When analyzed separately, data from studies provide only limited information with limited clinical generalizability, due to sometime to small sample size, or differing assessments, or limited scope.

Using a theoretical framework for performing meta-analysis of Bio Scan data obtained from disparate studies allows a calibration of the data from such studies and tests into a unified probability scale which can be used in screening score.

We apply the methods of Monastra et al. (1999) and Robeva et al., 2004 to combine the data from studies examining the diagnostic abilities of different diseases including diabetes, insulin resistance, metabolic syndrome, thyroid dysfunction, hepatitis, prostate cancer, major depression, ADHD children, dyslipidemia, coronary heart diseases, heart failure, kidney disorders, digestive disorders, and carotid atherosclerosis.

Each individual study results was statistically analyzed to detect statistically significant differences and provide a screening score for each one.

The used technologies to screen the above diseases were:

- The Bioimpedance at low frequencies in bipolar mode
- The bioimpedance at 50 KHz in tetrapolar mode
- The Heart Rate Variability analysis
- The Digital pulse Analysis (Photoelectrical plethysmography)
- And the SPo2 % measurement

We conclude that if data from various studies using various tests are made comparable the resulting combined sample size and the increased diversity of the combined sample lead to increased significance of the statistical tests and allow for cross-sectional comparisons which are not possible within each individual study.

Standardizing the Scores of Different Tests

In order to integrate the various study data from tests and the statistical results into a single assessment for each disease, we first need to standardize the output of these tests. In order to do so, we convert the output of each test into a probability for each disease.

Heuristically, justification of this paradigm would be the following: any test, for each disease, produces a score that is contingent upon certain characteristics. Therefore, a subject with a certain condition is expected to yield a lower score compared to a subject without that condition. Thus, a conditional probability of earning certain score, given a preexisting condition, which is a number between 1 and 6 (or 0 to 100%),

During each step of the overall disease assessment, each study receives a certain test score according to the specificity and sensitivity analysis, as well as on the severity of the disease.

In other words, the probability of earning a certain score depends on the study' condition.

In addition, each study has a suggested cutoff value, and these cutoff values are accepted for the calculation of the screening. Thus, for each test we can define indicator that represents the conditional probability of earning the specified score.

As in (Robeva et al., 2004), we use a linear mapping of a test score into a probability ranging from 1 to 6 with the test cutoff value mapped to 4, and the test minimal value indicating the

screening mapped to 1. Published diagnostic thresholds or cut-offs are used to produce the piecewise linear and continuous shape for the function. Figure 1 presents two examples of these mappings, where the X axis is the scoring cut-offs for the specified assessment, and the Y axis is the probability of disease (0–100%).

