Dynamic Venous Access Pressure Ratio Test for Hemodialysis Access Monitoring

Stanley Frinak, MSEE, Gerard Zasuwa, BS, Thomas Dunfee, MD, Anatole Besarab, MD, and Jerry Yee, MD

Background: Early recognition of arteriovenous graft (AVG) dysfunction in hemodialysis (HD) patients followed by prompt corrective procedures reduces AVG thrombosis rates and lengthens access survival. We developed a method to prospectively monitor AVGs that uses an algorithm to calculate venous access pressure (VAP) during HD from the venous drip chamber pressure (VDP).

Methods: Sham HD with blood was performed using standard blood tubing and a 1-in. 15-G needle. The pressure needed to overcome circuit resistance at an intra-access pressure of zero (VDP₀) was recorded at blood flow rates (Qb) from 0 to 600 mL/min and hematocrits varied in steps from 38.4% to 18.2%. An equation for VDP₀ was developed. VAP in patients was calculated as VAP = VDP – VDP₀. VAP ratio (VAPR) was defined as VAP/mean arterial pressure (MAP). VAPR was calculated only if MAP was greater than 75 mm Hg, Qb was greater than 200 mL/min, and VDP was greater than 20 mm Hg. A positive VAPR test (VAPRT) result was defined as three consecutive treatments with VAPR exceeding 0.55 during a given month. Sensitivity and specificity of VAPRT to predict a graft event, defined by AVG occlusion or requirement for angioplasty, were calculated.

Results: During a 3-month interval, 120 HD patients with AVGs underwent 359 VAPRTs while access outcomes were monitored for 6 months. After 3 months, sensitivity and specificity for detection of a graft event were 70% and 88%, and increased to 74% and 92% at 6 months, respectively.

Conclusion: The VAPRT is a valuable tool to prospectively monitor for adverse AVG events.

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INDEX WORDS: Hemodialysis (HD); access pressure ratio test; venous access pressure ratio test (VAPRT).

HEMODIALYSIS (HD) vascular access monitoring programs have been used to permit the early detection of evolving stenotic lesions. Several studies have shown that early detection of stenotic lesions followed by timely corrective procedures reduces the thrombosis rate and prolongs access survival. However, such monitoring programs are costly, with equipment, personnel, and data storage and analysis requirements. We developed an inexpensive method, the venous access pressure (VAP) ratio (VAPR) test (VAPRT), to prospectively monitor for arteriovenous graft (AVG) failure. This computer-based algorithm analyzes blood pressure, HD venous pressure, and blood pump flow data to identify patients at risk for access dysfunction that culminates in either thrombosis or percutaneous transluminal angioplasty or surgery to maintain AVG patency.

From the Department of Medicine, Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, MI. Received September 24, 2001; accepted in revised form May 20, 2002.

Address reprint requests to Stanley Frinak, MSEE, Henry Ford Hospital, Division of Nephrology and Hypertension, 2799 West Grand Blvd, CFP-5, Detroit, MI 48202. E-mail: stanfrinak@ghsrenal.com

© 2002 by the National Kidney Foundation, Inc. 0272-6386/02/0000-0000/0 doi:10.1053/ajkd.2002.35687

VAP = VDP – VDP₀ (1)

An elevation in VAP indicates stenosis in the venous outflow limb of the access and correlates with a higher risk of access failure. During HD, blood is drawn from the AVG at the arterial needle site by the dialysis machine’s blood pump. After traversing the dialyzer, blood passes through the venous drip chamber and returns to the access through the venous needle. The pressure required to infuse blood back into the AVG through the venous tubing and needle and overcome the pressure within the AVG is recorded as the venous drip chamber pressure (VDP). One component of VDP is the access pressure at the venous needle site, or VAP. Another component of VDP is the combined pressure required to overcome the low resistance to flow through the tubing distal to the drip chamber and the relatively high resistance through the venous return needle. VDP is also a function of needle size, tubing length, and blood viscosity, represented by hematocrit (Hct). If venous pressure in an AVG at its needle insertion site is 0 mm Hg, VDP can be defined as VDP₀, ie, the VDP at which access pressure is zero. Consequently, VDP₀ can be calculated for a given dialysis machine, tubing set, and needle size following measurements of blood flow rate (Qb), Hct, and VDP. After an equation for VDP₀ is determined, VAP can be calculated from measured VDP.
with an increased probability of access failure.\cite{6,8,11,12} To normalize variations in VAP attributed to changes in mean arterial pressure (MAP), VAPR is calculated by dividing VAP by MAP.

