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Preliminary evaluation of the Thermo Scientific Cascadion SM LC-MS/MS random access clinical analyser in a fully automated routine clinical laboratory

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Introduction

- Liquid chromatography mass spectrometry (LCMS) is considered the gold standard method for analysis of a number of key analytes because of its enhanced analytical specificity relative to immunoassay.
- Despite degrees of automation within systems, LCMS is still a labour intensive technique for clinical laboratories requiring large amounts of staff time to carry out sample preparation before analysis.
- The Thermo Scientific™ Cascadion™ SM Clinical Analyser (Cascadion) Fig 1, is a fully automated LCMS random access analyser that has been recently launched. The system incorporates on-line sample preparation and LCMS technology in a closed analytical system.
- Preliminary assays planned for availability on the Cascadion are total vitamin D (reported as a total of D2 + D3), an immunosuppressant panel (tacrolimus, sirolimus, cyclosporine, everolimus) and testosterone. Currently the total vitamin D is CE-IVD compliant.

Aim

- To carry out an independent evaluation of the Cascadion and to assess its acceptability within a busy routine clinical laboratory with no prior LCMS experience
- To carry out an analytical validation of the vitamin D3 assay component only due to the rarity of D2 bearing samples.

Figure 1: Cascadion at Frimley Park Hospital

Method

- Two state registered biomedical scientists with no previous experience of LCMS were selected as key operators. They received 3 days off-site training by Thermo Fisher Scientific and 2 days of on-site refresher training.
- Upon installation of the Cascadion in the laboratory the two scientists were tasked with running routine serum samples through the analyser for vitamin D analysis.
- User acceptability was defined as the ability to independently carry out this analysis as well as carry out routine maintenance.
- Vitamin D3 validation
  - Vitamin D stripped serum was run 20 times consecutively to assess limit of blank.
  - Carryover was assessed by analysing a high sample (D3 >301 nmol/L) in duplicate followed by a PBS sample in duplicate. This was repeated 10 times.
  - A high sample was diluted 1:2, 1:4, 1:8 and 1:16 to assess linearity.
  - Pooled serum samples were analysed 10 times consecutively to assess within batch precision and on 5 consecutive days to assess between batch imprecision.

Results

- The Cascadion is fully automated from sample preparation to result generation making it easy to operate.
- The two key operators had an automation background and no prior experience of LCMS. Following the 3 day off-site training and 2 day on-site refresher training staff were confidently able to run the Cascadion, carry out routine maintenance and perform basic trouble-shooting.
- The analyser has an automatic start-up. Routine daily maintenance takes a maximum of 10 minutes and routine monthly maintenance takes a maximum of 60 minutes

- Vitamin D3 validation
  - The vitamin D3 assay has an analytical range of 3.4 – 132 ng/mL (8.49 - 329.47 nmol/L).
  - No response was observed on a blank sample
  - No carryover was observed
  - Linearity of the assay was acceptable (r^2 = 0.9995)
  - Acceptable within batch and between batch precision was observed (tables 2a and 2b)

Sample	Mean ng/mL	SD	CV(%)
Low	19.13	0.57	2.96
Medium	87.15	3.94	4.53
High	131.16	4.01	3.06

Table 2a: Between batch precision

Sample	Mean ng/mL	SD	CV(%)
Low	18.60	0.95	5.10
Medium	87.93	3.22	3.66
High	128.10	1.93	1.51

Table 2b: Within batch precision

Conclusion

- In this study we have demonstrated that state registered scientists with no experience of LCMS are able to confidently run the Cascadion analyser with minimal training.
- Preliminary data for the D3 assay has demonstrated acceptable performance.
- A sample comparison for vitamin D3 and validation of the vitamin D2 assay is on-going.
- Further work is continuing to fully evaluate the Cascadion system including an assessment of sample throughput and walkaway time for 24-7 working.

Product is IVD/CE marked but not 510(k) –cleared and not yet available for sale in the U.S. Availability of product in each country depends on local regulatory marketing authorization status.

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