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Optimisation of the preparation of chemotherapy based on 5-fluorouracil by the use of peristaltic pumps

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Abstract

Objectives: Preparation of 5-FU elastomeric pumps is a time-consuming activity inducing musculoskeletal disorders (MSDs). Our unit has developed an automated filling system consisting of two peristaltic pumps (one for the diluent, one for the cytotoxic drug). The objective was to validate the accuracy of the assembly and evaluate the impact of automation on the compounding time, occurrence of MSDs and cost of preparation.

Methods: Accuracy was determined by calculating the total error on the volumes injected by the pumps. Measurements were made for 2 brands (AMF, Baxter), 3 different volumes; repeated 3 times at 3 times of the day. The time-saving study compared 24 measurements in manual filling and 24 in automated mode. Impact of automation on the occurrence of MSDs was evaluated by a self-assessment questionnaire. Finally, a comparison between the price of a manually prepared elastomeric pump and an automated prepared elastomeric pump was performed.

Results: Volumes administered by the pumps were accurate (total error < 2.5%). Preparation time was divided by 2. Occurrence of MSD decreased (8.7 manual filling vs. 23.5/28 automated filling). Overcost was moderate (14.7% for AMF; 10.3% for Baxter).

Conclusions: Using peristaltic pumps, 5FU preparation was optimized for moderate additional cost.

Keywords: automation; chemotherapies; elastomeric pumps; musculo-skeletal disorders; peristaltic pumps.

Introduction

Anticancer treatments present a risk both for the personnel who prepare the treatment by handling cytotoxic drugs and for the treated patient in case of preparation errors [1–8].

The risk of error is all the greater as the number of anticancer preparations increases from year to year and the preparations must be carried out faster, which also increases the mechanical stress and chemical contamination risk of the manipulators.

Portable elastomeric pumps with different volume reservoirs and that operate at different flow rates are marketed, adaptable to each patient's therapy needs (different doses and administration times) [9]. An elastomeric pump also enables the administration of chemotherapy in the outpatient setting, reducing both patients' length of stay and the workload of nurses and pharmacists. In addition, no manipulation is required after connection to the patient, reducing the risk of subsequent contamination.

One of the disadvantages of elastomeric pumps is the variability of the infusion flow rate. This rate varies depending on several factors including temperature, viscosity, and height of the reservoir and the Luer lock connector [10]. Medicines with a narrow therapeutic range should not be administered with an elastomeric pump because of the inaccuracy of the system. Moreover, the administration of drugs requiring patient monitoring cannot be done via such a pump. This does not pose a problem for the administration of 5-fluorouracil (5-FU) [9].

Additional important disadvantages include the preparation time of the elastomeric pumps [11] and the occurrence of musculo-skeletal disorders (MSD) [12]. Indeed, the preparation of cytotoxic drugs involves the permanent and sustained use of the upper limbs, fingers and upper body. When filling the elastomeric pump, an additional effort from users is required to oppose the resistance of the elastomeric membrane, which increases even more the risk of occurrence of MSD [13].

To the present day, cancer treatment activity continues to grow. Pharmacists have to prepare more and

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more chemotherapies (10% increase in 5 years in our center), without delay (less than 1 h according to national recommendations) to ensure the best patient satisfaction. In this context, automated systems have been shown to optimise the preparation time (several dozen chemotherapies an hour) improving the ergonomics of the work of hospital pharmacy technicians [13–16]. In the other hand, automated system installation is usually very expensive (several hundred thousand euros just for the robot).

That's why, in our center and with a view to optimising preparation time and improving the ergonomics of the work of hospital pharmacy assistants while keeping a lid on costs, we designed in Oscar Lambret Center, an automated filling system containing two Repeater® pumps for the infusion of 5-FU.

The first objective of the present study was to validate the automated filling system by evaluating the accuracy of volumes administered. The second objective was to evaluate the impact of automation on the preparation time and the risk of MSD (musculoskeletal disorders). The third objective was to assess the economic cost of the new device.

