drones

MDPI

Article

Preliminary Clinical Validation of a Drone-Based Delivery System in Urban Scenarios Using a Smart Capsule for Blood

Fabrizio Niglio [1], Paola Comite [1], Andrea Cannas [2], Angela Pirri [3,*] and Giuseppe Tortora [2]

1 Azienda Toscana Nord Ovest, Via A. Cocchi 7/9, 56121 Pisa, Italy
2 Smart Medical Theatre Laboratory, ABzero, Polo Tecnologico Navacchio, Via Mario Giuntini 63, 56023 Cascina, Italy
3 Istituto di Fisica Applicata "Carrara", IFAC, Consiglio Nazionale delle Ricerche, CNR, Via Madonna del Piano 10C, 50019 Sesto Fiorentino, Italy
* Correspondence: a.pirri@ifac.cnr.it

Abstract: In this paper, we report on the validation of an autonomous drone-based delivery system equipped with a smart capsule for the transportation of blood products in urban areas. The influence of some thermo-mechanical parameters, such as altitude, acceleration/deceleration, external temperature and humidity, on the specimens' integrity were analyzed. The comparison of the results carried out by hemolytic tests, performed systematically on samples before and after each drone flight, clearly demonstrated that the integrity of blood is preserved and no adverse effects took place during the transport; these results can be addressed to the smart-capsule properties, which allows integrating real-time quality monitoring and control of the temperature experienced by blood products and mechanical vibrations. In addition, we demonstrated this transport system reduces the delivery time considerably. A risk analysis (i.e., HFMEA) was applied to all delivery processes to assess possible criticalities. To the best of our knowledge, this is the first time a drone-based delivery system of blood products in an urban area has been validated to be employed in a future clinical scenario.

Keywords: smart capsule; artificial intelligence; drones; blood products; drone transport; risk analysis; HFMEA method

Citation: Niglio, F.; Comite, P.; Cannas, A.; Pirri, A.; Tortora, G. Preliminary Clinical Validation of a Drone-Based Delivery System in Urban Scenarios Using a Smart Capsule for Blood. *Drones* **2022**, *6*, 195. https://doi.org/10.3390/drones6080195

Academic Editors: Paul Royall and Patrick Courtney

Received: 14 July 2022
Accepted: 3 August 2022
Published: 5 August 2022

1. Introduction and Background

The first unmanned aerial vehicles (UAVs), commonly called drones, were used for civil activities (i.e., cargo drone) in 2014. In the last few years, their usage has increased significantly [1–3] in, for instance, humanitarian [4] and healthcare [5] settings, as well as in environmental emergencies due to climate change (fires [6], storms, landslides [7], etc.). Nowadays, in all countries, the civil defense employs drones for search and rescue operations in natural disasters whenever the areas to be monitored are dangerous for the safety of rescuers.

One of the most important advantages of drones is the ability to overcome, in urban areas, the car traffic by reducing delivery times with economic savings [8] or to reach rural areas where access by ambulances or cars is extremely difficult due to the scarcity of communication routes.

This feature has triggered medical-drone use [9,10]. It is known that in some emergency situations, the timely intervention of health professionals is essential to prevent patient death [11–13]. Nisingizwe et al. [14] clearly demonstrated, examining over 12,000 deliveries of blood products by drones to 20 hospitals in Rwanda in about 32 months, the delivery time decreased significantly (about 30%) and there was a 67% reduction in blood product expirations at 12 months.

Accordingly, drone-based delivery systems result in a useful alternative transport system with respect to road transport [15]. It is worth noting that air transport (airplane or helicopter) of blood products [16] has long been an alternative, used especially in developing countries for emergency or disaster situations [17,18].

Recently, the scientific communities have begun to investigate whether drones could be used to transport biological materials [19,20], such as blood products [21], as they require special arrangements. The temperature, for instance, plays a fundamental role to avoid adverse effects. Once blood cells have been collected, platelets and plasma units can be stored and transported in containers with specific temperatures (4 °C ± 2 °C for red cells, 22 ± 2 °C for blood platelets and −25 °C for frozen plasma).

