

# Drone Transport of Chemistry and Hematology Samples Over Long Distances

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**Key Words:** Drone; Stability; Temperature; Long flight; Chemistry; Hematology

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## ABSTRACT

**Objectives:** We addressed the stability of biological samples in prolonged drone flights by obtaining paired chemistry and hematology samples from 21 adult volunteers in a single phlebotomy event—84 samples total.

**Methods:** Half of the samples were held stationary, while the other samples were flown for 3 hours (258 km) in a custom active cooling box mounted on the drone. After the flight, 19 chemistry and hematology tests were performed.

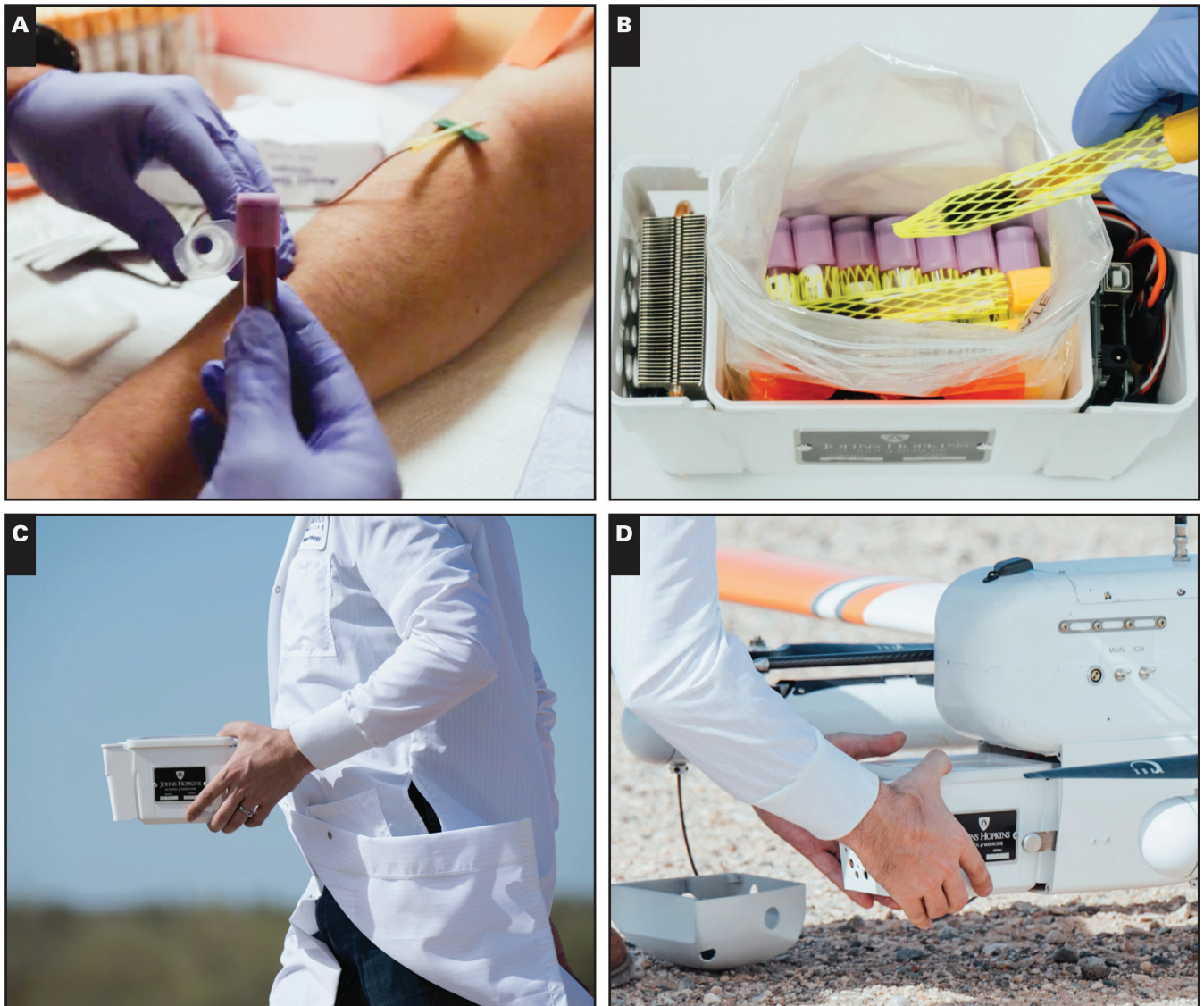
**Results:** Seventeen analytes had small or no bias, but glucose and potassium in flown samples showed an 8% and 6.2% bias, respectively. The flown samples (mean, 24.8°C) were a mean of 2.5°C cooler than the stationary samples (mean, 27.3°C) during transportation to the flight field as well as during the flight.

