BioMedInformatics

Review

A Comprehensive Survey of Digital Twins in Healthcare in the Era of Metaverse

Muhammad Turab [1] and Sonain Jamil [1,2,*]

[1] Department of Computer Science, Norwegian University of Science and Technology (NTNU) in Gjøvik, Postboks 191, NO-2802 Gjøvik, Norway; 18cs45@students.muet.edu.pk
[2] Department of Electronics Engineering, Sejong University, Seoul 05006, Republic of Korea
* Correspondence: sonainjamil@sju.ac.kr

Abstract: Digital twins (DTs) are becoming increasingly popular in various industries, and their potential for healthcare in the metaverse continues to attract attention. The metaverse is a virtual world where individuals interact with digital replicas of themselves and the environment. This paper focuses on personalized and precise medicine and examines the current application of DTs in healthcare within the metaverse. Healthcare practitioners may use immersive virtual worlds to replicate medical scenarios, improve teaching experiences, and provide personalized care to patients. However, the integration of DTs in the metaverse poses technical, regulatory, and ethical challenges that need to be addressed, including data privacy, standards, and accessibility. Through this examination, we aim to provide insights into the transformative potential of DTs in healthcare within the metaverse and encourage further research and development in this exciting domain.

Keywords: digital twin; healthcare; metaverse; machine learning; artificial intelligence

check for updates

Citation: Turab, T.; Jamil, S. A Comprehensive Survey of Digital Twins in Healthcare in the Era of Metaverse. *Biomedinformatics* **2023**, *3*, 563–584. https://doi.org/10.3390/biomedinformatics3030039

Academic Editors: Alexandre G. De Brevern and Pan Zheng

Received: 13 June 2023
Revised: 24 June 2023
Accepted: 18 July 2023
Published: 21 July 2023

1. Introduction

Digital twins (DTs) play a crucial role in the ongoing Industry 4.0 revolution, leveraging advanced data analytics [1,2] and the connectivity of Internet of Things (IoT) to drive transformative changes across industries [3]. The proliferation of IoT technology has substantially increased data availability across sectors, such as manufacturing [4], healthcare [5], and smart cities [6]. The abundance of data in various sectors like manufacturing and smart cities, coupled with robust data analytics capabilities, offers significant potential for applications, such as predictive maintenance, fault detection, and advancements in manufacturing processes and smart city infrastructure [7]. Furthermore, DTs enable anomaly detection in fault detection systems [8–10], patient care processes, and the efficient management of traffic in smart cities [11,12]. These applications demonstrate the significant value of DTs in optimizing processes [13,14] and enhancing operational efficiency across multiple domains [15]. The DT environment enables a smooth and seamless exchange of information between the physical and virtual realms, empowering organizations to derive valuable insights and make informed, data-driven decisions. This integration fosters a deeper understanding of complex systems, improves operational efficiency, and supports optimization efforts across various domains. By harnessing the potential of DTs, industries can unlock new opportunities for process improvement, predictive maintenance, and resource optimization, leading to enhanced productivity, cost savings, and overall business success.

The metaverse concept, first introduced by Neal Stephenson in his renowned science fiction novel *Snow Crash*, has captured considerable attention and transformed into the idea of a computer-generated universe that incorporates real-world economic systems. It encompasses immersive shared spaces that integrate elements from the physical, human, and digital realms [16]. The metaverse is gradually transitioning from a conceptual idea to a tangible reality as various technologies continue to advance. These technologies include wearable sensors [17], non-fungible tokens (NFTs) [18], augmented reality (AR) [19–21], 5G connectivity [16,22–24], DTs [3], blockchain [25–27], virtual reality (VR) [28,29], brain–computer interfaces [30], and artificial intelligence (AI) [31]. This progression has sparked global interest, leading major technology firms like "Meta" (formerly Facebook), Microsoft, Tencent, and NVIDIA to invest in its development [32]. The evolution of the metaverse [33] can be understood through three distinct phases: DTs [34], digital natives [35,36], and surreality. The initial phase focuses on creating highly detailed DT representations of humans and objects within virtual environments, effectively replicating physical reality in a vivid digital form. Subsequently, in the phase of digital twins, represented by avatars, active contribution to content creation and innovation occurs within the metaverse, erasing the traditional boundaries between the actual and virtual worlds. Finally, in the ultimate phase, the metaverse transforms into a persistent and self-sustaining surreality world, seamlessly integrating the physical and virtual realms and expanding beyond the physical world's limitations [37].

The metaverse, a conceptual technology, is digitalizing numerous facets of society, industries, and everyday life, presenting significant potential for advancing various services [38]. By merging virtual and physical assets within cyberspace, the metaverse empowers individuals to embody themselves through avatars [39]. Moreover, the integration of techniques and technologies, such as AI [40,41], machine learning (ML) [42–46], deep learning (DL) [47], DTs, IoT [48,49], edge computing [50,51], and cloud computing [52], further augments this transformative technology [53,54].

While the metaverse has witnessed notable advancements in platforms such as social media [55], diagnosis [56–59], and treatment planning [60], its utilization in the medical domain, specifically in cancer diagnosis, treatment, and examination, necessitates additional enterprise, deliberation, and research. Through the fusion of virtual and physical realms, the metaverse encompasses extended reality, mixed reality, AI, high-speed internet, blockchain, DTs, and augmented and virtual reality. This convergence holds immense potential to revolutionize healthcare and significantly impact overall health and clinical practice [61]. The immersive and interactive attributes of the metaverse present healthcare professionals with the opportunity to engage with patients in a personalized and captivating manner, ultimately resulting in enhanced care and patient satisfaction [62]. Furthermore, the metaverse enables seamless information and resource sharing, promoting more efficient and effective healthcare treatment. As a result, the metaverse has the potential to bring about transformative and substantial improvements to the healthcare industry.

In the past, healthcare has primarily relied on in-person interactions between patients and healthcare providers for crucial aspects, such as surgery, treatment, and diagnosis. While telehealth has introduced some changes by enabling remote consultations, exciting technological advancements such as the metaverse hold the promise to revolutionize the healthcare industry. The metaverse presents the potential for transformative changes in healthcare by offering virtual health services, supporting mental health, managing reality, and enabling virtual management [63]. These innovations have the capacity to enhance accessibility, convenience, and the overall patient experience, bringing healthcare closer to individuals and ensuring that they receive the necessary care, regardless of physical distance or limitations.

This paper aims to provide a comprehensive overview of the utilization of DTs in healthcare during the metaverse era. The survey makes the following contributions:

- It offers a comprehensive overview of the application of DTs in healthcare within the metaverse era.
- It provides an in-depth analysis of the current research landscape, including state-of-the-art models, approaches, datasets, and platforms that are relevant to the intersection of DTs and the metaverse.
- It identifies and explores the open research difficulties and challenges faced by academics and practitioners in these dynamic fields.

- It shares valuable perspectives and insights derived from extensive research on the subject matter.
- A valuable resource is created for researchers, practitioners, and stakeholders interested in exploring potential DT applications in healthcare and the metaverse.

The rest of the paper is organized as shown in Figure 1.

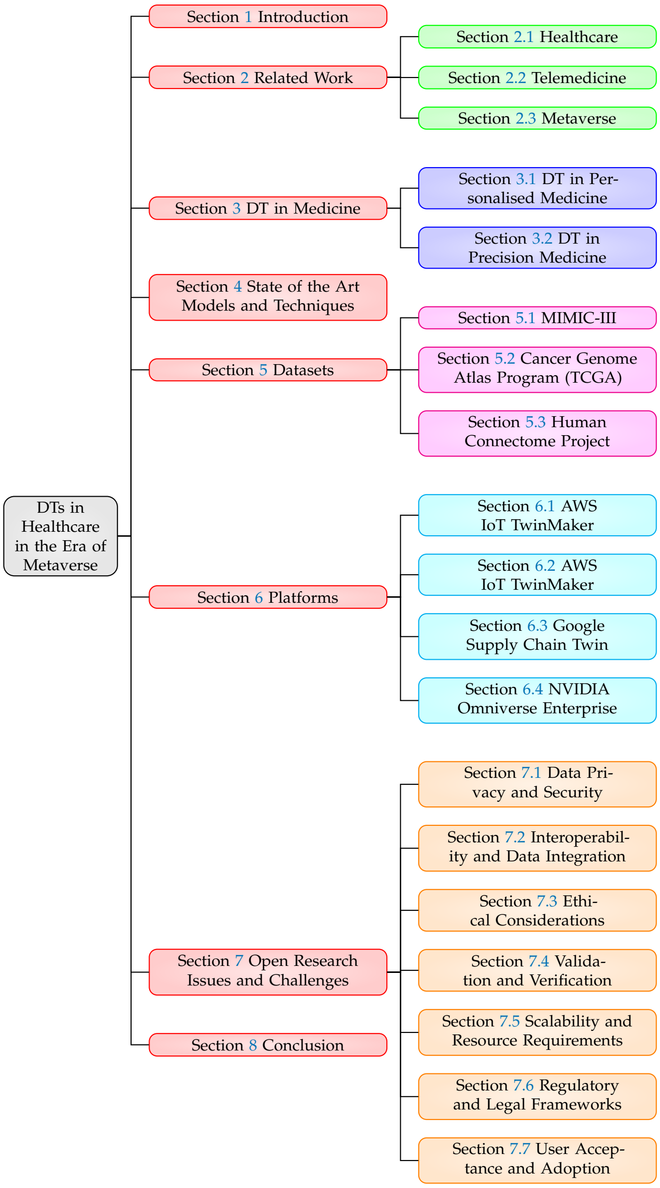

Figure 1. Organization of the survey.

2. Related Work

Numerous survey papers have investigated different aspects of DTs and the metaverse in the existing literature. However, it is worth noting that these surveys have yet to specifically address the application of DT in healthcare during the era of the metaverse. The specific intersection of DT, healthcare, and the metaverse still needs to be explored.

In their survey on DTs in the manufacturing industry [64], the authors explored important aspects of DT. They conducted interviews with two industry experts, and their findings highlighted the crucial role of digital modeling in creating DTs. Modeling allowed managers to accurately understand and analyze various factors within a factory, enabling them to make informed decisions. In this survey [65], the authors examined different techniques used in the construction of DTs for smart manufacturing and energy management. The findings revealed that no universally superior method exists for developing DTs. Instead, the optimal approach for leveraging the metaverse varies depending on the specific demands and needs of each individual application.

2.1. Healthcare

In recent studies, there has been emerging research on the utilization of DTs in healthcare [66]. Numerous practical implementations have been documented, covering a diverse range of areas. For example, DT has been successfully applied to promote well-being in smart cities [67], enhance fitness-related activities [68], simulate the spread of viral infections [69], facilitate remote surgical procedures [70], and improve healthcare management [66].

