

SUPPLEMENTAL TECHNICAL BULLETIN ST – 2007 – 01

Title: Area Under the Curve or AUC (aka ROC*)

Bulletin No: ST-2007-01

This Supplemental Technical Bulletin (ST) has been developed as a laboratory aid. This ST does not alter, revise or change the information provided in the Technical Bulletin included with each product. In accordance with Good Laboratory Practice and regulatory requirements, each laboratory must develop, validate and adopt its own written procedures.

Area Under the Curve or AUC (aka ROC*)

The ROC was initially applied to clinical diagnostics in 1982.¹ Since that time, use of the ROC has expanded in to many areas of clinical, laboratory and pharmaceutical medicine where it is used as a tool to evaluate test performance, identify normal and abnormal populations, or determine threshold levels for sampling and laboratory values.² In current literature and statistical software packages, the ROC is commonly referred to as the Area Under the Curve or AUC.³

In the clinical laboratory, Area Under the Curve is a measure of discrimination, or the ability of a test to correctly identify normal and abnormal test values.^{4,5} There are three primary methods used to determine the AUC: triangle, trapezoid and rectangle.⁷ Each gets its name from the geometric shape used to approximate the AUC. The trapezoid method is commonly used in clinical and pharmaceutical laboratories.

The PAP 8E automatically measures AUC for a fixed time period using the trapezoid approximation method. The parameters used to determine the AUC are:^{6,7}

Baseline (0% T)

% Final Aggregation

Agonist injection point (start time)

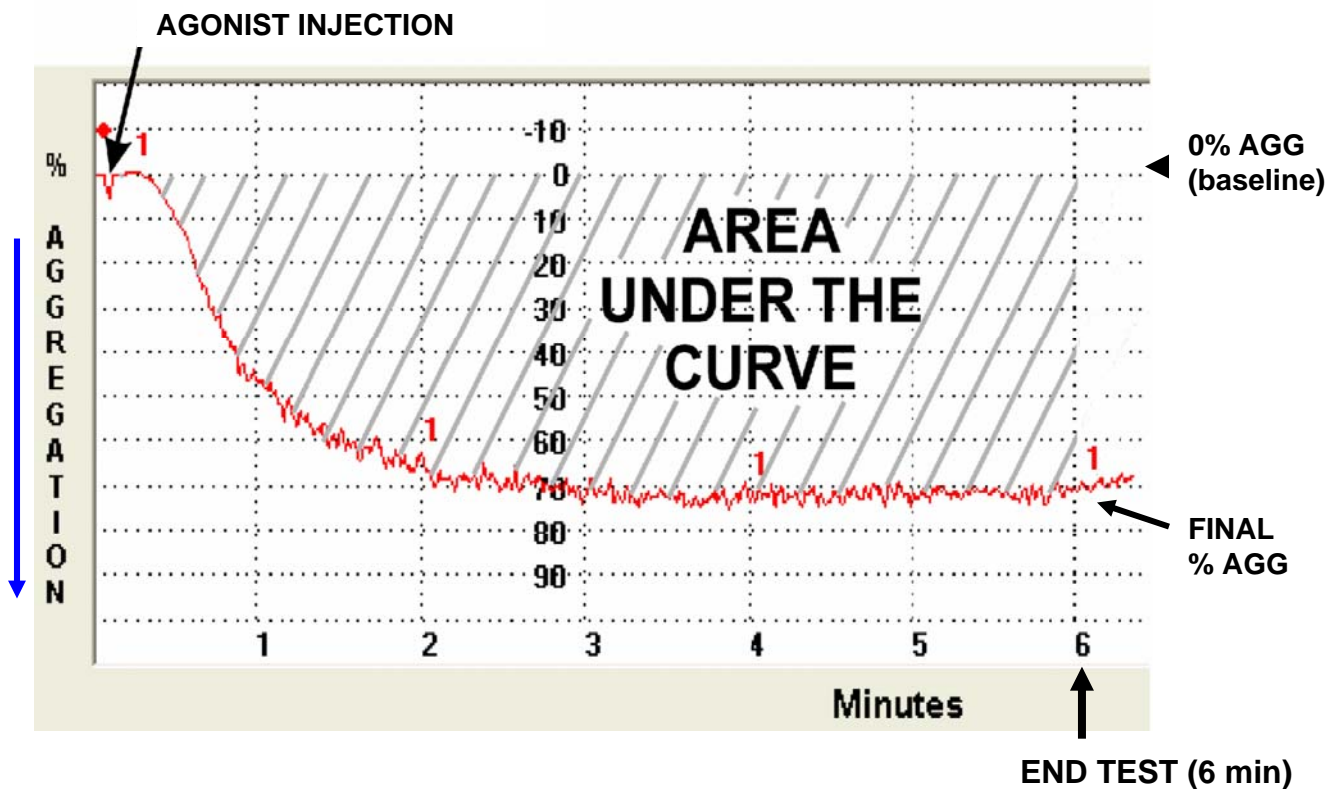
Test End Time: e.g. number of minutes at end of test

