Comparison of IV oncology infusions compounded via robotics and gravimetrics-assisted workflow processes

Bob Pang, PharmD, Cleveland Clinic, Cleveland, OH

Marc Earl, PharmD, BCOP, Cleveland Clinic, Cleveland, OH

Scott Knoer, PharmD, MS, FASHP, Cleveland Clinic, Cleveland, OH, and American Pharmacists Association, Washington, DC

Angela Yaniv, PharmD, BCSCP, Cleveland Clinic, Cleveland, OH

Marc Willner, PharmD, CPHIMS, Cleveland Clinic, Cleveland, OH

Anthony Boyd, PharmD, BCPS, Cleveland Clinic, Cleveland, OH

Address correspondence to Dr. Pang (pangb@ccf.org).

Twitter: @roBOBtics

Purpose. A study was conducted to compare an intravenous (IV) gravimetric technology–assisted workflow (TAWF) platform to an IV robotic system. In the study we reviewed both IV technology platforms using the same gravimetric quality assurance system, which allowed for direct comparison.

Methods. All oncology preparations compounded from January 2016 through December 2018 using either system were included in our retrospective analysis. Final preparation accuracy, IV system precision, and workflow throughput (analyzed using lean process methodologies) were evaluated.

Results. Data analysis indicated that use of the IV gravimetric TAWF system was associated with a significantly lower percentage of accuracy errors compared to the IV robotics system (1.58% vs 2.47%, $P < 0.001$), with no significant difference in absolute precision (1.12 vs 1.12 $P = 0.952$). Lean analysis demonstrated that overall completion time (17:49 minutes vs 24:45 minutes) and compound preparation time (2:39 minutes vs 6:07 minutes) were less with the IV gravimetric TAWF vs the IV robotics system.

Conclusion. Implementation of either an IV gravimetric TAWF system or IV robotics system will result in similar compounding accuracy and precision. Preparation time was less with use of the IV gravimetric TAWF vs the IV robotic system, but the IV robotic system required less human intervention. Both systems ensure medication safety for patients, although the IV robotic system has increased safeguards in place. Therefore, the primary driver for implementing these systems is alternative factors such as cost of systems implementation and maintenance, employee safety, and drug waste.

Keywords: gravimetric, i.v. robotics, oncology, patient safety, sterile compounding

Many national organizations have published guidance to improve the safety of chemotherapy prescribing, preparation, and administration for both oral and parenteral agents across all care settings.[1-3] Estimates of the number of medical errors occurring have increased over time, with an estimated 400,000 occurring annually, and medical errors been described as the third leading cause of death behind heart disease and cancer.[4] There have been cases described in the lay press where chemotherapy preparation errors have led to patient deaths over the last 2 decades.[4,5] Chemotherapy errors resulting in patient harm have prompted changes at a local level within institutions.[6]

The Institute for Safe Medication Practices (ISMP) published revised "Guidelines for Safe Preparation of Compounded Sterile Preparations" in 2016.[2] Data submitted to ISMP have demonstrated that the manual inspection of intravenous (IV) admixture ingredients by pharmacy technicians and pharmacists is not 100% effective in preventing all preparation and dispensing errors. ISMP has stated that barcode scanning of base solution and drug ingredients should be the minimum requirement for compounded sterile preparations to ensure the correct drug and diluent are used in IV preparations. ISMP has called for organizations to have a strategic plan for implementation of automation and technology solutions for sterile compounding that augment manual processes of preparing and verifying sterile products.[2] ISMP has highlighted the importance of using bar coding and gravimetric technology in chemotherapy preparation to ensure the expected weight of drug ingredients and base solutions for each compounded product.[2] The American Society of Health-System Pharmacists (ASHP) has recommended health systems adopt automation and information technology for preparing and dispensing compounded sterile preparations.[3]

Despite recommendations from various national organizations, there is a lack of commentary by standard-setting agencies regarding sterile compounding technologies to promote patient safety in sterile hazardous compounding.[8,9]

IV compounding robotic systems were developed to improve the safety of high-risk IV compounding and provide a self-contained compounding environment to reduce hazardous medication exposure.[10-16] Few studies comparing IV robotics systems to manual compounding have been completed; however, the data on these technologies have been inconclusive.[14-16] IV technology–assisted workflow (TAWF) systems implement multiple technologies into the sterile compounding process (eg, barcode verification, image capture, gravimetric verification) to ensure proper selection of medication and diluents and to provide for standardization of the IV preparation process. The available data on use of IV TAWF systems are conflicting, with reported error rates varying by system, and are challenging to interpret given that various systems use different technologies.[17-23] Although both IV robotic systems and IV TAWF systems have been studied in comparison to manual compounding processes, there is limited literature directly comparing both types of systems directly.[24]

The study described here was designed to compare an IV robotics system and an IV gravimetric TAWF system to provide insight into similar technologies available on the market. The primary objective of the study was to evaluate the accuracy and precision of an IV robotics system and an IV gravimetric TAWF system within a single infusion center over 3 years. The secondary objectives of the study were to compare workflow throughput and types of errors identified through use of both systems.

Methods

   Hospital setting. The retrospective study was conducted at the Cleveland Clinic, Cleveland, OH, a tertiary care, academic medical center with approximately 1,400 beds. Within the Cleveland Clinic main campus, the Taussig Cancer Center has 96 infusion chairs and the center's infusion pharmacy compounds oncology infusions for all adult outpatient oncology appointments and inpatient oncology admissions. The Taussig Cancer Center infusion pharmacy has 2 APOTECAchemo robotic systems (Loccioni, Angeli di Rosaro, Italy) and 5 APOTECAps IV gravimetric TAWF systems (Loccioni) incorporated into daily compounding operations. The study was approved by the institutional review board at the Cleveland Clinic.

