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***Abstract*— In order to monitor and assess the spread of the Omicron variant of COVID-19, we propose a Distributed Digital Twin that virtually mirrors a hemodialysis unit in a hospital in Toronto, Canada. Since the solution involves heterogeneous components, we rely on the IEEE HLA distributed simulation standard. Based on the standard, we use an agent-based/discrete event simulator together with a virtual reality environment in order to provide to the medical staff an immersive experience that incorporates a platform showing predictive analytics during a simulation run. This can help professionals monitor the number of exposed, symptomatic, asymptomatic, recovered, and deceased agents. Agents are modeled using a redesigned version of the susceptible-exposed-infected-recovered (SEIR) model. A contact matrix is generated to help identify those agents that increase the risk of the virus transmission within the unit.**

Keywords—Omicron variant, COVID-19, disease transmission, hemodialysis, digital twin, modeling and simulation, agent-based simulation, distributed simulation

I. INTRODUCTION

SARS-CoV-2 genetic variations continue to substantially modify the COVID-19 pandemic landscape. The B.1.1.529 (Omicron), a reported variant that emerged in late 2021, has quickly spread over the world and is currently the dominant variant responsible for the majority of COVID-19 cases in many countries [1], [2]. Several knowledge gaps exist about the Omicron variant, its transmissibility, pathogenicity, and severity, as well as the efficacity of the vaccines in preventing Omicron infection [1]. In comparison with patients infected with the Alpha or Delta variants, Omicron patients have required less intensive respiratory support and spent less time in the hospital, indicating a lower disease severity [2]. The Omicron variant has been found in more than 75 percent of COVID-19 positive tests in South Africa as of November 15, 2021 [3]. The World Health Organization named Omicron a variant of concern (VOC) on November 26, 2021. According to a study conducted in the Houston metropolitan area, the Omicron variant grew three times faster than the Delta variant in terms of relative frequency, and the Omicron variant was responsible for 98 percent of all new COVID-19 cases diagnosed in the Houston Methodist healthcare system by January 5, 2022 [2]. According to another study conducted in Denmark, Omicron's effective reproduction is 3.19 times greater than Delta's under equal epidemiological conditions [4].

The Omicron variant raises major concerns due to many mutations in the spike protein, which may limit antibody neutralization and increase the risk of reinfection. While there has been a dramatic increase in the number of Omicron cases reported around the world, the efficacy of vaccinations has been questioned until now.

For a variety of reasons, patients on maintenance hemodialysis (MHD) are more susceptible to COVID-19 infection and associated complications [5]. Many hemodialysis patients are elderly and have coexisting morbidities such as cardiovascular disease, diabetes, hypertension, and lung disease, as well as an underlying immune system deficiency [6]. In addition, MHD requires frequent physical presence at healthcare facilities, as well as physical contact during hemodialysis, both of which increase the risk of disease transmission. Patients on long-term dialysis are at increased risk of COVID-19 infection and mortality. Patients who receive dialysis at home have a distinct edge. They do not have to go to the hospital, which decreases social interaction and viral transmission risk.

Different modeling and simulation (M&S) methods and techniques can be used in order to improve the operations and management of hospitals and healthcare services. They can also be used to help in the training of existing staff and new hires. New simulation and visualization technologies, including virtual reality (VR) and digital twins (DTs), could play a critical role in the assessment of situations and in making rapid decisions to prevent further spread of COVID-19, while minimizing the risks associated with direct and field-based observations and analysis of various procedures and policies. The design of a virtual digital equivalent to a physical product

– or DT – was introduced in 2002 by Grieves [7] in connection with product lifecycle management (PLM). Although the application of DTs has gained some maturity in the manufacturing industry, research on the application of DTs in healthcare management is still young [7]. Nevertheless, digital assistance in patient pathways and treatment are now a hallmark and major concern of healthcare system development [8]. The development of DTs in healthcare management is challenging due to the complexity of the interactions and the non-uniform nature of the patient's case. For complex patient-centric engineering projects, the simultaneous use of models and data – e.g., model-based systems engineering (MBSE) – should be considered. Based on this assumption, the contribution of this paper deals with DTs and simulation for better planning and security in healthcare settings. In detail, some perspectives on the interest in the DT approach based on the model of the product service system are outlined, such as having simulation ready in the digital world to anticipate the future while preventing contamination. The relationship between service twins and ground data, and the connection to the decision level, is still open to discussion.

