

## ABSTRACT

Proton Pencil-Beam Scanning treatment plans are optimized using Single-Field Uniform Dose (SFUD), Multi-Field Optimization (MFO), or a combination of the two techniques into a Hybrid plan. In this study, we develop a method to evaluate plans using metrics applied to field-specific differential dose volume histograms (DVHs) from various treatment areas.

An application was developed to create normalized differential DVHs of the primary target volume for each field in a proton PBS treatment plan, and used five metrics to create a final ranking system for 235 patients plans. The results were then compared to their initially selected optimization technique, compared across treatment locations, and ran through statistical and machine-learning algorithms to test the validity of the ranking criteria.

Out of the 235 patient plans, our system reclassified 33 plans as MFO, 57 Hybrid, and 145 SFUD. Statistical analyses using ANOVA and T-test assuming unequal variances showed that the averages of metrics in each classification group were found to be statistically significantly different, and clustering and re-classification methods proved our ranking system to be a more accurate representation of the treatment plans than the initial automatic optimization.

By analyzing the uniformity of treatment plans, our method will aid future robustness evaluation, image guidance tolerance, and data analysis.

## INTRODUCTION

**Proton Radiotherapy** is a form of radiation treatment that uses energized protons to break DNA, leading to cell death and killing cancers.

**SFUD vs MFO** - planning optimization methods for Pencil Beam scanning

- Single-Field Uniform Dose, SFUD, is composed of multiple fields, each individually optimized at different locations to deliver a homogenous dose across a tumor (Fig. 2).
- Multi-Field Optimization, MFO, uses beams that are all optimized simultaneously, so that they can vary the intensity of radiation delivered at each voxel, working around organs at risk (Fig. 3).
- Fig 2&3 show differential Dose-Volume Histograms (dDVH), graphs displaying the percentage of full dosage delivered to every percentage of volume of dose, for a full SFUD and a full MFO plan.

**Hybrid**

- In practice, treatment plans are a combination of SFUD and MFO, or a hybrid plan
- As shown in Fig. 6&7, each beam deposits varying intensities of dosage to different voxels, the MFO component
  - The two beams have identical intensity distributions; delivering the same dosage, but coming in from different positions.

**Differential Dose-Volume Histograms**

- 2D representation of 3D dose-volume calculations; a histogram relating radiation dose to tissue volume
  - The height of each bar represents the amount of tissue that receives the amount of dose specified by the bin
- Our graphs are normalized to percentage of full volume for percentage of full dose

## METHODOLOGY

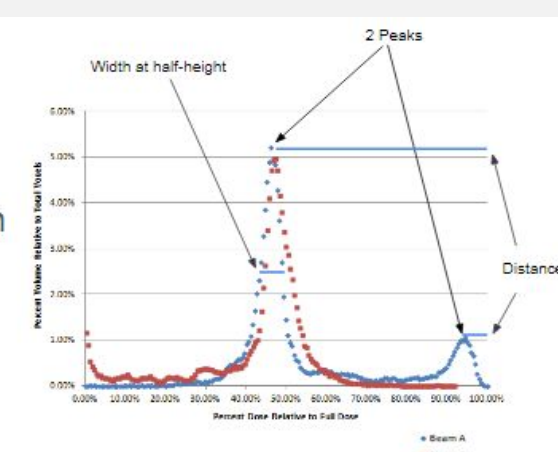
**Analysis** - Our goal was to analyze and classify the treatment plans into the SFUD-MFO spectrum. To do so, we created a python procedure that analyzes the beam distributions of treatment plans through dDVH graphs and goes through five weighted factors in the dDVH graphs to classify the type of plan being used (Fig. 1&6).

- **Number of Peaks** - Any more than a single peak per beam is an MFO component
- **Distance/Slope/Midwidth** - the smaller the distance from the peak to the end, the smaller the midwidth, and the steeper the slope is, the more SFUD it is.
- **Difference** - As seen in Fig. 2, the peaks in each of the two beams are almost identical in an SFUD plan as opposed to an MFO (Fig. 3). This means that the greater the difference is between the peaks of the beams, the more MFO the plan is.

