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# Analysis of red blood cell irradiation practices from South India

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## Abstract:

**INTRODUCTION:** Age of red blood cell (RBC) units at the time of irradiation is important and prolonged storage of preirradiated units is detrimental. The objectives were to determine RBC age at irradiation, days from expiry (DFE), and percentage of late transfusions of irradiated RBC. To estimate the concordance on expiry of irradiated RBC units with present American Association of Blood Banks (AABB)/Directorate General of Health Services (DGHS), New Delhi over British Committee for Standards in Hematology (BCSH) and Council of Europe (CE) guidelines.

**METHODS:** All the RBC units irradiated for a 1 year period were included. Retrieved data included date of collection, irradiation, revised expiry, and issue of blood. Late transfusions are units transfused in the last 2 week of RBC's shelf-life and wastage due to expiry was determined. Chi-square and Kruskal–Wallis test were used for comparisons between the guidelines.

**RESULTS:** Out of 1303 RBC units irradiated, the median age for irradiation was 2 (0–36) days and 99.3% units irradiated within day +14. Median DFE for these units transfused was 26 (0–28) days. 2.8% units expired as per local standards. Late transfusions happened in 121 (9.3%) units transfused. AABB/DGHS practice was not concordant with CE standards for 86 (6.6%) units and with BCSH 94 (7.2%) units. Overall discordance between the present practices was CE and BCSH was seen in 130 (10%) events.

**CONCLUSION:** Median RBC irradiation age and DFE was two and 26 days respectively at our center. Only 90% concordance was observed between AABB/DGHS and CE/BCSH guidelines with 9.3% units transfused as late transfusions. Restricting late transfusions of irradiated RBC can act as surrogate to improve the quality of units transfused through an inexpensive strategy.

## Keywords:

Irradiated red blood cell, packed red blood cell, quality control of red blood cell, red blood cell expiry

## Introduction

The presence of lymphocytes in cellular blood components can give rise to a fatal but rare complication known as Transfusion Associated Graft versus Host Disease (TA-GvHD).<sup>[1]</sup> The process of irradiation of cellular blood components inactivates the residual lymphocytes either using Gamma rays (from cesium-137 or cobalt-60) or X-rays thereby preventing TA-GVHD. Earlier studies concluded that both gamma irradiation and X-irradiation for blood

components are comparable, safe, and suitable for clinical application as concluded by the Joint Professional Advisory Committee of the UK Transfusion Services.<sup>[1]</sup>

Irradiated blood continues to be in a meager supply. In India, only few centers have the capability for on-site irradiation of blood. Few centers use Linear accelerators for meeting the requirements of irradiated blood. With the increase in bone marrow transplant programs in India, the transfusing facilities focus on maintaining adequate inventory of blood components.

To reduce the chances of issuing nonirradiated blood to hematology/oncology patients

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who are at risk of developing TA-GVHD, the universal irradiation policy was adopted in few centers.<sup>[2]</sup> Blood components irradiated soon after collection and stored can help maintaining a favorable inventory.<sup>[3]</sup> However, prolonged storage and overstocking of irradiated blood components can have detrimental effects and is not recommended either. Preirradiated red blood cell (RBC) units when stored for a prolonged time are shown to have high potassium levels, *in vitro* hemolysis, and decreased posttransfusion recovery.<sup>[4]</sup> Furthermore, there are odds of transfusing the irradiated units to the patients who otherwise do not require them.<sup>[5]</sup> National Advisory Committee (NAC) on Blood and Blood Products and Quebec's NAC on Transfusion Medicine Irradiation Working Group recommended to irradiate the units as close to the transfusion.<sup>[5]</sup>

Various recommendations and regulations exist to define the acceptable duration of RBC storage pre- and post-gamma irradiation.<sup>[4,6]</sup> Directorate General of Health Services (DGHS), New Delhi has adopted the American Association of Blood Banks (AABB) gamma-irradiation practices, which recommends that irradiation, may be done any time during RBC storage and postirradiation stored up to a maximum of 28 days.<sup>[7,8]</sup> While performing quality control (QC) of blood components is a mandatory requirement in India, not many centers have adopted or monitor QC of irradiated blood components.

The present study is the first attempt from India to analyze single center data on RBC irradiation practice and would provide a helpful guide for improving the utilization and wastage of irradiated RBC components. The secondary objectives were to estimate the RBC age at the time of irradiation, length of storage of RBC units postirradiation, and percentage of units transfused as late transfusions. And to estimate and compare the expiry dates of irradiated RBC units using AABB practice with the British Committee for Standards in Hematology (BCSH) and Council of Europe (CE) Guidelines.

