University of Groningen

An orchestra in need of a conductor

Doesburg, Frank

DOI:
10.33612/diss.165632361

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Doesburg, F. (2021). *An orchestra in need of a conductor: challenges and opportunities in multi-infusion therapy*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. https://doi.org/10.33612/diss.165632361

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 16-03-2025

CHAPTER 7

Multi-infusion with integrated multiple pressure sensing allows earlier detection of line occlusions

Frank Doesburg, Roy Oelen, Maurits H. Renes,
Pedro M. Lourenço, Daan J. Touw, Maarten W. Nijsten

Submitted

Supplementary
material

Abstract

Background

Occlusions of intravenous (IV) tubing can prevent vital and time-critical medication or solutions from being delivered into the bloodstream of patients receiving IV therapy. At low flow rates (≤1 ml/h) the alarm delay (time to an alert to the user) can be up to 2 hours using conventional pressure threshold algorithms. In order to reduce alarm delays we developed and evaluated the performance of two new real-time occlusion detection algorithms and one co-occlusion detector that determines the correlation in trends in pressure changes for multiple pumps.

Methods

Bench-tested experimental runs were recorded in triplicate at rates of 1, 2, 4, 8, 16, and 32 ml/h. Each run consisted of 10 minutes of non-occluded infusion followed by a period of occluded infusion of 10 minutes or until a conventional occlusion alarm at 400 mmHg occurred. The first algorithm based on binary logistic regression attempts to detect occlusions based on the pump's administration rate (Q(t)) and pressure sensor readings (P(t)). The second algorithm continuously monitored whether the actual variation in the pressure (P-SD-actual) exceeded a threshold of 2 standard deviations (SD) above the baseline pressure. When a pump detected an occlusion using either the regression or SD algorithm, a third algorithm correlated the pressures of multiple pumps to detect the presence of a shared occlusion. The algorithms were evaluated using the six bench-tested single-pump occlusion scenarios and seven multi-pump co-occlusion scenarios (i.e. with flow rates of 1+1, 1+2, 1+4, 1+8, 1+16, and 1+32 ml/h respectively). Alarm delay was the primary performance measure.

Results

In the single-pump occlusion scenarios, the overall mean ±SD alarm delay of the regression and SD algorithms were (1.8 ±0.8 min) and (0.4 ±0.2 min), respectively. Compared to the delay of the conventional alarm of 7.4 ±7.5 min this corresponds to a time reduction of 52 ±34% (P =0.003) and 90 ±6% (P =0.001), respectively. In the multi-pump scenarios a correlation >0.8 between multiple pump pressures after initial occlusion detection by the regression or SD algorithms had a mean ±SD alarm delay of 0.4 ±0.2 min. No occlusions were missed in the single-pump and multi-pump scenarios by any of the algorithms.

Conclusion

In single pumps, both the regression and SD algorithm considerably reduced alarm delay compared to conventional pressure limit-based detection. For multiple pumps the correlation algorithm reliably detected co-occlusions. The latter may be used to localize the segment of tubing in which the occlusion occurs.

Background

Occlusions of intravenous (IV) tubing can prevent vital and time-critical medication from being delivered into the bloodstream of patients. Conventional algorithms to detect occlusions sound an alarm when the pressure measured by the pump exceeds a certain threshold. A low pressure threshold will detect an occlusion sooner at the expense of an increase in the likelihood of false alarms, which is a known contributor to alarm fatigue.[1] Conversely, a high threshold will cause occlusions to be detected later, albeit with a decreased rate of false alarms. Using conventional pressure threshold algorithms it can take nearly up to 2 hours before an alarm is activated when administration rates are low (≤1 ml/h).[2] The use of higher rates (e.g. >10 ml/h) and low-compliance IV tubing may decrease the alarm delay, but many critical drugs are restricted to lower administration rates.[3]

Common statistical methods may be used to reduce alarm delays compared to conventional pressure threshold algorithms. One approach may use a binary logistic regression model, which describes the relationship of a binary (occlusion vs. non-occlusion) outcome with one or more predictors.[4] Based on the pump's administration rate Q(t) (ml/h) and its pressure P(t) (mmHg) such a model may be able to detect the occurrence of an occlusion. Another method could use the standard deviation (SD) of the a set of recent values of P(t) to define a real-time threshold for anomalies that occur during an occlusion (Figure 1). During stable infusion and assuming a normal distribution, 95% of pressure values will deviate less than 2 times the standard deviation (SD) from the mean pressure value.[5] A threshold to detect a pressure anomaly could be set at twice that SD. This approach requires one to know the standard deviation (SD) of the P(t) signal during stable infusion at different administration rates.

