Leksell GammaPlan version 10.0 preview: performance of the new inverse treatment planning algorithm applied to Gamma Knife surgery for pituitary adenoma

Clinical article

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Object. Treatment planning for Gamma Knife surgery has traditionally been a forward planning (FP)—only approach with results that depend significantly on the experience of the user. Leksell GammaPlan version 10.0, currently in beta testing, introduces a new inverse planning (IP) engine that may allow more reproducible results across dosimetrists and individual institutions. In this study the authors compared the FP and IP approaches to Gamma Knife surgery.

Methods. Forty-three patients with pituitary adenomas were evaluated after dose planning was performed using FP and IP treatment approaches. Treatment plans were compared for target coverage, target selectivity, Paddick gradient index, number of isocenters, optic pathways dose, and treatment time. Differences between the forward and inverse treatment plans were evaluated in a statistical fashion.

Results. The IP software generated a dose plan within approximately 10 minutes. The FP approach delivered the prescribed isodose to a larger treatment volume than the IP system (p < 0.001). The mean (± SD) FP and IP coverage indices were 0.85 ± 0.23 and 0.85 ± 0.13, respectively (no significant difference). The mean FP and IP gradient indices were 2.78 ± 0.20 and 3.08 ± 0.37, respectively (p < 0.001). The number of isocenters did not appreciably differ between approaches. The maximum doses directed to the optic apparatus for the FP and IP methods were 8.67 ± 1.97 Gy and 12.33 ± 5.86 Gy, respectively (p < 0.001).

Conclusions. The Leksell GammaPlan IP system was easy to operate and provided a reasonable, first approximation dose plan. Particularly in cases in which there are eloquent structures at risk, experience and user-based optimization will be required to achieve an acceptable Gamma Knife dose plan. (DOI: 10.3171/2010.7.GKS101033)

KEY WORDS  •   •   •   •
Gamma Knife  

Abbreviations used in this paper: FP = forward planning; GI = gradient index; GKS = Gamma Knife surgery; IP = inverse planning; LGP = Leksell GammaPlan.
that there may be a loss of control over the geometry of the resulting radiation dose distribution.

Elekta AB, the manufacturer of the Gamma Knife, recently developed a new set of IP tools that are currently in beta testing at a variety of Gamma Knife centers (Fig. 1). The tools allow a planner to define a target, fill the target with isocenters, and optimize the resulting dose distribution based on a prioritization of criteria including coverage, selectivity, dose falloff outside the target (GI), and beam-on time. The objective of this study is to evaluate the functionality and performance of the IP system proposed for the LGP version 10.0 release and to perform an initial evaluation of the system for delivering radiosurgery to a pituitary adenoma.

**Methods**

Studies to compare IP and FP were conducted in 52 pituitary adenomas treated by the Leksell Gamma Knife Perfexion (Elekta AB) in 2009 and 2010. Nine cases were excluded because the target (tumor) was not outlined as part of the treatment planning or the whole sellar area was outlined as a target; this left 43 treatment plans in the study. For treatment-planning purposes, axial T1-weighted unenhanced and contrast-enhanced 1- to 1.5-mm–slice thickness images were obtained through the entire volume of the head; these images were supplemented with coronal images through the pituitary fossa.

The GKS plans used for actual clinical treatments were created following the traditional FP method on the day of patient treatment by a team consisting of a neurosurgeon (J.P.S.), radiation oncologist, and medical physicist (D.J.S.) using Leksell GammaPlan version 9.0–9.3. The goal of FP was to maximize tumor coverage while limiting the maximum dose delivered to the optic apparatus to less than 8 Gy. The mean tumor volume across all treatments was 3.04 cm³ (range 0.09–17.61 cm³), the mean prescription dose was 20.23 Gy (range 14–25 Gy), and the mean treatment isodose was 49.8% (range 40%–50%).