In 2016, for the first time, a delivery system using a drone to carry blood sample tubes was taken into account [22], finding that no significant alterations in flown specimens occurred. Three years later, hundreds of non-centrifuged human blood specimens were flown by drones for around 40 min and their integrity was tested successfully [10].

In this paper, we report on the laboratory measurements, the activities and the tests to validate an autonomous drone delivery system of blood products in an urban area. We demonstrated by monitoring some parameters, which could influence the quality of the blood products, such as high altitude, temperature and acceleration/deceleration, the effectiveness and safety of blood-drone transport. Hemolytic tests performed on flown blood products confirmed the integrity of blood products. The smart capsule [23] attached to the drone, where blood products are placed, developed by Abzero and used for achieving our goal in the project, consists of a smart casing that is able to guide any autonomous aerial vehicle attached to it, specifically designed for transporting blood, as well as organs, tissues and so on. Equipped by artificial intelligence (AI), the smart capsule allows integrating real-time quality monitoring and control of the temperature, agitation and humidity; its intuitive control software, the possibility of preloading a route, set weights and temperatures required for each specific blood product make this a user-friendly product for this transport system [23].

The reliability of the entire delivery system was confirmed by a risk analysis (i.e., HFMEA (Healthcare Failure Mode and Effect Analysis), which was applied to assess possible criticalities, taking into account the observations performed during flights. Concerning the delivery times, it was estimated that drone transport reduces it up to 50% over short distances (up to 10 km) and up to 80% over medium distances (up to 40 km) in the scenario considered in this project.

The Smart Capsule and the Spoke App

The smart capsule is a box, which is equipped with artificial intelligence (AI), provided by an autonomous flight control, as no ground pilots are required [23]. The AI makes autonomous drone flight possible by reducing the risks associated with the flight (i.e., the capsule can react to unforeseen situations, such as a sudden battery drop). It fits all professional drones available on the market, as long as they comply with ABzero technical requirements (e.g., 10 kg load capacity, 60 km/h minimum speed, water and windproof). Its flexibility allows for adapting to the continuous evolution of drones thanks to a dedicated adjustable interface. GPS/GSM/5G connectivity permits modifying the route according to flight authorization requirements at any time. This kind of connectivity guarantees the recovery of the active control by drone operators in case of emergency as well. The capsule is equipped with many sensors, which allow for real-time monitoring and control of storing conditions and quality of the medical freight, as prescribed by the law (i.e., temperature, humidity and agitation). The AI coupled with smart sensors and cameras placed on the casing recognize possible obstacles, improving the safety during flight, take-off and landing. The capsule, flexible and modular, is able to adapt to any medical product (e.g., blood bags, organs, drugs, test samples) thanks to two casing sizes addressing different end-user needs. It is designed for the delivery of blood and blood components, fulfilling stringent delivery regulation, i.e., 4 ± 2 °C for red cells, 25 ± 2 °C for blood platelets and −25 °C for frozen plasma. It is worth noting that this smart capsule can be adapted for the delivery of any other medical products operating within less stringent regulation, such as test samples, equipment and other products, while preserving temperatures. For instance, transportation of organs will be carried out by means of a specific internal certified container and adjusting the temperature. Moreover, it can be used as a self-standing device if needed and also inside traditional means, such as cars and vans. The smart capsule is designed in full compliance with the EU Directive 2002/98/EC, prescribing quality and safety standards for the collection, testing, processing, storage and distribution of human blood and blood components, and the smart capsule is UN3373 certified (Transport Biological Substance, Category B by Air). Concerning the software, Spoke App (see Figure 1) is a software developed for fulfilling the needs of medical staff for activating and monitoring the delivery. It is based on advanced, commercial flight control systems, and thanks to an intuitive App, it is easy to use and the process of managing the flight is completely transparent to the user. Spoke allows the healthcare facility to manage the whole delivery process without the need for third-party couriers or licenses, thus, improving efficiency and reducing costs and waiting times. The Spoke app is functional and can be integrated with additional AI features in the near future after extensive usability tests have been performed.

Figure 1. Mobile app used for managing the system, the flight and medical information.