   Study design. All oncology preparations completed from January 2016 through December 2018 in either the IV gravimetric TAWF system or IV robotic system were considered for inclusion. The supplemental appendix describes the sterile compounding process for workflows using both technology platforms. Study data were provided through Loccioni-generated APOTECA reports from the system's internal engineering database. A summary of study data points can be found in the Box.

   Dosage accuracy. Dosage accuracy was calculated as final variance, which was defined as percent deviation of final product volume from prescribed dose. Oncology preparations were categorized as meeting or exceeding a variance threshold of ±4% based on a previously developed internal standard.[11] An accuracy error was defined for the purposes of this study as a preparation that fell outside that ±4% internal variance standard.

   Preparations that exceeded the internal ±4% variance threshold were further categorized as meeting or exceeding a ±10% threshold based on compendia standards. Any preparations that exceeded the ±10% variance threshold were automatically rejected by the

automation systems. Doses within the 4% to 10% variance threshold were evaluated by pharmacists for potential adaptation and subsequent utilization.

Dose precision. Dose precision was assessed between the IV gravimetric TAWF and IV robotic systems through distribution of final variances of completed preparations. Outliers, defined as those falling outside standard quartile ranges for dose precision, were trimmed from the analysis. A majority of the excluded outliers were preparations for which either the robot or pharmacy technician did not inject any drug product into the fluid bag, which resulted in a variance error of –100%.

Final variance was analyzed using a standard histogram and a normalized histogram to account for the difference in total numbers of preparations between systems. Distribution of final variance was assessed via a plotted qnorm function, as defined in R software (R Foundation for Statistical Computing, Vienna, Austria). Final variance was analyzed on the basis of mean variance and absolute mean variance, including associated standard deviations, to assess the distribution and precision of both workflows. Precision was assessed as the frequency of negative variance deviation (ie, the percentage of preparations that were underfilled) and magnitude of accuracy errors. The magnitude of accuracy errors (average absolute delta) was determined by calculating the absolute mean difference between the final variance and the ±4% variance threshold for preparations where an accuracy error occurred. This mean and standard deviation provided an evaluation of the magnitude of the variance deviation from accepted thresholds when an accuracy error occurred.

Error types and lean value stream map. Error types were separated into 4 categories: operator, wrong-diluent, wrong-drug, and preparation errors. Operator errors were related to deviations from the standard operating procedure of established workflows

(eg, scanning of an incorrect final item barcode). Wrong-diluent and wrong-drug errors were discrepancies between the prescribed components in a preparation and what was staged for preparation in both systems. Preparation errors were issues related to the compounding process, including failure of intermediary quality assurance checks and hardware faults.

Beginning in 2018, the gravimetric-assisted TAWF system received an upgrade that prompted pharmacy technicians to voluntarily adjust a final product dose closer to the prescribed amount, even when variance was within the accepted ±4% internal threshold. This voluntary prompt was recorded as an error despite quality assurance appropriateness. Preparation errors were indicated via a secondary statistic, with these events removed from the accuracy analysis, results of which are referred to herein as corrected error rates.

Error statistics, timestamps of compounding steps, and accuracy errors were used to generate a lean value stream map (VSM) of process times and first-pass yield (FPY). A lean VSM was used as a tool to graphically display efficiency metrics for individual workflow steps for the 2 platforms. Average process times were calculated for time prior to preparation, preparation time, and final validation time. FPY for each process step and overall FPY were used to identify the number of final products that would exit each process cell without human intervention or rework. Only drug products that could be compounded on both platforms (Appendix A) were analyzed in the lean VSM.

Statistical analysis. Data analysis was completed using Stata/IC 13.1 software (StataCorp LLC, College Station, TX) and Microsoft Excel (Microsoft Corporation, Redmond, WA). A quasi-experimental retrospective data analysis model was used. Differences in accuracy error rates between the IV gravimetric TAWF system and IV robotic system workflows were assessed using χ^2 analysis. Variance distribution between workflows was

assessed using Student's *t* test. A *P* value of ≤0.05 was considered to be statistically significant. Secondary outcomes were assessed through descriptive analysis.

Results

A total of 60,329 preparations were compounded using the APOTECAchemo IV robotics system (*n* = 42,129) and APOTECAps IV gravimetric TAWF system (*n* = 18,136) during the study period. Appendix A lists the oncology medications compounded through each automation workflow during the study period.

Dose accuracy. In the overall combined data set, there was a significant difference in accuracy error rates between the IV robotic system and IV gravimetric TAWF system (2.47% vs 1.58%, *P* < 0.001) (Table 1). Use of the IV robotics system was demonstrated to results in improvement in accuracy rates over the study period: from 3.11% in 2016 to 2.56% in 2017 and to 2.03% in 2018. Use of the IV gravimetric TAWF system was shown to results in larger improvements in accuracy rates over the study period: from 8.20% in 2016 to 2.37% in 2017 and to 0.89% in 2018 (Table 2). Quantities of preparations between ±4% and 10% variance, as a percentage of total accuracy errors, were comparable (75% vs 77.7%). The proportions of preparations exceeding the >10% variance standard were similar as well (25% vs 22.3%).

Dosage precision. Figure 1 displays the distribution of final variance for preparations between the 2 systems. The IV robotic system variance was centrally distributed around a single peak, with a slight left bias from the 0 point. There appeared to be a secondary peak centered around the −2% variance; however, this was an artifact of one misconfigured drug in the automation system drug library that was updated.

The IV gravimetric TAWF system variance was centrally distributed around a single peak over the 0 point, and the distribution was broader than that for the IV robotic system.

Figure 2 demonstrates a normalized histogram of variance based on occurrence as a percent of total doses, in which the distribution becomes more similar between the 2 systems.

