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BLOOD COMPONENTS

TRANSFUSION

Pathogen reduction of double-dose platelet concentrates from pools of eight buffy coats: Product quality, safety, and economic aspects

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Abstract

Background: Pathogen reduction (PR) of platelet concentrates (PCs) contributes to the safety of platelet (PLT) transfusion by reducing the risk of transfusion-transmitted infections and transfusion-associated graft-versus-host disease. In vitro quality of pathogen-reduced double-dose PC (PR-PC) made of eight whole blood (WB)-derived buffy coats (BCs) were evaluated.

Methods: Eight small-volume WB BCs from donors with at least 200×10^9 PLT/L were pooled with an additive solution to produce double-dose PCs (DD-PCs), which were treated with amotosalen/ultraviolet A light in a dual storage processing set, yielding 2 units of PR-PC. Quality controls were undertaken as per European Directive for the Quality of Medicines (EDQM) guidelines. PLT recovery rates were measured. Production costs and savings were compared over the 3 years before and after PR implementation.

Results: In the pre-PR period, 19 666 PCs were produced, compared to 17 307 PCs in the PR period. Single BC in the PR period had 41 ± 2 mL, hematocrit 0.39 ± 0.04 and $1.06 \pm 0.18 \times 10^{11}$ PLTs, and showed a recovery of 91% ± 8%. After pooling, separation, PR treatment of DD-PC, and splitting, each single PC had 189 ± 6 mL with $2.52 \pm 0.34 \times 10^{11}$ PLTs, compared to 2.48 ± 0.40 in the pre-PR period. The PLT recovery rate after PR was 87% ± 14%. EDQM requirements were met. An increase of about €12 (+7.5%) per PC from the pre-PR to the PR period was identified.

Conclusion: A new production method resulting in two PR-PCs made from pools of 8 BCs with use of one PR set was successfully introduced, and our experience of nearly 3 years demonstrated the high efficacy and in vitro quality of the PR-PCs obtained.

Abbreviations: BC, buffy coat; BC-PC, platelet concentrate made of buffy coat; BC-pool, pool of four to eight buffy coats and a unit of platelet additive solution; CAD, compound adsorption device; EDQM, European Directive for the Quality of Medicines; Hb, hemoglobin; Hct, hematocrit; OOS, out of specification; PAS, platelet additive solution; PB, peripheral blood; PC, platelet concentrate; PLT, platelet; PR, pathogen reduction; RBC, red blood cell; UVA, ultraviolet A; WB, whole blood; WBC, residual white blood cells.

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1 | INTRODUCTION

Pathogen reduction (PR) of platelet concentrates (PCs) for known and newly emerging pathogens significantly and proactively contributes to the safety of platelet transfusion by reducing the risk for transmitting bacterial, viral, and parasitic infections.[1,2] The INTERCEPT Blood System (Cerus Europe BV) for platelets (PLTs) uses amotosalen and ultraviolet A (UVA) light for PR and is widely used in clinical routine.[3,4] The functional and biochemical characteristics of PR-PC have mainly proven to be preserved over the storage period[5] and their therapeutic efficacy as measured by clinical outcome parameters, such as the occurrence of bleeding, was demonstrated in various patient populations.[6,7] Before the routine implementation of a PR technology for PC, a cost-benefit assessment and a proper alignment of all involved manufacturing subprocesses should be integrated for the purpose of optimization.

The extension of PLT storage time (PR allowed to increase the shelf life from 5 to 7 days in Austria) can contribute to the reduction of implementation costs by decreasing outdated PCs.[8] Moreover, by using the INTERCEPT Dual Storage Set for the preparation of two PR-PCs in one process, the production efficacy can be increased while costs can be reduced nearly by half.[9,10] Furthermore, INTERCEPT PR technology makes gamma irradiation obsolete,[11] as well as mandatory or optional bacterial testing.

The Blood Center in Graz is one of the first centers worldwide to have optimized PR of PC from both, a product quality and economic perspective. Therefore, we present our results obtained from a validation study of the production of pathogen-reduced double-dose PCs made of eight whole blood (WB)-derived buffy coats (BCs). Moreover, we focused on the economic impact by comparing the overall costs and savings before and after the implementation of PR.

