SESUG 2022 Paper 105

Use of JMP®'s Prediction Profiler to Predict Outcomes of Acute Spinal Cord Injury

Melvin Alexander- Independent Consultant

ABSTRACT

For 30 years JMP®'s Prediction Profiler (JPP) has been the cutting-edge, "secret-sauce" tool for finding optimal settings of predictor, regression factors that impact fitted responses from designed experiments and correlated observational data (Jones, 2021). Aarabi, Alexander et al. (2011) used stepwise regression to identify the key input variables from trauma admission, demographic, injury severity measures from Magnetic Resonance Imaging (MRI), and clinical indicators that impacted the response variables of the American Spinal Injury Association (ASIA) motor scores, Functional Independence Measure (FIM), manual dexterity, and dysesthetic pain (e.g., burning, prickling, or aching) experienced after surgery for trauma patients with acute traumatic central cord syndrome (ATCCS) due to spinal stenosis (spinal-cord narrowing that presses on the nerves passing through the spine). This paper uses JPP's Desirability functions and Simulator to gain additional the insights between 10 independent variables on four output response variables that were not considered in the original study. JPP's Desirability functions and Montel Carlo simulation helps to find the most robust data settings that achieves desirable goals for the dependent response variables, especially when some responses have conflicting objectives.

INTRODUCTION

JMP®'s Prediction Profiler (JPP) explores fitted responses with the objective of discovering how settings of multiple input variables impact single and multiple output, response variables. JPP provides useful visualizations for examining how changes in fitted models of various responses are affected by changing the settings of several individual predictor variables. JPP gives users the ability to set desirability goals for responses, find the optimal settings for factors, and much more.

JPP is an invaluable tool for exploring the relationships between multiple input variables on multiple output/outcome/response variables.

To illustrate the application, I will use a study by Aarabi, Alexander et al. (2011), designed to examine the relationship between 10 independent variables on four output response variables in patients with acute traumatic central cord syndrome (ATCCS) due to spinal stenosis.

ATCCS is the most common type of incomplete spinal cord injury that is characterized mostly by upper extremity weakness, variable sensory loss, bladder and sexual dysfunction. These injuries typically occur after traumatic events such as motor vehicle accidents, falls, sports and other injury mechanisms.

BACKGROUND

From January 1, 2000, until April 30, 2008, 914 patients with symptomatic cervical spinal cord injuries were admitted to the R. Adams Cowley Shock Trauma Center, 211 of them were clinically diagnosed with ATCCS. Forty-two patients meeting the study's inclusion criteria had at least 12 months of follow-up, which made up the study population. The study was approved by the Institutional Review Board of the University of Maryland School of Medicine. All patients underwent CT and MR imaging of their cervical spines. Measures of the independent variables were taken independently by two radiologists and the senior author in a blinded manner as displayed in Figure 1.

