

Apparatus dependence of normal brain tissue dose in stereotactic radiosurgery for multiple brain metastases

Technical note

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Object. Technical improvements in commercially available radiosurgery platforms have made it practical to treat a large number of intracranial targets. The goal of this study was to investigate whether the dose to normal brain when planning radiosurgery to multiple targets is apparatus dependent.

Methods. The authors selected a single case involving a patient with 12 metastatic lesions widely distributed throughout the brain as visualized on contrast-enhanced CT. Target volumes and critical normal structures were delineated with Leksell Gamma Knife Perfexion software. The imaging studies including the delineated contours were digitally exported into the CyberKnife and Novalis multileaf collimator–based planning systems for treatment planning using identical target dose goals and dose-volume constraints. Subsets of target combinations (3, 6, 9, or 12 targets) were planned separately to investigate the relationship of number of targets and radiosurgery platform to the dose to normal brain.

Results. Despite similar target dose coverage and dose to normal structures, the dose to normal brain was strongly apparatus dependent. A nonlinear increase in dose to normal brain volumes with increasing number of targets was also noted.

Conclusions. The dose delivered to normal brain is strongly dependent on the radiosurgery platform. How general this conclusion is and whether apparatus-dependent differences are related to differences in hardware design or differences in dose-planning algorithms deserve further investigation. (DOI: 10.3171/2011.1.JNS101056)

KEY WORDS • Gamma Knife • CyberKnife • Novalis • stereotactic radiosurgery • treatment planning • brain metastasis

STEREOTACTIC radiosurgery, with or without WBRT, is commonly used in the treatment of patients with a limited number of metastatic brain tumors. The clinical role of radiosurgery in patients with more than 4 or 5 brain metastases has not been established. Nevertheless, given the technical developments in SRS apparatuses in recent years, it is now practical to treat such patients with SRS with any of several various radiosurgery platforms, including Leksell Gamma Knife Perfexion (Elekta), CyberKnife (Accuray), and Novalis (Brainlab AG).

Perfexion uses a new sector-based collimator design with collimators that can be activated rapidly to permit a large combination of beam apertures at the isocenter, resulting in reduced procedure times and highly conformal

dose distributions for both individual and multiple targets.^{6,18} The CyberKnife and Novalis multileaf collimator–based systems have had marked technical improvements applicable to the treatment of multiple targets.^{4,10,15} In particular, there has been a several-fold increase in machine output and the speed of changing beam directions (CyberKnife) or individual multileaf-collimator leaf motions (Novalis). For treatment of a large number of brain lesions these technical features can be particularly beneficial.

For each of these technologies, there has been clinical concern regarding the dose to normal brain. For example, some studies have reported a possible relationship between normal brain volumes, such as the 10- or 12-Gy volume, and treatment-related toxicity,^{3,5} and we have previously reported the possible need for target dose reductions in patients with multiple metastases treated with SRS.¹² We have also previously examined dose distribu-

Abbreviations used in this paper: SRS = stereotactic radiosurgery; WBRT = whole-brain radiation therapy.

tions produced by different SRS apparatuses for single lesions without adjacent dose constraints and observed practically identical dose fall-off relationships and peripheral normal brain doses.⁸ This investigation reports our analysis of apparatus-dependent normal brain doses when treating multiple metastatic brain lesions.

Methods

As part of a multiinstitution study of SRS for multiple metastatic brain lesions, a single patient case was selected for a trimodality planning study involving Gamma Knife Perfexion, CyberKnife, and Novalis. This patient had been treated with Gamma Knife Perfexion and had undergone both CT and MR imaging with contrast. Because CyberKnife requires CT scans for planning purposes, we used those images for the present study. The CT study, which was performed with 1-mm spacing, demonstrated 12 metastatic brain lesions distributed throughout bilateral cerebral and cerebellar hemispheres with a total volume of 5.4 cm³ (range 0.03–1.0 cm³). Axial CT images showing the distribution of targets are presented in Fig. 1.