**Conclusions:** The changes in glucose and potassium are consistent with the magnitude and duration of the temperature difference between the flown and stationary samples. Long drone flights of biological samples are feasible but require stringent environmental controls to ensure consistent results.

Several recent reports demonstrate that biological samples can be transported by unmanned aerial vehicles (commonly referred to as drones) without affecting the laboratory results from the same samples.<sup>1-3</sup> However, the broad applicability of those studies to potential real-life drone transportation was limited by distance and temperature. Briefly, the earlier reports of drone-transported biologics were performed in ambient temperatures that were around room temperature<sup>1</sup> or cold,<sup>2,3</sup> and the maximal length of flight in those studies was 40 minutes (equivalent of 40 km) in a fixed-wing vehicle and 27 minutes (equivalent of 13-20 km) in a multicopter. While these times and distances were sufficient as proofs of concept, they are not long enough to address the needs of real-world drone networks.

To illustrate, let us consider a hypothetical drone network with four satellites and one central hub, where each satellite is 20 km from the hub. Such a network would either require several drones and complex logistics or a single drone flying a total distance of around 100 km. This hypothetical distance would increase with countervailing winds or increased distance from the hub. Thus, given the expected real-world demands on drone networks as well as the many regions and seasons that are characterized by high temperature, there is a need to examine long drone flights at relatively high temperatures. This report attempts to address these needs by presenting the results of a 3-hour, 258-km drone flight at 32°C ambient temperatures and low humidity (mean, 27.2%; range, 24.9%-28.8%).

In our earlier work on the impact of drone flights on chemistry clinical laboratory results, there were no specific



**Image 1** Schematic of the experiment. **A**, Phlebotomy of volunteers. **B**, Placement of sleeved Vacutainers in two biohazard bags inside the custom cooler box. **C**, Transfer of custom cooler to the drone. **D**, Insertion of custom cooler box into the custom box under the fuselage.

measures to stabilize temperature or pressure because ambient conditions were not extreme. Our test flights were performed at 100 m, and changes in temperature and atmospheric pressure with altitude were small.<sup>4,6</sup> In the current report, the flights were at high ambient temperatures, low humidity, and protracted. Consequently, we constructed a custom-built active cooling device that was designed to run using power from the onboard battery. In addition, as the engine in the current drone was gas powered, we reasoned that its vibration might be a significant environmental factor (<https://vimeo.com/medicaldrones/long-distance>). To mitigate these effects, we packed the primary Vacutainers individually in plastic mesh sleeves **Image 1**. The primary containers were sealed in two

flexible biohazard bags (Ziploc) with absorbent material, placed inside the custom cooler, and transferred to a custom-built foam-lined carrier attached to the bottom of the fuselage (**Image 1**). The purpose of our study was to examine the effects on samples during real-life drone flights that are greater than 3 hours in duration and in relatively high ambient temperatures.

## Materials and Methods

Paired chemistry and hematology samples were obtained from 21 adult volunteers in a single phlebotomy event (84 samples total). Forty-two samples were driven

