Irradiatinon of Blood and Blood Components

Background

Transfusion-Associated Graft-versus-Host Disease (TA-GvHD) is a rare, usually fatal, complication of transfusion resulting from the engraftment of transfused, immuno-competent, donor lymphocytes and subsequent damage to recipient tissues which are perceived as foreign by the engrafted lymphocytes. Patients at most risk include those who are severely immuno-compromised and those who fail to recognize the transfused lymphocytes as foreign, due to Human leucocyte antigen (HLA) homology. The risk associated with an individual transfusion depends on the number and viability of contaminating lymphocytes, immune status of the recipient and degree of HLA disparity between donor and patient. The minimum threshold for transfused lymphocytes necessary to induce TA-GvHD is unknown.

Since there is no effective treatment, prevention of TA-GvHD is of the utmost importance. Irradiation of blood components is a well-established method for the prevention of TA-GvHD.

Blood Components that need to be irradiated.

- For patients who are at-risk, all cellular blood components should be irradiated, except cryopreserved red cells after deglycerolization. Therefore, following components need irradiation
    - Whole blood
    - Packed red blood cells
    - Random donor platelet concentrates
    - Apheresis platelet concentrates
    - Granulocyte component
- It is not necessary to irradiate fresh frozen plasma, cryoprecipitate or fractionated plasma products; such as clotting factor concentrates, albumin and intravenous immunoglobulin.
- All cellular components obtained from first- or second-degree relatives should be irradiated, even if the patient is immuno-competent as there is increased risk of TA-GvHD because of HLA homology.
- All HLA-matched platelet components should be irradiated.
- Hematopoietic stem cells must not be irradiated.

Dose of Irradiation

- For red cells, platelets and granulocytes, it is recommended that blood component must receive a minimum central dose of 25 Gray, with no portion of component receiving less than 15 Gray.
- To ensure this dose distribution is achieved, it is very important to liaise with medical physicists in the hospital for regular and precise dosimetry.

Shelf - life and post irradiation storage of components

- Red cell components such as whole blood or packed red blood cells can be irradiated up to 28 days after collection.
- Irradiated cells must be transfused as soon as possible, but no later than 14 days after irradiation, and, no later than 28 days after collection, whichever is less.
- For intrauterinetransfusions or neonatal exchange transfusion, it is recommended that red cells be transfused within 24 hours of irradiation.
- Platelets can be irradiated at any stage during storage and can thereafter be stored up to their normal shelf life after collection.
- All granulocyte transfusions should be irradiated for recipients of any age, and they should be transfused as soon as possible after irradiation.

Labeling and documentation

- All Irradiated blood components must be appropriately labelled as “IRRADIATED” for positive visual verification.
- The label should be permanent and include the date of irradiation and any reduction in shelf life.
- To identify operator failure or instrumentation malfunction & to assure that components have been adequately irradiated, it is essential to put indicator labels that are sensitive to irradiation and change from ‘NOT IRRADIATED’ to ‘IRRADIATED’. Such indicators are commercially available. The dose at which the label changes to ‘IRRADIATED’ must be marked on the label.
- However, it may not be necessary to attach a radiation-sensitive label to every component unit, provided that the irradiation procedure follows a validated, documented and well-controlled quality system that permits retrospective audit of each stage of the irradiation process.Application of indicator tag on at least one unit every day of irradiation is acceptable evidence to assess the efficacy/ functional status of blood irradiator.
- Records should be maintained with information of all units irradiated, including details of irradiation batch and donation numbers, component type, the dose of irradiation, date & time of irradiation and signature of the individual performing irradiation.

Quality of Irradiated Blood Components

- Irradiated red cells have been shown to contain more cell-free haemoglobin (approximately 50% increase) & supernatant K^+ than control cells after equivalent periods of storage. There is no demonstrable, clinically significant effect of irradiation on red cell pH, glucose consumption, ATP or 2,3-Diphosphoglyceric acid (2,3-DPG) levels. It is therefore essential to monitor the quality of irradiated red cell components.
- Irradiation of platelets any time from day 1 to day 5 shows no demonstrable significant changes in platelet function & platelet quality during a 5 day storage period.

