**Supplemental Material**

*Abnormal and Contrived Samples*

The study population included 12 samples obtained from clinical patients with an abnormal coagulation profile as well as samples obtained from 18 normal volunteers whose samples were artificially contrived (2 different types of contrived samples per normal volunteer). The characteristics and preparations steps for these samples are described in Tables S1 and S2, respectively.

Table S1. Abnormal clinical samples.

| **Sample Type** | **Characteristics** | **Sample Description** |
| --- | --- | --- |
| Low platelet, normal fibrinogen | Moderately reduced PCS | Citrated whole blood from donor with platelet count= 119,000/uL and fibrinogen=388 mg/dL |
| High fibrinogen, high platelet | Greatly increased CS, PCS and FCS | Citrated whole blood from donor with fibrinogen=695 mg/dL and platelet count= 836,000/uL |
| High fibrinogen, high platelet | Greatly increased CS, PCS and FCS | Citrated whole blood from donor with fibrinogen=779 mg/dL and platelet count= 626,000/uL |
| Low platelet | Moderately increased PCS | Citrated whole blood from donor with platelet count= 37,000/uL |
| High platelet | Increased CS and PCS | Citrated whole blood from donor with platelet count= 567,000/uL |
| High platelet, moderately low fibrinogen | Increased CS and PCS | Citrated whole blood from donor with platelet count= 825,000/uL, fibrinogen=256 mg/dL |
| Low platelet | Greatly reduced CS and PCS | Citrated whole blood from donor with platelet count= 57,000/uL |
| Low platelet | Greatly reduced CS and PCS | Citrated whole blood from donor with platelet count= 10,000/uL |
| High platelet | Increased CS and PCS | Citrated whole blood from donor with platelet count= 587,000/uL |
| High platelet | Greatly increased CS and PCS | Citrated whole blood from donor with platelet count= 1,194,000/uL |
| High fibrinogen, low platelet | Increased FCS, reduced PCS | Citrated whole blood from donor with fibrinogen=611 mg/dL with platelet count= 42,000/uL |
| Low platelet | Greatly decreased CS and PCS | Citrated whole blood from donor with platelet count= 51,000/uL |

Table S2. Artificially contrived samples.

|  |  |  |  |
| --- | --- | --- | --- |
| **Number of samples** | **Samples Type** | **Characteristics** | **Samples Preparation** |
| 18 | High fibrinogen concentration | Increased CS and FCS values | Purified fibrinogen added to the native blood samples to achieve final concentrations of ~ 1,000 mg/dl |
| 12 | Low fibrinogen concentration | Reduced FCS; moderately reduced CT and CTH | The plasma component of the whole blood sample was replaced with a titration of fibrinogen-depleted and normal plasma to obtained final fibrinogen concentration below 100 mg/dl |
| 6 | FVIII deficiency | Increased CT and CTH | The plasma component of the whole blood sample was replaced with FVIII deficient plasma to achieve clot times greater than 250 sec |

*CCIs Analysis*

A series of clinical composite indexes (CCIs) were developed to describe the coagulation status of the patient on the basis of routine laboratory test results. Each QPlus parameter has a corresponding CCI, except for CTH (Heparinase Clot Time) as the information provided by this parameter is included in the combination of CT and CTR.

The definitions developed for each CCI, which are summarized in Table S3, incorporate the results of the aPTT, PT/INR, activated clotting time (ACT), fibrinogen level, and platelet count assays, as well as the presence of heparin. For each of the routine coagulation tests comprising the CCIs, specific thresholds were established to allow the classification of a sample into one of three categories:

* *High (H)* – representative of increased coagulation function
* *Low (L)* – representative of decreased coagulation function
* *Not Low and Not High (NL-NH)* – coagulation function within normal and subclinical ranges

The thresholds proposed for these characterizations are based on scientific and clinical literature, guidelines from the American and European Societies of Anesthesiologists, consultations with multiple physicians, and prior studies comparing results from the Quantra System to the conventional coagulation assays.

However, it is important to recognize that the clinical composite indexes are a limited and imperfect approximation since they represented a laboratory-centric definition of the clinical coagulation status of perioperative samples. For example, the laboratory-based assays are based on platelet poor plasma and do not provide information about the cross-functional interactions between plasmatic and cellular components.

