Assessment of an automatic robotic arm for dispensing of chemotherapy in a 2500-bed medical center

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Received 16 May 2011; received in revised form 1 November 2011; accepted 15 November 2011

Background/Purpose: Automation has long been awaited in parenteral drug dispensing. Pharmacists can benefit much in theory from a good automated device to handle the hazardous drugs used in chemotherapy. This paper describes the performance of the first chemotherapy-dispensing robot in the oncology pharmacy of a 2500-bed medical center. The objective of this paper is two-fold: (1) to assess the robot's performance in terms of its success rate and to summarize the causes of failure, and (2) to find out if the robot can decrease the full-time equivalents (FTEs) of the oncology pharmacy.

Methods: We used the computer-generated log from the first week of May 2010 to that of July 2010, supplemented with the pharmacists’ notes on the causes of failure, to determine the success rate and to analyze the incidences of failure. We also assessed the FTEs before and after implementing the robot.

Results: Data showed that the success rate rose slowly from 76.8% to 95.3% over the 2-month recording period. The major mechanical problems encountered were air, clamping, and waste bin problems. Manual errors, such as loading wrong drugs or syringes, also caused failures. In terms of manpower saving, CytoCare failed to decrease the number of FTE pharmacists/technicians in our oncology pharmacy practice.

Conclusion: We conclude that even though CytoCare could ease the risk of chemotherapy exposure and increase the precision of dosing, it was not able to improve the FTE pharmacists/technicians in our hospital.

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Introduction

The fact that healthcare workers, while preparing or administering chemotherapy, are exposed to the toxic effects of these hazardous drugs has been well documented.\textsuperscript{1–10} Manual dispensing of chemotherapy has been the norm in a hospital for a long time, although automation technology is on the rise in other dispensing work.\textsuperscript{11–16} This is mainly because the dispensing of parenteral chemotherapy needs to consider stringent environmental control standards and personnel safety. Automation technologies have failed to produce a system for this complicated task in the past until recently. CytoCare, manufactured by Health Robotics GmbH with its headquarters in Bolzano, Italy, is the first automatic processor for the preparation of chemotherapy injections in a sterile environment in the world.\textsuperscript{17}

Automation in chemotherapy dispensing has the ability to lower the exposure of pharmacists to hazardous drugs mainly because it replaces human manipulation of these drugs. However, in case of mechanical problems, ease of handling these problems needs to be assured as well. Besides the safety benefit, one would also hope that automation can elevate the accuracy and efficiency of the dispensing job. Many automated devices, such as carousel-dispensing technology, have been proved to improve the overall efficiency of medication distribution in inpatient service.\textsuperscript{18} The new chemotherapy-dispensing robot will also need to be validated to see if it can do the same. Many technicians or pharmacists are afraid of their roles being replaced by automation.\textsuperscript{19,20} However, the possibility of decreasing full-time equivalents (FTEs)\textsuperscript{21,22} can actually leave the pharmacists more time to help with clinical services.

Our hospital is one of the major medical centers in Taiwan. This tertiary medical center is located in the hub of the capital city and has over 2500 beds in total. Cancer patients are one of the main patient populations. The oncology pharmacy is equipped with facilities that meet USP 797 standards\textsuperscript{23} on the pharmaceutical compounding of sterile preparations and is responsible for chemotherapy for outpatients in the oncology clinic, as well as for inpatients. The oncology pharmacy, on average, dispenses more than 300 doses of chemotherapy per day. The pharmacy staff includes 11 FTE pharmacists and three FTE pharmacy technicians for the dispensing-related work. The pressure of filling so many prescriptions per day and the current knowledge of safety requirements\textsuperscript{24,25} in handling hazardous drugs prompted us to look for automated facilities. The search for an automated robot began in 2006. After installation and a testing period, we began its routine use in May 2010.

CytoCare consists of many different parts, its primary feature being a multiaxis robotic arm that does the main dispensing job. The machine is also equipped with five high-efficiency particulate air filters to provide an ISO class-5 environment for the dispensing process. It has a shaker, a camera for confirming the drug used, and an inbuilt scale to double-check the amount of the drug. A carousel for loading drugs, diluents, or syringes is located in the loading area. As CytoCare cannot handle glass ampoules, only drugs in vials are used. The whole robot is operated by computer software (CytoPlan). A pharmacist needs to key in a drug database in the preparatory stage. When the robot is used routinely, the pharmacist can key in necessary data from the prescription and, at the same time, arrange the sequence of all doses to be made. If an interface is developed to connect the in-house Computerized Physician Order Entry (CPOE) system with CytoPlan, the key-in process can be bypassed.

