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Review

Industry 4.0 and Digitalisation in Healthcare

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Abstract: Industry 4.0 revolution in healthcare involves using a wide range of modern technologies including digitisation, artificial intelligence, user response data (ergonomics), human psychology, Internet of Things, Machine learning, Big data mining, augmented reality to name a few. The healthcare industry is undergoing a paradigm shift – thanks to Industry 4.0 which is providing better user comfort through proactive intervention in early detection and treatment of various diseases. The sector is now ready to make its next move towards Industry 5.0, but certain aspects need further consideration that motivated this review paper. As a fruitful outcome of this review, we surveyed modern trends in this arena of research and summarised the bits-and-bobs of new features to guide and prepare the sector towards Industry 5.0 ready healthcare system.

Keywords: Industry 4.0; Healthcare; Digitalisation; Internet of Things; Big Data

Citation: Lastname, F.; Lastname, F.; Lastname, F. Title. *Materials* **2022**, *15*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Firstname Lastname

Received: date
Accepted: date
Published: date

1. Introduction

4th Industrial Revolution, namely, Industry 4.0 on the footings of digitisation, artificial intelligence and 5G telecommunications is advancing healthcare to unprecedented comfort levels [1,2]. These factors have helped in many ways to combat the ongoing crisis the world is facing in the wake of COVID-19 pandemic [3–6]. In this context, Table 1 summarise various definitions used currently in the context of Industry 4.0 to explain many of its sub systems.

Different digital projects have been developed globally by incorporating digital diagnostic systems which has significantly improved the agility in the XRay and MRI investigations. This has in turn allowed quick diagnosis of patient's healthcare data both retrospectively as well as clinical anamnesis to provide prompt feedback [7,8]. A question worthy to be asked at this stage, what's next? The answer to this question primarily drove this review. As shown in figure 1, the review begins by providing an insight into the interoperable development of the current ecosystem involving people, industry, business and the government which forms the backbone of Industry 4.0 – in sharp contrast to the previous industrial revolutions. By now, machines have become sufficiently smarter to take decisions in real time and to feed those decisions through cloud-based technologies [9] using neural networks [10,11] and decision-support systems [12]. Figure 2 shows the core components and essential elements of an Industry 4.0 system .

Table 1. Definitions of critical elements in an Industry 4.0 system

Name	Alternative term	Definition	Ref.
Internet of Things	Industrial Internet of Things; IoT IIoT	A single device or a system of devices having network access and communication with information networks and internet.	[13–15]
Artificial intelligence	AI Deep Learning Machine Learning	AI is a collective term for computer systems that can sense their environment, think, learn, and can take an action in response to a stimulus or pre-assigned goals.	[16–21] [22–25]
Neural networks	Artificial Neural Network; ANN	Mathematical model or computing system, as well as its software or hardware implementation, built on the principle of organization and functioning of biological neural networks - networks of neurons of a living organism.	[10]
Blockchain	Cryptographic ledger	A continuous chain of blocks, containing all the records of transactions, and safe distribution among participants.	[26–28]
Additive manufacturing	Digital manufacturing, 3D Printing	The process of manufacturing parts, which is based on the creation of a three-dimensional physical object from a digital geometric model, by adding material in a layer-by-layer manner.	[29–34]
Advanced materials	Composites; High Entropy Alloys, Hybrid materials	New groups of materials, which are out of standard classification – metals/alloys, ceramics, polymers.	[32,35–44]
Radio-frequency identification	RFID	A communication system that stands for radio frequency identification method. This is a method whose task is to recognize living or inanimate objects using radio waves. Fingerprints or retina, voice, clothing is used as Auto-ID.	[45,46]
Big data analytics	Big Data; BDA	This technology deals with a large array of data, enabling to derive information relevant for rapid decision-making	[47–49]
Digital medicine	Digitalisation in medicine; Hospital 4.0 H-IoT	The collective term of Industry 4.0 technologies used in medicine.	[15,50,51]
Virtual & augmented reality (including medical application)	VR & AR	Perceived mixed reality created with the help of a computer using "augmented" (visual/audio) elements of perceived reality, when real objects are projected in the field of perception.	[52–55]
Virtual and VR Experiments	VE & VRE	Virtual experiments and experiments with body part surrogates.	[56–58]