Table S3. Clinical Composite Indexes (CCIs) Definitions

| **CCI#** | **QPlus Test Result** | **Clinical Composite Indexes Definition** | | |
| --- | --- | --- | --- | --- |
| **Not Low/Not High**: Coagulation function within normal and subclinical ranges | **Low**:  Decrease in coagulation functions. Increased risk of bleeding | **High**:  Increase in coagulation function. Increased risk of thrombosis |
| **CCI1** | **Clot Time** | * If not Low and not High | * aPTT>55 sec   **OR**   * On heparin and ACT>140 sec | * aPTT≤10% below the lower bound of the local reference range **AND** INR≤1.2 |
| **CCI2** | **Clot Stiffness** | * If not Low and not High | * Fibrinogen <125 mg/dl   **OR**   * Platelet count <75,000/ul | * Fibrinogen > 500 mg/dl   **OR**   * Platelet count > normal range   **OR**   * Fibrinogen > 350 mg/dl **AND** Platelets > 300,000/ul |
| **CCI3** | **Fibrinogen Contribution** | * If not Low and not High | * Fibrinogen <125 mg/dl | * Fibrinogen > 500 mg/dl |
| **CCI4** | **Platelet Contribution** (calculated as Clot Stiffness – Fibrinogen Contribution) | * If not Low and not High | * Fibrinogen <125 mg/dl   **OR**   * Platelet count <75,000/ul | * Fibrinogen > 350 mg/dl **AND** Platelets > 300,000/ul   **OR**   * Fibrinogen > 400 mg/dl **AND** Platelets > 250,000/ul |
| **CCI5** | **Clot Time** **Ratio** (calculated as Clot Time / Heparinase Clot Time) | If not Low | If two or more are true:   * Heparin presence * Prolonged ACT * Prolonged aPTT | N/A |

The concordance analysis was performed as shown in the 3 x 3 confusion matrix below for each CCI vs QPlus parameter. The QPlus parameters were assigned Low, Not-Low/Not-High, or High values based on the respective reference ranges.

Table S4. Overall Clinical Concordance Analysis for each CCI – QPlus parameter

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **CCI** | | |  |
|  |  | **Low\*** | **Not Low / Not High\*** | **High\*** | **Total** |
| **QPlus** | **Low\*\*** | A | D | G | QL |
| **Not Low / Not High \*\*** | B | E | H | QNLNH |
| **High\*\*** | C | F | I | QH |
|  | **Total** | TL |  | TH | N |

\*Classification based on the CCI  
 \*\* Classification based on Quantra reference ranges

Overall, Low, Not Low / Not High, and High agreement will be calculated as follows:

Table S5 summarizes the overall agreement between each QPlus parameter and the corresponding CCIs as well as the agreement in each subcategory. This table shows the point estimates of the agreements along with the 95% confidence intervals. The squared brackets indicate the actual number of occurrences in each category. The overall agreement via the weighted kappa coefficient of the classification order [Low, Not Low – Not High, High] is also included to account for change agreement.

Table S5. Concordance Analysis Results

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **QPlus Parameter vs Clinical Composite Index** | **Overall Agreement (95% CI)** | **Low Agreement (95% CI)** | **Not Low – Not High Agreement (95% CI)** | **High Agreement (95% CI)** | **Weighted Kappa Coefficient\* (95% CI)** |
| **Clot Time (CT) vs CCI1** | 0.72  (0.69, 0.75)  [605/840] | 0.98  (0.96, 0.99)  [183/187] | 0.62  (0.58, 0.66)  [376/603] | 0.92  (0.83, 0.98)  [46/50] | 0.59  (0.55, 0.63) |
| **Clot Stiffness (CS) vs CCI2** | 0.80  (0.77, 0.84)  [670/833] | 0.80  (0.66, 0.91)  [39/49] | 0.81  (0.77, 0.85)  [585/721] | 0.73  (0.60, 0.85)  [46/63] | 0.46  (0.4, 0.53) |
| **Fibrinogen Contribution (FCS) vs CCI3** | 0.85  (0.82, 0.89)  [710/833] | 0.80  (0.63, 0.95)  [20/25] | 0.85  (0.81, 0.88)  [641/758] | 0.98  (0.93, 1.0)  [49/50] | 0.49  (0.42, 0.56) |
| **Platelet Contribution (PCS) vs CCI4** | 0.80  (0.77, 0.84)  [661/824] | 0.88  (0.76, 0.96)  [42/48] | 0.80  (0.77, 0.84)  [590/734] | 0.69  (0.50, 0.86)  [29/42] | 0.42  (0.35, 0.49) |
| **Clot Time Ratio (CTR) vs CCI5** | 0.98  (0.97, 0.99)  [821/838] | 0.94  (0.90, 0.98)  [156/166] | 0.99  (0.98, 1.0)  [665/672] | N/A | 0.94  (0.91, 0.97) |

The number in parentheses represent the 95% confidence intervals

The number is squared brackets represent the number of occurrences in each category

\*Cicchetti-Allison weighting