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Expanding the LC-MS/MS toolbox

Unlocking its full potential

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LC-MS/MS is a powerful analytical technique that, despite its potential to enhance patient care, has yet to be widely adopted by clinical laboratories. Here, Senior Biomedical Scientists from the Cardiff and Vale University Health Board share their experiences of LC-MS/MS, and discuss how a standardized and automated system with a broad and expandable testing menu could finally bring the technology to the forefront of clinical diagnostic testing.

Background information

Liquid chromatography linked to tandem mass spectrometry (LC-MS/MS) is an analytical tool that combines mass analysis by mass spectrometry with the physical separation capabilities of liquid chromatography, enabling the powerful separation, detection and identification of molecules in complex mixtures. Consequently, LC-MS/MS is a valuable technique in laboratory testing.

In particular, more recent technological advancements have enhanced the proficiency of LC-MS/MS systems, opening the door to a range of clinical applications with the potential to transform patient care. However, adoption among laboratories has been surprisingly slow due to a number of challenges associated with current LC-MS/MS technology.

We discussed these challenges with a team of Senior Biomedical Scientists from the Cardiff and Vale University Health Board. Gareth Jones, Paul Bramhall and Luke Griffiths speak from many years of experience on the importance and challenges of LC-MS/MS, and how a standardized and automated system with a broad and expandable testing menu could help to unlock the full potential of LC-MS/MS as a diagnostic tool.

Case Study: Cardiff and Vale University Health Board

The Cardiff and Vale University Health Board is one of the largest laboratories in Europe, providing diagnostic testing services for healthcare institutions across Wales. The laboratory operates six LC-MS/MS systems across several main specialisms all under one roof, including endocrinology, toxicology, metabolic and newborn screening.

The team emphasizes how important LC-MS/MS is in their laboratory. As a forward-looking facility, they are keen to provide the best service possible, so the quality of the tests they perform is paramount.

"Our major driving force has always been quality – and we view LC-MS/MS systems as the gold standard for this purpose," says Paul Bramhall.

Despite recognizing the benefits of LC-MS/MS systems and their importance in running powerful diagnostic analyses, the team acknowledges that their laboratory doesn't take full advantage of the functionality of their LC-MS/MS equipment. As with many other laboratories worldwide, this slow adoption of LC-MS/MS systems for diagnostic applications is due to several challenges presented by the LC-MS/MS technology that is currently available.

What are the barriers to LC-MS/MS adoption?

The team talks enthusiastically about potentially moving more of their testing over to the LC-MS/MS systems, including the screening of urine and serum samples for anti-epileptic drugs, anti-microbials and full steroid profiles, as well as using LC-MS/MS to develop and validate useful assays for a greater range of diagnostic tests. Although the current equipment in the laboratory can perform many of these functions, there just aren't enough staff trained to use it for these purposes. This is a particular problem for the out-of-hours service.

"Out of approximately 60 members of staff, only about half a dozen actually know how to run the LC-MS/MS systems because it's still a very specialist technique," explains Gareth Jones. "In such a big laboratory, with so many tests and LC-MS/MS systems, this is nowhere near enough trained personnel."

Based on the current configuration of their LC/MS-MS systems, the team believes they are not as cost-effective or efficient as they could be. Primarily, this is because the systems involve multiple, complex manual steps, including sample acquisition and preparation.

In addition, tests are often performed separately, such as when confirming the result from an immunoassay-based test or when a full steroid profile is requested. Jones, an endocrinology specialist, comments that obtaining a full steroid profile on LC-MS/MS systems following local protocols currently involves running multiple separate tests, which can take up to three to four days. "On one day, we would run androstrenedione, on another day we would run testosterone, and on the following day it would be 17-hydroxyprogesterone. But, if all these tests could be run on one instrument simultaneously, we could get the full picture much more quickly," he says.

The team points out that the limited menu of their current LC-MS/MS systems doesn't help matters either, because it makes it more time consuming for the laboratory to develop, review and validate new assays, and run a wider variety of tests.

Like in many similar laboratories around the world, such challenges are preventing the full potential of LC-MS/MS from being implemented as a powerful diagnostic tool. Instead, automated immunoassay-based methods are often used, which can provide healthcare facilities and their patients with potentially less reliable diagnostic test results.

LC-MS/MS versus immunoassay systems

The Cardiff team talks about using immunoassay-based tests for therapeutic drug monitoring (TDM), such as for immunosuppressant drugs. Yet, they admit they would much rather use LC-MS/MS for these tests, to benefit from improved accuracy and reliability of results.

The team describes the multiple advantages of using LC-MS/MS systems for TDM. "LC-MS/MS systems are much more specific than immunoassays, which can be subject to interference," Jones says. Additionally, LC-MS/MS systems provide a much quicker turnaround time. "Some LC-MS/MS-based tests take just two minutes compared to the 40 minutes needed to run an immunoassay-based test," explains Luke Griffiths.

