

A COMPARISON OF THREE POINT-OF-CARE PT TESTS VS. A LABORATORY REFERENCE STANDARD

M. Patsch, C. Cimini, Ph.D., International Technidyne Corporation, Edison, NJ

ABSTRACT

This study compared fingerstick results from three point-of-care (POC) prothrombin time assays used in the management of oral anticoagulant therapy. The POC assays were INRatio® (HemoSense®, Milpitas, CA) and two ProTime® assays (International Technidyne Corporation, Edison, NJ), original 5-channel (ProTime5) and low volume (ProTime3). A laboratory reference result (REF; venous 3.2% sodium citrate) was obtained using an MLA 900 (Medical Laboratory Automation, Pleasantville, NY) with Dade Innovin reagent (ISI=0.98, Dade Behring, Newark, DE). The lab reference was verified against a national reference lab (Midwest Hemostasis, Muncie, IN) and is substantiated by consistent mid-range performance within a proficiency test program (College of American Pathologists or CAP). The study was performed in two phases: (1) ProTime5 and INRatio vs. REF and (2) ProTime3 and INRatio vs. REF. Unique fingersticks were obtained for each POC assay. Regression analyses compared POC to REF Bias (POC-REF) was calculated with results categorized by INR <2.5 and ≥2.5. ANOVA compared POC and REF with categorized INR values.

ProTime5 (n=32) $y=0.99x+0.09, r=0.97$	ProTime3 (n=51) $y=0.89x+0.23, r=0.92$
INRatio (n=28) $y=1.25x-0.22, r=0.98$	INRatio (n=49) $y=1.32x-0.37, r=0.97$

Statistically significant differences (*) were found for INRatio vs. REF in the higher INR range.

BIAS (INR)	Bias < 2.5	Bias ≥ 2.5
ProTime5	0.06	0.08
INRatio	0.21	0.46*

Conclusion: All POC assays correlated well with the REF. INRatio demonstrated a significant positive bias vs. REF in the higher INR range. ProTime demonstrated small or no bias, regardless of INR range.

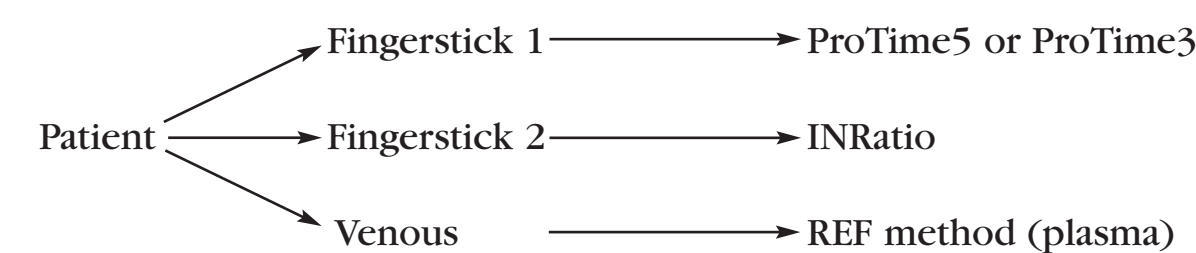
INTRODUCTION

The ProTime Microcoagulation System (ITC, Edison, NJ) has been used to manage patients on oral anticoagulant therapy (OAT) in professional and patient self-testing settings since 1995 and 1996, respectively. This system employs a 5-channel assay (ProTime5) which is unique with triplicate PT testing and on-board controls. A second assay, ProTime3, was added to the system in 2001 to meet the need for a PT test requiring less blood. This assay is a single PT test with on-board controls. Other test systems have entered the POC PT marketplace, including the INRatio system (HemoSense, Milpitas, CA). The objective of this study was to compare performance of these methods to that of a reference system.

STUDY

	ProTime5/INRatio	ProTime3/INRatio
OAT subjects	n=34	n=56
POC specimen	Fingerstick	Fingerstick
REF system*	MLA 900 (Medical Laboratory Automation, Pleasantville, NY), Dade Innovin reagent (ISI=0.98, Dade Behring, Newark, DE)	

