Artículo original

Status of management of children´s vaccine supply chain in Peru

Situación de la gestión de la cadena de suministro de vacunas infantiles en el Perú

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ABSTRACT

Introduction: Countries face different challenges in managing vaccine supply. In Peru, the process of vaccinating children has specific challenges such as geographical conditions, infrastructure and administrative issues. The vaccination process is important in all types of vaccines aimed at the population.
Objective: Determine the management state of the pharmaceutical supply chain of children vaccines in Peru.
Methods: An analytical cross-sectional study was conducted. An online interview was conducted with retail logistics experts, professionals from pharmaceutical companies and planning professionals from the Ministry of Health. The content of the personal interviews was validated by experts. Responses were focused on cold chain (last mile), distances and altitude, handling technology, human resources, management process, planning of vaccine supply and purchase, storage and transport personnel, storage spaces and technology, temperature, transport routes and availability of health professionals for vaccination.
Results: The lack of trucks with high technology for transportation, especially in the last mile, was detected, as well as the challenge of taking vaccines to distant cities because some routes are not available, the limited technology for the

traceability of the transport of vaccines, and the storage and distribution process with non-standard control. The lack of standardization of the training process of the personnel who handle the vaccines and the absence of certification requirements by the interested companies, including the government, were detected. There is absence of an integrated system that allows managers to know exactly where the vaccines are in real time, the stocks, the patients to whom the doses were applied, among others.
Conclusions: It is concluded that there is an urgent need for a systematized plan that ensures the purchase, storage, distribution and application of vaccines so that the entire management process of the pharmaceutical supply chain of children vaccines in Peru can be controlled in real time and efficiently.
Keywords: vaccine; pharmaceutical industry; vaccination; children; Peru; distribution; COVID-19.

RESUMEN

Introducción: Los países se enfrentan a diferentes retos en la gestión del suministro de vacunas. En el Perú, el proceso de vacunación de los niños tiene desafíos específicos como las condiciones geográficas, la infraestructura y las cuestiones administrativas. El proceso de vacunación es importante en todos los tipos de vacunas dirigidas a la población.
Objetivo: Determinar el estado de la gestión de la cadena farmacéutica de suministro de vacunas infantiles en el Perú.
Métodos: Se realizó un estudio transversal analítico. Se aplicó una entrevista en línea con expertos en logística minorista, profesionales de empresas farmacéuticas y profesionales de planificación del Ministerio de Salud. El contenido de las entrevistas personales fue validado por expertos. Las respuestas se orientaron a la cadena de frío (última milla), las distancias y la altitud, la tecnología de manipulación, los recursos humanos, el proceso de gestión, la planificación del suministro de vacunas y su compra, el personal de almacenamiento y transporte, los espacios y la tecnología de almacenamiento, la temperatura, las rutas de transporte y la disponibilidad de profesionales sanitarios para la vacunación.
Resultados: Se detectó la falta de camiones con alta tecnología para el transporte, especialmente en la última milla, también el reto de llevar las vacunas a ciudades lejanas porque algunas rutas no están disponibles, la limitada tecnología para la trazabilidad del transporte de las vacunas, y el proceso de almacenamiento y distribución con control no estándar. Se detectó la falta de estandarización del proceso de capacitación del personal que maneja las vacunas y la ausencia de requisitos de certificación por parte de las empresas interesadas, incluyendo el gobierno. Existe la ausencia de un sistema integrado que permita a los gestores saber exactamente dónde están las vacunas en tiempo real, las existencias, los pacientes a los que se aplicaron las dosis, entre otros.

Conclusiones: Se concluye que existe una necesidad urgente de un plan sistematizado que asegure la compra, almacenamiento, distribución y aplicación de vacunas para que todo el proceso de gestión de la cadena farmacéutica de suministro de vacunas infantiles en el Perú pueda ser controlado en tiempo real y de manera eficiente.
Palabras clave: vacuna; industria farmacéutica; vacunación; niños; Perú; distribución; COVID-19.