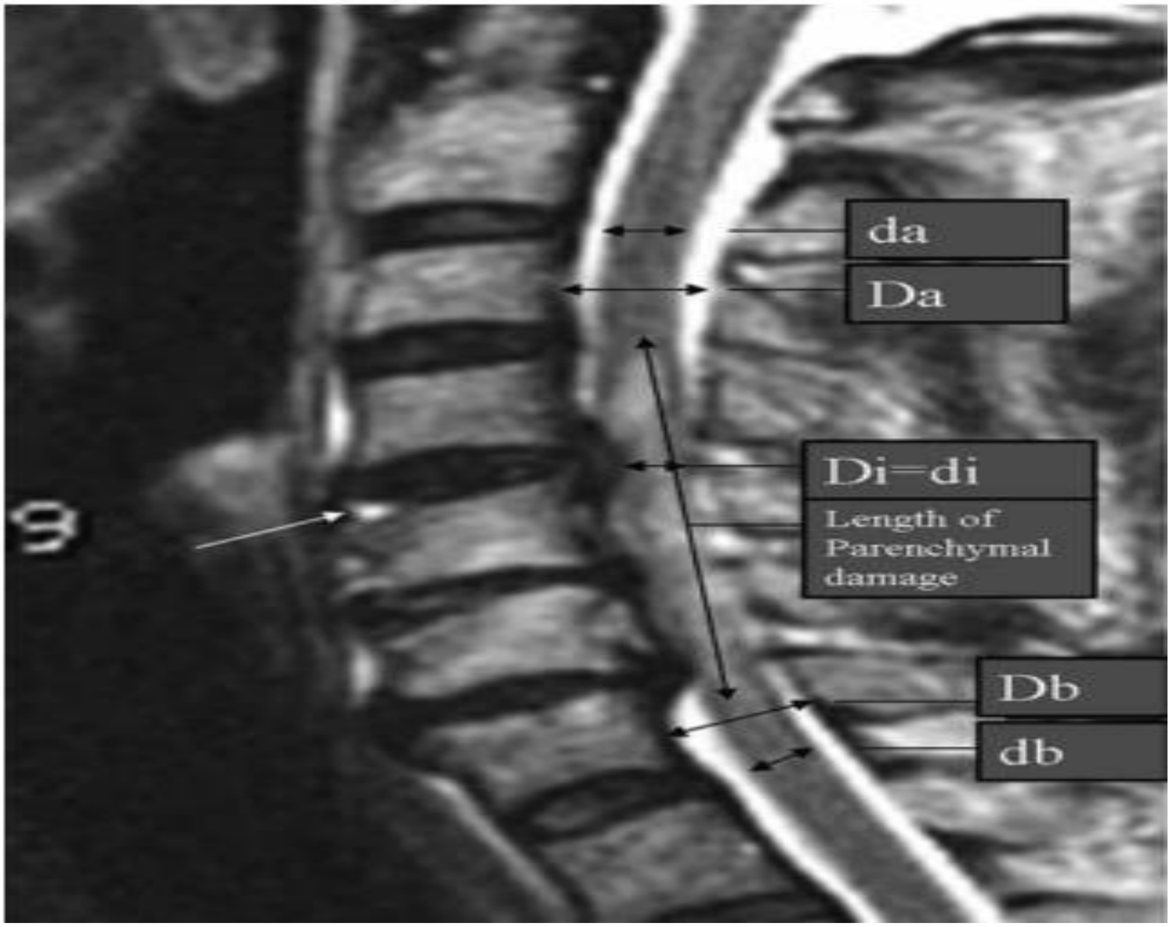


Fig. 1. Sagittal T2-weighted MR image obtained in a 56-year-old woman who sustained a fall and presented with ATCCS and an admission ASIA motor score of 39. The image depicts parameters used to measure midsagittal diameter, MCC, MSCC, and length of parenchymal damage. The white arrow indicates distractive extension injury Stage 1. The following measurements were obtained: spinal cord diameter 1 segment above the end of spinal stenosis (da) was 6.5 mm; sagittal diameter of the spinal canal 1 segment above the stenotic segment (Da) was 11.4 mm; sagittal diameter of spinal cord (di) and spinal canal (Di) at the point of maximum compression was 4.8 mm; length of parenchymal damage was 53.6 mm; sagittal diameter of spinal canal 1 segment below the stenotic segment (Db) was 11.4 mm; and the diameter of the spinal cord below the stenotic segment (db) was 5.6 mm. Calculations indicated a sagittal diameter of the spinal canal of 4.8 mm, MCC of 57.8%, and MSCC of 20.6%. This patient had a long-term ASIA motor score of 98, an FIM of 122, a manual dexterity of 25%, and a pain level of 5 on the analog scale. She had no bladder dysfunction.

Figure 1: MR Image from Aarabi, Alexander, et al. [2] of Acute Traumatic Central Cord Syndrome (ATCCS) due to spinal stenosis (Reprinted with permission from the *Journal of Neurosurgery: Spine*)

A major advantage of JPP is the ability to display *conditional* relationships between responses given current levels of the predictor variables. This feature allows the profiler to account for not only main effects of each predictor but also two-way interactions between pairs of predictors that other software products often ignore. Main effects without two-way interactions only represents the average of the data and are biased when the observed data design is not balanced which is not the (unbiased) least squares mean from the model. Multi-way Interactions in JPP allow fitted models to capture the full relationships between responses as levels of other predictors change**.** The interactions from the profiler allow the fitted model to capture relationships between the responses and each predictor that can be different when levels of other predictors change. Other software products tend to only show *unconditional* mean responses at each factor level. According to John Sall [1], SAS' co-founder and chief architect of JMP, "*th*e Profiler gives you an immediate understanding of which factors are important and the directions of their effects. Interactively changing a factor's value reveals any strong interaction effects."
The dataset consisted of 42 patients with spinal cord injury and central cord syndrome. The dependent variables of the are:

- **Follow-up recovery of Motor functions (F/U Motor Score)**, where Best is set to 100,
- Improved **Functional Independence Measures** (**FIM)** where Best is 126,
- **Hand Dexterity** where Best is 100%,
- **Level of Pain** where the Best is 0 for no pain and 10 is the most severe pain.