2. Material and Methods

2.1. Validation of the Transport System

The transport system of blood sample tubes by drone was validated in three different steps. First, the thermal stability of the smart capsule used to transport the blood sample tubes was tested in many different experimental conditions (weather conditions, acceleration/deceleration of the drones, altitude) in urban scenarios, etc. Second, the integrity of red cells on the blood samples was demonstrated by comparing the hemolysis tests performed on the specimens before and after the flight. Third, the reliability of the entire delivery system was assessed by the risk analysis method, i.e., HFMEA, to identify the parameters that could affect flight safety.

2.1.1. Smart Capsule Thermal Stability

The first prototype of the delivery system, see Figure 2, formed by a smart capsule attached on a DJI M600Pro drone was tested in areas with different geographical characteristics such as city, countryside, forest, airfield, etc. The DJI M600 is a hexacopter with a battery lifetime of 25 min.

The overall performance of the delivery system was tested in 8 different flights, each lasting between 13 and 17 min; the total distance covered was 105 km for 39 h flown. In Table 1, the experimental conditions for each flight are summarized.

Among the parameters that influence the quality of the blood, the temperature plays a crucial role. We monitored and acquired the temperature values during the whole flight at different altitudes, accelerations, decelerations, random speed, by a temperature system control (Plasma Check System, ExpertMed S.r.l., Verona, Italy). In particular, a time-strip sensor applied on the bag and a data logger were used (see Figure 3). As temperature increases, an alert is generated instantly: the data are acquired and stored by the software. In the future, an active solution for lowering the temperature will be integrated.

Figure 2. The drone-based delivery system equipped with the smart capsule.

Table 1. Experimental data of each drone flights.

Day	Duration (min)	Length (m)	Altitude (m) Min/Max	Forecast Weather	Wind (km/h)	Temperature (°C)
1	13	6042	60/90	Cloudy	8	6
2	14	7594	60/90	Cloudy	9	7
3	10	8961	60/90	Sunny	4	11
4	10	3802	60/150	Sunny	5	12
5	17	7870	60/90	Sunny	9	14
6	16	7593	60/90	Sunny	9	13
7	16	8961	60/90	Cloudy	23	8
8	15	6278	60/90	Cloudy	25	9

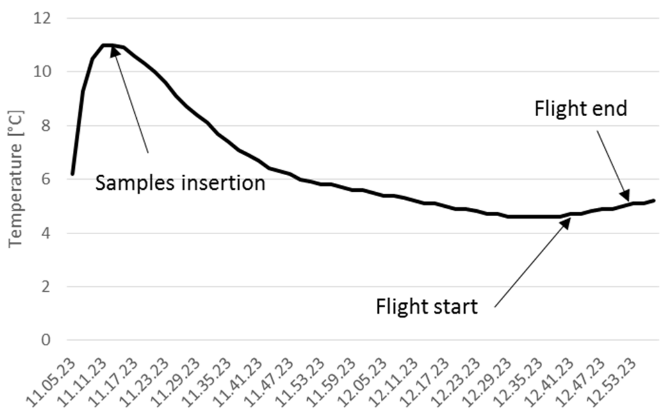

Figure 3. The temperature of the sample measured during the transport: from the refrigerator to the end of the flight. The time (hours, minutes, seconds) is shown on the x-axis.

Figure 3 reports the temperature changes in the blood during the transportation as a function of the time: from the refrigerator (6 °C) to the end of the flight. It is worth noting that as soon as the samples are outside of the refrigerator and manipulated, their temperature rises to 11 °C. Once placed in the UN3373 box, the blood tube samples return to the initial value (6 °C) in 42 min; to make up for lost minutes, the box should be placed in the refrigerator before being inserted into the smart capsule for flight.

In the first run of measurements the temperature variation in a physiological solution, placed in a UN3373-certified box, was monitored (see Figure 4). Later on, bags containing solutions having the physical–chemical characteristics of red blood cell concentrates (PRBC) were used. To prevent unauthorized opening of the smart capsule, it is equipped with a locking system.

Figure 4. Temperature check after the flight by means of time-strip sensor. The physiological solution bag is shown.

2.1.2. Validation of the Integrity of the Flown Blood Products

Here, 10 blood specimens from 10 different patients were tested in different weather conditions, see Table 2.

Table 2. Experimental conditions of the in-flight stress tests.