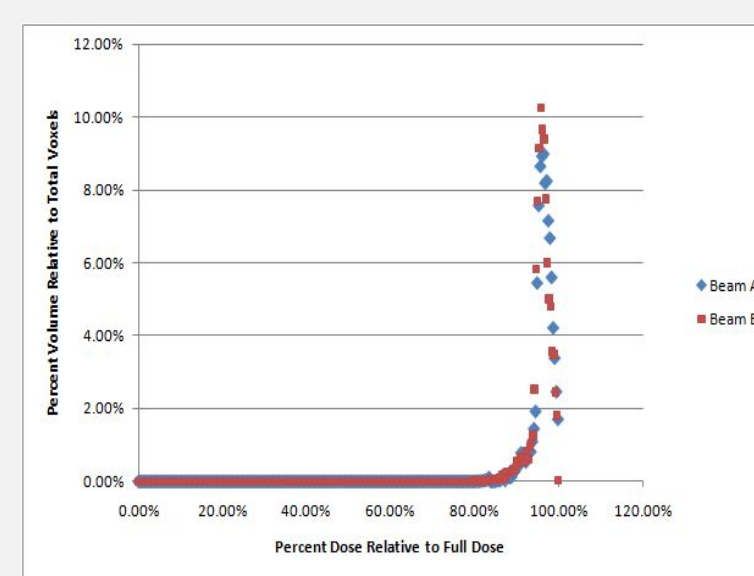
**Ranking** - We scaled all data from 100% (SFUD) down to 0% (MFO) to create an individual rank for each patient of where they lie on the spectrum. Each plan started at 100% SFUD, and based on if each of the five metrics represented a SFUD or MFO component, we added or subtracted from that initial value (Fig. 6).

**Machine Learning** - We ran all data through sklearn's agglomerative clustering algorithm, which sorted treatments into groups based on the similarity of metrics alone. We then ran a pipeline optimizer (TPOT) in attempt to find an accurate re-classification algorithm that would mimic the clustering results. Finally, we compared the results of TPOT's algorithm and our rankings to check for our ranking's accuracy.