Independent predictor Variables to be considered include:

- **Accident** (Fall=1, MVC=2, and other accidents= 3).
- **Age (years range 32-87)**,
- **Admission ASIA motor score** (ranging from 0- poor motor function to 100- maximal motor function),
- **Number of Skeletal segments** involved (1, 2, 3, 4, or 5). One (1) vertebra is one skeletal segment, two (2) vertebra is the second skeletal segment, etc.
- **Sagittal diameter** is the front to back diameter of spinal canal. Smaller diameters mean more narrowing and spinal cord compression.
- **MCC** is maximum canal compromise (or the percent narrowing) of the spinal canal, using Da, Di, and Db, (i.e., diameter of canal above, diameter at the lesion, and diameter below the lesion, respectively),
- We use the Da, Di, Db, to measure the degree or percent of spinal cord compression (**MSCC**).
- **Average Lesion length** is the length of signal change on MRI of patients with spinal cord injury. See the Figure attached.
- **Time Past Injury to surgery** (**TPI-S**, days) is the delay between the time when injury happened and surgery occurred at the Shock Trauma Center (STC).
- **Surgery** - technique of surgery at the front, back or circumferential part of the spine. Front means the surgery involved the front part of spine, back is the back part of spine, and circumferential includes front and back.

Spinal stenosis is the narrowing of spaces within the spinal-canal vertebrae that adds extreme pressure on the spinal cord (central stenosis) or nerves (lateral stenosis) passing through the spine. Spinal stenosis occurs in either the neck or lower back. Small, narrow spaces result in extreme pain, muscle weakness, impaired bladder, and bowel functions.

Table 1 shows the JMP data table of the patients from the case study.

42TCCS_MEL_010522 - JMP

	NO	Accident Fall=1 MVC=2 Other=3	AGE	Admission Motor Score	Skeletal Seg #	Sagittal Diameter of Spinal Canal	MCC % (% Maximum Canal Compromize)	MSCC (% Maximum Spinal Cord Compression)	Average Lesion Length	TPI-S (Time Past Injury to Surgery)	Surgery 1=Front 2=Back 3=Circumferential Front and back	F/U Motor Score	FIM (Functional Impairment Scale)	Dextrity of Hand (%)	Pain score 0-10
1	1	1	58	90	1	5.5	48.8	7.5	25.5	2	1	99	96	80	•
2	2	1	69	68	1	5.2	52.9	18.3	6.9	5.4	2	96	123	95	0
3	3	1	59	89	2	8.6	35.8	-21	28.1	3	1	100	126	90	0
4	4	2	53	80	1	7.1	43.9	5.9	24.7	16	1	100	124	70	6
5	5	1	58	84	2	4.4	64.5	28.4	35.9	7	2	100	125	75	3
6	6	1	51	81	2	6.9	45.7	12.6	29.9	5	1	100	•	•	•
7	7	3	43	50	2	6.6	42.1	8.9	43.1	3.1	1	92	120	70	9
8	8	2	65	56	2	6.1	47.1	27	25.6	2	1	94	121	65	0
9	9	3	64	92	3	4.8	56	26	36.6	1	2	100	126	100	4
10	10	1	50	24	4	5.1	58	30	24.1	90	2	86	108	55	0
11	11	1	56	39	2	4.8	57.8	20.6	53.6	1	1	98	122	25	5
12	12	1	48	38	3	4.1	58.6	34.9	34.3	1	3	97	122	30	7
13	13	2	43	56	3	6.2	42	-5	16.3	5	1	100	123	75	5
14	14	3	53	32	1	5.7	45.7	18.6	28	2	2	77	91	25	9
15	15	2	62	50	3	6.4	50	12	43.5	7	1	100	118	25	4
16	16	1	55	83	5	•	39.8	•	•	1	3	93	106	70	5
17	17	1	65	35	2	5.2	44.5	13.4	42.4	1	3	62	43	20	0
18	18	1	72	87	2	4.1	64	36	19.2	2	2	97	119	85	4
19	19	1	79	76	1	5.1	60	27	20.2	3.3	3	99	121	70	0
20	20	1	63	94	3	3.8	64.1	40.6	15.4	5	2	99	121	90	0
21	21	3	61	92	1	5.7	46.9	1	10	2	1	99	123	80	3
22	22	2	48	94	2	6.6	41.1	7.1	26.1	2	1	100	126	100	4
23	23	1	58	39	2	4.3	56.3	21.8	32.1	2	1	93	117	70	3
24	24	3	43	74	2	7.5	34.2	-8	44.4	2	1	90	121	35	4
25	25	3	47	34	2	7.8	37	12.8	27.5	1	1	100	120	60	3
26	26	1	57	34	4	5	58.1	23.6	35.1	5	2	91	106	40	6
27	27	2	61	89	4	6.1	42.7	5.6	•	2.5	1	97	107	75	0
28	28	1	32	64	1	7.1	42.3	-19.3	24.7	8.7	1	97	103	100	0
29	29	2	68	78	3	4.9	54.8	28	31.5	3.5	2	97	115	80	0
30	30	3	46	•	3	3.1	69.2	38	22	132	3	88	114	45	8

