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Calibration of Syringe Pumps Using Interferometry and Optical Methods

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***Abstract*—**Syringe pumps are commonly used for drug delivery in hospitals and clinical environments. These instruments are critical in neonatology and oncology, where any variation in the flow rate and drug dosing quantity can lead to severe incidents and even death of the patient. Therefore it is very important to determine the accuracy and precision of these devices using the suitable calibration methods. The Volume Laboratory of the Portuguese Institute for Quality (LVC/IPQ) uses two different methods to calibrate syringe pumps from 16 nL/min up to 20 mL/min. The Interferometric method uses an interferometer to monitor the distance travelled by a pusher block of the syringe pump in order to determine the flow rate. Therefore, knowing the internal diameter of the syringe with very high precision, the travelled distance, and the time needed for that travelled distance, it was possible to calculate the flow rate of the fluid inside the syringe and its uncertainty. As an alternative to the gravimetric and the interferometric method, a methodology based on the application of optical technology was also developed to measure flow rates. Mainly this method relies on measuring the increase of volume of a drop over time. The objective of this work is to compare the results of the calibration of two syringe pumps using the different methodologies described above. The obtained results were consistent for the three methods used. The uncertainties values were very similar for all the three methods, being higher for the optical drop method due to setup limitations.

***Keywords*—**Calibration, interferometry, syringe pump, optical method, uncertainty.

I. Introduction

Medical infusion instruments are widely used, as they are fundamental for primary health care, namely for providing drugs, nutrition and hydration to patients. Due to the widespread applications in critical health care treatments, infusion errors are often made, with reported dramatic effects in different applications in the health sector, especially in neonatology. Hence, it is crucial that volume and flow generated by these devices are as accurate and precise as possible. To ensure this, it is necessary to have appropriate calibration methods. The most common calibration method used by the National Metrology Institutes (NMI) for measuring low flow rates of fluids is the gravimetric method, which consists in the determination of the variation of mass of a liquid during a period of time. This methodology is used by the Volume and Flow Laboratory of the Portuguese Institute for Quality in a range down to 120 µL/h with an expanded uncertainty of 3% [10], being well defined in several publications, such as [1]-[3]; moreover, the calculation of the uncertainty is detailed in [4], [5]. But in order to determine which method is the most suitable for the specific instrument under test and to increase the used range and decrease the measurement uncertainty it was necessary to research and implement other methodologies for microflow determinations at the Volume Laboratory of the Portuguese Institute for Quality LVC/IPQ, as the interferometric and an optical method using a microscope. This work is currently being funded by the EURAMET EMPIR programs MeDDII – Metrology for drug delivery [6].

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II. Calibration Methods

The three methods studied and developed in the LVC/IPQ are described below.

A. Gravimetry

The gravimetric method relies on weighing the mass of the working fluid delivered by the instrument under test for a set time. The mass is converted to volume at a reference temperature. The volumetric flow rate (Q) is then determined by the quotient of the volume of the reference liquid and the time interval, including corrections according to (1), which consider evaporation, buoyancy and environment effects [1], [2]. This method is the one recommended by IEC 60601-2-24.

$$Q = \frac{1}{t_f - t_i}\left[\left((I_f - I_i) - (\delta m_{buoy})\right) \times \frac{1}{\rho_w - \rho_A} \times \left(1 - \frac{\rho_A}{\rho_B}\right) \times [1 - \gamma(T - 20)]\right] + \delta_{evap} \quad (1)$$

The method steps are conducted in a climate-controlled room insulated from vibration (reference temperature of 20 ºC, > 50% relative humidity). The flow is generated by a programmable syringe pump (Fig. 1). First, the syringe is filled with high ultrapure water. A high flow rate is imposed to the system in order to purge the flow line from air bubbles which can significantly affect flow stability and introduce flow errors. This procedure is repeated until the flow circuit is completely purged (normally 10 minutes of continuous water flow is enough). Additionally, the tube ending is immersed in the weighing vessel to prevent flow oscillations due to droplet detachment. The data are collected using a *LabVIEW* application during at least 15 min, depending on the instrument to be tested.