These reference FP treatment plans were loaded into the LGP version 10.0 beta IP station. All isocenters in each plan were deleted. The tumor outline used in the actual treatment plan was retained and set as the target. The outline of the optic pathway was also retained and marked as an “organ at risk.” The IP program was then used to establish a treatment plan (Fig. 2). The same target, critical structures, and prescribed doses used for the original treatment plan were used for IP. The IP software was set to allow the use of composite shots and sector blocking. The IP optimizer was allowed to run for a maximum of 10,000 iterations per plan.

Inverse planning results were compared with FP results for a variety of metrics including coverage, selectivity, GI, normalized beam-on time, maximum optic pathways dose, and number of isocenters. Statistics software (SPSS version 17.0, SPSS Inc.) was used to perform statistical analysis of the data. Comparisons of means were conducted using paired t-tests. Probability values < 0.05 were considered statistically significant. Mean values are presented ± SDs.

**Results**

**General Observations**

We observed that the IP system completed each treatment plan in approximately 10 minutes. Initial isocenter filling of the target took only a few seconds, and the rest of the time spent was for optimization of the plan. It was also noted that the learning curve was short—it took only a few trials for the operator to become familiar with the system and operate it in a timely manner. Another observation was that the optimizer allows for collimator configurations that are very different from those typically used in FP. For instance, in IP-generated dose plans, many isocenters used collimator ports of 3 different sizes.

**Treatment Volume**

Treatment volume is defined as the total volume of tissue (target or normal tissue) that receives a dose greater than or equal to the prescription isodose (\(V_{pi}\)). The mean volume receiving ≥ 50% of the prescription dose was 4.14 ± 3.45 cm³ for plans obtained through the FP approach, which was higher than the mean volume of 3.22 ± 3.09 cm³ for plans obtained using the IP system. The difference was statistically significant (p < 0.001) (Table 1).

**Coverage Index**

The coverage index is defined as the fractional volume of the target covered by the prescription isodose: coverage index = \(V_{Tp}/VT\), where \(V_{Tp}\) is the volume of target covered by the prescription isodose and \(VT\) is the volume of the target. Both treatment plans—FP and IP—showed similar coverage indices (0.85 ± 0.23 for FP and 0.85 ± 0.13 for IP, p = 0.967). The volume of tumor covered by the prescription isodose was 2.61 ± 2.88 cm³ for FP and 2.67 ± 2.79 cm³ for IP, which are similar volumes.

**Selectivity Index**

The selectivity index is defined as the volume of the tumor covered by the prescription isodose divided by the treatment volume: selectivity index = \(VT_{pi}/VT\). We observed that treatment plans obtained using IP were more selective. The mean selectivity of treatment plans formulated by the IP system was 0.83 ± 0.15, whereas that for FP was 0.58 ± 0.23. The difference in the selectivity index between the 2 groups was statistically significant (p < 0.001) (Table 1).

**Gradient Index**

The GI is a metric used to describe dose falloff outside the target. For this work we used the GI described by Paddick and Lippitz: \(GI = V_{1/2pi}/V_{pi}\), where \(V_{pi}\) is the volume of tissue covered by the prescription isodose and \(V_{1/2pi}\) is the volume of tissue covered by one-half of the prescription isodose. (For instance, if the prescription isodose is 50%, the GI would be the ratio of volumes of tissue covered by the 25% and 50% isodoses.) The GI for plans formulated using the FP approach was 2.78 ± 0.04, which was lower than that obtained using the IP system (3.08 ± 0.37). The difference between the 2 groups was statistically significant (p < 0.001) (Table 1).
Normalized Beam-On Time

Total beam-on time was reported by the treatment planning system as the dose rate used on the date of the plan. Total beam-on times were normalized to a common dose rate of 3.0 Gy/minute to allow for valid comparisons to be made. The normalized beam-on time was 97.04 ± 39.50 minutes for FP and 118.76 ± 53.02 minutes for IP (Table 1). The difference in normalized beam-on times between the 2 groups was statistically significant (p = 0.008) (Table 1).