$$\text{VAPR} = \frac{\text{VAP}}{\text{MAP}}$$  \hspace{1cm} (2)

The VAPRT algorithm uses an empirically derived formula to calculate VAP from dynamically obtained measurements of VDP during HD treatment sessions. The VAPRT algorithm analyzes VAPR values from each treatment and identifies individuals with consistently elevated intra-access pressures at risk for access failure. To eliminate such treatment errors as needle reversal or suboptimal needle insertion, which elevate VDP, we operationally defined an abnormal VAPRT result as VAPR greater than 0.55 at three consecutive HD treatments.

MATERIALS AND METHODS

Calculation of $\text{VDP}_0$

The VAPRT relies on a nonlinear regression formula developed during in vitro sham HD and calculates $\text{VDP}_0$ for a specific HD blood tubing set and access needle type at known $\text{Q}_b$ and Hct (Fig 1), using a Fresenius Model 2008H hemodialysis machine (Fresenius, Lexington, MA) with the blood pump calibrated before experiments by means of standard procedures. Exact flows were not measured during in vitro experiments because the intention a priori was to implement a system that used routine HD data obtained during each session. The reservoir is filled with 500 mL of human whole blood obtained from the hospital blood bank, and the blood pump transports blood from a reservoir through the dialyzer and venous drip chamber to a 15-G 1-in. backeye access needle. The venous needle is inserted into a section of large-bore tubing open at both ends; one end of the tubing returns blood to the reservoir; and the other end is elevated to prevent the escape of blood. This section of the circuit is designed to forego any resistance to flow at the tip of the venous access needle that would be recorded as increased VDP. The access needle is positioned 17 cm below the venous drip chamber transducer to simulate the average location of an angioaccess relative to the transducer during a typical HD treatment. The drip chamber transducer monitors the pressure created by blood flowing through the circuit, and $\text{VDP}_0$ readings are obtained directly from the HD machine.

A sample of blood is obtained for Hct determination from the reservoir. $\text{VDP}_0$ is recorded for each incremental increase (50 mL/min) in $\text{Q}_b$ from 0 to 600 mL/min. A separate transducer located directly behind the access needle measures the pressure intrinsic to the access needle resistance, and blood is diluted with matched human plasma to reduce Hct by approximately 4%. Blood is permitted to circulate at 500 mL/min for 5 minutes to ensure uniform mixing with the additional plasma before the next sample is obtained for Hct measurement. $\text{VDP}_0$ measurements are repeated at $\text{Q}_b$ varied from 0 to 600 mL/min. The circulated blood is diluted sequentially five times, which reduces the original Hct by approximately 20 percentage points. $\text{VDP}_0$ measurements were conducted at each of the five dilutions.

Description of the Algorithm for the VAPRT

This algorithm identifies persistent VAPR elevations that may signify an AVG requires additional evaluation. This algorithm calculates VAPR from VDP and blood pump flow data routinely collected at HD and determines persistent increases in VAPR. To limit variability related to differences in needle gauge, patients with less than 48 HD treatments were eliminated from analysis because smaller gauge needles are frequently used to cannulate new or poorly developed angioaccesses. The program extracts the most recent Hct and individual treatment data from a database, and VAPR is calculated when blood pressure is measured during HD at $\text{Q}_b$ of 200 mL/min or greater, VDP of 20 mm Hg or greater, and MAP of 75 mm Hg or greater. Data from the last 60 minutes of HD are excluded to eliminate the effect of ultrafiltration on Hct, blood pressure, and changes in systemic and vascular access resistances. The algorithm is then used to calculate mean VAPR for each HD session. In the majority of cases, three or four measurements are available. The VAPRT result is considered abnormal only after the eighth treatment during a given month and determines when VAPR exceeds 0.55 during three consecutive treatments.

Development of Criterion for the VAPRT

To determine the VAPR cut-off value most predictive of access failure, test data and follow-up data were analyzed from 117 patients treated at three separate HD facilities.
(Greenfield Health System, Southfield, MI), and VAPRs were correlated with AVG-related events during 6 months of follow-up because our unpublished observations and that of Sparks et al suggest that the primary unassisted patency for AVG is 64% at 6 months, with secondary assisted patency of 70% at 6 months. Overall, the conclusion of these studies indicates that during any 6-month interval, approximately 30% to 36% of AVGs will fail.