Another time-related issue is that immunoassay-based tests tend to be developed in a kit form and require FDA approval, so laboratories may experience extensive wait periods before the kits become available for use. “We’ve been waiting for two years for one immunoassay kit to come out, says Bramhall. “Instead, you could run the test immediately after completing validation and verification on an LC-MS/MS system.”

In addition to improved quality and quicker turnaround time, cost is another reason why the team views LC-MS/MS systems so favorably. “After the initial investment, the operating costs of LC-MS/MS systems are much lower than immunoassay-based tests,” says Jones.

Therefore, if the team could perform TDM and other tests on LC-MS/MS systems rather than using immunoassay-based analyses, they could produce more specific test results quicker with potential cost reductions, making the operation of their laboratory more cost-effective, efficient and productive. However, the limitations of current LC-MS/MS systems need to be resolved before this can be a reality.

The benefits of a broad and expandable testing menu

For the Cardiff team, enhancing current LC-MS/MS systems would ideally mean having a standardized and automated system with a broad and expandable testing menu. This would reduce system maintenance and the specialist knowledge needed to effectively use LC-MS/MS systems. Additionally, such a system would reduce sample preparation and other manual processes to improve turnaround times, and give labs the ability to routinely perform multiple tests and develop assays on one machine to heighten efficiency and increase productivity.

Having a broad and expandable LC-MS/MS testing menu is at the top of the Cardiff team’s wish list, because it would have a huge impact on the quality of the lab’s test results. Additionally, depending on how much the menu could be expanded, a wider variety of tests (e.g. TDM, full steroid profiles, urine testing) could be performed on such an LC-MS/MS system compared to what is possible now. Consequently, these improvements could translate to better patient care.

> “It’s absolutely vital to have a broad and expandable testing menu for our type of lab. We need an open system we can add to, so we can increase the number of tests we run, as well as manage the testing already being done to ensure we get the most reliable results possible,” says Bramhall.

It is also important to the team that any new LC-MS/MS system will increase their ability to develop and validate new assays (laboratory-developed tests or LDTs), as well as help to standardize them across different laboratories. “Regulatory certification has become essential. A readymade system with FDA approval and CE marked with traceability would benefit any laboratory introducing LC-MS/MS,” says Jones.

The broader impact of an enhanced LC-MS/MS system

The Cardiff team says that an automated system would be as simple to set-up as any other automated instrument, even if the laboratory had no prior experience of LDTs. Moreover, LDT-experienced laboratories, like the one in Cardiff, would also benefit from the additional time they would gain from running automated tests; time they could invest in more cutting-edge R&D and troubleshooting.

A ‘plug-and-play’ set-up would be suitable for clinical laboratories of all sizes – lending itself to both centralized and localized approaches to testing. Thus, diagnostic tests could be performed in a much more efficient way, improving testing turnaround times and, ultimately, patient care.

> “We’ve understood the value of our LC-MS/MS systems for a long time, but the challenge is how we optimize testing with the resources we have,” says Griffiths.

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Conclusion

Powerful LC-MS/MS systems are fast emerging as the first-choice tool for diagnostic testing in laboratories worldwide. However, their adoption is not as prevalent as their technological prowess suggests, possibly due to a number of problems associated with their implementation. We spoke about these challenges with a team of three Senior Biomedical Scientists, Luke Griffiths, Paul Bramhall and Gareth Jones, who work in one of the biggest laboratories in Europe, at the Cardiff and Vale University Health Board.

One of the key messages that arose from the discussion was that laboratories do not have enough staff trained in the specialist technicalities of current LC-MS/MS systems, meaning that they cannot perform as wide a variety of tests as they would like, and struggle to find the time to develop their own assays. The multiple, complex manual stages prevent them from being cost-effective or efficient. Instead, much to the team's frustration, they must rely on immunoassay-based analyses for a number of tests, like immunosuppressant drug monitoring, for which LC-MS/MS systems would give higher quality results.

The Cardiff team says that enhancing current LC-MS/MS systems – so that they are standardized and automated, with a broad and expandable testing menu – could solve many of these problems. The proposed technology would enable considerable time savings and reduce the need for training and specialization, allowing laboratories to operate more cost-effectively and efficiently. Most importantly, these improvements could translate to better patient care through quicker results based on the most reliable methods.

Thermo Fisher Scientific has a vision to make such a system a reality. By listening to and understanding the needs of laboratories currently struggling to implement LC-MS/MS systems, we envisage a standardized, automated LC-MS/MS system with a broad and expandable menu that resolves the challenges presented by current technology. Additionally, we believe in providing long-term support to laboratory personnel through comprehensive after-sales care. As such, we are poised to usher in a new era of diagnostic testing and, ultimately, assist in the transformation of patient care.

Find out more at **thermofisher.com/imagine**

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