

# Early Feasibility Study of an Electronically Controlled Gravity Feed Infusion Set for intravenous fluids in adults

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**Abstract**— A first in human single arm clinical study was conducted to determine the utility and safety of an Electronically controlled gravity feed (ECGF) infusion set, a low cost gravity feed infusion controller designed to improve intravenous administration of fluids and medication in resource constrained settings. The primary objective of this study was to estimate the accuracy and safety of the ECGF device in delivering a constant flow rate for therapies between 5 -100 drops/min in a sample adult population.

12 participants with an indication for intravenous fluid therapy that met the inclusion criteria and provided written informed consent were enrolled from the infectious diseases ward at Mulago National Referral Hospital, Kampala, Uganda and were all placed on the ECGF device for one infusion therapy. Patient physiological parameters were recorded over a period of 48hours. Maximum and minimum percentage variations  $E_p$  (max) and  $E_p$  (min) for analysis periods  $T_1$  (second hour) and  $T_2$  (last hour) showed a percentage error within  $\pm 7\%$  for all 12 patients. Physiological parameters for study participants over the 48 hour period were stable as would be expected from a correct infusion therapy.

The ECGF device was able to maintain flow rates within acceptable error during intravenous therapy and provide an appropriate level of safety for adult patients owing to its sensitivity in sounding alarms in the event of flow rate deviations. The ECGF has shown potential in improving the standard of care for intravenous therapy in resource limited settings.

**Keywords**— Clinical study, safety, intravenous fluids, infusion controller, device

## I. INTRODUCTION

Errors during the delivery of intravenous (IV) fluids and medication occur fairly frequent and compromise patient safety. A prospective observational study of nurses administering intravenous medication in two Australian hospitals showed clinical errors for 69.7% of infusion therapies which included flow rate errors for the prescribed therapy [1]. In low resource settings this challenge is compounded as nurses lack the requisite training on medical technology before it is used in a health facility. The existing standard of care in resource limited settings is manual regulation by a clinician which requires high skill to cor-

rectly set the flow rate. Available infusion pumps and their associated consumables are in limited supply and are prohibitively expensive to procure and maintain [2]. Access to a reliable power supply which is common in both semi-urban and rural areas also affects the utility of medical technology.

The Electronically Controlled Gravity Feed (ECGF) infusion set was designed to address these gaps. The ECGF is a low cost infusion controller device that automatically controls the flow rate of an IV therapy. It provides feedback on the status of the therapy through alarms and is battery operated utilizing a hybrid solar and electricity charging bed. In-vitro preclinical testing of the ECGF was completed to determine minimum safety, performance and repeatability. Black box tests were carried out to ascertain usability and safety by simulating adverse events such as slow flow rate, rapid flow rate and free flow. Results yielded a performance of  $\pm 1\%$  (deviation between actual and prescribed) for flow rates between 5-100 drops/min with an acceptable level of safety. However, the performance and safety of the ECGF in an actual patient population is unknown. Early feasibility studies allow for early clinical evaluation of devices to provide proof of principle and initial safety data, typically before the device has been finalized for a specific indication [3].

## II. MATERIALS AND METHODS

### A. Design of the ECGF

The ECGF device has been implemented as a microcontroller driven embedded system application. It comprises of four interrelated modules, a drop detector, actuator, user interface and a power supply unit as shown in figure 1. The drop rate detector consists of a sensor housing comprising of a light source and a photocell which is clamped onto the drip chamber of a fluid giving set [4]. Interference of the optical couple signals the presence of a drop. The actuator is the heart of the device and has been implemented with time steered control algorithms that regulate the drop rate in real time through constriction of the fluid giving set tube via a

stepper motor [4]. The user interface provides a keypad and indicators on alarms and the battery level status. A hybrid solar and AC electricity charging bed has been designed for the battery operated power supply to charge multiple batteries at a time.

Other infusion controllers have been developed to serve humanitarian contexts such as the DripAssist from Shift Labs and the Acuset IV flow

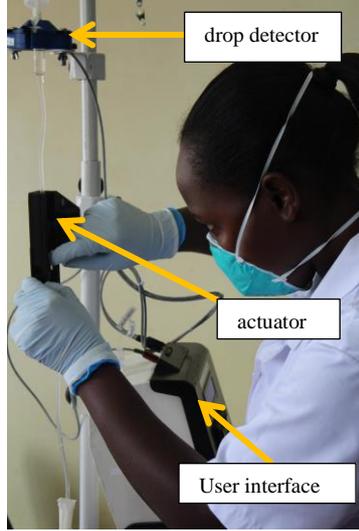


Fig. 1 Features of the ECGF device

controller by Medicine Mondiale, however, these devices only monitor the drop rate and do not dynamically adjust or maintain the flow rate.