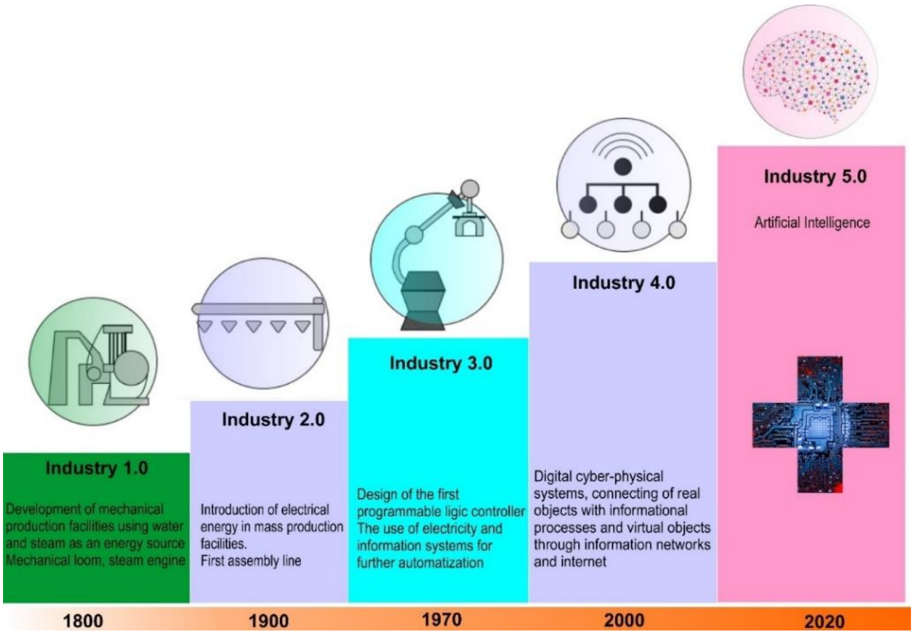

Figure 1. Evolution of industrial developments over time

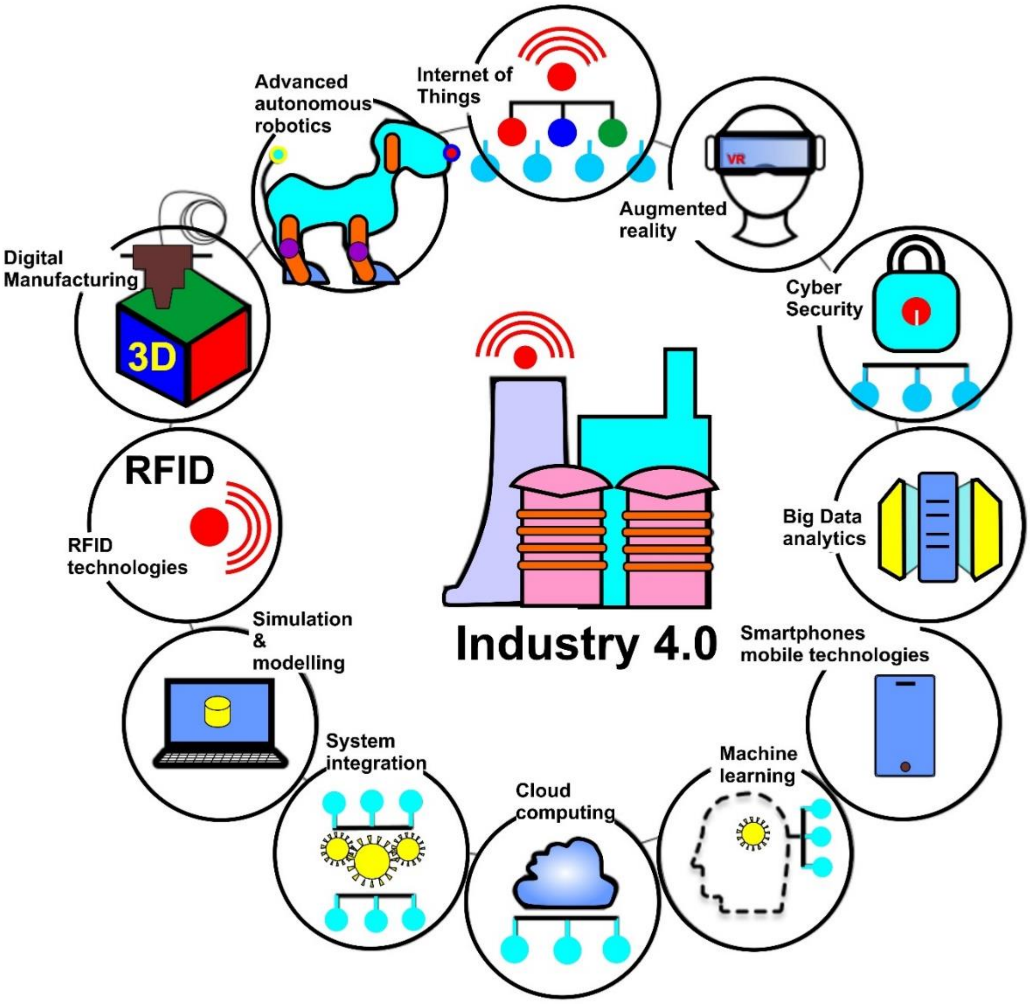

Figure 2. Building blocks of an Industry 4.0 system

In fact, the use of deep neural networks has enabled the AI to gain unprecedented quality of learning. For example, working with Alexa, Google Search and Yandex Disc has helped learning over time and the more it is used, the more the system becomes trained.

There are numerous examples of use of Internet of things (IoT) enabled systems which can be seen around in day-to-day life. An Amazon store without cash registers and sellers with capability of self-charging users based simply on their body movements is an excellent example while another involving use of IoT include Uber, Ola and GetTaxi. Recently Lv et al. [59] investigated the issue of quality service and network loading for next generation IoT systems. Additionally, Green aspects of Industry 4.0 are now also being explored [2,60].

Table 2 highlights state-of-the-art use of advanced technologies in healthcare and medicine revealed by different research papers. This review paper is the first to highlight the prospects of Industrial Internet of things (IIoT) in the healthcare sector and just second in the area of digital manufacturing. Table 2 highlights novelty of this review paper vis-a-vis increasing interest of the scientific community in this area.

Table 2: The key technologies discussed in the recent review publications (adapted and expanded from [15]). Here "V" stands for the presence, and "X" for the absence of the discussion on the relevant topics that makes an Industrial 4.0 system.

