The impact of drone transport on blood quality

J. Van Bael, MSc¹, N. Callewaert, Apr², C. Tersteeg, PhD¹

SUMMARY
Drone transport is employed in several countries to deliver blood products to remote locations difficult to access by cars. Additionally, it offers a swift and secure way of transporting blood tubes from collection sites to laboratories for subsequent analysis. However, during drone transport the blood is exposed to vibrations, g-forces and variable ambient temperatures. Ensuring the preservation of the quality of blood samples during aerial transportation is a crucial prerequisite for the widespread utilisation of drones for blood transportation. In this review, we will summarise the current knowledge on the impact of drone transport on hematological and biochemical parameters.

INTRODUCTION
The logistics sector is facing several major challenges. Ever shorter delivery times, a shortage of drivers and staff, climate challenges, fierce competition, low profit margins and increasing consumer demands are putting this sector under pressure. Transportation using unmanned aerial vehicles (UAV), commonly named drones, offers enormous potential to largely solve the above problems. A sector par excellence where the demand for reliable, flexible and time-critical deliveries is high is the medical sector for the transport of blood products (Figures 1A-B). Blood products are continuously transported between hospitals, patient homes, laboratories and blood banks, which must meet strict requirements on punctuality, quality and certification.

DRONE TRANSPORT OF BLOOD AND BLOOD PRODUCTS
Accidents and trauma require fast blood transfusions, where timely and safe distribution of blood products is often a major challenge. Drones were shown to be valuable in terms of reducing the delivery time of blood products, as congested traffic is avoided. Homier et al. tested the impact of drones on the delivery of simulated blood products to an urban trauma centre in a large-scale city-wide disaster simulation. After nine runs of simultaneous drone- and ground-based transportation of simulated blood products to trauma centres, the transport time using drones was significantly faster compared to ground transportation.¹ Li and colleagues performed a similar study in China and showed a reduction in time by 50% using drones, however not in all circumstances. Drones are limited in range due to their battery capacity, and some densely populated areas and airports impose restrictions preventing the drone to fly in a straight line. As a result, delivery time can be prolonged in some cases.² In remote locations particularly in Sub-Saharan Africa, the demand for blood transfusions is even higher resulting from anaemia caused especially by malaria and pregnancy related complications.³ Many areas in Sub-Saharan Africa face challenges resulting in a shortage of 40% for the total

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required blood units and an even higher shortage in platelets. The main reasons for this shortage include the lack of national blood transfusion services, low recruitment and retention of donors, commercial blood donation, and inadequate use of pharmacologic and non-pharmacologic alternatives to allogenic blood. Moreover, the conventional methods of delivering blood to its intended destinations usually relies on cars or ambulances, which are often subject to delays and limitations imposed by inadequate road conditions. Drone are a possible way to avoid this barrier, offering a logistic system enabling healthcare providers to bring medical products such as blood to remote locations in a fast and safe manner. In 2016, Zipline International together with the Rwandan government started a delivery operation in Rwanda. Blood products stored at two central hubs were transported with drones to 20 different healthcare facilities located within an 80 km radius effectively covering 90% of the country outside the capital. At the arrival location, blood is dropped using a parachute. Compared with the estimated driving time via the road, the delivery time using a drone was 79 minutes faster. More importantly, it resulted in a 67% decrease in blood and blood product expiration since the drone delivery program was put in place. In Switzerland, the US company Matternet together with Swiss Post, is successfully flying blood samples and pathology specimens between hospitals and laboratories since 2017 and is currently expanding to countries outside of Europe. This collaboration has proven the use of drones for blood and blood product transportation to be safe and effective in many cases. It is expected that it will be implemented on a much larger scale as drones are much more accessible, and changes in legislation make it easier to implement drone transport in current logistics. The success of drone implementation for blood transportation is depending on the geographics of departure and arrival location, as well as air and ground itineraries involved.

FIGURES 1A-B. Illustrative pictures of blood transport using drones at AZ Groeninge Hospital in Kortrijk, Belgium.
In addition, when transporting pathological blood, it will be a challenge to obtain approval to fly from the Civil Aviation Authorities. Together, these factors will determine whether drone transportation is a cost-effective manner of logistics. However, ensuring no impact on quality of blood samples during drone transportation is a crucial condition to utilise drones for blood transportation.