DT technology holds immense potential for improving healthcare management by leveraging AI, data science, and deep learning approaches. These advancements have the capacity to revolutionize the delivery of healthcare services, offering personalized and expedited care to individuals. The application of such technologies has already resulted in the development of innovative solutions, including vital sign monitoring apps, brain–computer interfaces, the detection of liver and cardiac diseases, and food-monitoring apps. In a recent study [66], a conceptual model known as the human digital twin (HDT) was proposed to address key security and social ethics challenges. The HDT aims to replicate an individual's physical body in a cyber–physical space by leveraging data from mobile phones, wearable sensors, and medical records. This model guarantees that its material is constantly updated via online services in order to retain up-to-date information [66]. The obtained data are analyzed with various technologies to produce pertinent assessments of the patient's health status. Furthermore, the HDT considers aspects like relationships with other people and environmental effects.

In their survey paper [71], the authors delve into the diverse applications of DTs across several industries, including manufacturing, construction, automotive, aerospace, and emerging applications in healthcare, specifically precision medicine. The authors emphasize the potential of DT to revolutionize connected care and transform the management of health, lifestyle, chronic diseases, and wellness. However, despite this potential, technical, regulatory, and ethical challenges impede consensus on the full extent of the revolutionary impact of DT in healthcare over the next decade. The paper discusses the technologies and applications of DT in healthcare. The technologies and applications emphasized in the article are shown in Figure 2. The paper comprehensively reviews current DT applications in healthcare, covering areas such as precision medicine, hospital operations, and clinical trial design. It identifies opportunities and challenges to the widespread adoption of DT in the healthcare domain. Additionally, the authors discuss current findings, opportunities, and challenges, and give recommendations to help with the further development of DT applications in healthcare.

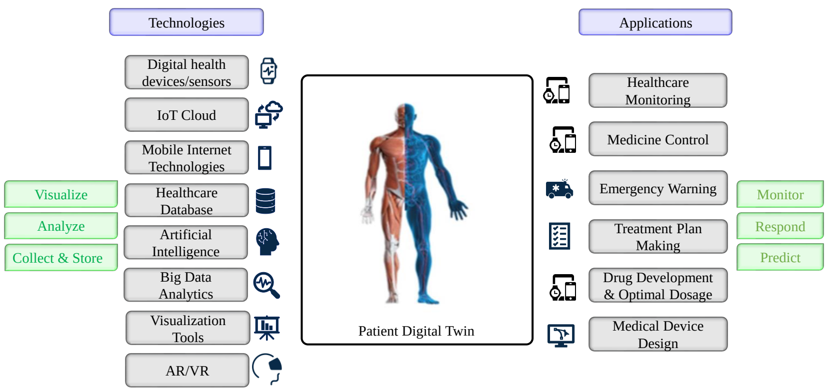

Figure 2. Technologies and applications of DT as illustrated in [71].

This study [72] explores the application of DTs in healthcare, specifically focusing on cancer care, with an emphasis on endometrial cancer. The study proposes a DT model integrated with AI to enhance clinical decision making and provide more patient-centric and individualized care. It investigates the role of AI techniques in developing DTs for cancer care and discusses challenges and facilitators from healthcare and technology perspectives.

2.2. Telemedicine

Telemedicine allows remote medical consultations and has several benefits, especially for patients living in disadvantaged and rural regions. Patients can remotely consult doctors and experts using the power of the metaverse, eliminating the need for travel and lowering healthcare expenses.

Telemedicine offers patients advantages, including convenience, effectiveness, and price. This substitute for conventional in-person consultations cuts down on appointment wait times, simplifies the recovery process, and is reasonably priced. Additionally, it promotes continuity of care by allowing patients to continue to receive assistance and direction from medical professionals, which results in improved treatment outcomes. Despite its advantages, telemedicine has a few challenges. These challenges include technological limitations, quality of care, low patient–provider communication, security and privacy concerns, and billing issues. Patients need adequate internet connections, computers, smartphones, and other devices to access telemedicine services fully. Some complex cases may not be possible with telemedicine. Limited connectivity and concerns about possible cyberattacks also threaten patient data privacy and security [73].

2.3. Metaverse

The metaverse has several applications in healthcare [74], as shown in Figure 3, and several surveys have explored this. Some of the enabling technologies of the metaverse for healthcare are shown in Figure 4. Enabling technologies of the metaverse include the following technologies:

- **Computer vision (CV)** is used for in-house disease diagnosis and medical imaging.
- **IoT** is used for surgery assistance, alerts, and providing vital information.
- **Human computer interface (HCI)** is used for remote assistance and better medical services.
- **AI** is used for obtaining valuable insights and making better decisions.
- **Quantum computing** is used in quantum resistance security for medical applications and provides improved computational speed.
- **Blockchain** is used for the security and privacy of medical data.
- **Big data** provides enhanced healthcare data management and better healthcare data visualization.
- **Extended reality (XR)** is used for virtual training, assistance and consultation.
- **DT** helps in staffing, care models, and operational strategies.
- **3D Modeling** helps in interactive anatomical representation.
- **5G and beyond** provides a high-quality immersive experience, low latency, and high-speed communication.
- **Edge computing** proves to be effective in efficient data transfer and better analytics.

Another technology that is highly used in the metaverse is virtual reality (VR). VR is a three-dimensional computer-generated world that is immersive and interactive and allows for interaction through various senses, including touch and position. Nowadays, thanks to technical advancements, VR technology has extended to various fields and industries, including surgical training, sports training, language learning, and even as a therapy to overcome stage fright. Depending on their function and the technology employed, VR systems can vary greatly from one to the next, but they often fall into one of the following three categories:

- **Non-immersive:** Typically, a 3D simulated environment that can be accessed through a computer screen is what this kind of VR means. Depending on the software, the surroundings could also produce sound. Using a keyboard, mouse, or other device, the user can influence the virtual world to some extent, but the environment does not communicate with the user directly. Non-immersive VR is exemplified by video games and websites that let users customize the look of a room.
- **Semi-immersive:** Through a computer screen, a pair of glasses, or a headset, this kind of VR provides a limited virtual experience. It does not involve physical movement as full immersion does and instead concentrates on the visual 3D part of virtual reality. The flight simulator, used by airlines and the military to train its pilots, is a typical example of semi-immersive VR.
- **Fully immersive:** The user is entirely submerged in the virtual 3D environment thanks to this form of VR, which offers the highest quality of virtual reality. It includes hearing, seeing, and occasionally touching. Even some attempts with the addition of scent have been conducted. Users are able to completely engage with their surroundings when they are wearing specialized gear like helmets, goggles, or gloves. To give consumers the feeling of movement across the 3D world, the environment may also include items like treadmills or stationary bicycles. Although fully immersive VR technology is still in its infancy, it has already had a significant impact on the gaming and, to a lesser extent, the healthcare industries, and it is sparking a lot of interest across a variety of other industries.

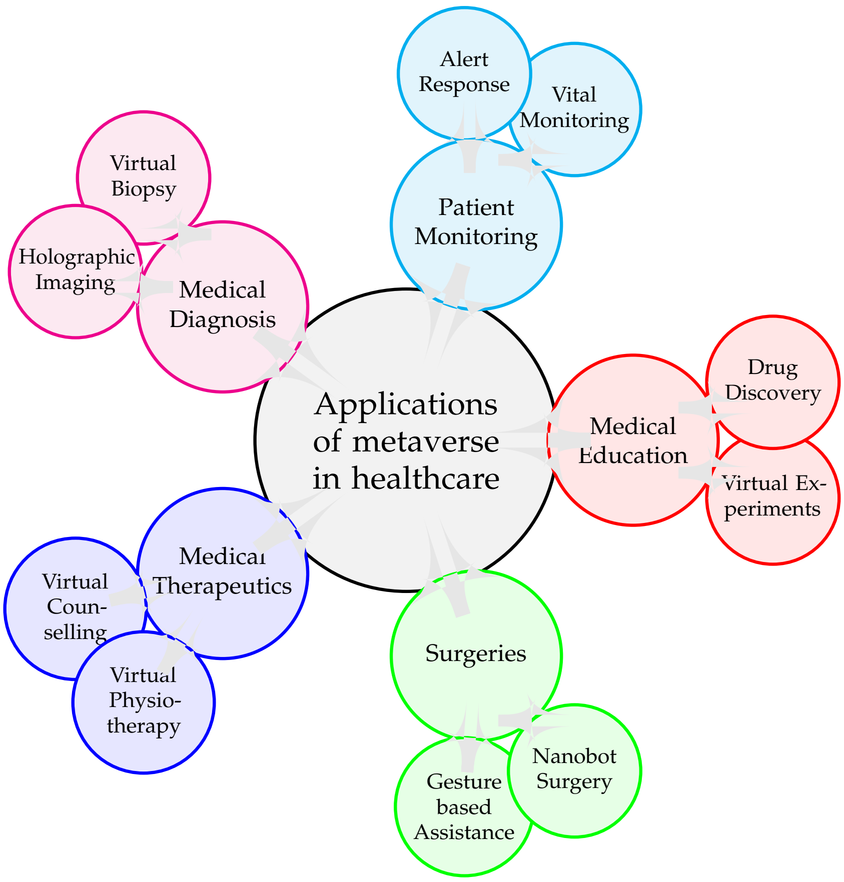

Figure 3. Application of metaverse in healthcare.

In this study [65], a comprehensive survey is presented, focusing on the fundamentals, privacy, and security aspects of the emerging concept of the metaverse. The authors emphasize the goal of building a virtual shared space that is immersive and highly spatiotemporal for human interaction. They also recognize the potential privacy invasions and security breaches that may impede the widespread adoption of the metaverse, along with addressing the fundamental challenges related to scalability and interoperability. The paper explores a distributed metaverse architecture, delves into security and privacy threats, reviews existing countermeasures, and outlines future research directions for developing metaverse systems. The continuous end-to-end metaverse experiences are considered crucial, and the authors likely discuss approaches or measures to ensure the seamless nature of such experiences.

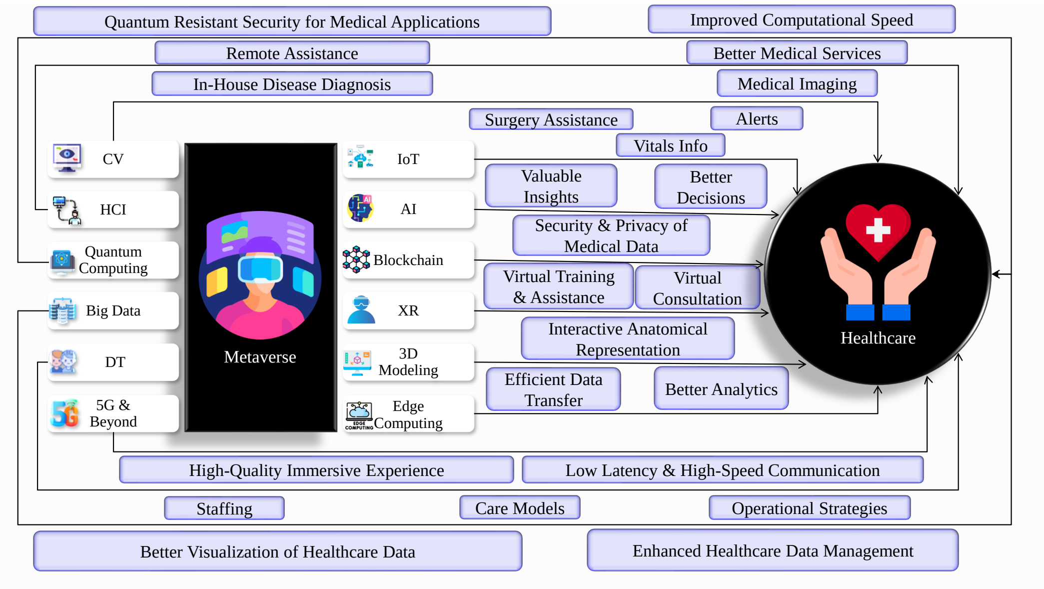

Figure 4. Enabling technologies of the metaverse in healthcare. The concept of illustration is inspired by [74].