2 | MATERIALS AND METHODS

2.1 | Preparation and storage of platelet units

WB units with a volume of 450 mL were collected on Day 0 by using a top and bottom blood bag system with 63 mL of citrate, phosphate, dextrose anticoagulant in the primary bag, a soft white blood cell (WBC) filter and 100 mL of saline, adenine, glucose, and mannitol as additive solution for the red blood cell (RBC) concentrate (LQT6281LU, Macopharma). WB units were immediately cooled down to 22 ± 2°C with use of 1,4-butanediol cooling plates (Compocool, Fresenius HemoCare GmbH) and stored overnight at room temperature. WB units were centrifuged the next morning (Day 1) with a water-cooled centrifuge (Roto Silenta 630 RS, Andreas Hettich GmbH & Co. KG) by hard spin centrifugation (4247 × g, 13:30 min, 22 ± 2°C) and separated by blood separator (LUXOmatic, LMB Technologie GmbH) into the components plasma, RBC units, and BC. The resulting small-size single BC from donors with at least 200×10^9/L PLT in peripheral blood (PB), rested between 2 and 4 hours at room temperature. Eight ABO and D identical BCs were thereafter pooled with 280 mL SSP+ platelet additive solution (PAS) (SSP2128U, Macopharma) in a "double train" configuration. The pools of four to eight BCs and a unit of PAS (BC-pools) had a resting time of 5 to 15 minutes before a second centrifugation.

The second centrifugation program ("soft spin", 461 × g, 9:40 min, 22 ± 2°C) was adapted to the volume and Hct of the BC-pool. PC had to meet the INTERCEPT guard bands before PR (volume between 300 mL and 420 mL, plasma ratio between 32% and 47%, PLT yield should not exceed 8×10^{11}). After soft-spin centrifugation of the pool in the last BC bag, the PLT-rich supernatant was separated automatically by LUXOmatic through a WBC filter in a platelet container (CompoStop flex, Fresenius Kabi GmbH). We produced PR-PCs made of eight single BCs with use of a dual storage processing set for PR with an amotosalen container; an illumination bag for exposure to UVA; a bag with a compound adsorption device (CAD) allowing reduction of the concentration of amotosalen and free photoproducts after illumination, whereas covalently bound photoproducts cannot be reduced equally[12]; and two bags for splitting and storage of 2 PC units (INT2504B, Cerus Europe BV). The PR processing set was connected to the PC bag with a sterile connector (TSCD-II Sterile Tubing Welder, Terumo Deutschland GmbH), and the PC was allowed to flow through the amotosalen bag in the illumination bag. After UVA illumination with 3.90 ± 0.01 J/cm^2 and a wavelength of 320 to 400 nm with use of the INTERCEPT illuminator INT-100, the PC was transferred to the CAD bag and stored on a platelet agitator (TA-1, Sarstedt AG & Co KG) for 6 to 16 hours. After being thoroughly mixed, the PC was split equally into the two storage containers; samples were drawn from only one of the two bags, but platelet yield was calculated by volume of each bag. No gamma irradiation or bacterial screening was performed on the PR-PC.

Before the implementation of PR ("pre-PR period"), the hard-spin centrifugation of WB differed from the PR period (4247 × g, 10:00 min, 22 ± 2°C), and the single BC had a mean volume of 52 ± 1 mL. Four BCs and 250 mL SSP+ were pooled in train. Soft-spin

centrifugation differed as well (320 × g, 6:00 min, 22 ± 2°C), and the PLT-rich supernatant was separated into the same filter-bag system as in the PR period. An additional sample (10 mL) from each PC, drawn at least 36 hours after WB collection, was sent for bacterial screening of aerobic and anaerobic strains (BacT/ALERT, bioMerieux) to the Department of Hygiene, and all PCs were gamma-irradiated with 25 to 30 Gray before release. The issue of the products was made on a negative-to-date strategy. An overview of the process of PC production in the pre-PR and the PR periods is shown in Figure 1.

