

INRatio® PT/INR Monitoring System: Correlations with Plasma-based Laboratory and Whole Blood-based Point-of-Care PT Measurement Systems

Introduction

The INRatio® PT/INR Monitoring System was developed for point-of-care (POC) testing, specifically to improve patient management for healthcare providers by using a simple finger-stick sampling of capillary whole blood and providing an immediate result. To facilitate a smooth transition to a new device such as the INRatio Monitor, comparisons to the current measurement system are sometimes performed. This paper provides examples of completed correlations comparing the INRatio system to plasma based lab systems and other POC whole blood based devices.

Purpose

The following correlations are provided as *examples only* of previous studies between INRatio and existing PT systems. These comparisons reinforce the strong correlation found between INRatio and other systems, including POC (whole blood) and lab-based (plasma samples), as well as to reference laboratories, and demonstrate acceptable performance of INRatio.

Procedure

The evaluations were performed using the HemoSense® Evaluations Guidelines, which recommend adherence to

Clinical Laboratory Standards Institute (CLSI), formerly known as NCCLS, guidelines for specimen collection, transportation, storage and processing to minimize the affect of pre-analytical variables on the lab sample. A minimum of 20 samples is recommended.

Factors to Consider

As described in previous INRatio Technical Bulletins [#101–105] there are many factors to consider when comparing PT results between different systems, including but not limited to, factors that affect warfarin metabolism, factors that affect the PT test itself, such as sample type, reagent source/sensitivity, and instrument measurement principle (Table 1). It is important to note that, as mentioned in Table 1, the INR calculation itself explains reasons for some differences:

$$\text{INR} = (\text{Patient PT} / \text{MNPT})^{\text{ISI}}$$

(MNPT= Mean Normal PT, ISI=International Sensitivity Index) The ISI is an exponent, so any error in the ISI can magnify errors in the calculation (hence, a low ISI due to a highly sensitive reagent will minimize errors). In addition, results exceeding 5.0 INR generally have reduced trueness, precision and linearity both in POC and lab based PT testing and should be interpreted accordingly.¹

Table 1: Factors that affect PT/INR results when comparing different systems.

Factors that affect warfarin mechanism or metabolism	Factors that affect the PT test itself can cause differences when comparing systems	Factors when comparing capillary whole blood lab-based plasma system	Incorrect ISI of thromboplastin
<ul style="list-style-type: none"> • Illness (e.g. congestive heart failure, hyper- & hypo-thyroidism, hepatic failure) • Drugs • Diet (foods containing vitamin K and alcohol) 	<ul style="list-style-type: none"> • Lack of comparability of INR between reagents when used at onset of warfarin therapy • Loss of accuracy and precision when using reagents with high ISI (low sensitivity thromboplastin) • Inherent variability with different instrumentation • Lack of reliability of ISI provided by manufacturer • Incorrect calculation of INR from use of inappropriate control plasmas used to determine the Mean Normal PT (MNPT) 	<ul style="list-style-type: none"> • Pretest variables (especially for plasma samples) • Contaminated line (Heparin) • Antiphospholipid antibodies • Hematocrit 	<ul style="list-style-type: none"> • Incorrect calibration • Change in ISI over time • Poor distribution of warfarin samples • Incorrect choice of reference

INRatio Monitor Characteristics

The INRatio Monitor determines the PT by measuring the change in impedance of the sample as clotting occurs. INRatio test strips use a recombinant thromboplastin reagent with a low ISI, as re-commended by ACCP, CAP and WHO.² Each lot of INRatio Test Strips is calibrated to a plasma based lab system traceable to the WHO standard.

Lot to lot variability is adjusted for by entering a test strip calibration code with each new strip lot. In the comparisons provided here, detailed reagent information (source and ISI value of comparative reagent) was not provided by the site.

Data Interpretation

In general terms, the “r” value may be interpreted as a measure of scatter in the data. A factor influencing the “r” value is the method of clot detection employed by the system. The closer the “r” value is to 1.0 the better the agreement between the individual points. Comparing systems with different clot detection methods may give rise to higher levels of scatter even when comparing lab systems (see fig. 9).