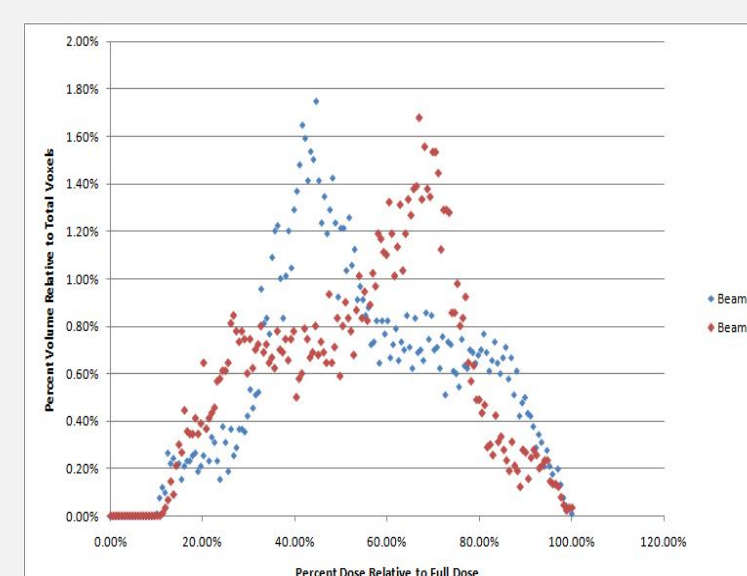
### Important Factors



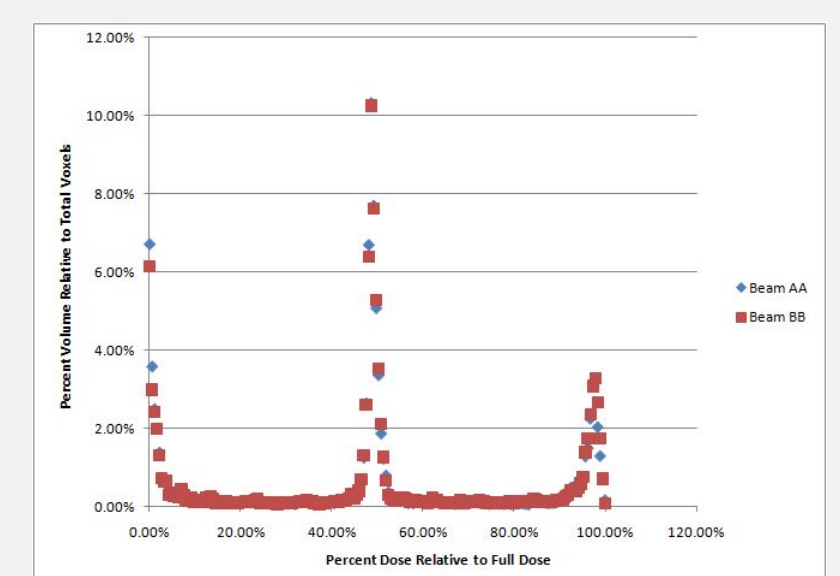
**Fig. 1 (above):** List of the five factors used to analyze a differential DVH to categorize the treatment plan. Four of the five are shown in the graph. The 5th, difference, is calculated by subtracting the two Ys for a given X.



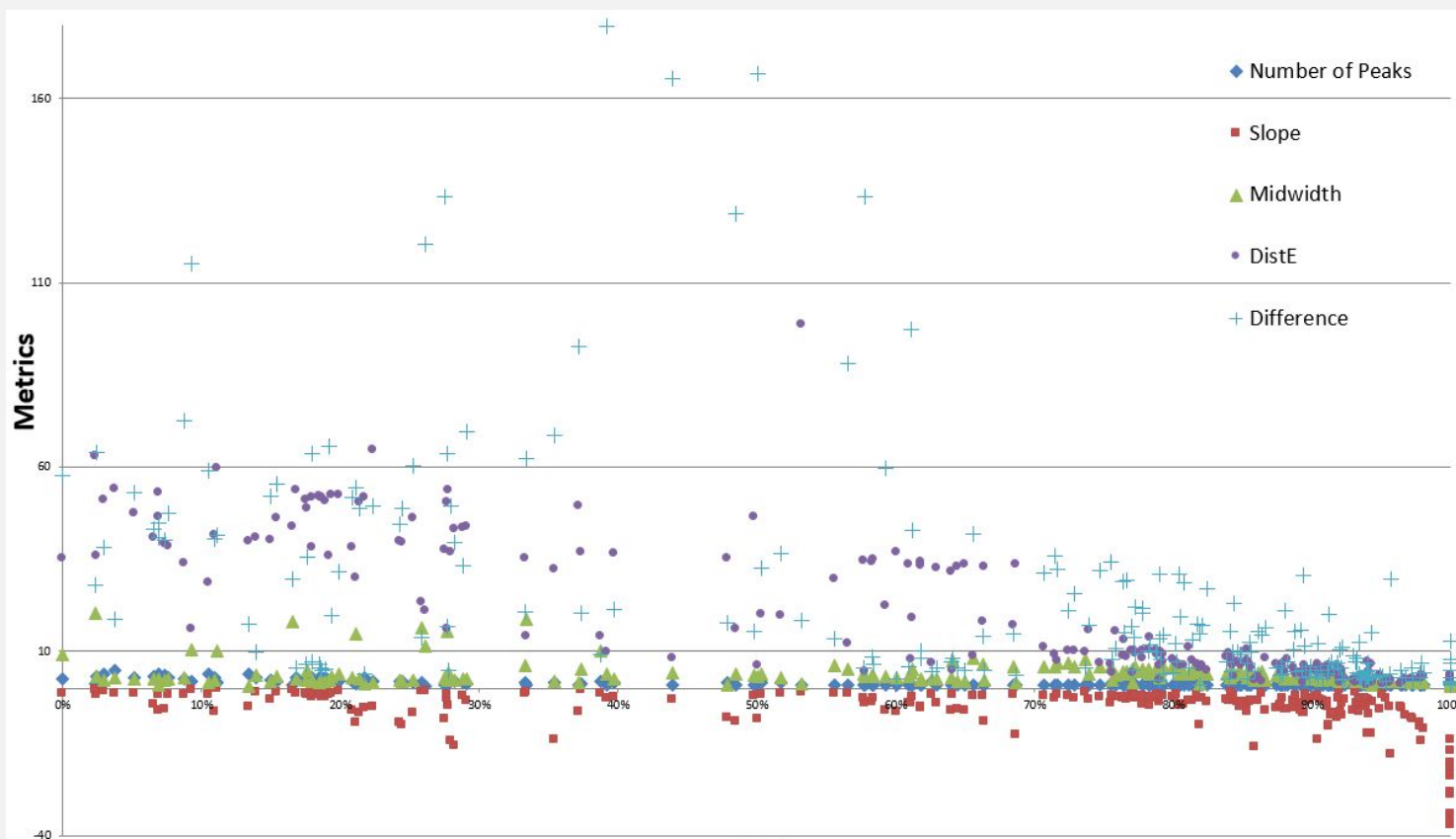
**Fig. 2 (left):** Differential DVH of SFUD plan, shown by uniform, identical peaks at 100% dose.