Flight	Altitudinal Max (m)	Forecast Weather	Drone Speed Km/h	Wind (km/h)	Temperature (°C)
1	150	Cloudy	60	No-wind	6
2	150	Sunny	60	No-wind	8–9
3	150	Sunny	60	23	22
4	150	Serene	60	29	6.5

The in-flight stress tests were performed with random values of accelerations, decelerations and rotations of the drone. Inside the UN3373 box containing the 10 blood specimens, a certified temperature tracker was inserted as temperature reference (data logger). Experiments were performed at the facilities of the association GAP "Gruppo Aeromodellistico Pontederese" and "G.A.P.L.", Gruppo Aeromodellistico Pisa Livorno. Figure 5 shows the box with blood specimens to be transported. Experimental video are available in Supplementary Materials.

Figure 5. UN3373-certified box with blood sample tubes before departure.

The entire clinical trial was carried out according to the medical official guidelines reported in DM 69—2 November 2015, Standard Transfusion Medicine III edition SIMTI 2017, Good Practice Guidelines (GPS) for blood establishments and Hospital blood banks (EU Directive 2016/1214).

To verify the integrity of the blood, the 10 specimens flown were investigated by Hemochromocytometric exam and hemolysis test; the latter test include aspartate transaminase (AST), alanine transaminase (ALT), direct and total bilirubin, lactated dehydrogenase (LDH) and potassium. The obtained values were compared with those carried out on the same 10 samples before each flight.

It is well known that the hemolysis test gives information on the breakdown of red blood cells. For sake of clarity, in Table 3 the potassium values are reported because this element is extremely sensitive to the hemolysis test. Comparing the measured values after and before the flight, variation of 0.24 (from 3.79 to 3.95 mEq/L) is found, which is a clear demonstration of the integrity of the red cells (see Table 3).

Table 3. Potassium values measured in a sample after and before drone transportation.

Potassium (K)	Value (mEq/L)	Reference Values
Antes-fligth	3.79	3.60–5.50
Post-fligth	3.95	3.60–5.50

2.1.3. HFMEA Risk Analysis

A risk analysis of the whole process was performed by means of Healthcare Failure Mode and Effect Analysis method (HFMEA), which is based on the Failure Mode and Effects Analysis (FMEA) tool developed in the 1950s in the frame of the NASA Apollo program.

FMEA allows calculating the Risk priority number (RPN), which is a combination of end effect probability (P) of the event occurring, the severity of the event (G) and the probability that the event would not be detected before the user was aware of it (D). RPN can be calculated by the following formula: $RPN = P \times R \times G$.

The risks were identified by analyzing the individual activities on the basis of scientific and regulatory guidelines (GPGs) already used to ensure transfusion safety. Accordingly, the critical factors taken into account during the transportation were: the hermetic closure of the tertiary container, the temperature of the sample and the integrity of the transported material.

The calculated RPN confirmed that the issues affecting the delivery system can be addressed to the control software of the drone. Although it is easy to use for health workers (setting temperature, routes, etc.) and is able to recognize obstacles and avoid them eventually, it is necessary to protect the software from harmful threats: adware, spyware, viruses, etc. An implementation of the software control is being studied to avoid cyber attackers.

3. Results and Discussion

The development of the smart capsule equipped with artificial intelligence (AI), which can be easily mounted on a drone, was the first goal of the project, as it preserves the thermal condition of the products transported. In all flight conditions (different altitudes, speed, acceleration, humidity), no significant change in temperature of the flown physiological solutions was measured. The integrity of the specimens was confirmed by chemical tests performed on the 10 blood specimens after each flight. No variation with respect to the test results obtained on the blood specimens stored in laboratory was measured. The mentioned chemical tests were performed according to the general guidelines and procedures of the European medical testing laboratories.

As the project involved two different hospitals in two different Italian cities (Pontedera and Volterra), we estimated the saved time by using drones with respect to the common ambulance transport; it was obtained by comparing the delivery time on the road (from Google maps) with the calculations obtained considering the transport by drone traveling at 60 km/h. The delivery times decrease up to 50% for distances of about 10 km and up to 80% for a distance of about 40 km. This result is addressed to the ability of the drone-based delivery system to overcome traffic issues, as well as the winding of rural roads. For the sake of clarity, Figure 6 shows the route of the ambulance (blue line) and that of the drone (straight black line) between Pontedera and Volterra hospitals.