Target volumes, the whole brain volume, and critical structure volumes were delineated on a Leksell GammaPlan workstation. The imaging sets including all delineated structures were transferred via DICOM-RT (Digital Imaging and Communications in Medicine–radiotherapy) functionality to the CyberKnife MultiPlan and Brainlab iPlan systems for treatment planning. Treatment plans were created at each apparatus's respective workstation following these dose specifications and constraints: 20 Gy was prescribed to each target and was required to cover at least 99% of the target volume; the maximum dose to each critical structure was required to be < 800 cGy to the pituitary, < 600 cGy to the pituitary stalk, < 800 cGy to the optic chiasm and optic nerves, < 600 cGy to the globes, < 200 cGy to the lens, and < 1200 cGy to the brainstem; and the prescription isodose line was selected based on standard practice for each apparatus. Multiple planning iterations were performed to meet the above requirements while achieving good dose conformity. Four subsets of target combination with 3, 6, 9, or 12 targets were selected for separate planning with these 3 treatment modalities. In each instance, targets were selected so as not to be closely bunched.

For Perfexion treatment planning, multiple collimators (4, 8, and 16 mm) with composite sectors were used. Individual targets were planned sequentially and the final dose distribution was manually adjusted by normalizing the dose to each target to a global maximum dose value among all the targets. For CyberKnife treatment planning, we adopted a newly developed 2-step optimization method⁹ in which individual targets were first planned independently, disregarding the contributions of other lesions, and then a final linear optimization was performed to adjust the weighting of individual contributions to produce an acceptable plan. This approach was specially designed for planning a large number of targets so that a sufficient number of non-isocentric beams could be employed to generate an acceptable treatment plan satisfying the dose requirements and the dose-volume constraints.

This approach results in a substantially lower dose to normal brain than that obtained using only the commercially available CyberKnife software. For Novalis treatment planning, only the central portion of its 3-mm micro-multileaf collimator was used. For each target, a separate isocenter was assigned (we used 3, 6, 9, and 12 isocenters for 3, 6, 9, and 12 targets, respectively). For each isocenter, 5 noncoplanar dynamically shaped arc beams were applied at couch angles of $\pm 10^\circ$, $\pm 50^\circ$, and 90° . These dynamic arc beams spanned 100° and were all optimized as fixed beams spaced 10° apart in the treatment planning system. Typically, each arc requires approximately 1–2 minutes to deliver, making the overall beam-on plus isocenter setup time similar to the overall CyberKnife treatment procedure time. Computer-automated planning was used for both CyberKnife and Novalis to create final treatment plans.

Dose-volume histograms and related indices for the targets and the normal brain structures were tabulated and compared for each of the target combinations to ascertain their dependence on increasing number of targets and SRS apparatus.

Results

Each modality satisfied the specified normal-tissue dose constraints. Figure 2 shows Paddick conformity indices¹¹ for all 4 treatment plans for each of the 3 modalities. The conformity indices were in the range of 0.41–0.70. However, the Perfexion plans were consistently superior to those of CyberKnife or Novalis. No obvious degradation in dose conformity for any platform was noticed with increasing number of targets. In addition, the central target dose was typically higher for Gamma Knife than for CyberKnife or Novalis. For example, the average prescription isodose values were $61\% \pm 11\%$, $78\% \pm 5\%$, and $71\% \pm 3\%$ of the maximum dose inside a target for Gamma Knife, CyberKnife, and Novalis, respectively.

The relationship of absolute volume of normal brain tissue receiving a specified dose to increasing number of targets is illustrated in Fig. 3. As expected, there is a notable but nonlinear trend of increase in the volume of normal brain tissue receiving a peripheral dose of 4–20 Gy among the 3 modalities. This nonlinear increase in the normal brain dose volume is consistent with our previous report on multitarget Gamma Knife treatments.¹²

