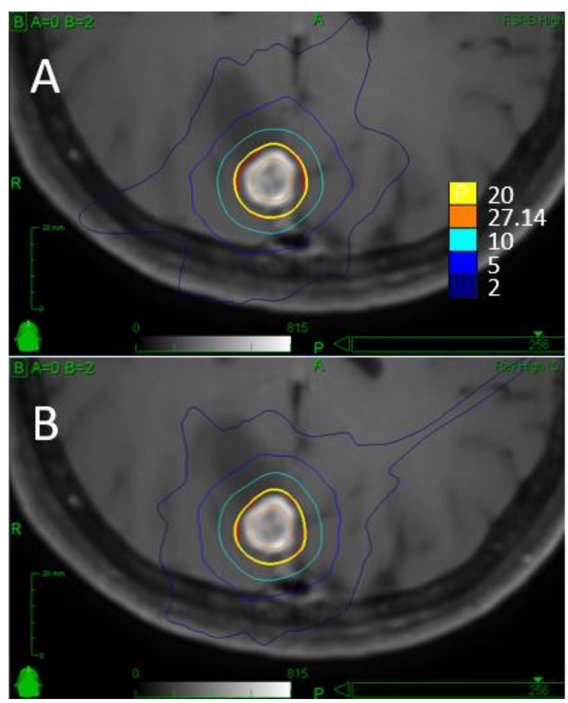

Figure 1: Example for a metastasis in the right occipital lobe prescribed to 20Gy. A) MLC plan with isodose legend in Gy, 27.14Gy equals the 95% isodose. B) IRIS plan.

4 Discussion

The findings considering plan quality and delivery efficiency are in accordance with [7], where treatment plans for a cohort of very diverse brain metastases in size, number of targets per plan and fractionation scheme were optimized with the InCise1, the previous version, which differs mainly in leaf width and had only a few installations. One major difference is the much better conformity in the optimized plans here, both for MLC and circular fields, which perhaps is an effect of prescribing to the 80% isodose in [7] instead of the 70%.
As the number of nodes and segments/beams is less for the MLC and the penumbra shows no substantial differences to the IRIS, the reason for the steeper high-dose gradient in MLC plans might be in the segment placing algorithm and optimization process not controllable by the user.

The MLC promises good delivery efficiency for larger targets where fractionation might be needed as well, because no correlation between target size and treatment time could be found as opposed to the IRIS.

4.1 Treatment planning strategies

Aiming for an MLC plan with very high conformity, the following considerations can be made:

- Adjusting the leaf margin either for “leading edge” larger than 0mm or for “middle edge” smaller than 0mm in smalls steps for segment generation only just giving 100% PTV coverage.
- Optimizing the shells after the coverage step of the PTV in the sequential optimization should be repeated 4-5 times with setting of adjusted maximum dose constraints for all shells in between to decrease the *CI* while preserving enough coverage.
- To preserve GTV coverage during the shell iteration, it is beneficial to insert a GTV minimum dose optimization as first step.
- For large PTV volumes the MLC tends to produce a cold spot in the central part of the lesion, like the “donut-shaped” dose distributions also known for the circular fields. Here it is especially useful to not only include a smaller inner volume in the optimization steps, but to generate extra segments for this volume, e.g. with “isocentric conformal, trailing edge”. This problem cannot be addressed through not using the peripheral MLC shapes as this will lead to a coverage drop.
- As shown here MLC plans end up with much less nodes and segments as possible regarding geometry and shape generations. This leads to the suggestion to permit the maximum number of nodes and use all types of segment shapes.

5 Conclusion

For all cases, both collimators provide a reasonable plan with a very good conformity. The results show higher conformity for the IRIS plans but a steeper high-dose gradient for the MLC plans. MLC plan delivery is more time and MU efficient. Further analyses covering more tumor entities and fractionation schemes should be made to evaluate the broadened range of treatment opportunities of a CyberKnife equipped with an MLC.

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