iLine® microsystems friendly technology

Performance of the microINR® System: Precision and Accuracy Assessment by Healthcare Professionals and Self-Testing Patients

Introduction

Vitamin K Antagonist (VKA) drugs, such as warfarin, are the cornerstone of oral anticoagulation therapies for prevention of thromboembolic events. Point-of-care (POC) devices for INR measurement provide advantages, such as ease-of-use, fast turnaround time and fingersticking versus venous draw, allowing better therapy management which can maximize the time in therapeutic range (TTR).

The microINR System (iLine Microsystems, Donostia-San Sebastián, Spain) is a worldwide marketed device for INR determination in patients undergoing oral anticoagulation therapy with VKA. The innovative microINR System is designed to exploit the advantages of both microfluidics and Lab-on-a-Chip (LOC) technological concepts under the company´s proprietary core technology.

The specific characteristics in the design and the usability of the microINR System, such as the automatic strip lot calibration, low sample volume and minimum testing steps, provide key advantages over existing POC/INR systems, in the hands of both healthcare providers (HCP) and self-testing patients (PST).

In addition to multiple evaluations conducted in the past, this whitepaper focuses on the results obtained in two recent independent multisite clinical trials performed in the US, under real-life conditions by both HCP and PST. These studies are described in detail in the following sections.

Precision and Accuracy by Healthcare Professionals

Method

The first clinical trial was performed at three US medical centers involving 68 normal non-anticoagulated donors and 245 patients anticoagulated with warfarin.

The goal was to assess the accuracy and precision of the microINR System against both a reference laboratory method and a US FDA-cleared PT/INR POC device.

HCP performed testing using capillary blood samples for POC systems and venous blood samples for laboratory testing.

Results

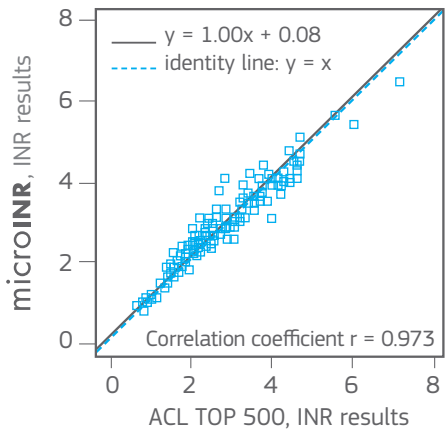

Figure 1: Passing–Bablok regression plot. INR results from microINR system vs. INR results from the ACL system.

Passing–Bablok regression analysis between the results of the microINR System and the reference system (Fig.1) showed a strong correlation.

The regression analysis of the microINR system against the PT/INR POC device also showed remarkable agreement.

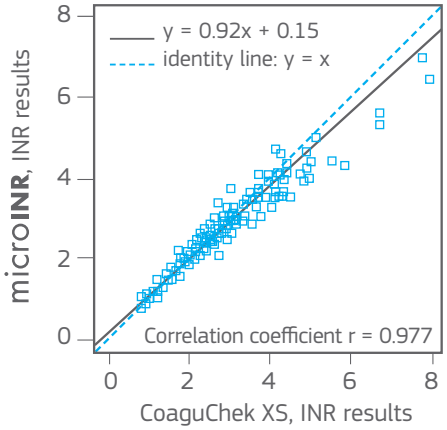

Figure 2: Passing–Bablok regression plot. INR results from microINR system vs. INR results from the CoaguChek XS system.

Precision performance was evaluated by comparing duplicate measurement results on the microINR System with capillary blood. The microINR System showed remarkable precision of 5.0%, from a total of 305 duplicate results. The Coefficient of Variation (CV) in the therapeutic INR range (i.e., 2.0–3.5) reached 4.68%.

Precision and Accuracy by Self-Testing Patients

Method

The second clinical trial was conducted at four US clinical sites and included 117 self-testing patients.

The goal was to assess the accuracy of the microINR System comparing the INR test results obtained by trained PST to those of HCP, using the microINR System after two visits to the sites.

Additionally, INR test results obtained by PST on a second visit were compared to a laboratory reference method, in order to evaluate the system accuracy by trained PST vs. a reference.

The microINR precision was also assessed, based on duplicate measurements performed by the PST on their second visit to the site.

Finally, in order to assess the usability of the system, all self-testing patients enrolled in the trial filled out a questionnaire with 20 statements about the ease of use, handling and functionality of the microINR System.

Results

Passing–Bablok regression analysis between the results of PST and HCP (Fig.3) showed a strong correlation. 228 results were included in this regression.