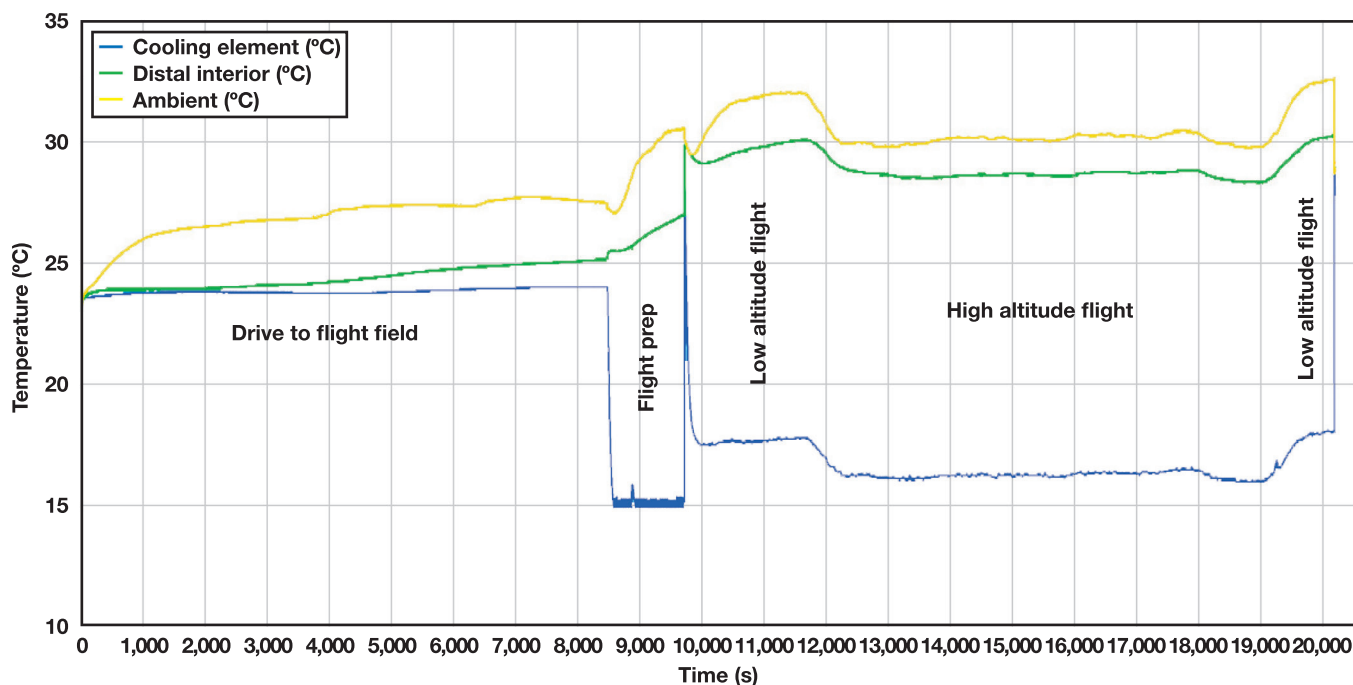
to the flight field and held stationary. The other 42 samples were flown in the drone for 3 hours. There was temperature monitoring of the samples before and during the flight using the Sensor Push sensor (SensorPush, Brooklyn, NY; temperature accuracy [0°C-60°C]:  $\pm 0.3^\circ\text{C}$  typical,  $0.5^\circ\text{C}$  maximum; humidity accuracy:  $\pm 4.5\%$  typical,  $\pm 7.5\%$  maximum). Nineteen of the most common chemistry and hematology tests were performed after the flight. Standard statistical methods for the performance of laboratory method comparisons (linear regression and difference plots) as well as relevant performance criteria from four external bodies<sup>7-10</sup> were used to evaluate the results.

### Study Design

Twenty-one volunteers were recruited for the study: 14 females and 7 males. Four samples were obtained from each of the 21 adult volunteers. Two of the samples were 3.5-mL serum separator tubes, and the other two were 3-mL potassium EDTA whole-blood tubes. All four samples were collected in a single event using a standard phlebotomy technique. The samples were de-identified and there was no key linking the participants to the samples or results. The study was approved by the University of Arizona Institutional Review Board (Tucson).

One set of the paired tubes was driven to the flight site and flown in the drone for 174 minutes. Samples were flown in a custom-built active cooling device that was designed to run using power from the onboard battery. There was temperature monitoring at three sites in the flown payload (Figure 1). These were (1) the coldest part of the payload box (just outside the cooling element), (2) the most warmest part of the payload box, and (3) the ambient temperature. The second sample set was driven to the flight site but not flown. This second set was held in the car where there was active cooling, using the car's air conditioning, to maintain mean (range) ambient temperatures of  $26^\circ\text{C}$  ( $24^\circ\text{C}$  to  $28^\circ\text{C}$ ). The maximum temperatures in the transport vehicles and at the flight site were  $28^\circ\text{C}$  and  $32^\circ\text{C}$ , respectively.

Approaches for the packing of samples for flight have been previously described.<sup>1</sup> Briefly, the samples were packed in a sample payload module that served to control the in-flight environment as well as to contain the samples in the unlikely event of a leak or breakage (Image 1). The flights were conducted in compliance with Advisory Circular 91-57,<sup>11</sup> Model Aircraft Operating Standards, and the International Air Transport Association's guidelines for the packaging of potentially infectious liquid biological materials (REF 6.1).<sup>12</sup> Each sample was enclosed by three layers of packaging and enough absorbent material (SAF-T-PAK, Hanover, MD) to absorb twice the full volume of all the samples in the payload. The primary



**Figure 1** Temperature tracing of the payload during the drive to the flight field as well as during flight. The blue tracing shows the temperature at the coolest part of the payload just outside the cooling element, the green tracing shows the warmest part of the interior of the payload, and the yellow shows the ambient temperature just outside the payload.



receptacles were the original sample tubes, separated from each other by a mesh sleeve around individual tubes. The secondary receptacle was a sealed biohazard bag wrapped around all the primary receptacles. The tertiary receptacle was the rigid custom drone refrigerator that was placed in a specially constructed payload bay underneath the aircraft's fuselage.