## Methods

This study was a retrospective descriptive study, data relating to irradiation practice and utilization of irradiated RBC component for 1 year at tertiary cancer center from South India.

### Blood transfusion service

Universal irradiation and leukoreduced RBC policy were adopted at the hospital for all hemato-oncology patients. The blood center performs leukoreduction either by inline filtration of whole blood on day 0 or by lab-side filtration of buffy coat-reduced RBCs based on the inventory requirements. Irradiation was carried out

using BioBeam GM 2000, Germany. The intended RBCs were stacked in the canister and a standard dose of 25 Gy was delivered between day 0 and day +42 of collection and subsequently stored for 0–28 days without exceeding the storage time of 42 days as per AABB/DGHS guidelines.<sup>[4]</sup> The irradiation indicator labels on the blood bags used during irradiation ensured adequate dose delivered at the end of the procedure. Regular dose mapping of equipment was undertaken and the exposure time was revalidated at suitable intervals.<sup>[9]</sup>

### Study parameters

The data on irradiated RBC components such as collection date, original expiry date, revised expiry, transfusion date, and wastage were retrieved from the irradiation register and blood banking information system. The following parameters were analyzed.

- RBC age: Days to irradiation from collection date
- Days from expiry (DFE): Subtracting transfusion date from the expiration date<sup>[10]</sup>
- Late transfusions: Units transfused in the past 2 weeks of RBC's shelf-life
- Percentage of irradiated RBC issued out of the group
- Percentage of irradiated RBC issued for nonhemato-oncology patients.

Table 1 discusses the regulations with respect to the maximally acceptable storage time of RBCs before and after gamma irradiation. The date of irradiation and revised date of expiry was subtracted from the calculated maximum allowable day of irradiation and revised expiry between BCSH, CE, and AABB guidelines. The existing practice was compared with the adherence to BCSH and CE guidelines on irradiated RBC components.

### Statistical methods

Data were first entered in MS Excel and later analyzed using SPSS 20.0 SPSS 20.0 IBM, Chicago, Illinois, United States. Results were tested for normal distribution by Shapiro–Wilkes tests. Descriptive statistics were used for determining RBC age, length of storage of RBC units postirradiation, etc., Analysis using Mann–Whitney U-test was performed for nonparametric methods. The concordance rates among the three guidelines were

**Table 1: Regulations with respect to the maximally acceptable storage time of red blood cells before and after irradiation<sup>[1,7-9]</sup>**

Parameter	AABB/DGHS	CE	BCSH
Days to irradiation from collection	No limit	28	14
Days to expiry from irradiation	28 days or original expiry	14	14

AABB=American Association of Blood Banks, DGHS=Directorate General of Health Services, CE=Council of Europe, BCSH=British Committee for Standards in Hematology

analyzed. Chi-square and Kruskal–Wallis test were used for comparisons between the guidelines. A  $P < 0.05$  was considered significant.

## Results

Out of 2400 RBC units prepared, 1303 (54%) units were leukoreduced and irradiated. All patients under hemato-oncology unit received only irradiated blood. Seventy-two irradiated RBC units were issued to nonhematooncology patients, i.e., surgical and radiotherapy patients as inventory management. Thirty-six (2.8%) units expired as per AABB/DGHS standards, where irradiated units could not be utilized within 28 days of irradiation. To manage inventory, out-of-group transfusion was necessary in 46 units.

The median RBC age of RBC for irradiation was day +2 (interquartile range [IQR]: 1–3; range: 0–36) days [Figure 1]. 93.4% units irradiated within 1 week of collection and 99.3% units within day +14 of collection. Nine units were irradiated beyond day +14 with one unit irradiated after day +28 of collection (day 36) [Figure 2].

The median DFE for these units transfused was 26 (IQR: 21–28; range: 0–28) days. Seventy-seven percent of units transfused had more than 21 DFE and 90.7% had more than 14 DFE. Late transfusions happened in 121 units (9.3%) which had <14 DFE after irradiation [Figure 3]. Moreover, 4.5% of units which were transfused had <7 DFE.

The blood centre irradiation practice was in full compliance with AABB/DGHS recommendations. However, the practice was not concordant with CE

standards for 86 (6.6%) units and with BCSH 94 (7.2%) units. Overall discordance between the present practice against CE and BCSH was seen in 130 (10%) units.