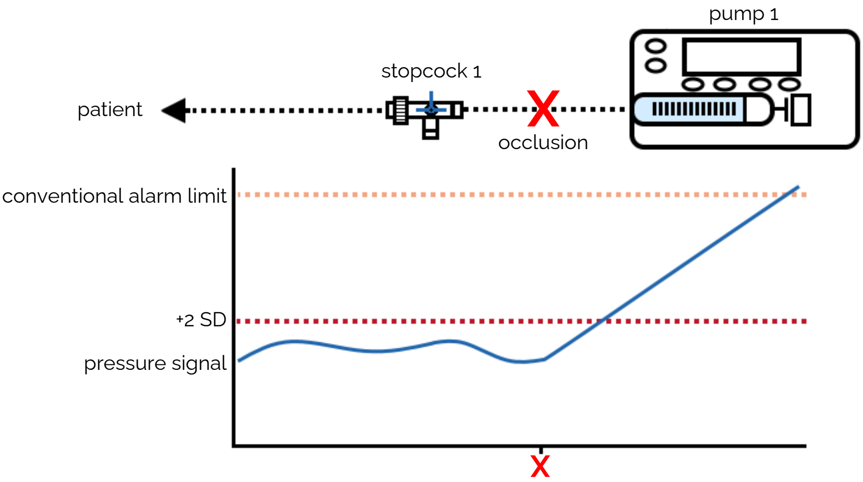

Figure 1. Single-pump occlusion detection using the standard deviation (SD). During stable infusion pressure values will deviate less than 2 times the SD from the mean pressure value. When the pressure exceeds the threshold set at twice the SD, an occlusion is likely.

With increasing complexity of patients, multi-infusion systems are increasingly employed. Such systems are increasingly integrated with respect to monitoring and control of multiple pumps from a centralized single controller.[6] When the number of infusion pumps is larger than the number of available intravenous (IV) access points several pumps have to be connected to the same IV access point.[7] In case of an obstruction in the pathway between such pumps and the patient, one or more pumps may be affected by the obstruction, depending on where the physical obstruction is present.

In multi-infusion settings combining the pressure signals P1(t), P2(t), etc. from several pumps might allow both earlier and more specific detection of obstructions in a common line to the patient. In case the pressures in two or more pumps that deliver to the same IV access show a coincident rise, then an obstruction in the final common pathway is likely (Figure 2A). In case the pressure of only one pump increases, this suggests an obstruction in the infusion line between that specific pump and the common infusion line (Figure 2B).