evaluations done

Table 1. JMP data table of the ATCCS data, highlighting the patient record from Figure 1.

The prediction profiler is a dynamic matrix plot of all input variables as columns and output responses as rows. The grey regions (for continuous factors) and error bars (for categorical factors) about the profiler lines show the 95% confidence interval for the mean dependent variable responses that reflect prediction error for each factor. The slopes of each predictor indicate the linear (or nonlinear) trend and direction each predictor has as values change.

Figure 2 shows the Prediction Profile Plot the relationships between the response variables and the predictors.

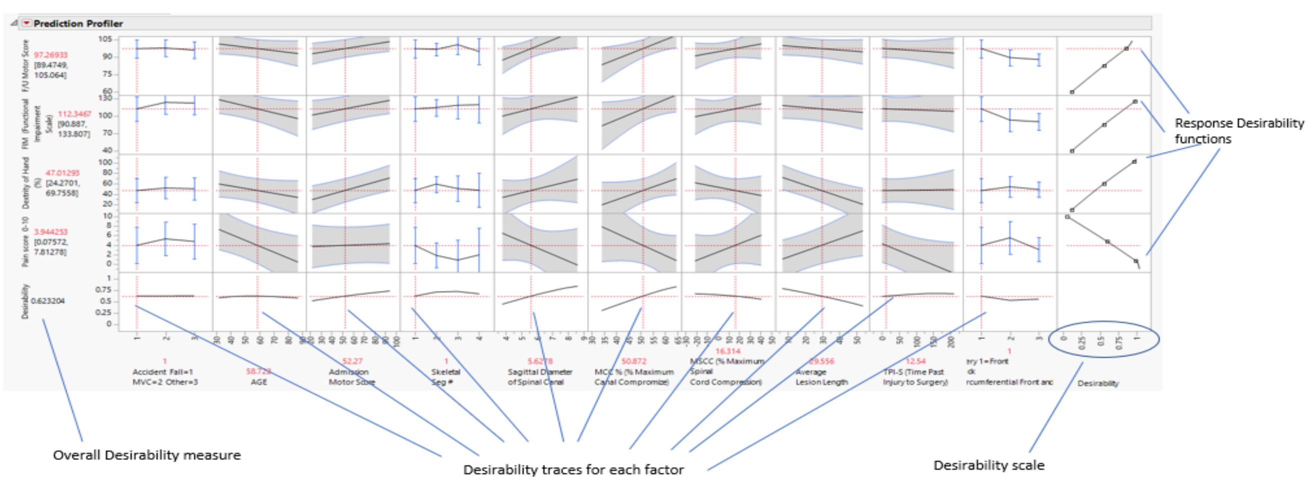


Figure 2: ATCCS Model Profiler Plot

Values and vertical lines over each predictor represent their current settings. Dragging the vertical lines left or right dynamically changes the corresponding values of the predicted responses, along with the associated confidence intervals of the left side of the plot. Desirability functions define an objective function (goal) ranging from zero to one for a single response variable or for several response variables. Desirability functions are well suited to optimize several response variables that have competing criteria. For example, one objective seeks to maximize one response, minimize another, and keep a third response close to some target value.

