Quantifying and improving the efficiency of Gamma Knife treatment plans for brain metastases: results of a 1-year audit

Clinical article

GAVIN WRIGHT, M.PHIL., PAUL HATFIELD, PH.D., F.R.C.R., CARMEL LOUGHREY, F.R.C.R.,
BEATRICE REINER, M.SC., AND PETER BOWNES, M.SC.

St. James's Institute of Oncology, St. James's University Hospital, Leeds, United Kingdom

Object. A method for quantifying the efficiency of Gamma Knife treatment plans for metastases was previously implemented by the authors to retrospectively identify the least efficient plans and has provided insights into improved planning strategies. The aim of the current work was to ascertain whether those insights led to improved treatment plans.

Methods. Following completion of the initial study, a 1-year audit of metastasis plans created at St. James's Institute of Oncology was carried out. Audited recent plans were compared with the earlier plans of the initial study, in terms of their efficiency and dosimetric quality. The statistical significance of any differences between relevant plan parameters was quantified by Mann-Whitney U-tests. Comparisons were made between all plans and repeated for a reduced set of plans from which the smallest lesions treated with a single 4-mm shot were excluded. The plan parameters compared were a plan efficiency index (PEI), the number of shots, Paddick conformity index (PCI), gradient index (GI), and percent coverage (of the lesion by the prescription isodose).

Results. A total of 157 metastatic lesions were included in the audit and were compared with 241 in the initial study. In a comparison of all cases, the audited plans achieved a higher median PEI score than did the earlier plans from the initial study (1.08 vs 1.02), indicating improved efficiency of the audited plans. When the smallest lesions (for which there was little scope for varying plan strategy) were discounted, the improvement in median PEI score was greater (1.23 vs 1.03, $p < 0.001$). This improvement in efficiency corresponds to an estimated mean (maximum) time saving of 15% (66%) per lesion (11 minutes [64 minutes] on the day of treatment). The modified planning strategy yielding these efficiency improvements did not rely on the use of significantly fewer shots (median 11 vs 11 shots, $p = 0.924$), nor did it result in significant detriment to dosimetric quality (median coverage 99% vs 99%, median PCI 0.84 vs 0.83, $p = 0.449$, and median GI 2.72 vs 2.67, $p = 0.701$, audited plans vs initial plans, respectively).

Conclusions. Choice of planning strategy can substantially affect plan efficiency and thus strongly influence treatment time. Through increased emphasis on efficiency, resulting from the introduction of PEI combined with a modified planning strategy informed by previous work, it has been possible to reduce times for metastatic plans without compromising their dosimetric quality. Although the average time savings achieved per lesion are moderate, the potential benefits per patient are greater for those with multiple metastases. Reducing treatment times has clear benefits with regard to patient comfort and throughput. In addition, optimization of plan efficiency may potentially affect the biologically effective dose from Gamma Knife treatments and offers opportunity for further work.

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KEY WORDS • Gamma Knife • radiosurgery • treatment planning •
treatment time • efficiency • metastases • stereotactic radiosurgery

GAMMA Knife treatment planning involves placing one or more radiation isocenters (shots) within a tomographic imaging study of the brain, such that the combined radiation distribution delivers a therapeutic dose to the target while minimizing the dose to surrounding healthy tissue. The treatment planner determines the total number of shots in the plan, selecting for each shot

its position (stereotactic coordinates), collimation, and relative weighting. The treatment planning system, Leksell GammaPlan (Elekta AB), then automatically calculates the required duration of each shot needed to deliver the prescribed dose.

In addition to creating a plan of suitable dosimetric quality, another important consideration during treatment planning is the minimization of treatment time, that is, the total duration of all shots in the plan. As well as benefiting patient throughput, minimizing treatment time improves patient comfort by reducing the time spent immobilized

Abbreviations used in this paper: GI = gradient index; nTRP_{corr} = attenuation-corrected, normalized treatment time–dose rate product; PCI = Paddick conformity index; PEI = plan efficiency index.