The slope of the regression line may be interpreted as a reflection of a systematic bias between the systems. A factor influencing the slope is the calibration of the system. All systems are calibrated differently, a fact reflected in the slopes of the lab to lab comparisons (see fig. 7, 8 and 9). The closer the slope is to 1.0, the less the bias between the systems.

Comparisons between whole blood POC systems:

POC systems with the same sample type i.e. whole blood fingerstick show very good agreement even though the measurement principals are quite different.

Fig. 1

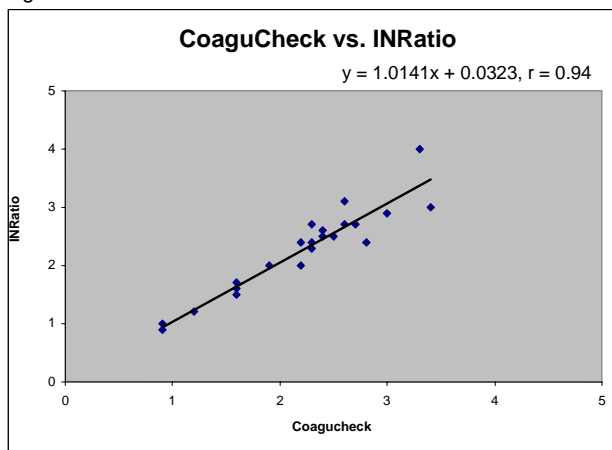
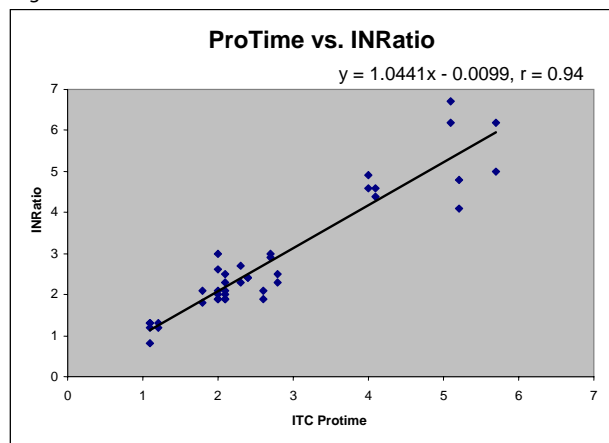


Fig. 2



Comparisons between whole blood POC and lab-based plasma systems:

Even with the differences in sample types added to the mix, the following comparisons between INRatio and several laboratory-based plasma samples continue to show good correlations ranging from 0.93 to 0.99. Few (if any) clinical discrepancies that would result in different dosing decisions are apparent. In each case the evaluating site implemented the INRatio system due to acceptable agreement coupled with the additional features of the INRatio system.