A receiver operator curve (ROC) for VAPR was constructed with cutoff ratios from 0.2 to 0.8. Respective sensitivities and specificities were calculated at each VAPR cutoff level while other test parameters were held constant. Integration of area under the curve was with Mathcad Plus, version 6.0 (MathSoft Inc, Cambridge, MA). Clinical data were analyzed with StatView for Windows, version 5.0 (SAS Institute Inc, Cary, NC) and DeltaGraph 4.0 (SPSS Inc, Chicago, IL). Clinical data were analyzed with StatView for Windows, version 5.0 (SAS Institute Inc, Cary, NC) and DeltaGraph 4.0 (SPSS Inc, Chicago, IL). Grouping variables for unpaired t-tests were true positive (TP; test predicted intervention or access clotting), true negative (TN; test correctly predicted the absence of an access event), false positive (FP; test falsely predicted an access event would have occurred), and false negative (FN; test falsely predicted that an access event would not occur). A VAPR cutoff value of 0.55 was selected for further clinical testing because it provided a compromise between sensitivity (75%) and specificity (83%).

**Clinical Application of VAPRT**

After determining the optimal VAPR cutoff value of 0.55, a total of 359 VAPRT results were obtained from our stated HD population from January through March 1999. Data were analyzed retrospectively from January (n = 112), February (n = 113), and March (n = 134) 1999. Medical records were examined to identify individuals who required intervention for an access event, defined as an obviously low access flow (<250 mL/min), inability to provide adequate dialysis within the predetermined treatment time, or necessity for surgical or angioplasty intervention to maintain AVG patency. Patients tested in January, February, and March 1999 were followed up for 6 months, and outcomes were evaluated at 3 and 6 months after each test period.

**RESULTS**

**In Vitro Modeling of VAPR**

Results of the sham dialysis study are shown in Fig 2, and mathematical modeling of VDP0 data is described in Appendix A. The analysis yielded the following second-order polynomial equation:

\[
VDP_0 = 0.00042 \cdot Q_b^2 + (0.62116 \cdot Hct^2 + 0.01203 \cdot Hct + 0.12754) \cdot Q_b - 17.32509
\]

Equation 3 was evaluated for accuracy by curve-fitting the raw data to equation 3 with a nonlinear regression program (DataFit; Oakdale Engineering, Oakdale, PA). The adjusted coefficient of multiple determination is \( r^2 = 0.99982 \). Note that the common average intercept, \(-17.325, \) was established empirically and is directly related to the 17-cm difference in height between the needle and drip chamber transducer at \( Q_b = 0 \) mL/min. When pressure is measured from the transducer proximal to the access needle, the offset is zero, and the relationship between pressure and flow remains curvilinear (Fig 2;
venous needle pressure at Hct of 29.1). Thus, VDP₀ increases in relationship to increasing Qₑ and Hct.

Equation 3 can be used to calculate VDP₀ for any Qₑ at known Hct. For example, at Qₑ of 500 mL/min and Hct of 18.2%, VDP₀ is 163 mm Hg and increases to 200 mm Hg when Hct is 38.4%. VAP may be calculated from VDP recorded at HD by using equation 1, and VAPR is calculated by using equation 2. At an Hct of 38.4%, Qₑ of 500 mL/min, VDP of 265 mm Hg, VDP₀ of 200 mm Hg, and MAP of 100 mm Hg, VAPR = 0.65 = (265 – 200)/100.

ROC Evaluation

Patients for whom data were used for ROC analysis had a mean treatment Qₑ of 438 ± 61 mL/min, Hct of 34.0% ± 4.2%, MAP of 102 ± 14 mm Hg, VDP ranging from 48 to 430 mm Hg (mean, 214 ± 43 mm Hg), and mean VAPR of 0.64 ± 0.35 (Fig 3). Area under the curve corresponds to an 82% probability of correctly ranking the two test alternatives, persistence of access patency or occurrence of access failure within 6 months.¹⁴,¹⁵

Figure 4 shows the distribution of individual mean treatment VAPR values for all patient observations with AVGs in January 1999 (see Appendix B for equations). The monthly mean VAPR for each patient was calculated from VAPRs obtained during each treatment. Patients with a TP test result by VAPRT had a median VAPR of 0.89 (mean, 0.91 ± 0.24) that was

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**Fig 3.** ROC curves for the January 1999 VAPRT results for grafts (117 results). An area of 1 represents an ideal test, and an area of 0.5 indicates the test has only a 50% probability of determining the correct outcome. An area from 0.80 to 0.90 implies a good test result.