In this study [34], the authors investigate the crucial factors involved in creating metaverse services and propose a framework that integrates DTs, 6G communication networks, blockchain, and AI. They aim to ensure continuous end-to-end metaverse experiences. The study also outlines the prerequisites for a comprehensive DT-enabled metaverse architecture and provides insights into potential future advancements in this emerging domain. Similarly, in this study [75], the authors initially discuss the definitions, applications, and challenges of both DT and the metaverse. They then propose a three-layer architecture that incorporates a user interface to bridge the gap between the real world and the metaverse. Additionally, the study addresses privacy and security issues that arise when utilizing DT in the metaverse, suggests potential solutions, and explores future research directions. These studies contribute to the understanding of integrating DT with the metaverse and shed light on the architecture, privacy concerns, security considerations, and potential advancements in this field. In [76], the authors explore the utilization of DTs in the construction of the metaverse, which is a virtual digital space that reshapes the physical world. Their focus lies in integrating tangible objects and social relations within the metaverse, including interpersonal connections and ethical considerations. The authors introduce principles such as the small-world phenomenon, broken windows theory, survivor bias, and herd behavior to guide the development of a DT model for social relations. The aim of the review is to provide insights into the mapping of real-world objects to the metaverse and to contribute to the understanding of how DT influences social dynamics within this virtual realm. The summary of the existing surveys is presented in Table 1.

Table 1. Summary of the available surveys on DT, healthcare, and the metaverse.

Survey	Year	Scope			Contributions and Limitations
		DT	Healthcare	Metaverse	
[16]	2022	✗	✗	✓	• Countermeasures to overcome the challenges. • A novel distributed metaverse architecture. • Ternary-world interactions. • Exploration of the state-of-the-art approaches.
[71]	2022	✓	✓	✗	• Applications of DTs in healthcare. • Exploration of precision medicine, clinical trial design, and hospital operations using DTs. • Identification of opportunities and challenges in the adoption of DTs in healthcare.
[72]	2023	✓	✓	✗	• Endometrial cancer case study with AI-based DT model. • The role of AI in developing cancer care DTs and identifying barriers and facilitators from healthcare and technology perspectives.
[34]	2022	✓	✗	✓	• Key strategies for establishing metaverse services. • Framework for integrating DT, 6G communication networks, blockchain, and AI. • Demonstration of framework to solve issues in metaverse services.
[57]	2023	✗	✓	✓	• The development of a method for creating digital representations of cancer. • Explanation of cancer DTs for simulating diagnosis and development. • Description of the proposed cancer DT with ML techniques and algorithms.
[77]	2022	✓	✗	✗	• Comprehensive view of DT in relevant domains and applications in engineering and beyond. • Focus on understanding the challenges and limits of DT implementation.
[78]	2022	P	✓	✓	• Explores metaverse's impact on healthcare industry in seven areas: telemedicine, clinical care, education, mental health, physical fitness, veterinary care, and pharmaceuticals. • Examines current metaverse use and technical challenges for reliable healthcare systems. • Highlights potential benefits and addresses challenges for widespread metaverse integration in healthcare.
[74]	2023	P	✓	✓	• Comprehensive review of metaverse in healthcare, including state-of-the-art, enabling technologies, applications, and projects. • Identifies challenges and suggests future research directions for metaverse in healthcare.
[79]	2022	✓	✓	✗	• Promotes a better understanding of DT. • Clarify some common misconceptions, and review the current trajectory of DT applications in healthcare.
[80]	2020	✓	✓	✗	• Explore how DT can achieve precision healthcare for patients and systems. • The role of DT, frameworks, benefits, and challenges are also discussed.
Our survey	2023	✓	✓	✓	• Applications of DT in healthcare. • Application of DT in healthcare with respect to the metaverse. • State-of-the-art techniques and methods. • New outlook to the open research gaps.

Note: ✓— fully explained; P—partially explained; ✗—not explained.

3. DT in Medicine

DT has immensely evolved the medical field as it found its utilization in the diagnosis and treatment of diseases [81]. Table 2 presents state-of-the-art articles summarizing the DTs in medicine, including DTs of hospitals, heart, patients, etc.

Table 2. Summary of the articles presenting DT in the medical field.

Ref.	Year	Name of DT	Scope
[82]	2019	HospiT'Win	DT of hospital
[83]	2019	Cardio Twin	DT of human heart
[84]	2021	–	DT of the vaccination centers of COVID-19
[79]	2022	–	Exploration of the different DT in healthcare
[85]	2022	–	Exploration of different for cardiovascular diseases
[86]	2022	–	Exploration of different human DT for personalized healthcare
[87]	2023	–	Exploration of the different DT in healthcare

We also summarized the types of DT as discussed in [88] in Table 3. The applications of DT in medicine can be further categorized in terms of personalized medicine and precision medicine. Based on this, the organization of Section 3 is shown in Figure 5.

Table 3. Summary of the DT types in healthcare.

Research	DT Types	Description
[56,89–93]	Entire body	An interactive digital model of the entire human body constructed using a variety of noninvasive clinical sensors and self-reported data, such as pain or symptom reports.
[94–96]	Body system	Represents all components of the 11 basic organ systems, which include the integumentary, skeletal, muscular, lymphatic, respiratory, digestive, nervous, endocrine, cardiovascular, urinary, and reproductive systems. These systems control all fundamental functions of the body.
[97–99]	Organ	DTs of human organs are utilized for in silico testing and/or to develop patient-specific substance or surgical techniques.
[99,100]	Cellular	Human cell digital twins can be utilized to simulate cell responses to potential medication candidates.
[101,102]	Molecular	ML may be used to simulate molecular processes, including the sequencing of the human genome.
[103]	Disease	The immune system's DT can be employed to treat a variety of diseases.

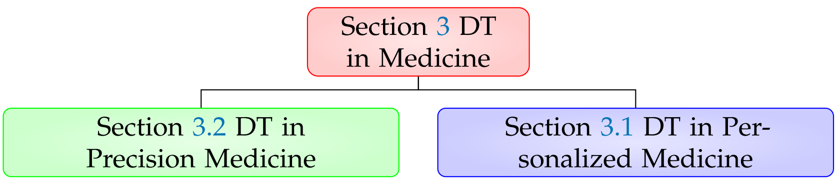

Figure 5. Organization of Section 3.

3.1. DT in Personalized Medicine

Over the past few years, the Internet of Things (IoT) has played a vital role in the field of healthcare [104]. It has revolutionized data collection by allowing instant monitoring through interconnected sensors in medical facilities and various health and environmental conditions. Additionally, IoT has facilitated seamless communication between various devices, equipment, and individuals. This has led to the availability of crucial data through electronic medical records, remote monitoring, diagnostic processes, and patient-generated reports.

Parallel to the advancements in IoT, other technologies, such as artificial intelligence (including machine learning) and cloud computing, have emerged as vital tools in healthcare. Artificial intelligence offers sophisticated data analysis capabilities, while cloud computing provides on-demand access to powerful computational resources. These technologies are instrumental in processing massive amounts of IoT data and enabling real-time analysis and knowledge discovery. Integrating these technologies yields synergistic effects, enabling timely and valuable insights for medical professionals and individual patients. Consequently, they empower informed decision making and proactive healthcare approaches. Moreover, these technologies hold the potential to transform healthcare by prioritizing precision and preventive care. However, integrating DTs further enhances this vision, completing the comprehensive picture of high-quality care.

In [105], the authors put forth a fascinating concept called "virtual twins" or "guardian angels" to revolutionize personalized care and disease prevention in Europe. Their idea involves creating digital models that mimic the biology of European patients and their health conditions. These models use data from various domains, such as clinical records, imaging, and sensor data. With advancements in computing resources and big data technologies, developing these personalized digital models becomes increasingly feasible. Physicians can then use these models to simulate and test different treatments and measures before implementing them on real patients. This approach holds tremendous potential for improving the quality of life for European citizens while reducing healthcare costs.

In addition to the overarching vision of personalized care, some studies have focused on utilizing DTs to assist in understanding and managing specific medical conditions. For example, a case study by researchers [106] explores the concept of a "mirror world" for trauma management. This virtual environment captures the patient's condition and considers the contextual information surrounding the patient, such as the hospital environment, physicians, and trauma team. By incorporating cognitive, social, and temporal augmentations, the researchers aim to enhance the trauma team's decision-making process and support their DT counterparts.

Another study [107] demonstrates the application of DTs in orthodontic treatment for Korean adult females. By analyzing facial scans and three-dimensional (3D) imaging data, specifically cone-beam computed tomography (CBCT), the researchers develop individualized 3D DTs for each patient. These DTs allow for more precise assessments of the "sagittal relationship" between the maxillary central incisors and the forehead, taking into account the facial structure variations observed in Korean and Caucasian patients.

In the field of multiple sclerosis management, there has been growing interest in leveraging DTs [108,109]. Multiple sclerosis is a complex and diverse disease that often leads to neurological disabilities in young adults. With the vast amount of collected data, data-driven approaches utilizing DTs offer valuable opportunities. Creating diverse genomic prototypes of patients as DTs can help evaluate the effects of various intervention strategies and therapies. Additionally, by incorporating external factors like environmental influences, treatment side effects, and disease management costs, the DTs can predict disease progression and treatment outcomes.

Precision cardiology is another significant area of research exploring the potential of cardiac DTs (CDT) [110]. The cardiovascular system is a vital component of the human body, and developing a twin model for it aims to enhance our understanding of its anatomical, mechanistic, and functional aspects. By combining this understanding with advanced analytical models built around relevant data, researchers aspire to transition from mere descriptions to accurate predictions of cardiac conditions. Both industry and academia have shown great interest in this field. In fact, a commercial implementation of DT technology called "Living Heart" was introduced in 2015. This software transformed two-dimensional (2D) scans into comprehensive models of the heart, allowing users to interact with and manipulate the virtual heart model. Recent research has also focused on automating the generation of CDTs, prioritizing the fidelity of the replicated model and computational efficiency [98].