There was a significant difference in average variance between the IV robotic system and IV gravimetric TAWF system (mean [SD], –0.79% [1.33%] vs –0.51% [1.46%]; $P < 0.001$), which corresponded to the left bias seen in Figures 1 and 2. There is no significant difference in mean (SD) absolute variance between the IV robotic system and IV gravimetric TAWF system (1.12% [1.07%] and 1.12% [1.07%], respectively; $P = 0.952$) (Table 3).

There was a statistically significant between-system difference in the magnitude of accuracy errors, with use of the IV robotic system resulting in a smaller percentage of accuracy errors in comparison to use of the IV gravimetric TAWF system (mean [SD], 0.84% [1.68%] and 1.91% [3.05%], respectively; $P < 0.001$) (Table 3). For both systems there was a consistent change in precision statistics over time during the 2016-2018 period (Table 4).

Errors and productivity analysis. 16,608 errors were assessed through analysis of data available from the final report. Table 7 summarizes data on frequency of errors in each of the 4 categories for products that could be associated to a completed preparation ($n = 9,800$). The IV gravimetric TAWF system had a greater absolute and percent error rate in comparison to the IV robotic system (an 8.73% error rate vs a 19.11% corrected error rate). This difference in error rates was primarily driven by wrong-diluent and wrong-drug scanning in the IV gravimetric TAWF system (11.43% of errors) vs the IV robotic system (1.52% of errors).

Using these error rates and timestamps, a lean VSM was generated and is shown in Figure 3. The VSM shows the robot workflow had greater process times in the steps prior to preparation and during preparation. Drug orders designated for preparation using the IV robotic system spent more time prior to preparation (13:57 minutes vs 10:23 minutes), and

more time being compounded or prepared (6:07 minutes vs 2:39 minutes) when compared to those prepared using the IV gravimetric TAWF system. The increased average process time was offset by higher FPY in both process cells (97.5% vs 88.1% for time to start preparation and 93.6% vs 91.3% *[corrected]* for preparation time), which demonstrated that more human intervention was required with use of the IV gravimetric TAWF system to address deviations from standard operating procedures.

Discussion

Given the importance of safety and accuracy when compounding chemotherapy preparations, it is critical that IV automation systems are designed to minimize errors. To our knowledge, ours was the first study to directly compare an IV robotics system and an IV gravimetric TAWF system.

Accuracy. Our study identified a significant difference in accuracy error rates for completed IV preparations, with IV gravimetric TAWF workflows proving to be more accurate than use of the IV robotics system within our data (2.47% vs 1.58%, *P* = 0.028). Previous studies compared manual IV compounding processes to IV robotic workflows and demonstrated a 2- to 3-fold improvement in accuracy.[14,16] When comparing our results with findings in other robotics studies, the accuracy error rates we documented were lower than that reported by Masini et al[15] (mean [SD], 3.8% [5%]) but higher than those reported by Yaniv et al[11] (mean [SD], 1.8% [4%]) and Seger et al[14] (mean [SD], 1.6% [5%]). Although it is challenging to compare accuracy across different robotics systems and institutional workflows, 3 of the pertinent studies (the studies by Yaniv et al[11] and Masini et al[15] and the study described here) involved use of the same IV robotics platform, which provides for more robust comparison. Of note, relative to those other 2 studies, our study evaluated an

increased number of medications (*n* = 25) and an increased number of preparations (*n* = 42,219) over a longer study period and is therefore likely the best representation of accuracy error rates over a prolonged period of routine usage. There was 1 study that analyzed an IV gravimetric TAWF system; however, due to differences in workflow it is not a reliable comparator to our study.[23]

Given that initial IV robotics studies demonstrated significant improvements in comparison to IV manual compounding processes, the results of our study demonstrating increased accuracy of final preparations with use of the IV gravimetric TAWF system may be unexpected. During the manual IV preparation of sterile compounds, the intermediate quality assurance (QA) check relies on pharmacy technician and/or pharmacist visual examination. There is potential for variation in interpretation of syringe markings by different individuals and inherent variability in syringe manufacturing that allows for certain tolerances. These factors result in very limited and potentially inaccurate feedback being presented to technicians during QA checks. These limitations are one of the many reasons that robotic compounding is growing in popularity, given that mechanical and gravimetric checks throughout the workflow are able to remove much of the subjectivity and variability present in manual processes.

IV gravimetric TAWF systems, which include QA checks similar to those enabled by IV robotic systems, also address the limitations present in manual compounding. The detailed percentage variance report provides more granular and consistent feedback to technicians to help meet quality thresholds. Technicians are able to gain practical feedback in mitigating interdrug and syringe variability that may be present (eg, in preparation of small-volume syringes where variability in syringe markings may result in large percent variance deviations in gravimetric measurements).

An important note: Our study demonstrated improvements over time for both systems. With regard to the IV robotics system, this finding can be explained by the platform receiving regular software upgrades to improve accuracy across the medication library. As for the improved results seen with the IV gravimetric TAWF system, the large accuracy improvement is more difficult to explain. There is no clear explanation supported by the data collected within the study of the rationale behind improvement over time seen within the IV gravimetric TAWF system. However, the results warrant further study.

While we identified a significant difference in accuracy rates between the IV robotics system and IV gravimetric TAWF system, it is important to acknowledge that the majority of accuracy errors that occurred would not have been considered clinically significant, with weight deviations ranging from 4% to 10%. As reported in our study, only 0.5% of 60,625 preparations across both platforms had weight deviations greater than 10% and were therefore automatically rejected by the system in use. Although use of the robot resulted in a slightly higher percentage of errors that exceeded 10% variance, the IV robotic system and IV gravimetric system had the same error percentage in 2018 and the figures improved for both systems over time. In addition, the IV robotic system, by design, has a propensity to underfill preparations, resulting in preparations that can be most often be corrected manually.