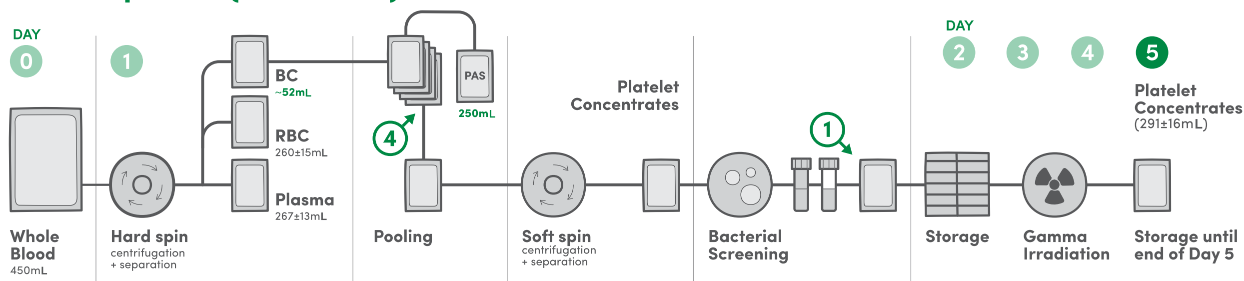
2.1.1 | Analysis of process and quality control parameters

After a resting time of at least 2 hours for single BCs and PCs and thoroughly mixing, samples were taken from each single BC from the BC-pool and from the PC before and after PR (Days 2, 5, and 7). Additionally, a PB sample from the donor was used for calculation of the platelet recovery. Measurements included volume (we used 1.06 g/mL as specific gravity of the single BC and BC-pool and 1.01 g/mL for the PC) and platelet count (Advia 2120i, Siemens Healthcare Diagnostics GmbH) from all samples, Hct from WB, single BC, and BC-pool, as well as pH (Cobas b221 at 22°C, Roche Diagnostics Deutschland GmbH) and swirling (visually determined; 0 indicates no swirling and 3 indicates great swirling) on PR-PC on Days 2, 5, and 7 of storage. Residual WBCs and RBCs were tested in the PC before PR, using flow cytometry (BD FACSCalibur with Trucount absolute count tubes, Becton Dickinson Austria GmbH). Residual amotosalen was tested in PR-PC with a high-performance liquid chromatography method (University Hospital Jena, IKCL). Platelet recovery was calculated in BC with use of WB, in PC with use of the BC-pool, and in PR-PC with use of PC as baseline value. After the validation of the PR process, revalidations regarding the recovery rates were undertaken on an annual basis additionally to the routine quality controls, which were performed monthly on the end products.

2.2 | Cost-benefit assessment

We compared the economic aspects of almost 3 complete years of PR of platelet concentrate made of buffy coat (BC-PC) (1 March 2016-31 December 2018; Period 2) with a historic control of 3 years before implementation of the PR technology (1 January 2013-31 December 2015; period 1). Costs of the PR set (one set for 2 PCs) and illuminator acquisition and maintenance costs were considered. No additional staff was employed after PR implementation; nevertheless, labor costs were considered for better comparability. On the other hand, the savings included the omission of bacterial screening and gamma irradiation, the lower outdating rate (percentage

Pre-PR period (2013-2015)



PR period (2016-2018)

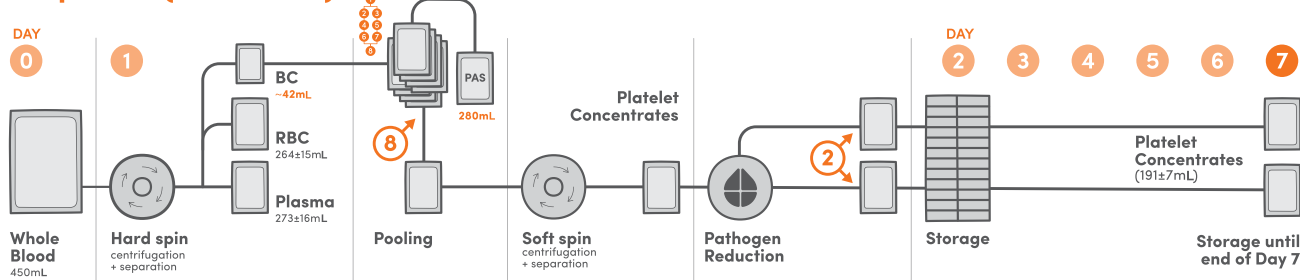


FIGURE 1 Process of preparation and storage of BC-PC in the pre-PR and PR period [Color figure can be viewed at wileyonlinelibrary.com]

of released products that are discarded at the end of storage time) caused by the extension of storage time and the lower scrap rate (percentage of discarded products caused by test or production reasons before release) caused by higher efficiency and better process control of the entire manufacturing and testing process.