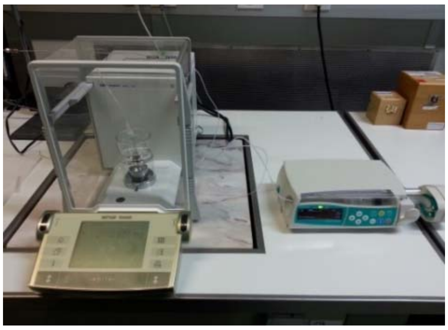

Fig. 1 Gravimetric setup

B. Interferometry

The Interferometric method uses a Hewlett-Packard, model 5528A interferometer that operates at 633 nm (the signal is processed using a LabVIEW application) to monitor the distance travelled by a pusher block of the syringe pump in order to determine the flow rate of the measuring device [7].

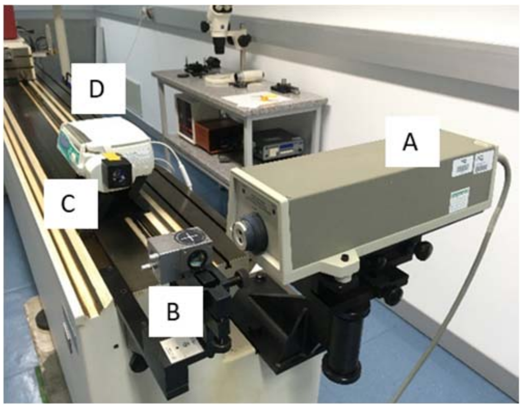

Fig. 2 Interferometric setup

The use of interferometry for flow measurement involved the use of the following components: a laser unit (A) with a detector incorporated (an optical arrangement composed by two retroreflector cubes (C) (one of which with a beam splitter attached (B)), a Control Unit, and the syringe pump (D) (Fig. 2)

The generation of flow was accomplished by a stepper motor which drove a screw that is connected to a pusher block that itself pushed the syringe piston. Therefore, knowing the internal diameter of the syringe, the travelled distance, and the time needed for that travelled distance, it is possible to calculate the flow rate of the fluid inside the syringe and its uncertainty.

The flow in the presented setup is expressed by (Q) [1] and is given by (2), where v is the velocity of the fluid and A is the internal cross-section circular area of the syringe (πr^2). Also, the velocity is obtained by dividing the displacement d (in the x-axes between point 1 and 2) of the syringe piston through a period of time t. If we add the expansion correction factor γ of the syringe glass for a reference temperature, T of 20 ºC then we will get (3):

$$\boldsymbol{Q = v \times A = \frac{x_2 - x_1}{\Delta t} \times \pi r^2 = \frac{d\pi r^2}{t}} \tag{2}$$

$$\boldsymbol{Q_{20} = \frac{d\pi r^2}{t} \times [1 - \gamma(T - 20)]} \tag{3}$$

C. Optical Drop Method

As an alternative to the gravimetric and the interferometric method, a methodology based on the application of optical technology was also developed to measure low flow rates.

The syringe pump is set to a specific flow rate, the delivered liquid flow was determined by observing the volume increase of a drop at the end of the flow line placed inside an evaporation trap (Fig. 3). This observation was performed at a specific time by using photographs taken by a digital USB microscope with 400X magnification.

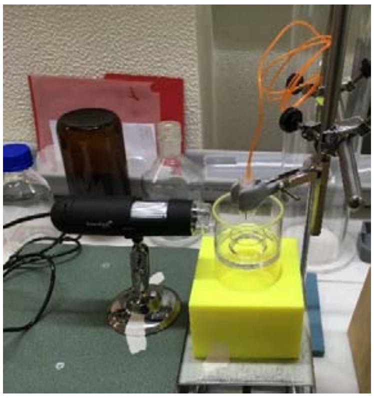

Fig. 3 Optical drop setup

The projected area of the drop was obtained geometrically with the assistance of a Pyton software (by dividing the image into slices), with pixel resolution, and considering the tube diameter where the drop is hanging, 1,49658 mm, measured by interferometry, as the reference value for length (Fig. 4). This value was then converted to an equivalent sphere volume and later to a flow rate based on time acquired (Δt) and on volume change (ΔV), according to (4).

Fig. 4 Image using Pyton software

$$\boldsymbol{Q = \frac{\Delta V}{\Delta t}} \tag{4}$$

III. Uncertainty Calculation

The measurement's uncertainty method used for microflow determination is normally estimated according to the Guide to the expression of Uncertainty in Measurement (GUM) [8].

The measurement model is determined along with the standard uncertainties' components, the sensitivity coefficients' values, the combined standard uncertainty and the expanded uncertainty.