### B. Study design

A first in human single arm study was conducted with a sample size of 12 patients. Patients that met the inclusion criteria and provided written informed consent were enrolled onto the study. All patients had one infusion therapy administered using the ECGF investigative device. The patients suffered from three main conditions; cryptococcal meningitis, tuberculosis and diabetes. Therefore the main infusates were amphotericin B, metrogyl and 0.9% normal saline.

### C. Data Collection Procedure

Clinical data and data on the device performance were collected. Patient vitals recorded included pulse rate, respiratory rate, blood pressure and temperature. An infusion bag retrofitted with a 20 drops/ml Korean fluid giving set (K203T) were clamped onto the ECGF device as shown in Figure 1. An RS-232 to USB cable was connected to a computer running Termite 3.2 RS-232 terminal software which collects real time data on the total drop count  $N_x$  and the associated total infusion time stamp  $t_x$  every 12 seconds. The amount of fluid infused was recorded in drops/minute. To ensure the accuracy of the device, a weighing scale (Medio-Line 40600) with a precision of 0.3% was used as a control. The weight of the infusion bag was taken after flushing and after completion of the therapy. The difference

in volume was recorded and compared against volume infused as recorded by the ECGF device.

### D. Drip rate analysis methods

Data was analysed using equations specified in the International Electrotechnical Commission (IEC) 60601-2-24 standard [5]. These equations show the calculation of the actual drip rate as well as calculations for maximum and minimum percentage variations. The drip rate  $Q_i$  at each sample interval for the analysis period was calculated using equation (1)

$$Q_i = \left( \frac{N_i - N_{i-1}}{S} \right) \quad (1)$$

where  $N_i$  is the  $i^{\text{th}}$  total drop count sample from the test period and  $S$  the sample interval (min).

The maximum  $E_p(\text{max})$  and minimum  $E_p(\text{min})$  percentage variations within observation windows of duration period  $P$  (min) for the 1, 2, 5, 11, 19 and 31 minutes over the analysis period  $T_1$  (min) of the second hour as well as over the analysis period  $T_2$  (min) of the last hour of the test period are calculated using equations (2) and (3)

$$E_p(\text{max}) = \text{MAX}_{j=1}^m \left[ \frac{S}{P} \times \sum_{i=j}^{j+\frac{P}{S}-1} 100 \times \left( \frac{Q_i - r}{r} \right) \right] (\%) \quad (2)$$

$$E_p(\text{min}) = \text{MIN}_{j=1}^m \left[ \frac{S}{P} \times \sum_{i=j}^{j+\frac{P}{S}-1} 100 \times \left( \frac{Q_i - r}{r} \right) \right] (\%) \quad (3)$$

where  $Q_i$  is the actual drip rate calculated from (1),  $P$  is the observation window duration (min),  $S$  is the sample interval (min),  $r$  is the set drip rate (drops/min) and  $m$  is the maximum number of observation windows. The equation to calculate  $m$  is derived in (4)

$$m = \frac{T_x - P}{S} + 1 \quad (4)$$

where  $T_x$  is the analysis period (min). The overall mean percentage drip rate error,  $A$  is derived using equation (5)

$$A = \frac{100(Q - r)}{r} (\%) \quad (5)$$

where  $Q$  is the mean drip rate of the analysis period  $T_1$  and the overall mean percentage drip rate error  $B$  derives equivalent to  $A$ , where  $B$  is measured over the analysis period  $T_2$  (the last hour of the test period).

### III. RESULTS AND DISCUSSION

#### A. Drip rate results

Results from a patient receiving 41drops/min are analyzed and discussed in detail. Startup graphs were plotted with MATLAB showing the actual and ideal flow rates against time. Trumpet curves for the maximum and minimum error margins (deviation between the prescribed and actual flow rates  $E_p$  (max) and  $E_p$  (min)) over the analysis periods  $T_1$  and  $T_2$  are shown in figures 2 and 3 respectively.