2.3 | Statistical analysis

Data are presented in mean and SD for continuous data or by frequencies and proportions (%) for categorical data. Computer software (SPSS version 25.0, IBM Corporation) was used for statistical analyses. The nonparametric Mann-Whitney U test was used to test for significant differences in volume, PLTs, and residual WBCs of PCs, in volume of plasma and in hemoglobin of RBC units in the pre-PR versus PR period. *P* greater than .05 was considered statistically significant.

3 | RESULTS

3.1 | Validation study

In the initial validation study (Table 1) we achieved a BC volume of 41 ± 2 mL, a Hct of 0.39 ± 0.04 and a platelet content of $1.06 \pm 0.18 \times 10^{11}$ per single BC (recovery rate

TABLE 1 Results of the initial validation study

	Parameter	Mean ± SD	Limits
Single BC (n = 24)	Volume (mL)	41 ± 2	
	Hct	0.39 ± 0.04	
	Plasma (mL)	25 ± 2	
	RBC (mL)	16 ± 2	
	PLT × 10^{11}	1.06 ± 0.18	
	PLT recovery (%)[a]	91 ± 8	
Pool (n = 6) consisting of 8 BC + PAS	Volume PAS (mL)	280	
	Volume pool (mL)	580 ± 7	
	Hct	0.20 ± 0.01	
	PLT × 10^{11}	8.2 ± 0.4	
	Plasma ratio	0.40 ± 0.01	0.32-0.47
Double-PC before PR (n = 6)	Volume (mL)	408 ± 9	≤420 mL
	PLT × 10^9/L	1441 ± 60	
	PLT × 10^{11}	5.8 ± 0.2	2-8 × 10^{11}
	WBC × 10^6/U	0.01 ± 0.01	≤1 × 10^6/U
	RBC × 10^9/L	1.3 ± 0.6	≤4 × 10^9/L
	PLT recovery (%)[b]	71 ± 3	
PR-PC after split (n = 12)	Volume (mL)	189 ± 6	
	PLT × 10^9/L	1333 ± 231	
	PLT × 10^{11}	2.5 ± 0.5	≥2.0 × 10^{11}
	PLT recovery after PR (%)[c]	87 ± 14	
	Amotosalen μmol/L	0.3 ± 0,1	≤2.0 μmol/L
	pH on Day 7 (22°C)	7.21 ± 0.11	≥6.4
	Swirling on Day 7[d]	+++	

Note: This study was performed to achieve the manufacturing license for split pathogen-inactivated PC derived from eight BCs with INTERCEPT Blood System.

Abbreviations: BC, buffy coat; Hct, hematocrit; PAS, platelet additive solution; PC, platelet concentrate; PLT, platelet; PR, pathogen reduction; RBC, red blood cell.

[a]PLTs in BC/PLT in WB (volume of WB without additive solution x PLT of the donor).

[b]PLTs in double PC pre-PR/PLT in pool.

[c]PLT in double PC after PR/double PC pre-PR.