The biopharmaceutical industry is also delving into the realm of DTs, exploring their potential in diverse applications, including drug discovery and development [99,100]. An intriguing example is provided by Subramanian, who discusses the creation of a DT specifically for the liver. This virtual model integrates a wealth of knowledge and understanding regarding various liver functions, diseases, and the effects of drugs. Achieved through a mathematical framework of ordinary differential equations, this DT accurately replicates normal liver functioning and allows for simulations of disease progression and the impact of different drug treatments. Furthermore, by connecting the liver twin with experimental measurements, researchers have gained valuable insights into drug-induced liver injury [111].

3.2. DT in Precision Medicine

DT holds significant importance in advancing the field of precision medicine. Precision medicine seeks to improve the efficiency and effectiveness of healthcare systems by departing from the current model of standardized treatments for all individuals. Instead, it emphasizes acknowledging and embracing the distinctive variations and characteristics that exist among patients [110]. Precision medicine places its emphasis on utilizing advanced diagnostic tools and therapies that are specifically customized to meet the unique needs of each patient. These personalized treatments consider numerous factors, including the patient's genetic composition, biomarkers, physical characteristics, and even psychological and social circumstances. The main aim is to ensure that patients receive the most optimal medications precisely when they are most needed, maximizing their effectiveness [112].

However, the healthcare systems we have today often struggle to provide personalized care for diseases that require multiple stages of diagnosis and treatment. This challenge becomes particularly evident when we consider diseases such as cancer, where there is a wide variation in how the disease presents and responds to therapy [113]. One of the major problems in precision medicine is the varying responses among patients with the same diagnosis when they undergo identical treatments. This variability can be attributed to the intricate nature of the condition, where interactions among thousands of genes can differ among individuals sharing the same illness. Consequently, it becomes essential to identify multiple disease subtypes within a single diagnostic category. However, the present healthcare system relies on limited biomarkers with restricted sensitivity or specificity, creating a gap between disease complexity and diagnostic tools [114,115].

To overcome these problems, DTs could potentially offer a solution. DTs involve creating a comprehensive model of an individual that incorporates their structural, physical, biological, and historical attributes. This model can then be compared to vast amounts of data from other individuals, enabling the identification of significant genetic characteristics. Consequently, DTs can facilitate disease prediction by analyzing an individual's personal history alongside contextual factors like location, time, and activity [110,112]. Moreover, DTs can simulate the potential impact of various treatments on these patients, thereby providing valuable decision support to physicians and other healthcare professionals, including hospital pharmacists. By leveraging DTs, healthcare practitioners can make more informed decisions regarding treatment options based on individualized patient models and simulations.

The study [116] focuses on addressing the increasing demand for personalized medicine in critical diseases like multiple sclerosis (MS) and specific cases such as trauma or elderly management. Timely and precise intervention is vital in such situations. Although the implementation of DTs in these areas is not yet fully established, the researchers propose a reference framework for future application. Their framework, known as CloudDTH (cloud healthcare system based on DT healthcare), specifically targets healthcare management for elderly patients. By utilizing DTs within a cloud-based healthcare system, the researchers aim to enhance the quality of care and support provided to elderly individuals. The study presents the application scenario of CloudDTH, highlighting its potential benefits in elderly healthcare management. The framework offers a promising avenue for leveraging DTs to analyze and interpret complex patient data, leading to personalized care strategies and interventions tailored to the unique needs and conditions of elderly patients.

Although DTs in precision medicine are still limited in scope, there have been significant developments in creating DTs for specific organs or body parts. One notable example is the Living Heart project by Dassault Systèmes, which has successfully developed a functioning computer model representing the complete heart, encompassing aspects such as blood flow, mechanics, and electrical impulses. This pioneering DT has applications in designing medical devices, analyzing drug safety, planning personalized surgical treatments, and advancing biomedical education. The availability of the Living Heart model to a global audience signifies a substantial step forward in utilizing DTs for precision medicine, enabling researchers, healthcare professionals, and educators to explore new possibilities, enhance medical device design, ensure drug efficacy and safety, and improve personalized approaches to surgery.

4. State-of-the-Art Models and Techniques

In a study [110], the CardioInsight noninvasive 3D mapping system was introduced. This innovative system combines chest electrocardiogram (ECG) signals with computerized tomography (CT) scan data to generate and visualize simultaneous 3D cardiac maps. By utilizing personalized heart models, physicians can gain a better understanding and characterization of abnormal heart rhythms.

Siemens Healthineers introduced a digital twin (DT) model for the heart, which has been employed for research purposes by cardiologists at Heidelberg University Hospital in Germany. Although the study is still undergoing data evaluation, the preliminary results are promising. The Siemens Healthineers DT model utilizes a comprehensive database comprising over 250 million annotated images, reports, and operational data. This DT model, which makes use of AI, allows for the digital construction of the heart based on patient-specific data, combining parameters like size, ejection fraction, and muscle contraction that closely match the particular patient's situation.

The Blue Brain Project, a collaboration between HP and EPFL, aims to create a DT of the brain. This research, which is part of the larger human brain research, focuses on developing physiologically realistic digital reconstructions and simulations of the mouse brain. In 2018, researchers produced the first ever 3D cell atlas for the whole mouse brain, which marked a significant milestone [117]. Researchers in their work presented a prototype of a human DT named "virtual human V1.0". This DT model depicts the respiratory system in detail, including the conducting and respiratory zones, lung lobes, and body shells. The major goal of this study is to explore and optimize the efficacy of cancer-targeted medications by selectively targeting tumor areas, hence enhancing cancer therapy success rates [112]. In this study [112], a digital twin (DT) was developed specifically for the treatment of aneurysms. Aneurysms, characterized by swollen blood arteries that can potentially result in strokes or blood clots, pose a significant health risk. By constructing 3D models of the aneurysm and the surrounding blood arteries, brain surgeons can utilize DT simulations to better understand the dynamic interplay between the implant and the aneurysm. Although the initial trials yielded encouraging outcomes, additional research is required to comprehensively evaluate the effectiveness of this approach.

In this study [108], multiple sclerosis (MS), often referred to as the "disease of a thousand faces", is observed to exhibit a high level of complexity, multidimensionality, and heterogeneity in terms of disease progression and treatment options among individuals. This complexity leads to the generation of large amounts of data that require careful administration and analysis. The development of human DTs holds great promise for individuals with MS (pwMS) in the field of precision medicine. The concept of this DT is shown in Figure 6. DTs enable medical professionals to efficiently manage and monitor large datasets, closely monitor patients, and provide more individualized care tailored to their specific needs and conditions.

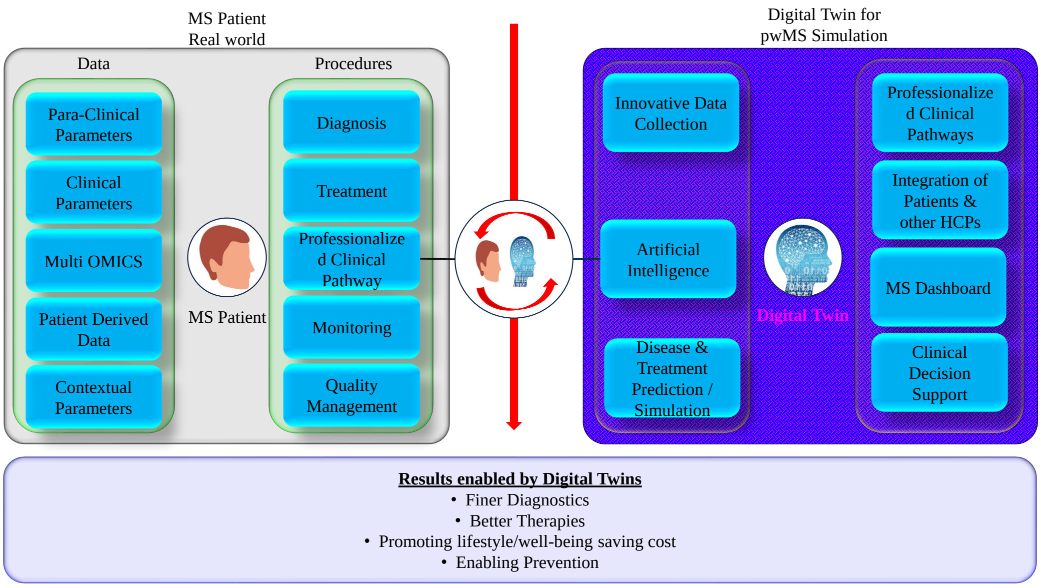

Figure 6. Concept of DT for MS patient as proposed in [108].

Human DTs have shown the ability to predict viral infections or immune responses in patients with viral illnesses in a study mentioned by [69]. This is achieved by integrating the current knowledge of human physiology and immunology with population and individual clinical data, which are then utilized to construct AI-based models. Healthcare practitioners can make better decisions regarding patient treatment by utilizing these cutting-edge models to acquire insights into how viral infections develop and the related immune responses. The urgent nature of traumatic injuries necessitates quick and well-coordinated care in the field of trauma management. DTs have tremendous promise in this setting as is highlighted in [106]. The use of DTs in trauma management spans several stages, beginning with the critical pre-hospital stage where urgent medical attention is given, moving on to the pain-free transfer of the patient to the hospital emergency room, and concluding with the operative stage, where the specialized trauma team provides individualized care. Even if a fully functional system might not yet exist, the creation of a prototype shows how far DTs have come in terms of being used for trauma care.

The field of diabetes management also benefits from the application of DTs, as discussed in [118]. Twin Health, a California-based start-up, has successfully leveraged DTs to develop models that simulate patient metabolism. These DT models keep a close eye on a number of variables, including variations in physical activity, sleep patterns, and dietary practices. They also closely monitor important health markers, including weight, liver function, and blood sugar levels. Current clinical trials have shown encouraging findings that show that people with type 2 diabetes can benefit significantly from receiving individualized, precise dietary advice.

5. Datasets

In this section, we discuss some of the state-of-the-art datasets available.

5.1. MIMIC-III

The MIMIC-III dataset [119] is a noteworthy dataset in the field of digital twins in healthcare. It comprises de-identified health-related information from approximately 40,000 patients hospitalized in the critical care units of Beth Israel Deaconess Medical

Center between 2001 and 2012. The dataset encompasses a wide range of data, including demographics, vital sign readings collected hourly at the bedside, laboratory test results, interventions, drug information, caregiver notes, imaging reports, and post-hospital discharge data, including mortality. Researchers can leverage the MIMIC-III dataset for various analytical investigations, such as epidemiology, the development of electronic tools, and the improvement of clinical decision rules. Researchers commonly utilize the MIMIC-III dataset for research in areas such as predictive modeling, clinical decision support systems, and outcomes analysis.

5.2. Cancer Genome Atlas Program (TCGA)

TCGA [120] was a significant initiative driven by the combined research power of the National Human Genome Research Institute and the National Cancer Institute, beginning as early as 2006. Based solely on this collaboration, almost 20,000 examples of cancerous and healthy samples from 33 individual conceptions of pertinent diseases were assessed. This phase lasted for an extensive 12-year period, resulting in more than 2.5 petabytes of scraped genomic, epigenomic, transcriptomic, transcriptomic, and proteomic records.