Materials and methods

The filling system

The assembly studied is presented in Figure 1. The two Repeater® peristaltic pumps (Baxter; ref: H938099E) are connected to the 5-FU and diluent (3,000 mL 0.9% NaCl Aguettant, ref: 5620730) reservoir bags through a transfer tubing (Baxter; ref: H93833). The other end of the tubing is connected to the elastomeric pump through a Y connector (ICU; ref: 011-MC33128) and a Spiros® (ICU; ref: CH2000S-PC) luer [17].

The 5-FU bag was prepared from 10 vials of 5-FU (ACCORD; 5,000 mg/100 mL) filled into an empty bag (MACOPHARMA; ref: PB1000512T20CPP075). The amount of 5-FU is intended to contain enough cytotoxic drug to prepare all elastomeric pumps of the day.

Peristaltic pumps are intended for use in isolators. The dimensions of a pump are 20.5 × 28 × 24.5 cm. A working space of about 90 cm is required for the installation and use of the pumps. Our isolators are sized to accommodate these two pumps.

Six different elastomeric pumps were studied:

- FOLFusor® LV 2 (BAXTER, ref: 2C4008K)
- FOLFusor® LV 5 (BAXTER, ref: 2C4009K)
- FOLFusor® LV 10 (BAXTER, ref: 2C4036K)
- AutoFuser® 2.5 mL/h (AMF, ref: AA2011-1-S)
- AutoFuser® 4 mL/h (AMF, ref: AA2004-1-S)
- AutoFuser® 10 mL/h (AMF, ref: AA2010-1)

Calibration of the peristaltic pumps

A daily calibration of the two pumps was performed by infusing 40 mL of 0.9% NaCl in 60 mL syringes (BD; ref 300865). For practical reasons

Figure 1: The studied assembly.

and in order not to impact the production of chemotherapy for patients, calibration and measurements were performed outside of the controlled-atmosphere area by replacing the 5-FU with 0.9% NaCl, which has a similar density and viscosity. The adjustment between the 0.9% NaCl volumes theoretically injected by the Repeater® pumps and the volumes actually injected was done by reading the syringes. The speed of the pumps chosen for this study, “Medium 5”, was that intended for routine use.

Accuracy of the volumes delivered by the pumps

After calibration, the accuracy of the volumes delivered by the pumps was measured using the gravimetric method. Volumes were weighted with a Mettler Toledo® precision-controlled balance (MS3002 TS/M ref: 30133561). The weight of the diluent actually delivered by the pump was compared with the weight of the volume theoretically delivered.

The measurements were performed on the six elastomeric pumps. For each of them, the measurements were made on three different volumes, repeated three times at three times of the day (at start, middle and end of production). So, nine measurements for one elastomeric pump and one volume were done.

For Baxter pumps, with a nominal volume of 240 mL, the volumes of 5-FU studied were 10 mL (+230 mL of diluent), 120 mL (+120 mL of diluent) and 230 mL (+10 mL of diluent).

For AMF pumps, with a nominal volume of 275 mL, the volumes of 5-FU studied were 10 mL (+265 mL of diluent), 137 mL (+138 mL of diluent) and 265 mL (+10 mL of diluent).

The accuracy of the volumes delivered by the two pumps was calculated and expressed as the total error in percent (sum of accuracy/bias and precision/trueness) as described for the validation of quantitative analytical procedure.

Objective 2.1: optimisation of the preparation time

This part of the study involved 48 time measurements. Six different pharmacy technicians filled the FOLFusor® LV 5 and the AutoFuser® 4 mL/h, automatically and manually, and each measurement was repeated twice.

For this study, 80 mL of 5-FU for 150 mL of diluent were used, which represents the average volume of most reconstituted elastomeric pumps used in our center.

The steps for the manual and automated preparation processes of the filling systems are detailed in Table 1: and 2:, respectively.

In order to determine the time gained by the use of pumps, the median and mean filling times for automatic vs. manual filling were described and a statistical analysis (Student's test) between the two was performed.

To ensure that the type of elastomeric pump and the user chosen for the study did not have any impact on the results, a statistical analysis (Wilcoxon Mann–Whitney test) on the filling time with Baxter vs. AMF pumps and a statistical analysis (Wilcoxon Mann–Whitney test) on the filling time according to the pharmacy technician were performed.