The design of the robot has the benefit of avoiding direct human contact with the hazardous drugs, thus improving safety. Another feature of the robot is that it can use drug density and the dose required to get the calculated volume. It also measures the actual weight of the vial before and after the liquid has been drawn up in a syringe to confirm the exact volume drawn. If the volume of the drawn liquid differs by more than 5% from the calculated volume, the robot will reject the product and label it as a failure. From the manufacturer's data, the accuracy of the chemotherapy dispensed by the robot shows an error rate of less than 2.5%. For a syringe to draw 20 mL liquid, the error rate is less than 0.5%. Manual work can never reach this precision, because of not only the limitations in human hands and eyes, but also the lack of precision in the graduations on the syringe. Thus, the robot should provide more accurate dosages to patients.

The purpose of this study is to describe the performance of this novel robot in dispensing chemotherapy in terms of its success rate and the major causes of its failures. We also want to compare the efficiency of automation to that of manual work by comparing the FTEs. As far as we know, this is the first report on this specific type of automated robotics used for the dispensing of chemotherapy.

Methods

We collected the related data of CytoCare for 2 months from May 4, 2010 to July 9, 2010. Out of the 10 weeks, CytoCare operated routinely only on 47 days (94% of the 50 pharmacy work days). This was because the engineer needed to test the robot on certain days and routine use of the robot was not possible. The robot had its own computer-generated daily and monthly log of the drugs that it dispensed, with the number, but not the cause, of failures being recorded. After CytoCare finished a daily assignment, the pharmacists would edit the log to explain the reasons for its failure. The definition of failure for the robot was a self-detected difference of greater than 5% between the drawn dose and the calculated dose (air failure), or when the robot aborted the operation due to other mechanical or manual problems (non-air failure). Air failure was caused when air, in addition to drug, was drawn into the syringe, resulting in a difference of greater than 5% from the calculated volume. If the robot failed to produce an acceptable dose, it would eject the syringe to its loading area and warn the pharmacist by showing the status of "failure" on the operation screen. All the other doses were counted as successful.

The daily number of failures and the weekly success rate were documented. Causes of failure were further analyzed. In the analysis, we used cumulated doses because these
represented the total doses that the robot made, and the cumulative failed doses could be compared to total prepared doses. This was done in the hope of detecting the most frequent cause of failure during this period of time.

We also tried to perform linear regression analyses on the failed doses. This would mainly show if the failure occurs at a steady rate. If the linear regression line is a best fit for all dots, it indicates that the failure is occurring at the same rate. If, however, the dots are best fit with two different lines, it would imply that other factors have come into play in changing the failure rate.

The influence on the saving of manpower was assessed by summarizing what we viewed from the logs. Prior to the use of the robot, we had 14 FTEs of pharmacists/technicians. We assumed that a pharmacist/technician could dispense 20 doses of chemotherapy per hour (data on file). This was then compared with the average number of doses made by CytoCare per hour to see how many person-hours it saved. Every 8 person-hours were equivalent to one FTE. This was the gross impact of CytoCare on manpower saving.

**Results**

**Chemotherapy dispensed by CytoCare**

We used CytoCare in our pharmacy for two purposes. The first was a preparatory purpose. 5-Fluouracil (5-FU) was one of the most frequently prescribed chemotherapeutic agents at our hospital. Because the daily number of doses was large, we used CytoCare as the main tool for pre-filling 5-FU syringes. The pharmacists/technicians then adjusted the dosages and completed the dilution process. Secondly, we used CytoCare to help with daily online prescriptions. So far, only a limited number of chemotherapeutic agents were used in CytoCare, namely, 5-FU 1 g/vial, carboplatin 150 mg/vial, cisplatin 50 mg/vial, cyclophosphamide 500 mg/vial, cytarabine 500 mg/vial, epirubicin 50 mg/vial, ifosfamide 2 g/vial, methotrexate 1 g/vial, oxaliplatin 50 mg/vial, and leucovorin 50 mg/vial (not a chemotherapeutic agent itself, but is commonly used in our pharmacy). For most of the total doses made in this study 5-FU was used (551 doses, 53.6%), followed by cyclophosphamide (22.3%), cytarabine (6.8%), carboplatin (4.7%), methotrexate (4.6%), and ifosfamide (4.2%); each of the rest of the drugs made up less than 2% of the total. The reason for the limitation of drugs used was that some chemotherapeutic agents available in Taiwan are either glass ampoules or available in small volumes; it would take much longer to draw large doses of these than of agents that are available in larger-volume vials. We, thus, chose more widely used chemotherapeutic agents to be dispensed by the robot. Vials of water for injection were not available in Taiwan; hence, we were unable to use CytoCare to reconstitute powdered drugs.

