COMPARATIVE STUDY OF THE
COAG-SENSE™ AND INRatio2 PT/INR MONITORING SYSTEMS

Introduction
Oral anticoagulant treatment has in recent years experienced a surge due to increased number of indications and its demonstrated effectiveness. This increase in demand has led to development of new portable monitoring systems that are devised to utilize capillary blood for Prothrombin Time (PT) determination.

The primary means of monitoring the response to Warfarin therapy is the Prothrombin Time (PT) test reported in seconds. The PT can vary widely depending on the method of measuring clotting and the Thromboplastin reagent used. For that reason the World Health Organization (WHO), in conjunction with the International Council for Standardization in Hematology and the International Committee for Thrombosis and Hemostasis, developed a measure of coagulation called the International Normalized Ratio (INR).

The Coag-Sense PT Monitoring System is a new in vitro diagnostic device that provides quantitative Prothrombin time (PT) results, expressed in seconds and INR units. It is the first portable device capable of directly detecting a clot using fresh capillary whole blood obtained from a finger stick. This system is used for monitoring oral anticoagulation therapy.

The purpose of this study was to compare the INR values obtained with Coag-Sense System and the Alere INRatio2 system along with the values from a traditional plasma based lab system, in a group of long term anticoagulated patients.

Material and Methods
The study was performed using a group of people under chronic oral anticoagulant treatment with a target INR range between 2 and 4. As per CLSI Guidelines for method comparison a number of non-anticoagulated samples were also included in the study.

Two separate finger sticks were performed and the capillary whole blood samples were tested, to obtain duplicate INR results on each point-of-care system. Manufacturer’s guidelines were followed for sample application. The order of sample application to the devices was sequenced so that it was not one particular device that got the first drop each time. The patterns allowed for each device to be first in the sequence multiple times.

Venous samples were also collected in two separate tubes. The first draw was in a red top with no anticoagulant and whole blood from this was immediately applied to all the point of care devices. It should be noted that the Alere INRatio2 is not intended for use with venous sample. Because the Coag-Sense system is capable of directly detecting the clotting endpoint, visual confirmation of clot formation on this system was also performed.

A second tube of 3.2% dehydrate of trisodium citrate was drawn and subsequently spun to produce platelet poor plasma and tested on the lab system. CLSI recommended guidelines were followed for collection and processing. The citrated tube was spun to produce platelet poor plasma and subsequently aliquoted. A plasma aliquot was run on the Diagnostica STAGO STA Compact analyzer with Siemens Dade® Innovin®. Remaining aliquots were frozen and stored as per required guidelines for any future analysis. To ensure proper function of the elements of each system two levels of quality control samples were tested on Coag-Sense and the lab system. Alere INRatio2 system does not allow for use of external controls.
The systems and their principle of measurement are tabulated below.

<table>
<thead>
<tr>
<th>Name of System</th>
<th>Principle of Measurement</th>
<th>PT Time (endpoint) Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coag-Sense PT/INR Monitoring System</td>
<td>Direct micromechanical detection of clot</td>
<td>Direct- Light beam interruption by clot</td>
</tr>
<tr>
<td>Alere INRatio2</td>
<td>Electrical Impedance</td>
<td>Look up table based on current change</td>
</tr>
<tr>
<td>STA Compact system with Dade® Innovin®</td>
<td>Viscosity based detection</td>
<td>Look up table based on steel ball movement</td>
</tr>
</tbody>
</table>

### Results

The statistical methodology for comparing the INR results obtained with the different methods included determination of the mean, standard deviation (SD), orthogonal regression analysis, and the plot of the average value of a pair of measurements versus their difference using the Bland-Altman method. When the new Coag-Sense system is compared against the INRatio2, the STA Compact, and itself using venous whole blood sample instead of capillary whole blood, in all cases a good correlation is observed as shown in Table 1.

An “r” value (correlation coefficient) of greater than 0.90 is generally recommended as acceptable. A difference in the slope value from 1.0 is expected when comparing methodologies using reagents with different ISI values. The y-intercept in the linear regression defines the elevation of the trend line.

The lower slope value with INRatio2 suggests that it is biased higher when compared to the Coag-Sense system. This is confirmed in the Bland Altman graph shown in figure 1 below. The mean difference between results obtained in this study was of 0.4 INR units. The Bland Altman plot is useful in showing how well two different testing methods agree with each other and also indicates where in the INR range a bias may be occurring. The regression analysis in figure 2 below shows good correlation between the Coag-Sense and INRatio2 systems.

![INRatio2 vs. Coag-Sense](image1)

**Table 1:** Orthogonal regression analysis of Coag-Sense PT/INR system average fingerstick INR results compared with INR results from the INRatio2 (fingerstick) and the STA Compact (plasma).

![INRatio2 vs. Coag-Sense](image2)
Comparison between point-of-care and plasma-based lab PT/INR systems

Figures 3-4 below are Bland-Altman plots comparing the whole blood first finger stick INR values from the point-of-care systems with the plasma INR values from Diagnostica STAGO STA Compact laboratory system. The Alere INRatio2 system showed a slightly higher bias when compared with the STA Compact system which was not the case with Coag-Sense system. The mean difference between results obtained on INRatio2 and STA Compact was of 0.7 INR units, with INRatio reading higher evident in the waterfall-like spread of data points. The mean difference between results obtained on Coag-Sense and STA Compact was 0.2 INR units, with Coag-Sense reading slightly higher than the STA Compact lab system.

Fig. 3: Bland-Altman bias plot of STA compact average INR results compared with the first fingerstick INR result from the INRatio2 system. A test strip failure reduced the sample size to 19.

Fig. 4: Bland-Altman bias plot of STA compact average INR results compared with the first fingerstick INR result from the Coag-Sense system.

Duplicate Measurement Variability Graph (Precision)

Two separate finger sticks were performed and the capillary whole blood samples were tested to obtain duplicate INR results on both of the point-of-care PT/INR systems. Figure 5 below is a variability plot showing how the first duplicate sample compared to the second duplicate sample for each subject on each of PT/INR system. The Alere INRatio2 device demonstrated significantly greater duplicate measurement (precision) variability than the Coag-Sense system. This variability appears inline with the INRatio2’s package insert which claims precision performance of 10.9% CV compared to Coag-Sense’s claim of 2.53% CV.

Figure 5: Anticoagulated patient first and second fingerstick INR standard deviation plot. This graphic representation illustrates the precision of the two point-of-care systems when performing duplicate fingerstick measurements. A test strip failure was encountered with the INRatio2 system during testing of patient CSI08; therefore a duplicate INR result was not available for that patient.
Discussion
The comparisons presented in this study show strong performance results for the Coag-Sense system relative to Alere INRatio2 as well as to the Diagnostica Stago STA Compact laboratory system. The study also shows that the Coag-Sense system compares well against itself when performing duplicate measurements or whether using venous or capillary whole blood sample types.

REFERENCES