Response Desirability functions on the right of Figure 2 assigned desired goals for the each of the response variables ranging from 0 (least desirable) to 1 (most or ideal desirable). The left lower-to-upper right desirability lines for FU Motor Score, FIM, and Hand Dexterity reflect goals to *maximize* the responses. The downward slope for Pain reflects *minimizing* the response objective. The overall desirability function is determined by computing the geometric mean of the individual desirability functions for each response. Denote the individual desirability functions for four (k= 4) responses by d_1, d_2, d_3, d_4, where: d_1 = Follow-Up ASIA motor score (Best is set to 100), d_2 = FIM (Best is set to 126), d_3 = Hand Dexterity (Best is 100%), d_4 = Level of Pain (Best is 0 for no pain and 10 is the most severe pain).

The overall desirability function (D) is the geometric mean of the individual desirability functions, i.e.,

$$D = d_1^{1/4}\ d_2^{1/4}\ d_3^{1/4}\ d_4^{1/4} = \sqrt[4]{d_1 d_2 d_3 d_4}.$$

Current settings of the 10 inputs in red reflected in Figure 2 yielded an overall desirability of 0.623. Changing the input levels can yield a higher desirability over 0.93 in Figure 3.

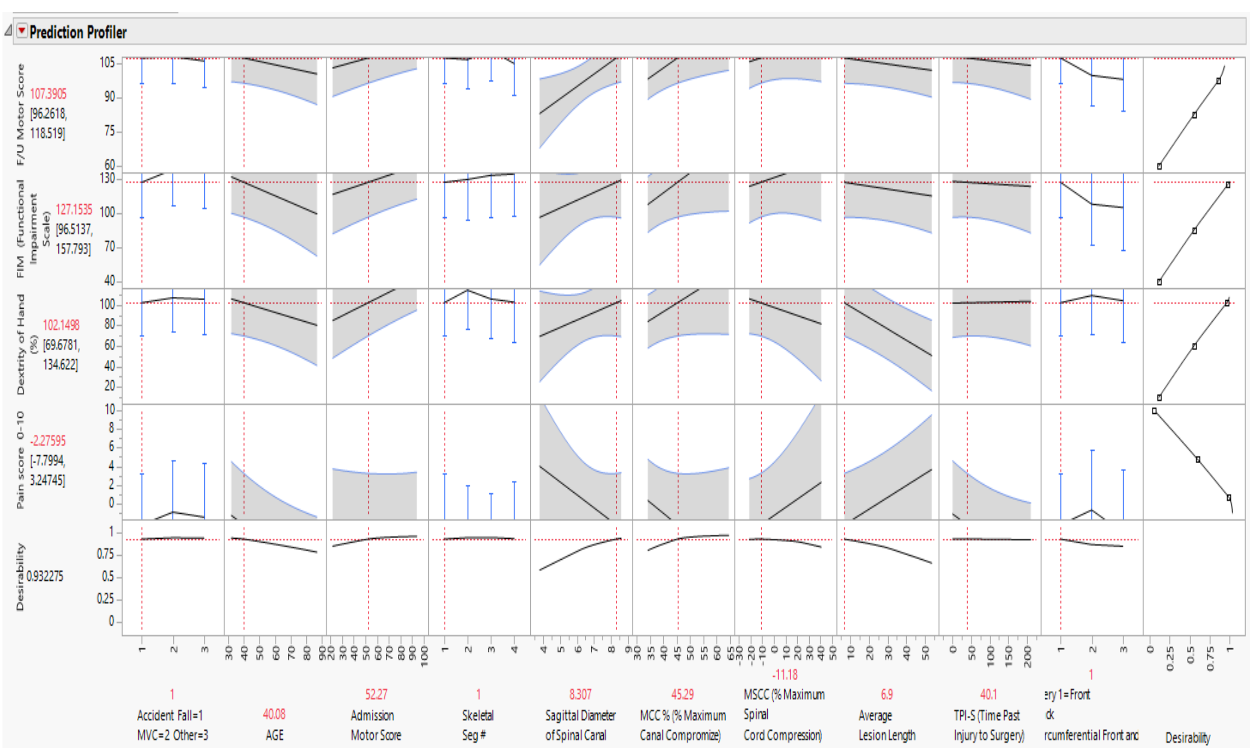
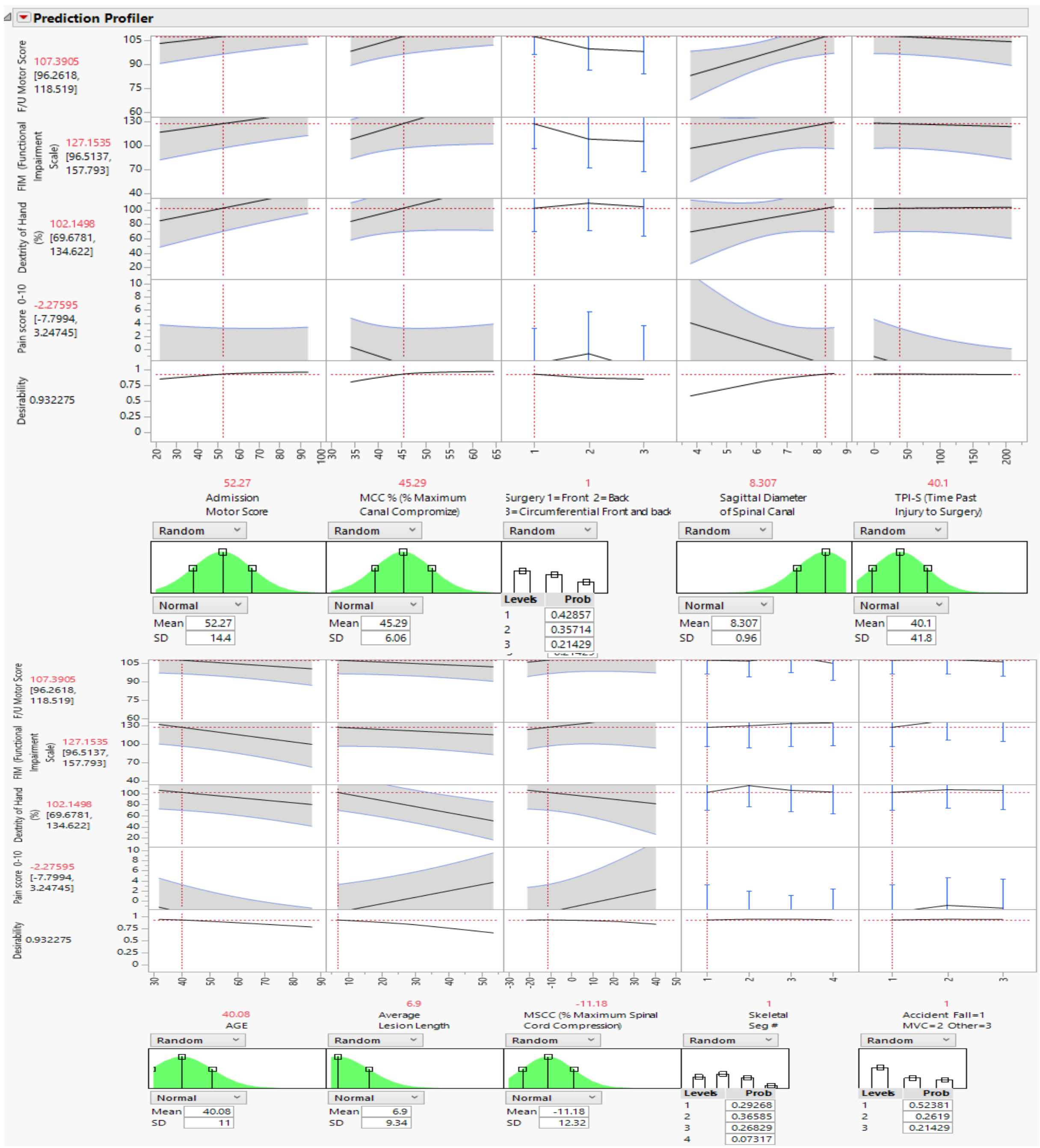


Figure 3: ATCCS Model Profiler Plot to yield higher Desirability

Details about constructing JPP's Desirability functions are available at [3]. Figure 3 gives an indication of better conditions for the surgical team to expect that would satisfy desirability levels and increase the chances of survival and recovery for patients with ATCCS.

