

PLENARY

ISOTOPE RATIO MASS SPECTROMETRY IN MEDICAL RESEARCH AND DIAGNOSIS

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From the early days following their discovery, the light gas stable isotopes have been applied to biomedical applications. Von Hevsey¹ exploited deuterium to measure total body water very soon after supplies of heavy water became available. The Neir-type gas source isotope ratio MS was introduced and, once these isotopes had been isolated and suitable tracer materials synthesised, Shoenheimer, Rittenberg and co-workers^{2, 3} exploited ²H and ¹⁵N in pioneering metabolic research. Stable isotope applications continued to be developed in a select group of research laboratories^{4, 5} with the greater emphasis being on the use of GCMS to measure relatively high enrichment stable isotope labelled metabolites⁶. However, it has been the introduction of automated on-line sample preparation systems, principally continuous-flow isotope ratio mass spectrometry^{7, 8}, that has facilitated much wider use of IRMS in medical research and diagnosis. Applications of stable isotope tracers and IRMS now span a very wide range of research. The most obvious example of diagnostic use of stable isotopes is in non-invasive ¹³C-breath tests, such as the urea breath test for *Helicobacter pylori* infection^{9, 10}. Future developments of stable isotope applications and IRMS are likely to be in the following areas:

- a) Nutritional assessment (total body water); energy expenditure (doubly-labelled water); non-invasive breath and urine tests of organ function
- b) Extending compound-specific isotope analysis for medical use: glucose homeostasis; availability of essential nutrients; interpretation of ¹⁵N natural abundance in terms of nitrogen 'stress'
- c) Developing applications of LC-IRMS: underivatized molecules (e.g., amino acids); extension to high molecular compounds (proteins, nucleotides); other tracers besides ¹³C (e.g., ¹⁵N)

IRMS will continue to have an important niche as it has excellent sensitivity for detecting low tracer enrichment, but organic MS techniques will be used in parallel as, unlike IRMS, they permit isotopologue analysis. As conversion systems to produce simple gases from key organic molecules separated on-line become ever more sophisticated, the greatest limitation yet to be overcome in IRMS is the poor efficiency of the electronic impact ionisation source.

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