**Failure and success rate of CytoCare**

Fig. 1 showed the daily total number of doses dispensed by the robot on Day 1 through Day 47 of CytoCare operation. From the data, we could see that the number of doses that CytoCare produced daily was between 1 and 47. The total number of doses made by CytoCare during this period of time was 1028. The number of doses made per day gradually increased as the days went by, largely due to the pharmacists’ increasing familiarity with the machine over time. The pharmacists gradually tried to make online orders in the morning, while in the less busy hours they used CytoCare for preparatory doses (pre-filled 5-FU). Another reason for this steadily rising trend was that the onsite engineer solved many problems and the process became much smoother. In the sixth week (Days 24—28), the engineers were changing the syringe system from a BD to a Terumo mode, which resulted in lowering of the daily totals. Regular dispensing work was delayed by much testing.
The success rate also increased from 76.8% in the first week to 95.3% in the 10th week (Fig. 2), indicating a smoother process in the later stages.

Air failures and non-air failures

Out of the total of 1028 doses made by CytoCare during this period of time, 123 doses (12.0%) failed. The causes of failure were categorized into two groups: air and non-air failures (Fig. 3A). The non-air failures included loading, clamping, waste bin, and others (Fig. 3B). The loading failure was caused by manual errors, while all other were mechanical failures.

From the cumulative failing doses, one could see that the most frequent failure was an air failure (98 of 1028 total doses, 9.53%), which was caused by drawing of air in addition to drug into the syringe, resulting in a difference of greater than 5% from the calculated volume. This was followed by non-air failures, namely, loading failure, clamping failure, waste bin failure, and others. If we examine the air failures in more detail, 5-FU was associated with the highest number of failing doses due to an air problem (63 doses) because it was the most frequently dispensed drug. The drugs with the highest percentage of failure due to this problem also included epirubicin (eight failures out of 48 doses for carboplatin, 12.5%), and cisplatin (two failures out of 16 doses for cisplatin, 12.5%).

It can be seen from Fig. 3A that the data were best fit by two least-squares lines for both the air and non-air failures. Line "Air a" describes the initial operation period, whereas line "Air b" describes the second period. The slope of line "Air a" is about half of the slope of line "Air a", indicating that the failure rate was approximately halved (from 11.5% to 6.0%) in the second period. This transition in failure rate occurred around a cumulative dose of 500. This was in the sixth week, when we switched our syringe system. Since the installment of the new syringe grips, the air problem dramatically decreased. The failure rate of non-air problems was also reduced (2.6% to 1.7%) around the cumulative dose of 450, which was in the fifth week (Days 20–23). At this time, the engineers were fine-tuning the robot to help maintain the system. The stability of the robot seemed to improve (fewer clamping and waste bin failures). This might have contributed to the lower failure rate in the second period ("Non-air b" line).

The second most frequent failure, loading failure (seven in 1028 doses, 0.68%), was a manual problem, as seen in Fig. 3B. While loading the syringe, one had to make sure that the plunger was completely pushed in; otherwise, the robot could not put the syringe into the drawing position (too long a syringe). In many cases, the failure occurred if the plunger was not properly pushed in.

The next cause of failure was a mechanical one, namely, the clamping failure. It had the same frequency as the loading failure (seven in 1028 doses, 0.68%). The fourth most frequent failure was also a mechanical problem, the waste bin failure (six in 1028 doses, 0.58%). Lastly, the causes behind "others" included two power failures and three failures that occurred during testing (five of 1028 failed doses, 0.49%).