See Figure 1.

The Area Under the Curve is a calculation of the activity of aggregation from the base line (the injection zero point) to the final percent aggregation for the elapsed time selected for the test. The PAP 8E averages the data points at half second intervals, then divides that average by 120 seconds. The result is % Aggregation/minute.

Expected results depend on the end of test time selected by the operator and the concentration of the agonist. AUC use has been reported for both traditional platelet agonists and the ristocetin cofactor assay.^{7,8} There is no standardized definition for the use or reporting of AUC. Each laboratory must determine its own end time and reference ranges. *AUC is intended for Research Use Only.*

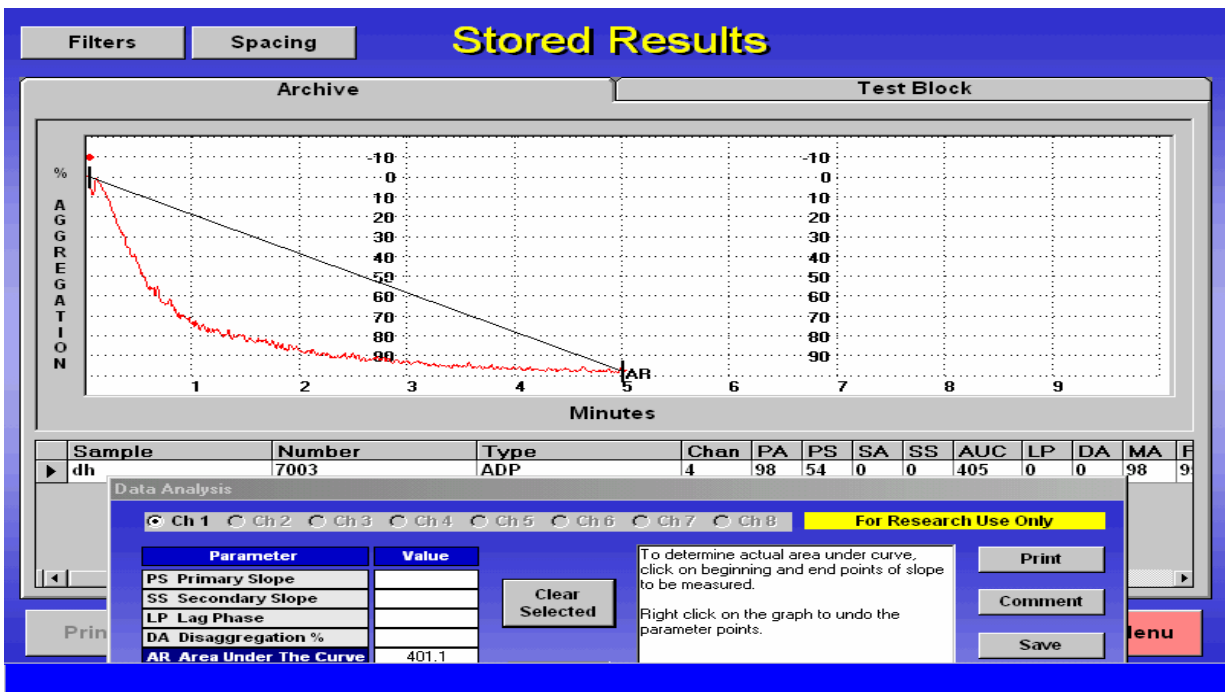
Figure 1



The PAP 8E has two additional options for determining the AUC. One uses the PAP 8E's Data Analysis software, and the other is provided in the Graphpad Prism software.