METHOD

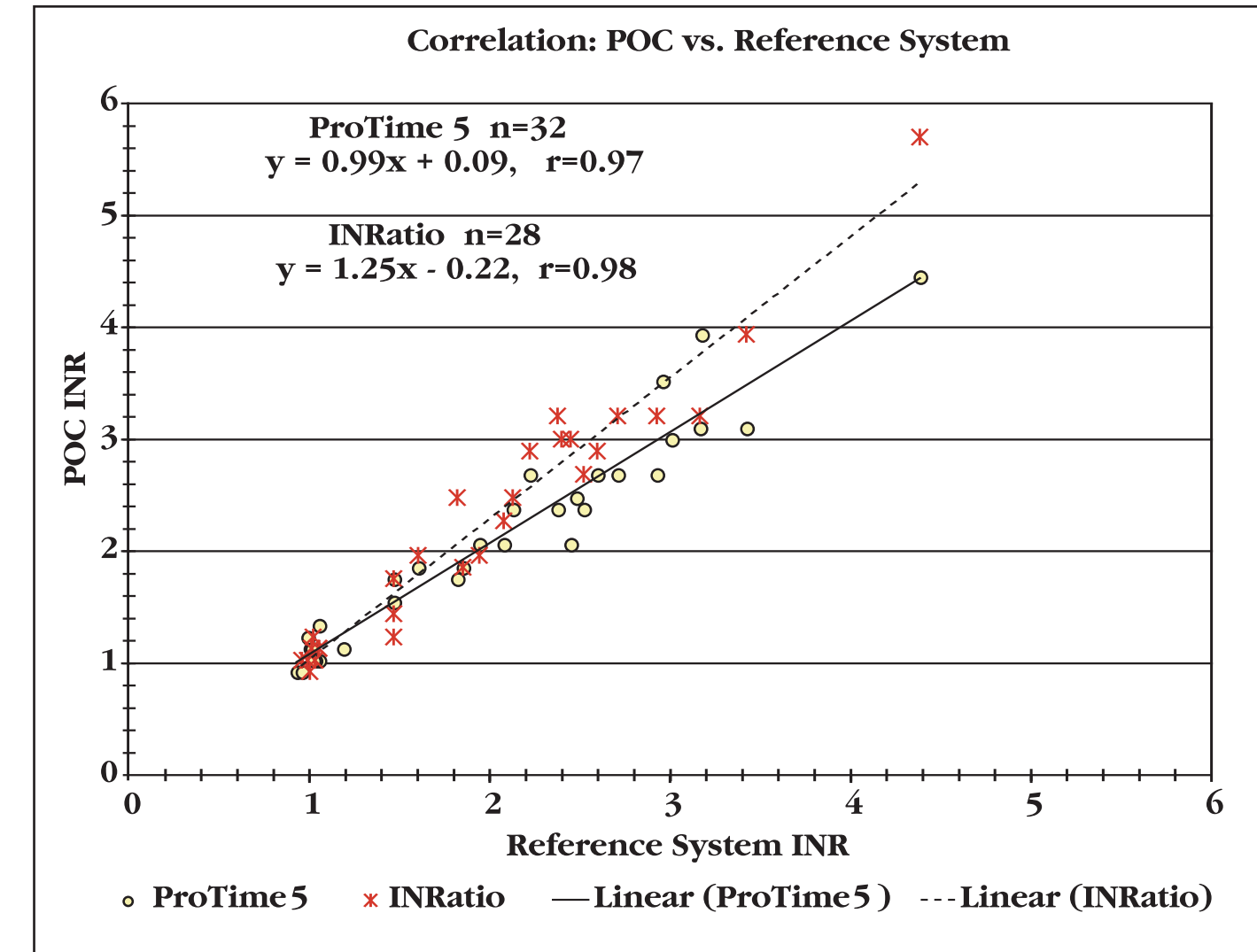


ANALYSIS

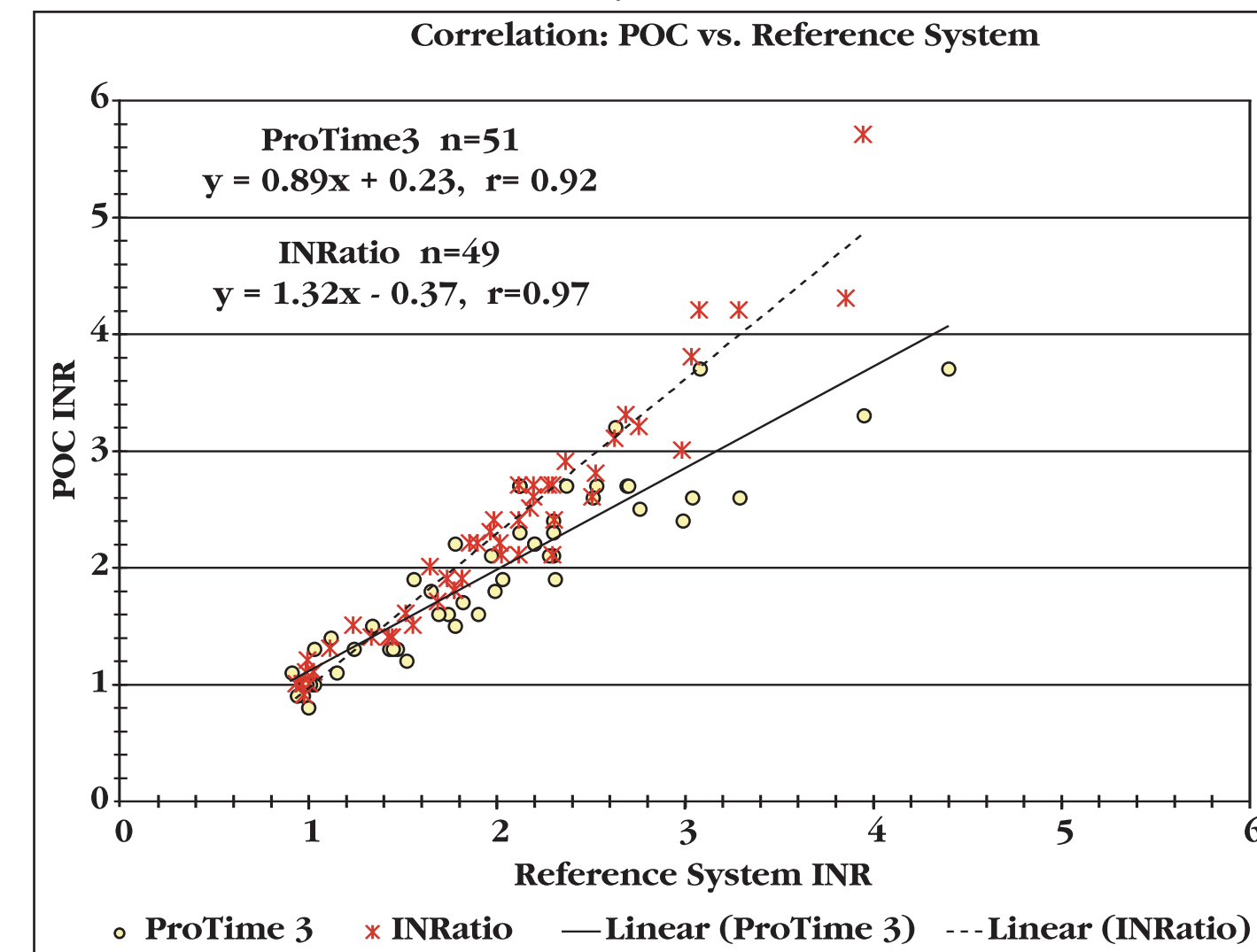
Linear regression, bias and outlier analyses, and analysis of variance (ANOVA) were used to assess agreement between each POC system and the REF. ANOVA and bias and outlier analyses were performed with data separated into two INR classes, <2.5 and ≥2.5. This arbitrary INR separation was established to provide study balance for meaningful evaluation. Classification was determined by the REF. Paired differences [POC-reference] were categorized by agreement within 0.4 INR, and as discrepant by 0.7 or 1.0 INR. INR differences of 0.4 and 0.7 have been used as benchmarks in comparative evaluations of the prothrombin time test¹. Clinically significant inter-laboratory variations in INR have been documented^{2,3,4,5}, 0.4 INR is considered acceptable variation¹.

RESULTS

ProTime 5 and INRatio vs. Reference System



ProTime 3 and INRatio vs. Reference System



Bias Analysis [POC-Reference System]

		ProTime5	INRatio
<2.5 INR*	n	23	22
	population avg. (INR)	1.55	1.70
	avg. relative difference vs. Reference	0.06	0.21
	within 0.4 INR (n, %)	22 (96%)	17 (77%)
≥2.5 INR*	n	9	6
	population avg. (INR)	3.13	3.57
	avg. relative difference vs. Reference	0.08	0.46**
	within 0.4 INR (n, %)	7 (78%)	3 (50%)