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on the treatment couch, and additionally can reduce time demands on staff supporting the service.

Studies have compared the treatment efficiency of different models of Gamma Knife,^{3,6,9} but only recently has a study investigated the efficiency of the treatment plans themselves.¹¹ In the early study from our center (St. James's Institute of Oncology), a new time-related quantity—the attenuation-corrected, normalized treatment time–dose rate product ($nTRP_{corr}$)—was presented. Derived from the treatment time multiplied by a series of correction factors, $nTRP_{corr}$ accounts for the effect of varying attenuation conditions (the size of the patient's head and the location of the lesion within that head) and prescription, and of decay of the cobalt-60 sources. Between lesions of similar size and shape, a comparison of $nTRP_{corr}$ values therefore provides a more meaningful assessment of relative plan efficiency than does a comparison based on treatment times alone. By retrospectively calculating $nTRP_{corr}$ for 241 metastatic lesions treated at our center from March 2009 to September 2011, a curve was derived to indicate how $nTRP_{corr}$ typically varied with volume for these lesions. Plotting the $nTRP_{corr}$ value of any individual lesion's plan against this “expectation curve” provides a visual indication of the efficiency of the plan; a plan with an $nTRP_{corr}$ value that lies above the curve is less efficient than the average plan for a lesion of comparable volume, and a plan with an $nTRP_{corr}$ value that lies below the curve is more efficient. Furthermore, the equation describing the expectation curve enables calculation of an exact value for expected $nTRP_{corr}$ for a lesion of specified volume. By calculating the ratio of the expected $nTRP_{corr}$ value to the $nTRP_{corr}$ value actually achieved by a plan, a single figure of merit for the efficiency of that plan, independent of prescription, attenuation, and source decay, is obtained. This figure of merit we termed the plan efficiency index (PEI).

One outcome of that study (hereafter referred to as the first study) that was of interest locally was insight into what constitutes an efficient planning strategy. By using the newly presented PEI, we retrospectively identified our least efficient plans; subsequently, we demonstrated that by modifying our strategy, these cases could be replanned to achieve significant increases in PEI scores and corresponding reductions in treatment times (on average 42%, or 29 minutes on the day of treatment) without detriment to dosimetric quality.

Of course, there is little value in only replanning historic cases; of greater value is determining whether the introduction of the PEI and the associated emphasis placed on efficiency during planning, along with our newly gained insights into planning strategy, would have any general effect on our future treatments. To answer that question, we conducted a 1-year audit of metastatic lesions treated at our center since that first study. The aim of the audit was to determine whether the efficiency of these recent plans was significantly improved over the efficiency of the earlier plans of the first study.

Methods

All results presented relate to treatment plans pro-

duced on Leksell GammaPlan versions 8.2 to 10.2 for Leksell Gamma Knife Perfexion (Elekta AB).

Data Collection

Plans for all lesions that met the selection criteria of the first study were included: metastatic lesions whose maximum-to-minimum dimension ratio did not exceed 2.2, for which there were no critical structures of such close proximity so as to necessitate blocking (shielding) of source sectors, and for which the half-prescription isodose for a lesion in a patient with multiple metastases did not overlap that of a neighboring lesion. At our center, patients with metastatic lesions constitute the most commonly treated group and thus provided the greatest amount of data for comparison.

For each case, lesion volume was recorded along with the prescription, the treatment time, the number of shots, and calculated values for $nTRP_{corr}$ and PEI. In addition, dosimetric quality, quantified in terms of coverage (of the lesion by the prescription isodose), Paddick conformity index (PCI),⁷ and gradient index⁸ (GI) were recorded.

From these data, a subset of cases was further selected, which excluded the smallest lesions treated with a single 4-mm shot (hereafter referred to as the reduced-data subset).