In some circumstances, using a traditional simulation technique is insufficient, necessitating the introduction of a distributed technology. In this study, we provide a Distributed Digital Twin (DDT) that virtually mirrors a hemodialysis unit in a hospital in Toronto, Canada, in order to monitor and assess the spread of the Omicron variant of COVID-19 within the unit. To develop this distributed system, AnyLogic was utilized for the discrete event and agent-based M&S, while Unity was used as a 3D engine to create the virtual reality environment. In order to integrate both of the aforementioned heterogeneous tools, the IEEE international high-level architecture (HLA) standard was applied to address interoperability and distributed simulation challenges. This would allow users to engage with the simulation and explore/review various hemodialysis unit settings and their effects. The rest of this paper is organized as follows. Section 2 offers an overview of recent research studies as well as pertinent existing literature. The DS system architecture, including the simulation models in AnyLogic and Unity, as well as their integration and methodology, are described in Section 3. The hemodialysis case study is also defined in Section 3. Section 4 of the study includes a discussion of simulation findings, and Section 5 offers a summary and conclusion.

II. Literature Review

By the 15th of December 2021, in the presence of the Omicron VOC, daily infections among healthcare workers in South Africa were three times higher than at the Delta VOC peak [9]. According to the same research study, Omicron infected a higher percentage of healthcare workers aged 18 to 30, compared to the Delta VOC, which infected mainly healthcare workers aged 55 and over. Some 91% of healthcare workers who were hospitalized during the Omicron phase required general care, 6% required high care, and 3% required intensive care [9]. During the Delta phase, 89% needed general care, 4% needed high care, and 7% needed intensive care, while during the Beta phase, 43%, 7%, and 16% required general care, high care, and intensive care, respectively. Although one may deduce that the Omicron VOC is less severe than prior versions, the concern is that it spreads roughly three times faster than Delta VOC [10], which is 87 percent faster than Beta, and which, in turn, is 73 percent faster than its preceding variant [11]. The widespread infection from the Omicron VOC poses a serious threat, particularly in hospitals and among healthcare workers. According to a European study, the risk of healthcare system saturation is critical, particularly with the Omicron VOC, and more refined mitigation strategies and techniques that safeguard the most vulnerable people and healthcare systems are urgently needed [12].

The Omicron variant raises substantial concerns about vaccine effectiveness and the increased reinfection risk [13]. The Omicron VOC was revealed to escape antibody neutralization by the RNA vaccine Pfizer BioNTech. In a study conducted in South Africa, scientists discovered a vaccination effectiveness of 70% during the Omicron phase, based on data collected over the period November 15-December 7, 2021. This vaccine effectiveness rate was significantly lower than the rate of 93% calculated in the period September 1-October 31, 2021, when Delta was the prevalent variant [3]. The Omicron VOC has a considerable impact on neutralizing activity against mRNA vaccine response. However, after receiving a booster dose, the vast majority of individuals maintained neutralizing activity against the Omicron variant for at least one month [14]. These data back up the necessity for a booster dose to preserve neutralizing activity against the Omicron variant [15], [16].

For in-center patients on MHD, the requirement for frequent visits to the hemodialysis unit, as well as the unavoidable clustering of patients during dialysis shifts, enhance the risk of viral transmission [17]. Interactions with transportation staff and other passengers on public transit systems may be required when traveling to hemodialysis centers. Furthermore, the MHD unit's everyday activities include a number of patient-patient and patient-caregiver interactions that raise the potential of COVID-19 transmission [18]. This is due to synchronous dialysis schedules, in which patients enter and exit the department at the same time, as well as intimate contact with healthcare personnel who engage with other patients in a similar manner. MHD patients are extremely sensitive to COVID-19 infections and vulnerable to their severe repercussions, according to early findings from Canadian healthcare facilities [18]. According to data collected between March and August 2020 in Ontario, Canada, 187 out of 12,501 dialysis patients were diagnosed with COVID-19 infection. Of the 187 who were infected, 117 (62.6%) were admitted to hospitals, with a 28.3% death rate [19]. According to another study in France between March and May 2020, the mortality rate was 40% for peritoneal dialysis patients [20]. As a result, adequate preventive strategies and procedures must be established in hemodialysis centers in order to protect patients from any infection risk [18], [21]. In some in-center dialysis facilities, outbreaks involving dialysis patients, nursing staff, and physicians have occurred, resulting in clinical staff shortages in an already overwhelmed healthcare system [22]. To our knowledge, there are currently no modeling studies on Omicron VOC dissemination and control in hospital settings, particularly in hemodialysis units where COVID-19 susceptible patients require special attention.