The apparatus dependence of the peripheral normal brain dose for the 3 modalities is illustrated in Fig. 4. For the purpose of consistent comparison, the normal brain volume for the y-axis was normalized to the total target volume obtained with each individual modality. This was done to prevent rounding or scaling errors associated with different dose grid resolutions from computations at each treatment planning system. This effect is mostly negligible for large target volumes but can be significant for small target volumes. The Gamma Knife Perfexion plans result in much smaller normal brain volumes receiving any particular dose as compared with the CyberKnife and Novalis plans. The discrepancy was typically on the order of a factor of 2–3 favoring Gamma Knife Perfexion for all the cases. Although the CyberKnife and Novalis curves are somewhat similar, it is important to note

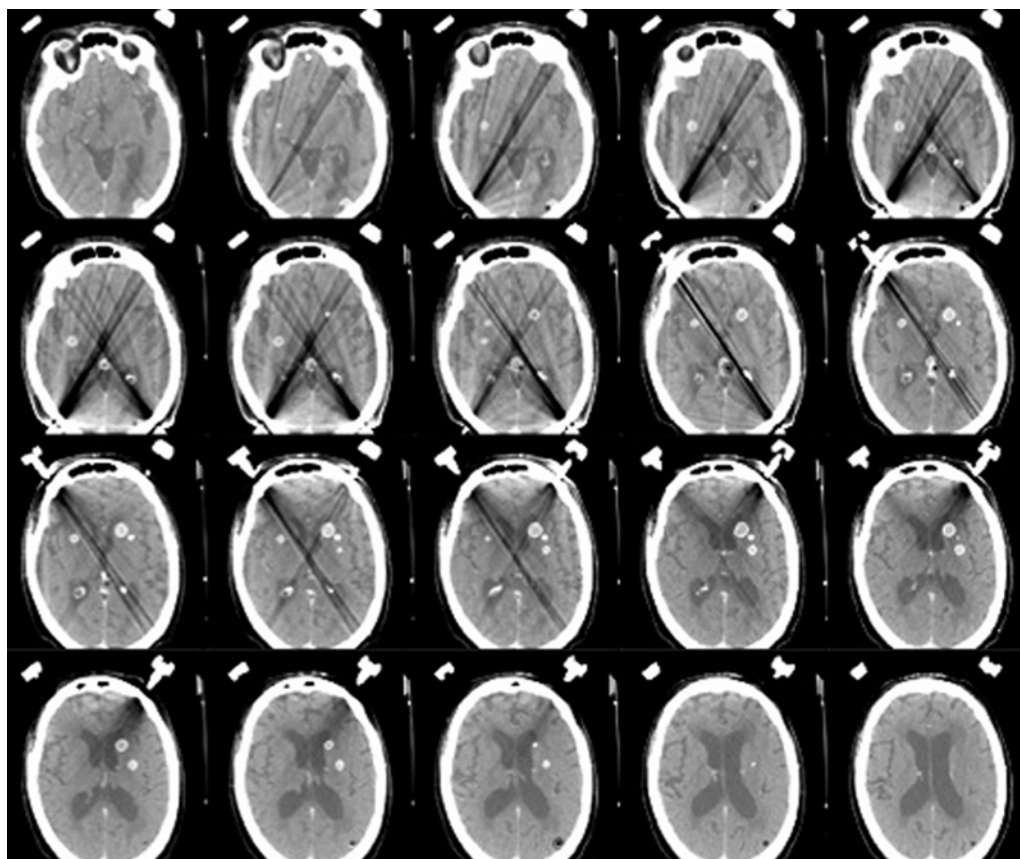


Fig. 1. Axial images showing target distribution.

that CyberKnife dose-volume histograms obtained using only the commercially available CyberKnife planning software (not shown) are even less favorable than those shown here (which were obtained with the commercially available software plus our in-house optimization technique⁹).

Discussion

This is the first report to demonstrate large apparatus-dependent differences in dose to normal brain with multiple target radiosurgery. We find that the volumes of normal brain enclosed by peripheral isodose volumes can be several times lower for Gamma Knife Perfexion versus CyberKnife and Novalis.

