DG04

A Picture is worth 3000 words!! 3D Visualization using SAS®

Suhas R. Sanjee, Novartis Institutes for Biomedical Research, INC., Cambridge, USA

ABSTRACT

Data visualization is an important aspect in clinical research. Graphs provide means to convey information efficiently in a concise manner and three dimensional (3D) graphs are even better given that they provide another dimension. In general, 3D graphs seem to be under utilized in clinical research. Fortunately, SAS has a number of procedures that support data visualization in three dimensions. This paper explores the G3D procedures in detail and provides examples in the Oncology therapeutic area. 3D graphs are especially useful in oncology trials where the primary endpoints typically depend on a number of variables. For example, overall response computed using Response Evaluation In Solid Tumors, RECIST criteria depends upon change from baseline, change from nadir, appearance of new lesions etc. Plotting these variables in 3D allows for the visualization of all these variables together. Also, 3D surface plot can be used to visualize multiple PK concentration profiles at once and also provide means to make decisions about dose escalation and Maximum Tolerated Dose (MTD).

INTRODUCTION

The G3D procedure can be used to generate three-dimensional surface and scatter plots.

Surface plots depict shape of the surface that is described by the values of three variables, X, Y, and Z. The values of the X and Y variables are plotted on the horizontal plane. The values of the Z variable create a vertical axis that is perpendicular to the X-Y plane. Combined, these three axes form a three-dimensional surface.

Scatter plots represent the data as points. As with surface plots, the values of the X and Y variables are plotted to form a horizontal plane. The values of the Z variable create a vertical axis that is perpendicular to the X-Y horizontal plane. The values of the Z variable are represented as individual symbols. By default, these symbols are connected to the horizontal plane with lines, referred to as needles.

DATA OVERVIEW

All the data used here is simulated. Structure of the datasets used follow CDISC SDTM/ADAM so that the techniques presented can be easily adopted across studies.

SAS PROGRAMMING OVERVIEW

This section will discuss the steps and mechanics involved in the generating 3D surface plots and bar charts using PROC G3D. Following is the syntax for the G3D procedure.

```
PROC G3D <DATA=input-data-set>
<ANNOTATE=annotate-data-set>
<GOUT=<libref.>output-catalog>;
PLOT plot-request</option(s)>;
SCATTER plot-request</option(s)>;
```

SAS also has ability to produce GIF files and by including 3D plots generated from using different tilt/rotation can be very valuable when presented in clinical forums.

Using DEVICE=ACTIVEX, the end user can view the graphs with different angles of tilt and rotation. DEVICE=GIFANIM can produce GIF images which are useful for slide shows and animations that don't need to be controlled by the end user. TILT and ROTATE options of PROC G3D can be used to produce graphs with different views for animations.

For both surface plots and scatter plots, the X-Y plane can be rotated around the Z axis, or the X-Y plane can be tilted towards the user. When the plot is rotated, the data can be viewed from any angle around the three-dimensional graph. Rotating a plot is useful for bringing into view data points that might be obscured by other data points. Tilting a plot enables you to accentuate the location of data points.

3D BAR CHARTS

Bar charts are very useful in general to visualize a number of variables in clinical trials. They are especially useful in Oncology trials to visualize different components of RECIST criteria. Three dimensional graphs come in handy since RECIST involves a number of variables.
An example of a bar chart depicting RECIST components is shown in Figure 1. Red bars signify increase and green bars signify decrease from the reference point. Type=1 represents % change from baseline and Type=2 represents % change from nadir. Annotations can be used for denoting status of new lesions. You can notice that some of the % change from nadir bars are not visible since they are obscured by % change from baseline bars. This can be resolved by tilting/rotating the plot which will also be discussed in detail in this section.