Recent technologies have required the design and development of DS systems that integrate different heterogeneous simulators [23], [24]. Such simulators may be running on different simulation environments and utilizing different modeling methods such as discrete event simulation (DES), agent-based modeling (ABM) and system dynamics [25], [26]. Consequently, DS systems have become more and more complex in terms of both the level of dynamism and the level of heterogeneity within the system. In [24], the authors identify four main levels of heterogeneity which may pose barriers to integration and interoperability: (1) data, (2) middleware, (3) application, and (4) non-functional heterogeneities. In order for a DS solution to be considered fully interoperable, it must overcome barriers at all four levels [28]–[31].

In the 1990s, Defense Advanced Research Projects Agency of the Department of Defense (DoD) in the United States (US) developed the HLA standard over an entire decade resulting in the US DoD 1.3 HLA standard [32]. The primary goal of this standard's development was to address problems with reusability and interoperability amongst diverse heterogeneous systems. Later, in year 2000, it was named HLA IEEE 1516 after being adopted by IEEE. It was improved in 2010, resulting in HLA Evolved. HLA 4 is a new version now under development. This version will encompass new object modeling possibilities, as well as new simulation security-related features [33]. In its current form, HLA is now the most popular standard for DS.

A digital twin (DT) is a digital replica of an object, process or system that can be used for various purposes [34]. In this work on the propagation of a virus inside the hemodialysis unit, it seems necessary to consider an environment to embark the users and to allow a better visualization of the contact situations and thus better understand the problems encountered. Nevertheless, to our knowledge, no DT has yet been developed to study the impact of the transmission of the Omicron variant inside hemodialysis centers.

III. Materials and Methods

A. DS architecture

The integration of AnyLogic and Unity, two powerful but heterogeneous technologies, was made possible through the HLA standard. For both application platforms, an HLA interface layer has been developed in order to enable the communication and data exchange (Figure 1). The purpose of this research is to use Unity3D as an engine that is synced with AnyLogic's process flow, ABM, and DES to have a process/simulation-based VR environment. On the one hand, AnyLogic is a Java-based engine, with models mapped to Java code. On the other hand, C#, JavaScript/UnityScript, and Boo are the scripting languages supported by Unity.

The federated object model (FOM) file, which contains all the details about the objects/attributes, interactions/parameters, and communication between the two federates (AnyLogic and Unity), is attached to both HLA interfaces. With the use of the HLA interface, AnyLogic and Unity can both build the HLA federation. Once one of the two components has established the federation, the other one joins it. AnyLogic and Unity are both referred to as the HLA federates. The publish/subscribe (p/s) mechanism of HLA serves as the foundation for communication between the two components [29]. When one of the federates publishes an object or interaction, the other federate receives a callback if it has subscribed to that object or interaction.

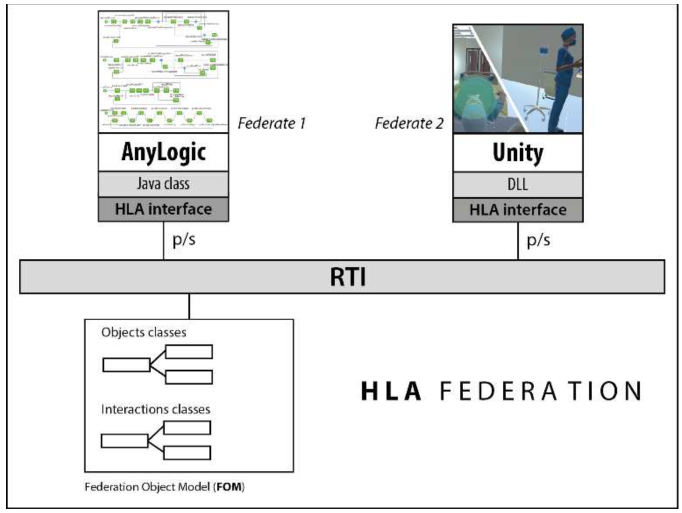

Figure 1 Distributed Digital Twin architecture

B. Case Study

In this study, we model and simulate the dialysis unit of the University Health Network (UHN) which is located at the Toronto General Hospital. The unit operates from Monday to Saturday under three daytime shifts (7:30 AM – 12:30 PM, 1:00 PM – 5:00 PM, and 5:30 PM to 9:00 PM) and one nocturnal shift from 11:00 PM to 6:00 AM. The unit patient capacity is 308. Of these, 278 patients undergo hemodialysis during daytime three to six days a week and 30 at nighttime three times a week. There are a total of 55 dialysis chairs available at the UHN dialysis unit. Staff consists of nephrologists, nephrology fellows, nurses, technicians, pharmacists, dieticians, social workers, and other support personnel.