Ref	**IoT**	**IIoT**	**AI**			**Blockchain**	**Digital manufacturing**	**VR & AR**	**Hospital 4.0 H-IoT**	**RFID**	**Big Data**
			Deep Learning	**Machine Learning**	**Neural networks**						
[15]	V	X	V	V	V	V	X	V	V	V	V
[61]	V	X	X	V	X	X	X	X	X	X	X
[62]	V	X	X	X	X	X	X	X	X	X	X
[63]	V	X	V	V	X	X	X	X	X	X	V
[25]	V	X	V	V	X	X	X	X	X	X	X
[51]	V	X	V	V	X	X	V	X	V	X	V
[64]	V	X	X	V	V	X	X	X	X	X	V
[65]	V	X	X	X	X	X	X	X	V	V	V
[66]	V	X	X	X	X	X	X	X	X	X	X
[67]	V	X	V	V	V	X	X	X	V	X	X
[68]	V	X	X	X	X	X	X	X	X	X	X
This work	V	V	V	V	V	X	V	V	V	X	V

Recently Austin et al. [7] investigated collaboration between academia, SME's and digital health industries for the promotion of innovative digital solutions in healthcare. Qadri et al. [15] presented an extensive review of IoT applications in healthcare with careful articulation of the previous literature in this field. They introduced the term H-IoT (Healthcare IoT) to emphasize the importance of IoT in the field of healthcare and medicine. Marques et al. [62] presented a review on IoT applications in healthcare highlighting the need of medical professionals, students and engineers. They discussed the advantages of IoT platforms in achieving personalized healthcare and developing smart devices for diagnosis and monitoring. They also pointed out the limitations on social readiness [62]. Hau et al. [69] showed how digital tools of Industry 4.0 could be used to combat COVID-19 pandemic. Von Eiff et al. [51] in their short review discussed prospects of digitalisation in healthcare. Their work partly discussed digital development and the use of Industry 4.0 tools in medicine development.