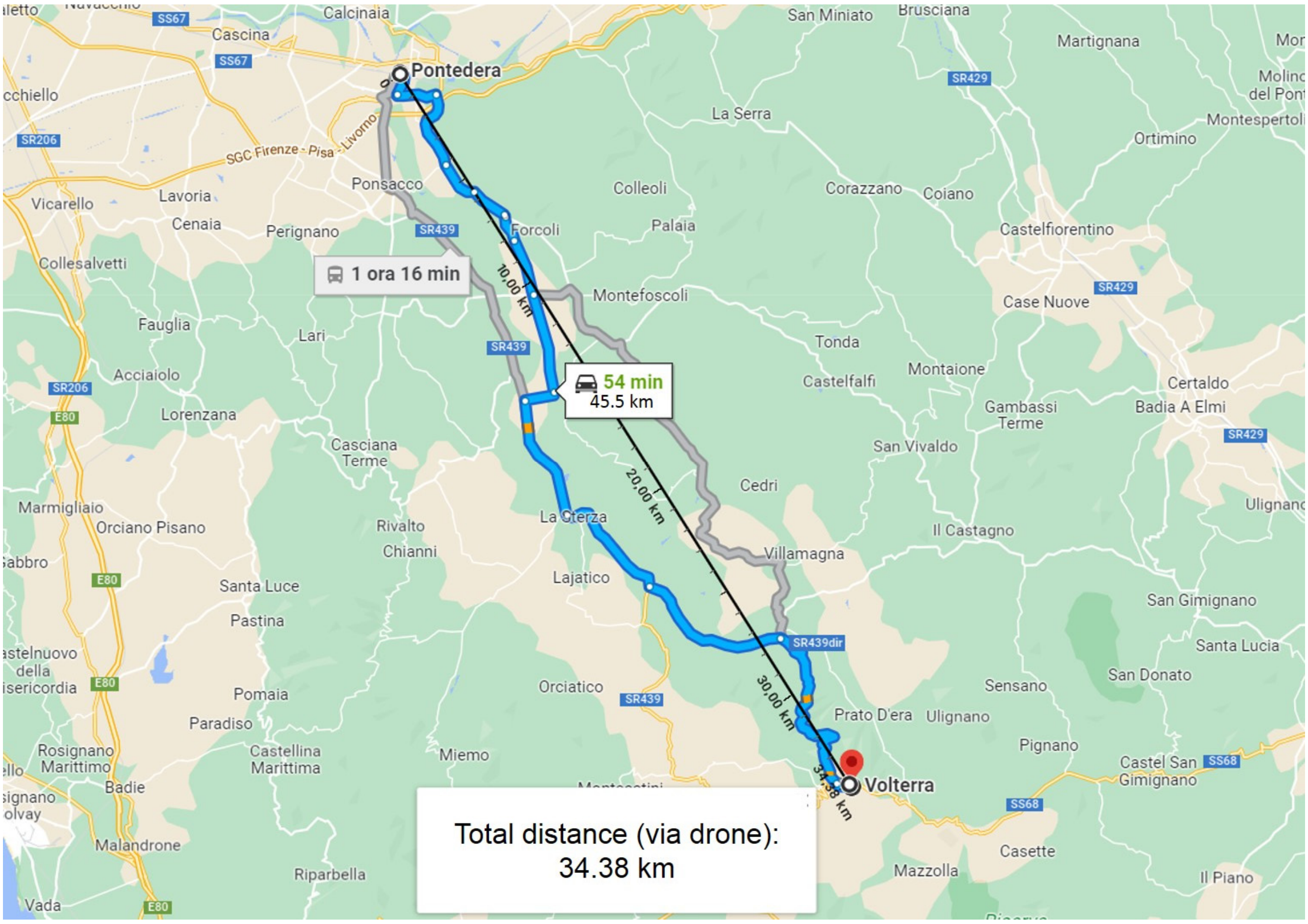

Figure 6. Route between Pontedera and Volterra cities for ambulance (blue line, distance 45.5 km) and drone (straight black line, distance 34.38 km).