The units which are compliant with CE had strong positive correlation with BCSH recommendations also ( $r = 0.95$ ), while the centres irradiation practice (AABB/DGHS) had no correlation with either CE ( $r = -0.04$ ) or BCSH ( $r = -0.04$ ).

## Discussion

In recent years, there has been a surge in the percentage of irradiated RBCs from 4.5% (2004–2005) to 6.7% (2015–2016).<sup>[5]</sup> Our center is a multidisciplinary tertiary cancer center where more than half of the RBC units utilized were irradiated and served mostly to patients with hematology disorders. To our knowledge, this was the first audit on irradiation practices in RBC units from India providing comprehensive details on RBC age and DFE. Almost all units (99.3%) were irradiated within day +14 of the collection with median RBC age at the time of irradiation of 2 days. 90.7% units had more than 14 DFE at the time of transfusion with median DFE of 26 days. The blood center practices RBC leukodepletion by filtration before subsequent irradiation in all units as this process has exhibited improved *in vivo* 24 h survival when stored with the additive solution by earlier studies.<sup>[6]</sup>

Blood centers adopt irradiation practices based on the infrastructure facility available and also blood requirements. For a center with gamma irradiation facility and with regular need for irradiated RBC

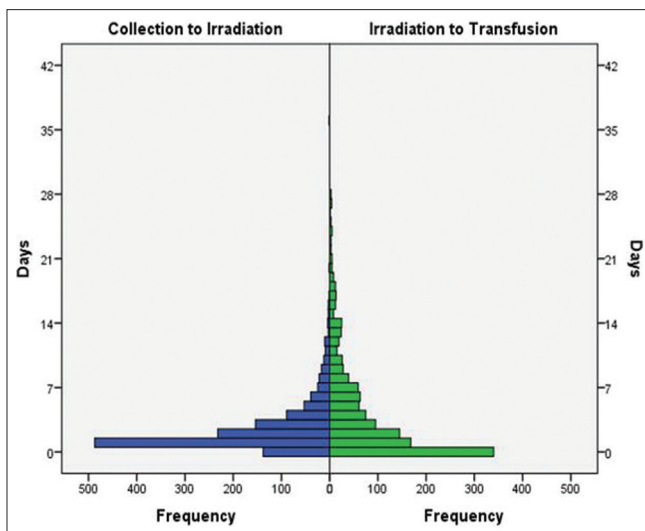


Figure 1: Distribution of red blood cells age and length of storage of irradiated red blood cells units at tertiary cancer centre

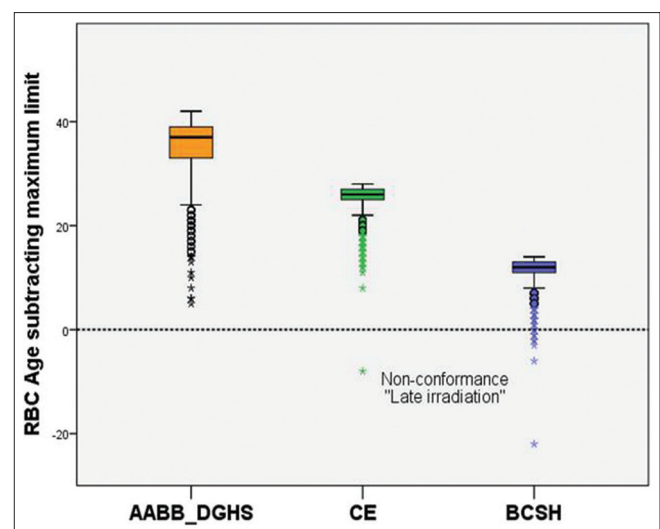
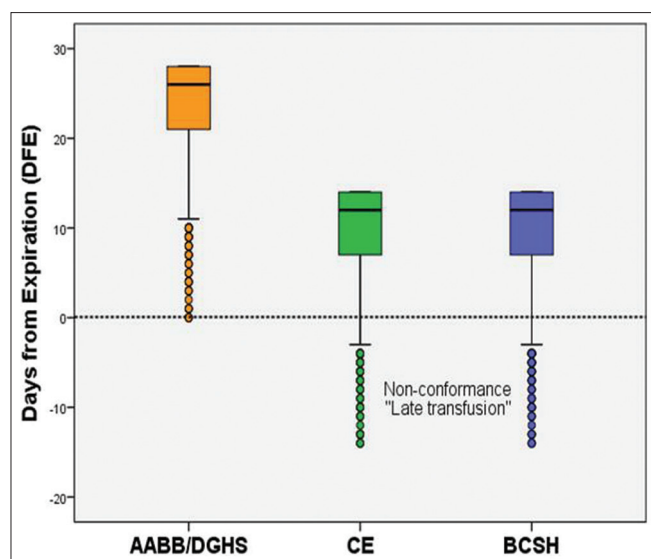


