Midterm Report
IPRO Team 304C
Submitted 3/25/2005

BACKGROUND:

Human blood is a suspension of three types of blood cells (red blood cells, white blood cells, and platelets) in an aqueous solution called plasma. Each type of cell plays a specific role in maintaining life. The current trend in blood transfusion is to deliver to the patient only cells of the required type. This allows efficient use of the existing blood supply. Therefore, when whole blood is collected from a donor, it is typically separated into its cellular and plasma components.

With the use of appropriate additive solutions, red blood cells may be stored for up to 42 days at 1-6 °C. If frozen, however, they may be safely stored for ten years or more. In order to freeze and thaw red blood cells without inducing cell rupture (hemolysis), it is necessary to use a cryoprotective agent such as glycerol. After the cells have been thawed, this cryoprotective agent must be removed before the cells can be transfused to a patient.

The use of glycerol as a cryoprotective agent for red blood cells was first reported by Smith in the early 1950s. During the next decade, the clinical effectiveness of frozen red blood cells was confirmed. The only obstacle was to generate a procedure for glycerolization and deglycerolization of red blood cells.

In 1960, Tullis et al were able to transfuse several units of deglycerolized red blood cells with a continuous-flow centrifugal cell washing device which was capable of avoiding hemolysis. However, there were still many problems with sedimentation of the glycerolized red blood cells that made this procedure impractical.

During the 1960s, a number of workers, including Latham, Tullis, Haynes, Valeri, and others refined this technique, and, in 1969, the American Red Cross accepted this method as the primary method for use in its blood banks. This provided a new market and created possibilities for new research in the field.

In the late 1960s and early 1970s, a number of commercial devices based on this technique became available. These include the IBM 2991 Blood Cell Processor, the Haemonetics Cell Washer, and the Fenwal Elutramatic. All of these devices provided high blood cell recovery with low residual glycerol levels. The United States military currently employs the Haemonetics ACP215, a centrifugal device based on the Haemonetics Cell Washer.

As an alternative to these centrifugal cell-washing devices, various membrane separation devices have been considered. Membrane technologies are widely used for numerous blood cell processing applications, including hemodialysis, hemofiltration, and plasmapheresis. However a membrane filtration device for deglycerolization of thawed red blood cells is not available currently. Potential advantages of membrane devices compared to centrifugal devices include reduced weight and reduced cost, as well as reduced risk of contamination when compared to open-circuit centrifugal devices.

In 1980, Zelman et al reported on the use of a novel blood bag constructed of a semipermeable membrane material for glycerolization and deglycerolization of red blood cells. In the late 1980s and early 1990s, workers including Radovich and Van Reis investigated deglycerolization procedures using hollow fiber and flat sheet membranes, respectively. In 1996, Castino and Wickramasinghe described methods for designing a hollow fiber microfiltration system for deglycerolization of red blood cells.

As part of this project, we have designed a membrane-based system for deglycerolizing packed red blood cells. This system should be able to compete successfully with the centrifugal cell-washers in the blood banking industry. This objective and the methods we have and will use to accomplish our goal are outlined below.

OBJECTIVE:

The objective of this project is to develop a system for washing multiple units of frozen red blood cells in emergency situations. The key parameters that would be emphasized in the project are:

- Selection of the optimal technology for the washing process.
- Making the system portable by considering parameters like weight, dimensions, and alternative power sources.
- Automation of the system.
- Minimization of wash-solution usage by considering techniques such as recycling.
- Minimization and efficient disposal of biological waste.
- Compliance of the washed blood with the blood transfusion standards such as hematocrit values.

METHODOLOGY:

To accomplish the goals set forth in the project plan, the team divided into three groups which were the standards, membrane, and centrifuge groups. The membrane and centrifuge groups then conducted research to decide which method, centrifugation or membrane separation, would be the most effective to meet the criteria as defined by the standards group. During this research phase, we consulted with Dr. Radovich and are continuing to refine our goals. The team selected the membrane-based washing process, and will continue to conduct research into which kind of membrane will be most effective and which operating variables will affect the portability of the device. In order to complete the project, we will form new groups to perform cost analysis and market need. We will also assign specific tasks to group members to complete the deliverables for the project day. The entire team will review all tasks, but specific members will be charged with heading certain tasks. We will design a process flow diagram complete with refined calculations for the membrane-based method. Finally, we will continue to accumulate research so that this IPRO may continue in the future.