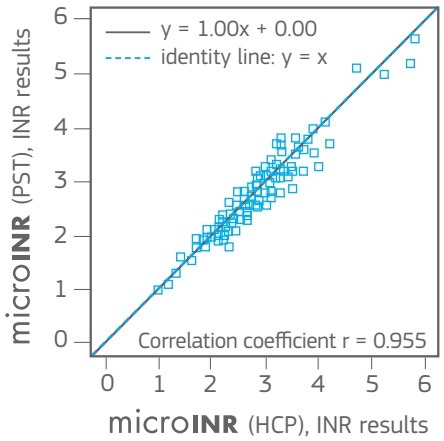

Figure 3: Passing–Bablok regression plot. INR results from microINR system obtained by PST vs. INR results from microINR system obtained by HCP.

Analytical agreement with both HCP and laboratory were assessed according to three different acceptance criteria: ISO-17593:2007, FDA at the 2016 Workshop and CLSI POCT14-Ed2.

Table 1: Analytical agreement from the PST results with the HCP results and the ACL system results.

Acceptance criterion		ISO 17593:2007	FDA Workshop 2016	CLSI POCT14 Ed2
< 2.0 INR		±0.5	±0.4	±0.4
≥ 2.0 - 4.5 INR		±30%	±20%	±20%
> 4.5 - 6.0 INR		NA	±25%	±25%
> 6.0 INR		NA	±25%	±30%
Overall agreement		≥ 90%	≥ 95%	≥ 95%
microINR results	**PST vs. HCP**	**100%**	**99.1%**	**99.1%**
	PST vs. Lab	**100%**	**100%**	**100%**

The precision of the microINR System was determined from duplicate measurements performed at four clinical sites by PST on the second visit to the site. The obtained CV from 111 paired results reached 4.9%.

Regarding the usability questionnaire, questions were rated by the patients (n=117) on a scale of 1 (strongly disagree) to 5 (strongly agree) obtaining an overall score of 4.7.

Discussion and Conclusion

In the first clinical trial comparison the results obtained with microINR showed significant correlation with the reference laboratory system and a commercial INR POC System. This is also confirmed in the second clinical trial, in which the INR test results obtained by PST were compared to the same laboratory system. In fact, analytical agreements values were excellent (>99%) between the microINR System and the reference laboratory and also when comparing the INR values obtained by HCP and PST.

Concerning the precision, the microINR System showed good CV, below 5.0% when used by both HCP and PST users. In fact, the CV achieved in the second clinical trial was obtained during the patient's second visit, having performed few tests prior to their visit.

Noteworthy, most enrolled patients on both clinical trials, had one or more comorbid conditions. Many also suffered from different conditions affecting physical, sensorial and cognitive capabilities. The educational or cultural level was not considered in the inclusion/exclusion criteria.

In relation to the usability evaluation, self-testing patients felt comfortable using the microINR System according to the questionnaire they filled out at the end of the trial. The majority agreed on the convenience of use of the system both in terms of its simple design and the ease of performing the test.

Key design features of microINR, such as automatic lot identification and calibration, the low sample volume required (at least 3 µL), the test result reported only in INR units and the simplicity of the test, ensure that the microINR System is safe, uncomplicated and easy to use. Furthermore, the acoustic signals and Chip illumination also contribute to the interaction with the device and reinforce the easy adoption of the system by a wide range of HCPs and patients.

These results demonstrate the user-friendliness and reliability of microINR, as none of the different patient conditions seemed to affect the use of the system or biased the results obtained, with an easy and quick adoption of the system by both HCPs and PST of different abilities and ages.

In conclusion, the first multicenter trial demonstrated that the microINR System has equivalent performance to both a laboratory INR method and an established INR POC device and thus was granted FDA clearance for professional use in January 2019 (510(k) number K180780).

The second multicenter trial demonstrated that briefly trained self-testers could obtain satisfactory results when using the microINR System and thus FDA cleared microINR for self-testing and professional use with the CLIA waiver (510(k) number K201185).

References

- Refaai MA, Shah V, Fernando R. *Performance of the microINR Point-of-Care System: A Multicenter Clinical Trial.* Thromb Haemost. 2020;120(4):687-691.
- ISO 17593:2007 *Clinical Laboratory Testing and in Vitro Medical Devices - Requirements for in Vitro Monitoring Systems for Self-Testing of Oral Anticoagulant Therapy.* International Organization for Standardization; 2007.
- Goehe R, Riddick K. *FDA Regulatory Oversight of POC PT/INR In Vitro Diagnostic Devices.* In: FDA CDRH Public Workshop; 2016.
- CLSI POCT14-Ed2 *Point-of-Care Coagulation Testing and Anticoagulation Monitoring* - Second Edition. Clinical and Laboratory Standards Institute; 2020.
- 510(k) number K180780 Decision Summary: https://www.accessdata.fda.gov/cdrh_docs/reviews/K180780.pdf
- 510(k) number K201185 Decision Summary: https://www.accessdata.fda.gov/cdrh_docs/reviews/K201185.pdf

iLine Microsystems S.L.

Paseo Mikeletegi, 69
20009 Donostia - Gipuzkoa (SPAIN)

www.ilinemicrosystems.com