Magnetic resonance thermometry derived solution for the problem to measure transient red blood cell temperature during transport

Poster No.: C-1066
Congress: ECR 2013
Type: Scientific Exhibit
Authors: G. Reiter¹, U. Reiter¹, T. Wagner¹, N. Kozma¹, J. Roland², H. Schoellnast¹, F. Ebner¹, G. Lanzer¹, ¹Graz/AT, ²Erlangen/DE
Keywords: MR physics, Haematologic, MR, Physics, Experimental investigations, Health policy and practice, Blood
DOI: 10.1594/ecr2013/C-1066
Purpose

Temperature is a key measure in red blood cell concentrate (RBC) quality control. Recommended by current guidelines, RBC temperature should not exceed 10°C during transport, else being used or discharged [1-3]. In clinical routine, RBC transport temperature is commonly estimated applying the "30 minute rule" or controlled by temperature sensitive labels attached to the surface of RBC pouch [4-9]. Definition of time RBC units can be exposed to ambient temperature without exceeding the recommended temperature limit of 10°C challenges the investigation of the three-dimensional temperature distribution of RBC during warming, which is the basic prerequisite for describing and predicting thermodynamic processes.

Magnetic resonance (MR) proton resonance frequency (PRF) temperature mapping is the method of choice for fast, stable and accurate temperature measurements [10-12]. Discrete time-series of mean, surface and core temperatures of RBC units during warm up can be derived from PRF images, which allow analytical modelling of warm up processes. As RBC pouch's surface resistance to heat transfer can be assumed to be larger than the thermal resistance within RBC, time-dependence of RBC units' mean temperature during warm up should be well described by a lumped capacitance model of heat transfer, with relative mean to ambient temperature differences following an exponential decay [13,14]. Additionally, similar time-shifted exponential decays might provide adequate descriptions of surface and core temperature time courses during warm up.

The aim of the present study was to evaluated to which extend RBC warm up temperature distributions, derived from MR PRF thermometry measurements can be described by a lumped capacitance model of heat transfer and to derive analytical formulas to predict core, mean and surface temperatures during RBC warm-up.
Methods and Materials

RBC sample collection

Whole blood donations were obtained according to the Austrian regulations for blood donation from healthy volunteer blood donors after informed written consent and collected into triple bags (LCR5 filtration set) containing 63 ml citrate phosphate dextrose (MacoPharma LAB, Pharmaceutiques, Tourcoing, France). After centrifugation at 4000·g for 10 min at 20°C, RBC and plasma were separated from buffy coat fraction and transferred into satellite containers using an automated separator (Compomat G4, NPBI, Amsterdam, Netherlands). Within 30 min after separation RBC was leukoreduced using the LCR5 leukoreduction filter (MacoPharma LAB, Pharmaceutiques, Tourcoing, France) and re-suspended in 100 ml of saline adenine glucose mannitol (SAGM containing 900 mg of glucose monohydrate, 877 mg of sodium chloride, 525 mg of mannitol and 16.9 mg of adenine).

RBC sample storage and handling

Forty-seven RBC units, investigated by proton resonance frequency thermometry, were stored at temperatures between 1°C to 6°C (MobiCool W35 12/230V, Zhuhai, China). Storage temperature was recorded in 5 minute time intervals by two RFID data loggers (SensoTag Siemens HFST-T109, Vienna, Austria, overall accuracy of ± 0.5°C) mounted in the box. To prevent uncontrolled thermal transfer processes and motion as well as ensure a fast and reproducible experimental onset, RBC units were stored, transported and investigated in upright position in a two-layer plastic holder (Lego®) with minimum distance of 1 mm between frame and RBC (refer to Figure 1). Withdrawn from storage, RBC samples were plugged into an adjustment unit positioned in the MR system in the center of a 12 channel matrix head coil.
Fig. 1: Experimental setup for temperature measurements. Schematic drawing (a): The RBC pouch was mounted in a plastic frame (F) with 1-2 mm distance between holder and RBC. For temperature mapping, the frame was fixed on an apron (A) equipped with two reference phantoms (RP). The RBC-unit was positioned in the center of the matrix head coil MHC. Unit position was marked by markers M (B) MR adjustment and shim was performed by a reference RBC-unit, which thereafter was replaced by the cold RBC-unit for temperature mapping (C).