Data Analysis

The $nTRP_{corr}$ values of all audited plans were plotted against the expectation curve from the first study to provide a graphical indication of any overall change in efficiency. To numerically quantify any differences between the audited recent plans and the earlier plans from the first study, we compared the median values of relevant plan parameters and investigated the statistical significance of any differences by means of Mann-Whitney U-tests; *p* values < 0.05 were considered statistically significant. Plans were compared in terms of efficiency and dosimetric quality.

Analysis was repeated on the reduced-data subset. For this subset, expected treatment times were estimated (using the source activity on the day of treatment) for each lesion from the $nTRP_{corr}$ expectation curve. Derived from expected $nTRP_{corr}$, these expected treatment times are those that would have been typically achieved during the period of the first study for a lesion of comparable size, all else (attenuation, source activity, and prescription) being equal. Comparing estimated and actual treatment times provided an indication of any time savings achieved over the times that would have been expected during the period of the first study.

Results

Data Collection

Data were collected for metastatic lesions treated at our center from July 2012 to July 2013. A total of 157 lesions met the selection criteria for the study. Of these 157 lesions, 111 originated from patients with multiple metastases (43 patients, mean of 2.6 lesions/patient), and the remaining 46 were in patients with a single metastatic le-

sion. For the majority of the lesions (69%, 14%, and 13%), plans were created by 1 of 3 individuals; the remaining 6 cases were planned by a fourth.

The volume of the lesions ranged from 3.8 mm³ to 19,260 mm³. In the reduced-data subset of lesions, the minimum volume was 31 mm³. This reduced-data subset consisted of 118 lesions; 42 of these constituted single-metastasis cases.

Data Analyses

Figure 1 shows the nTRP_{corr} values achieved by the 157 audited cases, plotted against lesion volume. Also shown is the expectation curve from the first study. A point lying below the curve corresponds to a plan that is more efficient than was typical for a lesion of similar volume during the first study. Conversely, points lying above the curve correspond to plans that are less efficient. The equation of the expectation curve (indicated on the graph) allows for calculation of expected nTRP_{corr} for any given lesion of specified volume and, thus, subsequent calculation of PEI.

Figure 2 shows the distribution of PEI scores achieved by the audited plans compared with those scores achieved during the first study. Figure 2 also shows the distribution of PEI scores for the reduced-data subset. These PEI scores are again compared with those from the first study; these earlier data were similarly filtered to eliminate those lesions treated with a single 4-mm shot.

Table 1 details average values for various efficiency and dosimetry parameters for the recent audited plans compared with those of the earlier plans in the first study. Comparisons are included for the full data sets and for the reduced-data subsets. For the 118 plans in the reduced-data subset, Fig. 3 shows the estimated time savings achieved by the recent plans. These estimated time savings are based on the dose rate (activity) of the sources on the day of treatment. Of these 118 lesions, 89 (75%) had a treatment time that was less than the expected estimate. The mean (maximum) estimated time saved over all 118

lesions was 11 minutes (64 minutes), equivalent to 15% (66%). For the reduced-data subset, Table 2 summarizes the PEI scores achieved and associated estimated time savings, stratified by lesion volume.

Discussion

The aim of this investigation was to answer a question that arose following our first study: whether by modifying our planning strategy we were able to improve the efficiency of our metastatic treatment plans without compromising their dosimetric quality. By the method of quantification presented in that first study, our recent plans do indeed tend toward greater efficiency.

Efficiency Improvements

As shown in Fig. 1, the nTRP_{corr} values for the majority of our plans now lie below their expected values. In many cases, the degree to which they improve over their expected mean value is much greater than 1 standard deviation, alluding to the statistical significance of the improvement. Although a comparison between the distributions of PEI scores achieved by the recent plans and those of the earlier plans is not remarkable (Fig. 2 upper), it is important to note in Fig. 1 that a substantial proportion of lesions were of small volume. At our center, the very smallest metastases tend to be treated with a single 4-mm shot prescribed to a high percent isodose; clearly, for these lesions there is little scope for varying the plan strategy. Consequently, for such cases the nTRP_{corr} values tend to cluster close to their expected mean value, skewing the PEI distributions inevitably toward a value of 1.