Objective 2.2: decrease of MSD

The occurrence of MSD was measured with a self-questionnaire. Each of the six pharmacy technicians filled the questionnaire for each of the 2 elastomeric pumps both for an automated and for a manual filling (24 in total).

The questionnaire is based on the OSHA (Occupational Safety and Health Administration) checklist used by the American institute NIOSH (Health National Institute for occupational Safety and Health) for the detection of work situations likely to be at risk for upper limb MSD.

This checklist is divided into seven items: repetitiveness, manual effort, awkward postures, skin pressure, vibration, work environment and control of the work pace. These items are themselves subdivided into items that are scored individually [18].

In this study, the questionnaire was adapted to the preparation of the filling system and the following items were selected: repetitiveness, manual effort, awkward postures (divided into 5 sub-items) and skin pressure. The pharmacy technicians scored each item according to the intensity. The higher the score, the more intense the criterion studied. All individual scores were then summed to obtain a total score ranging from 0 to 28 (Figure 2).

The Wilcoxon Mann Whitney Test for paired data was applied to each question to test the difference between automatic and manual filling.

Objective 3: economic cost

The final part of the study compared the production price of a manual filling system with that of an automated system. The production costs of a manual and automated preparation were calculated considering the material used for each system. In a second step, the price of assembly was calculated and integrated into the price of automated preparations. The preparation price according to the number of preparations was represented in a graphic in order to estimate the price of the assembly taking into account the number of daily preparations.

Table 1: Steps necessary for the preparation of the elastomeric pump without the use of peristaltic pumps.

Step 1	Control of vials: Scan of the 5-FU vials identification DataMatrix bar code
Step 2	Elastomeric pump control: Scan of the pump DataMatrix bar code
Step 3	Weight of the elastomeric pump
Step 4	Weight of the empty syringe
Step 5	Collection of the 50-mL of NaCl 0.9% bag
Step 6	Weight of the syringe + volume of NaCl 0.9%
Step 7	Injection of the diluent into the elastomeric pump
Step 8	Collection of the 50-mL of NaCl 0.9% bag
Step 9	Weight the syringe + volume of NaCl 0.9%
Step 10	Injection of the diluent into the elastomeric pump
Step 11	Collection of the 50-mL of NaCl 0.9% bag
Step 12	Weight of the syringe + volume of NaCl 0.9%
Step 13	Injection of the diluent into the elastomeric pump
Step 14	Weight of the elastomeric pump with the diluent
Step 15	Weight of the empty syringe
Step 16	Collection of 40 mL of 5-FU
Step 17	Weight of the syringe + 5-FU
Step 18	Injection of the 5-FU into the elastomeric pump
Step 19	Collection of 40 mL of 5-FU
Step 20	Weight of the syringe + 5-FU
Step 21	Injection of the 5-FU into the elastomeric pump
Step 22	Final weight of the elastomeric pump
Step 23	Labeling of the preparation

Results

Accuracy of the volumes delivered by the peristaltic pumps

The results obtained for the two pumps and for each type of elastomeric pump are presented in Table 3.

For all measurements, the total error was less than 2.5%. For all the volumes studied, the measurements were accurate with a bias ranging between -0.90 and 1.61% .

Table 2: Steps necessary for the automated preparation of the elastomeric pump.

Step 1	Elastomeric pump control: Scan of the pump DataMatrix bar code
Step 2	Weight of the elastomeric pump
Step 3	Weight of the diluent bag
Step 4	Injection of 150 mL of diluent
Step 5	Bag control: Scan of the 5-FU bag Identification DataMatrix bar code
Step 6	Injection of 80 mL of 5-FU into the elastomeric pump
Step 7	Weight of the diluent bag
Step 8	Final weight of the elastomeric pump
Step 9	Labelling of the preparation

Items	Manual	Automated	Maximum score
I1: Repetitiveness			/7
I2: Manual effort			/6
Awkward postures			
I3: Neck: rotation/flexion			/2
I4: Shoulders: upper limb without support or elbow higher than the middle of the chest			/3
I5: Rapid movement of the fore-arm			/2
I6: Wrist: flexion/extension			/3
I7: Fingers			/1
I8: Skin pressure			/4
Total score			/28

Abbreviations: I= item

Figure 2: Self-evaluation questionnaire.