Precision. There were no significant differences in precision or final variances found between the two systems. The low final variances recorded for the IV robotics system (mean [SD], 1.12% [1.07%]) correlate with results of other studies that evaluated dose deviations.[14,16] For the IV robotics system, there was very little change in this metric over time from 2016 through 2018. These results were expected, as IV robotic systems have the benefit of robotic precision achieved through designed engineering tolerances. There were

not any major changes in precision over time, given that the system did not undergo any significant hardware changes. Interestingly, the IV gravimetric TAWF system also had the same mean (SD) variation (1.12% [1.07%]). The system demonstrated improvements in average absolute variance over time from 2016 through 2018. One of the main drivers of choosing IV robotics systems over manual IV compounding processes is the purported benefits of robotic precision, which should result in less variation in drug doses prepared. In our study, we were able to demonstrate comparable precision with a pharmacy technician manually preparing IV oncology infusions in a guided fashion with gravimetric verification steps.

A potential explanation for the similarity in precision seen between the 2 systems is the guided feedback being provided to pharmacy technicians compounding doses. As mentioned above, the feedback being provided allows technicians to minimize the effect of interdrug and syringe variability and allow for more precisely drawn-up doses on the initial withdrawal and injection. In addition to this, beginning in 2018 the system began to prompt pharmacy technicians on whether they would like to adjust the dose for preparations that already met acceptable dose deviation thresholds (ie, ±4%). This voluntary change in dose preparations, which the pharmacy technicians often undertook, likely drove the improvement in precision seen from 2017 to 2018. Notably, the improvement from 2016 to 2017 was most likely caused by sample size differences, as data for this period were collected post implementation of the first IV gravimetric TAWF system in the latter part of 2016.

While the overall final variance figures for both systems were similar, it is important to note that there were 2 significant differences between the 2 systems related to precision. The IV robotic system has a tendency to underfill preparations, which can be seen with the

left bias in final variance in both Figures 1 and 2. In addition, the IV robotic system, when making an accuracy error, tends to deviate less from accepted variance thresholds than the IV gravimetric TAWF system (mean [SD] deviation, 0.84% [1.68%] vs 1.91% [3.05%]; $P < 0.001$). While there was no overall difference in variance between the 2 systems, the IV robotic system had an advantage when it came to salvaging failed preparations, as underfilled preparations are more easily adjusted by adding drug to reach the prescribed dose. Oftentimes, overfilled preparations cannot be salvaged and therefore have to be wasted; therefore, an IV robotic system has an advantage over an IV gravimetric TAWF system in this regard. Both of these are purposeful engineering features of the IV robotics system compared to the IV gravimetric TAWF system.

Error types and efficiency. Error rates between the 2 systems differed considerably based on available data in Table 6. This is the first study to our knowledge to describe error types experienced during use of 2 different IV automation systems.

Operator errors are primarily comprised of incorrect barcode scans of system-generated barcodes. The IV robotic system was associated with a lower percentage of operator errors, which was expected as operation of the IV robotic system is much more regimented, with specific scan and loading steps that must be done in sequence with no deviation.

There were considerably more wrong-diluent (fluid bag) and wrong-drug errors with use of the IV gravimetric TAWF system vs the IV robotic system. Given that both systems require a pharmacy technician to stage the diluent and drug product before compounding, one might expect the error rates to be similar. However, there are differences in workflow that can explain these findings, including (1) pictorial guidance within the IV robotic system on loading of materials and (2) staging of materials being performed by different pharmacy

technician outside of an IV engineering control in the IV gravimetric TAWF system workflow. In both systems, the barcode scans need to happen in a specific order; therefore, the errors captured by the system may be inflated by technicians scanning diluent bags and drug product out of order. These errors would not represent true instances of incorrect products being selected for compounding; rather, they result from the system capturing technicians scanning the correct drug and diluent but doing so in an incorrect sequence. It is important to note that despite the difference in errors seen with these 2 systems, the systems are designed to identify and correct these errors in order to ensure correct drug and diluent selection before beginning IV compounding.

Compounding errors during use of the IV robotic system are primarily comprised of mechanical faults such as calibration errors with sensors or robotic actuators. Compounding errors seen with use of IV gravimetric TAWF systems are primarily comprised of dose adjustments reported to the pharmacy technician or reconstituted drug adjustments prior to final preparation. The difference in compounding errors was primarily driven by the voluntary dose adjustment prompt implemented in 2018. If these voluntary "errors" had been expressed in terms of a corrected error rate, the difference between the systems would have become less substantial. This category of error type is not easily compared.

The lean value stream map generated from study data seen in Figure 4 demonstrates the differences in time and FPY seen within both systems. There was a notable difference in preparation times (2:39 minutes vs 6:07 minutes) in favor of the IV gravimetric TAWF system compared to the IV robotics system. This finding was expected and corroborated by previous literature demonstrating the challenges with throughput in IV robotics systems. [14-15,24] Pharmacy technicians performing IV compounding are more dexterous compared to a robotic actuator arm designed to mimic human movement, which limits the efficiency of

many current IV robotic systems on the market. The IV robotic system also has additional safety checks built into compounding workflow to ensure that each withdraw and injection are performed as programmed, which contributes to the increased compounding time (Figure 1). In addition, certain sites that use robotics systems have developed optimization strategies such as batching and limiting compounding to certain drugs. These strategies were not used in the Taussig Cancer Center infusion pharmacy and may have decreased preparation times.