During a shift, patients are admitted in groups of three or four and in a staggered manner. A cohort is admitted approximately 30 minutes after the one preceding it. A clerk goes into the waiting area and gives each patient a wrist band containing the patient's identification. Patients walk in and weigh themselves. They then walk to their assigned station next to which a nurse is waiting. The latter helps patients getting settled onto the machine, assesses them, and checks their blood pressure. While this is taking place, the clerk admits the next cohort. Meanwhile, patients are lining up in the corridor outside the doorway maintaining a 2 m distance between each other, as per protocol.

After setting up a patient, the nurse calls in the next patient. When patients have completed their dialysis, the nurse will take them off the machine, decannulate the attached arteriovenous (AV) fistula, or central venous catheter, and check their blood pressure in both a seated and a standing position. The entire process of starting and stopping the dialysis takes between 15 and 20 minutes for each patient. The following is to be noted: (1) nurses are assigned to stations (and not to patients) in a random manner on the day of the shift, and (2) patients are assigned to stations in a random manner (although some of them indicate their preference for certain stations over others).

Hemodialysis assistants (HAs) oversee setting up the dialysis machines. The task consists of cleaning and sterilizing the machines according to a protocol, putting dialyzers and tubing onto them, and ensuring all equipment is available at the stations for the nurses and patients to use. HAs perform the task before and between shifts.

The UHN hemodialysis unit has two wings (east and west) operated by 10 different nephrologists available during all shifts. The latter are assisted by a nurse practitioner (NP) during morning and afternoon shifts. Nephrologist fellows conduct rounds in the unit on behalf of the most responsible physician (MRP) who, like the NP, spends between 1 and 2 hours in the dialysis unit, once a week, while a nephrology fellow spends approximately 1 to 2 hours per shift circulating in both wings. NPs or nephrologist fellows leave the unit or wait in their office area when not actively seeing patients.

C. DDT parameters and configuration

Predicting the efficacy of vaccinations and the transmission of Omicron VOC inside the hemodialysis unit requires the collection of a significant amount of data. The first stage consists of gathering information about patients and personnel who were either vaccinated or not. The vaccinated patients or personnel are divided into those who have had one, two or three doses of the vaccine. Splitting the patients by age group is another interesting information that improves model efficacy. Table 1 shows the key parameters used to build the ABM. Some of these parameters are collected from the medical staff of the hemodialysis unit – such as the length of time spent performing each stage of dialysis, the patient's age group, staff/patient walk speed, and others. The likelihood that infection spreads among susceptible agents who are in close contact with an infected agent is determined by a metric called "attack rate".

Table 1 Data and parameters of the Agent-Based Model

Agent	Parameter	Value	Unit
Staff/Patients	Speed	0.16	m/s
Staff	Time spent in the locker room	5-10	minute
Staff	Break time	20-40	minute
Assistant	Required time for setting up station materials	2-4	minute
Assistant	Time spent at the dialysis station	1-2	minute
Nurse	Visiting time at the dialysis station	3-5	minute
Nurse	Time spent to connect/disconnect the patient and the machine	20-40	minute
Physician	Visiting time at the dialysis station	3-5	minute
Patient	Time spent in the screening process	0.5-1.5	minute
Patient	Time spent receiving treatment at the dialysis station	210-270	minute
Patient	Time spent in the lobby before leaving the hospital	4-6	minute
All agents	Omicron attack rate	35.4-50.4	%
All agents	Omicron incubation period	2-4	days
78% of the agents	Omicron infectiousness	3-6	days PSO
16% of the agents	Omicron infectiousness	7-9	days PSO
5% of the agents	Omicron infectiousness	10-13	days PSO
1% of the agents	Omicron infectiousness	14	days PSO
10.7% of the patients	Age	18-44	years old
33.4% of the patients	Age	45-64	years old
25.6% of the patients	Age	65-74	years old
29.7% of the patients	Age	> 74	years old

According to seven experiments presented in a recent research [35], the attack rate employed in the ABM setup is between 35.4% and 50.4%. The time between meeting an infected agent and the onset of the first symptoms is represented by an incubation period, a metric used in the ABM model. The incubation period used in this study is two to four days based on recent research [36]–[39]. The Omicron variant's period of infectiousness peaks at three to six days post symptom-onset (PSO). At 7 to 9 days PSO, up to 16% of infected people may still be contagious, compared to 5% at 10 to 13 days PSO and 1% at 14 days PSO [10], [40].