[d]Assessment from - to +++.

of 91% ± 8% based on PLTs in WB). After pooling of 8 BCs and 280 mL of PAS, the volume of the resulting BC-pool was 580 ± 7 mL, Hct 0.20 ± 0.01, the platelet yield was $8.2 \pm 0.4 \times 10^{11}$, plasma ratio was 0.40 ± 0.01. Double-PC before PR had a volume of 408 ± 9 mL, a platelet yield of $5.8 \pm 0.2 \times 10^{11}$ resulting in a platelet recovery rate of 71% ± 3% after soft-spin centrifugation. The residual cells were below the limits of the European Directive for the Quality of Medicines, Guide to the Preparation, Use and Quality Assurance of Blood Components: WBC $0.01 \pm 0.01 \times 10^6$/U and RBC $1.3 \pm 0.6 \times 10^9$/L. After PR and splitting, the volume of each single PC was 189 ± 6 mL with a total PLT count of $2.5 \pm 0.5 \times 10^{11}$ and a PLT concentration of $1333 \pm 231 \times 10^9$/L. The PLT recovery rate after PR was 87% ± 14%. The residual amotosalen concentration was 0.3 ± 0.1 μmol/L (below the limit of 2.0 μmol/L). Measured pH at the end of storage was 7.2 ± 0.1. Visual evaluation of swirling was excellent until Day 7.

3.2 | Revalidation of the process

After implementation of PR, we did a revalidation of the whole process on an annual basis with 24, 16, and 60 runs for the years 2016, 2017, and 2018, respectively. We analyzed the quality of the single BC, the pool of eight BCs with PAS and the double PC before and after PR and product splitting. The results (mean ± SD) were stable over the 3-year period, with final PLT content of 2.5 ± 0.3, 2.5 ± 0.2, and $2.4 \pm 0.3 \times 10^{11}$ in 2016, 2017, and 2018, respectively; residual WBCs/RBCs and amotosalen were far below the limits; the PLT recovery rate after soft-spin centrifugation of the pool was 70%, 70%, and 68%, respectively; and the PLT recovery rate after PR was 87%, 91%, and 90%, respectively. A slight adaptation of the automated separation of the PLT-rich supernatant was undertaken and resulted in a 2-mL volume increase for each PR-PC. During the whole study period, we did not perceive any visible aggregates in the PCs either before or after the PR process.

During the study time, the INTERCEPT double set changed, and the new set was introduced into routine in March 2018 after a validation phase. Especially the CAD bag volume increased from 1000 mL to 1300 mL. We did not find higher residual amotosalen amounts, although fewer interaction opportunities for molecules with the CAD were expected. During the validation of the new set, we observed a reduction of remaining amotosalen from 0.3 ± 0.1 in the old set to 0.2 ± 0.0 μmol/L in the new sets respectively.

TABLE 2 Results (mean ± SD) from routine quality control

	Parameter (limit)	Pre-PR period	PR period	Change in PR vs pre-PR	*P* value
PC/PR-PC	**Number of controls**	**972**	**1823**[a]		
	Vol mL	291 ± 16	191 ± 7		< .001
	WBC × 10^6/U (<1.0)	0.05 ± 0.15	0.03 ± 0.16		.156 n.s.
	OOS WBC	0.50%	0.10%		
	PLT × 10^{11}/U (≥2.0 × 10^{11}/U)	2.48 ± 0.40	2.52 ± 0.34		.003
	OOS PLT	10.80%	4.80%		
Plasma	**n**	**1989**	**1843**		
	Vol mL	267 ± 23	273 ± 16	+2.4% (+6.5 mL)	< .001
	WBC × 10^6/L (<100)	28 ± 24	24 ± 20		
	OOS WBC	1.60%	0.80%		
	PLT × 10^9/L (<50)	14 ± 5	12 ± 4		
	OOS PLT	0.00%	0.00%		
RBC units	**n**	**1989**	**1837**		
	Vol mL	260 ± 15	264 ± 15		
	WBC × 10^6/U (<1.0)	0.14 ± 0.26	0.32 ± 0.16		
	OOS WBC	1.7%	0.8%		
	Hb g (>40)	49.4 ± 5.1	50.0 ± 5.1	+1.2% (+0.6 g)	<.001
	OOS Hb	2.7%	1.7%		

Note: Results of PC, plasma, and RBC units in the pre-PR and PR period (random samples from routine quality control).

Abbreviations: Hb, hemoglobin; OOS, out of specification; PC, platelet concentrate; PR, pathogen reduction; RBC, red blood cell; WBC, white blood cell.

[a]In the first year of the PR period the frequency of controls was higher for better process control.