From this brief discussion, the importance of Industry 4.0 in the healthcare sector is obvious. Thus, this review highlights the state-of-the-art in digitalisation of medicine and healthcare and alludes to the sharp transition this sector is facing while moving towards Industry 5.0. This review also aims to discuss the trends in digital medicine and healthcare and to provide future directions in this area.

2. Ingredients of an Industry 4.0 healthcare system

2.1. Internet of things (IoT)

IoT is a term that refers to any device with a network access [13,26,70,71]. Modern devices/objects/networks of objects/systems are equipped with sensors, software, and network equipments. These network equipments and sensors are capable of compiling and processing data arrays using Internet [2,70,72–75] protocols.

5G has made an enormous impact on the IoT technology and economy due to its superior level of connectivity and improved functionality. The key 5G technology drivers are superfast broadband, ultra-reliable low latency communication, massive machine-type communications, high reliability/availability, and efficient energy usage [73,76–78].

The main areas of application of 5G enabled IoT are tracking of goods and materials; asset monitoring; remote data collection; self-service systems; remote service delivery systems; real-time market data and flexible pricing models [71,79]. As per the review of Likens et al. [80], it would appear as shown in Fig 3 that the Internet of Things will lead to be the most promising techniques that will change the gamut for industries and academia in the Post 4th Industrial revolution era.

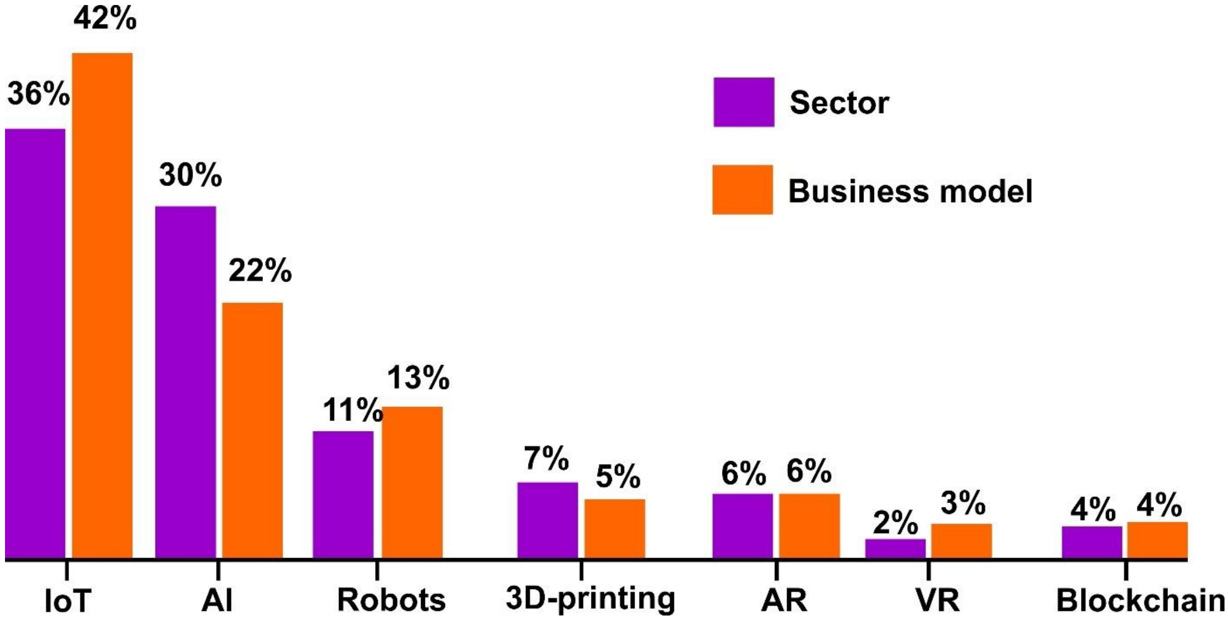

Figure 3. Leading position of IoT in Industry 4.0 structure [80]