On comparing data for time to start preparation for the IV gravimetric TAWF system vs IV robotic system workflow, there was a difference (10:23 minutes vs 13:57 minutes), which can be explained by a queuing effect that was multifactorial. The pharmacy technicians using the IV gravimetric system are often more readily available to be tasked with compounding medications requiring a quicker turnaround time, whereas medications due later are often queued in the IV robotics system. There were more available IV gravimetric TAWF platforms within our pharmacy (5 IV gravimetric TAWF systems vs two 2IV robotic systems), which might have contributed to increased queuing. In addition, the time to start preparation includes a longer queue time, as individual preparations in the lean VSM will be impacted by the difference in compounding speed between the 2 systems. The IV robotic system has additional QA checks performed during the staging/loading process prior to the start of the preparation process.

There was no significant difference between the 2 systems in terms of final validation, as the final variance reports on preparations compounded with the 2 systems were similar.

The results of the lean VSM demonstrated that overall preparation time per individual preparation was faster in the IV gravimetric TAWF system; however, this was

partially offset by the need for additional human intervention in the periods of time before and during IV compounding. Our results differed from those of the study by Bhakta et al.[24] That study also compared an IV TAWF system with an IV robotic system. Bhakta et al found a decrease in turnaround time between the 2 systems in favor of the IV robotic system. However, it should be noted that the IV TAWF system used in the study of Bhakta et al was not described as performing gravimetric verification. In addition, Bhakta et al recorded preparation times that showed an improvement of aggregate preparation times from technician to robot (44.2 minutes vs 34.7 minutes) when comparing similar time slices, which was unique to their study. These factors suggested significant variation in workflow processes in comparison to our study.

Due to the additional safety parameters, the IV robotics system is considered the gold standard from a patient and staff safety perspective. However, the findings from our study illustrate that preparation with the IV gravimetric TAWF system was faster than with the IV robotic system, with comparable accuracy and precision. Many of the current IV robotic systems on the market have been designed with a robotic actuator arm designed to mimic human movement, which limits the overall efficiency and throughput of these IV systems. The pressure on pharmacy departments to be more efficient and cost-effective highlights the limitations of throughput as a concern with the current generations of IV robotic systems. Given the cost of implementation and maintenance of IV robotic systems, there are many sites that are unable to justify these expenses when implementation of an IV gravimetric TAWF system could provide similar outcomes. In order for IV robotic systems to remain cost-effective in a competitive market, automation vendors must continue to design more efficient systems while maintaining a level of safety and efficacy demanded of these products. Ultimately, the next generation of IV robotic systems must be more efficient than

their human counterparts, increase productivity, provide an increased level of safety in complex processes, and lower operating costs.

There were limitations of our study that should be acknowledged. The retrospective design of our analysis meant data available was dependent on the engineering reports the vendor was able to provide. There was a potential for underreporting of accuracy error rates for the IV gravimetric TAWF system due to reporting limitations; however, additional data validation analysis demonstrated the effect was insignificant. The wide SD ranges for precision metrics was another potential weakness in the data analysis. Precision was measured as an aggregate of all oncology preparations completed, even though there is known variability in the ability of both the robot and technicians to achieve a fixed level of precision due to numerous factors that were not examined in our analysis. Future research that compares precision should take into account these potential confounding factors (eg, volume, dose, geometry of components).

There was also potential for overreporting error rates with use of the IV gravimetric TAWF system through voluntary dose adjustments being coded as errors, which we captured through the corrected error rate. There were slight differences in workflows between the IV gravimetric TAWF system and IV robotic system, but comparison was possible because such differences were minimized, given that both platforms are designed by the same automation vendor. Since our department had already begun using these IV automation systems in practice, we were not able to compare them to completely manual IV compounding processes. As our study was a single-center analysis, the results may not be generalizable to institutions with vastly different IV automation systems.

Conclusion

The study demonstrated that implementation of either an IV gravimetric TAWF system or an IV robotics system will result in similar accuracy and precision in preparation of oncology infusions. Both systems are also able to effectively prevent medication errors in IV compounding from reaching the patient. Preparation time was less with use of the IV gravimetric TAWF system, but the IV robotic system required less human intervention. Both systems in our practice are used interchangeably. Therefore, the decision as to which system to implement will be dictated by other factors such as drug waste, financial costs (eg, closed-system transfer device costs, personnel costs, system costs, implementation costs), physical space availability for various automation systems, and/or employee safety considerations (eg, repetitive strain injury, hazardous drug exposure, USP chapter 800 compliance). Future work will be required to effectively quantify these factors within other health systems and to address data limitations of our study.

Disclosures

The authors have declared no potential conflicts of interest.

References

1. Neuss MN, Gilmore TR, Belderson KM, et al. 2016 updated American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards, including standards for pediatric oncology. *Oncol Nurs Forum.* 2017;44(1):31-43.

2. Institute for Safe Medication Practices. *Guidelines for Safe Preparation of Compounded Sterile Preparations.* https://www.ismp.org/sites/default/files/attachments/2017-11/Guidelines%20for%20Safe%20Preparation%20of%20Compounded%20Sterile%20Preperations_%20revised%202016.pdf. Revised 2016. Accessed July 30, 2019.

3. American Society of Health-System Pharmacists. ASHP policy positions: automation and information technology. https://www.ashp.org/-/media/assets/policy-guidelines/docs/policy-positions/policy-positions-automation-information-technology.ashx?la=en&hash=1D84F59B06027E2138FE8E74F78A06B23DB517BC. Accessed July 30, 2019.

4. Makary MA, Daniel M. Medical error—the third leading cause of death in the US. *BMJ.* 2016;353:i2139.

5. Marquard B. Mildred Lehman, launched campaign to reduce medical errors. Boston Globe, April 15, 2012. https://www.nytimes.com/1995/03/24/us/big-doses-of-chemotherapy-drug-killed-patient-hurt-2d.html?pagewanted=all Accessed June 16, 2019.