References: Siemens AG, Healthcare Division - Graz/AT

RBC temperature mapping

Immediately after exposition to ambient temperature (mean setup time = 16 ± 3 s) temperature images were acquired with a 2D multislice gradient echo sequence (TR = 33.15 ms, TE = 20 ms, flip angle = 14°, voxel size = 1.1×1.1×7.5 mm³, FoV = 170×170 cm², BW = 65 Hz/Pixel, number of slices = 7, data acquisition time = 38 s) covering the entire RBC volume with equidistant slices (gap = 90%-95%) for a total investigation time of 69.7 min.

MR images were transformed to RBC temperature maps by dedicated software developed in Matlab (R2010b. The MathWorks Inc. Natick, Massachusetts) employing a PRF thermal coefficient of RBC derived from calibration measurements [15]. RBC unit height, width (w_pouch) and center (c_{RBC}) were determined from the central slice. Thermal RBC core (RBC_{core}) was defined as region with minimum temperature in the central slice throughout warm up. Its position was specified as relative distance from c_{RBC} (refer to Figure 2).
Fig. 2: TSE images were used to segment RBC volume, SAGM and reference phantoms RP (A). Sample height $h$ and width $w_{pouch}$ and center $c_{RBC} = h/2$ was determined from the central slice. RBC volume was calculated as sum of segmented RBC areas in the 7 slices multiplied by slice distance (B). Phase drift were corrected via medians of reference phantom phases (C). Corrected RBC difference phases were recalculated to temperatures, which are visualized color encoded. Thermal RBC core ($RBC_{core}$) was defined as region with minimum temperature in the central slice throughout warm up. Its position was specified as relative distance from geometric RBC pouch center $c_{RBC}$ (d).

References: Siemens AG, Healthcare Division - Graz/AT

RBC temperature image analysis

RBC mean temperature $T_{\text{mean}}$, associated with the thermal state of RBC after "gently mixing", was defined as mean value of temperatures measured in the entire RBC volume at a specific time during warm up. The time-resolved temperature maps were employed to determine discrete time courses of RBC mean temperature $T_{\text{mean}}$. Linear extrapolation at half maximum of volume fraction-time curve was used to specify the time when RBC volume starts to exceed 10°C, interpreted as surface temperature $T_{\text{surface}}$ and the time when 100% of RBC volume exceeds 10°C, interpreted as core temperature $T_{\text{core}}$. 
For the analytical description of RBC's warm up processes, it was hypothesized, that mean temperature $T_{\text{mean}}$ during warm up is described by a lumped capacitance model of heat transfer [13,14]. Consequently relative mean temperature difference $\#_{\text{mean}} = (T_{\text{ambient}} - T_{\text{mean}})/(T_{\text{ambient}} - T_{\text{store}})$ to ambient temperature $T_{\text{ambient}}$ should fulfill

$$\theta_{\text{mean}} = \exp\left(-\frac{t}{\tau_{\text{mean}}}\right)$$

Table 1

References: Siemens AG, Healthcare Division - Graz/AT

where $t$ is the time the RBC pouch is exposed to ambient temperature and $\#_{\text{mean}}$ is a RBC pouch specific time constant, not dependent on storage temperature $T_{\text{store}}$ or difference between ambient and storage temperature $T_{\text{ambient}} - T_{\text{store}}$, respectively. Moreover, for RBC surface and core temperatures it was hypothesized, that relative surface and core temperature differences $\#_{\text{surface}}$ and $\#_{\text{core}}$ to ambient temperature $T_{\text{ambient}}$ follow "shifted" exponential decays. Thus, $\#_{\text{surface}}$ and $\#_{\text{core}}$ should fulfill

$$\theta_{\text{surface}} = \exp\left(-\frac{t}{\tau_{\text{surface}}} - \Delta_{\text{surface}}\right)$$

Table 2

References: Siemens AG, Healthcare Division - Graz/AT

$$\theta_{\text{core}} = \exp\left(-\frac{t}{\tau_{\text{core}}} + \Delta_{\text{core}}\right)$$
Table 3