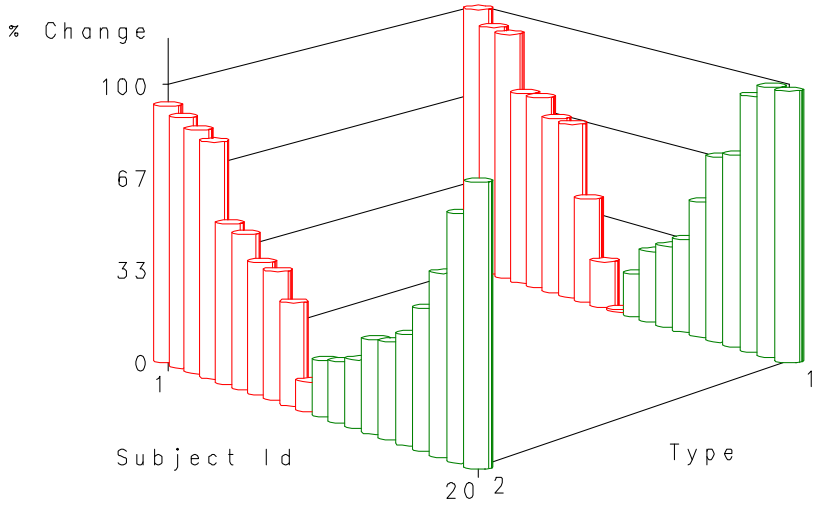

Figure 1: 3D plot of RECIST components (Type=1 represents % change from baseline Type=2 represents % change from nadir)

This approach can be used to generate graphs whenever two variables need to be visualized in three dimensions.

3D SURFACE PLOTS

The G3D procedure can be used to generate surface plots and these can be very valuable to study the relationship between 3 variables. Two such scenarios are presented here.

PK Concentration:

Figure 2 shows surface plot of PK concentrations. This is very helpful since it shows multiple PK profiles at once. Color gradient can be used for classification by any variable such as treatment group.