**Fig. 3 (left):** Differential DVH of MFO plan, shown by varied percent dose deliverance.



**Fig. 4 (above):** Differential DVH of Hybrid plan, shown by combinations of SFUD and MFO components.



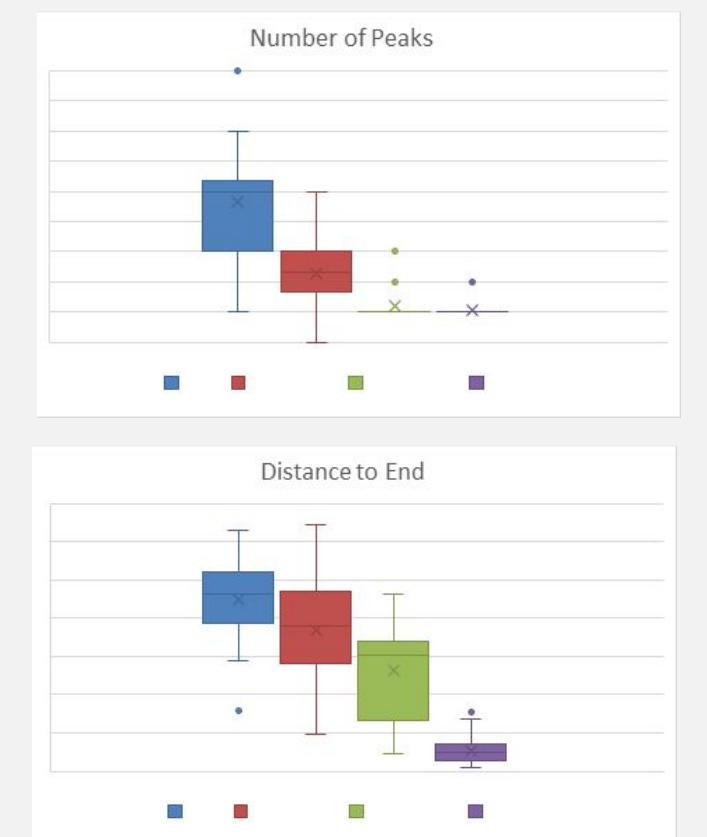
**Fig. 5 (above):** Graph showing distribution of each of the five factors of a treatment plan according to the rank it was given 0%-100%.