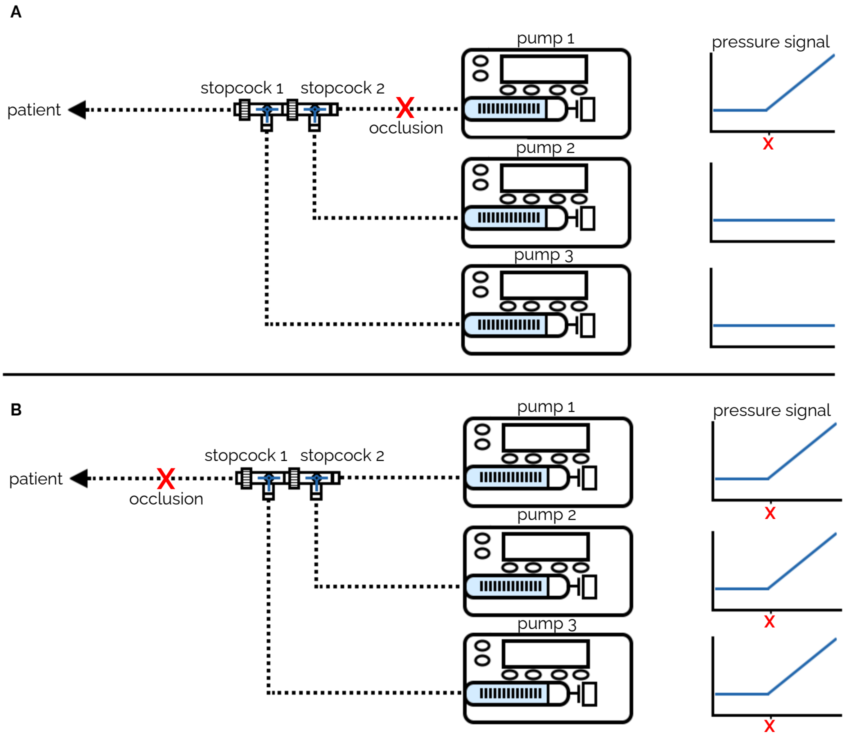

Figure 2. Multi-pump and single-pump occlusions in a multi-infusion set-up. During an occlusion in the shared pathway between the pumps the pressures measured by each pump will rise coincidently (Panel A). During a single-pump occlusion the pressure in only one pump is expected to rise, while the pressure of the other pumps remains stable (Panel B).

In this study we aimed to reduce the alarm delay in single and multi-pump occlusion scenarios while maintaining a high level of accuracy. We therefore developed and tested two occlusion detection algorithms for single pumps using common statistical methods. Secondly, we developed and tested an algorithm designed to detect co-occlusions in IV tubing by correlating the pressure signals in multiple pumps, thereby providing a framework for occlusion localization. To our knowledge no studies have previously assessed the feasibility of a multi-infusion system to detect and pinpoint occlusions.

Methods

Materials

Three Alaris Asena GH Syringe pumps (Carefusion, United Kingdom) with firmware v2.3.6 were connected to an Alaris DS docking station. A generic laptop running Windows 10 (Microsoft Corporation, United States of America) was used to run custom pressure logging software written in Java 1.7 (Oracle Corporation, United States of America). Algorithm evaluation software was also written in the Java environment. Communication between the computer and the pumps followed the pumps' RS232 communication protocol.[8] A StarTech ICUSB2324X USB to serial adapter (StarTech, United Kingdom) and 3 generic RS232 cables were used for RS232 connectivity.

Tubing consisted of two Steritex 3W three-way stopcocks (Codan, Denmark), three Vygon VGreen IV (2 meter length, 2 ml volume, 1 mm internal diameter) tubes (Vygon, France), and an Arrow-Howes MC-12703 triple-lumen central venous catheter (Teleflex Inc., United Kingdom). Three BD Plastipak 50 ml syringes (Becton-Dickinson, United States of America) were used. A generic plastic waste container was used as the end point of the catheter.

Experimental setup

Three infusion pumps were attached to a docking station in a vertically stacked fashion. The docking station was attached to a wall so that the middle pump was at approximately the same height as the tip of the triple-lumen catheter. The three syringes were filled with 50 ml of tap water and connected to an IV tube. Subsequently, two stopcocks were connected to the tubes. One stopcock connected to the distal (16 Ga., 0.39 ml priming volume) lumen of the catheter. The tip of the catheter was submerged in approximately 7 cm of tap water, corresponding to a counter pressure of 5.2 mmHg simulating a normal central venous pressure (2-8 mmHg).[9,10] The syringes were placed in the pumps, followed by priming of the tubing using the pumps' built-in priming functionality until there was no more air present in the tubing.

Gathering of experimental data for the development and evaluation of the algorithms

Baseline single-pump occlusion scenarios

In order to determine the baseline pressure characteristics experimental runs were recorded using three separate pumps simultaneously. Runs were recorded at administration rates of 1, 2, 4, 8, 16, and 32 ml/h and consisted of two phases. The first phase consisted of ten minutes of non-occluded infusion. Subsequently an occlusion phase was started by closing both stopcocks and clicking a designated button in the logging software that created a timestamped occlusion event entry. Every 2 seconds the software generated a log entry for each pump which contained a pump-identifier (numbers 0, 1, and 2), a timestamp, the administration rate (ml/h), an event code (no-event or occlusion event), and the pressure as measured by the pumps' internal sensors (mmHg). The experiment ended after ten minutes of occlusion or when an occlusion alarm was generated by the pump.

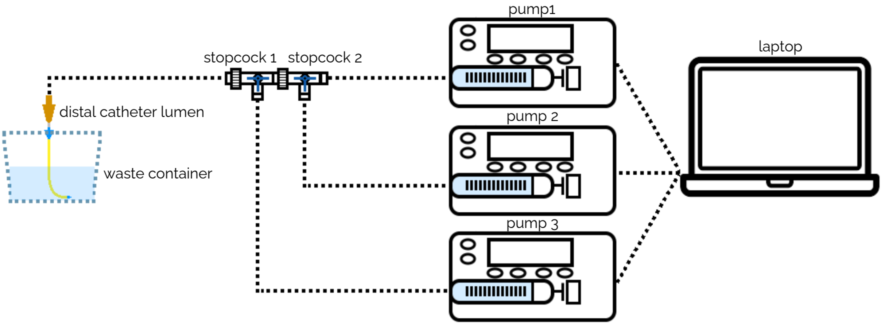

Figure 3. Experimental setup.