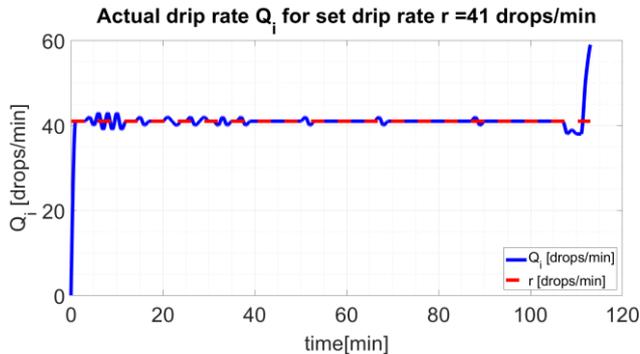


Fig. 2 Startup graph for patient on 41drops/min therapy

From figure 2,  $Q_i$  tends close to the ideal flow rate. The small ripples at the start of the therapy are due to the device's feedback regulation mechanism as it corrects deviations in the flow rate caused by hydrostatic pressure and movement artefacts in a clinical environment at the start of the therapy.

In figure 3 as the therapy progresses the regulation is seen to stabilize where  $E_p$  (min) is denoted by the red line and  $E_p$  (max) is denoted by the blue line. In the first five minutes the device begins to regulate the therapy, this progression is fairly common for most infusion pumps on the market, by the 10 min mark both  $E_p$  (max) and  $E_p$  (min) tend towards the zero-error line (purple). The maximum and minimum percentage variations  $E_p$  (max) and  $E_p$  (min) for analysis periods  $T_1$  and  $T_2$  from all 12 study participants was less than  $\pm 7\%$ .

Due to interruptions in the therapy (over and under infusion alarms) caused by either the patient folding their arm causing flow rate restriction inducing a slow flow rate or leakage from the point of contact between the fluid giving set and the infusion bag the error margins varied between patients. Excessive fluid entering the drop rate detector erroneously caused the activation of a rapid flow rate alarm which would terminate the therapy. The study clinician therefore had to dry the drop rate detector casing before restarting the therapy.

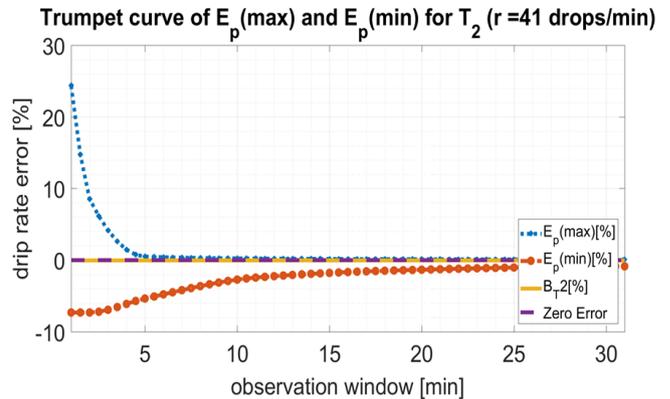


Fig. 3 Trumpet curves depicting  $E_p$ (max) and  $E_p$ (min) for the 41 drops/min therapy

Three runs were recorded during the 41 drops/min therapy that ran for a total of 227 minutes as shown in Table 1. Since there were no continuous runs for more than two hours without alarm interruptions, trumpet curves for  $T_1$  are similar to those of  $T_2$ . The maximum error for this infusion therapy was an  $E_{total}$  of 4.065%.

Table 1 Drip rate analysis parameters for patient on 41drops/min therapy

Run	Run time (min)	R (drops/min)	$Q_{total}$ (drops/min)	$E_{total}$ (%)	$Q_{T1}$ (drops/min)	$Q_{T2}$ (drops/min)	$B_{T2}$ (%)
1	4	41	42.667	4.065	-	-	-
2	113	41	41.402	0.980	-	40.983	0.043
3	110	42	42.000	0.000	-	42.000	0.000

Adverse events that subsequently caused alarm activation and subsequent intervention by a nurse were noted by study observers for this particular therapy and are summarized in the Table 2. This patient experienced various alarms where the clinician had to intervene. In particular the patient experienced phlebitis on the wrist [6] as a result of poor cannulation, which is a common occurrence with patients receiving IV treatment. A limitation with the ECGF device is its inability to 'pause' a therapy resolve an adverse event and resume as opposed to restarting causing several runs. The ECGF device was also not able to determine when the infusion bag was running empty. The device assumed that the clinician had input values for fluid either equal to or less than the quantity of fluid in the infusion bag. As a result this particular therapy did not have an 'end of therapy' alarm because the clinician turned off the device as the bag was almost empty, see table 2. As a safety feature the ECGF terminates a therapy for extremely slow flow rates and as such would have inevitably terminated the therapy even if

the therapy had continued to run. These features will be incorporated into the technology development of the next version of the device.