4. Conclusions

In conclusion, we demonstrated that a drone delivery system using a smart capsule, which preserves the temperature conditions needed for the integrity of the blood products, can be used successfully in a hypothetical clinical setting. The smart capsule was effective in comparison with other drone delivery systems. This was one of the major outcomes of this study. These performed clinical trials have, for the first time, to the best of our knowledge, technically validated the drone transport of blood specimens in an urban area. As in this first step of the project, we verified the integrity of red cells flown, our future goal will be demonstrating the safety of blood products for transfusions in emergency situations, with previous authorization from the Ethics Committee of the hospitals. Concerning the flight safety from cyberattacks, we are studying an algorithm capable of preventing them because it is the most critical aspect of our delivery system.

Generally speaking, technological progress will allow redesigning health processes, allowing the optimization of human resources and an improvement in performance in terms of efficiency as the drones provide more rapid and less cost-effective healthcare.

Prospectively, the drones could represent a development in the current pneumatic mail within hospital buildings, as well as an alternative delivery system for dangerous biological material from hospital wards to laboratories in pandemic crises.

Supplementary Materials: Videos are available online at www.youtube/abzerox, accessed date 13 July 2022.

Author Contributions: Conceptualization, A.C. and G.T.; medical supervision F.N. and P.C.; methodology, F.N., P.C., A.C. and G.T.; software, A.C. and G.T.; validation, P.C., F.N., A.P. and G.T.; formal analysis, P.C.; investigation, G.T., F.N. and P.C.; data curation, P.C.; writing—original draft preparation, A.P. and P.C.; writing—review and editing, A.P.; supervision, G.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research was partially funded in the framework of the project Mini-lysis, JUMP (Joint Universities prograM for Poc), Ministero dello Sviluppo Economico (MISE), Italy.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Blood donors were used during the study. The informed consent of patients was waived by the Ethical Committee of ASL Toscana Nord Ovest, Pisa, Italy.

Data Availability Statement: Not applicable.