Most modern industries utilise modelling and simulations for process monitoring, control, diagnosis, optimization and design. Industry 4.0 and massive digitization has made it possible to collect and process large arrays of data resulting in the development of data-driven decisions and modelling tools [81]. It is worth mentioning that the data-driven, statistical or empirical models do not require broad initial knowledge about the studied system, but strongly rely on the presence of collected data from the process [82]. Modern simulation tools are used for predicting natural disasters, which can lead to many victims (e.g., tsunami) [83–86]. A new trigger for modelling advancement reemerged in recent years due to the development of machine learning techniques and a variety of technologies of Industry 4.0. Big Data and modern modelling and analytical tools provide new horizons even to address the old legacy issues and also open new scenarios for realising out-of-the-box ideas.

2.2. Artificial Intelligence

Artificial intelligence (AI) allows computers to learn from their own experience, adapt to the given parameters and perform tasks that were previously only possible for human. In most AI implementations such as computer chess players, self-driving cars the role of deep learning and natural language processing is critical. AI allows automating repetitive learning and searching processes using data acquisition to identify the trends. Forms of AI in use today include digital assistants, chatbots, deep learning and machine learning amongst others [16–23,87–89].

2.3. Big Data analytics (BDA)

Big Data analytics (BDA) is one of the key components of Industry 4.0. Big Data technology deals with large arrays of data, enabling to derive the information relevant for rapid decision-making. The derived data is transformed to the relevant goal-oriented knowledge for achieving agility in problem-solving [47,48]. The successful application of BDA in online trade can be seen through AliExpress, Amazon, and eBay. Technologies for image data are also rapidly developing enabling target recognition, photo filtering, and stereoscopic three-dimensional (3D) contents [90–93].

2.4. Digital manufacturing and advanced materials processing

One of the main outcomes of the advances in digital manufacturing is the 3D printing technology, also called as additive manufacturing (AM) [29–33]. AM enables processing of polymers, ceramics, glass and metallic alloys. Using approaches such as the Design for Additive Manufacturing (DfAM) [94] and Materials Design by Additive Manufacturing (MaDe-by-AM) [95], novel materials can now be manufactured with ease, which include tailored composition as well as structural and functionally graded materials [32,35–39,96–98]. By shape and composition complexity, the success of design of new porous materials and metamaterials can also be realised. Moreover, the flexibility of manuvering printing head allows on-site printing of freeform shapes which are potentially useful to develop custom sized implants or prostheses [31,99,100]. Digitalisation of industrial manufacturing is developing due to the implementation of design strategies for new materials development [95,96,101,102]. Now, these additive technologies allow printing of concrete buildings/structures [103]. Additive manufacturing of concrete structures is much more promising for fast construction in complex nature environments compared to other techniques [104–106].

2.5. Green aspects of Industry 4.0

Among other aspects, green aspects of Industry 4.0 deserve a special mention. Some of those aspects in relation to the food-water-energy nexus are highlighted below:

1. The survival of humanity will largely depend on how we address the following concerns in the upcoming years:
- global energy shortage and depletion of raw materials (energy crisis) [107–109];
- reduction of arable land, decrease in soil fertility and food shortage (food crisis) [110];
- depleting availability of clean water [111]
- catastrophic state of the environment (ecological crisis) [60,112–114].
2. The main spheres of life have received a new form and content - industry, transport, the fuel and energy complex, the economy, public administration, security, etc. This is due to the penetration of digital technologies into everyday life and development of alternative energy and electrical vehicles [115].
3. The modern industrial development could not proceed without efficient re-use and recycling procedures [116–119].