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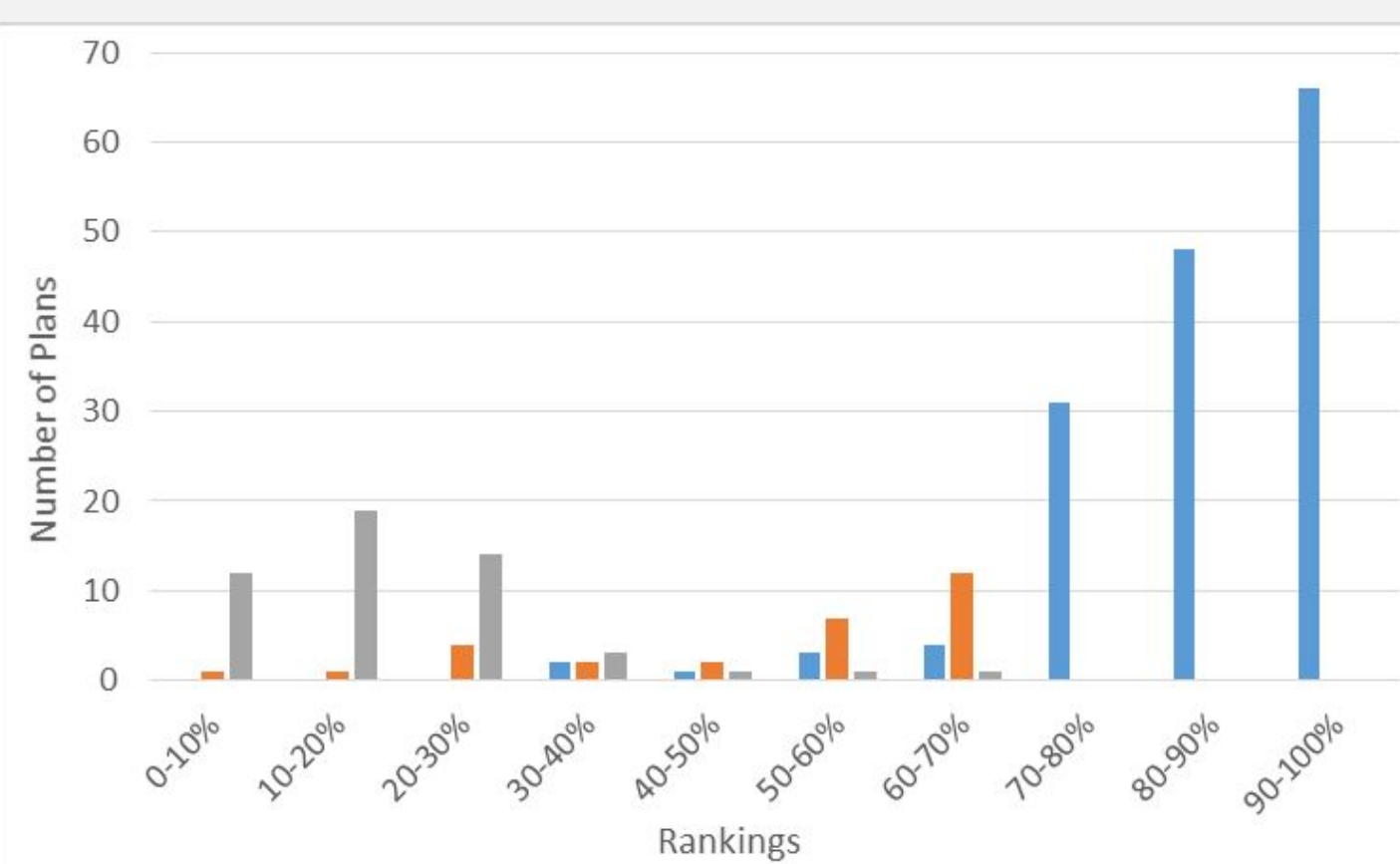
ranking = 100.0
if (avgBeamPeak > 1):
    ranking = ranking - (25*(1-.5**((avgBeamPeak-1)/.5)))
    print("ranking after peak count: " + str(ranking))
if (avgDist >= 40):
    ranking = ranking - 40
else:
    ranking = ranking - avgDist
print("ranking after distance: " + str(ranking))
ranking = ranking - avgMidwidth
print("ranking after midwidth: " + str(ranking))
if (avgAbsDiff >= 1):
    ranking = ranking - 25
else:
    ranking = ranking - avgAbsDiff*25
print("ranking after diff: " + str(ranking))
ranking = ranking - avgSlope/2
print("ranking after slope: " + str(ranking))
if (ranking > 100):
    ranking = 100
if (ranking < 0):
    ranking = 0
    