A. Gravimetry

The main standard uncertainties considered are: mass measurements (m), density of the mass pieces (ρ_B), density of the water (ρ_W), density of the air (ρ_A), evaporation rate (δQ_{evap}), water temperature (T), time (t), expansion coefficient (γ), standard deviation of the measurements (δQ_{rep}) and buoyancy on the immersed dispensing needle (δQ_{mbuoy}). More information can be found in [5].

B. Interferometry

The main standard uncertainties considered are: distance (d), time (t), radius of the syringe (r), stability of the setup (δQ_{sta}), water temperature (T), time (t), expansion coefficient (γ), standard deviation of the measurements (δQ_{rep}). More information can be found in [7].

C. Optical Method – Drop

The main standard uncertainties considered are: Volume determination by drop method (V) that includes the inaccuracy of the contour of the drop and the pixels determination, evaporation (δQ_{evap}), time (t) and standard deviation of the measurements (δQ_{rep}). More information can be found in [9].

IV. Results

A Braun perfusor space syringe pump was calibrated using the gravimetric method, the interferometric method and the optical drop method at 4 different flow rates: namely 5000 µL/h, 1000 µL/h, 500 µL/h, and 100 µL/h. The calibrations were performed under the following conditions:

a) Controlled temperature equal to 20 ± 3 ºC;
b) Humidity above 50 %;
c) 10 mL plastic syringe (diameter of 15,66 mm);
d) Results collected every 30 s during 15 min;
e) Water used as calibration liquid.

The results of the measured flows and the expanded uncertainty for the gravimetric method (U for k = 2,0) are presented in Table I.

TABLE I
GRAVIMETRIC RESULTS

Nominal flow (µL/h)	Measured flow (µL/h))	Uncertainty (µL/h)	Uncertainty (%)
100	97,83	3,89	4,0
500	498,27	4,54	0,9
1000	998,85	22,3	2,2
5000	5008,90	24,3	0,50

The results of the measured flows and the expanded uncertainty for the gravimetric method (U for k = 2,0) are presented in Table II.

The results of the measured flows and the expanded uncertainty for the optical drop method (U for k = 2,0) are presented in Table III. It was not possible to perform the 5000 µL/h test due to setup limitations, mainly the drop was increasing too fast and it was not possible to take several pictures of it.

TABLE II
INTERFEROMETRIC RESULTS

Nominal flow (µL/h)	Measured flow (µL/h))	Uncertainty (µL/h)	Uncertainty (%)
100	100,21	3,6	3,6
500	496,92	15,0	3,0
1000	1004,00	24,9	2,5
5000	5035,30	107,5	2,1

TABLE III
OPTICAL DROP RESULTS

Nominal flow (µL/h)	Measured flow (µL/h))	Uncertainty (µL/h)	Uncertainty (%)
100	97,1	12,0	12,4
500	518,0	60,2	11,6
1000	1005,1	81,3	8,1

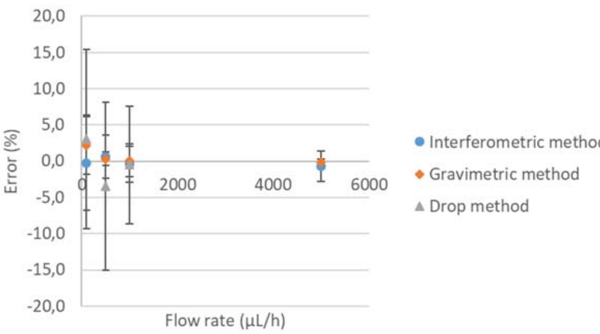

Fig. 5 Comparison between methods

From Tables I-III and Fig. 5, it can be seen that the results from the gravimetric method, the interferometric method and the optical drop method are consistent with each other, being the uncertainty values very similar for the gravimetric method and the interferometric method. The optical method presents uncertainties higher that the other methods due to the limitation of the camera used. The majority of the values are within the maximum permissible error defined by the manufacturer, 2%.

V. Conclusion

The aim of this work is to provide and compare the obtained calibration results of a syringe pump at low flow rates, using three different methods, in order to define the most suitable one that can give better uncertainty and accuracy.

The results obtained were consistent for the three methods used. The uncertainties values were very similar for all the three methods, being higher for the optical drop method due to setup limitations.

In general the most easy and reliable method to be used in the calibration of the syringe pump is the gravimetric method, but the interferometric method can also be a good substitute, if the instrumentation is available.

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