Given that similar differences were not found for solitary targets planned without adjacent dose constraints in our previous study,⁸ we suspect that our current findings may be due to beam interplay effects and the relatively large number of imposed dose-volume constraints, both of which would be of less importance for a single lesion treatment plan. For multiple lesion treatment plans, the total number of beams plus the number of constraints approximately scale proportionally with the total number of targets. Differences in dose calculation algorithms, such as in the volume-rendering schemes in the computation of dose-volume histograms, may partially explain the current findings. However, these differences are unlikely to

explain the large differences in dose-volume histograms observed in the current study. This is because the calculations in the brain are in the relatively homogenous medium, and all systems have been well validated with published in-phantom dosimetry measurements.^{1,2,7,16,17} Finally, it is well known that CyberKnife low-isodose lines (such as 10%–20%) often show fingers or islands of dose in nontarget regions, a phenomenon not seen in Novalis or Perfexion plans. These isodose lines are presumably associated with CyberKnife's non-isocentric planning al-

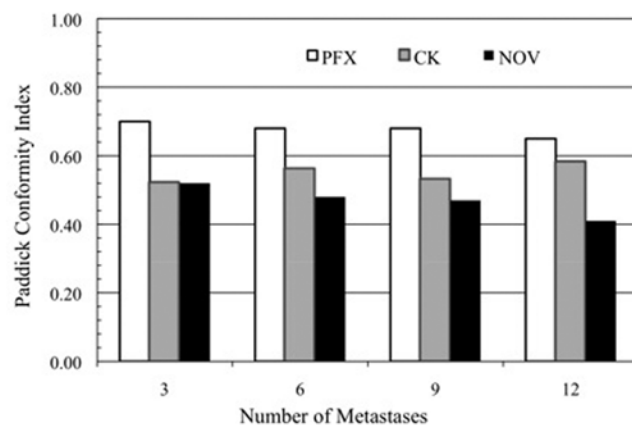


Fig. 2. Comparison of Paddick dose conformity indices for 3, 6, 9, and 12 targets. PFX = Gamma Knife Perfexion; CK = CyberKnife; NOV = Novalis.

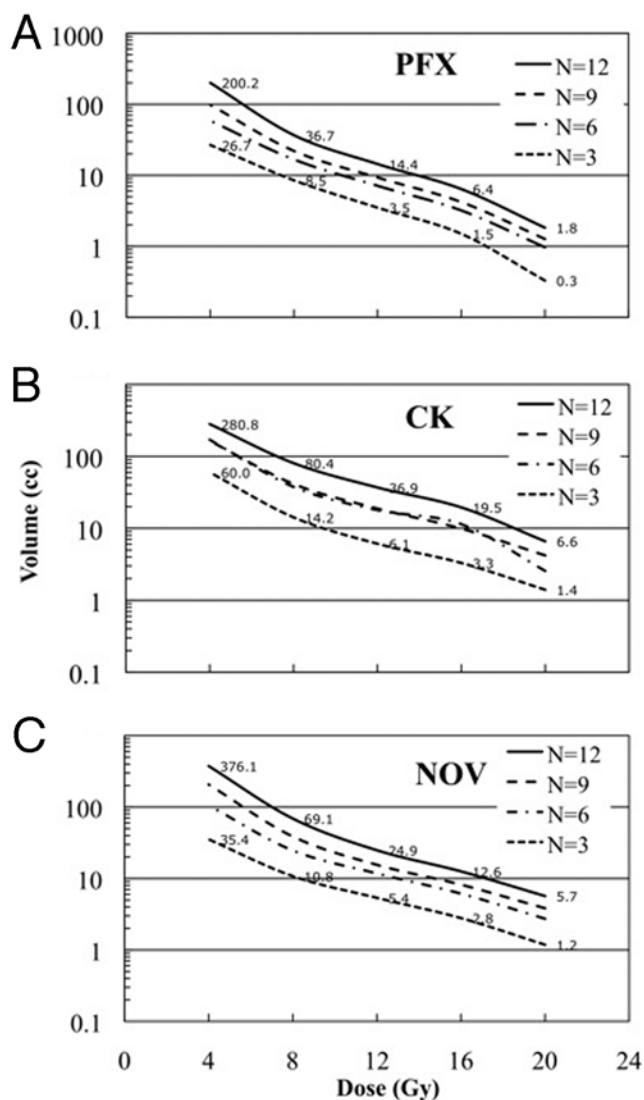


FIG. 3. Semilogarithmic plots of normal brain isodose volumes versus dose for Gamma Knife Perfexion (A), CyberKnife (B), and Novalis (C). The numbers on the upper and lower curves are the absolute total target volumes for Gamma Knife Perfexion and CyberKnife for 4, 8, 12, 16, and 20 Gy, respectively. N = number of targets.