```

**Fig. 6 (left):** Python code calculating rank of each treatment plan based on the five weighted factors.

Patient Number	Rank	Peak	Slope	MW	DTE	Diff
1	0.000%	3	-1.32	9.17%	35.14%	57.74%
14	10.50%	4	-1.73	1.58%	28.72%	58.92%
34	20.88%	2	-6.09	2.95%	38.30%	51.82%
52	33.34%	1.5	-1.4	6.23%	35.12%	20.76%
60	43.93%	1	-3.15	4.03%	8.26%	165.29%
65	50.31%	1.5	-1.67	3.94%	19.88%	32.46%
78	61.21	1	-2.46	5.17%	18.99%	42.74%
92	70.69%	1	-2.11	5.71%	11.11%	31.31%
129	81.12%	1	-3.40	4.01%	11.21%	5.36%
175	90.74%	1	-3.55	2.29%	5.62%	3.33%
235	100%	1	-28.86	0.83%	2.15%	1.44%



**Fig. 7 (above):** 11 example patients of the 235 we tested. One patient from every 10% rank to show distribution of factors. Graphs on the right display trends of certain metrics (number of peaks/beam and distance from peak to end) grouped in rankings from 1-20%, 20-40%, 40-70%, and 70-100%.

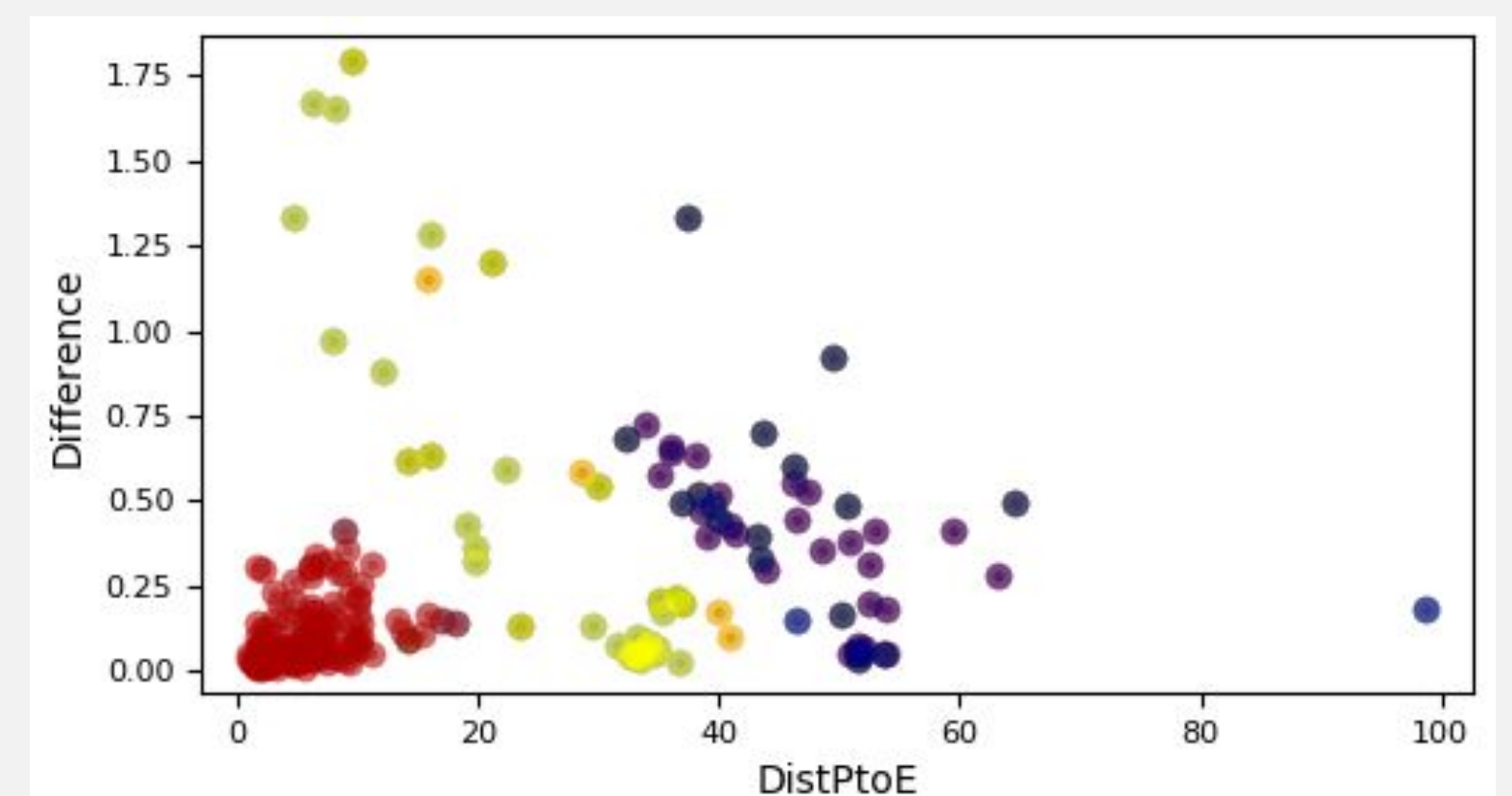
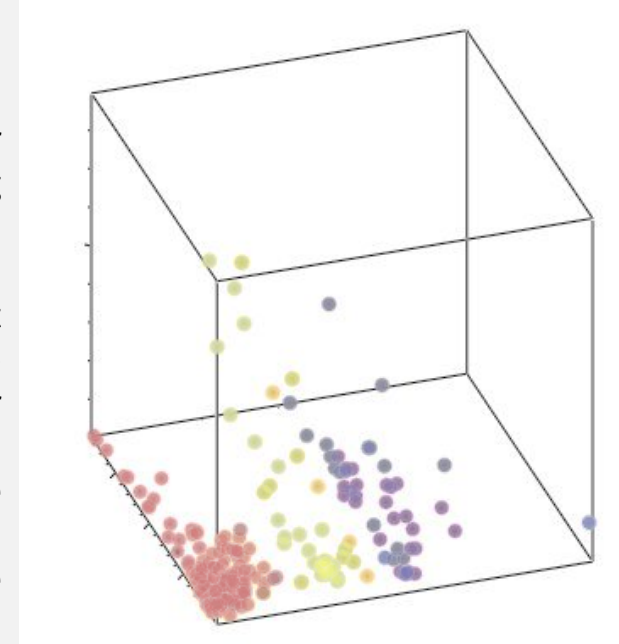


**Fig. 9 (above):** Graph depicting the types of plans our algorithm sorted plans into versus the ranking our system assigned it. The type of plan matches almost exactly with the progression of rankings.

Ranking Range	Treatment Area
55-65%	Prostate & Lymph Nodes
70-80%	Brain
~80%	Neck
90-100%	Prostate

**Fig. 8 (above):** Table showing most common area treated with each range of ranks. Treatment areas closer to 100% rank would more likely receive an SFUD plan, while areas with a lower rank would receive more MFO components.

**Fig. 10 (right):** 3D graphing of the 235 patients based on their 5 metrics using Agglomerative Clustering (see Fig 9). Principal Component Analysis was used to project data in a lower dimensional space. X-Axis (across): Distance Y-Axis (back): Slope Z-Axis (up): Difference



**Fig. 11 (above):** 2D cluster analysis of the 235 patients based on their 5 metrics which have been reduced down to two degrees showing difference between the distributions and their distance from the end. One can see that the collection of red points are tight together, representing the SFUD. Yellow then represents hybrid plans, while purple represents the MFO plans.

