INRATIO®

651 River Oaks Parkway 1-877-436-6444
San Jose, CA 95134 408/719-1393 tel
www.hemosense.com 408/719-1184 fax

A Comparison of the HemoSense™ INRatio™ Prothrombin Time Monitoring System to the MLA™ Electra 900C™ by Regression and Bland-Altman Analysis

Introduction

Prothrombin time (PT) testing is the standard of care for monitoring the extrinsic clotting pathway in patients on oral anticoagulant therapy. Oral anticoagulation drugs are members of the coumarin family, which includes warfarin, also known by its trade marked name of Coumadin®. This study examined the performance of the HemoSense INRatio System, a new PT monitoring device that provides a measurement of a patient's prothrombin time expressed in seconds and as an International Normalized Ratio.

The International Normalized Ratio (INR) is the primary unit used to report and monitor the clotting propensity for patients on anticoagulation therapy in the United States and Europe. The PT test result is derived mathematically to the International Normalized Ratio (INR), based on a model that uses the relationship between the logarithms of clotting times determined with different thromboplastins and methods. As a result, the INR has been used effectively to compensate for the differences between laboratories, laboratory methodologies and thromboplastin sensitivities and allows for across test and across laboratory comparisons. The following formula is used to calculate the patient's INR:

$$INR=(PT\ seconds/mean\ normal\ PT\ in\ seconds)^{Thromboplastin\ ISI}$$

As an explanation of the terms, in which PT is patient's prothrombin time, mean normal PT in seconds (MNPT) is the mean normal PT that is calculated from a range of normal, non-medicated patients, and the ISI is the international sensitivity index of the measurement system.

To trigger coagulation in a laboratory system, thromboplastin is added as a reagent. Thromboplastins manufactured by different manufacturers are assigned a value for each batch of thromboplastin called the International Sensitivity Index (ISI). Manufacturers assign the ISI value to each batch of thromboplastin reagent after comparing the particular batch to a "working reference" reagent preparation. This "working reference" has been calibrated against internationally accepted standard reference preparations. By definition, the more sensitively manufactured thromboplastins have an ISI near 1.0 and the less sensitive are greater than 1.0. The ISI value is critical for calculation of the INR, because the ISI value is the exponent in the formula defined above. Consequently, small errors in the ISI assignment will affect the calculated INR substantially. From a clinicians point of view, the American College of Chest Physicians recommends the use of thromboplastins with a low ISI, because laboratory methodologies or systems that use thromboplastin reagents that have higher ISI values may produce INR results that are less precise than systems that use thromboplastin with a lower ISI value.

Purpose of the Study

The primary objective of this trial was to demonstrate that the HemoSense INRatio System is substantially equivalent to PT/INR systems currently on the market. The HemoSense INRatio was evaluated for accuracy determined by regression analysis and analytical sensitivity as determined by a Bland-Altman analysis. These were demonstrated by comparative testing with a standardized reference method using the MLA Electra 900C in an Institutional Review Board (IRB) approved clinical trial.

Materials and Methods

The trial included 152 subjects at three locations in the US. Testing on the INRatio was performed by health care professionals (HCP) without laboratory training. Both normal volunteers and patients undergoing warfarin therapy were selected to encompass the measuring range of the INRatio device. All evaluations were conducted under IRB approval. All samples were collected on site from subjects who had been recruited by the trial investigator and who had provided informed consent. There was no medical intervention based on the study results.

Fresh capillary whole blood samples were tested on the HemoSense INRatio System, which incorporates a thromboplastin reagent into a test strip. The results were compared to matched plasma samples tested on an MLA Electra 900C using Innovin, a thromboplastin reagent with an ISI also near 1.0.

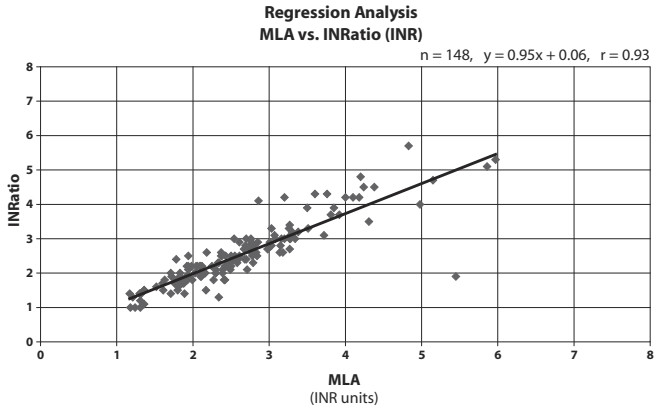
Results

Results were analyzed using regression analysis and Bland-Altman analysis. Although the MLA Electra 900C has frequently been referred to as an established laboratory instrument standard, the use of the Bland-Altman analysis serves as a valuable statistical tool for the practicing clinician because it assumes that neither system is a "gold standard"; it is only a comparison between the two systems.

A Bland-Altman analysis is used to assess the level of agreement between two methods in the comparison of a new technique to an established one. For the Bland-Altman analysis, the paired differences were plotted against the mean of the two data values. INR values were expected to lie between ± 0.5 INR units from the mean. As an example, if the HemoSense INRatio reported an INR of 2.6 and the MLA result for the same sample was 2.9, the average value for the sample would be 2.75. A Bland-Altman plot is constructed from the differences between each of the instrument's reported value and the average value: In this example, for the HemoSense INR result, 0.15 below the mean (2.6-2.75) and for the MLA INR result, 0.15 above the mean (2.9-2.75).

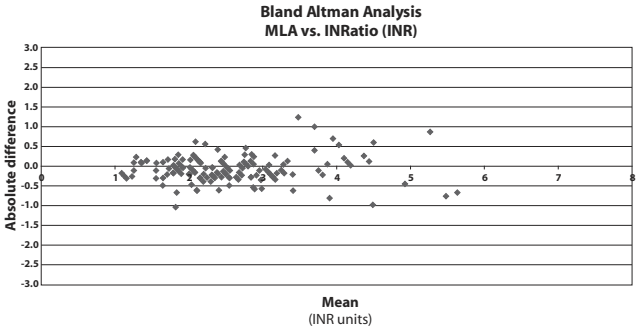
As seen in the regression analysis in Figure 1, the results from the HemoSense INRatio system compared well to the results from the MLA Electra 900C. An overall correlation coefficient or R value of 0.93 was observed with one outlier removed.

FIGURE 1:



The Bland-Altman analysis shown in Figure 2 shows that the majority of the compared INR results fall within ± 0.5 INR units from the calculated paired result mean.

FIGURE 2:



Conclusion

These study results confirm that the HemoSense INRatio Prothrombin Time Monitoring System compares closely to the well established laboratory instrument, the MLA Electra 900C in both regression and Bland-Altman analyses.

The HemoSense INRatio system offers the clinician an easy-to-use, whole blood, fingerstick system that provides reliable prothrombin time results in both PT seconds and a computed INR.

HemoSense®

HemoSense, Inc.
651 River Oaks Parkway, San Jose, CA 95134
1.877.436.6444 • 408.719.1393 tel • 408.719.1184 fax
moreinfo@hemosense.com • www.hemosense.com