When PEI scores for the reduced-data subsets are compared, the improvement achieved by recent plans is more marked (Fig. 2 lower). However, even in these reduced-data subsets, small lesions remain; these lesions may have been treated with 2 close neighboring 4-mm shots or with a single 8-mm shot prescribed to a high percent isodose. Regardless, these cases represent instances in which a choice was made during the planning process to adopt a strategy alternative to the single 4-mm shot approach, irrespective of the small lesion size. Therefore, for the purposes of this study, in which the planning strategy choice is central, we believed it appropriate that these cases remain in the analysis.

Effect on Dosimetric Quality

Despite the relatively narrow scope of plan strategies available for the smallest lesions, a statistically significant improvement in efficiency overall has been achieved (Table 1). Importantly, this improvement has been achieved without any significant detriment to the coverage or conformity of our plans. Although a comparison of the full data sets indicates a statistically significant increase in GI, the median GI of our recent plans still meets our locally set planning aim of a GI less than 3.0. It is outside the scope of this study to comment on any possible clinical significance of this observation, but it should be noted that there is a greater proportion (39/157) of these single 4-mm shot plans in the data set of recent plans than in the data set

FIG. 1. nTRP_{corr} value versus volume. Diamond-shaped points represent the individual plans included in the recent audit. The solid line (described by the equation) represents the expected relation, as derived from the plans of the first study. The broken lines represent 1 standard deviation from the mean expectation curve.

Fig. 2. The distributions of PEI scores achieved by the plans included in the recent audit (after July 2012) compared with those achieved by the earlier plans of the first study (before September 2011). **Upper:** Graph showing PEI scores for all plans. **Lower:** Graph demonstrating PEI scores for the data-reduced subset, which excluded single 4-mm shot plans.

of the early plans (53/241). Prescribed to a high isodose, the GI for these single 4-mm shot plans is unavoidably high; when these plans are eliminated from the analysis, there is no statistically significant difference between the median GI of our recent and early plans.

Estimated Time Savings

With regard to the estimated time savings achieved,

Fig. 3 clearly indicates that for most cases, our treatment times are now shorter than would have been previously expected. Although an average time saving of 11 minutes is moderate, this value pertains to a single lesion only; for patients with multiple metastases, the potential time saved per patient is more noteworthy. The fact that metastatic treatments can often involve multiple targets makes optimizing plan efficiency particularly relevant for this

TABLE 1: Select plan parameters*

Parameter	All Plans			Reduced-Data Subset of Plans		
	Before Sep 2011	After Jul 2012	p Value†	Before Sep 2011	After Jul 2012	p Value†
cases, no.	241	157	—	188	118	—
vol, mm ³	840 (102–4675)	957 (71–5050)	0.492	2200 (417–6300)	2030 (530–6545)	0.912
dose, Gy	24 (18–24)	20 (18–24)	—	22 (18–24)	20 (18–24)	—
isodose, %	50 (48–60)	50 (50–64)	—	50 (48–50)	50 (49–51)	—
shots, no.	7 (1–16)	7 (1–14)	0.742	11 (4–17)	11 (4–16)	0.924
PEI	1.02 (0.90–1.19)	1.08 (0.94–1.40)	0.002	1.03 (0.87–1.26)	1.23 (1.01–1.58)	<0.001
coverage, %	99 (98–99)	99 (99–99)	—	99 (98–99)	99 (99–99)	—
PCI	0.80 (0.67–0.87)	0.80 (0.59–0.86)	0.171	0.83 (0.77–0.88)	0.84 (0.77–0.87)	0.449
GI	2.74 (2.62–3.13)	2.82 (2.65–3.20)	0.050	2.67 (2.60–2.81)	2.72 (2.62–2.89)	0.701

* All data are medians (interquartile ranges) unless otherwise stated. — = not applicable.