5.3. Human Connectome Project

The Human Connectome Project dataset [121] is a beneficial resource that has facilitated the exploration of the brain's intricate structure and function. It comprises extensive neuroimaging data from over 1200 healthy adults, providing exceptional detail regarding the brain's neural activity and connectivity.

6. Available Platforms

The digital twin platforms discussed below offer powerful capabilities for creating and utilizing DTs in various domains.

6.1. AWS IoT TwinMaker

One notable platform in the realm of digital twins is the AWS IoT TwinMaker [122]. Designed for real-world systems, such as buildings, factories, industrial equipment, and production lines, the AWS IoT TwinMaker platform simplifies the development of digital twins. It offers developers a comprehensive set of tools to optimize building operations, enhance production output, and improve equipment performance. AWS IoT TwinMaker supports the construction of comprehensive digital twin representations by using data from many sources and integrating them with virtual representations and 3D models. This provides a comprehensive perspective of operations, allowing for increased efficiency, predictive maintenance, and informed decision making. AWS IoT TwinMaker, with its sophisticated features and capabilities, enables developers to utilize the promise of digital twins in a variety of sectors, promoting innovation and operational excellence.

6.2. Azure Digital Twins

Azure DTs [123] is a robust platform-as-a-service (PaaS) product that allows for the development of twin graphs based on digital models of diverse settings, such as buildings, industries, farms, energy networks, trains, stadiums, and even cities. Azure DTs give significant information for driving product innovations, optimizing operations, saving costs, and providing excellent customer experiences by exploiting these digital models. One of the primary benefits of Azure DTs is their seamless integration into a larger cloud solution, which allows for simple connecting with IoT Hub device twins and the sharing of real-time data. This connection enables organizations to utilize the power of real-time data streams and digital twin capabilities to make informed decisions, monitor performance, and open new prospects for innovation.

6.3. Google Supply Chain Twin

Supply chain twin [124] by Google enables companies to consolidate and analyze data from diverse sources, facilitating a comprehensive view of suppliers, inventories, and other pertinent information. This platform supports informed decision-making processes by providing insights into the supply chain, enabling companies to optimize their operations and enhance overall efficiency.

6.4. NVIDIA Omniverse Enterprise

Powered by NVIDIA OVX, it empowers enterprises to create physically accurate DTs enhanced with AI capabilities. This platform [125] grants businesses the ability to design, simulate, and optimize products, equipment, and processes in real time before transitioning to production. By leveraging the power of AI, NVIDIA Omniverse Enterprise equips enterprises with the tools to develop highly accurate digital representations that enable efficient decision making and optimization across various domains.

7. Open Research Issues and Challenges

DTs in healthcare have shown promising opportunities, but their implementation faces a number of problems and issues that may prevent them from reaching their full potential. As DTs incorporate multiple technologies such as AI, IoT, and robotics, each introduces its own unique challenges and issues. Furthermore, the integration of these technologies and DT in healthcare is still in an early stage. Figure 7 presents the organization of the section.

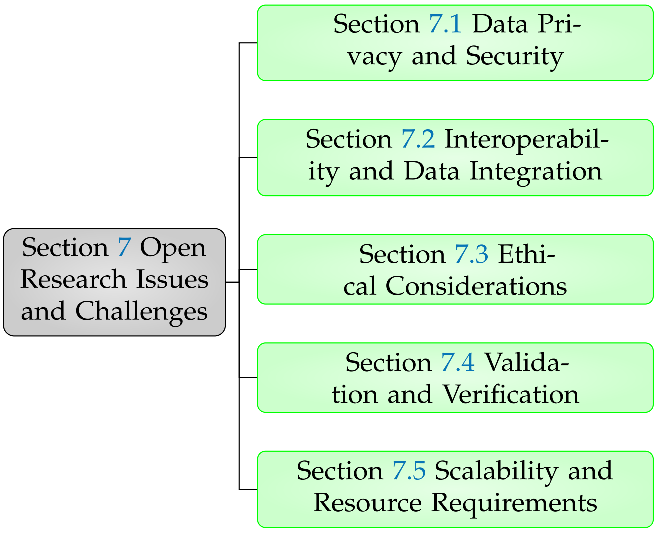

Figure 7. Organization of Section 7.

7.1. Data Privacy and Security

One of the foremost concerns surrounding DTs in healthcare is data privacy and security. The collection and storage of vast amounts of sensitive patient data raise the risk of data breaches, unauthorized access, and the potential misuse of information. Safeguarding patient privacy while enabling data sharing and analysis poses a significant challenge. Robust security measures, encryption techniques, and access controls must be implemented to ensure the confidentiality and integrity of patient data within DT ecosystems.

7.2. Interoperability and Data Integration

Healthcare systems often consist of diverse and fragmented data sources, hindering the seamless integration and synchronization of data across different platforms and devices. Achieving interoperability among various DT components, such as electronic health records, medical devices, and wearable sensors, is a complex task. The challenge lies in establishing standardized data formats, communication protocols, and data-exchange mechanisms to enable the efficient flow of information across systems. Overcoming these interoperability challenges is crucial to harnessing the full potential of DTs in healthcare.

7.3. Ethical Considerations

The use of DTs in healthcare raises ethical concerns that must be carefully addressed. Informed consent, data ownership, and patient autonomy are paramount in ensuring the responsible and ethical implementation of DTs. Clear guidelines and regulations are needed to navigate the ethical implications of using patients' personal health information for DT modeling. Respecting patients' rights and maintaining transparency throughout the process is vital to fostering trust between healthcare providers and patients.

7.4. Validation and Verification

Validating and verifying DTs in healthcare poses significant challenges. The complexity and variability of human physiology, disease progression, and individual patient characteristics make it difficult to ensure an accurate representation of real-world patients. Rigorous testing, validation methodologies, and clinical studies are necessary to ensure that DTs deliver reliable results. The continual refinement and validation of the models against real-world patient data are essential to enhance their predictive capabilities and increase their clinical utility.

7.5. Scalability and Resource Requirements

Building and maintaining DTs in healthcare require substantial computational resources, storage capacities, and data-processing capabilities. Scalability becomes a critical challenge, as healthcare organizations must handle large volumes of data generated by digital twins and ensure efficient resource allocation for real-time monitoring and analysis. Developing scalable infrastructure that can accommodate the growing demand for DTs while maintaining high performance is essential for their successful adoption in healthcare settings.

7.6. Regulatory and Legal Frameworks

The regulatory landscape for DTs in healthcare is still evolving. As the use of DTs becomes more widespread, it is crucial to establish clear guidelines and policies. In conclusion, the adoption of digital twins in healthcare brings forth a range of open issues and challenges that must be addressed. These challenges encompass data privacy, consent management, liability, intellectual property rights, and regulatory compliance. Regulatory frameworks play a crucial role in striking a balance between fostering innovation and safeguarding patient rights, providing clarity to healthcare organizations, and facilitating the responsible implementation of digital twins.

7.7. User Acceptance and Adoption

Another critical aspect of successful implementation is user acceptance and adoption. Resistance to change, concerns regarding accuracy and reliability, and challenges in integrating digital twins into existing healthcare workflows can hinder their adoption. To overcome these challenges, it is essential to implement education and training programs that familiarize healthcare professionals with the benefits and limitations of digital twins. Additionally, engaging patients and involving them in the decision-making process can contribute to their acceptance and adoption.

In conclusion, the adoption of digital twins in healthcare necessitates a multidisciplinary approach involving technology, policy, ethics, and stakeholder collaboration. By addressing the challenges mentioned above, we can fully realize the promise of digital twins to improve patient care, enhance healthcare outcomes, and transform the healthcare environment. Further research and development are imperative to address these challenges and establish robust frameworks for the responsible and effective implementation of digital twins in healthcare.

8. Conclusions

In this comprehensive review of DTs in healthcare, we explored their technology, applications, and challenges. DTs offer significant potential for solving complex medical problems, such as real-time monitoring, dynamic analysis, and precise treatment, which traditional methods struggle to address. By modeling the perception and action of relevant medical facilities and coupling them with the physical entity, DTs enable a quantitative understanding of health and disease, paving the way for personalized treatment and precision medicine. Moreover, the emergence of DT applications across various domains, coupled with enabling technologies like big data, ML, advanced modeling, simulation, and communication interfaces, empower data-driven decision making. While each domain may have specific requirements, the underlying concept and basic architecture of DTs remain prevalent. Although universal standards for DT technology still lack widespread adoption, the increasing attention and publications on DTs signal the need for standardization efforts by organizations like ISO. While the predictions for the DT market are favorable, realizing the full potential of DTs requires addressing significant limitations and challenges. These include privacy, ethical considerations, maintenance, lack of standards and regulations, and user acceptance concerns. Evaluating DTs based on technology readiness, societal readiness, and maturity is crucial, and currently, most applications are still in the early stages. Future research efforts should focus on simulation and modeling techniques, 5G communication, IoT data processing, interoperability, integration of software tools, and advanced computing capabilities to overcome these challenges. By understanding the holistic view of DTs across domains and addressing the proposed research efforts, we can unleash the full potential of DTs for the future. As technology develops under the principles of innovation and sustainability, these obstacles will become more manageable, enabling autonomous, sustainable, and widely accepted DT implementations in real environments. The application of DTs extends beyond the private sector, with governments and public agencies also considering their use in smart city development and public services management, aligning with citizen well-being and sustainable development goals.

In conclusion, while DT technology is still in its early stages, its potential to transform healthcare and various other domains is significant. By solving the challenges and working on development and research, we can overcome limitations and fully harness the potential of DTs to improve decision making and patient outcomes, and make a contribution to a more sustainable future.