References: Siemens AG, Healthcare Division - Graz/AT
with time constants $\tau_{\text{surface}}$ and $\tau_{\text{core}}$ and shifts $\delta_{\text{surface}}$ and $\delta_{\text{core}}$. The shifts characterize (in units of time constants) how much earlier (or later in case of core) the decay of $\tau_{\text{surface}}$ (and $\tau_{\text{core}}$) is starting than the instantaneous decay of $\tau_{\text{mean}}$. 
**Fig. 1:** Experimental setup for temperature measurements. Schematic drawing (a): The RBC pouch was mounted in a plastic frame (F) with 1-2 mm distance between holder and RBC. For temperature mapping, the frame was fixed on an apron (A) equipped with two reference phantoms (RP). The RBC-unit was positioned in the center of the matrix head coil MHC. Unit position was marked by markers M (B) MR adjustment and shim was performed by a reference RBC-unit, which thereafter was replaced by the cold RBC-unit for temperature mapping (C).

© Siemens AG, Healthcare Division - Graz/AT
Fig. 2: TSE images were used to segment RBC volume, SAGM and reference phantoms RP (A). Sample height h and width wpouch and center c_RBC = h/2 was determined from the central slice. RBC volume was calculated as sum of segmented RBC areas in the 7 slices multiplied by slice distance (B). Phase drift were corrected via medians of reference phantom phases (C). Corrected RBC difference phases were recalculated to temperatures, which are visualized color encoded. Thermal RBC core (RBC_core) was defined as region with minimum temperature in the central slice throughout warm up. Its position was specified as relative distance from geometric RBC pouch center c_RBC (d).

© Siemens AG, Healthcare Division - Graz/AT
Results

Qualitative description of RBC warm up temperature distributions

Similar qualitative warm up phenomena were observed in all RBC units irrespectively of storage temperatures ranging from 1 to 6°C (mean $T_{\text{store}} = 3.6 \pm 1.4°C$). A typical example of RBC temperature maps derived from PRF thermometry measurements is shown in Figure 3.

Withdrawn from steady storage conditions, RBC’s temperature at the surface of the pouch and at SAGM border immediately started to rise. During warm up heat was continuously transferred from RBC surface to the adjacent inner layers, causing an increasingly non-uniform temperature distribution in the sample with isotherms located symmetrically around temperature core RBC$_{\text{core}}$ in both transversal (horizontal and latitudinal) extensions of the unit. In vertical extension RBC$_{\text{core}}$ was displaced by 13 ± 4% from pouch center. Highest temperatures, the respective $T_{\text{surface}}$, were reached at the surface at sections with smaller width at the top of the pouch.

Increases in mean, surface and core temperatures (or decreases of relative mean, surface and core temperature differences) decreased with increasing warm-up time.
**Fig. 3**: Typical RBC warm up temperature distribution. Color encoded temperature maps of RBC withdrawn from 4°C storage temperature exposed to 21.25°C room temperature.

**References**: Siemens AG, Healthcare Division - Graz/AT

**Mean, surface and core temperatures during warm up**

Measured relative temperature differences $\#_{\text{mean}}$, $\#_{\text{surface}}$ and $\#_{\text{core}}$ fulfilled lumped capacitance model of heat transfer (Eq. (1) and "shifted" exponential decays Eqs (2) and (3)) close to perfect. Mean $R^2$ were $0.999 \pm 0.001$, $0.996 \pm 0.004$ and $0.998 \pm 0.002$, respectively. The resulting mean time constants were $\#_{\text{mean}} = 55.3 \pm 3.7$ min, $\#_{\text{surface}} = 41.4 \pm 2.9$ min and $\#_{\text{core}} = 76.8 \pm 7.1$ min, resulting mean time shifts $\#_{\text{surface}} = 0.07 \pm 0.02$
and \( \#_{\text{core}} = 0.04 \pm 0.01 \). Average time courses of \( \#_{\text{mean}}, \#_{\text{surface}} \) and \( \#_{\text{core}} \) together with corresponding uncertainties are shown in Figure 4.

**Fig. 4:** Average time courses (solid lines) and corresponding uncertainties (dotted lines) of relative temperature differences of mean, surface and core temperature to ambient temperature of RBC during warm up. Recalculation of relative temperature difference scale to temperature scale at the right hand side was done (for convinience) for \( T_{\text{store}} = 3.6^\circ \text{C} \) and \( T_{\text{ambient}} = 21.25^\circ \text{C} \).