Clinical Situations requiring gamma irradiated blood components

- All transfusions from first degree blood relatives must be irradiated, even if the recipient is immunocompetent.
- All HLA-matched platelets must be irradiated, even if the recipient is immunocompetent.
- All granulocyte products must be irradiated & transfused with minimum delay.
- Patients treated with purine analogue drugs (fludarabine, cladribine and deoxycoformicin) should receive irradiated blood components indefinitely. All patients receiving alemtuzumab (anti-CD52) should be administered only irradiated blood components
- Patients with aplastic anaemia who are receiving immunosuppressive therapy such as ATG must receive irradiated red cells and platelets
- Patients with Hodgkin disease should receive irradiated cellular blood components at all stages of disease and therapy
- Consideration should be given to transfusing irradiated cellular blood components to patients with B and T cell non-Hodgkin's lymphoma (NHL).
- All patients undergoing autologous haematopoietic stem cell transplantation (HSCT) must receive gamma irradiated cellular blood components from the initiation of conditioning chemo/radiotherapy until at least three months post-autograft (or six months if total body irradiation used).
- All recipients of allogeneic HSCT/ bone marrow transplant (BMT) must receive irradiated cellular blood components from the time of initiation of conditioning chemo/radiotherapy. Transfusion of only irradiated cellular blood components should be continued while the patient remains on post-transplant GVHD prophylaxis, usually for a minimum of twelve months or until lymphocytes are $>1x10^9$/L.
- Irradiation of cellular components is recommended for all infants/children with suspected or diagnosed T-cell immune deficiency states.
- Premature infants <28 weeks or weighing less than 1300g should be given irradiated cellular components.
- All red cells and platelets for intrauterine transfusion & exchange transfusion must be irradiated.
- Patients who do **NOT** routinely require irradiated products
    - Top up transfusions or other blood products unless
        - An infant who has received IUT of blood or platelets (then required for 6 months post expected delivery date)
        - Products from a donor who first or second degree relative
    - Chronic or acute leukaemia
    - Solid tumours
    - Cardiac transplants
    - Other organ transplants (Unless alemtuzumab has been used in the conditioning regimen).
    - Patients with HIV/AIDS
    - Other acquired immunodeficiency
    - Aplastic anaemia unless treated with anti-thymocyte globulin (ATG)

- Thalassemia

Technical Information

- Institutions should have policies and procedures in place to ensure that all transfusion recipients who require irradiated components are identified and receive appropriate components.
- All facilities performing irradiation of blood components must ensure compliance with guidelines of Atomic Energy Regulatory Board (AERB) of India for use of radioactive material. Specific guidelines for gamma irradiation chambers are provided in AERB document No AERB/RF-RPF/SG-2 (www.aerb.gov.in)
- It is recommended that irradiation of blood components is carried out using dedicated blood irradiation machines with a gamma emitting source (cesium-137 or cobalt-60), or X-ray based irradiators. If radiotherapy machines (linear accelerators) are used, equivalent validated protocols should be developed.
- Gamma rays and X-rays are similar in their ability to inactivate T lymphocytes in blood components at a given absorbed dose. This X-irradiation may be regarded as equivalent to gamma irradiation. Guidelines with regard to dose and permitted post irradiation storage time are the same, as are the required labelling and dosing for gamma irradiation.
- Laboratories performing irradiation of blood components are strongly recommended to work closely with a medical physicist and/or Radiation safety officer (RSO). The defined irradiation procedure must be validated and there must be regular monitoring of the
- Radiation safety, dosimetry and personnel safety issues should be under the responsibility of a suitability qualified person in accordance with guidelines of AERB of India.
- The irradiator manufacturer, or their agent, should commission the irradiator and, on completion of commissioning, provide a calibration certificate for a dose rate at a specified point in the canister calibrated to traceable national standards.
- Following calibration, a table must be produced which gives irradiation times for specified doses for a set period. Both the dose rate and the dose distribution must be checked upon installation, at least annually, and after any source change or mechanical alterations, particular to the rotating turntable, as applicable.
- It is necessary to periodically lengthen the time of irradiation to correct for decay of the isotopic source. With the half-life for Cs-137 being 30 years, annual lengthening of the timer setting is appropriate. Half-life of Co-60 being only 5.27 years, the time of irradiation should be increased on a quarterly basis, as applicable.
- Quality control procedures must be implemented and all operators must have been adequately trained in the use of the equipment.
- Preventative maintenance procedures must be in place and “wipe tests” must be carried out at regular intervals, preferably six monthly, to check for leakage of radioactive contamination.
- Irradiated components not used for the intended recipient can safely be used for recipients who do not require irradiated components provided the other requirements with regard to quality of component have been satisfied. However, any reduction in shelf life resulting from the irradiation process must be observed.

- Blood centers which do not have facility for irradiation can get blood component irradiated from a facility having a blood irradiator and necessary approval and license (such as AERB). There should be an agreement or memorandum of understanding (MOU) for this purpose.