Author Contributions: Conceptualization, M.T. and S.J.; methodology, M.T.; software, M.T.; validation, M.T. and S.J.; formal analysis, M.T.; investigation, S.J.; resources, M.T.; data curation, M.T.; writing—original draft preparation, M.T.; writing—review and editing, S.J.; visualization, M.T.; supervision, S.J.; project administration, S.J.; funding acquisition, S.J. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

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

Abbreviations

The following abbreviations are used in this paper:

2D	Two-dimensional
3D	Three-dimensional
AI	Artificial intelligence
AR	Augmented reality
CBCT	Cone-beam computed tomography

CDT	Cariac digital twin
CT	Computerized tomography
DL	Deep learning
DT	Digital twins
EPFL	L'École Polytechnique Fédérale de Lausanne
HDT	Human digital twin
IoT	Internet of things
MS	Multiple sclerosis
NFT	Non-fungible token
VR	Virtual reality

References

1. Fuller, A.; Fan, Z.; Day, C.; Barlow, C. Digital twin: Enabling technologies, challenges and open research. *IEEE Access* **2020**, *8*, 108952–108971. [CrossRef]
2. Molinaro, R.; Singh, J.S.; Catsoulis, S.; Narayanan, C.; Lakehal, D. Embedding data analytics and CFD into the digital twin concept. *Comput. Fluids* **2021**, *214*, 104759. [CrossRef]
3. Jamil, S.; Rahman, M.; Fawad. A comprehensive survey of digital twins and federated learning for industrial internet of things (IIoT), internet of vehicles (IoV) and internet of drones (IoD). *Appl. Syst. Innov.* **2022**, *5*, 56. [CrossRef]
4. Kalsoom, T.; Ahmed, S.; Rafi-ul Shan, P.M.; Azmat, M.; Akhtar, P.; Pervez, Z.; Imran, M.A.; Ur-Rehman, M. Impact of IOT on Manufacturing Industry 4.0: A new triangular systematic review. *Sustainability* **2021**, *13*, 12506. [CrossRef]
5. Kashani, M.H.; Madanipour, M.; Nikravan, M.; Asghari, P.; Mahdipour, E. A systematic review of IoT in healthcare: Applications, techniques, and trends. *J. Netw. Comput. Appl.* **2021**, *192*, 103164. [CrossRef]
6. Syed, A.S.; Sierra-Sosa, D.; Kumar, A.; Elmaghraby, A. IoT in smart cities: A survey of technologies, practices and challenges. *Smart Cities* **2021**, *4*, 429–475. [CrossRef]
7. Bilberg, A.; Malik, A.A. Digital twin driven human–robot collaborative assembly. *CIRP Ann.* **2019**, *68*, 499–502. [CrossRef]
8. Jain, P.; Poon, J.; Singh, J.P.; Spanos, C.; Sanders, S.R.; Panda, S.K. A digital twin approach for fault diagnosis in distributed photovoltaic systems. *IEEE Trans. Power Electron.* **2019**, *35*, 940–956. [CrossRef]
9. Huang, H.; Yang, L.; Wang, Y.; Xu, X.; Lu, Y. Digital twin-driven online anomaly detection for an automation system based on edge intelligence. *J. Manuf. Syst.* **2021**, *59*, 138–150. [CrossRef]
10. Lu, Q.; Xie, X.; Parlikad, A.K.; Schooling, J.M. Digital twin-enabled anomaly detection for built asset monitoring in operation and maintenance. *Autom. Constr.* **2020**, *118*, 103277. [CrossRef]
11. Mandolla, C.; Petruzzelli, A.M.; Percoco, G.; Urbinati, A. Building a digital twin for additive manufacturing through the exploitation of blockchain: A case analysis of the aircraft industry. *Comput. Ind.* **2019**, *109*, 134–152. [CrossRef]
12. Deren, L.; Wenbo, Y.; Zhenfeng, S. Smart city based on digital twins. *Comput. Urban Sci.* **2021**, *1*, 1–11. [CrossRef]
13. Singh, M.; Fuenmayor, E.; Hinchy, E.P.; Qiao, Y.; Murray, N.; Devine, D. Digital twin: Origin to future. *Appl. Syst. Innov.* **2021**, *4*, 36. [CrossRef]
14. Ibrahim, M.; Rjabtšikov, V.; Gilbert, R. Overview of digital twin platforms for EV applications. *Sensors* **2023**, *23*, 1414. [CrossRef]
15. Lo, C.; Chen, C.; Zhong, R.Y. A review of digital twin in product design and development. *Adv. Eng. Inform.* **2021**, *48*, 101297. [CrossRef]
16. Ning, H.; Wang, H.; Lin, Y.; Wang, W.; Dhelim, S.; Farha, F.; Ding, J.; Daneshmand, M. A Survey on the Metaverse: The State-of-the-Art, Technologies, Applications, and Challenges. *IEEE Internet Things J.* **2023**. [CrossRef]
17. Dai, N.; Lei, I.M.; Li, Z.; Li, Y.; Fang, P.; Zhong, J. Recent advances in wearable electromechanical sensors—Moving towards machine learning-assisted wearable sensing systems. *Nano Energy* **2022**, *105* , 108041. [CrossRef]
18. Hammi, B.; Zeadally, S.; Perez, A.J. Non-Fungible Tokens: A Review. *IEEE Internet Things Mag.* **2023**, *6*, 46–50. [CrossRef]
19. Arena, F.; Collotta, M.; Pau, G.; Termine, F. An overview of augmented reality. *Computers* **2022**, *11*, 28. [CrossRef]
20. Yin, Y.; Zheng, P.; Li, C.; Wang, L. A state-of-the-art survey on Augmented Reality-assisted Digital Twin for futuristic human-centric industry transformation. *Robot.-Comput.-Integr. Manuf.* **2023**, *81*, 102515. [CrossRef]
21. Devagiri, J.S.; Paheding, S.; Niyaz, Q.; Yang, X.; Smith, S. Augmented Reality and Artificial Intelligence in industry: Trends, tools, and future challenges. *Expert Syst. Appl.* **2022**, 207, 118002. [CrossRef]
22. Adil, M.; Song, H.; Khan, M.K.; Farouk, A.; Jin, Z. 5G/6G-Enabled Metaverse Technologies: Taxonomy, Applications, and Open Security Challenges with Future Research Directions. *arXiv* **2023**, arXiv:2305.16473.
23. Jamil, S.; Rahman, M.; Tanveer, J.; Haider, A. Energy Efficiency and Throughput Maximization Using Millimeter Waves–Microwaves HetNets. *Electronics* **2022**, *11*, 474. [CrossRef]
24. Jamil, S.; Rahman, M.; Abbas, M.S.; Fawad. Resource allocation using reconfigurable intelligent surface (RIS)-assisted wireless networks in industry 5.0 scenario. In Proceedings of the Telecom, Virtual, 13–15 July 2022; MDPI: Basel, Switzerland, 2022; Volume 3, pp. 163–173.
25. Huynh-The, T.; Gadekallu, T.R.; Wang, W.; Yenduri, G.; Ranaweera, P.; Pham, Q.V.; da Costa, D.B.; Liyanage, M. Blockchain for the metaverse: A Review. *Future Gener. Comput. Syst.* **2023**, *143*, 401–419. [CrossRef]

26. Yang, Q.; Zhao, Y.; Huang, H.; Xiong, Z.; Kang, J.; Zheng, Z. Fusing blockchain and AI with metaverse: A survey. *IEEE Open J. Comput. Soc.* **2022**, *3*, 122–136. [CrossRef]
27. Fu, Y.; Li, C.; Yu, F.R.; Luan, T.H.; Zhao, P.; Liu, S. A survey of blockchain and intelligent networking for the metaverse. *IEEE Internet Things J.* **2022,** *10*, 3587–3610. [CrossRef]
28. Kamińska, D.; Sapiński, T.; Wiak, S.; Tikk, T.; Haamer, R.E.; Avots, E.; Helmi, A.; Ozcinar, C.; Anbarjafari, G. Virtual reality and its applications in education: Survey. *Information* **2019**, *10*, 318. [CrossRef]
29. Wu, D.; Yang, Z.; Zhang, P.; Wang, R.; Yang, B.; Ma, X. Virtual-Reality Inter-Promotion Technology for Metaverse: A Survey. *IEEE Internet Things J.* **2023**. [CrossRef]
30. Abdelghafar, S.; Ezzat, D.; Darwish, A.; Hassanien, A.E. Metaverse for Brain Computer Interface: Towards New and Improved Applications. In *The Future of Metaverse in the Virtual Era and Physical World*; Springer: Berlin/Heidelberg, Germany, 2023; pp. 43–58.
31. Hwang, G.J.; Chien, S.Y. Definition, roles, and potential research issues of the metaverse in education: An artificial intelligence perspective. *Comput. Educ. Artif. Intell.* **2022**, *3*, 100082. [CrossRef]
32. Press Release: Global Internet of Things Market to Grow to 27 Billion Devices, Generating USD3 Trillion Revenue in 2025. Available online: https://iotbusinessnews.com/2016/08/03/97077-global-internet-things-market-grow-27-billion-devices-generating-usd-3-trillion-revenue-2025 (accessed on 21 June 2023).
33. Zhou, M. Evolution from AI, IoT and Big Data Analytics to Metaverse. *IEEE/CAA J. Autom. Sin.* **2022**, *9*, 2041–2042. [CrossRef]
34. Aloqaily, M.; Bouachir, O.; Karray, F.; Al Ridhawi, I.; El Saddik, A. Integrating Digital Twin and Advanced Intelligent Technologies to Realize the Metaverse. *IEEE Consum. Electron. Mag.* **2022**. [CrossRef]
35. Prensky, M. Digital natives, digital immigrants part 2: Do they really think differently? *On the Horizon* **2001**, *9*, 1–6. [CrossRef]
36. Evans, C.; Robertson, W. The four phases of the digital natives debate. *Hum. Behav. Emerg. Technol.* **2020**, *2*, 269–277. [CrossRef]
37. Lee, L.H.; Braud, T.; Zhou, P.; Wang, L.; Xu, D.; Lin, Z.; Kumar, A.; Bermejo, C.; Hui, P. All one needs to know about metaverse: A complete survey on technological singularity, virtual ecosystem, and research agenda. *arXiv* **2021**, arXiv:2110.05352.
38. Daneshfar, F.; Jamshidi, M.B. An octonion-based nonlinear echo state network for speech emotion recognition in Metaverse. *Neural Netw.* **2023**, *163*, 108–121. [CrossRef] [PubMed]
39. Carey, B. Metaverse Technologies, Behavioral Predictive Analytics, and Customer Location Tracking Tools in Blockchain-based Virtual Worlds. *Rev. Contemp. Philos.* **2022**, *21*, 188–204.
40. Huynh-The, T.; Pham, Q.V.; Pham, X.Q.; Nguyen, T.T.; Han, Z.; Kim, D.S. Artificial intelligence for the metaverse: A survey. *Eng. Appl. Artif. Intell.* **2023**, *117*, 105581. [CrossRef]
41. Mozumder, M.A.I.; Armand, T.P.T.; Imtiyaj Uddin, S.M.; Athar, A.; Sumon, R.I.; Hussain, A.; Kim, H.C. Metaverse for Digital Anti-Aging Healthcare: An Overview of Potential Use Cases Based on Artificial Intelligence, Blockchain, IoT Technologies, Its Challenges, and Future Directions. *Appl. Sci.* **2023**, *13*, 5127. [CrossRef]
42. Khan, N.; Khan, S.U.; Baik, S.W. Deep dive into hybrid networks: A comparative study and novel architecture for efficient power prediction. *Renew. Sustain. Energy Rev.* **2023**, *182*, 113364. [CrossRef]
43. Turab, M.; Kumar, T.; Bendechache, M.; Saber, T. Investigating multi-feature selection and ensembling for audio classification. *arXiv* **2022**, arXiv:2206.07511.
44. Jamil, S.; Abbas, M.S.; Habib, F.; Umair, M.; Khan, M.J. Deep learning and computer vision-based a novel framework for himalayan bear, marco polo sheep and snow leopard detection. In Proceedings of the 2020 International Conference on Information Science and Communication Technology (ICISCT), Karachi, Pakistan, 8–9 February 2020; IEEE: Manhattan, NY, USA, 2020; pp. 1–6.
45. Khan, N.; Haq, I.U.; Ullah, F.U.M.; Khan, S.U.; Lee, M.Y. CL-net: ConvLSTM-based hybrid architecture for batteries' state of health and power consumption forecasting. *Mathematics* **2021**, *9*, 3326. [CrossRef]
46. Khan, W.; Turab, M.; Ahmad, W.; Ahmad, S.H.; Kumar, K.; Luo, B. Data Dimension Reduction makes ML Algorithms efficient. *arXiv* **2022**, arXiv:2211.09392.
47. Upadhyay, K.; Dantu, R.; He, Y.; Badruddoja, S.; Salau, A. Auditing Metaverse Requires Multimodal Deep Learning. In Proceedings of the 2022 IEEE 4th International Conference on Trust, Privacy and Security in Intelligent Systems, and Applications (TPS-ISA), Atlanta, GA, USA, 14–17 December 2022; IEEE: Manhattan, NY, USA, 2022; pp. 39–46.
48. Mozumder, M.A.I.; Sheeraz, M.M.; Athar, A.; Aich, S.; Kim, H.C. Overview: Technology roadmap of the future trend of metaverse based on IoT, blockchain, AI technique, and medical domain metaverse activity. In Proceedings of the 2022 24th International Conference on Advanced Communication Technology (ICACT), Virtual, 14–16 December 2022; IEEE: Manhattan, NY, USA, 2022; pp. 256–261.
49. Veeraiah, V.; Gangavathi, P.; Ahamad, S.; Talukdar, S.B.; Gupta, A.; Talukdar, V. Enhancement of meta verse capabilities by IoT integration. In Proceedings of the 2022 2nd International Conference on Advance Computing and Innovative Technologies in Engineering (ICACITE), Greater Noida, India, 28–29 April 2022; IEEE: Manhattan, NY, USA, 2022; pp. 1493–1498.
50. Wang, Y.; Zhao, J. Mobile Edge Computing, Metaverse, 6G Wireless Communications, Artificial Intelligence, and Blockchain: Survey and Their Convergence. *arXiv* **2022**, arXiv:2209.14147.
51. Liu, C.; Wang, Y.; Zhao, J. Mobile Edge Computing for the Metaverse. *arXiv* **2022**, arXiv:2212.09229.