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Introduction

In 2019, 5.2 million children under the age of 5 died from preventable causes.[1] It is important to understand that societies have extended their survival due to the use of vaccines,[2,3,4,5,6,7,8,9,10,11,12,13] estimating that two to three million deaths are prevented annually;[14] however, approximately 19.7 million children annually are not vaccinated.[15] In Peru, it has been reported 76.7% of coverage of vaccination in children under one year old and 60.7% of coverage in children under 3 years old.[16] More recently, *Vásquez-Uriarte*[17] has estimated that, according to the measles vaccine card, the coverage for the first dose was 70.2%, and for the booster dose, it was 52.0%. All the efforts made to improve the population's health are also framed in the Sustainable Development Goals (SDG). Goal 3.2 establishes that by 2020 the preventable deaths of newborns and children under 5 years of age, with all countries trying to reduce neonatal mortality to at least 12 per 1,000 live births, and mortality of children under 5 years of age to at least 25 per 1,000 births alive.[18] According to Instituto Nacional de Estadística e Informática (INEI),[19] the educational level of the mother establishes differences in the risks of infant mortality: the children of mothers with primary education have a greater probability of dying during the first year of life (24 per thousand) than those of mothers who have secondary studies (17 per thousand), or higher studies (14 per thousand).

The infant mortality levels calculated in the Demographic and Family Health Survey[19] present estimates of infant and child mortality for the three five-year periods before the survey, calculated using direct estimation methods based on the history of births and deaths obtained in interviews with women of reproductive age. Of every 1,000 girls and boys who were born in Peru during the 0 to 4 years before the survey (central date: January 2012), 17 died during the first year compared to 20 for the period 5 to 9 years prior (central date: January 2007) and 23 for the period 10 to 14 previous years (central date: January 2002). The estimates are reasonable if the population's increased access to health services is considered, mainly in rural areas. Child mortality, measured as deaths before the

fifth birthday for every 1,000 live births, reached 20 during the last five years; while for the immediately preceding five-year period, it was 23; and, for the previous five-year period 10 to 14 years, it was 30 children for every thousand live births.

Vaccination processes are a cornerstone in preventing infant death. The vaccine supply chain involves all activities after the manufacture of these until their application since vaccines are drugs that are highly sensitive to temperature and that at the same time are related to public health,[20,21,22] which includes distribution, transportation, handling, conservation, and storage, involves many actors.[23,24,25,26,27,28,29] The vaccine distribution process is generally necessary in an environment of uncertainty, as in the case of COVID-19 that arose without anyone expecting it.

Proper vaccine distribution is challenging, especially in developing countries with limited transportation infrastructure, inaccessible geographic areas, and marked climatic diversity.[20,21,22,23] The World Health Organization (WHO)[14] notes that critical areas of logistical support include vaccine management and monitoring, cold chain management, and immunization safety. The difficulties in the distribution of vaccines increase if it is a large-scale operation.[24] The vaccine distribution chain must work efficiently since this protects people against the diseases these vaccines prevent[25,26,27] This study aims to know the current supply chain management situation of children's vaccines in Peru in line with this need. Some actors are involved in this process, so the information they can supply is relevant to improve the understanding of supply chain management.

The paper is structured as follows: Section 2 presents relevant background, including different concepts about the supply chain about vaccines. The methodology, with a description of the qualitative instrument, sample, and data process, is provided in Section 3. Section 4 gives the results and outcomes according to the questionnaire applied, and Section 5 discusses the findings. Conclusions with theoretical, practical, and societal implications and recommendations, including potential future research, are provided in Section 6.

Theoretical background

The supply chain of vaccines: According to the WHO,[28] the cold chain is a term that refers to the supply chain necessary to store vaccines in such conditions that their effectiveness is not affected. Based on their studies, these conditions are mainly concerned with ranges of temperatures and light conditions required for proper storage and are recommended by the manufacturer. Likewise, these must be respected throughout the distribution process, from its manufacture to its application. Each manufacturer must specify the conditions in which the vaccines

must be stored. This requirement varies according to the composition that each sample may have. According to the WHO,[28] some vaccines are sensitive to freezing, others to heat, and others to ultraviolet rays transmitted by sunlight. For example, some vaccines should be stored between +2 ° C and +8 ° C and avoid temperatures below 0, but others require temperatures between -15 ° C and -25 ° C, or even lower, which are they can only hold temporarily for a few days in the range mentioned initially. For its part, the Centers for Disease Control and Prevention (CDC)[29] warns that care must be taken with experiencing interruptions in the power supply of this equipment since these inconveniences can destroy an entire batch of vaccines.