6. McCoy K, Brady E. Rx for errors: drug error killed their little girl. ABC News website. https://abcnews.go.com/Business/story?id=4338158&page=1. Published March 6, 2008. Accessed June 16, 2019.

7. Fischer DS, Alfano S, Knobf MT, et al. Improving the cancer chemotherapy use process. *J Clin Oncol*. 1996;14:3148-3155.

8. Pharmaceutical compounding—sterile preparations (general information chapter 797). In: The United States pharmacopeia, 40th rev., and the national formulary, 35th ed. Rockville, MD: United States Pharmacopeial Convention; 2017.

9. Hazardous drugs—handling in healthcare settings (general information chapter 800). In: The United States pharmacopeia, 40th rev., and the national formulary, 35th ed. First Supplement. Rockville, MD: United States Pharmacopeial Convention; 2017.

10. Chen WH, Shen LJ, Guan RJ, et al. Assessment of an automatic robotic arm for dispensing of chemotherapy in a 2500-bed medical center. *J Formos Med Assoc.* 2013;112(4):193-200.

11. Yaniv AW, Knoer SJ. Implementation of an i.v.-compounding robot in a hospital-based cancer center pharmacy. *Am J Health-Syst Pharm*. 2013;70(22):2030-2037.

12. Nurgat Z, Faris D, Mominah M, et al. A three-year study of a first-generation chemotherapy-compounding robot. *Am J Health-Syst Pharm.* 2015;72(12):1036-1045.

13.   Palma E, Bufarini C. Robotized compounding of oncology drugs in a hospital pharmacy. *Int J Pharm Compd*. 2014;18:358-364.

14.   Seger AC, Churchill WW, Keohane CA, et al. Impact of robotic antineoplastic preparation on safety, workflow, and costs. *J Oncol Pract.* 2012;8(6):344-349.

15.   Masini C, Nanni O, Antaridi S, et al. Automated preparation of chemotherapy: quality improvement and economic sustainability. *Am J Health-Syst Pharm.* 2014;71(7):579-585.

16.   Iwamoto T, Morikawa T, Hioki H, et al. Performance evaluation of the compounding robot, APOTECAchemo, for injectable anticancer drugs in a Japanese hospital. *J Pharm Health Care Sci.* 2017;3:12.

17.   O'Neal BC, Worden JC, Couldry RJ. Telepharmacy and bar-code technology in an i.v. chemotherapy admixture area. *Am J Health-Syst Pharm*. 2009;66(13):1211-1217.

18.   Speth SL, Fields DB, Schlemmer CB, et al. Optimizing i.v. workflow. *Am J Health-Syst Pharm.* 2013;70(23):2076, 2078-2080.

19.   Moniz TT, Chu S, Tom C, et al. Sterile product compounding using an i.v. compounding workflow management system at a pediatric hospital. *Am J Health-Syst Pharm*. 2014;71(15):1311-1317.

20.   Deng Y, Lin AC, Hingl J, et al. Risk factors for i.v. compounding errors when using an automated workflow management system. *Am J Health-Syst Pharm.* 2016;73(12):887-893.

21.   Wright KR, Dekarske B, Clark JS, Chaffee B. Parenteral product error detection before and after implementation of intravenous workflow management technology [published online ahead of print August 4, 2017]. *J Oncol Pract.* 2017. doi:10.1177/1078155217723695.

22.   Eckel SF, Higgins JP, Hess E, et al. Multicenter study to evaluate the benefits of technology-assisted workflow on i.v. room efficiency, costs, and safety. *Am J Health-Syst Pharm*. 2019;76(12):895-901.

23.   Reece KM, Lozano MA, Roux R, et al. Implementation and evaluation of a gravimetric i.v. workflow software system in an oncology ambulatory care pharmacy. *Am J Health-Syst Pharm.* 2016;73(3):165-173.

24.   Bhakta SB, Colavecchia AC, Coffey W, Curlee DR, Garey KW. Implementation and evaluation of a sterile compounding robot in a satellite oncology pharmacy. *Am J Health-Syst Pharm.* 2018;75(suppl 2):S51-S57.

Figure 1. Histogram of final variance between intravenous (IV) robotic system (APOTECAchemo) and IV gravimetric technology–assisted workflow system (APOTECAps).

Figure 2. Normalized histogram of final variance between intravenous (IV) robotic system (APOTECAchemo) and IV gravimetric technology–assisted workflow system (APOTECAps).

Figure 3. Lean value stream map for intravenous (IV) gravimetric technology–assisted workflow system (APOTECAps) compared to IV robotic system (APOTECAchemo). Asterisk denotes frequency of preparation errors excluding those involving voluntary dose adjustments performed by a pharmacy technician.

Key Points

- A study was conducted to compare an intravenous (IV) robotics system to an IV gravimetric technology–assisted workflow (TAWF) system by examining all mixtures prepared at a major cancer center for accuracy, precision, and measures of efficiency.

- Data analysis indicated that compared to the IV robotics system, the IV gravimetric TAWF system was similarly accurate, similarly precise, and completed compounding more quickly; however, differences were slight.

- The decision of whether an institution should use either technology will be dependent on other factors such as cost, employee safety, and waste.

Table 1. Dose Accuracy Analysis of IV Robotic System (APOTECAchemo) and IV Gravimetric TAWF System (APOTECAps)

System and Variance Analysis	APOTECAchemo (n = 42,129)	APOTECAps (n = 18,136)	P Value
Accuracy error, No. (%)	1,042 (2.47)	287 (1.58)	<0.001
Preparations with 4%–10% variance, No. (%)	782 (1.86)	223 (1.23)	<0.001
Preparations outside 10% variance threshold, No. (%)	260 (0.62)	64 (0.35)	<0.001

Abbreviations: IV, intravenous; TAWF, technology-assisted workflow.