The precision error between the measurements was low, ranging from 0.11 to 1.60% for all results. The repetition of measurements over time had little or no influence on the accuracy of the infusion volumes.

In addition, the accuracy of pump A (precision between 0.11 and 1.24%) and pump B (precision between 0.19 and 1.60%) for both elastomeric pumps was the same.

For all the volumes measured using the Baxter pumps, the total error ranged between 0.34 and 1.62% with a bias

between -0.72 and 0.73% and a precision error between 0.14 and 1.06% .

For all the volumes measured using the AMF pumps, the total error ranged between 0.52 and 2.42% with a bias between -0.90 and 1.61% and a precision error between 0.11 and 1.60% .

Results of objective 2.1: automatic vs. manual filling times

Mean (SD) time for automatic filling was 156.8 (15.2) seconds vs. 301.5 (15.7) seconds when done manually (student test: $p < 0.001$).

Filling time depending on the type of elastomeric pump

The filling time difference was not statistically significant between the two elastomeric pump types, neither globally nor depending on manual/automatic filling ($p = 0.089$, Wilcoxon Mann-Whitney test) (Table 4).

Filling time depending on pharmacy technicians

The filling time was not significantly different between the six pharmacy technicians ($p = 0.895$, Wilcoxon Mann-Whitney test) (Table 5).

Table 3: Accuracy of the volumes administered by the pumps (each values of accuracy, precision and total error are based on the results of the nine repetitions (3 times at start, middle and end of production)).

		PUMP A (5FU)				PUMP B (Diluent)			
		Theoretical volume (mL)	Accuracy (bias) (%)	Precision (trueness) (%)	Total error (%)	Theoretical volume* (mL)	Accuracy (bias) (%)	Precision (trueness) (%)	Total error (%)
BAXTER	10 mL/h	10	0.44	0.54	0.99	230	0.05	0.29	0.34
		120	0.64	0.50	1.14	120	0.19	0.39	0.59
		230	0.35	0.34	0.69	10	-0.33	0.75	1.08
	5 mL/h	10	-0.56	1.06	1.62	230	-0.72	0.82	1.54
		120	-0.25	0.24	0.49	120	-0.64	0.90	1.54
		230	-0.26	0.14	0.40	10	0.00	0.96	0.96
	2 mL/h	10	0.11	1.00	1.11	230	0.14	0.59	0.73
		120	0.52	0.23	0.75	120	0.51	0.38	0.89
		230	0.73	0.50	1.23	10	0.33	1.01	1.35
AMF	10 mL/h	10	0.00	1.12	1.12	265	-0.42	1.60	2.02
		137	0.42	0.69	1.11	138	-0.90	1.52	2.42
		265	0.43	0.30	0.73	10	0.11	1.28	1.39
	4 mL/h	10	1.33	0.87	2.20	265	1.03	0.49	1.52
		137	1.31	0.36	1.66	138	1.23	0.19	1.43
		265	1.61	0.11	1.71	10	0.67	0.74	1.41
	2.5 mL/h	10	0.62	1.24	1.91	265	-0.19	0.47	0.66
		137	0.79	0.41	1.20	138	0.23	0.30	0.52
		265	0.01	0.70	0.70	10	0.67	0.74	1.41

*Complementary volume to pump A (pump containing 5-FU).

Table 4: Automatic and manual filling times for AMF and Baxter elastomeric pumps.

	Time (s)		p
	AMF pump	Baxter pump	
Automatic	n = 12	n = 12	0.089 (Wilcoxon)
Median (range)	149 (138–172)	158.5 (131–183)	
Mean (SD)	152.5 (12.9)	161.2 (16.6)	
Manual	n = 12	n = 12	
Median (range)	291 (277–316)	310 (296–338)	
Mean (SD)	291.8 (11.9)	311.2 (12.9)	

Objective 2.2: decrease of MSD

Table 6 presents the scores obtained for each question for the automatic or manual filling and overall. A total mean (SD) score of 23.5 (2.8) was obtained for manual preparations vs. 8.7 (4.5) for automated preparations. For all except for question 3 (neck rotation/flexion), there was a significantly lower score (lower risk of MSDs) for automatic filling compared with manual filling.