Also, it is important to consider ensuring the correct management of all processes related to distribution to optimize costs.[30,31] According to the CDC, two important factors for this objective are an adequately prepared staff and accurate vaccine inventory management. The personnel in charge of administering the vaccines and the temperature control equipment must be adequately trained to ensure the conditions that the vaccine requires and protocols to follow in cases of emergency.[32,33,34,35] Likewise, the correct management of the cold chain, the quality and quantity of the vaccines received, and the constant review of the conditions of the stored batches must be guaranteed.

Distribution of vaccines in Peru: Having a broader knowledge of what is involved in the distribution of a vaccine, it is pertinent to start talking about how it is carried out in Peru. The Peruvian state places orders to purchase vaccines through the Revolving Fund of the Pan American Health Organization (PAHO), allowing it to access quality products at lower costs for immunization programs. Likewise, it provides you with the air waybill or bill of lading before dispatching the order made.[36] All vaccines are kept in specialized warehouses categorized into 3 levels, each with its cold chain: the first is the national one, where all the acquired vaccines are located and can supply the country for long periods. Next, it is the regional one, which is located in each department and, due to geographic accessibility, some have up to 3 warehouses. Finally, there is the local level, which are the vaccinations that make up the health facilities.[37]

Due to the need to improve the country's technological infrastructure to preserve vaccines in the different departments that make up Peru, the Ministry of Health has been implementing improvements in various health facilities in our country for the past decade. For example, in 2013, the cold chain was strengthened by implementing 13,630 refrigeration units distributed throughout the national territory. After years, projects were developed to improve provincial health centers, technical standards to optimize cold chain procedures, regional vaccine warehouses, and technical assistance.[38,39,40,41,42]

Likewise, through the Technical Health Standard N° 141,[43] the state has established a mandatory National Vaccination Scheme throughout the country. This rule guarantees free vaccines in public health centers and those private that

have agreements with the Ministry of Health. In addition, the same document establishes that there are 17 vaccines to which every citizen must undergo, organized in a calendar of the application according to age and which we can see in Table 1.[43] On the other hand, in Table 2, the National Vaccination Scheme for children under 5 years of age has been compiled, in which we can also note that childhood is a fundamental stage for immunization since 12 of the 17 mandatory vaccines are applied in is.

In table 1 is shown the national schedule of compulsory vaccines in Peru.

Table 1 - Compulsory vaccinations of the national vaccination scheme

Vaccine	Storage temperature	Storage time once opened	Vaccination schedule	
			Pediatric	Adult
Tuberculosis (BCG)	+2 °C to +8 °C	6 hours	In the first 12 hours after birth	---
Hepatitis B (HvB)	+2 °C to +8 °C	Immediate use	In the first 12 hours after birth	From 16 to 59 years of age, not having received before
Pentavalent	+2 °C to +8 °C	Inmediate use	2, 4 and 6 months	Continue pediatric scheme
Pediatric Distothane Toxoid (Dt)	+2 °C to +8 °C	4 weeks	4 and 6 months	---
Influenzae Type B (Hib)	+2 °C to +8 °C	Immediate use	4 and 6 months	---
Inactivated polio (IPV oo Salk)	+2 °C to +8 °C (do not expose to sunlight or freeze)	Immediate use	2 and 4 months	---
Oral Poliovirus (bAPO or SABIN)	+2 °C to +8 °C	---	6 months, with 2 boosters at 18 months and 4 years	---
Rotavirus	+2 °C to +8 °C	---	2 and 4 months Cannot exceed the age of 5 months, 29 days	---
Pneumococcal	+2 °C to +8 °C	Immediate use	2, 4, and 12 months of age	Ages 60 and over receive a dose
Against measles, mumps, and rubella (MMR)	+2 °C to +8 °C	6 hours or immediate use depending on the presentation	12 months and 18 months	It can be applied in children and adolescents
Against measles and rubella (SR)	+2 °C to +8 °C	Immediate use	---	From 5 to 49 years of age, if not received MMR previously

Against varicella	+2 °C to +8 °C	---	From 12 months to before 3 years	-
Yellow fever vaccine	+2 °C to +8 °C	---	15 months	From 2 to 59 years of not having previously received
Against diphtheria, pertussis, tetanus (DPT)	+2 °C to +8 °C	---	2 booster doses at 18 months and 4 years	---
Against adult dT (tetanus and diphtheria)	+2 °C to +8 °C	---	---	1 dose at the first contact with the health service, another 2 months after the first dose, and another (only for women) 4 months after the second
Combined dTpa (only for pregnant women)	+2 °C to +8 °C	---	---	In the third trimester of pregnancy
Against Human Papilloma Virus (HPV)	+2 °C to +8 °C	---	---	Girls in the 5th grade of primary school

Source: Norma Técnica de Salud N° 141 (2018).

