Volumetric Quality Control for Sample Management Automated Applications Using Low-Coherence Interferometry

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Abstract

We report on proof-of-concept (POC) experiments demonstrating the use of a novel interferometric volume measurement technology for quality control in Sample Management. Our results demonstrate the successful measurement of nanoliter droplets dispensed into dry wells, and of volume changes resulting from dispensing nanoliter droplets into wells that already contain a liquid meniscus, two key applications in the preparation of assay ready plates (ARP's) in our sample management workflow. We further demonstrated successful measurement of inventory volume in opaque, racked storage tubes for use with acoustic liquid handlers.

Introduction

Quality Control (QC) continues to be an utmost priority for Sample Management (SM). Cutting-edge technologies are used to ensure that all of our automated systems are validated prior to, and after, their deployment. As SM moves to an Acoustic tube platform, we have the need to continue traditional Automation QC, as well as the potential for real time QC -- a capability previously unobtainable. There are also some unique challenges. The acoustic storage vessel is opaque, making volume determination very difficult. To combat these challenges, Global Innovation Technologies (GLINT) has collaborated with Meniscense to develop a next-generation volume quantification system for quality control that can meet the future QC needs of Sample Management at AstraZeneca.

Acoustic Tube Description:
Acoustic storage tubes (FluidX AcoustiX Sample Tube, Brooks Life Sciences, Chelmsford, MA) have a flat bottom and their axial cross section in the usable lower portion is a rectangle with rounded corners. The tubes are made of opaque material and equipped with a screw cap. 96 tubes are held in SBS format racks, allowing for rearrangement and removal of individual tubes.

Methods

The experiments described here use a previously described low-coherence Michelson interferometer.[1,2] The interferometer allows for high-resolution liquid fill height measurements, from which the volume of liquids in wells of microplates or other containers are derived. Measurements of the volume of liquid droplets resting on a planar surface use this interferometer to measure the height of the droplet at its apex. Image processing is used to determine the radius of the contact area between the droplet and its support surface. In some experiments, an internally calibrated precision weighing module with a repeatability and readability of 0.1 mg was used for an independent gravimetric verification. Nanoliter droplets were dispensed with a PipeJet NanoDispenser. The interferometer was tested on multiple labware types and fill volumes and both accuracy and repeatability were measured. For some experiments ball bearings were used to create precise incremental volume changes seen in chart 2.

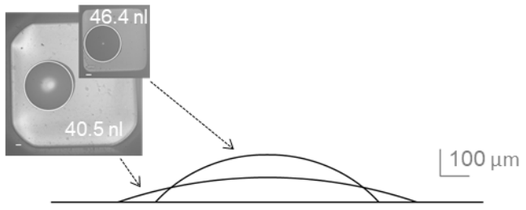


Image and Surface Profile of Nanoliter Droplets

Chart 1 Fill Volume vs Fill Height:
Volumes in acoustic tube

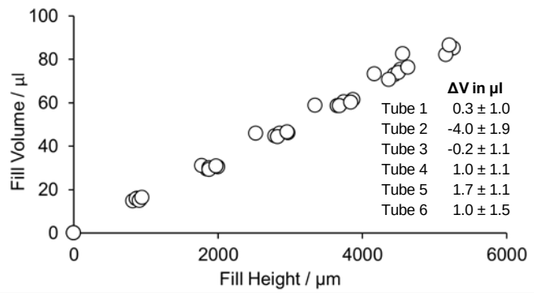
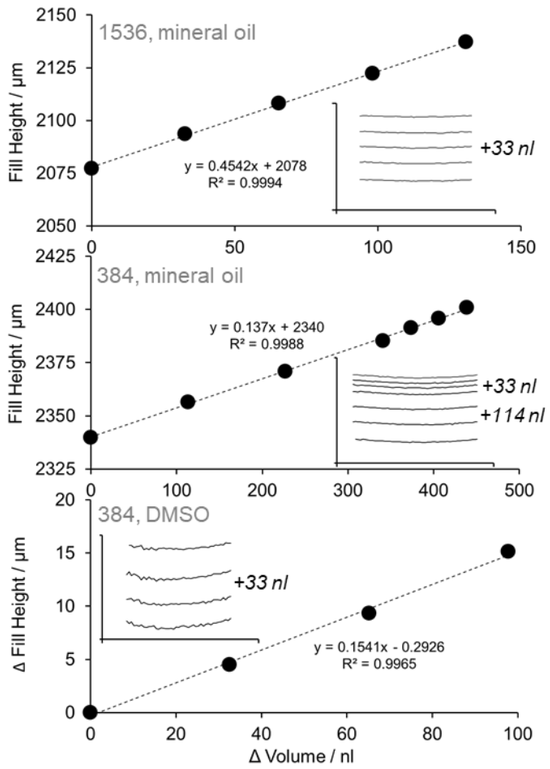


Chart 2 Fill Volume vs Fill Height:
Volumes in plates with incremental nanoliter dispenses[3]



Results

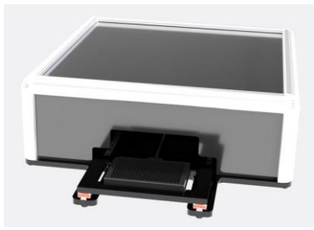
The proof of concept experiments met the goals for detection capabilities in sample management's process labware. The capabilities are summarized in table 1 and demonstrated in chart 2 for the three labware types and the measurements volumes tested. The technology shows the capabilities that we need to move quality control process forward with our increase in dispensing capabilities,.

Table 1 Labware Parameters and Tests
Summary of Labware Tests

Labware Type	Max Volume	Verified Volumes
Acoustic Tubes	85uL	15 - 85 uL
384 Well Plate	80uL	30-100 nL additions
	Dry	1 – 100 nL
1536 Well Plate	15uL	30-100 nL additions
	Dry	1 – 100 nL

Conclusions & Next Steps

- Low-coherence interferometry promises to deliver the next generation of volume verification.
- The proof of concept work demonstrates that the technology is compatible with all of our labware types.
- Following the completion of POC work, we are currently building a beta system for in-process testing. Anticipated delivery of beta test system is December 2019



Conceptual Design of Instrument

References
1. Luedemann, Interferometric Volume Measurement in Microplates, SLAS Technol. 2017; 22(1) 89-97
2. Luedemann, Interferometric Measurement of Liquid Volumes, U.S. Pat. 10,094,695, Oct. 9, 2018
3. Luedemann et al., Volumetric Quality Control for Sample Management Automated Applications Using Low-Coherence Interferometry, manuscript in preparation

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