		ProTime3	INRatio
<2.5 INR*	n	39	38
	population avg. (INR)	1.7	1.9
	avg. relative difference vs. Reference	0.02	0.17
	within 0.4 INR (n, %)	35 (90%)	33 (87%)
≥2.5 INR*	n	12	11
	population avg. (INR)	2.9	3.7
	avg. relative difference vs. Reference	-0.16	0.62**
	within 0.4 INR (n, %)	5 (42%)	3 (27%)

* INR classification determined by Reference System result

** Statistically significant difference (p<0.05) when compared to Reference System

Discrepant INR Results [Comparison of POC and Reference System]

		ProTime5	INRatio
<2.5 INR*	n	23	22
	values discrepant by > 0.7 INR (n, %)	0 (0%)	1 (5%)
	values discrepant by > 1.0 INR (n, %)	0 (0%)	0 (0%)
≥2.5 INR*	n	9	6
	values discrepant by > 0.7 INR (n, %)	1 (11%)	1 (17%)
	values discrepant by > 1.0 INR (n, %)	0 (0%)	1 (17%)

		ProTime3	INRatio
<2.5 INR*	n	39	38
	values discrepant by > 0.7 INR (n, %)	0 (0%)	0 (0%)
	values discrepant by > 1.0 INR (n, %)	0 (0%)	0 (0%)
≥2.5 INR*	n	12	11
	values discrepant by > 0.7 INR (n, %)	0 (0%)	4 (36%)
	values discrepant by > 1.0 INR (n, %)	0 (0%)	2 (18%)

OBSERVATIONS

- All POC systems were highly correlated to the REF system.
- ProTime demonstrated closer agreement to the REF system compared to INRatio.
- INRatio demonstrated a statistically significant bias vs. REF for INR ≥ 2.5.

SUMMARY

Results demonstrate all POC systems were highly correlated to a standard laboratory reference method. The slopes generated from the regression analysis show directional differences of the ProTime and INRatio systems relative to the MLA. INRatio demonstrated a positive bias that was exaggerated in the higher INR range resulting in significantly different results compared to the MLA for INR values ≥2.5. The ProTime Microcoagulation System (ProTime5 and ProTime3) demonstrated a smaller bias and accurate INR results across the entire INR range evaluated, with few discrepant values, consistent with published reports^{6,7}. Results confirm both ProTime assays are appropriate for monitoring the coagulation status of patients on oral anticoagulant therapy. It is important that all sites establish their own correlation with the local laboratory to identify institutional variation between POC systems and their unique reference systems.

REFERENCES

- Lassen, J.F., Brandslund, I. and Antonsen, S. (1995) International Normalized Ratio for prothrombin times in patients taking oral anticoagulants: Critical difference and probability of significant change in consecutive measurements. Clin. Chem. 41 (3) 444-447
- Becker, D.M., Humphries, J.E., Walker, E.B., Demong, L.K., Bopp, J.S. and Acker, M.N. (1993) Standardizing the prothrombin time: Calibrating coagulation instruments as well as thromboplastin. Arch. Pathol. Lab. Med. 117 602-605
- Preston, F.E. (1995) Quality control and oral anticoagulation. Thromb. Haemost. 74 (1) 51-520
- Ng, V.L., Levin, J., Corash, L. and Gottfried, E.L. (1993) Failure of the International Normalized Ratio to generate consistent results within a local medical community. Am. J. Clin. Pathol. 99 (unbold the highlighted for consistency) 689-694
- Horsti, J., Uppa, H., Vilpo, J.A. (2005) Poor Agreement among Prothrombin Time International Normalized Ratio Methods: Comparison of Seven Commercial Reagents. Clin. Chem. 51 (3) 553-560
- Oral Anticoagulation Monitoring Study Group* (2001): Point of care prothrombin time measurement for professional and patient self-testing use. Am J Clin Path 115: 288-296 (*Group consists of Maureen Andrew, M.D., Jack Ansell, M.D., Daniel Becker, M.D., Richard Becker, M.D., Douglas Triplett, M.D.)
- Oral Anticoagulation Monitoring Study Group* (2001): Prothrombin time measurement using a patient self-testing system. Am J Clin Path 115: 280-287. (*Group consists of Maureen Andrew, M.D., Jack Ansell, M.D., Daniel Becker, M.D., Richard Becker, M.D., Douglas Triplett, M.D.)

*The reference system has been verified against a national reference lab (Midwest Hemostasis, Muncie, IN) and is substantiated by consistent mid-range performance within a proficiency test program