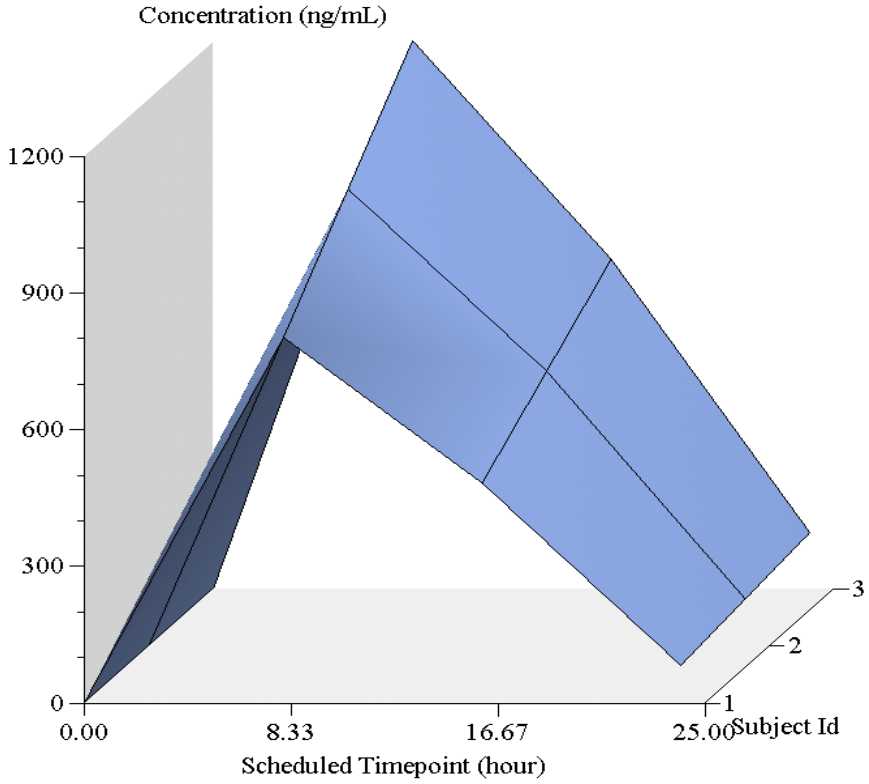

Figure 2: 3D Surface Plot of PK Concentrations

Probability of DLT

The surface plot depicting relationship of probability of DLT with dosages of drugs A & B is very useful to make decisions about dose escalation and MTD in combination trials. Figure 3 shows one such example. Probability greater than or equal to 0.5 signifies higher toxicity of drugs and is represented in orange. Probability of DLT lesser than 0.5 signifies lower toxicity of drugs and is represented in blue. The threshold of 0.5 can be changed if needed. The G3D procedure is used in conjunction with annotate facility to accomplish this. G3D procedure is used to draw the three dimensional axes and the annotate facility is used to draw the contours. This approach is very useful and can be used to depict relationship between any 3 variables.

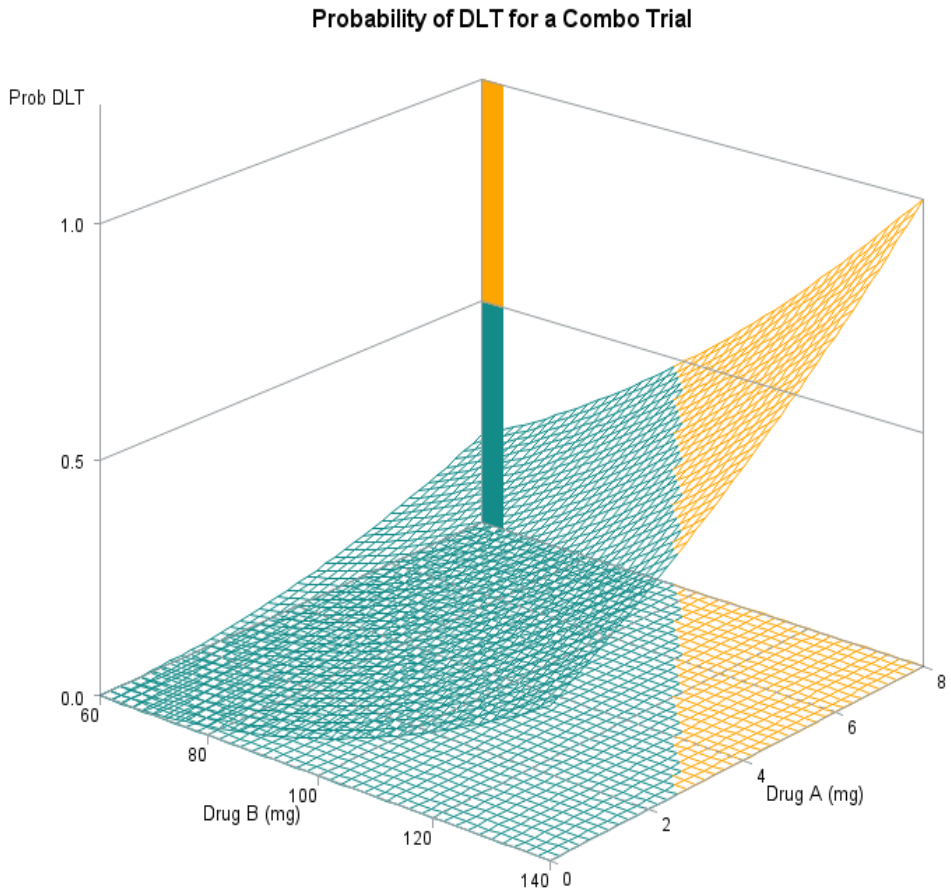

Figure 3: 3D Surface Plot of Probability of DLT

3D KAPLAN-MEIER PLOT

The Kaplan-Meier survival curve is defined as the probability of surviving in a given length of time while considering time in many small intervals. Kaplan Meier plot in three dimensions allows clear visualization of survival plots of patients in different treatment arms without overlapping of data points. Figure 4 shows a three dimensional Kaplan Meier plot generated using PROC G3D.