Manual problems, as reflected in the loading failures, lessened as pharmacists became more familiar with the process. Mechanical problems, such as the waste bin and clamping failures, were not frequent and normally could be fixed by the local engineer instantly, so they posed no serious trouble. The air failure remained the unresolved issue despite its rate being decreased by 50% over time. As we have explained earlier, the change of the syringe system was one of the factors that contributed to lowering of the failure rate. The complete solution to this failure remained to be elucidated, although selecting proper-sized vials to be dispensed by CytoCare might lower future air problems.

FTEs saved

We compared the number of doses that CytoCare made in a day with daily manual production. In this period of
testing, the maximum number of doses made per day by CytoCare was 47. This was approximately equivalent to a gross saving of 2 person-hours a day, based on the data that a trained pharmacist can dispense 20 doses per hour. However, we had to have a pharmacist or a technician to switch on and off CytoCare repeatedly during the whole day. This included keying-in commands for the robot, preparing and loading the robot with appropriate drugs and syringes, as well as taking out products, handling problems, and so on. The work was approximately 6 person-hours per day (75% of the daily work). So the time and personnel saved were not able to compensate for the time spent on maintaining the routine operation of the machine. In addition, an onsite engineer was required to stand by to monitor and to help sort out possible failure issues, adding to the time and personnel involved. CytoCare was not able to lower FTEs for our oncology pharmacy.

Figure 3  (A) Cumulative number of air and non-air failures graphed as a function of cumulative total doses. Linear regression analysis determined the failure rates as shown. (B) Main contributors to the non-air failures in Fig. 3A. Problems are listed in order of frequency. A detailed description may be found in the "Causes of failure" section.
Discussion

Causes of failures

Air failure
According to the results, epirubicin, carboplatin, and cisplatin had the highest air-failure rates. The main reason for the failure with these drugs was that the dosages prescribed were relatively large and they used up almost all the contents in the vial. For example, for 100 mg of epirubicin (available as 50 mg/25 mL vials), CytoCare would need to draw up two 25-mL vials. Because of the lack of dexterity in the robotic arm, it tended to draw up too much air when it came to the last bit of liquid.

Other reasons for air failures included our use of a vented needle for the syringe to avoid spraying contaminating aerosols in the machine. When the vented needle was inserted into the drug vial, it could easily introduce air into the vial, causing air to enter into the syringe as well. Even though the robot always tilted the vial at an angle of around 15° to try to keep the tip of the needle below the surface of the liquid, it was unable to adjust the position of the vial to always do this. It was thus possible to draw air in addition to the liquid, it was unable to adjust the position of the vial to the correct position and thus be unable to pick up the needle cap; this would result in failure.

Waste bin failure

When CytoCare’s robotic arm threw away the used vials or other waste into the waste bin, the lid of the bin had to move away and then reposition itself back to home position. Sometimes, it was not able to move back to home position and would cause an alarm to go off, reflecting failure. After our local engineer adjusted some parameters to control the moving of the lid, this problem was mainly solved, except some occasional instances when it would still come up.

Other failures

The two power failures were unavoidable and unpredictable. Although CytoCare was hooked to a UPS system, in this type of instant electrical interruption, the task that was underway would be aborted. One could still take out the syringe manually and finish the task either by re-entering it into the robotic system or by hand. As to the remaining failures, the manual record only noted that these were the doses tested by the engineer and gave no further explanation.

Lack of influence of the robot in daily practice

Speed
The manufacturer of CytoCare stated its benefits of safeguarding the staff from chemotherapy contamination and ensuring precise dosing (>95% precision). However, the use of CytoCare did not have a great influence on our practice because of its several limiting factors. One major limitation of CytoCare was its lack of speed in making the doses. Since our pharmacy was located in a medical center, the number of doses of chemotherapy to be prepared each day was more than 300; in contrast, the maximum number of doses that CytoCare can prepare, in our experience, was approximately 50. Manually drawing the drug into a syringe could be done within 3–5 minutes. The average time required for CytoCare to do the same job was about 10–20 minutes, depending on the dosage and the availability of larger drug vials. This was the main reason why CytoCare could only make a limited number of doses of chemotherapy. This facet of CytoCare’s performance limited its use mainly to inpatients, because outpatients normally could not tolerate waiting for more than 30–60 minutes for their chemotherapy to arrive.