3. Digitalisation in medicine

The term Medicine 4.0 is closely related to Industry 4.0: it describes the fourth stage in the development of medicines. Modern Medicines which emerged around 150 years ago are undergoing digital journey with help of robotics, internet and artificial intelligence. The introduction of AI system in medicine is one of the most important modern trends in world healthcare. Modern medical treatments cannot achieve their full potential without using advanced computing technologies. AI technologies are fundamentally changing the global healthcare system, allowing to radically redesign the system of medical diagnostics, the development of new drugs, advanced analysis, testing, treatment to enable advances in the field of transplantation surgeries [50,51,120,121]. Computational simulation using finite element analysis (FEA) is a crucial part of the digitalisation process in medicine [122,123]. FEA allows medical engineers / industrial designers to study many interrelated concepts including for instance, device stability and durability (e.g., patient-specific implant) to predict its end-of-life. FEA enables modelling of stresses within a material under different thermodynamic conditions[124]. In an FEA model, the part is simulated and analyzed using representative physical behavior [122,125–127]. Such approach demonstrates weak areas of the part, and it allows to redesign and strengthen the geometrical shape of it. Digitalisation and AI generally improve the quality of healthcare services while reducing costs for medical clinics. Fig.4 highlights key technologies enabling digitalisation of medicines.

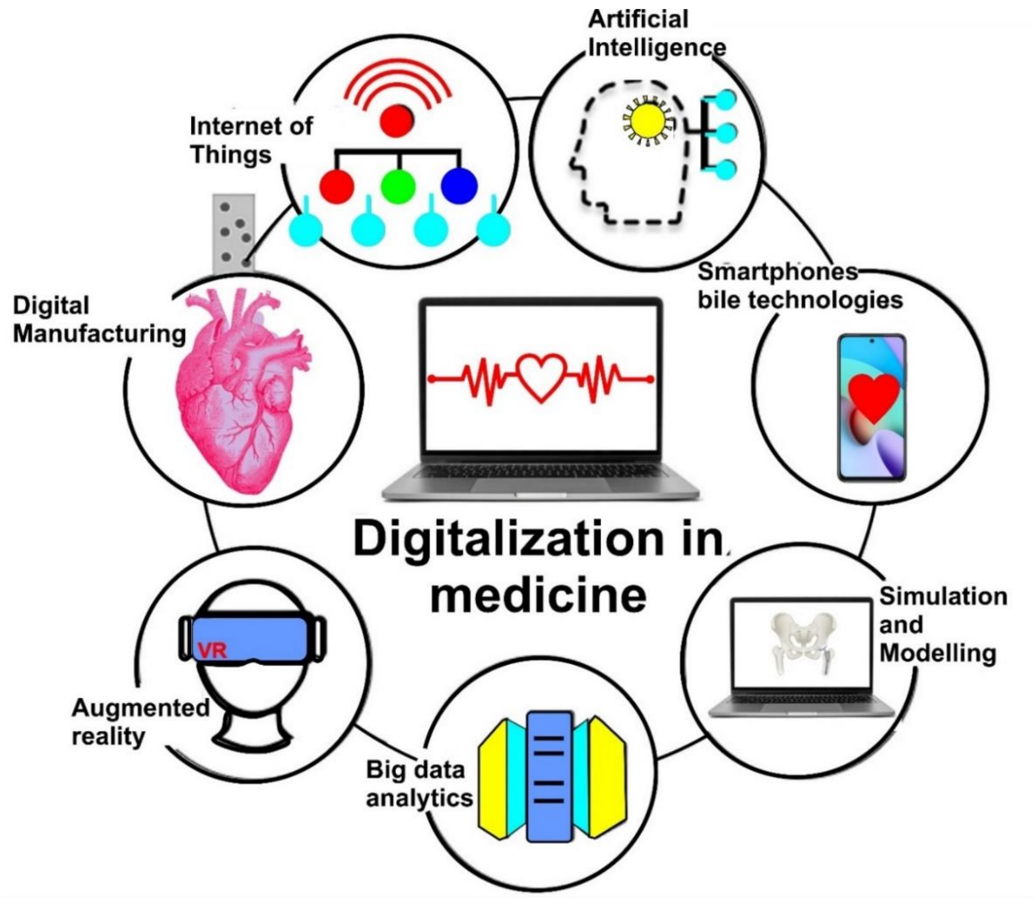

Figure 4. Digitalisation in medicine – main technologies.