The objective of the present study was to determine the status of the pharmaceutical supply chain management of childhood vaccines in Peru.

Methods

Design and population: An analytical cross-sectional study was carried out. An online interview was conducted, selecting experts non-probabilistically for convenience. These experts included professionals in retail logistics (4), pharmaceutical company's professionals (2), and planning professionals in the Ministry of Health (2). The instrument was validated for review of content by experts. The instrument includes the following questions:

1. What are the processes of the vaccine logistics chain?
2. How much do you consider that the logistics chain has allowed an essential advance in childhood immunization?
3. What are the factors that should be analyzed to optimize vaccine distribution?
4. What are the main challenges for vaccine application, and how could we address them?

5. What is the security protocol that companies that transport vaccines from the port/airport to the warehouse of the pharmaceutical companies usually have?
6. What are the difficulties that companies that transport vaccines usually face?
7. What are the types of transport that vaccine transport companies usually use? Do the companies own them, or are they contracted?
8. What kind of license or permit, or certification do they need to transport vaccines? How easy is the process of obtaining this permit?
9. What type of tender exists by the pharmaceutical companies to carry out the transport contract? What is the criterion?
10. What type of training do the personnel involved in the transport of vaccines usually receive?
11. How do you measure the skills of workers in vaccine transport companies?
12. What are the criteria for hiring new staff?
13. What are the specific measures that companies have in place to avoid breaking the cold chain?
14. What is the contingency plan that companies have in the event of a cold break during transport?
15. What traceability system do vaccine transport companies have for their trucks? What technology do they use?
16. It is usually commented that the vaccine distribution system is not so efficient in Peru. What do you think about the role of companies in this process? Why?
17. What specific suggestions would you have for pharmaceutical companies to improve the distribution of vaccines nationwide?
18. What specific suggestions would you have for the Ministry of Health to improve the distribution of vaccines at the national level?
19. How is the payment process for transportation services?
20. How good is the State payer?
21. Specifically, what has changed in the distribution of vaccines with the arrival of COVID-19?

Data analysis: To develop the analysis of the information collected by the interviews, we established the following issues:

1. Cold chain (last mile)

2. Distances and altitude
3. Handling technology
4. Human resource
5. Management process
6. Planning provisioning of vaccines
7. Purchase of vaccines
8. Storage and transportation staff
9. Storage spaces and technology
10. Temperature
11. Transportation routes
12. Availability of health professionals for vaccination

Results

The participants expressed different information about the issues described in table 2.

Table 2 - Items, percentage of responses and level of importance

Item	Percentage of responses	Level of importance
Cold chain	100%	High
Distances and altitude	100%	High
Handling technology	87.5%	High
Human resource	87.5%	High
Management process	87.5%	High
Planning provisioning of vaccines	75%	Intermediate
Purchase of vaccines	75%	Intermediate
Storage and transportation staff	75%	Intermediate
Storage spaces and technology	75%	Intermediate
Temperature	75%	Intermediate
Transportation routes	50%	Low
Availability of health professionals for vaccination	50%	Low

Source: Interview of experts.

Cold chain (last mile): There is an efficient distribution in general vaccines from the central warehouses to the warehouses of large hospitals, the Ministry of Health, and the Pan American Health Organization; this distribution is done by trucks with temperature control systems. However, it has also been possible to report that the distribution from the big cities to the most remote cities is carried out by the same trucks up to a certain point, but then in the last mile, the distribution is carried out by trucks that do not necessarily have the sophisticated systems of control.