† p values relate to those of a Mann-Whitney U-test. p values are not reported for coverage, prescription dose, or prescription isodose because these parameters have a narrow range of discrete values that do not meet the continuous data requirements of the statistical test.

Fig. 3. Estimated time savings achieved by plans included in the recent audit, excluding plans for a single 4-mm shot. Negative values indicate time saved (over that previously expected); positive values indicate time lost.

group of patients. Furthermore, these 11 minutes still represent an average time saving of 15%; the absolute time saving to which this finding corresponds will be extended as the sources decay, a period over which considerations around optimizing plan efficiency become increasingly important. As indicated in Table 2, typical time savings were much greater for lesions larger than 3000 mm³ in volume.

An Efficient Planning Strategy

Consistent with the findings of the first study, it is interesting to note our efficiency improvements have been achieved without the use of significantly fewer shots (Table 1). Others have previously proposed the use of a quantity termed “unit isocentres” (number of shots divided by lesion volume), and it has been suggested that low unit isocenters would indicate a less complex, more efficient plan of shorter treatment time.^{5,12} However, the evidence from both this study and our first study indicates that creating an efficient plan is not simply an exercise in minimizing the number of shots alone, but rather that what is important is minimizing the proportion of small shots (thus maximizing the proportion of large shots), both in terms of their numbers and weightings, irrespective of the total shot count. Although this is perhaps a statement of the obvious, it should be noted that this aim can be achieved only by accepting a greater degree of overlap

between shots. Consequently, efficient planning becomes an exercise in carefully controlling dose normalization at the point of dose maximum, where shot overlap is great. Indeed, it is simple to envisage 2 plans of equal shot count and comparable dosimetry but one with a greater contribution from large shots than the other. Figure 4 shows a schematic illustration. Although this example is simplistic, this approach used consistently over a large volume can significantly reduce treatment time (Fig. 5).

The authors do not claim to present a planning strategy that is necessarily novel; we simply felt it pertinent to illustrate the technique used to achieve the demonstrated improvements. Of more novelty is the presentation of analysis, based on hundreds of plans collected over several years, which specifically quantifies the degree to which planning strategy can affect Gamma Knife treatment times. Through a concerted effort to optimize planning efficiency, driven by the introduction of the PEI and enabled by a modified planning strategy, it has been possible to reduce our treatment times without compromising the dosimetric quality of our plans.

The use of a single 4-mm shot prescribed to a high isodose has been mentioned as a strategy for treating our smallest lesions. For intermediate-sized lesions (those larger than the minimum 4-mm collimator but smaller than the maximum 16-mm collimator), an analogous planning approach could be used, that is, a single (8-mm or 16-mm) shot prescribed to a high percent isodose. Although prescribing to a higher percent isodose could yield further treatment time gains in addition to those resulting from the planning strategy described in this study, it is stressed that doing so would probably require a compromise of dosimetric quality, particularly the GI. Shiue et al.¹⁰ have discussed prescribing to higher percent isodoses for Gamma Knife metastasis treatments. Although they found no effect on local control, they did not investigate any possible effect on toxicity resulting from poorer GI. Furthermore, it should be noted that choosing to prescribe

TABLE 2: Improvements achieved after July 2012*

Vol (mm ³)	PEI	Estimated Time Saved, %
<1000	1.06 (0.88–1.25)	5.5 (–14.3 to 20.2)
1000–3000	1.20 (0.94–1.75)	16.6 (–6.7 to 42.9)
>3000	1.44 (1.17–1.63)	30.6 (14.7–38.5)

* All data are medians (interquartile ranges). Negative values for estimated time saved indicate treatments longer than expected.