gorithm rather than with CyberKnife's hardware design. We therefore speculate that the observed differences in dose-volume histograms between the 3 systems are due in part to differences in planning algorithms. Whether they are also due to individual apparatus-dependent beam profile differences is unknown.

In terms of clinical considerations, the observed differences in the reported peripheral normal brain volume might be compensated for by decreasing the prescription dose. However, we have found that a reduction of prescription dose on the order of 20%–30% is needed,¹² a finding that was confirmed by matching a peripheral isodose volume such as the 12-Gy volume among all the plans in our study. This means reducing 20 Gy to the range of 14–16 Gy for our cases. Evidently, this is not a sensible compromise, based on standard practice guidelines or reports.^{13,14}

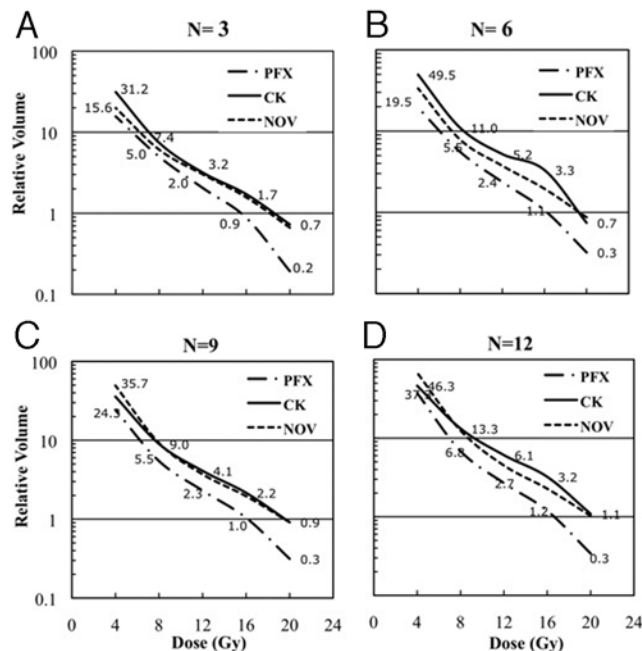


FIG. 4. Apparatus dependence of normal brain isodose volumes for multitarget treatment plans with 3 (A), 6 (B), 9 (C), and 12 (D) targets. The numbers on the curves are the normalized total target volumes for Perfexion and CyberKnife for 4, 8, 12, 16, and 20 Gy, respectively.

Conclusions

Our findings indicate that caution should be used in considering the peripheral normal brain dose when performing multitarget SRS. Future studies of different treatment scenarios such as varying the total target volume and number of targets, as well as those designed to further improve planning techniques, are needed. Studies of the cause of apparatus-dependent dose-volume histogram differences are needed to resolve the relative contributions of hardware design and treatment planning algorithms.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Ma, Petti, Wang, Kunwar, Shrieve, Sahgal, Larson. Acquisition of data: Ma, Petti, Wang, Kunwar, Larson. Analysis and interpretation of data: Ma, Petti, Wang, Larson. Drafting the article: Ma, Sahgal, Larson. Critically revising the article: Ma, Barani, Shrieve, Sahgal, Larson. Reviewed final version of the manuscript and approved it for submission: Ma, Descovich, Chuang, Barani, Shrieve, Sahgal, Larson. Statistical analysis: Larson. Administrative/technical/material support: Descovich, Chuang, Barani, Sahgal, Larson. Study supervision: Ma, Larson.

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