Number of Shots (Isocenters)

The number of shots, or isocenters, per plan was recorded. The mean number of shots was similar for both treatment plans: 13.42 ± 4.17 for FP and 13.81 ± 8.29 for IP (p = 0.710) (Table 1).

Fig. 1. Leksell GammaPlan version 10.0 IP workflow. The planning system can fill a target with shots and then optimize dose distribution based on prioritized criteria such as selectivity, coverage, GI, and beam-on time.

Fig. 2. The optimization functionality of the IP system demonstrating how to prioritize constraints and visualize the number of iterations and the progress of the optimization.
TABLE 1. Summary of results*  

<table>
<thead>
<tr>
<th>Factor</th>
<th>FP System</th>
<th>IP System</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>coverage index</td>
<td>0.85 ± 0.23</td>
<td>0.85 ± 0.13</td>
<td>0.967</td>
</tr>
<tr>
<td>selectivity index</td>
<td>0.58 ± 0.23</td>
<td>0.83 ± 0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>treatment volume (cm³)</td>
<td>4.14 ± 3.45</td>
<td>3.22 ± 3.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GI</td>
<td>2.78 ± 0.20</td>
<td>3.08 ± 0.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>normalized beam time (min)</td>
<td>97.04 ± 39.50</td>
<td>118.76 ± 53.02</td>
<td>0.008</td>
</tr>
<tr>
<td>no. of isocenters</td>
<td>13.42 ± 4.17</td>
<td>13.81 ± 8.29</td>
<td>0.710</td>
</tr>
<tr>
<td>max dose to optic pathways (Gy)</td>
<td>8.67 ± 1.97</td>
<td>12.33 ± 5.86</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Values are presented as means ± SDs. Although it has better selectivity and a smaller prescribed isodose volume than the FP system, the IP system has a larger gradient index, longer beam-on time, and higher maximum dose delivered to the optic pathways.

Radiation Dose Directed to the Optic Pathways

The maximum dose of radiation directed to the optic pathways using the FP system (8.67 ± 1.97 Gy) was less than that using the IP system (12.33 ± 5.86 Gy), and this difference was statistically significant (p < 0.001) (Table 1).

Discussion

A number of automated planning systems for GKS have been studied with the goal of achieving some of the advantages of the IP systems used elsewhere in radiation oncology. Using these techniques, isocenters are placed to fill the target, and then isocenter configurations, locations, and weights are optimized. The optimization model can include dose constraints applied to both the target and sensitive structures. Different approaches have included a sphere-packing approach, a modified Powell method, simulated annealing, and mixed integer programming. In several studies, the treatment plan produced by an IP system resulted in plans with fewer shots, an improved conformity index, a higher minimum target dose, and a reduced volume within the 30% isodose line as compared with the manual plan. However, these techniques have not yet been generally adopted in the clinic and are not included in the LGP treatment planning software that is used in the majority of clinics.

A major requirement for any semiautomated planning system is that it must be fast, because the treatment planning process begins after the patient’s stereotactic head frame is in place and MR or CT images have been obtained. Therefore, it is unacceptable to have a planning procedure that takes hours to complete. Treatment planning in traditional radiation oncology takes place off-line, often days or even weeks before treatment begins. Thus, IP systems used in such cases have plenty of time for calculation, and in some cases treatment planning occurs in batch mode, wherein optimization of multiple plans occurs overnight, with the results evaluated the next day.

An IP system should take into consideration patient comfort and also facilitate better workflow in a GKS center. The IP system used in this study satisfied that requirement. The 10-minute time frame for completing a treatment plan for GKS is shorter than that required to complete the same task manually, even in the hands of experienced operators. The short learning curve is another obvious advantage of the IP system.