**References:** Reiter G et al. (2013) Thermometry of red blood cell concentrate: Magnetic resonance decoding warm up process. PLOS ONE (in print)

Neither time constants nor shifts depended on storage temperature \( (T_{\text{ambient}}-T_{\text{store}}) \), respectively. Variations in geometric RBC pouch parameters volume \( (255 \pm 17 \text{ ml}) \), height \( h \) \( (13.1 \pm 0.5 \text{ cm}) \) and width \( w_{\text{pouch}} \) \( (3.4 \pm 0.2 \text{ cm}) \) were small and shifts did not depend on these parameters. Time constants depended strongest on \( w_{\text{pouch}} \).
Temperature prediction from surface temperature

Average dependencies of relative mean and core temperature differences $\Delta_{\text{mean}}$ and $\Delta_{\text{core}}$ on relative surface temperature difference $\Delta_{\text{surface}}$ together with corresponding uncertainties and the influence of storage temperature $T_{\text{store}}$ on the prediction of absolute mean or core temperature from absolute surface temperature are shown in Figure 5.

![Graph showing temperature prediction](image)

**Fig. 5:** Dependence of relative mean and core temperature differences on relative surface temperature differences (solid lines) together with corresponding uncertainties (dotted lines) during warm up.

**References:** Reiter G et al. (2013) Thermometry of red blood cell concentrate: Magnetic resonance decoding warm up process. PLOS ONE (in print)
**Fig. 3:** Typical RBC warm up temperature distribution. Color encoded temperature maps of RBC withdrawn from 4°C storage temperature exposed to 21.25°C room temperature.

© Siemens AG, Healthcare Division - Graz/AT
Fig. 4: Average time courses (solid lines) and corresponding uncertainties (dotted lines) of relative temperature differences of mean, surface and core temperature to ambient temperature of RBC during warm up. Recalculation of relative temperature difference scale to temperature scale at the right hand side was done (for convinience) for $T_{\text{store}} = 3.6^\circ\text{C}$ and $T_{\text{ambient}} = 21.25^\circ\text{C}$.

© Reiter G et al. (2013) Thermometry of red blood cell concentrate: Magnetic resonance decoding warm up process. PLOS ONE (in print)
**Fig. 5:** Dependence of relative mean and core temperature differences on relative surface temperature differences (solid lines) together with corresponding uncertainties (dotted lines) during warm up.

© Reiter G et al. (2013) Thermometry of red blood cell concentrate: Magnetic resonance decoding warm up process. PLOS ONE (in print)
Conclusion

Simple analytical formulas for the calculation of transient RBC mean, surface and core temperatures are presented allowing for calculation of RBC temperatures for arbitrary storage and ambient temperature conditions. This might be a helpful tool in RBC temperature monitoring and quality control performed either by temperature sensitive labels or by estimation of time RBC is out of stock.


9. Perry HE, Prasad P, Kirwan S, Huang YQ. Core temperature changes in resuspended red blood cells (RBCs) and pediatric RBCs removed from refrigerated storage. Transfusion. 2010;50(1):174-177.


Personal Information

Gert Reiter PhD, Siemens AG, Healthcare Sector, Graz, Austria;
gert.reiter@siemens.com.

Ursula Reiter PhD, Division of General Radiology, Department of Radiology, Medical University of Graz, Austria;
ursula.reiter@klinikum-graz.at.

Thomas Wagner MD, Department of Blood Group Serology and Transfusion Medicine, Medical University of Graz, Austria;
thomas.wagner@medunigraz.at.

Noemi Kozma MD, Department of Blood Group Serology and Transfusion Medicine, Medical University of Graz, Austria;
noemi.kozma@medunigraz.at.

Jörg Roland PhD, Siemens AG, Healthcare Sector, Erlangen, Germany;
joerg.roland@siemens.com.

Helmut Schöllnast MD, Division of General Radiology, Department of Radiology, Medical University of Graz, Austria;
helmut.schoellnast@medunigraz.at.

Franz Ebner MD, Division of Magnetic Resonance, Department of Radiology, Medical University of Graz, Austria;
franz.ebner@klinikum-graz.at.

Gerhard Lanzer MD, Department of Blood Group Serology and Transfusion Medicine, Medical University of Graz, Austria;
gerhard.lanzer@klinikum-graz.at.