Acknowledgments: The authors wish to thank Angela Pirri for her valuable support during the organization of public demonstration in Pontedera (PI) and all the personnel of the Transfusion Center of F. Lotti Hospital of Pontedera (PI) and Azienda USL Toscana Nord Ovest.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Alkouz, B.; Shahzaad, B.; Bouguettaya, A. Service-Based Drone Delivery. In Proceedings of the IEEE 7th International Conference on Collaboration and Internet Computing (CIC), Atlanta, GA, USA, 13–15 December 2021; pp. 68–76. [CrossRef]
2. Islam, A.; Al Amin, A.; Shin, S.Y. FBI: A Federated Learning-Based Blockchain-Embedded Data Accumulation Scheme Using Drones for Internet of Things. *IEEE Wirel. Commun. Lett.* **2022**, *11*, 972–976. [CrossRef]
3. Hiebert, B.; Nouvet, E.; Jeyabalan, V.; Donelle, L. The Application of Drones in Healthcare and Health-Related Services in North America: A Scoping Review. *Drones* **2020**, *4*, 30. [CrossRef]
4. Cawthorne, D.; Cenci, A. Value Sensitive Design of a Humanitarian Cargo Drone. In Proceedings of the 2019 International Conference on Unmanned Aircraft Systems (ICUAS), 2019, Atlanta, GA, USA, 11–14 June 2019; pp. 1117–1125. [CrossRef]
5. Rosser, J.C., Jr.; Vignesh, V.; Terwilliger, B.A.; Parker, B.C. Surgical and medical applications of drones: A comprehensive review. *J. Soc. Laparoendosc. Surg.* **2018**, *22*, 18. [CrossRef]
6. Cohen, J. Drone spy plane helps fight California fires. *Science* **2007**, *318*, 727. [CrossRef] [PubMed]
7. Al-Rawabdeh, A.; Moussa, A.; Foroutan, M.; El-Sheimy, N.; Habib, A. Time series UAV image-based point clouds for landslide progression evaluation applications. *Sensors* **2017**, *17*, 2378. [CrossRef] [PubMed]
8. Amukele, T. The economics of medical drones. *Lancet Glob. Health* **2020**, *8*, e22. [CrossRef]
9. Cawthorne, D.; Robbins-van Wynsberghe, A. An Ethical Framework for the Design, Development, Implementation, and Assessment of Drones Used in Public Healthcare. *Sci. Eng. Ethics* **2020**, *26*, 2867–2891. [CrossRef] [PubMed]
10. Amukele, T. Current State of Drones in Healthcare: Challenges and Opportunities. *J. Appl. Lab. Med.* **2019**, *4*, 296–298. [CrossRef]
11. Laksham, K.B. Unmanned aerial vehicle (drones) in public health: A SWOT analysis. *J. Fam. Med. Prim. Care* **2019**, *8*, 342–346. [CrossRef]
12. Arcury, T.A.; Preisser, J.S.; Gesler, W.M.; Powers, J.M. Access to transportation and health care utilization in a rural region. *J. Rural Health* **2005**, *2*, 31–38. [CrossRef]
13. Tanser, F.; Gijsbertsen, B.; Herbst, K. Modeling and understanding primary health care accessibility and utilization in rural South Africa: An exploration using a geographical information system. *Soc. Sci. Med.* **2006**, *63*, 691–705. [CrossRef] [PubMed]
14. Nisingizwe, M.P.; Ndishimye, P.; Swaibu, K.; Nshimiyimana, L.; Karame, P.; Dushimiyimana, V.; Musabyimana, J.P.; Musanabaganwa, C.; Nsanzimana, S.; Law, M.R. Effect of unmanned aerial vehicle (drone) delivery on blood product delivery time and wastage in Rwanda: A retrospective, cross-sectional study and time series analysis. *Lancet Glob. Health* **2022**, *10*, e564–e569. [CrossRef]
15. Amukele, T.K.; Sokoll, L.J.; Pepper, D.; Howard, D.P.; Street, J. Can unmanned aerial systems (Drones) be used for the routine transport of chemistry, hematology, and coagulation laboratory specimens? *PLoS ONE* **2015**, *10*, e0134020. [CrossRef]
16. Ling, G.; Draghic, N. Aerial drones for blood delivery. *Transfusion* **2019**, *59*, 1608–1611. [CrossRef]
17. Carrillo-Larco, R.M.; Moscoso-Porras, M.; Taype-Rondan, A.; Ruiz-Alejos, A.; Bernabe-Ortiz, A. The use of unmanned aerial vehicles for health purposes: A systematic review of experimental studies. *Glob. Health Epidemiol. Genom.* **2018**, *3*, e13. [CrossRef]

18. Knoblauch, A.M.; de la Rosa, S.; Sherman, J.; Blauvelt, C.; Matemba, C.; Maxim, L.; Defawe, O.D.; Gueye, A.; Robertson, J.; McKinney, J.; et al. Bi-directional drones to strengthen healthcare provision: Experiences and lessons from Madagascar, Malawi and Senegal. *BMJ Glob. Health* **2019**, *4*, e001541. [CrossRef]
19. Lippi, G.; Mattiuzzi, C. Biological samples transportation by drones: Ready for prime time? *Ann. Transl. Med.* **2016**, *4*, 92. [CrossRef]
20. Amukele, T.K.; Street, J.; Carroll, K.; Miller, H.; Zhang, S.X. Drone transport of microbes in blood and sputum laboratory specimens. *J. Clin. Microbiol.* **2016**, *54*, 2622–2625. [CrossRef]
21. Glauser, W. Blood-delivering drones saving lives in Africa and maybe soon in Canada. *Can. Med. Assoc. J.* **2018**, *190*, E88–E89. [CrossRef]
22. Amukele, T.; Ness, P.N.; Tobian, A.A.R.; Boyd, J.; Street, J. Drone transportation of blood products. *Transfusion* **2017**, *57*, 582–588. [CrossRef]
23. Amicone, D.; Cannas, A.; Marci, A.; Tortora, G. A Smart Capsule Equipped with Artificial Intelligence for Autonomous Delivery of Medical Material through Drones. *Appl. Sci.* **2021**, *11*, 7976. [CrossRef]