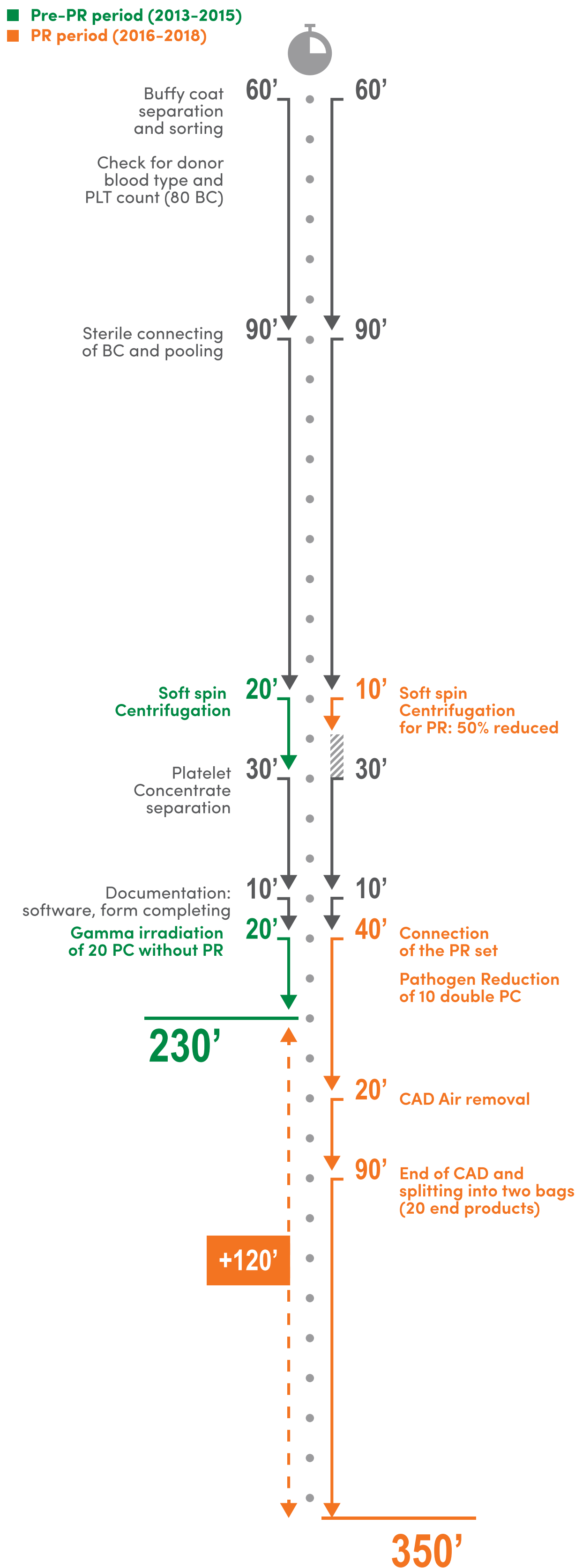


FIGURE 2 Comparison of working time for conventional and pathogen reduced PC (20 end products for each group) [Color figure can be viewed at wileyonlinelibrary.com]

3.3 | Comparison of PC in the pre-PR and PR periods including the concomitant products plasma and RBC units

In the pre-PR period, 19 666 PCs were produced compared to 17 307 PCs in the PR period. When comparing the random sample quality controls of the blood components manufactured in the period before and after PR implementation, we are able to show positive volume effects in favor of the concomitant plasma and RBC unit related to necessary volume reduction of each single BC. As shown in Table 2, the volume of each single PC was markedly reduced from 291 ± 16 mL to 191 ± 7 mL in the pre-PR versus PR period. The platelet content of each PC increased slightly but significantly despite the inherent loss through the PR process. The rate of out-of-specification (OOS) products (PLTs $<2.0 \times 10^{11}$/U) could be reduced, and so did the OOS rate for RBC units regarding hemoglobin (Hb) content and WBC contamination. In addition, the Hb content of the RBC units increased by 1.2% and the volume of the WB-derived plasma increased by 2.4% in the PR period (in both cases $P < .05$). The reduced OOS rates, the higher mean amount of Hb content in RBCs, and especially the higher volume of plasma brought an incremental revenue and had an impact on the economic aspects since in our case most of the plasma is sold to the plasma industry for fractionation.