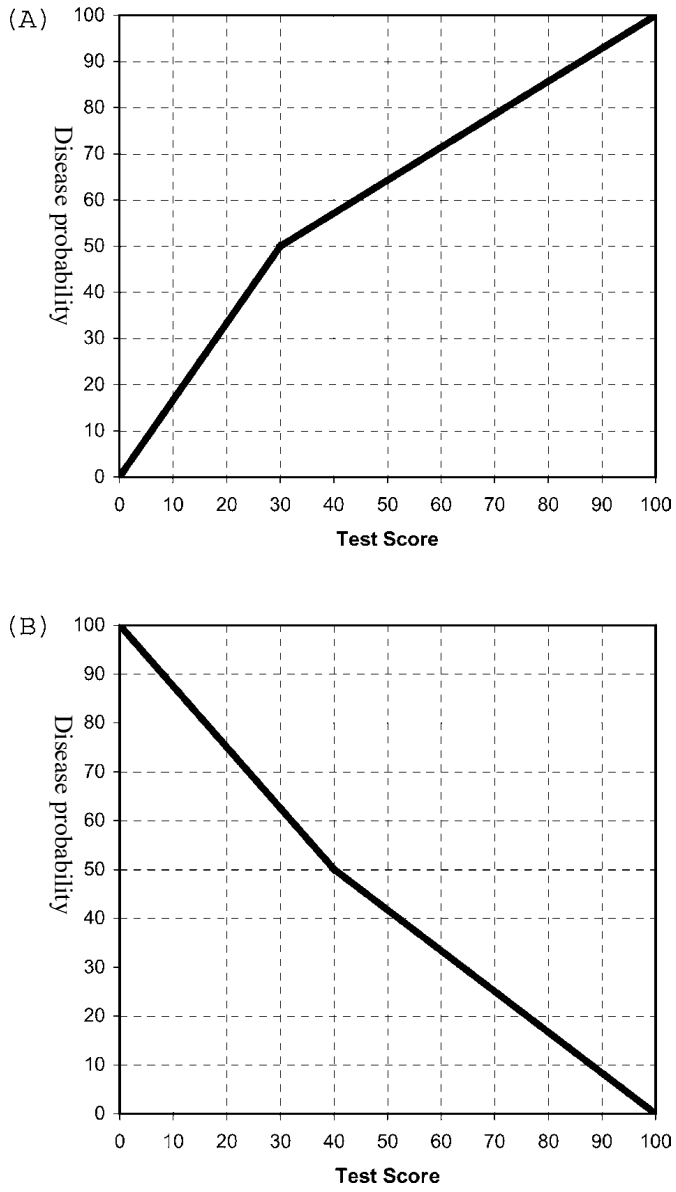

Fig.1

The computing of the conditional probabilities of Fig. 1 is carried out as follows:

1) Disease diagnostic by conventional methods: The score on the disease-SI ranges from 0 to 36 with scores >12 indicating the disease. The mapping formula is then:

$$\begin{cases} x \le 12 & P(\text{disease} \mid x) = \dfrac{x}{24} \\ x \ge 12 & P(\text{disease} \mid x) = \dfrac{x}{48} + \dfrac{1}{4} \end{cases}$$

2) Disease screening: The score ranges from 0 to 100 with scores (>93 indicating disease). The mapping formula is then:

$$\begin{cases} x \le 93 & P(\text{disease} \mid x) = \dfrac{x}{186} \\ x \ge 93 & P(\text{disease} \mid x) = \dfrac{x}{14} - \dfrac{43}{7} \end{cases}$$

3) The Test Consistency Index (CI) based upon p value: The Consistency Index ranges from 0 to 100% with a CI < 40% indicating disease .The mapping formula is then:

$$\begin{cases} x \le 40 & P(\text{disease} \mid x) = 1 - \dfrac{x}{80} \\ x \ge 40 & P(\text{disease} \mid x) = \dfrac{5}{6} - \dfrac{x}{120} \end{cases}$$

Once the standardization of measures is completed, a Bayesian algorithm for calculating the combined probability for disease for each study is provided. We present an outline for the algorithm below. Additional details can be found in Robeva et al., 2004. The algorithm works as follows: At step 0, probability for disease $P^0_{\text{disease}} = 0$ is assigned to each study regardless of the cut off. Then, $P^{\text{test}}_1 = \text{P}$ is assigned to each study regardless of the cut off and $P^{\text{test}}_2 = 1 - \text{P1}$ are used to calculate a posterior probability P^1_{disease} for disease, using the formula:

$$P^1_{\text{disease}} = \frac{P^{\text{test}}_1 \, P^0_{\text{disease}}}{P^{\text{test}}_1 \, P^0_{\text{disease}} + P^{\text{test}}_2 \left(1 - P^0_{\text{disease}}\right)}$$

Disease Assessment

From here on the procedure is recursive - after each step the posterior probability becomes a prior probability for the next step; for example in the formula above P^{0}_{disease} is replaced by P^{1}_{disease}, P^{test}_{1} and P^{test}_{2} derived from the second test, and so forth. In general, the posterior probability from step (n−1) becomes a prior probability in step (n) and then posterior probability is computed for step (n) using the results from the assessment at step (n). At each step we may have a "gray zone" of a non definitive assessment, however, at each sequential step the gray zone will become smaller and the final result is an assessment that is substantially more precise than any of its individual steps. The final outcome of the Bayesian algorithms is a combined probability for disease assigned to each study (0 to 100%), for example a placement of each study on a continuum of disruption, with greater number and severity of disruptions resulting in placement on the high extreme end of the continuum. Since the final outcome is based upon the combination of all of the diagnostic, it has increased specificity/sensitivity beyond any single measure.

Statistical Analysis

Roc curves were used to compare the probabilities for disease/no disease, estimated by each tests, across the disease versus No disease groups.