After recording the experimental runs the pressure log files were examined by testing for a normal distribution, and the baseline characteristics (pressure mean and standard deviation for each rate) were calculated for the non-occluded phase. In case the pump was not immediately pressurized at the start of a run (i.e. the pressure was still rising to a stable pressure), those 'start-up' values were omitted from the calculation of the baseline characteristics.

Linear regression was used to determine the pressure increase per second during occlusions at different administration rates during the occlusion phase. The resulting regression lines were used to calculate the alarm delay (time from the start of the occlusion to the alarm) for a range of alarm thresholds found in literature (300-800 mmHg) assuming a 'worst case' baseline pressure of 150 mmHg.[3,11–13]

Experimental data for the evaluation of co-occlusions

A series of experimental runs was performed in triplicate where two pumps were co-occluding on the same lumen. The same experimental procedure and set-up used to collect the baseline single-pump measurements was followed, with a few differences: The administration rate of one pump was kept constant at 1 ml/h, and the rate of the second pump was varied in each run, resulting in rates of 1+1, 1+2, 1+4, 1+8, 1+16, and 1+32 ml/h. Pump 3 (Figure 3) was not used and during the non-occlusion phase stopcock 1 was configured so that water could not flow from or towards pump 3. Finally, in order to create a shared occlusion only stopcock 1 (Figure 3) was closed instead of all stopcocks.

Real-time occlusion detection algorithms

Regression algorithm

Two single-pump detection algorithms were created and evaluated. The first detection algorithm involves a binary logistic regression model. The (rounded) output of such a model is either 0 or 1, which makes it suitable for a binary classification (non-occlusion vs. occlusion). The regression model was trained using the data collected using baseline single-pump occlusion scenarios. Cases were labeled as corresponding to a non-occlusion, or an occlusion (the dependent variable). Independent variables were administration rate (ml/h) and pressure (mmHg). This resulted in the following regression model:

$$output = \frac{1}{(1 + e^{-(-1.345 - 0.177 \cdot rate + 0.040 \cdot pressure)})}$$

Where a rounded output of 1 corresponds to an occlusion, and 0 to a non-occlusion.

Standard deviation (SD) algorithm

The second algorithm assumes that pressures measured by the pump during non-occluded infusion are normally distributed around the mean pressure. In that case 95% of these values are within 2 SDs from the mean.[5] When the pressure exceeds the detection threshold that is twice the baseline SD, an occlusion is likely.

The use of both single-pump algorithms is illustrated in Figure 4. We used a moving window of 30 measurements (60 seconds) in which the mean pressure and SD were calculated. The size of the window was determined by testing window sizes between 2 and 60 seconds and selecting the size that had the best accuracy (%; Supplementary material: Figure S1).

Both the regression and the SD algorithms can produce a preliminary occlusion classification belonging to a single time point based on an administration rate (ml/h) and a pressure (mmHg). As these preliminary classifications are sensitive to outliers and noise, additional criteria were added to improve accuracy: The mean slope in pressure over the last 30 seconds had to be >0.0. Also, if in the most recent 10 classifications at least 6 were positive, the final classification was also positive.

Correlation algorithm

For multi-pump scenarios a correlation algorithm was coupled with the regression and SD algorithms. When either the regression or SD algorithm made a final occlusion classification, the correlation between the pump's pressure and that of every other connected pump was evaluated over the previous 60 seconds. If the correlation between the pressures of two pumps was >0.8, the final classification of the correlation algorithm was that both pumps were co-occluding.