52. Mandala, V.; Jeyarani, M.R.; Kousalya, A.; Pavithra, M.; Arumugam, M. An Innovative Development with Multidisciplinary Perspective in Metaverse Integrating with Blockchain Technology with Cloud Computing Techniques. In Proceedings of the 2023 International Conference on Inventive Computation Technologies (ICICT), Atlanta, GA, USA, 1–3 November 2023; IEEE: Manhattan, NY, USA, 2023; pp. 1182–1187.
53. Jamil, S.; Piran, M.J.; Rahman, M.; Kwon, O.J. Learning-driven lossy image compression: A comprehensive survey. *Eng. Appl. Artif. Intell.* **2023**, *123*, 106361. [CrossRef]
54. Jamil, S.; Jalil Piran, M.; Kwon, O.J. A comprehensive survey of transformers for computer vision. *Drones* **2023**, *7*, 287. [CrossRef]
55. Khader, J. Welcome to the Metaverse: Social Media, the Phantasmatic Big Other, and the Anxiety of the Prosthetic Gods. *Rethink. Marx.* **2022**, *34*, 397–405. [CrossRef]
56. Yang, D.; Zhou, J.; Chen, R.; Song, Y.; Song, Z.; Zhang, X.; Wang, Q.; Wang, K.; Zhou, C.; Sun, J.; et al. Expert consensus on the metaverse in medicine. *Clin. Ehealth* **2022**, *5*, 1–9. [CrossRef]
57. Moztarzadeh, O.; Jamshidi, M.; Sargolzaei, S.; Jamshidi, A.; Baghalipour, N.; Malekzadeh Moghani, M.; Hauer, L. Metaverse and Healthcare: Machine Learning-Enabled Digital Twins of Cancer. *Bioengineering* **2023**, *10*, 455. [CrossRef] [PubMed]
58. Moztarzadeh, O.; Jamshidi, M.; Sargolzaei, S.; Keikhaee, F.; Jamshidi, A.; Shadroo, S.; Hauer, L. Metaverse and Medical Diagnosis: A Blockchain-Based Digital Twinning Approach Based on MobileNetV2 Algorithm for Cervical Vertebral Maturation. *Diagnostics* **2023**, *13*, 1485. [CrossRef]
59. Skalidis, I.; Muller, O.; Fournier, S. CardioVerse: The cardiovascular medicine in the era of Metaverse. *Trends Cardiovasc. Med.* **2022**. [CrossRef] [PubMed]
60. Ali, S.; Abdullah; Armand, T.P.T.; Athar, A.; Hussain, A.; Ali, M.; Yaseen, M.; Joo, M.I.; Kim, H.C. Metaverse in healthcare integrated with explainable ai and blockchain: Enabling immersiveness, ensuring trust, and providing patient data security. *Sensors* **2023**, *23*, 565. [CrossRef] [PubMed]
61. Wang, G.; Badal, A.; Jia, X.; Maltz, J.S.; Mueller, K.; Myers, K.J.; Niu, C.; Vannier, M.; Yan, P.; Yu, Z.; et al. Development of metaverse for intelligent healthcare. *Nat. Mach. Intell.* **2022**, *4*, 922–929. [CrossRef]
62. Musamih, A.; Yaqoob, I.; Salah, K.; Jayaraman, R.; Al-Hammadi, Y.; Omar, M.; Ellahham, S. Metaverse in healthcare: Applications, challenges, and future directions. *IEEE Consum. Electron. Mag.* **2023,** *12*, 33–46. [CrossRef]
63. Yang, Y.; Siau, K.; Xie, W.; Sun, Y. Smart Health: Intelligent Healthcare Systems in the Metaverse, Artificial Intelligence, and Data Science Era. *J. Organ. End User Comput. (JOEUC)* **2022**, *34*, 1–14. [CrossRef]
64. Neto, A.A.; da Silva, E.R.; Deschamps, F.; de Lima, E.P. Digital twins in manufacturing: An assessment of key features. *Procedia CIRP* **2021**, *97*, 178–183. [CrossRef]
65. Wang, Y.; Kang, X.; Chen, Z. A survey of digital twin techniques in smart manufacturing and management of energy applications. *Green Energy Intell. Transp.* **2022**, *1*, 100014. [CrossRef]
66. Shengli, W. Is human digital twin possible? *Comput. Methods Programs Biomed. Update* **2021**, *1*, 100014. [CrossRef]
67. Laamarti, F.; Badawi, H.F.; Ding, Y.; Arafsha, F.; Hafidh, B.; El Saddik, A. An ISO/IEEE 11073 standardized digital twin framework for health and well-being in smart cities. *IEEE Access* **2020**, *8*, 105950–105961. [CrossRef]
68. Barricelli, B.R.; Casiraghi, E.; Gliozzo, J.; Petrini, A.; Valtolina, S. Human digital twin for fitness management. *IEEE Access* **2020**, *8*, 26637–26664. [CrossRef]
69. Laubenbacher, R.; Sluka, J.P.; Glazier, J.A. Using digital twins in viral infection. *Science* **2021**, *371*, 1105–1106. [CrossRef] [PubMed]
70. Laaki, H.; Miche, Y.; Tammi, K. Prototyping a digital twin for real time remote control over mobile networks: Application of remote surgery. *IEEE Access* **2019**, *7*, 20325–20336. [CrossRef]
71. Armeni, P.; Polat, I.; De Rossi, L.M.; Diaferia, L.; Meregalli, S.; Gatti, A. Digital Twins in Healthcare: Is It the Beginning of a New Era of Evidence-Based Medicine? A Critical Review. *J. Pers. Med.* **2022**, *12*, 1255. [CrossRef] [PubMed]
72. Kaul, R.; Ossai, C.; Forkan, A.R.M.; Jayaraman, P.P.; Zelcer, J.; Vaughan, S.; Wickramasinghe, N. The role of AI for developing digital twins in healthcare: The case of cancer care. *WIley Interdiscip. Rev. Data Min. Knowl. Discov.* **2023**, *13*, e1480. [CrossRef]
73. Bhugaonkar, K.; Bhugaonkar, R.; Masne, N. The trend of Metaverse and augmented & virtual reality extending to the healthcare system. *Cureus* **2022**, *14*, e29071. [CrossRef] [PubMed]
74. Chengoden, R.; Victor, N.; Huynh-The, T.; Yenduri, G.; Jhaveri, R.H.; Alazab, M.; Bhattacharya, S.; Hegde, P.; Maddikunta, P.K.R.; Gadekallu, T.R. Metaverse for healthcare: A survey on potential applications, challenges and future directions. *IEEE Access* **2023,** *11*, 12765–12795. [CrossRef]
75. Far, S.B.; Rad, A.I. Applying digital twins in metaverse: User interface, security and privacy challenges. *J. Metaverse* **2022**, *2*, 8–15.
76. Lv, Z.; Xie, S.; Li, Y.; Hossain, M.S.; El Saddik, A. Building the Metaverse by Digital Twins at All Scales, State, Relation. *Virtual Real. Intell. Hardw.* **2022**, *4*, 459–470. [CrossRef]
77. Botín-Sanabria, D.M.; Mihaita, A.S.; Peimbert-García, R.E.; Ramírez-Moreno, M.A.; Ramírez-Mendoza, R.A.; Lozoya-Santos, J.d.J. Digital twin technology challenges and applications: A comprehensive review. *Remote Sens.* **2022**, *14*, 1335. [CrossRef]
78. Bansal, G.; Rajgopal, K.; Chamola, V.; Xiong, Z.; Niyato, D. Healthcare in Metaverse: A Survey on Current Metaverse Applications in Healthcare. *IEEE Access* **2022**, *10*, 119914–119946. [CrossRef]
79. Hassani, H.; Huang, X.; MacFeely, S. Impactful Digital Twin in the Healthcare Revolution. *Big Data Cogn. Comput.* **2022**, *6*, 83. [CrossRef]