3.4 | Working time

Working time including documentation steps and labor costs are calculated for a staff member producing 20 PCs without PR (230 minutes) vs 10 double PCs and treating them to obtain 20 PR-PCs covering the mean daily PC production (350 minutes). Consequently, each INTERCEPT-treated PC required only 6 more minutes of working time and €4 of additional personnel cost per produced PR-PC (Figure 2).

3.5 | Scrap and outdating rates

We compared the scrap and outdating rates for the two 3-year periods. Scraps are related to the products eliminated due to positive or discrepant test results from infectiology and immunohematology, which were not present at the time of production and by production waste caused by machine or human errors. Although the PR process has a higher complexity, the scrap rate could be slightly reduced by higher efficiency and better process control of the testing and production process: 6.9%

TABLE 3 Scrap rate and outdating rate

PC/PR-PC	Pre-PR period 2013-2015	PR period 2016[a]-2018	
PC produced	19 666	17 307	
PC released	18 303	16 464	
PC scrapped prior release	1363	843	
Scrap rate	6.9%	4.9%	Drop down of ~1/3
PC outdated	3214	976	
Outdating rate	17.6%	5.9%	Drop down of ~2/3

Outdating rate, percentage of released products which are discarded at the end of storage time; scrap rate, percentage of discarded products caused by test or production reasons before release.
[a]Data of 2016 started in March (extrapolated to 12-mo period).
PC, platelet concentrate; PR, pathogen reduction.

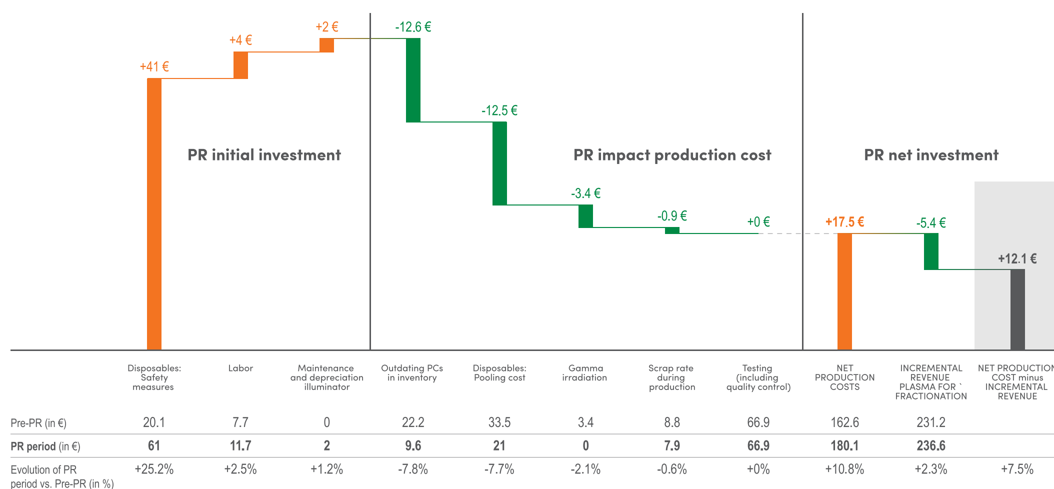


FIGURE 3 Health economics. Comparison of the costs and savings of the pre-PR and PR period by platelet concentrate [Color figure can be viewed at wileyonlinelibrary.com]

in the pre-PR vs 4.9% in the PR period). Not surprisingly, the outdating rate could be markedly reduced by the extension of storage time. The outdating rate in the observed period dropped down from 17.6% to 5.9% (Table 3).

3.6 | Economic aspects

The overall economic aspects of the implementation of PR by comparing the pre-PR period with the post-PR period include the labor time, disposables, bacterial testing, and gamma irradiation (pre-PR period), maintenance and depreciation costs, scrapped and outdated PCs, and incremental revenue. The incremental costs in the PR period for one single PC associated mainly with disposables, labor time, and scrap and outdating rate was €17.5. Due to the incremental revenue of the plasma for fractionation the costs were reduced to €12.1 or 7.5% per single PC (Figure 3). The higher safety of the product or the theoretically reduced septic transfusion reaction rate and associated costs are not considered in this model.