Figure 2: Comparison of American Association of Blood Banks/American Association of Blood Banks with British Committee for Standards in Hematology and Council of Europe on the distribution of red blood cells age available after irradiation (days to irradiation subtracted from maximum allowable days for irradiation from collection)



**Figure 3:** Comparison of American Association of Blood Banks/American Association of Blood Banks with British Committee for Standards in Haematology and Council of Europe on the distribution of days from expiration among transfused irradiated red blood cells units

usually prefer storage of a large number of irradiated units within maximally acceptable storage time. While others adopt irradiation policies based on demand either using gamma irradiation or outsource blood to radiation oncology facility for irradiation. Our center adopted maintaining half of the RBC units' inventory as irradiated RBC.

Multiple studies investigated the effects of early irradiation and subsequent storage versus late irradiation of units before the shelf life (stored longer than 14 days) on RBC quality. Age of RBC at time of irradiation is important and prolonged storage of preirradiated units is detrimental.<sup>[11]</sup> Hemolysis in irradiated RBC was strongly explained by prolonged storage of preirradiated units.<sup>[4]</sup> Similarly, prolonged storage of irradiated units was also associated with high potassium levels, reduced RBC adenosine triphosphate levels, increased RBC rigidity, and decreased posttransfusion recovery.<sup>[3,4,12,13]</sup> It was also recommended that irradiation of RBCs therefore should occur as near-to as possible to the time of transfusion.<sup>[5]</sup>

AABB/DGHS permits storage of irradiated RBC up to 28 days, while BCSH/CE guidelines allow only 14 days of storage postirradiation [Table 1]. Serrano *et al.* Observed that RBC when irradiated in their 4<sup>th</sup> week of storage and subsequently stored for 15–21 days exhibited the highest level of hemolysis.<sup>[4]</sup> Zimmermann *et al.* also reported RBCs that are irradiated later than day +14 may be subsequently stored for a maximum of 7 days, at least if they are irradiated before day +28.<sup>[6]</sup> And units irradiated later than day +28 and when stored should be avoided in patients who are sensitive to enhanced

potassium levels.<sup>[6]</sup> Only nine (<0.01%) units were irradiated beyond day +14 at our center, while 9.3% units transfused beyond 14 days from irradiation. These transfusions were considered as late transfusions of irradiated RBC and were noncompliant as per BCSH/CE guidelines [Figures 2 and 3].

In an ideal setting, outdated and wastage of blood and blood products would never occur. To limit the outdated of irradiated RBC units, 5.8% units were issued to nonhematology patients where irradiation was not indicated. Further, the wastage of irradiated RBC was 2.8%. Due to the inherent need to maintain adequate blood stocks at all times and also often unpredictable demands for other components such as platelets, an inevitable outdated of RBC components in blood can be accepted.<sup>[14]</sup> With the available evidence, units stored longer can result in poor *in vitro* quality.<sup>[4]</sup> Serrano *et al.* From Canada reported there is a need for reconsideration in the timing of RBC irradiation and storage time postirradiation to avoid transfusions of poor quality units.<sup>[4]</sup>

This study being retrospective one, the only information available in the irradiation records was used for the study. Due to this limitation, it was not possible to determine the change in biochemical parameters in irradiated RBC components during the study period.

## Conclusion

This study was an attempt to analyze the center's irradiation practice with the focus on areas to review late transfusions of stored irradiated units and reduce wastage. The current irradiation practice had only 90% concordance with CE/BCSH guidelines with 9.3% units transfused as late transfusions. Although the quality assurance in blood banking have established efficacy in blood component production, the efficacy of transfusion of prolonged storage of irradiated RBC without measuring plasma hemoglobin or extracellular K + is said to be less than optimal. Restricting late transfusions of irradiated RBC can act as surrogate to improve the quality units transfused through an inexpensive strategy. Finally, the study hopes to draw attention toward early versus late irradiation of RBC in future studies from India to avoid transfusion of inferior quality of RBC units.

## Ethics consideration

Institutional review board (IRB) approved the present study without ethical approval through Ref. No: 1616/IRB-SRC/13/MCC/12–10-2019/5; dated: October 18, 2019, before the start of the study.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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