A Gap Analysis of Research in Apheresis – Knowledge Gained from Systematic Review of Clinicaltrials.gov

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American Society of Apheresis Research Subcommittee
Introduction

• Apheresis procedures can be defined as two types:
  – **therapeutic apheresis**: designed to directly treat a disease
  – **donor apheresis**: designed to collect blood components and cellular populations from healthy donors or patients.

• For **therapeutic apheresis**, the ASFA 2013 third edition *Guidelines on Therapeutic Apheresis* showed 78 separate diseases and 156 conditions with approximately 50% were defined as “optimum role of apheresis is not yet established”. (Schwartz et al, *Journal of Clinical Apheresis* 2013)

• In **donor apheresis**, there has been considerable heterogeneity in protocols for collection of specialized products such as stem cells, in contrast to basic blood components that have been standardized by industry and regulatory agencies. (Akkök et al, *Cytotherapy* 2011)
Research Question and Methods

**Research Question:** What are the characteristics of funded clinical trials involving apheresis medicine, and are these characteristics informative of future applications of apheresis medicine?

**To answer this question we analyzed clinical trials involving apheresis from 2001 to 2013 registered in Clinicaltrials.gov**

**We queried Medical Subject Headings (MeSH) with 14 search terms:**

- Apheresis
- Erythrocytapheresis
- Immunoadsorption
- LDL apheresis
- Leukapheresis
- Leukocytapheresis
- Lipoprotein apheresis
- Photopheresis
- Plasma Exchange
- Plasmapheresis
- Platelet Apheresis
- Red Cell Exchange
- Rheopheresis
- Thrombocytapheresis
Methods

• The trials were selected from the results query with the following inclusion criteria:
  1. Technical studies in apheresis.
  2. Apheresis was a therapeutic intervention, a fundamental component of a novel therapy, a source for cellular collection for novel cellular therapeutics, or was part of a novel multimodal therapeutic approach.

• We excluded studies based on the following criteria:
  1. Apheresis was a source for standard G-CSF mobilized peripheral blood mononuclear cells for transplantation of hematopoietic progenitors.
  2. The role of apheresis was not related to the research question or critical for the study, has been clearly established in the literature, or studies granting Expanded Access for the compassionate use of a drug required in apheresis.
Methods

- ClinicalTrials.gov study fields were used for analysis of the data.

- Intervention field was used to disease related groups and procedure related groups

- Study Start Date field was used to temporally classify studies

- Funded By field was used to classify study funding source. (Goswami, PLOS ONE, 2013)

- Study Location was used to classify study location
Apheresis Trials (2000-2013)
Current Status of Apheresis Trials (2001-2013)

- Donor (n=238)
  - Open: 140
  - Completed: 70
  - Aborted: 28

- Therapeutic (n=110)
  - Open: 40
  - Completed: 30
  - Aborted: 20
Increase in Apheresis Trials is Secondary to an Increase in Studies in Donor Apheresis

**Graph:**

- **X-axis:** Study Start Date
- **Y-axis:** Number of Apheresis Trials Registered/year in ClinicalTrials.gov

Legend:
- Blue: Total Trials
- Red: Donor Trials
- Green: Therapeutic Trials

Statistical Note: *** (p<0.001)
Procedure Related Grouping of Apheresis Trials (n≥10)

- LDL Apheresis
- Cell Depletion
- CC for Regenerative...
- Immunoadsorption
- ECP
- CC for DCI
- Plasmapheresis
- CC for HSCT
- CC for LI

CC = cell collection
DCI= dendritic cell therapy
HSCT= hematopoietic stem cell transplant
LI= Lymphocyte immunotherapy
ECP = extracorporeal photochemopheresis
Location of Apheresis Trials in ClinicalTrials.gov

The chart shows the number of registered apheresis trials categorized by region and type. North America has the highest number of trials, with a significant portion being therapeutic. Europe and Asia also have notable numbers, with Europe having a mix of therapeutic and donor trials. Multinational trials and other regions have fewer trials compared to North America.
Funding for Donor Versus Therapeutic Apheresis Trials by Year

Funding Source, By Year

* = p<0.05
Conclusions

- The increase in registered trials involving apheresis is secondary to an increase in trials involving donor apheresis cellular collections.

- The proportion of aborted trials is higher in therapeutic apheresis than in donor apheresis.

- There are more trials involving apheresis in solid and liquid tumors than all other disease related groups combined.

- The proportion of clinical trials involving therapeutic apheresis compared to donor apheresis is higher in Europe than in North America.

- Since mandatory registrations, NIH funding has grown for clinical trials involving donor apheresis. Industry funding has grown for therapeutic apheresis.
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Most scientists regarded the new streamlined peer-review process as “quite an improvement.”

Cartoon by Nick D Kim, strange-matter.net

Errm... what kind of cells do you think you're working with?

Labtimes Online April 23rd, 2010
Apheresis Research in Cellular Collections

- **Mobilization**: Novel factors and factor combinations that enhance or enrich specific progenitor, precursor, or mature cell mobilization in normal donors and patients with specific disease. An example is cytokines combinations targeting megakaryocyte progenitors recruitment.

- **Collection**: Novel methods to enrich specific cell collection through density separation, column purification through negative and positive selection, and filtration technology.

- **Storage and Cryopreservation**: Identifying optimal storage conditions for collected cells to ensure predictable effect with minimal or more than minimal ex-vivo manipulation. An example is studies in optimal cryopreservation for donor lymphocytes.

- **Cellular Characterization**: Quantitation, phenotype, and genotype of cellular populations, subpopulations, and single cells in collections.

- **More than Minimal Manipulation of CT and Regenerative Medicine**: Clinical Outcomes & Guidelines