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CARDIOVASCULAR DISEASE

Metabonomics reveals blocked pipes

For those of us who don't like needles, there may be some comfort in the work published in the December issue of *Nature Medicine*. A non-invasive technique known as metabonomics allows the rapid diagnosis of the presence and severity of arterial blockages in coronary heart disease (CHD), according to researchers from Imperial College, London, Cambridge University and GlaxoSmithKline.

CHD is an important cause of mortality and morbidity in developed countries, and although risk factors for CHD have been identified, they cannot diagnose the presence of the disease on an individual basis. Currently, the gold standard for CHD diagnosis is angiography, which requires the insertion of a catheter into an artery, the injection of a contrast agent and an X-ray of the area to reveal the location and severity of any arterial blockages. Metabonomics — a nuclear magnetic resonance (NMR)-based system — exploits changes in low-molecular-weight metabolites in biofluids, such as urine or blood serum, in healthy compared with diseased states.

The researchers applied pattern-recognition techniques to NMR spectra of serum taken from both healthy individuals and from those with severe CHD, as characterized by angiography. Visual inspection of the spectra from the two groups revealed

few systematic differences. However, after reducing the complexity of the NMR data and performing principal components analysis and partial least squares-discriminant analysis, clustering within each group became evident. A further analysis using orthogonal signal correction considerably improved the separation achieved between the healthy and CHD groups.

But is the model predictive? The study showed that it is possible to predict the arterial status of unknown samples, using just over 50 healthy and diseased individuals to set the standards. Furthermore, another statistical analysis was able to distinguish the severity of CHD present, indicating stenosis of one, two or three major coronary arteries.

One of the benefits of this type of analysis is that understanding the underlying complex molecular differences associated with CHD is not necessary to be able to correctly classify patients with high sensitivity and specificity. This assay, alongside angiography, would be a relatively cheap and noninvasive addition to the diagnostic toolkit for CHD, potentially allowing widespread population screening and targeting of those most in need of treatment with drugs such as statins. Unfortunately, for the needle-shy, a blood sample would still be required!

Melanie Brazil

References and links

ORIGINAL RESEARCH PAPER Brindle, J. T. *et al.* Rapid and noninvasive diagnosis of the presence and severity of coronary heart disease using ¹H-NMR-based metabonomics. *Nature Med.* **8**, 1439–1444 (2002)

FURTHER READING Nicholson, J. K., Connelly, J., Lindon, J. C. & Holmes, E. Metabonomics: a platform for studying drug toxicity and gene function. *Nature Rev. Drug Discov.* **1**, 153–161 (2002)

WEB SITE

MaGiCAD, a large on-going trial which is testing the use of this new diagnostic technology in the clinic. <http://www.magicad.org.uk>