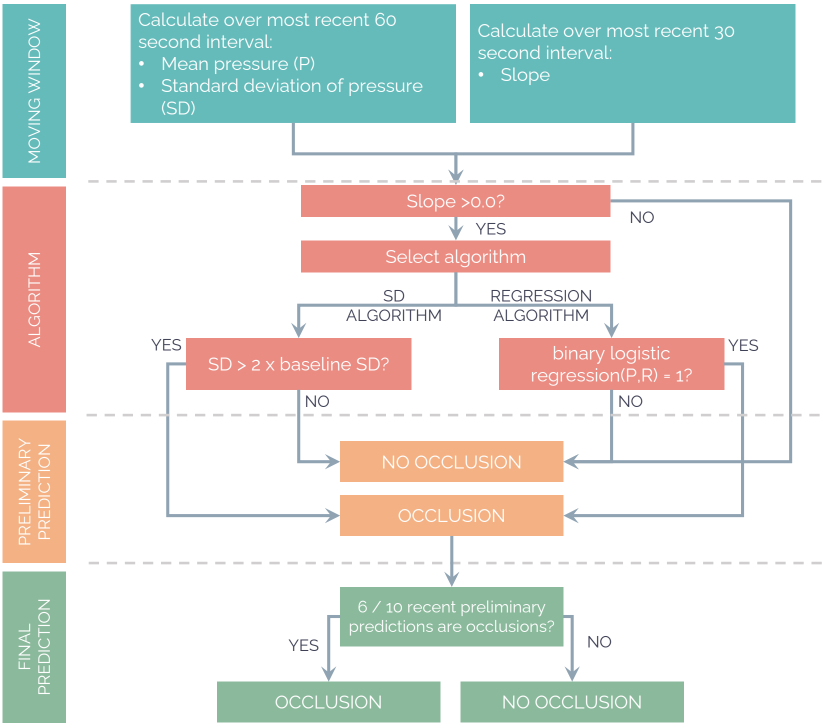

Figure 4. Flow chart of the two single-pump occlusion detection algorithms

Evaluation of algorithms

All three algorithms were programmed into custom algorithm evaluation software. The software was able to process pump log files, run each algorithm and export a report that detailed the performance of each algorithm in terms of alarm delay (min) and accuracy (percentage of correct classifications). The software also exported a .csv file for each pump with the preliminary and final occlusion classifications from the algorithm as well as correlations with other pump pressures at each time point.

The baseline single-pump measurement log files were used to evaluate the performance of the regression and SD algorithms at administration rates of 1, 2, 4, 8, 16, and 32 ml/h. The correlation algorithm was evaluated using the log files of the multi-pump scenarios. At the start of a measurement the pressure was not always immediately stable (e.g. P(t) was still increasing to a stable level), and in such case the unstable interval was omitted from analysis. The primary performance measure was alarm delay (min).

Statistics

IBM SPSS Statistics V23.0 for Windows (IBM Corporation, Armonk, NY) was used for the statistical analysis. When normally distributed the mean ±standard deviation (SD) are presented, otherwise the median and interquartile range (IQR) are shown.

By default, statistical significance was concluded at a two-sided P-value <0.05. In the single pump scenarios overall statistically significant differences in alarm delay between the regression and SD algorithms were determined using the Student's t-test. Comparisons of alarm delays of the regression and SD algorithms vs. conventional pressure threshold levels (300-800 mmHg) were evaluated using pairwise t-tests.

In the multi-pump scenarios, the alarm delay of the three algorithms was compared using a one way analysis of variance (ANOVA) with post hoc Bonferroni tests at a corrected significance level of $0.05/6 = 0.0083$.

Results

Single pump scenarios

Alarm delays for the regression and SD algorithms, and for conventional pressure limits between 300 and 800 mmHg are shown in Figure 5. Numerical values for all conventional pressure limits corresponding to Figure 5 are listed in the supplementary material (Supplementary material: Table S1). Pairwise comparisons between alarm delays of the regression and SD algorithms with our local alarm limit of 400 mmHg at different administration rates are listed in Table 1.

False negative alarms did not occur, i.e. our algorithm did not generate an alarm before the conventional pressure alarm threshold was reached. Likewise, there were no false positive alarms in the single-pump scenarios.

