Evaluation of \textit{in-utero} Erythropoiesis in preterm infants

\textbf{Purpose:} Determination of red blood cell (RBC) lifespan is important in order to evaluate the pharmacodynamics of erythropoietin in the stimulation of RBC production aimed at reducing or eliminating the need for RBC transfusions to treat neonatal anemia. We have developed a method for multi-density biotin labeling of RBCs that can be used to determine the RBC lifespan of both the adult donor RBCs and neonatal RBCs concurrently. The current investigation is aimed developing a mathematical model to describe the \textit{in-utero} RBC production under non steady state conditions in critically ill, very low birth weight infants.

\textbf{Methods:} Separate populations of neonatal autologous and adult allogeneic donor RBCs were labeled at two discrete biotin densities. The two biotin labeled RBC (BioRBC) populations were transfused into seven premature infants (mean±SD: birth weight: 784±164 g, gestational age: 25.9±0.7 weeks, and study age: 4.1±4.5 days). A pharmacodynamic hemoglobin mass balance model was used to account for the dynamic changes due to laboratory phlebotomies, RBC transfusions and growth. Post birth elimination of the transfused BioRBCs was assumed to be due to senescence. All modeling and simulation were conducted using WINFUNFIT/FORTRAN, using ordinary least squares fit to each individual subject’s Hb amount-time data.

\textbf{Results:} General agreement between the model fit and enrichment data was observed. The in vivo lifespan of neonatal and adult RBCs were similar 63±12 and 75±19 days, respectively, \(P=0.10\). The model was able to simulate the survival curve of the in-utero produced cells under non-steady state \textit{in-utero} RBC production.
Conclusions: This study demonstrates the utility of concurrent multi-density BioRBC method in determining in vivo RBC lifespan. Contrary to previous published infant studies, in vivo RBC lifespan of neonatal and adult RBC were not statistically different. In addition, the model developed can be used to estimate the rate of in-utero production under non-steady state conditions.