After flight operations were completed, all the samples (flown and stationary) were transported back to the core laboratory at Mayo Clinic in Arizona, Scottsdale campus, Scottsdale, Arizona. The time from the first drawn sample to the last result was less than 8 hours for all 84 samples in this experiment. The time from phlebotomy to arrival at the laboratory was uniform for both sample sets. Serum samples were centrifuged at 3,000g for 10 minutes at 22°C and analyzed. Chemistry testing was performed on the Roche Cobas c501 analyzer (Roche Diagnostics, Indianapolis, IN) and hematology (CBC) testing performed on the Sysmex XE-5000 hematology analyzer (Sysmex America, Lincolnshire, IL). Tests were performed from the original primary sample tubes without decantation or intervening storage.

### Flight Protocol

Specimens were flown in a hybrid vertical take-off and landing aircraft (HQ-40, Latitude Engineering, Tucson, AZ). Distance flown was 160.22 miles (257.5 km) over an elapsed time of 3 hours, 3 minutes, and 34 seconds. The altitude of the airfield was 475 feet above mean sea level (MSL). The aircraft's maximum altitude was 950 feet MSL, 475 feet above ground level.

A hybrid aircraft was selected over other aircraft types because it combines the ability to launch and land vertically (like a helicopter) with a range several times that of a helicopter or multirotor aircraft. The HQ-40 launches, with lift provided by four vertical propellers, and at 75 feet makes a transition to a traditional horizontal flight by engaging a forward thrust motor and a short time later stopping the vertical thrust propellers. Landing is performed by the inverse procedure.

Among other precautions, the test was conducted away from populated areas, and the aircraft was under the control of a certified remote pilot. The aircraft was controlled via a radio link between the onboard flight computer and the ground control station. The flight was performed in restricted airspace at a military aircraft test range, cleared of other air traffic.

### Statistical Analysis

Deming regression was used to compare flown with stationary results for sodium, potassium, chloride, CO<sub>2</sub>

**Table 1**  
Summary of the Hematology Results From Flown and Stationary Samples

Analyte	Regression Equation	r <sup>2</sup>
Hb	y = 0.98x + 0.32	0.99
Hct	y = 0.99x + 0.52	0.98
RBC	y = 1.01x - 0.02	0.98
MCV	y = 1.03x - 3.15	0.94
RDW	y = 0.97x + 0.37	0.98
Plt	y = 0.94x + 16.6	0.82
WBC	y = 1.00x - 0.02	0.99
Neut	y = 1.00x	0.99
Lymph	y = 1.01x - 0.04	0.98
Mono	y = 1.12x - 0.09	0.79
Eos	y = 0.97x	0.94
Baso	y = 1.08x	0.41

Baso, basophils; Eos, eosinophils; Hb, hemoglobin; Hct, hematocrit; Lymph, lymphocytes; MCV, mean corpuscular volume; Mono, monocytes; Neut, neutrophils; Plt, platelet count; RDW, RBC distribution width.

**Table 2**  
Summary of the Chemistry Results From Flown and Stationary Samples

Analyte	Regression Equation	r <sup>2</sup>
Gluc	y = 0.82x + 6.5	0.89
SUN	y = 0.98x + 0.43	1.00
Cr	y = 1.1x - 0.1	0.93
Sodium	y = 1.2x - 31.6	0.49
Potassium	y = 1.0x - 0.29	0.87
Chloride	y = 0.8x + 20.9	0.69
CO <sub>2</sub>	y = 1.2x - 5.2	0.72

Cr, creatinine; Gluc, glucose; SUN, serum urea nitrogen.

(bicarbonate), serum urea nitrogen, creatinine, glucose, WBCs, RBCs, hemoglobin, hematocrit, mean corpuscular volume, RBC distribution width, platelet count, lymphocytes, monocytes, neutrophils, eosinophils, and basophils. To determine if our results met clinical and regulatory quality criteria, we compared the 95% limits of agreement of our results with the intervals describing acceptability criteria from four distinct clinical, academic, and regulatory bodies.<sup>7-10</sup> Analyse-it Software for Microsoft Excel Version 3.90.1 (Analyse-it Software, Leeds, UK) and Excel (Microsoft, Redmond, WA) were used to do the analysis.