FIG. 4. Illustration of 2 planning strategies. **A and B:** Starting from a target volume (A), planning could proceed by placing 2 greatly overlapping large shots (*broken lines*); the resulting 50% isodose (*white line*) of the net dose distribution is smaller than the extent of the individual shots because of normalization to the dose maximum in the region of overlap (B). Coverage of the 50% isodose can be regained by boosting the underdosed regions with small shots of low weighting, placed peripherally inside the first 2 shots. **C:** The result is 5 greatly overlapping shots: 2 heavily weighted large shots and 3 low-weighted small shots. **D:** Alternatively, a similar dose distribution could be achieved with 5 equally weighted, minimally overlapping shots: 1 large shot and 4 small shots. Relying on a greater contribution from small shots, this latter approach is less efficient than the former, although both approaches use the same number of shots.

to a higher percent isodose is simply an act of accepting a lower maximum dose and lower integral energy delivered to the target. In contrast to the planning strategy we advocate, a high prescription isodose does not necessarily imply an inherently more efficient means of delivering that dose.

Future Work

It is worth noting that, in quantifying dosimetric quality, this study has considered only physical dose parameters. Further comparisons between efficient and inefficient plans could be made in terms of their biological effective dose. Previous studies have investigated the effect on biological effective dose of variations in overall treatment time resulting from the decay of the sources, gaps in treatment, and the order of shot delivery.^{1,2,4} The study reported here provides evidence that planning strategy might further influence biological effective dose; investigation of this influence provides potential opportunity for future work.

Conclusions

Choice of planning strategy can substantially affect plan efficiency and thus plays a pivotal role in determining treatment time. By introducing a metric of plan efficiency—the Plan Efficiency Index—a greater emphasis

FIG. 5. Two plans for the same lesion prescribed to 18 Gy at 50%, both consisting of exactly 24 shots and having comparable dosimetric quality (99% coverage; PCI, GI = 0.90, 2.54 [*upper*] vs 0.92, 2.62 [*lower*]). In the example in the upper panel, the treatment time is 72 minutes. Greatly overlapping a more substantial proportion of large shots in the lower panel, treatment time is reduced to 37 minutes.

has been placed on efficiency during our planning process. This emphasis on efficiency, combined with a deliberate modification to our planning strategy, informed by insights from previous work, has enabled us to systematically reduce the treatment times of our metastatic lesions. Although an average time saving of 15% (11 minutes on the day of treatment) per lesion is moderate, for patients with multiple metastases, the benefits are potentially greater. Furthermore, our modified planning strategy has yielded efficiency improvements without detriment to dosimetric quality. Importantly, it has been demonstrated that the efficiency of a plan can be improved, and its dosimetric quality maintained, not necessarily through reducing the number of overall shots but by reducing the proportion of small shots. This approach therefore relies on the opposite—increasing the proportion of large shots used—and thus demands a greater degree of overlap be-

tween shots within a given volume. Consequently, efficient planning relies on careful control of dose normalization.

Although minimizing treatment time through optimized planning has obvious benefits with regard to patient comfort and throughput, of additional interest is the potential effect it might have on biologically effective dose. An investigation into any such impact provides potential for future work.

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Disclosure

Drs. Hatfield and Loughrey are employed by Leeds Teaching Hospitals NHS Trust but work in collaboration with Nova Healthcare to provide treatment for patients at Leeds Gamma Knife Centre. The authors alone are responsible for the content of this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Wright, Hatfield, Bownes. Acquisition of data: Wright, Hatfield, Loughrey, Reiner. Analysis and interpretation of data: Wright. Drafting the article: Wright. Critically revising the article: Wright, Hatfield, Reiner, Bownes. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Wright. Statistical analysis: Wright. Administrative/technical/material support: Wright, Hatfield, Loughrey. Study supervision: Bownes.

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Address correspondence to: Gavin Wright, M.Phil., Department of Medical Physics & Engineering, St. James's Institute of Oncology, Bexley Wing, St. James's University Hospital, Beckett St., Leeds, LS9 7TF, United Kingdom. email: Gavin.Wright@leedsth.nhs.uk.