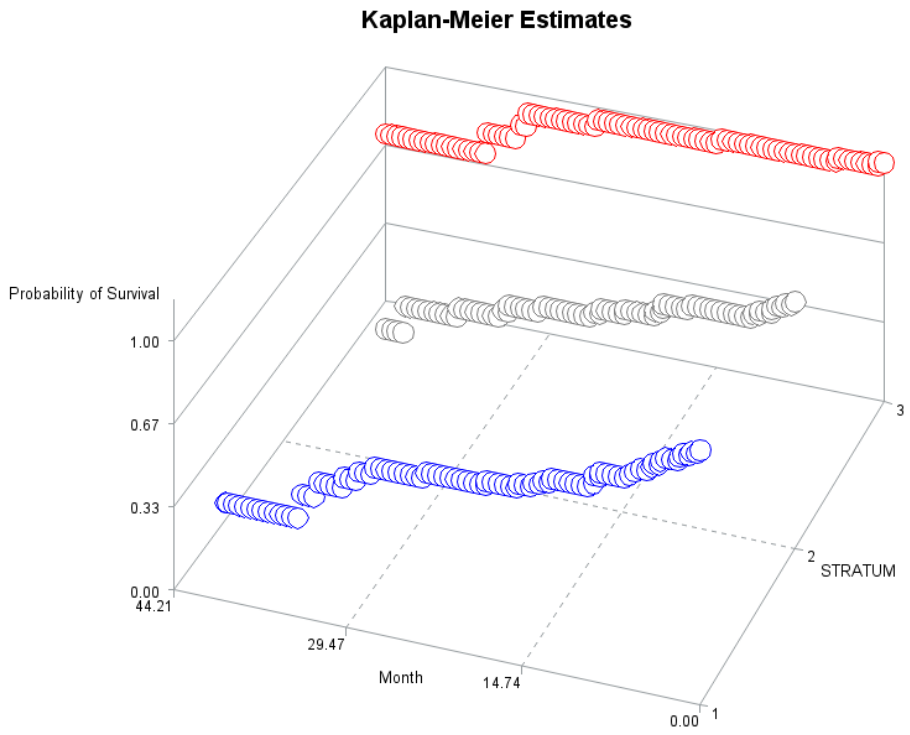

Figure 4: Kaplan-Meier Estimates of Overall Survival

CONCLUSION AND SUMMARY:

3D data visualization techniques have significant potential for enhancing the analysis of Oncology clinical trials and perhaps clinical trials in other therapeutic areas. These data visualization methods may increase the odds of getting interesting and clinically significant insights. Surface plots of PK concentration profile can provide the clinical team a method of juxtaposing multiple profiles. Also, 3D bar charts can be used to visualize multiple components of RECIST simultaneously.

While 3D graphs provide great way of visualizing clinical trial data, it is sometime hard to interpret since some information can be hidden. However, when it is viewed at an appropriate tilt/rotation they can provide valuable insights.

ACKNOWLEDGEMENTS:

I would like to thank my manager Christelle Navarro for her guidance and support. I would also like to thank David Demanse, Senior Statistician, and Karma Tarap, Senior Statistical Programmer of Novartis Pharmaceuticals for their valuable inputs.

REFERENCES:

1. SAS Knowledge Base / Samples & SAS Notes: http://support.sas.com/kb/24/861.html
2. Robert Allison's SAS/Graph Examples! http://robslink.com/SAS/Home.htm
3. Jack Shostak, SAS Programming in the Pharmaceutical Industry.
4. SAS/GRAPH(R) 9.2: Reference, Second Edition

TRADEMARK INFORMATION:

DISCLAIMER:

The opinions expressed in this presentation and on the following slides are solely those of the presenter and not necessarily those of Novartis. Novartis does not guarantee the accuracy or reliability of the information provided herein.

CONTACT INFORMATION:

Author Name: Suhas R. Sanjee
Designation : Systems Consultant - Business
Company : Novartis Institute for Biomedical Research INC.
Address : 220 Massachusetts Ave
City : Cambridge State: MA Zip: 02139
Email : suhas.sanjee@novartis.com