One goal of radiosurgery is to design a treatment plan in which the prescription isodose line covers the target with minimal excess volume and a sharp dose falloff outside the target volume. The IP system provided similar tumor coverage but better selectivity, as evidenced with a smaller treatment volume (prescription isodose volume) in this study. One of the most important quality metrics used for radiosurgery treatment plans is a conformity index, which in the formulation by Paddick is simply the product of fractional coverage and the selectivity index. The IP system had better overall conformity, indicating that the system was capable of formulating a treatment consistent in quality to those created using the FP system.

Although the conformity index is an objective measure of how well the distribution of radiation conforms to the size and shape of a target, the dose falloff outside the target is of equal, if not greater, importance as a measure of treatment plan quality, particularly with regard to the prediction of complications. This point is even more valid when the target is close to critical structures, as often occurs in cases of pituitary adenomas, where the optic apparatus and mesial temporal structures lie in the vicinity of the treatment target. Although the IP system has better selectivity and a smaller prescription isodose volume, it has a larger GI. Since the mean number of isocenters was similar for both treatment plans, the larger GI in plans obtained using the IP system is most likely a reflection of the distribution and configuration of isocenters. In the LGP IP system, isocenters appear to be placed closer to the edges of the target volume. In addition, large elongated isocenters, created by blocking sectors, are often used, and this can have the effect of broadening the dose falloff outside the target (Fig. 3). This point is further reinforced by the observation that when the maximum dose was considered, exposure of optic pathways to radiation was greater when IP was used.

Another drawback of the IP system was that the treatment beam-on time was longer than that obtained using the FP system. Cases of pituitary adenoma tend to have some of the longest treatment times in the Gamma Knife repertoire due to the relatively high doses required and the need for extensive blocking. Any unnecessary increase in time reduces overall patient satisfaction with the treatment. While one could argue that an average of 20 minutes difference (97.04 ± 39.50 minutes for FP and 118.76 ± 53.02 minutes for the IP) over a total of almost 2 hours is not clinically relevant, our experience is that ignoring treatment time as a measure of plan quality increases the risk that a patient will refuse to complete a treatment. It should be noted that the increase in beam-on time is somewhat mitigated by a decrease in treatment planning time. The complexity of pituitary adenoma treatment plans often requires extended effort by the planning team, as there are a large number of factors to
consider and parameters to optimize manually. The much shorter time required using the IP system helps minimize the overall time patients wait with a stereotactic frame on their heads.

It should be noted that the intent of this study was to perform a preliminary investigation of a beta version of the new Elekta IP system with a focus on evaluating performance and usability. By using a single set of parameters for IP optimization, we used the planning method in a manner somewhat different from its intended clinical workflow. A more typical IP session will resemble that shown in Fig. 1. After filling the target with shots, optimization will proceed in an iterative fashion: the results of one optimization iteration will be evaluated based on criteria such as those presented in this paper, constraints will be adjusted, and a new optimization iteration will be run. This, combined with a manual adjustment of shots, if required, will be repeated until an acceptable plan has been generated. While this will require more planning time than that reported in this work, we still expect significant savings in overall time compared with using a purely manual method.

Conclusions

The LGP IP system is easy to operate and is likely to have a short learning curve. Even using the default settings, the functionality of the new IP can quickly achieve plans comparable to (and in some cases better than) those of traditional FP. Experience will likely make it possible to choose the most appropriate optimization settings while minimizing the number of required iterations. In the present study IP had better selectivity and a smaller prescription isodose volume than FP, although IP did have a larger GI. This may indicate that it will be more useful in cases in which the target is not too close to radiosensitive vital structures. For these kinds of targets, some manual optimization following IP will likely be necessary to protect critical structures.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Sheehan, Schlesinger, Yen. Acquisition of data: Schlesinger, Sayer, Yen. Analysis and interpretation of data: Schlesinger. Drafting the article: Sayer, Schlesinger. Critically revising the article: Sheehan, Schlesinger, Yen. Reviewed final version of the manuscript and approved it for submission: Sheehan, Schlesinger. Statistical analysis: Schlesinger.

References