Objective 3: economic cost

Considering the material used, the manufacturing cost of a manual elastomeric pump is 23.72 € (all taxes included) with a Baxter pump and 16.52 € (all taxes included) with an AMF pump (Table 7).

The cost of an automated preparation includes the price of the peristaltic pump, the price of the assembly and the material necessary for the calibration of pumps, smoothed out with regard to the number of preparations per day. Considering that Baxter Repeater® pumps have an estimated life expectancy of 7 years, the annual cost for both pumps would be of 1 964.69 € (all taxes included). Considering an approximate number of working days of

250, the price of the pumps for a working day is estimated at 7.86 € (all taxes included). For a day of activity, the price of assembly and calibration is 75.56 € (all taxes included), leading to a total cost of 83.42 € (all taxes included) (Table 8).

The cost difference for the preparation of an elastomeric pump using either Baxter or AMF peristaltic pumps between the automatic and manual systems was 70.44 € (all taxes included).

Considering that the daily assembly will be used 10 times, the total cost of Baxter elastomeric pumps is 261.6 € (all taxes included) for the automatic system and 237.2 € (all taxes included) for the manual system. Similarly, the total cost for the preparation of 10 automated and manual AMF elastomeric pumps is of 189.56 € (all taxes included) and 165.20 € (all taxes included), respectively. The difference in cost between automatic system and manual system for both AMF and Baxter elastomeric pumps is the same: 2.44 € (all taxes included) for one preparation.

The cost of assembly is smoothed out by the 10 preparations thus reducing the additional cost of an automated preparation. The price of the automated preparation of an elastomeric pump using AMF pumps was estimated at 18.96 € (including all taxes) (15% increase compared to manual preparation) and 26.16 € (including all taxes) for a Baxter broadcaster (10% increase over manual preparation).

The cost of an automatic Baxter or AMF elastomeric pump is lower than that of a manual system for 19 preparations or over.

Discussion

This study demonstrates that the assembly developed in our center allows optimising the preparation of 5-FU elastomeric pumps without reducing the level of safety of the product and of the personnel.

Table 5: Automatic and manual filling times depending on the pharmacy technician.

	Time (s)					
	Pharmacy technician 1	Pharmacy technician 2	Pharmacy technician 3	Pharmacy technician 4	Pharmacy technician 5	Pharmacy technician 6
Automatic	n = 4	n = 4	n = 4	n = 4	n = 4	n = 4
Median (range)	158 (140–181)	159.5 (146–176)	143.5 (131–155)	159.5 (144–183)	153 (139–176)	165.5 (142–173)
Mean (SD)	159.3 (20.3)	160.3 (13.4)	143.3 (10.8)	161.5 (17.5)	155.3 (15.3)	161.5 (13.6)
Manual	n = 4	n = 4	n = 4	n = 4	n = 4	n = 4
Median (range)	294.5 (277–338)	303.5 (291–310)	289.5 (277–311)	306.5 (293–323)	297 (284–321)	310.5 (287–321)
Mean (SD)	301 (26.2)	302 (9.1)	291.8 (15.1)	307.3 (14.1)	299.8 (15.5)	307.3 (15.1)

Table 6: Questionnaire scores for automatic and manual fillings and overall.