**Fig 4.** Distribution of access pressure ratio values within the four possible test groups: TP, TN, FP, and FN, for patients with grafts.
significantly different from the other three possibilities of FP, TN, and FN (Table 1). Patients with TN test results had a median V APR of 0.48 (mean, 0.52 ± 0.15) that differed from FP results (median V APR, 0.70; mean, 0.70 ± 0.13; P < 0.0001), but not from FN results (median V APR, 0.57; mean, 0.62 ± 0.23). All test groups had some V APR values exceeding 1.0. In this case, VDP/VDP<sub>0</sub> exceeds the MAP for data obtained during treatment and may reflect problems of needle-site insertion or needle reversal.

**Assessment of VAPRT**

Figure 5 shows study results during 3 months of VAPRTs. Twenty-six of 112 patients (23%) had a positive VAPRT result in January 1999. During the next 3 months, 13 individuals (50%) experienced access failure, which increased by month 6 to 19 individuals (73%) in the group with a positive test result. For the January test, 8 patients who ultimately tested negative experienced access failure (FN; 7% of tested population). Statistical analysis of the VAPRT is listed in Table 2 and represents average values obtained 3 and 6 months after each test. For the 3-month follow-up period, the mean test sensitivity of VAPRT was 70% ± 8% and specificity was 88% ± 2%, which improved to a mean sensitivity of 74% ± 5% and specificity of 96% ± 3% during the 6-month follow-up period. The VAPRT’s positive predictive value was 84% ± 10%, and the negative predictive value was 92% ± 3% during this interval.

**DISCUSSION**

The location of an access stenosis will determine in part the ability of a monitoring system to detect dysfunction. In most AVGs, a stenotic lesion develops in the region of the venous anastomosis. A stenosis at this locus or in the distal runoff will impede flow and increase VAP, which is observed as an increase in VDP. VDP, measured during treatment, represents the sum of three components: pressure created by flow through the tubing and needle, static pressure created by the difference in height between the access site and venous pressure transducer in

| Table 1. Comparison of Monthly Mean Graft VAPR Values for the Different Test Groups |
|----------------|-----------|---------|---------|
| Result | Count | Mean   | SD      | SE       |
| TP     | 27    | 0.909  | 0.237   | 0.046    |
| TN     | 67    | 0.515  | 0.149   | 0.018    |
| FP     | 9     | 0.616  | 0.215   | 0.072    |
| FN     | 14    | 0.698  | 0.125   | 0.033    |
| Mean Difference |  | 0.394  | <0.0001 |
| P      | | 0.293  | 0.0024  |
| TP, TN | 0.183 | <0.0001 |
| TN, FN | 0.102 | 0.0734  |
| FP, FN | 0.082 | 0.2595  |
| Mean Difference |  | 0.211  | 0.0036  |
| P      | | 0.082  | 0.2595  |

![Fig 5. Access pressure ratio test results for 3 separate months of testing. Patients were followed up for 6 months after each test for an access failure event.](image)
the HD machine, and VAP. VDP will vary with treatment Qb, VAP, and Hct. The difference in height between the access site and venous pressure transducer also will vary, but will not differ by more than 5 cm from the value of 17 cm used in our model in most cases. This results in a ±5.1-mm Hg variation in VAP, and at MAP of 100 mm Hg, a ±0.05 variation in VAPR will be seen. VAP also will vary with MAP, and changes in MAP will be reflected in VDP. Mapping the access pressure gradient from the arterial to venous anastomosis has shown that the slope of the midgraft pressure gradient increases during the development of stenosis.11 Therefore, VDP increases with increasing distance between the venous needle and venous anastomosis.

Initially, it appears that VAPR values greater than 1.0 are biologically impossible; however, all test groups had some VAPR values greater than 1.0, reflecting that physiologically calculated VAP exceeded MAP. For VAPR data shown in Fig 4, of all values, 9.8% were greater than 1.0, with 27.9% of these in the TP group. Several conditions may lead to greater than expected VAPR values. Reversal of arterial and venous needles is probably the most common and occurs in nearly 25% of treatments.18 It also should be noted that the small diameter of the venous needle creates turbulent flow in the access and augments resistance to flow through the access. The degree of turbulent flow increases when access flow is reduced from venous stenosis and results in increased resistance and increased VAP. Lodgment of the venous needle against or partially in the access wall will produce an increase in measured VDP and result in episodically high VAPR values. Finally, a difference in MAP between the access extremity and nonaccess arm, typically used to monitor blood pressure during HD,19 will produce an elevation of VAPR.