Table 2. Dose Accuracy of IV Robotic System (APOTECAchemo) and IV Gravimetric TAWF System (APOTECAps), 2016–2018

| System and Variance Analysis | 2016 (*n* = 10,867) | | 2017 (*n* = 21,160) | | 2018 (*n* = 28,238) | |
	APOTECAchemo (*n* = 10,684)	APOTECAps (*n* = 183)	APOTECAchemo (*n* = 13,623)	APOTECAps (*n* = 7,537)	APOTECAchemo (*n* = 17,822)	APOTECAps (*n* = 10,416)
Accuracy errors, No. (%)	332 (3.11)	15 (8.20)	349 (2.56)	179 (2.37)	361 (2.03)	93 (0.89)
Preparations with 4%–10% variance, No. (%)	188 (1.76)	10 (5.46)	264 (1.94)	138 (1.83)	330 (1.85)	75 (0.72)
Preparations outside 10% variance threshold, No. (%)	144 (1.35)	5 (2.73)	85 (0.62)	41 (0.54)	31 (0.17)	18 (0.17)

Abbreviations: IV, intravenous; TAWF, technology-assisted workflow.

Table 3. Dose Precision Statistics for IV Robotic System (APOTECAchemo) and IV Gravimetric TAWF System (APOTECAps)

System and Variance Analysis	APOTECAchemo (*n* = 42,129)	APOTECAps (*n* = 18,136)	*P* Value
No. of accuracy errors	1,042	287	<0.001
Underfilled preparations (outside variance), No. (%)	1,025 (98.4)	139 (48.4)	<0.001
Average variance, mean (SD)	−0.79 (1.33)	−0.51 (1.46)	<0.001
Average absolute variance, mean (SD)	1.12 (1.07)	1.12 (1.07)	0.952
Average absolute delta, mean (SD)	0.84 (1.68)	1.91 (3.05)	<0.001

Abbreviation: IV, intravenous; TAWF, technology-assisted workflow.

Table 4. Dose Precision Statistics for IV Robotic System (APOTECAchemo) and IV Gravimetric TAWF System (APOTECAps), 2016-2018

System and Variance Analysis	2016 (*n* = 10,867)		2017 (*n* = 21,160)		2018 (*n* = 28,238)	
	APOTECAchemo (*n* = 10,684)	APOTECAps (*n* = 183)	APOTECAchemo (*n* = 13,623)	APOTECAps (*n* = 7,537)	APOTECAchemo (*n* = 17,822)	APOTECAps (*n* = 10,416)
No. of preparations outside variance	332	15	349	179	361	93
Underfilled preparations, No. (%)	332 (100)	6 (40.0)	345 (98.9)	97 (54.2)	348 (96.4)	36 (38.7)
Average variance, mean (SD)	−0.61 (1.38)	0.11 (2.81)	−0.87 (1.27)	−0.65 (1.61)	−0.85 (1.32)	−0.41 (1.29)
Average absolute variance, mean (SD)	1.05 (1.09)	1.53 (2.36)	1.13 (1.04)	1.28 (1.18)	1.15 (1.08)	1 (0.91)
Average absolute delta, mean (SD)	1.35 (2.48)	5.58 (7.49)	0.57 (0.77)	1.91 (2.81)	0.75 (1.58)	1.27 (1.40)

Abbreviations: IV, intravenous; TAWF, technology-assisted workflow.

Frequency and Error Type	APOTECAchemo n=42129	APOTECAps n=18136
Total **[N (%)]**	3677 (8.73)	6123 (33.76) *3468 (19.11)

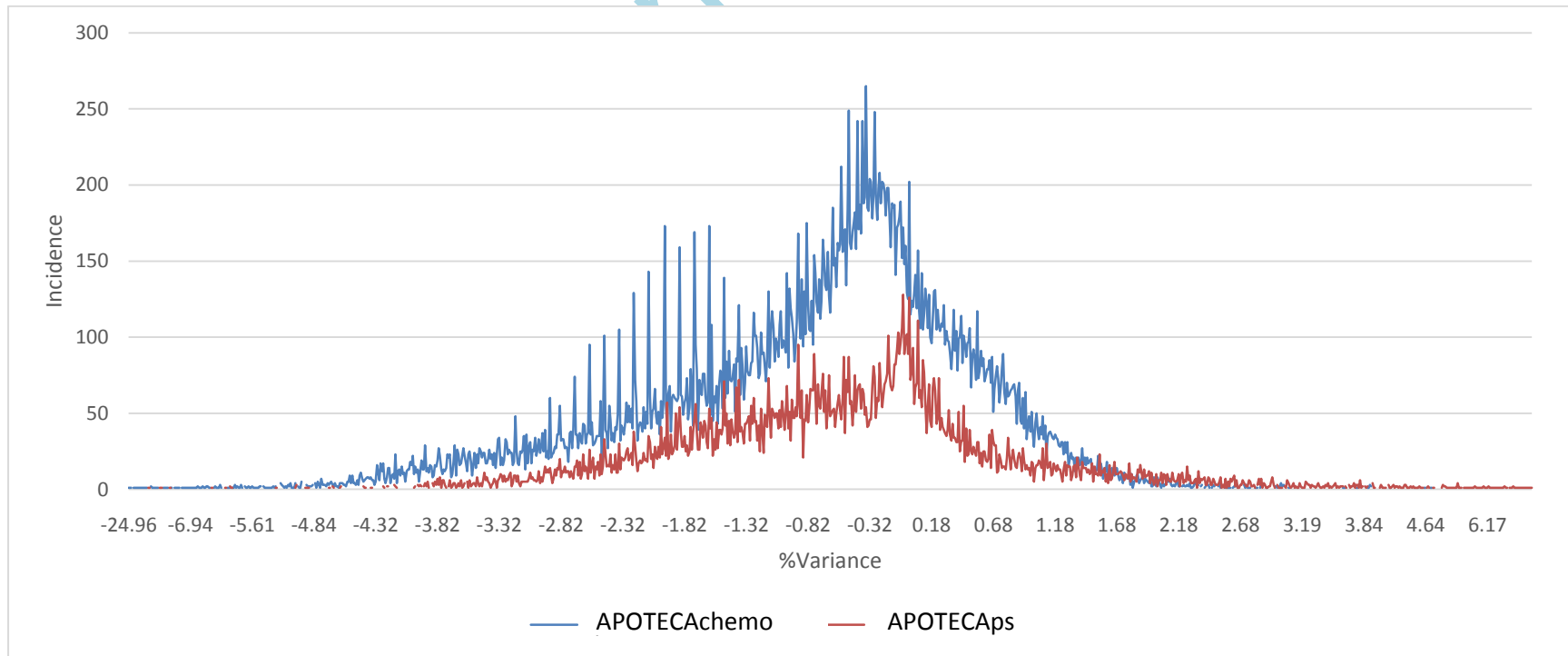|		
Operator	409 (0.97)	89 (0.49)
Wrong Diluent	580 (1.38)	1136 (6.26)
Wrong Drug	59 (0.14)	937 (5.17)
Preparation	2629 (6.24)	3961 (21.84) *1306 (7.20)