Questionnaire MSD items	Automatic (n = 12)	Manual (n = 12)	Total (n = 24)	p (Wilcoxon test)
I1: Repetitiveness				0.002
Median (range)	2 (1–6)	6 (5–7)	5.5 (1–7)	
Mean (SD)	3 (1.7)	6.3 (0.6)	4.6 (2.1)	
I2: Manual effort				0.002
Median (range)	2 (0–4)	5 (4–6)	4 (0–6)	
Mean (SD)	1.6 (1.1)	5.3 (0.7)	3.5 (2.1)	
I3: Neck: rotation/flexion				0.343
Median (range)	1 (0–2)	1 (0–2)	1 (0–2)	
Mean (SD)	0.7 (0.7)	0.9 (0.8)	0.8 (0.7)	
I4: Shoulders				0.002
Median (range)	1 (1–2)	2.5 (2–3)	2 (1–3)	
Mean (SD)	1.2 (0.4)	2.5 (0.5)	1.8 (0.8)	
I5: Rapid movement of the fore-arm				0.03
Median (range)	0.5 (0–2)	1.5 (0–2)	1 (0–2)	
Mean (SD)	0.6 (0.7)	1.4 (0.7)	1 (0.8)	
I6: Wrist: flexion/extension				0.002
Median (range)	1 (0–2)	3 (2–3)	2 (0–3)	
Mean (SD)	1 (0.6)	2.7 (0.5)	1.8 (1)	
I7: Fingers				0.002
Median (range)	0 (0–1)	1 (1–1)	1 (0–1)	
Mean (SD)	0.2 (0.3)	1 (0)	0.6 (0.5)	
I8: Skin overpressure				0.002
Median (range)	0 (0–2)	3.5 (2–4)	2 (0–4)	
Mean (SD)	0.5 (0.7)	3.4 (0.7)	2 (1.6)	
Total				0.002
Median (range)	8 (3–18.5)	23 (20–28)	19.3 (3–28)	
Mean (SD)	8.7 (4.5)	23.5 (2.8)	16.1 (8.4)	

Table 7: Materials used for manual preparation of elastomeric pump.

Materials	Provider	Reference number	Unit Price (tax included)	Quantity	Total Price (tax included)
Elastomeric pump	BAXTER	FOLFusor® LV2: 2C4008K, FOLFusor® LV5: 2C4009K, FOLFusor® LV10: 2C4063K	18.6 euros	1	18.6 euros
	AMF	AutoFuser® 2.5 mL/h AA2011-1-S, AutoFuser® 4 mL/h AA2004-1-S, AutoFuser® 10 mL/h AA2010-1	11.40 euros	1	11.40 euros
Spiros®	ICU	CH2000S-PC	1.74 euros	3	5.22 euros
Take Set®	CODAN	16.4200	1.16 euros	1	1.16 euros
Bag of sodium chloride solution (250 mL) EASYFLEX +	MACOPHARMA	ACG0419FR	0.69 euros	2	0.69 euros
Syringe (60 mL)	BD	300865	0.22 euros	2	0.44 euros
Spike®	ICU	CH-70	1.31 euros	10	13.1 euros

We developed a filling system consisting of two Repeater® peristaltic pumps. Although several studies have shown the benefits of automated preparations with the help of pumps [15, 19–23], there are no reports on the use of a two-pump assembly injecting the diluent and then the 5-FU without prior disconnection of the pump.

The analysis validated the accuracy of the volumes administered by the pumps on a day of activity (total error of less than 2.5%) and thus our assembly for the Baxter and AMF filling system preparation.

These results are consistent with those of Humbert et al. [19]; who studied the accuracy of the volumes

Table 8: Materials used for automated preparation of elastomeric pump.

Materials	Provider	Reference number	Unit Price (tax included)	Quantity	Total Price (tax included)
Elastomeric pump					
	BAXTER	FOLFusor® LV2: 2C4008K, FOLFusor® LV5: 2C4009K, FOLFusor® LV10: 2C4063K	18.6 euros	1	18.6 euros
	AMF	AutoFuser® 2.5 mL/h AA2011-1-S, AutoFuser® 4 mL/h AA2004-1-S, AutoFuser® 10 mL/h AA2010-1	11.40 euros	1	11.40 euros
Assembly					
Peristaltic pump (Repeater®)	BAXTER	H938099E	6876.43 euros	2	13752.86 euros
Transfer tubing	BAXTER	H938331	18 euros	2	36 euros
Y-connector	ICU	011-MC33128	1.548 euros	1	1.548 euros
Spiros®	ICU	CH2000S-PC	1.74 euros	3	5.22 euros
Take Set®	CODAN	16.4200	1.16 euros	1	1.16 euros
Empty bag (1 L)	MACOPHARMA	PB10005122T20CPP075	4.68 euros	1	4.68 euros
Bag of sodium chloride solution (1 L)	FRESENIUS KABI	8025-2	0.85 euros	2	1.70 euros
Daily calibration					
Empty bag (100 mL)	MACOPHARMA	YZG0219EU	2.7 euros	1	2.7 euros
Syringe (60 mL)	BD	300865	0.22 euros	2	0.44 euros
Female coupling	ICU	011-DC	0.576 euros	2	1.152 euros
Spike®	ICU	CH-70	1.31 euros	10	13.1 euros