## Results

### Correlations

**Table 1** and **Table 2** show data describing the linear relationship between the flown and stationary sample chemistry, as well as hematology results. The slopes of the regression equations were between 0.80 and 1.2 for all 19

tests and between 0.90 and 1.10 for 15 of the 19. Thus, for 15 of the 19 tests, the results obtained from the flown and stationary sample pairs were within 10% of each other. Fifteen analytes had an intercept close to zero. The other four—sodium, potassium, chloride, and CO<sub>2</sub>—had intercepts (constants) that were more than 25% of their mean values.

Thirteen of the 19 tests had coefficients of determinations ( $r^2$ ) (between the results from the flown and stationary sample pairs) above 0.9, and the remaining six tests had  $r^2$  less than or equal to 0.8.

### Bland-Altman Comparisons

Figure 2 and Figure 3 show the percent differences in the results obtained between individual flown and stationary sample pairs. The dashed lines delineate the 95% limits of agreement. The blue lines show the mean difference for analytes where this difference was more than

0.5% of the mean value. Glucose, potassium, and basophils had a mean difference more than 5.0%. Glucose and potassium in flown samples showed an 8% and 6.2% bias, respectively.

Three of the seven chemistry analytes (glucose, potassium, and CO<sub>2</sub>) had a 95% limit of agreement greater than 10%. Four of the 12 hematology tests (platelets, monocytes, eosinophils, and basophils) had a 95% limit of agreement greater than 10%. Of note, three of these four analytes had the lowest mean levels, a characteristic that increases random errors.

### Allowable Performance Limits

With the exception of glucose and potassium, the 95% intervals for sample pairs in this study met the four distinct clinical and/or regulatory acceptability criteria we used in this study.<sup>7-10</sup> In particular, the 95% interval for glucose in our study (8%) did not meet two (<7%, <8%) of the four