LABORATORY ANALYSIS

Amukele et al. were the first in demonstrating the influence of drone transportation on the stability of blood samples, as well as its consequential effects on the laboratory analyses conducted with those samples. Blood specimens were transported either by car or by a fixed wing drone for a duration of 6-37.5 minutes, while kept at ambient temperatures. Their results demonstrated that drone transportation had no impact on the accuracy of routine chemistry, haematology, and coagulation test results. Nevertheless, it led to slightly reduced precision for certain analytes. In a follow up study, the same research group demonstrated the impact of drone transportation on blood products, where size and storage requirements are significantly different from routine blood specimens. Platelet concentrates, red blood cell (RBC) concentrates and plasma were flown for 22 minutes using a multicopter drone with a cooler container. The authors showed no detectable impact on the test samples, as no visual RBC or platelet lysis or platelet clumping was observed. However, no laboratory analyses were performed to support these findings. They furthermore demonstrated the ability to effectively regulate the temperature of blood products during flight, even with significant fluctuations in ambient temperature. In a subsequent study by Amukele et al., blood specimen quality was determined after a prolonged duration of drone transportation. Blood specimens were either transported by drone for three hours using a hybrid aircraft or stored in a stationary car for the same duration. In this setup, glucose and potassium levels were higher in samples that were transported by drone. The authors suggested that this was an effect of the 2.5°C temperature difference between samples stored in the drone compared to the car and not a result of the vibration and turbulence caused by the drone. They strengthened these finding by demonstrating no effect on the laboratory parameters after shaking blood for 3 hours at 3000 rpm. Earlier studies have indeed described a temperature dependent effect on potassium and glucose levels; glucose levels decrease faster at a higher temperature due to increased glycolysis, and potassium levels increase faster at a lower temperature because of inhibition of the sodium potassium pump. Perle et al. compared blood samples transported by drone or by car with samples that were not transported. In this study, a fixed wing drone was used and samples were stored in an isolating box. They showed a clinically significant increase in lactate dehydrogenase (LDH) levels, indicating haemolysis. This could potentially be attributed to movement during transport, which can be addressed by optimising the stabilisation of blood tubes within the transport box. Also in this study, glucose levels decreased in samples transported by drones, suggestively due to the decreased temperature during transport. In Japan, additional studies have been performed using RBC concentrates transported using a quadcopter for 4-35 minutes using a refrigerator box. No differences were observed in LDH, potassium, glucose or other laboratory parameters. The same authors furthermore studied the impact of dropping blood products from a fixed wing drone, as is currently being conducted in Rwanda, on blood quality. RBC concentrates dropped from ten meters height had a significant increase in LDH compared to control samples that were transported by drone without dropping.

All studies described above have all included samples from healthy individuals rather than patients that present with values outside the normal reference range. Therefore, Johannessen et al. developed an in vitro model to simulate vibration and turbulence, and studied the effect on blood samples from patients with a wide range of abnormal blood values. They demonstrated that these blood samples could tolerate substantial vibration and turbulence during the two hours of the testing. Only blood samples containing a separator gel that were centrifuged before the simulation resulted in significant changes in test results, emphasising the need to avoid centrifugation of these blood samples before drone transport. In this study, temperature was kept stable for the duration of the experiment.

FUTURE DIRECTIONS

Ensuring the preservation of the quality of blood samples during aerial transportation is a crucial prerequisite for the widespread utilisation of drones for blood transportation. In different studies it has been shown that the impact of vibrations and turbulence are minimal, but that temperature changes affect blood quality, especially glucose and potassium levels. The ideal storage temperature of blood specimens and blood products depend on the assay to be performed or the blood product that is transported. For blood tubes, the ideal storage temperature is depending on the laboratory assay that needs to be performed, but most guidelines recommend storage between 20-24°C.
For transfusion purposes, RBC are best kept at 4°C and platelet concentrates at 20-24°C. For this purpose, well isolated and, if needed, temperature-controlled transport boxes are needed to ensure blood sample quality. Further research is needed to study the impact of drone transportation on patient samples, as current studies investigating drone transportation have only included healthy individuals thereby lacking pathological samples outside the reference intervals. In addition, the effect of drone transport on platelets has not been studied yet. These cells are very sensitive to vibration and turbulence, and become easily activated. Platelet activation parameters could be of benefit to include in future drone studies to understand the effect on platelet dependent clinical laboratory assays and platelet concentrates used for transfusion purposes.

REFERENCES