To reduce errors in the VAPRT, patient VAPR values must exceed 0.55 for three consecutive treatments. Initial dynamic access pressure testing developed by Schwab et al1 used three consecutive treatments that exceeded predefined limits to indicate a positive test result. HD treatments at the end of the month were selected for evaluation because test results were included in a monthly patient report, and patients may have had an access intervention during the early part of the month. Our objective was to maintain a minimal FP rate to preclude unnecessary evaluations of AVG.

Figure 2 shows problems that must be resolved when using dynamic VDP measurements to monitor access pressure. As blood flow increases, VDP increases, and this is attributable primarily to augmented resistance created by the venous needle. Elevation in Hct also will increase VDP. The variability in VDP values from Qb and Hct can be reduced if measurements are made at a fixed relatively low blood flow, as shown by Schwab et al.1

However, the appropriate warning level for VDP will vary among individuals, depending on MAP and Hct. For example, with a 15-G needle and Qb of 200 mL/min, VDP0 is 33 mm Hg at an Hct of 20% and 42 mm Hg at an Hct of 36%. Using our criteria that a patient is at risk when VAPR is greater than 0.55, an MAP of 120 mm Hg would require an access pressure greater than 66 mm Hg (66/120 = 0.55) to receive a warning for that treatment. Therefore, at Qb of 200 mL/min, the VDP warning level should be between 99 (33 + 66) and 108 (42 + 66) mm Hg for a patient because Hct varies between 20% and 36%. Applying the same criteria, a patient with an MAP of 75 mm Hg would need a VDP warning level between 74 and 83 mm Hg. Thus, it is difficult to select a single VDP warning value for patients at risk for VDP between 74 and 108 mm Hg. After calculating VAPR, the VAPRT adjusts the VDP warning level for each access pressure measurement in relationship to Qb, Hct, and MAP. Notably, this absolute pressure range of 74 to 108 mm Hg is significantly less than that originally reported by Schwab et al,1 who used 16-G needles in his investigation. The component of VDP caused by flow through the needle therefore would be expected to be significantly greater with a 16-G needle.6 Therefore, our algo-

| Table 2. Statistical Analysis of the VAPRT for Grafts Showing Mean Values for 3 Months of Testing |
|-----------------|-----------------|-----------------|
| Sensitivity (%) | Specificity (%) | Positive predictive value (%) |
| 70 ± 8          | 86 ± 2          | 52 ± 10          |
| 74 ± 5          | 96 ± 3          | 84 ± 10          |
| Negative predictive value (%) | 94 ± 2          | 92 ± 3          |
| 4 ± 3          |
| FP rate (%)     | 12 ± 2          | 4 ± 3            |
rithm must be applied only when 1-in. 15-G needles are used, at least until newer investigations are completed.

An alternative method of determining VAPR is to monitor static venous pressures and calculate the static venous access pressure ratio (SVPR) to test for a functionally significant stenosis. Previously, we determined that SVPR was an accurate method for access monitoring. However, this method involves intensive training of HD staff and ongoing monitoring to ensure the validity of data. The VAPRT does not require specific training, and the algorithm examines data currently entered in our patient database and evaluates the patient’s access at each dialysis treatment. Last, another method measures static intra-access pressures directly before HD by using a proprietary hydrophobic filter. This method has not been widely applied.

Stenosis at the arterial input side of the access or within the access would not be detected by the VAPRT because this type of lesion reduces access flow and VAP simultaneously. Thus, it may be feasible to detect an arterial stenosis with a model that examines prepump arterial drip chamber pressure for values more negative than empirically determined. It also may be possible to determine the presence of intra-access lesions if arterial intra-access pressure and VAP can be determined. In this regard, Polaschegg et al described a method to detect and locate an access stenosis using dynamic arterial and VAP measurements.