4 | DISCUSSION

PR of PC contributes to the safety of platelet transfusions. Jutzi et al.[1] reported that, since 2011 when PR was introduced to treat 100% of the PLTs produced in Switzerland, no further transfusion-transmitted bacterial infection was recorded compared to 16 - including three fatalities - reported in the 7-year period before PR was implemented.

The overall advantage of PR-PC is greater if an extended shelf life is generally accepted by the national authorities. Although the Graz Blood Center had screened for aerobic and anaerobic bacteria in the pre-PR era at the beginning of storage of PC on Day 1, storage

time was not extended from 5 to 7 days. Nevertheless, two septic transfusion reactions were observed over a period of 15 years, one with BC-PC and one with apheresis PC,[13] both after 4 days of storage. An overview of different approaches on precaution measures to mitigate the risk of bacterial transmission in Europe is given by Prax et al.[14] regarding several aspects such as the shelf life of PLTs, time of sampling, and the applied control measures. The analysis revealed a broad heterogeneity of procedures. The Food and Drug Administration has recently released a guidance[15] to mitigate bacterial risk with strategies for blood collection establishments to safeguard the PLT supply. The reported rates of septic transfusion reactions from PLTs vary from 1 in 100.000 to 1 in 10.000, following testing with single aerobic culture performed no sooner than 24 hours after collection.[16,17] Failure of culture-based bacteria screening methods to prevent septic transfusion reactions keeps being reported on a regular basis and is now supported by a number of publications.[18–23] In addition, the annual SHOT Report for 2018[24] states that screening of PLT components cannot guarantee bacteria-free PC. The investigation of suspected bacterial incidents is time and cost consuming. In the theoretical work of Kacker et al.,[25] which compared the financial impact of three approaches to reduce bacterial contamination of apheresis PCs, PR is said to have the greatest effect on the reduction of this risk but has the highest per-unit costs seen from the perspective of a hospital transfusion service.

Cost implications associated with implementation of PR for apheresis PCs were analyzed by McCullough et al.,[26] who reported that there are potential cost reductions, especially after extension of the shelf life to 7 days, but differences in institutional practices require case-by-case analyses. In addition, McCullough et al. considered the added benefit that, with PR, the need for new blood screening test implementation, especially for emerging infectious diseases, could be avoided. This benefit of PR is occasionally discussed by expert committees. As it is unclear which tests could be avoided if PR is implemented, such considerations were not included in our analysis.

4.1 | Limitations

We have to emphasize limitations of our work, too. Besides the storage parameters pH and swirling effect, we did not perform in vitro quality parameters like platelet morphology, ultrastructure, phenotypic alterations, release reactions, or function tests such as aggregation or adhesion under flow. Furthermore, we have not collected clinical data such as corrected count increment or bleeding outcomes of the transfused patients. We hereby refer to the results of clinical studies.[27,28]

During the study period some conditions changed. The infectious test results could be obtained more rapidly in the PR period because of the implementation of new laboratory technologies. Therefore, positive results could be considered before production started, so scrap rate could be reduced. As mentioned above, the INTERCEPT double set changed, and the new one was used for the last 10 months of the PR period.

Finally, the processing costs are related to special conditions of the Graz Blood Center and can give only general information to readers, but it must be replicated individually on each site. In practice, the implementation of a new technology in the production process of BC-PC provides the opportunity to reconsider each processing step, to better coordinate processing and to review procedures, which can lead to higher efficacy, yield, and quality, each of which can result in cost savings.

The "one PR treatment for two PR-PCs" approach could be successfully implemented at the Graz Blood Center. The results obtained from a 3-year period before and after PR implementation with the INTERCEPT Blood System has been found to meet process requirements, control of the overall costs, and improving the safety profile of PR-PCs.

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CONFLICT OF INTEREST

The Graz Blood Center performs company-funded trials for Cerus and is under contract to perform routine PR for platelets and plasma in. KR and WH declare no conflicts of interest. PS has received honorarium and reinbursement for travel expenses in the past 5 years.

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