## DISCUSSION/CONCLUSIONS

- The rankings presented trends about the uniformity of certain treatments as seen in Fig. 8.
- These trends can help dosimetrists more readily identify the most efficient treatment plan to use for future patients and the program allows them to confirm that they have the safest and most efficient plan before applying it to the patient
- Raystation originally optimized 98 patients as SFUD, 107 Hybrid, and 30 MFO; our system reclassified 33 plans as MFO, 57 Hybrid, and 145 SFUD
- Statistical analyses using ANOVA and T-test assuming unequal variances showed all values to be significantly different, proving our ranking system to be a more accurate representation of the treatment plans than the initial automatic optimization.
- The results of running clustering (Agglomerative Clustering) and optimizing tools (TPOT) on our data values also show a significant divide between the three optimization techniques, which will allow us to create superior classification and regression algorithms for the uniformity of treatment plans in the future.
- SFUD accounted for 80% of brain patients, and 70% of prostate patients
- Craniospinal and torso patients had an even spread across all techniques
- 50% of Head/Neck treatment plans were MFO, the other half SFUD, with very few hybrid plans

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## ACKNOWLEDGEMENTS

- Thank you to the medical physics department at Northwestern Medicine for providing us with this opportunity and mentorship.
- Thank you to IMSA for providing us with transportation and the opportunity to participate in a research project.