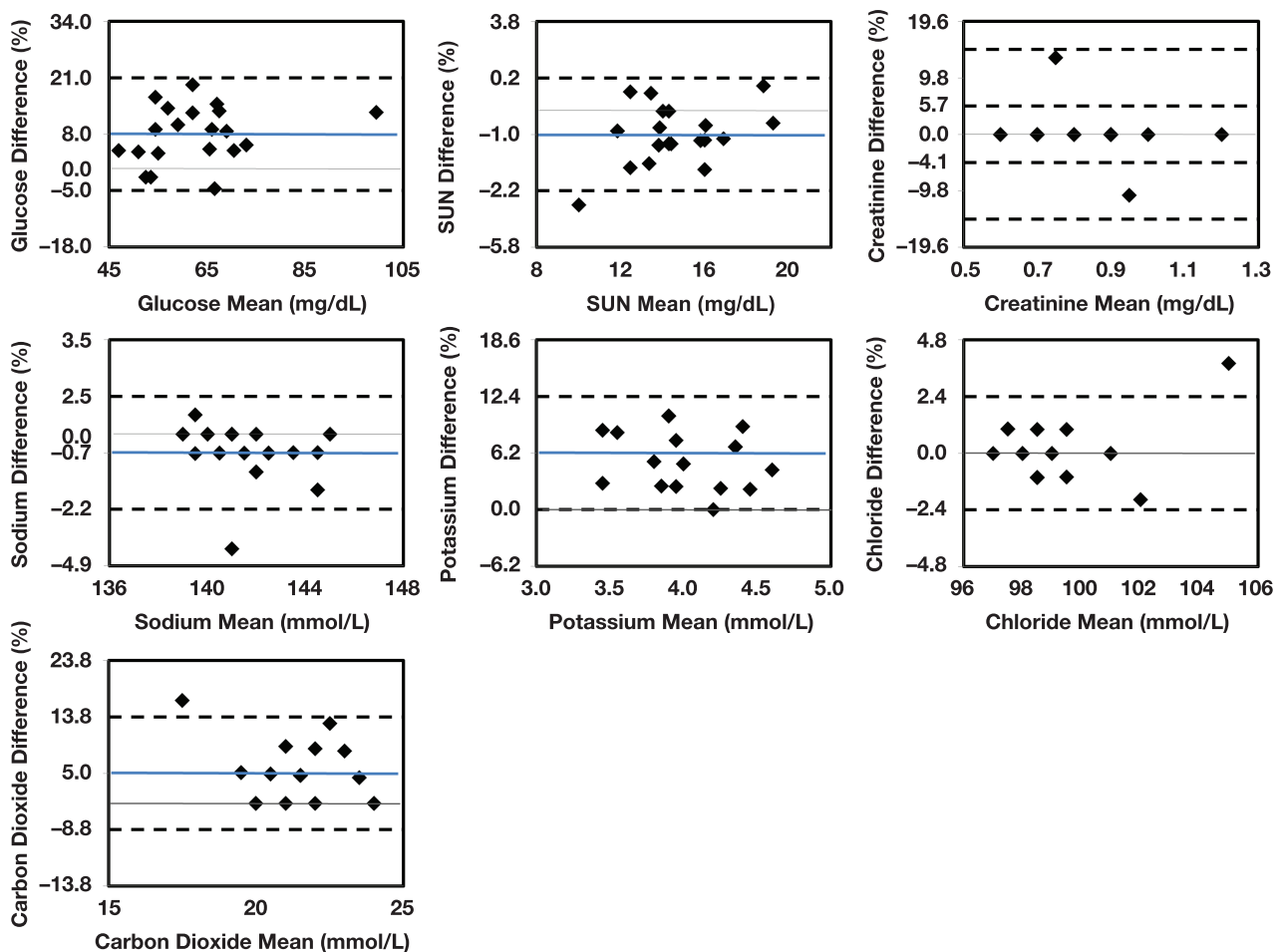
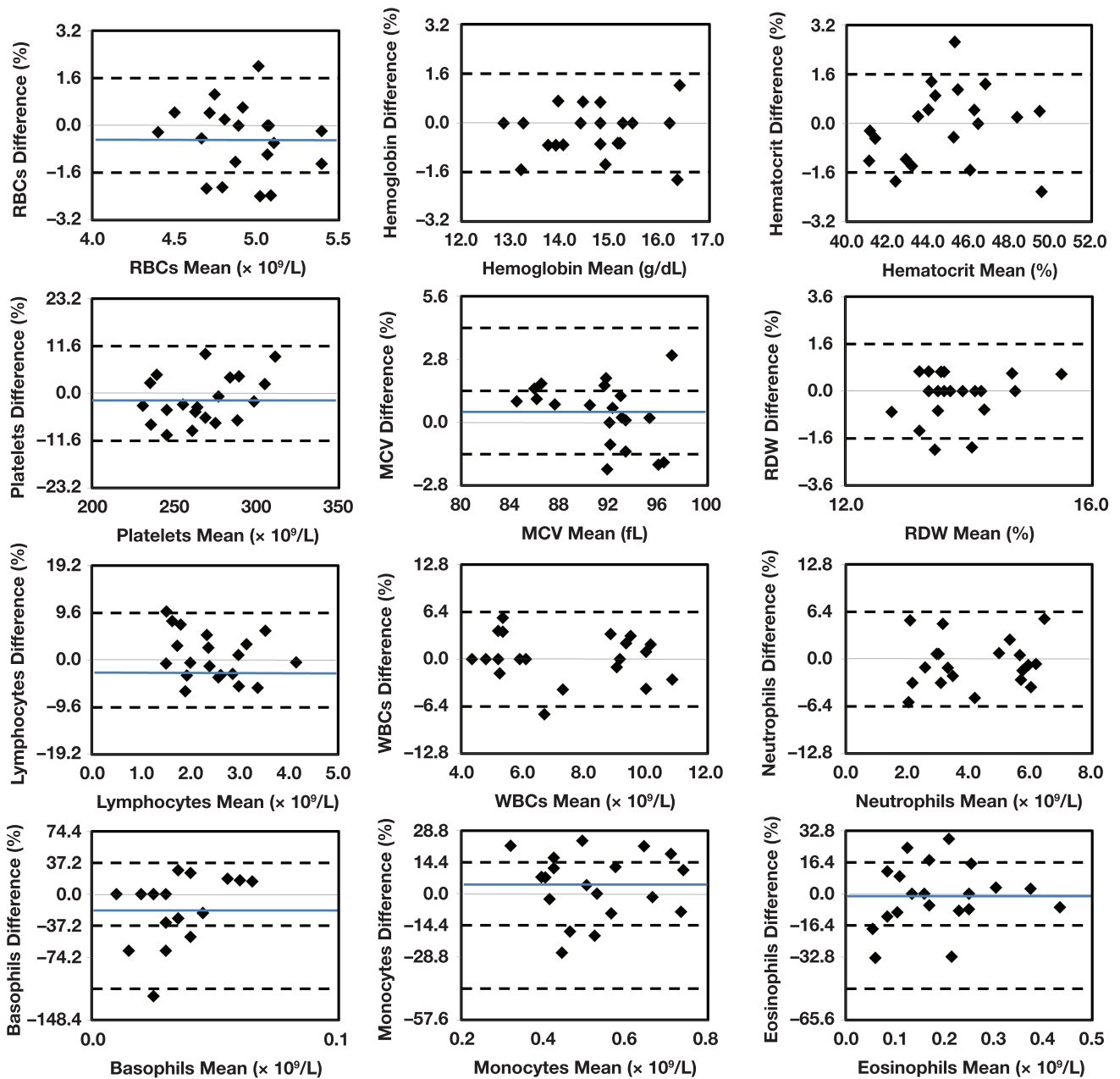


