**Outline:**

Automated treatment planning for a dedicated multi-source intracranial radiosurgery treatment unit using projected gradient and grassfire algorithms

1. **Introduction**
2. The new Leksell Gamma Knife (LGK) Perfexion (PFX), used to deliver radiosurgery for brain cancer treatment, allows for greater automation and customizability than earlier LGK models.
3. We develop an optimization-based method based on intensity modulated radiation therapy (IMRT) models to automatically develop good PFX treatment plans.
4. **Methods and materials**
5. Our method consists of two parts: isocenter selection and sector duration optimization (SDO).

	1. **Isocenter selection**
		1. Isocenters, assumed to be spherical in this phase, are optimized using a purely geometric algorithm.
		2. The algorithm is a hybrid of grassfire and sphere-packing (GSP) methods and uses tunable scoring parameters.
		3. The scoring method requires the identification of the deepest voxels in the non-covered target area.
		4. The isocenter candidate with the highest boundary and depth scores is selected as the next isocenter.
		5. Parameters α and *f* in GSP are tuned to obtain good target coverage with a user-defined number of isocenters.
	2. **Sector duration optimization model**
		1. Using the GSP-selected isocenters, sector-collimator radiation delivery durations are optimized.
		2. The SDO is similar to fluence map optimization in IMRT.
		3. Dose is calculated as a linear sum of the duration decision variables.
		4. Voxel underdose or overdose is penalized according to each structure.
		5. The dose penalty function is a convex quadratic function.
		6. The SDO model minimizes total penalty, resulting in a convex problem with only non-negativity constraints.
	3. **Projected gradient algorithm**
		1. A projected gradient algorithm with an Armijo line search is used to solve SDO.
		2. The algorithm terminates when relative objective function improvement is less than 10e-4.
	4. **Evaluation of algorithm**
		1. The method was tested on seven radiosurgery patient cases.
		2. There are clinical guidelines that must be followed.
		3. The method was tested for a range of isocenters per case.
6. **Results**
7. The optimized treatments outperformed the clinical treatments in target coverage and conformity.
8. Dose levels and conformity are illustrated in dose-volume histograms and isodose lines.
9. As more isocenters were used, conformity improved, but beam-on time exhibited no clear correlation.
10. Isocenter selection took less than 3s, while SDO took 215min on average.
11. **Discussion**
12. Our approach yields clinically acceptable treatment plans, though treatment times are longer.
13. Our results compare favorably in both conformity and organ sparing to previous LGK optimization studies.
14. Our methods are more flexible and computationally tractable than those in previous LGK optimization studies.
15. Unlike previous LGK optimization studies, we explicitly consider organ sparing and are not limited to single-target scenarios.
16. GSP extensions could provide improvements, but simultaneous isocenter optimization and SDO is likely computationally intractable based on similar IMRT studies.
17. A beam-on time penalty could be incorporated into SDO for improved treatment times.
18. Computation times could be improved through faster languages and parallelization.
19. **Conclusions**
20. Mathematical frameworks successful in IMRT optimization can be applied to PFX to obtain quality treatments.