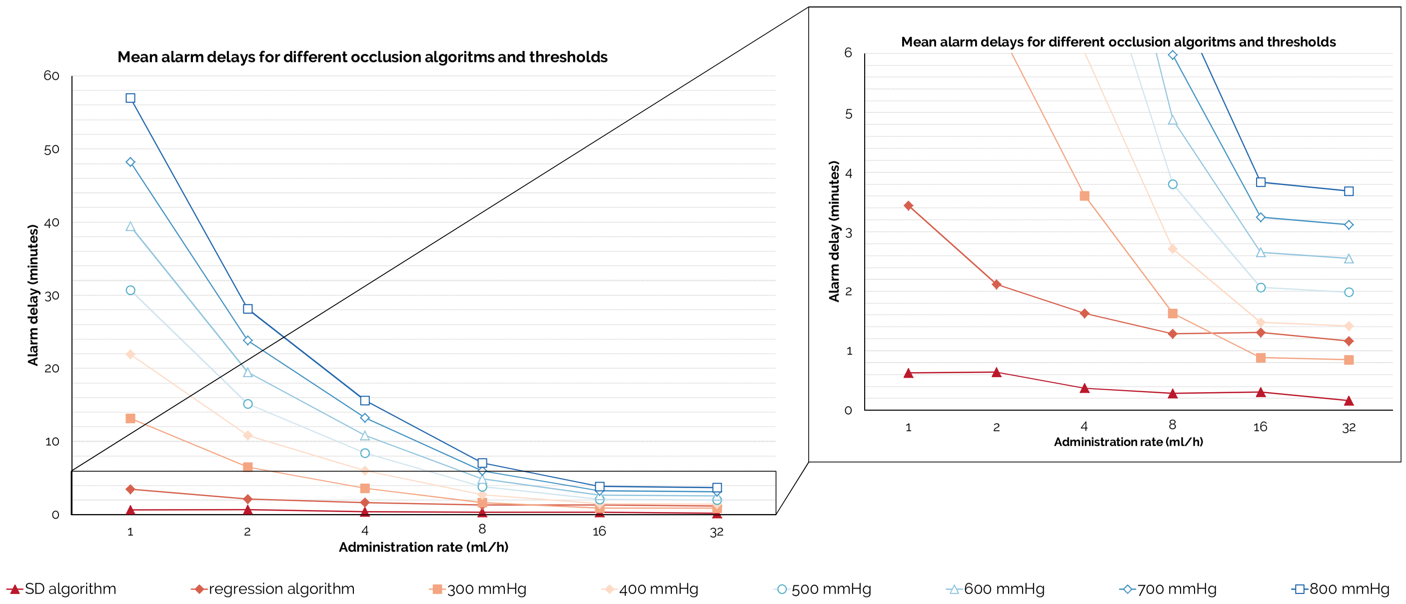

Figure 5. Mean alarm delays for calculated conventional alarm thresholds (300-800 mmHg) and the SD and regression algorithms in physical pump occlusion scenarios at different administration rates. A detailed view is shown on the right-hand side.

Table 1. Alarm delays in minutes for the regression and SD algorithms compared to calculated conventional alarm delays with an alarm threshold set at 400 mmHg

Rate	Detection algorithm	Alarm delay mean ±SD (minutes)	Conventional alarm delay mean ±SD (minutes)[a]	*P*[b]
1	SD	0.6 ±0.1	21.9 ±1.9	*<0.01*
	Regression	3.4 ±0.6		*<0.01*
2	SD	0.6 ±0.1	10.8 ±1.1	*<0.01*
	Regression	2.1 ±0.2		*<0.01*
4	SD	0.4 ±0.0	6.0 ±1.1	*<0.01*
	Regression	1.6 ±0.1		*0.03*
8	SD	0.3 ±0.0	2.7 ±0.2	*<0.01*
	Regression	1.3 ±0.1		*<0.01*
16	SD	0.3 ±0.0	1.5 ±0.1	*<0.01*
	Regression	1.3 ±0.2		*0.88*
32	SD	0.2 ±0.0	1.4 ±0.5	*0.05*
	Regression	1.2 ±0.2		*0.54*
Overall	SD	0.4 ±0.2	7.4 ±7.5	*<0.01*
	Regression	1.8 ±0.8		*<0.01*

[a] Calculated alarm delay for our local threshold setting of 400 mmHg
[b] Paired Student t-test

Multi-pump scenarios

In the multi-pump scenarios, the overall mean ±SD alarm delay of the SD algorithm (0.4 ±0.2 min) and the correlation algorithm (0.4 ±0.2 min) was lower than that of the regression algorithm (2.1 ±0.9 min), *P <0.001* in both cases. The difference in alarm delay between the SD and the correlation algorithms was not significant. False negative alarms did not occur. One false positive alarm occurred in a scenario with a combined rate of 17 ml/h. In this particular case the SD alarm was triggered for a period of 14 seconds during a brief fluctuation in pressure, after which the algorithm self-corrected.

Figure 6 shows the alarm delays for two pumps using the correlation algorithm. Alarm delays for the regression and SD algorithms can be found in the supplementary material (Supplementary material: Figures S2 and S3).