Distances and altitude: There are many limitations in the distribution time from Lima, the capital of Peru, to different regions in the country. The cities on the coast are based on good roads that allow a safe and short distribution in time. The same does not happen with the case of distributions towards the mountains of the country, where it is necessary to have trucks that can carry the vaccines through winding, uneven, and more distant roads. On the other hand, this same Andean zone presents altitude, which also impacts the conservation of vaccines and the effect on transporters who must be prepared to face these conditions in the destination sites.

Handling technology: Some trucks have the technology to ensure the traceability of vaccines throughout the journey, which implies that they have GPS traceability that allows knowing in real-time the truck's progress and taking concrete actions when stoppages on the route, accidents, or other accidents contingency are detected. However, the number of trucks that have this technology is limited; It was even reported that given the contingency of the current COVID-19, companies from other productive sectors that have trucks equipped with these technologies were requested to collaborate with the transport of vaccines to be able to carry out the distribution successfully.

Human resource: About human resources, that is, the workers who perform the roles of driver and stevedore, it was striking that it has been reported that there is no specific certification at the national level to develop these functions, considering the relevance of the products that are being carried out transporting. The state also does not request certifications from the drivers and stevedores from the companies that are hired to outsource the distribution of vaccines. Internal training that each company carries out independently, the same ones carried out with a particular frequency, but that is not reflected in any specific individual certificate for those who are trained.

Management process: Concerning the management of the distribution of the vaccines, there were different approaches. The delivery times are programmed correctly, but the orders are often not made with enough anticipation to avoid stock breakdown, generating that the vaccines arrive late to the vaccination sites.

Planning provisioning of vaccines: Also, the annual vaccination schedule is deficient because they order based on historical consumption in certain places,

which only considers the number of vaccines applied the previous year. However, the number of vaccines that were not applied due to lack of stock is not taken into account; in other words, in many cases, scheduling is done without adding the unattended demand.

Purchase of vaccines: The purchase of vaccines is basically articulated by the PAHO, which selects the laboratories from which it purchases the vaccines; later, in coordination with the Ministry of Health, it distributes to the central warehouse and even to decentralized warehouses for later distribution. In this regard, it is reported that the process is carried out in an efficient and standardized way.

Storage and transportation staff: Warehousing personnel usually have standard training in companies that provide outsourced warehousing services. The same happens with the store personnel of the Ministry of Health; However, in both cases, the need for a specific type of certification for the handling of vaccines is not reported, considering that they are high-cost pharmaceutical products of high importance in public health and highly susceptible to being altered in its composition due to environmental alterations.

Storage spaces and technology: Another aspect recognized is that the spaces for the storage of vaccines are very varied in the country. In certain cities, the regional health department has specialized warehouses in which vaccines are stored under all humidity and temperature conditions; However, some health centers keep vaccines in small refrigerators, even with other unrelated products.

Temperature: The temperature in the country is very varied due to the different geographical areas. In this sense, the cities of the jungle have a high environmental temperature. There are no problems in the rest of the country because you can have the equipment to maintain the required temperature and humidity. However, in the jungle, there are electricity restrictions with which there are rainy days that affect the supply of electricity and therefore put the electricity supply at risk stability of vaccines.

Transportation routes: Regarding the quality of the roads for the transportation of vaccines, the vast majority of the routes in the country are in good condition; many cities are difficult to access because there are no tracks, paved roads, or that the current state of these paved roads in the past is not the most suitable for efficient transport in general, generating an impact on the distribution of pharmaceutical products such as vaccines.

Availability of health professionals for vaccination: A critical aspect that could be reported is that although planning can be carried out from the central level of the Ministry of Health in health centers, the allocation of personnel for the specific task of childhood vaccination is very varied. For example, it was reported that two nurses for the vaccination process for 3 days, only one of them is assigned, and the other is entrusted with other functions of the health center. Another

modality is that the 2 nurses are appointed but only for two days, the third day being used to carry out other activities.