The PAP 8E's analysis function allows the operator to select alternate start and end points on the platelet aggregation curve, or a different time base for the measurement. The Data analysis software also uses the trapezoid method to calculate AUC.⁶

Figure 2
PAP 8 E DATA ANALYSIS SCREENSHOWING ADP AUC at 5 MINUTES



The operator can also use the Prism software to calculate AUC. That option is in the Laboratory Statistics section of Prism.⁵ Prism uses the trapezoidal method for calculating the AUC. See Figure 3. Refer to the Prism Manual provided with the PAP 8E.


Figure 3
PRISM AUC DIALOG SCREEN


1. Enter ROC data

From the Welcome or New table dialog, choose the one-way tab, and then choose a scatter plot. If you are not ready to enter your own data, choose the sample ROC data.

Enter diagnostic test results for controls into column A and patients in column B. Since the two groups are not paired in any way, the order in which you enter the data in the rows is arbitrary. The two groups may have different numbers of subjects.

2. Create the ROC curve

From the data table, click  Analyze | bar, and then choose Receiver-operator characteristic curve from the list of one-way analyses.



In the ROC dialog, designate which columns have the control and patient results, and choose to see the results (sensitivity and 1-specificity) expressed as fractions or percentages. Don't forget to check the option to create a new graph.

Note that Prism doesn't ask whether an increased or decrease test value is abnormal. Instead, you tell Prism which column of data is for controls and which is for patients, and it figures out automatically whether the patients tend to have higher or lower test results.

3. View the graph

Results are usually reported as arbitrary units, or decimal equivalents of fractions between 0.0 and 1.0.^{5,6,7}

Refer to the PAP 8E Operations Manual or the Prism Users Manual for further information.

Note:

*ROC: receiver operating characteristic curve. ROC came from Signal Detection Theory and was initially used by World War II radar operators to differentiate enemy targets from friendly vessels and background.^{4,5}

References:

1. Hanley, JA and McNeil, BJ. The Meaning and Use of the Area Under a Receiver Operating Characteristic (ROC) Curve. Radiology. 1982 Apr; Vol 143 (1): 29 – 36.
2. Schisterman, EF, Faraggi, D, Reiser, B, and Trevisan, M. Statistical Inference for the Area under the Receiver Operating Characteristic Curve in the Presence of Random Measurement Error. Am J Epidemiol. 2001. Vol 254 (2): 174 – 179.
3. Lasko, TA, Bhagwat, JG, Zou, KH, and Ohno-Machado, L. The Use of Receiver Operating Characteristic Curves in Biomedical Informatics. J Biomed Info. 2005 Vol 38 (5): 404 – 415.
4. Tape, TG. Interpreting Laboratory Tests. 2004. <http://gim.unmc.edu/dxtests/Default.htm>.
5. Motulsky, H. GraphPad PRISM® Statistics Guide: Statistical Analyses for Laboratory and Clinical Researchers. GraphPad Software Inc. San Diego. 2003.
6. Platelet Aggregation Profiler, Model PAP 8E Operations Manual. Doc No 106221 Rev H. Bio/Data Corporation, Horsham, PA. 2007.
7. Jarviss, GE, Humphries, MJ, Robertson, MJ and Leff, P. ADP Can Induce Aggregation of Human Platelets via Both P2Y₁ and P_{2T} Receptors. Brit J Pharm. 2000. Vol 129: 275 – 282
8. Stranderg, K, Lethagen, S, Andersson, K, Carlson, M, and Hillarp, A. Evaluation of a Rapid Automated Assay for Analysis of von Willebrand Ristocetin Cofactor Activity. Clin & Appl Thromb Heme. 2006. (1): 61 – 67.