Fig. 3

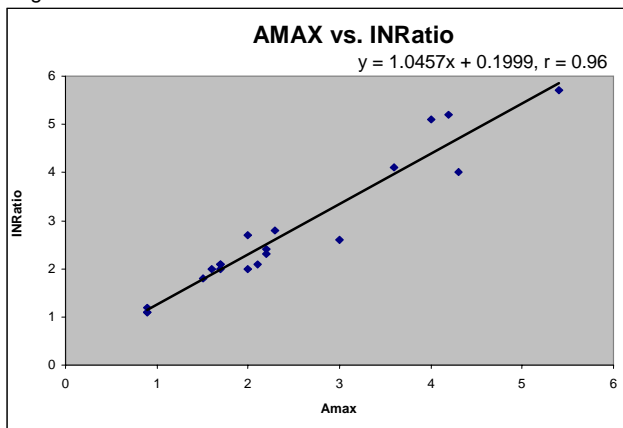


Fig. 4

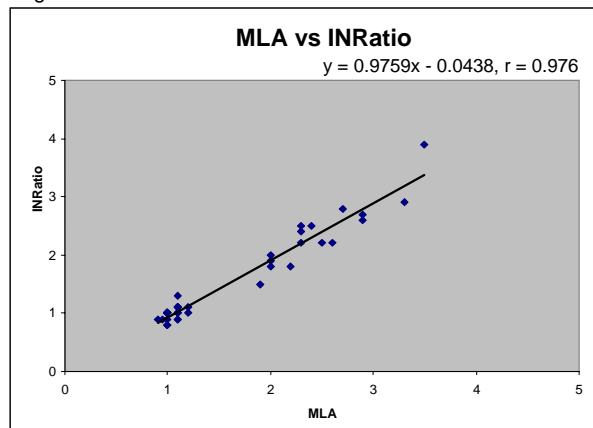


Fig. 5

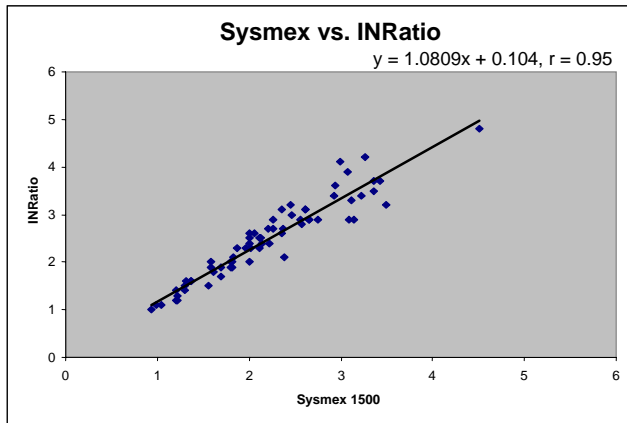
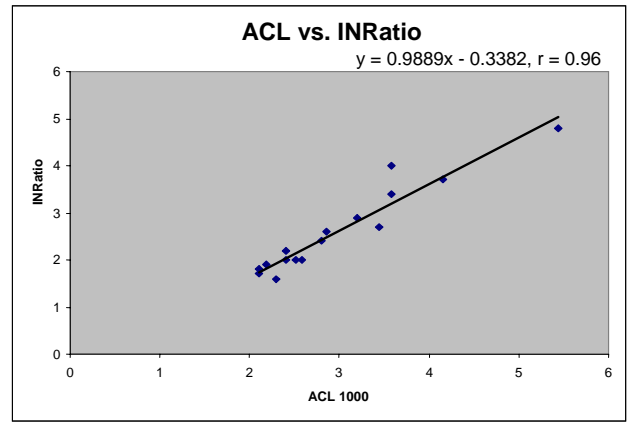


Fig. 6



Commentary: Variability between laboratory analyzers is recognized and reported by others

To understand the variability among PT methodologies better, three comparisons are provided in Figures 7, 8 and 9 between lab systems commonly used: MLA, Sysmex, STA and AMAX. In addition, according to data provided by Dr. Alan Jacobson, observed variation in INR can be high even between laboratory and reference laboratory analyzers (Fig 10). Plasma samples tested on 18 different instrument/reagent combinations demonstrated that as much as 2.5 INR differences can be observed for a single sample run on multiple systems.