One of the important aspects that affects COVID-19 vaccine efficacy is the weeks from vaccination parameter. As seen in Figure 2, the vaccination efficacy diminishes weeks following the second injection [41]. The vaccine's efficacy peaks at 90-95 percent during the first three weeks, then drops to about 25% after 90 weeks following the second dose immunization.

Another key factor that influences vaccination efficacy is the type of vaccine used. 98% of the patients and staff have been vaccinated with Pfizer-BioNTech Cominaty or Moderna Spikevax. As a result, the efficacy of Pfizer and Moderna on Omicron VOC was of particular interest in the developed ABM. In terms of vaccine efficacy, according to the Institute for Health Metrics and Evaluation, Pfizer/BioNTech and Moderna are quite similar, with both vaccines preventing severe disease caused by the Omicron variant by 72-73% and infection by 44-48% [41]. According to recent studies, the booster dose of Pfizer/BioNTech increases the vaccine effectiveness up to 90-93% against COVID-19 infection [3], [42].

All the agents that exist in the DDT are linked to a susceptible, exposed, infected, recovered (SEIR) model (Figure 3). In this study, we use a redesigned SEIR model that has undergone various changes, including the addition of symptomatic and asymptomatic states that in turn comprise new states. These changes may be discovered in earlier research work [43].

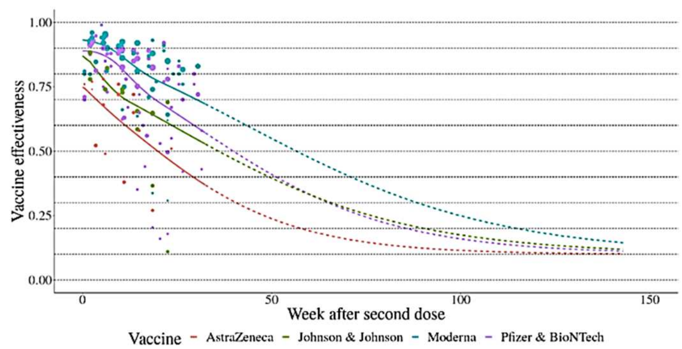

Figure 2 Vaccine effectiveness per week after second dose [41]

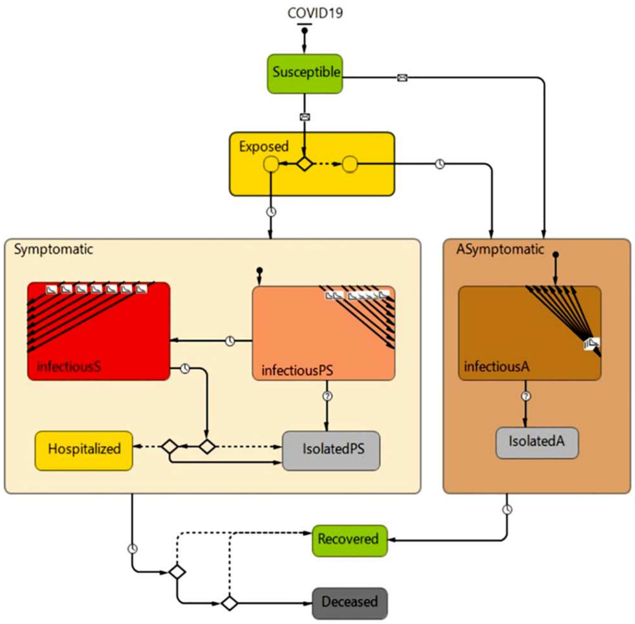

Figure 3 Redesigned SEIR model

IV. Results and Discussion

We employ two modeling phases to create the hemodialysis agent-based simulation model. The first phase consists of developing a contact matrix that can be used for comprehensive disease modeling and for the analysis of various mitigation techniques. Based on previously defined methodology, a contact matrix keeps track of, and summarizes, agent interactions [18]. The highest risk of viral transmission is between the HAs, as seen in Figure 4. Additionally, there is a considerable risk that nurses and HAs spread the virus within the unit. This contact matrix was crucial for the medical staff's efforts to determine the source of viral transmission and limit its spread within the facility, especially with the Omicron variant, which has a roughly three-fold higher likelihood of transmission than the Delta VOC [10]. This created contact matrix is utilized for the second stage of M&S, which is defined in the paragraph that follows.

