Can MSPC techniques characterize healthy humans? Diagnosing inborn errors of metabolism

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Introduction

Identification of complex diseases is often based on (multivariate) statistical techniques. Commonly, the starting point of such models is a particular disease, and e.g. discriminant analysis is used to distinguish healthy and diseased individuals. Such approaches, however, may not be useful in practice due to the large number of (un)known diseases with possibly low incidence that have to be considered.

Goal: develop a general tool for diagnosis of (rare) diseases.

Method and Results

1 Disease identification

- Multivariate statistical process control (MSPC) [1] was used to separate healthy and diseased individuals [4].

![Diagram of MSPC showing three types of outliers.](image)

- Urine NMR data of 60 healthy and 42 “non-healthy” children was used for validation.

![Q-statistic chart with 99% confidence limit; the dots represent the validation samples.](image)

- A sensitivity and specificity of 94.6 and 95.2% were obtained, respectively.

2 Disease diagnosis

- Complete decomposition (CDC) of the Q-statistic [2] was used to identify the deviation from NOC leading to detailed diagnosis [4].

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\[ \text{CDC}: Q = \sum_{i=1}^{\text{NOC}} Q_i = \sum_{i=1}^{\text{NOC}} e_i^2 = \text{CDC}_i = e_i^2 \]
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- Relative contribution: \( e_i^2 / \text{UCL}_i \)

![Relative contribution of each process variable to Q-statistic for one patient.](image)

- Visualisation into the original NMR data allows for incorporation of the proposed method into current clinical practice. In this case Alkaptonuria was diagnosed.

![Diagram of Alkaptonuria process.](image)

- Correct detection of more complex disease signatures requires more sophisticated decomposition methods.

Conclusions / Outlook

- Application of process control strategies is very valuable for disease identification.
- Correct identification of a multitude of diseases at the same time was demonstrated.
- Variable decomposition allows for correct diagnosis of some diseases.
- The method potentially allows for a personalized health approach by establishing NOC for each individual.