Figure 2 Bland-Altman plots showing percentage differences in results for 21 flown vs stationary sample pairs. The dashed lines delineate the 95% limits of agreement. The blue lines show the mean difference for analytes where this was 5% or more of the mean values for each analyte. SUN, serum urea nitrogen.



**Figure 3** Bland-Altman plots showing percentage differences in results for 21 flown vs stationary sample pairs. The dashed lines delineate the 95% limits of agreement. The blue lines show the mean difference for analytes where this was 5% or more of the mean values for each analyte. MCV, mean corpuscular volume; RDW, RBC distribution width.

criteria,<sup>7,8</sup> and the 95% interval for potassium in our study (6.2%) also did not meet two of the four criteria.<sup>7,10</sup>

### Temperature

Temperature monitoring of the payload was conducted during the drive to the flight field as well as during flight (Figure 1). The blue tracing shows the temperature inside the payload (sample container), just outside the

cooling element. The green tracing shows the temperature of the part of the payload most distal (warmest) from the cooling element, and the yellow shows the ambient temperatures just outside the payload. The actual temperature experienced by the samples was an average of the coolest (blue) and the warmest (green) points inside the payload. During the drive to the flight field, the temperatures of these two points were almost identical. However, during powered flight, there were increased ambient

temperatures and increased heat loss due to higher airflow (see green tracing). The cooling element appropriately responded to this by cooling more aggressively. This is the reason for the relatively large differences in temperature between these two graphs during flight. The average temperature in the payload remained similar to that during car transportation, 24.8°C. The temperature of the stationary samples was at an average of 27.3°C during the car transportation and remained at this temperature while held in the car.

## Discussion

This report examines the impact of a long (3-hour, 258-km) drone flight on chemistry and hematology results obtained from the flown blood samples (<https://vimeo.com/medicaddrones/long-distance>). The results from flown vs stationary sample pairs were compared using several statistical approaches to determine the presence and magnitude of any differences between them. In addition, any changes in the mean results were compared with “allowable limits” performance criteria from four independent clinical, regulatory, and expert groups.<sup>7-10</sup> Results from flown and stationary sample pairs were similar for 17 of the 19 tests. However, glucose and potassium showed 8% and 6.2% bias, respectively, and only met two of the four performance criteria. The glucose and potassium levels were higher overall in the flown samples. The other 17 analytes met all four performance criteria.

This change in the mean results obtained for glucose and potassium could have been due to a number of factors, including the intrinsic variability of the assay, prolonged time to analysis, differences in temperature, or physical alteration of the cellular viability of the samples due to the proximity to the drone engine<sup>13-15</sup> (<https://vimeo.com/medicaddrones/long-distance>). However, the intrinsic variability of the assay and prolonged time to analysis would be expected to affect both flown and stationary sample sets in similar ways. To address the physical alteration of the samples due to shaking, we performed additional experiments where EDTA-coagulated blood-filled Vacutainers were shaken for 3 hours at 3,000 rpm using a Barnstead Thermolyne M16715 (Thermo Fisher, Waltham, MA). Glucose and potassium levels measured before and after the shaking did not show any systematic changes (Table 3). Thus, the systematic changes in the glucose and potassium results appear to be due to temperature differences between these two sample groups.

