Modern Clinical Analysis and Mass Spectrometry

Rogatsky E*
Biomarker Analytical Resource Core Laboratory, Einstein-Montefiore Institute for Clinical and Translational Research, Albert Einstein College of Medicine, Bronx, NY 10461, USA

Clinical analysis has a long tradition in science. First attempts to analyze human specimens for diagnostic purposes were conducted in ancient times. Pregnancy testing for example, it was assayed by adding urine into a vessel with fish. Progesterone, the main hormone of pregnancy, is absorbed by fish, causing aggressive behavior, providing a positive test.

Today main methodologies in clinical assay are UV-based enzymatic/chemical reactions and immunoassays. Modern clinical chemistry offers thousands of clinical assays, which can be conducted rapidly, simply and inexpensively. Disadvantages of these methodologies are a lack of calibration (many assays calibration curves are constructed with only 2-4 points); poor accuracy (for immunoassays of small molecules, error can easily be 50%, and up several fold for peptides/proteins). As result, there may be poor agreement between measurements of the same sample in different laboratories. Another disadvantage of immunoassays is their poor selectivity caused by cross reactivity of antibodies to various analytes with similar chemistry, which is a permanent source of false-positive results. Alternatively, human anti-mouse antibodies can result in false high or low levels. Implementation of mass spectrometry in the field of clinical analysis has greatly improved specificity, sensitivity, minimizes errors and increased accuracy and precision.

Mass spectrometry is a relatively young field of science. The first publication of J.J. Thomson in 1913, "Rays of Positive Electricity", discussed formation of positively charged ions (a precursor advance, leading in the future to mass spectrometry as a science and technology). The American Society for Mass Spectrometry (ASMS) was organized in 1969. For many decades Gas Chromatography with electron impact ionization (GC/MS) was the main mass spectrometry tool for environmental, forensic and clinical analysis. Liquid chromatography-electrospray ionization mass spectrometry (LC/MS) was introduced in 1980s, however sensitive triple quadrupole mass spectrometers LC/MS/MS, equipped with robust and efficient for dirty clinical samples electrospray ionization source, become available about 10-15 years ago. Recent advances (from 2000) in liquid chromatography have dramatically moved the field forward: design of fully spherical stationary phase particles, reduction of the particle size to 3um and next development of sub-2 um particle size and fused core stationary phases along with instrumental advancement in chromatography and mass spectrometry hardware have lead to constant progress in LC-MS methodologies and new applications in drug development and discovery, biochemistry, chemistry and clinical analysis. At the 2004 annual ASMS meeting (Nashville, TN) the number of attendees reached 6000, demonstrating the dramatic world wide growth of the field of mass spectrometry. Liquid chromatography interfaced with triple quadrupole mass spectrometry has become the workhorse of modern analytical chemistry and steady substitute for GC/MS.

The progress of mass spectrometry for clinical analysis can be described in the following facts: at the American Association for Clinical Chemistry meeting in July 2008 (Washington DC), only Applied Biosystems /MDS SCIEX had a booth at the expo out of all the mass spectrometry vendors. At the last AACC meeting in 2013 (Houston, TX), most of the mass spectrometry and robotics vendors were represented. Also in 2008, the first meeting of Mass Spectrometry Applications in Clinical Lab (MSACL) took place in San Diego (CA, USA). The aim of this conference was to provide a forum for discussion clinical applications of mass spectrometry by bringing together academic and industrial experts in the field with those driven to explore and understand more about the potential application and benefits. The mission of MSACL is to accelerate the implementation of mass spectrometry in the clinical laboratory, improve patient standard-of-care, and reduce health care costs (according to their web site msacl.org). At the first meeting, 270 attendees and 10 vendors participated. At the 2013 meeting, there were 771 attendees, 40 vendors, 68 podium presentations and 237 posters. The attendance for 2014 USA meeting was already 861 participants; the growing interest in clinical mass spectrometry has lead to the organization of a similar event in Europe (Salzburg, Austria, September 2-5, 2014).

Progress in clinical mass spectrometry is based on simultaneous advancements and detailed understanding of sample preparation and expertise in chromatography and mass spectrometry. While the future is bright for mass spectrometry in clinical analysis, higher equipment costs, a long learning curve and staff training requirements has slowed its widespread adoption, but continued progress can be anticipated.