administered by a single Repeater® pump at different flow rates and for volumes ranging from 10 to 250 mL. Between each series/set of measurement, a calibration of the pump was performed with a calibration volume of 40 mL. For the pump flow rate of “Medium 5”, the total error was between 1 and 3% with coefficients of variation of less than 1%.

The analysis confirmed our method for pump calibration, which consisted on the visual reading of a 40 mL injection volume syringes. This one-time calibration method before the start of the activity ensured the accuracy of volumes injected throughout the day.

The time gained in the preparation by the use of pumps was evaluated by comparing the time of manual preparation and automated preparation over a total of 48 time measurements. With the automated procedure, over 2 min per preparation were gained. Parameters such as the preparation of the reservoir bags and of the assembly were not measured since their impact on the preparation time could not be estimated. Nevertheless, the important saving of time will make it possible to reduce the waiting time of the patient when the assembly will be used in routine.

The decrease in the risk of MSD occurrence through the automation of the preparation was confirmed by the third part of this study. Pharmacy technicians completed a self-

assessment questionnaire on the risk of MSD occurring after manual and automated preparation. The repeatability of gestures, the manual effort, the physical posture constraints of the shoulders, forearms, wrists and fingers and the skin overpressure were significantly diminished by the automation of the preparations. Only the decrease in neck posture constraints was not significant based on statistical analyses. Other teams have used the motorization of infusion pumps with the aim of minimizing the risk of MSDs [24–28]. Bourget et al. developed a motorized apparatus able to suppress the risk of MSDs caused by the manual filling of portable infusion pumps [24]. However, the impact of the automation on MSDs was not evaluated as part of the study.

Despite these advantages, some limitations could be identified: during the installation, a stage is particularly risky. Indeed, the risk of connecting the reservoir bag filled with 5-FU to the pump identified as “diluent” and connecting the reservoir bag of 0.9% NaCl to the pump identified as “5-FU” could have serious consequences. This risk is however limited by the double control of the assembly imposed in the procedure. In addition, the risk of injecting the wrong volume was limited by gravimetric system implemented in our center that detects volume errors at 5% of the theoretical volume.

Second, the calibration of the pumps before use strongly impacts on the accuracy of the volumes [29, 30]. The calibrations of the pumps are performed by visual reading of the syringe.

This method is more or less precise and remains dependent on the user performing the calibration, which implies an adapted and rigorous training of the staff. Improper calibration increases the risk of error in the administered volumes. However, the risk of injection of a volume too small or too large is limited, since our gravimetric system detects volume errors at more or less 5% of the theoretical volume [31].

Last, the automation of the preparation generates and additional cost of 70.44 € (including all taxes) if only one preparation is made during the day, the cost of assembly having a strong impact on the total cost. However, this extra cost of preparation, mainly due to the price of the material, decreases with an increase of the number of preparations carried out daily to reach 2.44 € (including all taxes) for 10 preparations, thus allowing to even the price of the assembly. On the other hand, the economic evaluation was carried out on the current market prices. When the automation of the preparations is used routinely, price can be negotiated in view of the increase in the use of consumables.

In addition, the cost of acquiring pumps is still affordable compared to other more expensive and cumbersome automated assemblies that sometimes require a rearrangement within the unit that generates additional costs.

The filling system developed by our unit therefore responds to the objectives of saving time and of decreasing the risk of MSD occurrence while remaining accurate on the volumes injected. The assembly is fully compatible with our gravimetric control system and ensures a safety level equivalent to that achieved with a manual preparation. Finally, the economic study shows that the additional cost generated by the automation of the preparations can be evened by considering the number of preparations made by our unit (average of 10 5-FU elastomeric pumps per day).

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