Table 5. Frequency and Types of Errors Identified in Review of IV Robotic System (APOTECAchemo) and IV Gravimetric TAWF System (APOTECAps)

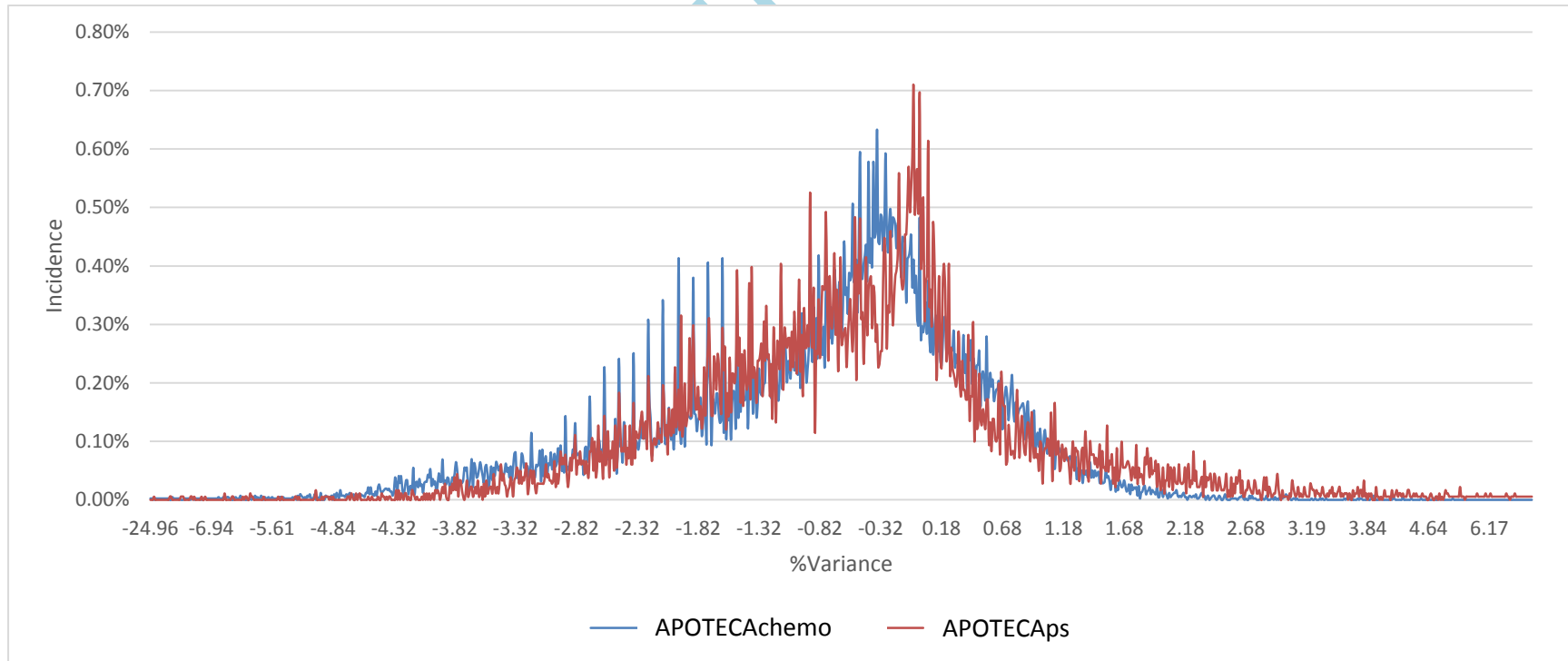|	APOTECAchemo (*n* = 42,129)	APOTECAps (*n* = 18,136)
All errors, No. (%)	3,677 (8.73)	6,123 (33.76)
		3,468 (19.11)[a]
Errors by type, No. (%)		
Operator	409 (0.97)	89 (0.49)
Wrong diluent	580 (1.38)	1,136 (6.26)
Wrong drug	59 (0.14)	937 (5.17)
Preparation	2629 (6.24)	3,961 (21.84)
		1,306 (7.20)[a]

Abbreviations: IV, intravenous; TAWF, technology-assisted workflow.

[a]Denotes error count (frequency) after exclusion of preparations corrected by pharmacy technicians through voluntary dose adjustments.

[Fig 1]

[Fig 2]

[Fig 3]