Monte Carlo simulation is possible using the Prediction Profiler because it is likely there may be some random variation in the factors and responses, see Kadapa [4]. The Simulator [5] lets you estimate the expected range of response values for the implemented factor settings. To do this, we select Simulator from the red triangle for the Prediction Profiler. For each factor and response, we add random variation that follows specified distributions and standard deviations. To simulate responses, click the Simulate button. Figure 4 shows the simulated distributions for each of the responses and a summary table for the simulation.



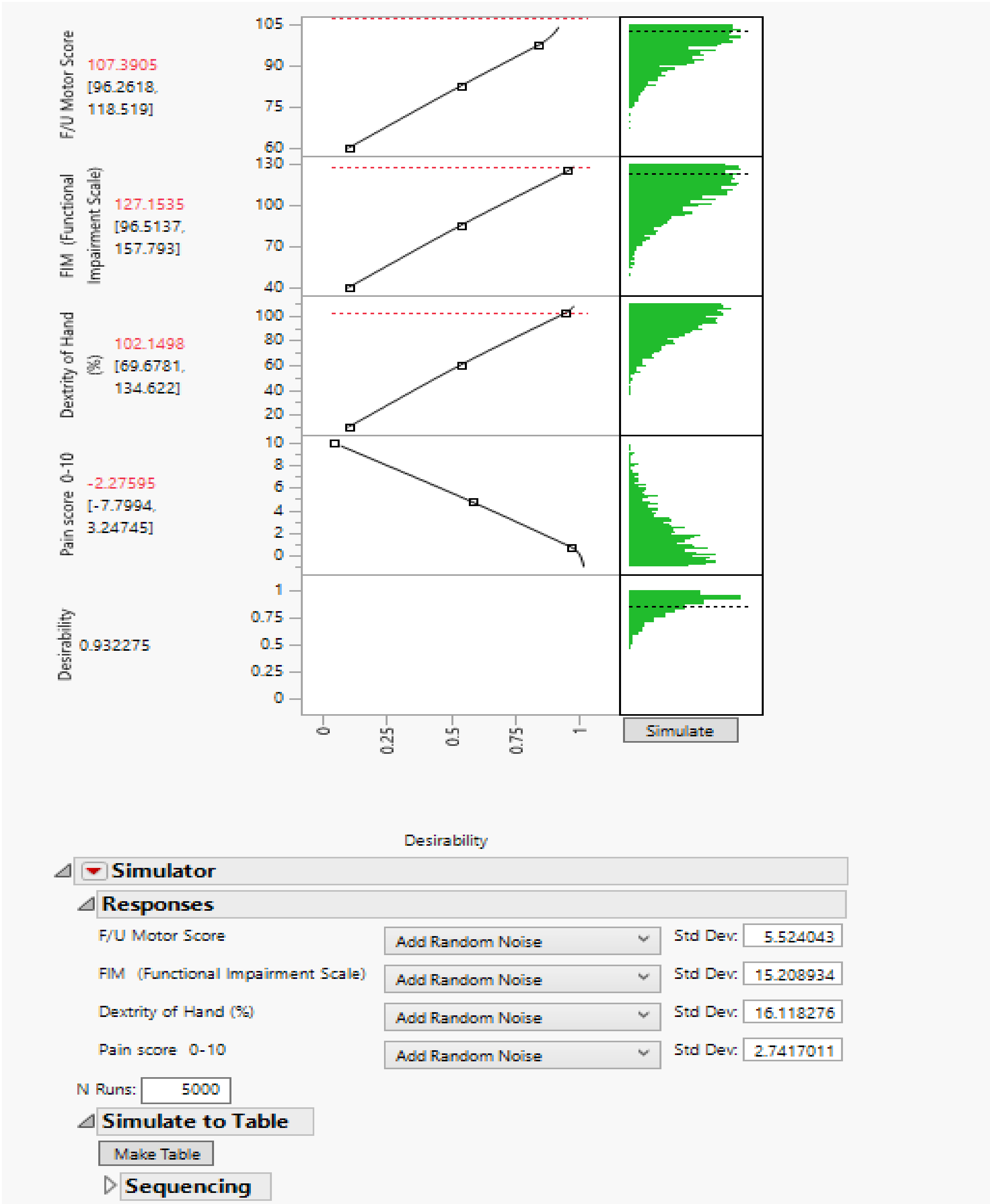


Figure 4: Prediction Profiler and Simulator Responses for each Predictor

The default number of simulated values is 5000 which can be changed and saved into a JMP Data Table by clicking Make Table. Figure 5 lists other random distribution choices that can be used for running simulations for each factor. Applying goodness-of-fit techniques helps to decide the best distribution to choose for fitting the data.