Previous reports have demonstrated that the magnitude of decreases in glucose due to temperature alone depends on the temperature in question and the length

**Table 3**  
Glucose and Potassium Results From EDTA Whole-Blood Samples Before and After 3 Hours of Shaking at 3,000 rpm

Before 3-Hour Shaking		After 3-Hour Shaking	
Glucose (mg/dL)	Potassium (mmol/L)	Glucose (mg/dL)	Potassium (mmol/L)
206	3.5	210	3.5
85	4.0	86	3.9
132	3.8	134	3.8
58	3.2	57	3.2
256	4.1	258	4.1
65	3.8	65	3.8
71	3.6	69	3.6
70	3.4	70	3.4
68	3.2	65	3.2
70	3.5	69	3.5

of the incubation. For example, Ono et al<sup>15</sup> demonstrated a 22%, 54%, and 71% decrease in glucose levels after 48 hours at 4°C, 23°C, and 30°C, respectively. The reason for this finding is that glycolysis is more efficient at higher temperatures. Similar patterns have been demonstrated for potassium, but the mechanisms are different.<sup>15</sup> Intraerythrocyte concentrations of potassium are 40-fold higher than those in serum, and thus the mild changes in RBC membrane permeability that occur with increasing temperature lead to spurious increases in serum potassium levels.<sup>14,16</sup> There was no impact of the flight on hemolysis rates, under the conditions of our experiment. Based on the hemolysis indices of the flown and stationary sample sets as measured on the Roche Cobas c501 analyzer, none of our samples were hemolyzed. It is likely that the plastic mesh socks into which the primary tubes were placed helped to stabilize them in transit. As described in the Results section, the temperature of the flown samples was an average of 2.5°C cooler than the stationary samples during transportation to the flight field, as well as during the flight. The magnitude and direction of the changes in glucose and potassium are consistent with the magnitude and duration of the aforementioned temperature difference between the flown and stationary sample sets. For example, the amount of change in glucose levels in the range of interest (24°C-27°C) is around 10% after 2 hours, with lower glucose concentrations in samples kept at higher temperatures.<sup>13,15</sup>

The  $r^2$  of 13 of 19 tests was 0.9 or more. The other five tests had  $r^2$  values less than 0.8, but these were for reasons that were unrelated to agreement between the two result sets. As previously described,<sup>1</sup>  $r^2$  is also affected by a low mean value of a cohort, a narrow range of values (highest to lowest) in a cohort, or only a few possibilities within a cohort (eg, a dichotomous



variable). In our case, all five of these tests with an  $r^2$  of less than 0.8 (sodium, chloride, CO<sub>2</sub>, monocytes, basophils) had either low mean normal values or narrow normal range (Supplemental Table 1; all supplemental materials can be found at *American Journal of Clinical Pathology* online).

At the inception of this work, there was no precedent for packaging samples for long drone flights in hot conditions. To address this, we attempted to mitigate the impacts of vibration, acceleration, and temperature. We mitigated vibration by using a plastic mesh sock around each Vacutainer, acceleration by close packing of the primary tubes (Image 1), and temperature by constructing an active cooling box that could run using the drone's power source (Image 1). The cooling element in the box was set to a minimum temperature of 15.5°C so as not to overcool the samples, as laboratory results from many analytes are also affected by cooling.<sup>13,15</sup> The cooling element appropriately cooled to this minimum temperature during much of the flight, as ambient temperatures reached 32°C (Figure 1). We were unable to measure the actual temperatures inside the primary Vacutainers, since the conditions of the experiment precluded that. However, the mean temperatures in the payload box were 24°C.

As with the previous study of sample stability in drones,<sup>1</sup> this study's most significant limitation is that the volunteers were mostly healthy individuals and so their results were in the relatively narrow normal range, rather than spread across the full assay range (low to high) for each test. Consequently, it does not address the impact of drone transport on results that are outside of the normal reference range. Nevertheless, as previous reports of this kind were performed either in cold ambient temperatures<sup>2,3</sup> or at around room temperature,<sup>1</sup> this report is the first of its kind to examine long drone flights as well as flights at relatively high temperatures and low humidity, as seen in the southwestern United States. The 3-hour, 258-km flight selected to examine this question was not chosen because it is appropriate to all testing situations but rather because it may be necessary for some. In fact, the length of the flight alone exceeds recommendations from the World Health Organization and the Clinical Laboratory Standards Institute for times between sample procurement and arrival in the laboratory.<sup>17,18</sup> Adoption of long drone flights such as that in this report will require a careful selection of analytes that are stable under the conditions and remain clinically useful even with delayed reporting of results. Our findings demonstrate that transportation of laboratory specimens via small drones for long flights at high temperatures does not appear to affect the accuracy for 17 of the 19 test types in this study.

However, time- and temperature-sensitive analytes such as glucose and potassium will require good preplanning and stringent environmental controls to ensure reliable results.

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