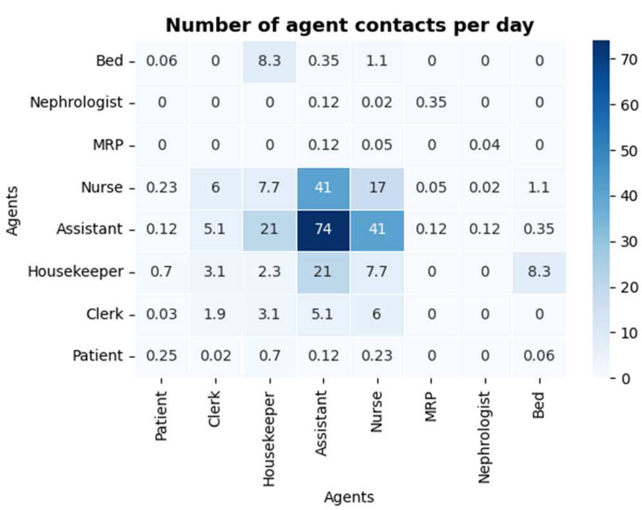

Figure 4 Generated contact matrix

A primary goal of this study has been to extend previously published work [18], [44] by adding vaccination settings and parameters as well as Omicron variant parameters. Figure 5 compares our simulated outcomes of the propagation of the original SARS-CoV-2 virus with the spread of the Omicron variant inside the hemodialysis unit. One can see that the Omicron VOC spreads more quickly to, but has less severe effects on, hemodialysis patients than the original COVID-19 virus, with a death rate that has nearly dropped to 4% as opposed to the original virus' death rate of close to 20%. The fact that there was no vaccination available during the original SARS-CoV-2 (the upper part of Figure 5), however, may also have contributed to the higher death rate among hemodialysis patients.

Until now, the developed DDT performs an offline simulation by replaying the situation or anticipating possible situations, it embeds users in a role-playing game but it does not process the data in real time.

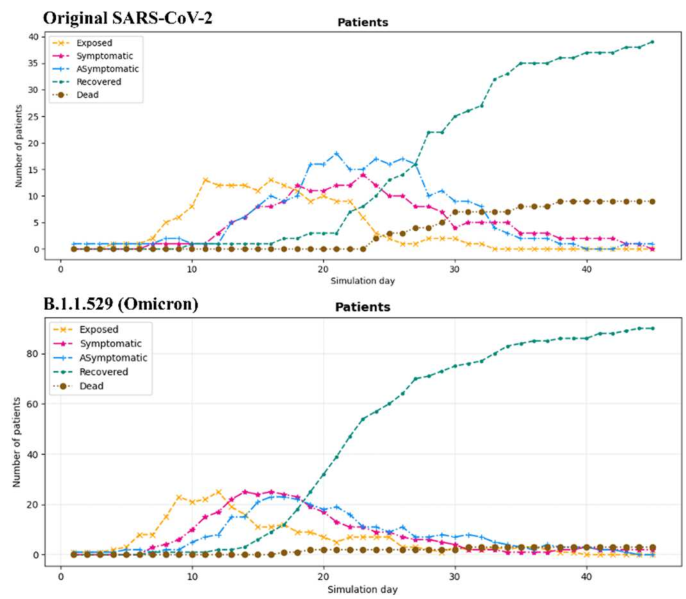

Figure 5 Original SARS-CoV-2 vs Omicron variant spread inside the hemodialysis unit

V. Conclusion

In this paper, we present a DDT system designed for the hemodialysis unit of a hospital in Toronto, Canada, to provide the medical staff with predictive analytics and visual models that aid them in identifying solutions to enhance the efficacy, safety, and quality in highly contagious disease environments.

The IEEE HLA distributed simulation standard has been used to resolve the interoperability concerns between heterogeneous components. A discrete event simulator has been integrated with a virtual reality environment based on HLA in order to provide an immersive experience to the medical staff in addition to platform showing the number of exposed, symptomatic, asymptomatic, recovered, and dead agents (patients, nurses, physicians, clerks, and others) during the simulation run. A contact matrix has also been generated to identify the agents that raise the risk of viral transmission inside the unit.

One of the study's limitations is that the models reported here do not yet consider portable equipment (e.g., portable X-ray machines, mobile dialysis machines, temporary beds). One future venue to explore may be the use of an SEIR network to model the problem and the application of artificial intelligence techniques to predict the spread of the virus. This can be done through the use of some neural network architectures or the design of heuristics that learn the weights on the network edges.

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