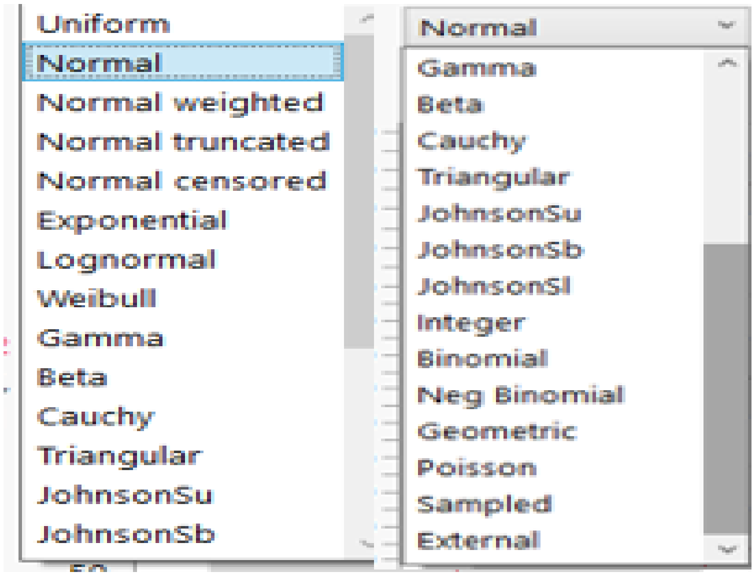


Figure 5: List of Random Statistical Distributions running simulations for each factor

The simulator lets you explore the robustness of the fitted responses with respect to variation in the model factors by defining random inputs, running the simulations, and producing output tables of simulated values.

CONCLUSION

Since 2011, the original research paper was cited over 121 times in the medical literature according to Google Scholar [6], with nine citations since 2022. Studies have shown that ATCCS has gained more attention from spinal cord surgeons and clinicians. Key predictors identified in this case study (Admission ASIA motor score, Sagittal diameter, MCC percentage, Average Lesion length of MRI signal change, and the patient's Age) and others serve as guides to the need and timing of surgery that have resulted in satisfactory neurological recovery of trauma patients with ATCCS. JPP visualizations in this presentation demonstrates one advance towards better understanding acute cervical spinal-cord injury research.

REFERENCES

[1] Jones, B., 2021, "The Profiler at 30,"

https://www.jmp.com/en_us/articles/the-profiler-at-30.html, (accessed 01/12/2021).

[2] Aarabi, B., Alexander, M., Mirvis, S.E., Shanmuganathan,K., Chesler, D., Maulucci, C., Mark I., Aresco, C., and Blacklock, T., 2011, "Predictors of outcome in acute traumatic central cord syndrome due to spinal stenosis." *Journal of Neurosurgery: Spine* 14.1, pp. 122-130.

[3] "Construction of JMP's Desirability Functions," https://www.jmp.com/support/help/en/16.2/index.shtml#page/jmp/construction-of-desirability-functions.shtml# (accessed 08/02/2022)

[4] Kadapa, V., Feb, 11, 2021, https://richardvigilantebooks.com/what-is-a-desirability-function/ gives a discussion of Desirability Function analysis. (accessed 01/07/2022).

[5] https://community.jmp.com/t5/Learning-Library/Simulating-Data-Using-the-Prediction-Profiler/ta-p/272000 (accessed 01/12/2022)

[6] https://scholar.google.com/scholar?oi=bibs&hl=en&cites=6089317106442657124 (accessed 01/12/2022).

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Melvin Alexander
3701 Gramercy Road
Greensboro, NC 27410-2863
Phone: (410) 458-7129
E-mail: Melvin.Alexander@verizon.net

DISCLAIMER

The views expressed in this presentation are the author’s and do not represent the views of SAS Institute, Inc. or other cited organizations and institutions.