Because of this limitation, pharmacists had to work on the rest of the prescription orders, plus one person always needed to keep an eye on the robot for the loading requirements and other possible alarms.

Another limiting factor in terms of its performance was the delicacy of the robotic arm. Any minor alteration of the vial shape, labeling of the vial, or change in the axis of

Non-air failure

Loading failure
Loading failure was a manual problem. It could only be prevented by teaching the pharmacists to ensure that all the plungers of the syringes are tightly pushed in and placed into the robot in the proper direction so that the needle can effectively draw up the liquid.

Clamping failure

During the weighing procedure, the robotic arm would occasionally fail to put the vial at the correct position, and later be unable to clamp onto the vial and pick it up. This failure required the engineer to adjust the position of the clamp by trial and error. It would still occur occasionally, mainly because of variations in the packaging of vials. The differing shapes and sizes of vials could cause some difficulties. A certain set of parameters regarding the shape and size of vials was saved in the database; if the shape of a vial was different from the average, for example in the curvature of the neck area, the system would show a failure sign. Furthermore, when the clamp was about to pick up the upper portion of the vial, it would sometimes hit the top and thus be unable to secure the vial in an upright position. This unpredictable problem required a manual adjustment to be fixed. Another problem occurred when the robot had already completed drawing the chemotherapy and wanted to put the needle cap back onto the syringe. If for some reasons the axis of the robot had been moved, as might happen in the cleaning procedure every afternoon, it would not aim at the correct position and thus be unable to pick up the needle cap; this would result in failure.
the robot could result in an error. Some of the failures listed in Fig. 3A and 3B resulted from a minor maladjustment of the robotic arm. The engineers are still working on the air failure and hopefully would be able to decrease it, improving the performance of CytoCare. The performance will also improve once larger chemotherapy vials are available. A similar situation exists with the less frequent clamping and waste bin failures. An onsite engineer is needed to stand by to readjust the positioning of the robotic arm and the waste bin to curtail these problems.

FTEs

The guarantee period of the robot was limited (2 years in our hospital). In special cases, engineers from Italy, or an engineer who was in the Asia district, would fly to the site to fix the robot. This service was provided for free within the guarantee period. If an onsite engineer is needed for adjusting the many minor problems that can block the normal functioning of CytoCare, we would need to hire this personnel at an extra cost after the guarantee period expires. A contingency plan should be developed for our own personnel to be trained further to understand more day-to-day operation details in order to maintain a smooth run. The local engineer recently provided us with a problem-solving brochure, so pharmacists could try to solve some of the issues themselves prior to asking the engineer to help.

In terms of cost saving, so far the net influence on FTEs was a negative one. The requirement for personal protective equipment (including hair covers, shoe covers, waterproof gowns, gloves, and masks) was not reduced, and the use of other consumables, such as syringes or vented needles, was the same as, if not more than, in manual work. Person-hours saved could not offset the attention needed by extra manpower.

Conclusion

Reports have shown that informatics and automation are important tools for the reduction of work, error, and cost in a hospital pharmacy.11–17 CytoCare is the first automatic dispenser for parenteral chemotherapy.17 From our preliminary experience, this robot could so far save approximately 2 person-hours per day, although it was not able to make up for the person-hours spent on running the robot, i.e., it had no real benefit in cutting FTEs. If the inherited problems can be further solved—for example, if the air issue can be taken care of by having larger vials available and if the engineer can develop ways to increase the stability of the machine—the performance will improve. If we can also develop the interface between our CPOE system and the software (CytoPlan), the speed and scope of the operation of CytoCare in our hospital will be improved. Despite these facts, we are still much obliged to the hospital for purchasing this first robot for chemotherapy in the pharmacy department, and we will try our best to accommodate the robot in our working schedule and maximize its usage.

Acknowledgments

We owe the hospital our gratitude for purchasing CytoCare for the oncology pharmacy. We also thank the local engineers, as well as the foreign engineers from the distributor and headquarters of CytoCare, for fixing the robot and helping our pharmacists gain knowledge needed for operating and maintaining CytoCare. We also thank Professor and Mrs John Suppe for painstakingly helping us to proofread this manuscript; without their encouragement and input as well as their prayers, this manuscript would not have been completed.

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