Access flow measurements, performed in the HD unit, can determine when there is a clinically significant reduction in access flow, indicating the need for intervention. However, the location of the obstruction to flow cannot be definitively identified. Disadvantages of flow measurements include requirements for costly equipment, trained personnel, and dialysis time for setup and measurement. Moreover, Paulson et al indicated that a single access flow measurement is a relatively poor indicator of graft failure. To achieve a sensitivity of 80%, the FP rate was 34% for testing grafts. A low FP rate (20% for grafts) was selected to avoid a large number of interventions by either vascular surgeons or interventional radiologists. Trend analysis, which may be a better predictor of access failure when using access flow, requires more frequent flow measurements and greatly increases the cost of monitoring. The VAPRT calculates a VAPR for each HD treatment, thus rendering it an ideal method for trend analysis. The current VAPRT models VAPRT trend after the eighth treatment of the month. To minimize spurious alarms, we imposed a triplet rule whereby three consecutive treatments with a VAPR greater than 0.55 were necessary to elicit a warning of impending graft failure. Although it may be possible to improve the VAPRT if trend analysis of all data is included in the algorithm, this hypothesis has not been tested. Greater emphasis could be placed on the analysis of temporal trends or implementation of data filters to exclude clearly erroneous measurements. In addition, analysis of data from two or more consecutive months may increase the accuracy of the VAPRT to detect access dysfunction.

Results of this study show that the VAPRT is a valuable noninvasive screening test that identifies HD patients at risk for AVG failure. The key component in implementing this system is computer access to the required treatment and laboratory data. The software algorithm to analyze HD data is incorporated as a standard end-of-month report and as an Internet-based accessible vascular access monitoring system. All patients showing a warning are identified in the database, and their status is available online to create a report for any HD location or period. Patient care is enhanced because warning status can be tracked, permitting immediate follow-up with timely cost-saving interventions.

APPENDIX A

Data from Fig 2 were analyzed by fitting each individual curve with an equation of form:

$$VDP_0 = A \cdot Q_b^2 + B \cdot Q_b + C$$

The constant C equals VDP at Q_b of 0 mL/min, and the average value of -17.325 mm Hg was used during further data analysis. Because
coefficient A varied minimally from 0.0004232 to 0.0004327, a mean value of 0.00042329 was used, ie, an increase of only 1.5 mm Hg in VDP_0 at Q_b of 400 mL/min. Coefficient B varied to a greater extent, from 0.145289 to 0.231968, as Hct increased over the range of clinically encountered Hcts. Raw data then were fit with equation 2a.

\[
VDP_0 = 0.00042329 \cdot Q_b^2 + B \cdot Q_b - 17.325 \quad (2a)
\]

Coefficient B values were obtained for each Hct value. Figure 6 shows the plot of coefficient B versus Hct, and equation 3a was fit to the data.

\[
B = 0.62116 \cdot Hct^2 + 0.01203 \cdot Hct + 0.12754 \quad (3a)
\]

Equations (2a) and (3a) were combined to yield equation (4), which relates VDP_0 to Q_b and Hct.

\[
VDP_0 = 0.00042 \cdot Q_b^2 + (0.62116 \cdot Hct^2 + 0.01203 \cdot Hct + 0.12754) \cdot Q_b - 17.32509 \quad (4a)
\]

Equation 4a was evaluated for accuracy using a nonlinear regression program (DataFit). The adjusted coefficient of multiple determination \( r^2 = 0.99982 \) validated the accuracy of equation 4a as a data model.

### APPENDIX B

Equations for curves fit to AVG histogram data from Fig 4.

TN

\[
y = 7.396 e^{\frac{-(x - 0.468)^2}{2}} \cdot 4.895^2 + 0.472 e^{-(0.315 \cdot (x - 2.049))} \quad (1)
\]

\[ r^2 = 0.9800 \]

TP

\[
y = 21.88 e^{\frac{-(x - 0.863)^2}{2}} \cdot 3.457^2 + 0.188 e^{-(0.00012 \cdot (x - 3.045))} \quad (2)
\]

\[ r^2 = 0.9192 \]

FN

\[
y = 6.440 e^{\frac{-(x - 0.512)^2}{2}} \cdot 3.093^2 + 0.192 e^{-(0.291 \cdot (x + 0.083))} \quad (3)
\]

\[ r^2 = 0.8754 \]

FP

\[
y = 17.28 e^{\frac{-(x - 0.717)^2}{2}} \cdot 7.422^2 + 0.803 e^{-(1.002 \cdot (x - 1.143))} \quad (4)
\]

\[ r^2 = 0.9301 \]

### REFERENCES