Table 2 Study observer notes for patient on 41drops/min therapy

Device infusion log	Observer's report	Clinician's action
Under infusion	Slow rate alarm Rapid rate alarm Under infusion alarm	Clinician closed roller clamp and restarted the device
Over infusion	Over infusion/ Swollen hand due to incorrect insertion of cannula	Changed position of cannula to another site on the patient's other arm
No feedback	Bag empty/ Device was turned off by the clinician	Turned off device

### B. Clinical data results and discussion

Patient vitals for the study participants had an overall slight improvement or maintained stability as expected with a properly carried out infusion therapy. The study participants were not in critical condition therefore improvement appeared to be slight. The most significant clinical outcome was observed with a study participant who suffered from hypertension with sepsis. This patient was however put on anti-hypertensive medication on day 2 which was one of the major contributing factors for a significant improvement in their blood pressure levels. For this participant diastolic and systolic blood pressures showed a significant improvement over a 48-hour period. No Unanticipated adverse device events were noted with the ECGF except for the erroneous activation of a rapid rate alarm for therapies with extreme leakage of fluids.

## IV. COMPLIANCE WITH ETHICAL REQUIREMENTS

### A. Statement of Informed Consent

All patients enrolled on the study provided written informed consent and all potential risks with using the ECGF investigative device were clearly explained. All patients on the study were protected by insurance in the event that they obtained injuries related to participating in the study.

### B. Statement of Human Rights

This clinical study was conducted in compliance with ISO standards for clinical investigation of medical devices and national laws and regulations of the Uganda National Council for Science and Technology. The ECGF device was cleared by the Uganda National Drug Authority for use in a clinical study. This early feasibility study was committed to complying with the Makerere University School of Medicine Research and Ethics Committee (SOMREC) to ensure the protection of human participants [7]. This study was approved by SOMREC under study identification (ID) REC REF 2017-101 and administratively cleared by the Mulago Hospital Research and Ethics Committee under study ID MREC 1273.

## V. CONCLUSION

The ECGF device was able to provide an appropriate level of safety and accuracy for adult patients. The device performance analyzed for maximum and minimum error margins for all 12 study participants was within  $\pm 7\%$ , which is acceptable for the clinical setting. The device met minimum safety requirements however additional safety features will need to be incorporated in a future version. Alarms sounded within the recommended timeframes and the device was able to subsequently effect an action after the alarms persisted beyond the required timeframe. These results confirm the utility and safety of the ECGF device for use in clinical settings and its potential to address existing limitations with infusion equipment in resource limited countries.

## ACKNOWLEDGEMENTS

This project is supported by Grand Challenges Canada. Grand Challenges Canada is funded by the Government of Canada and is dedicated to supporting Bold Ideas with Big Impact. This work recognizes contributions from Dr. Sabrina Bakeera-Kitaka, Dr. Noah Kiwanuka, clinical staff and study participants from Mulago National Referral Hospital - Kiruddu and the staff at the Instrumentation Division at Uganda Industrial Research Institute.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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#### REFERENCES

1. H. H. Hoefel, C. Lautert, C. Schmitt and et al., "Vancomycin administration: mistakes made by nursing staff," *Nurs Stand*, vol. 22, pp. 35-42, 2008.
2. A. Juarez, K. Maynard, E. Skerrett, E. Molyneux, R. Richards-Kortum, Q. Dube and M. Z. Oden, "AutoSyP: A Low-Cost, Low-Power Syringe Pump for Use in Low-Resource Settings," *Am J Trop Med Hyg*, vol. 95, no. 4, p. 964-969., 2016.
3. FDA, "Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including certain First in Human Studies," Food and Drug Administration, 2013.
4. S. Ssekitoleko, P. Niyitanga, M. Ocheng, P. N. Makobore and P. Rolfe, "Design of a Low Cost Electronically Controlled Gravity Feed Infusion Set," in *IEEE Africon*, Addis Ababa, 2015.
5. International Electrotechnical Commission, "Medical electrical equipment Part 2-24 Particular requirements for the basic safety and essential performance of infusion pumps and controllers," IEC, 1998.
6. J. Westbrook, R. Marilyn, A. Woods and D. Parry, "Errors in the administration of intravenous medications in hospital and the role of correct procedures and nurse experience," *BMJ Qual Saf*, vol. 20, no. 12, p. 1027-1034, 2011.
7. M. University, "Faculty of Medicine Research and Ethics Committee," Makerere University College of Health Sciences, Kampala, 2016.