80. Ahmadi-Assalemi, G.; Al-Khateeb, H.; Maple, C.; Epiphaniou, G.; Alhaboby, Z.A.; Alkaabi, S.; Alhaboby, D. Digital twins for precision healthcare. In *Cyber Defence in the Age of AI, Smart Societies and Augmented Humanity*; Springer: Berlin/Heidelberg, Germany, 2020; pp. 133–158.
81. Eftimie, R.; Mavrodin, A.; Bordas, S.P. From digital control to digital twins in medicine: A brief review and future perspectives. *Adv. Appl. Mech.* **2023**, *56*, 323–368.
82. Karakra, A.; Fontanili, F.; Lamine, E.; Lamothe, J. HospiT'Win: A predictive simulation-based digital twin for patients pathways in hospital. In Proceedings of the 2019 IEEE EMBS International Conference on Biomedical & Health Informatics (BHI), Chicago, IL, USA, 19–22 May 2019; IEEE: Manhattan, NY, USA, 2019; pp. 1–4.
83. Martinez-Velazquez, R.; Gamez, R.; El Saddik, A. Cardio Twin: A Digital Twin of the human heart running on the edge. In Proceedings of the 2019 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Istanbul, Turkey, 26–28 June 2019; IEEE: Manhattan, NY, USA, 2019; pp. 1–6.
84. Pilati, F.; Tronconi, R.; Nollo, G.; Heragu, S.S.; Zerzer, F. Digital twin of COVID-19 mass vaccination centers. *Sustainability* **2021**, *13*, 7396. [CrossRef]
85. Coorey, G.; Figtree, G.A.; Fletcher, D.F.; Snelson, V.J.; Vernon, S.T.; Winlaw, D.; Grieve, S.M.; McEwan, A.; Yang, J.Y.H.; Qian, P.; et al. The health digital twin to tackle cardiovascular disease—A review of an emerging interdisciplinary field. *NPJ Digit. Med.* **2022**, *5*, 126. [CrossRef]
86. Okegbile, S.D.; Cai, J.; Yi, C.; Niyato, D. Human digital twin for personalized healthcare: Vision, architecture and future directions. *IEEE Netw.* **2022**, 1–7. [CrossRef]
87. Haleem, A.; Javaid, M.; Singh, R.P.; Suman, R. Exploring the revolution in healthcare systems through the applications of digital twin technology. *Biomed. Technol.* **2023**, *4*, 28–38. [CrossRef]
88. Song, Y.T.; Qin, J. Metaverse and Personal Healthcare. *Procedia Comput. Sci.* **2022**, *210*, 189–197. [CrossRef]
89. Rodríguez-Aguilar, R.; Marmolejo-Saucedo, J.A. Conceptual framework of Digital Health Public Emergency System: Digital twins and multiparadigm simulation. *EAI Endorsed Trans. Pervasive Health Technol.* **2020**, *6*, e3. [CrossRef]
90. Khan, S.; Arslan, T.; Ratnarajah, T. Digital twin perspective of fourth industrial and healthcare revolution. *IEEE Access* **2022**, *10*, 25732–25754. [CrossRef]
91. Bagaria, N.; Laamarti, F.; Badawi, H.F.; Albraikan, A.; Martinez Velazquez, R.A.; El Saddik, A. Health 4.0: Digital twins for health and well-being. In *Connected Health in Smart Cities*; Springer: Cham, Switzerland, 2020 ; pp. 143–152._7. [CrossRef]
92. Qi, Q.; Tao, F.; Hu, T.; Anwer, N.; Liu, A.; Wei, Y.; Wang, L.; Nee, A. Enabling technologies and tools for digital twin. *J. Manuf. Syst.* **2021**, *58*, 3–21. [CrossRef]
93. Schwartz, S.M.; Wildenhaus, K.; Bucher, A.; Byrd, B. Digital twins and the emerging science of self: Implications for digital health experience design and "small" data. *Front. Comput. Sci.* **2020**, *2*, 31. [CrossRef]
94. Chen, X.; Feng, Y.; Zhong, W.; Kleinstreuer, C. Numerical investigation of the interaction, transport and deposition of multicomponent droplets in a simple mouth-throat model. *J. Aerosol Sci.* **2017**, *105*, 108–127. [CrossRef]
95. Feng, Y.; Zhao, J.; Chen, X.; Lin, J. An in silico subject-variability study of upper airway morphological influence on the airflow regime in a tracheobronchial tree. *Bioengineering* **2017**, *4*, 90. [CrossRef] [PubMed]
96. Chen, X.; Feng, Y.; Zhong, W.; Sun, B.; Tao, F. Numerical investigation of particle deposition in a triple bifurcation airway due to gravitational sedimentation and inertial impaction. *Powder Technol.* **2018**, *323*, 284–293. [CrossRef]
97. Bende, A.; Gochhait, S. Leveraging digital twin technology in the healthcare industry—A machine learning based approach. *Eur. J. Mol. Clin. Med.* **2020**, *7*, 2547–2557.
98. Gillette, K.; Gsell, M.A.; Prassl, A.J.; Karabelas, E.; Reiter, U.; Reiter, G.; Grandits, T.; Payer, C.; Štern, D.; Urschler, M.; et al. A framework for the generation of digital twins of cardiac electrophysiology from clinical 12-leads ECGs. *Med. Image Anal.* **2021**, *71*, 102080. [CrossRef]
99. Portela, R.M.; Varsakelis, C.; Richelle, A.; Giannelos, N.; Pence, J.; Dessoy, S.; von Stosch, M. When is an in silico representation a digital twin? A biopharmaceutical industry approach to the digital twin concept. In *Digital Twins: Tools and Concepts for Smart Biomanufacturing*; Springer: Berlin/Heidelberg, Germany, 2021; pp. 35–55.
100. Canzoneri, M.; De Luca, A.; Harttung, J. Digital twins: A general overview of the biopharma industry. In *Digital Twins: Applications to the Design and Optimization of Bioprocesses*; Springer: Berlin/Heidelberg, Germany, 2021; pp. 167–184.
101. Telenti, A.; Pierce, L.C.; Biggs, W.H.; Di Iulio, J.; Wong, E.H.; Fabani, M.M.; Kirkness, E.F.; Moustafa, A.; Shah, N.; Xie, C.; et al. Deep sequencing of 10,000 human genomes. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 11901–11906. [CrossRef]
102. Lloyd-Price, J.; Abu-Ali, G.; Huttenhower, C. The healthy human microbiome. *Genome Med.* **2016**, *8*, 51. [CrossRef]
103. Angulo, C.; Gonzalez-Abril, L.; Raya, C.; Ortega, J.A. A proposal to evolving towards digital twins in healthcare. In Proceedings of the Bioinformatics and Biomedical Engineering: 8th International Work-Conference, IWBBIO 2020, Granada, Spain, 6–8 May 2020; Springer: Berlin/Heidelberg, Germany, 2020; pp. 418–426.
104. Kamel Boulos, M.N.; Al-Shorbaji, N.M. On the Internet of Things, smart cities and the WHO Healthy Cities. *Int. J. Health Geogr.* **2014**, *13*, 10. [CrossRef]
105. Lehrach, H.; Ionescu, A.; Benhabiles, N. The Future of Health Care: Deep data, smart sensors, virtual patients and the Internet-of-Humans. *White Paper* **2016**, *11*, 1–7.
106. Croatti, A.; Gabellini, M.; Montagna, S.; Ricci, A. On the integration of agents and digital twins in healthcare. *J. Med. Syst.* **2020**, *44*, 1–8. [CrossRef]

107. Cho, S.W.; Byun, S.H.; Yi, S.; Jang, W.S.; Kim, J.C.; Park, I.Y.; Yang, B.E. Sagittal relationship between the maxillary central incisors and the forehead in digital twins of korean adult females. *J. Pers. Med.* **2021**, *11*, 203. [CrossRef] [PubMed]
108. Voigt, I.; Inojosa, H.; Dillenseger, A.; Haase, R.; Akgün, K.; Ziemssen, T. Digital twins for multiple sclerosis. *Front. Immunol.* **2021**, *12*, 669811. [CrossRef]
109. Walsh, J.R.; Smith, A.M.; Pouliot, Y.; Li-Bland, D.; Loukianov, A.; Fisher, C.K. Generating digital twins with multiple sclerosis using probabilistic neural networks. *arXiv* **2020**, arXiv:2002.02779.
110. Corral-Acero, J.; Margara, F.; Marciniak, M.; Rodero, C.; Loncaric, F.; Feng, Y.; Gilbert, A.; Fernandes, J.F.; Bukhari, H.A.; Wajdan, A.; et al. The 'Digital Twin'to enable the vision of precision cardiology. *Eur. Heart J.* **2020**, *41*, 4556–4564. [CrossRef]
111. Subramanian, K. Digital twin for drug discovery and development—The virtual liver. *J. Indian Inst. Sci.* **2020**, *100*, 653–662. [CrossRef]
112. Barricelli, B.R.; Casiraghi, E.; Fogli, D. A survey on digital twin: Definitions, characteristics, applications, and design implications. *IEEE Access* **2019**, *7*, 167653–167671. [CrossRef]
113. Wickramasinghe, N.; Jayaraman, P.P.; Forkan, A.R.M.; Ulapane, N.; Kaul, R.; Vaughan, S.; Zelcer, J. A Vision for Leveraging the Concept of Digital Twins to Support the Provision of Personalized Cancer Care. *IEEE Internet Comput.* **2021**, *26*, 17–24. [CrossRef]
114. Raden, N. Digital Twins for Personalized Medicine-A Critical Assessment. Diginomica 2020. Available online: https://diginomica.com/digital-twins-personalized-medicine-critical-assessment (accessed on 21 June 2023).
115. Björnsson, B.; Borrebaeck, C.; Elander, N.; Gasslander, T.; Gawel, D.R.; Gustafsson, M.; Jörnsten, R.; Lee, E.J.; Li, X.; Lilja, S.; et al. Digital twins to personalize medicine. *Genome Med.* **2020**, *12*, 4. [CrossRef]
116. Liu, Y.; Zhang, L.; Yang, Y.; Zhou, L.; Ren, L.; Wang, F.; Liu, R.; Pang, Z.; Deen, M.J. A novel cloud-based framework for the elderly healthcare services using digital twin. *IEEE Access* **2019**, *7*, 49088–49101. [CrossRef]
117. Erö, C.; Gewaltig, M.O.; Keller, D.; Markram, H. A cell atlas for the mouse brain. *Front. Neuroinform.* **2018**, *12*, 84. [CrossRef] [PubMed]
118. Shamanna, P.; Saboo, B.; Damodharan, S.; Mohammed, J.; Mohamed, M.; Poon, T.; Kleinman, N.; Thajudeen, M. Reducing HbA1c in type 2 diabetes using digital twin technology-enabled precision nutrition: A retrospective analysis. *Diabetes Ther.* **2020**, *11*, 2703–2714. [CrossRef] [PubMed]
119. Johnson, A.E.; Pollard, T.J.; Shen, L.; Lehman, L.w.H.; Feng, M.; Ghassemi, M.; Moody, B.; Szolovits, P.; Anthony Celi, L.; Mark, R.G. MIMIC-III, a freely accessible critical care database. *Sci. Data* **2016**, *3*, 1–9. [CrossRef] [PubMed]
120. The Cancer Genome Atlas (TCGA). Available online: https://www.cancer.gov/ccg/research/genome-sequencing/tcga (accessed on 21 June 2023).
121. The Human Connectome Project. Available online: https://www.humanconnectome.org/ (accessed on 21 June 2023).
122. Services, A.W. AWS IoT TwinMaker. Available online: https://aws.amazon.com/iot-twinmaker (accessed on 21 June 2023).
123. Azure Digital Twins Overview. Available online: https://learn.microsoft.com/en-us/azure/digital-twins/overview (accessed on 21 June 2023).
124. Supply Chain Twin Solution. Available online: https://cloud.google.com/solutions/supply-chain-twin (accessed on 21 June 2023).
125. NVIDIA Omniverse Digital Twins. Available online: https://docs.omniverse.nvidia.com/digital-twins/latest/index.html (accessed on 21 June 2023).