Discussion

The cold chain is recognized as a critical path, especially in vaccines that are highly susceptible to being altered by variations in temperature and humidity. Current evidence recognizes the importance of securing the last mile,[44] including the need to digitize the last-mile process.[45] However, while it is easy to advise that traceability should be digitized, the associated costs should be considered, especially in smaller companies tasked with the last mile. A significant investment may be required to have trucks equipped with traceability systems. The latter can reduce the profits of companies that hire these small businesses for the last mile; likewise, it could lead to large companies demanding a higher price to cover these increased expenses and maintain the established profit margin. The last mile logistics for the distribution of vaccines should constantly be optimized.[46,47]

Technology is increasingly providing different alternatives for the storage and distribution of vaccines. The distance and altitude create limitations for the distribution of the vaccines[48] since in the most remote cities, there are electricity limitations 24 hours a day or that the refrigerator is not the most suitable for the vaccine or that it breaks down and cannot be repaired in time before the vaccines have a problem with stability. Technology is increasingly providing different alternatives for control of temperature in the storage and distribution of vaccines[48] to avoid the stoppage of the cold chain;[49] also, it needs to evaluate what is the real effectiveness of vaccines through different kinds of a test as immunogenicity.[50,51] Thus, it is increasingly possible to see that preliminary information helps predict storage conditions, as with machine learning.[52] The need to have vaccines available in storage conditions and efficient delivery can be ensured have already been discussed.[53] It is relevant that they can be evaluated in future studies and implemented in real processes, which also leads to thinking about how to maintain the constant flow of vaccines to the population,[54] which is a current problem, increased by COVID-19, and that needs different alternatives to achieve the necessary supplies.

Various technologies can be gradually implemented so that the storage and distribution processes are safe and traceable, regardless of the distance that the vaccine trucks must travel, the height of the cities, or other conditions of the route or destination; this is the case of the use of blockchain,[55,56] ensuring traceability also reduces the probability of distribution of counterfeit vaccines.[57,58] However, in developing countries, different characteristics make the processes very different from those that occur in other regions where the

processes are standardized, so evaluating the processes in developing countries must consider multiple variables to be evaluated.[59]

Concerning human resources, it can be seen that there is no specialization in the personnel in charge of the storage and distribution of vaccines. Although they have specific training in most cases, they do not have certified training so that companies that hire storage or transportation services can be sure that the personnel in charge of handling the vaccines have standardized training and are certified by an independent institution. The certifications such as ISO 9001 improve general level processes, ensuring the traceability of processes and records;[60] it can undoubtedly be a starting point to optimize the management of the vaccine supply chain process, but it can be precious to have specific training programs aimed at generating knowledge and developing specific competencies in vaccine management. The COVID-19 pandemic has once again made the subject of vaccines relevant and requires more controlled processes, improving workers' skills. However, the concern about the vaccines for COVID-19 does not generate problems in managing other vaccines, such as those intended for childhood vaccination. Likewise, it is expected that this greater empowerment of human resources for the management of vaccines not diminish when the pandemic is controlled and the demands and care be relaxed.

Planning has also been recognized as a limitation that allows the established programs to be fully implemented. Human resources are not always allocated to comply with the vaccination schedule, which is a great weakness and limits vaccination coverage. In the case of developing countries, such as Peru, the management process needs to be standardized, but at the same time, it requires unified information; that is, all the information on vaccines, including the information on the companies that supply the vaccines, the purchases made, the distribution of the vaccines nationwide, the institutions where they are distributed, the certified warehouses, the workers who have the national certifications, among others. These health centers may have a limited number of professionals to cover other activities, but the vaccination processes should not be altered or postponed since fewer professionals who do the vaccination directly impact coverage.

Final considerations

The cold chain was recognized as high level the importance for experts and all of them agreed that it is a crucial element in the vaccination process. The same has been reported with respect to distances and altitude since Peru has many remote cities, with difficult access roads and many located in the Andean zones where there is a considerable altitude, with cities at more than 3000 meters above sea level. Human resource and management processes were also identified as being of high importance. Planning provisioning of vaccines, purchase of vaccines,

storage and transportation staff, storage spaces and technology and temperature were recognized as of medium importance, which shows that although these aspects can be fulfilled, they may not be receiving the greatest attention. Planning is the most critical of the aspects as it is not widely recognized by the experts as an element of high relevance. Finally, transportation routes availability of health professionals for vaccination were reported as of low importance, which could explain the weaknesses in the application of vaccines, as there is always a limited number of health professionals to apply vaccines to children.

It is concluded that there is an urgent need for a systematized plan to ensure the purchase, storage, distribution, and application of vaccines so that the entire management process of the pharmaceutical supply chain of childhood vaccines in Peru can be controlled in real-time and efficiently.

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Conflicts of interest

The Authors declares that they have no conflicts of interest to disclose.

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