Fig. 7

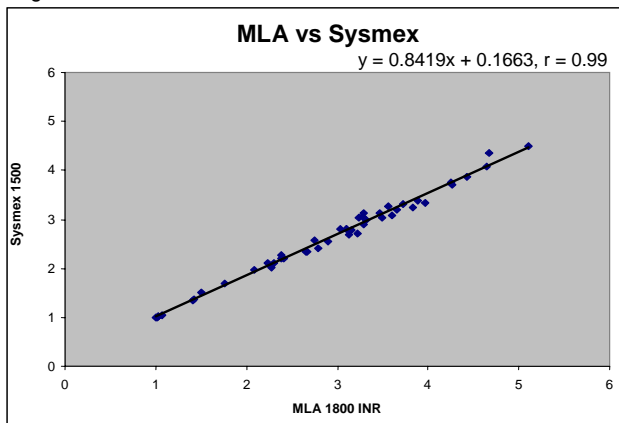


Fig. 8

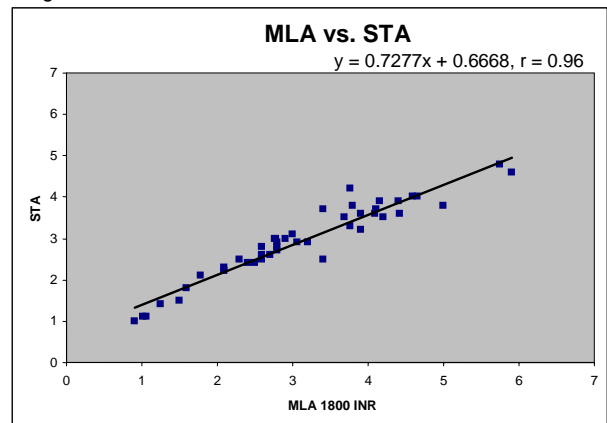


Fig. 9

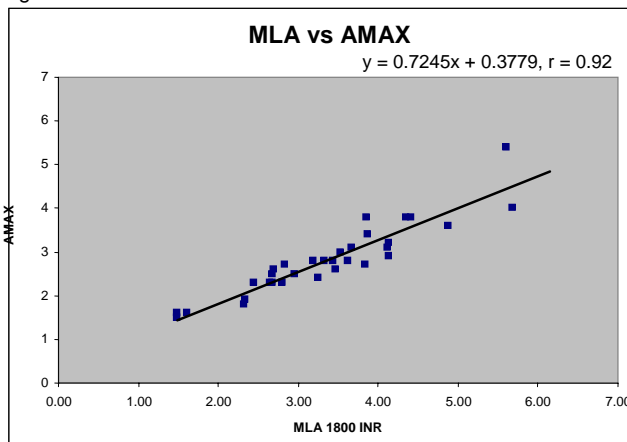
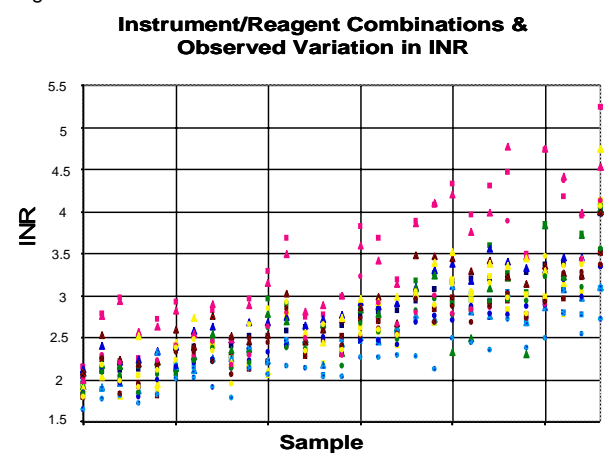


Fig. 10



Conclusions

Transitioning to a new coagulation measurement system for PT is not difficult but has several points to consider due to the many variables that exist across all PT/INR testing modalities. In the context of this variability, the correlations presented here show strong performance for INRatio versus commonly used lab systems.

The frequently asked question “Will it match?” should be carefully considered. However, in the end consistency of test method is the key to the management of patients on oral anticoagulant therapy. The INRatio provides that consistency together with an easy to learn and easy to use system.⁴



Measurement Principles of Comparison Systems

INRatio detects clot formation by a change in the electrical impedance of the blood sample that occurs when fibrinogen is converted to fibrin.

CoaguChek uses alternating magnetic fields in the device which cause iron particles on the strip to move within the sample; the endpoint is reached when the blood clot stops the iron particles from moving.

ProTime Microcoagulation System pumps the sample back and forth until a clot forms. The clot is detected optically as the motion of the blood decreases with clotting.

Plasma based systems generally detect clot formation via mechanical (AMAX) or optical means (ACL, MLA, STA, Sysmex).

References

¹ NCCLS Point of Care monitoring of anticoagulation therapy; approved guideline, NCCLS document H49-A Vol. 24 No. 23 (TSBN 1-56238-540-2). NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA, 19087-1898 USA, 2004.

²The Seventh ACCP Conference on Anticoagulation Therapy: Evidence-Based Guidelines, Supplement to Chest, Volume 126, No. 3 (Supplement). September 2004: 2085-2095. ACCP: American College of Chest Physicians, CAP: College of American Pathologists, WHO: World Health Organization.

³Unpublished Abstract, Alan Jacobson, Loma Linda VA

⁴Self management of oral anticoagulation with the INRatio system: impact of a structured teaching program on patient's knowledge of medical background and procedures; European Journal of Cardiovascular Prevention and Rehabilitation 2004, 11:000-000; Heinz Völler, Clemens Dovifat, Johannes Glatz, Heinrich Körte, Uwe Taborski and Karl Wegscheider.

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