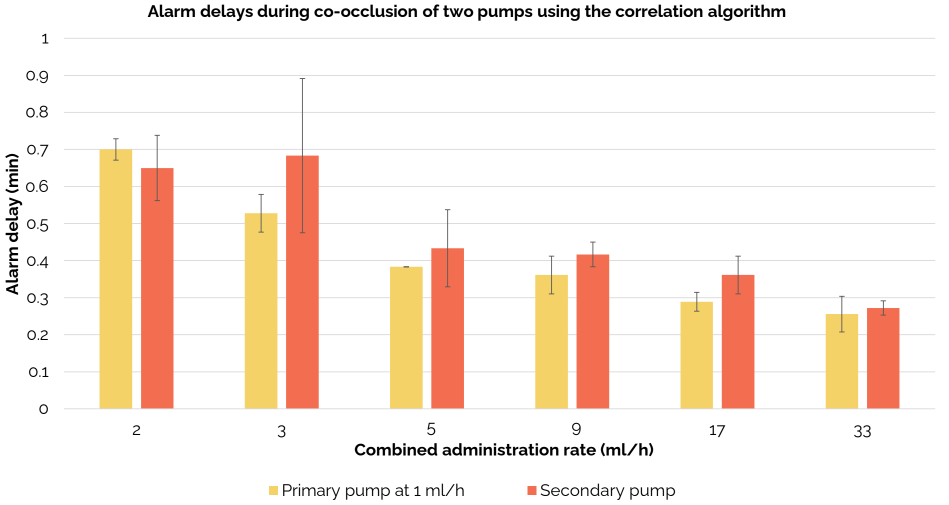

Figure 6. Mean alarm delays for two pumps during a co-occlusion. The primary pump was running at a rate of 1 ml/h in every scenario, while the rate of the secondary pump was increased, resulting in increasing combined rates.

Discussion

In this study we aimed to develop and test the performance of two single-pump occlusion detection algorithms and one multi-pump occlusion detection algorithm. In the single-pump scenarios we found that both the regression and SD algorithms were able to detect occlusions much faster than conventional pressure threshold algorithms. The SD algorithm was both faster and more accurate than the regression algorithm. In the multi-pump scenarios, the SD and correlation algorithms showed a similar performance, and both were faster and more accurate than the regression algorithm.

Compared to our local alarm threshold of 400 mmHg the mean time reduction was 52 ±34% and 90 ±6% respectively using the regression and the SD algorithms. The reduction in alarm delay was significant at administration rates ≤8 ml/h. This is an important result as conventional occlusion detection generally has a poor performance at low rates.[2]

False negative alarms did not occur. If there was an occlusion, it was always detected by our algorithms before our local conventional alarm limit of 400 mmHg was reached. A single false positive occurred during a multi-pump scenario. The low incidence of false alarms will prevent many unnecessary alarms in a clinical situation and could reduce alarm fatigue.[1]

To our knowledge there are no existing studies that investigated the feasibility of occlusion localization using the pressure measurements from multiple pumps. Our correlation algorithm was able to detect a co-occlusion with a high degree of accuracy at different combinations of administration rates. When two pumps show a coincident rise in pressure, it is likely that both pumps are affected by an occlusion located in a segment of the IV tubing that is shared between them. Such information may help nurses to pinpoint and resolve occlusions faster.

The fact that our current design obtains pressures every 2 seconds may seem an overly high sampling frequency. But in particular in multi-pump set-ups this can lead to far more rapid detection of occlusions.

During the co-occlusion of both pumps the tubing acts like a closed system with pumps at both sides. In a static closed system with fluid, Pascal's law holds. It states that pressure exerted on the fluid is transmitted almost instantaneously in all directions.[14] Therefore, using a high pressure sampling frequency makes sense and allows for rapid detection of a correlation between pressure changes detected by multiple pumps.

In the multi-pump experiments the primary pump was running at the same rate (1 ml/h) in each scenario. As the combined rate increased, the alarm delay of the primary pump decreased (Figure 6). The same phenomenon can be seen in the alarm delays of the regression and SD algorithms (Supplementary material: Figures S2 and S3). The primary pump at 1 ml/h will detect a much larger pressure increase caused by the second pump compared to a single-pump occlusion. The detection delay of a pump running at a low rate becomes shorter when it shares tubing with another pump running at a higher rate.