SCHEDULE OF TASKS/TIMELINE:

DATE	TENTATIVE TASKS
01/18	▪ Introduction
01/20	▪ An understanding of the project and goals for the project was determined. ▪ Pre-IPRO Experience Survey (w/briefing) was done.
01/25 - 01/27	▪ Team divided into three groups and one system: o Centrifugation group o Membrane filtration group o Standards group o IKNOW system
02/01	▪ Members of the group volunteered to write different sections of the project plan. o Background: BROGAN o Tasks: SUMAN o Objective: JEN o Methodology: KAREN
02/04	▪ Finalized Project Plan and submitted to IPRO office.
02/08	▪ Individual team groups brain stormed on their assigned tasks.
02/10	▪ Some information required of the standards group was completed and posted online.
02/15	▪ Some information required of the membrane group was completed and posted online.
02/17	▪ Consulted with Dr. Radovich.
02/22	▪
02/24	▪ The calculations for centrifugation group were completed.
03/01	▪ The calculations for membrane group were completed.
03/03	▪ Outlined Midterm Progress Report
03/08	▪ Consulted with Dr. Radovich

DATE	TENTATIVE TASKS
03/10	▪ Decided on membrane technology over centrifugation.
03/15	▪ Spring Break
03/17	▪ Spring Break
03/22	▪ Members of the group volunteered to write different sections of the mid term progress report. o Objective- VENKATA o Background- OSCAR / DAVE o Methodology - BROGAN o Tasks- SUMAN o Milestone events- CLARA o Expected results-ERIC
03/25	▪ Mid-Term Progress Report
03/29	▪ Assigned new tasks for the rest of the semester. Tasks include o Cost of membranes- SUMAN/AHLAM o Optimization-JEN/KAREN/BROGAN/VEN o Cost of pump/ pressure sensors/Cad image- JOE o Glycerol detection/cost- DAVE/OSCAR o Biowaste standards- DEREK
03/31	▪
04/05	▪
04/07	▪
04/12	▪ Finish Final Report
04/14	▪ Finish Presentation
04/19	▪ Practice Presentation
04/25	▪ Poster and project abstract
04/27	▪ Final Oral Presentation

05/03	▪ IPRO Day
05/06	▪ Team information, Comprehensive Deliverables CD, and final report.
05/09	▪ IPRO Survey

MILESTONE EVENTS:

DATE	MILESTONE EVENTS
01/25	▪ The team recognized that there were three main areas that needed to be researched to solve the problem at hand and as a result, split into three groups (standards, membrane filtration and centrifuge)
02/04	▪ The project plan was submitted.
02/12	▪ All information required of the standards group was completed and posted online.
02/21	▪ It was discovered that the iKnow system had the three sections of IPRO 304, which are being treated as separate IPROs, as one IPRO.
02/22	▪ The calculations for centrifugation system (settling velocity, residence time, and total system time) were completed using to the following parameters: angular velocity & bowl radius (maximum centrifugal force), particle diameter, particle density, liquid density, liquid viscosity, & maximum flow rate. An Excel sheet was created to display these calculations and the file was uploaded to yahoo groups.
02/24	▪ The formula to calculate the density of blood as a function of H (hematocrit) was found.
02/27	▪ The ultra-filtration coefficients of different membranes were obtained. This information was used in forming the material balance system for the membrane filtration system.

DATE	MILESTONE EVENTS
03/03	▪ The mass balance of the system was formed and the steps of the centrifugation deglycerolization process were noted down in detail by creating a sketch for the process flow diagram. The JPEG of the work was uploaded to Yahoo groups.
03/05	▪ The material balance of the membrane filtration system was formed and the details on obtaining the values for various parameters were posted online.
03/08	▪ The meaning of 40% W/V glycerol in the glycerolized red blood cells, which is percent weight by volume, was determined. This is the mass (in grams) of a substance dissolved or mixed in 100 mL of solution or mixture.
03/10	▪ The material balance calculations and process flow diagram was completed for the centrifuge process, which includes inlet and outlet compositions and volume amounts of all components to each stage (shaker table, centrifuge bowl, waste bag, and product bag). Two Excel sheets were made and both files were uploaded to Yahoo groups: one with the material balance calculations and the other with the centrifuge system process diagram.

EXPECTED RESULTS:

By the conclusion of project, we plan to optimize the membrane filtration process with respect to membrane area, system size, volume of wash and washing time to remove glycerol from thawed red blood cells. This will be done by running a simulation for the process for many different combinations of membrane area, size of apparatus, and washing time. From these trends the best combination will be chosen. The final design configuration should be an improvement over the centrifugal technology used currently in the washing process.

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