In our experiments the counter pressure consisted of the tubing's compliance and an artificial central venous pressure of approximately 5.2 mmHg.[10] Depending on the use of additional disposables such as filters, anti-siphon and anti-reflux valves, counter pressure may be as high as 50 mmHg in neonates and 150 mmHg in adults.[15] As our algorithms only take the deviation from the mean pressure into account (and not the absolute value of the mean itself) during occlusion detection, the alarm delay will still be relatively short, regardless of the mean baseline pressure.

Tubing compliance (the extent by which the volume increases under pressure) will have affected all scenarios as it takes some time until the system is pressurized and the pressure starts to rise throughout the tubing.[11] In order to reduce the time until a stable pressure was reached the tubing was primed prior to each run using the pumps' priming functionality.

In this study we used thin, rigid tubing and syringe pumps. In clinical practice thick, flexible tubing is also commonly used, in particular for volumetric pumps. Flexible tubing has a higher compliance and thus it will take longer before an occlusion can be detected compared to thin tubing used in this study. Similarly, when longer tubing is used a larger detection delay can be expected. We would expect that under conditions of higher compliance our algorithms would also considerably reduce the time to obstruction detection. Additional studies are required to assess the performance of our algorithms under clinical conditions where many different tubing lengths and thicknesses are used, as well as the possible impact of fluid viscosity.

Conclusion

Both the regression and SD algorithms were able to considerably reduce alarm delays in single-pump occlusion scenarios. The performance of the SD algorithm was superior to the regression algorithm in terms of alarm delay. During multi-pump occlusions the correlation algorithm reliably and very rapidly detected co-occlusions, which may also be useful to pin-point the segment of tubing in which an occlusion is present.

Acknowledgments

The authors would like to thank JunLong Xu for his assistance in this study.

Supplementary material

Supplementary material can be downloaded from https://ivcompatibility.org/thesis/supplements.html.

References

1. Sendelbach, S. & Funk, M. Alarm fatigue: a patient safety concern. *AACN Adv. Crit. Care* **24**, 378-86–8.
2. Donmez, A., Araz, C. & Kayhan, Z. Syringe pumps take too long to give occlusion alarm. *Pediatr. Anesth.* **15**, 293–296 (2005).
3. Joe, H. B., Moon, B.-K., Lee, Y.-J. & Min, S.-K. Arrangements of the intravenous parallel infusions with anti-reflux valves decreasing occlusion alarm delay. *Korean J. Anesthesiol.* **66**, 300–5 (2014).
4. Ranganathan, P., Pramesh, C. S. & Aggarwal, R. Common pitfalls in statistical analysis: Logistic regression. *Perspect. Clin. Res.* **8**, 148–151.
5. Altman, D. G. & Bland, J. M. Standard deviations and standard errors. *BMJ* **331**, 903 (2005).
6. Doesburg, F. *et al.* Improved usability of a multi-infusion setup using a centralized control interface: A task-based usability test. *PLoS One* **12**, e0183104 (2017).
7. Doesburg, F. University of Groningen Master thesis: Developing a System for Integrated Automated Control of Multiple Infusion Pumps. 1–87 (2013).
8. Richardson, M., Templeton, P. & Fry, T. *Alaris ® Syringe Pump Communications Protocol*. (2006).
9. Moore, T. & Woodrow, P. *High Dependency Nursing Care*. (Routledge, 2004).
10. Klingensmith, M. E. The Washington manual of surgery. in (eds. Aziz, A., Bharat, A., Fox, A. C. & Porembka, M. R.) 512 (Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008).
11. Managing Occlusions of the Delivery System. in *The Biomedical Engineering Handbook* (ed. Bronzino, J. D.) (CRC Press, 1999).
12. Deckert, D. *et al.* The Effects of Multiple Infusion Line Extensions on Occlusion Alarm Function of an Infusion Pump. *Anesth. Analg.* **108**, 518–520 (2009).
13. Chua, J. & Ratnavadivel, A. Comparison of flow pressures in different 3-way infusion devices: an in-vitro study. *Patient Saf. Surg.* **12**, 19 (2018).
14. Hodanbosi, C. Pascal's Principle and Hydraulics. https://www.grc.nasa.gov/www/k-12/WindTunnel/Activities/Pascals_principle.htm (1996).
15. Keay, S. & Callander, C. The safe use of infusion devices. *Contin. Educ. Anaesth. Crit. Care Pain* **4**, 81–85 (2004).