3.1. On-demand healthcare

According to Fox et al. [128], consumers are increasingly using online platforms to obtain medical information due to the following reasons:

- 47% wishes to know more about their doctor

- 38% would like to check a hospital and its medical facilities
- 77% would prefer online medical appointments.

In the new regime of digital economy, medical professionals just like freelance professionals can provide their skills, talents, and expertise directly to the patients.

Several healthcare companies provide an online marketplace that connects medical workers directly with the required medical facilities. It results in a much more effective way to provide on-demand medical procedures and services to consumers. In turn, healthcare workers have now become a part of digital healthcare industry providing patient-oriented treatments [129].

3.2. Telemedicine

Telemedicine is a rather modern trend that became especially popular during the COVID19 pandemic [130]. Such an approach enables support and care of patients in a non-crucial state. Telemedicine minimises the number of contacts between ill patients. Moreover, such educational support is important for chronic patients, and to prevent diseases [131]. According to the data of John Hopkins, before first global lockdown in March 2020, the number of televisits were nearly 50-70 per month. By May 2020, this number radically increased to 94,000. Moreover, after the healthcare services were broadly reopened, the number of monthly visits remained about 35,000 [132].

Technologically, this kind of telecommunication provides direct transmission of medical information in various formats (medical history, laboratory data, X-ray images and CT scan results, video images, ultrasound, etc.), as well as real-time video conferencing between medical institutions or a doctor and patients.

The use of telemedicine enables providing consultative medical services in those areas where patients do not have the opportunity to receive the help of narrow specialists directly at a medical institution. Telemedicine is of no less importance even in developed countries. With its incorporation, treatment costs have significantly reduced, the quality of diagnostics has improved and remote monitoring of health has become accessible. This is especially important for elderly patients and patients with chronic diseases. For example, St. Luke University Health Network in Pennsylvania regularly hosts video conferencing to help elderly patients. They recognize that this social group is less likely to use applications and is more comfortable with technologies that target desktops or laptops.

According to the Global Telemedicine Market Outlook, the global telemedicine market reached $ 56.2 billion in 2020, and is expected to reach $ 175.5 billion by 2026. The annual growth rate is about 19.2% [133]. Patient telemonitoring accounts for the main share of the world market are in a ratio of 48% to 32% (see Table 3). The leading countries in terms of spending on telemedicine and the development of the telemedicine technology market are China and the United States [133].

Table 3: Telemedicine directions

Telemedicine directions	Application
Teleconcilium	Communication between consultant doctors from different medical institutions, or different professional areas, and the attending doctor
Telemonitoring	Monitoring patients with chronic diseases
Teleconsultation	Remote consultations "doctor-patient"
Medical archive, patient's personal account	Maintaining and storing patient health records
Data integration	The ability to merge and exchange information between different clinics, health authorities, insurance companies, etc.
Maintaining a register, making an appointment with a doctor	Remote appointment with a doctor

Remote access to equipment	Control over the condition of the equipment, remote diagnosis of the patient
Tele-teaching	Conducting lectures, video seminars, conferences, inclusions from operating rooms

The global telemedicine market can be segmented according to several criteria, including:

- The nature of remote interaction (clinic - clinic, clinic - patient's home);
- Technological parameters of interaction (monitoring systems, communication and communication channels, measuring instruments and sensors, video conferencing systems, databases, mobile and "wearable" technologies);
- Purpose of application (medical education, diagnostics, monitoring, consultation, treatment).

Depending on this, different approaches to design and development of software solutions are augmented and, accordingly, different tools are used. However, as these segments are closely intertwined, the developer must have skills and expertise in a wide variety of development areas, including experience with embedded solutions, mobile, cloud technologies and protocols specific to the medical industry. It can be concluded that for the telemedicine technologies to flourish, it is crucial to provide:

- Remote interaction of medical workers with each other, with patients and (or) their legal representatives;
- Identification and authentication of specified persons;
- Documenting their actions during consultations and remote medical monitoring of the patient's health.

3.3. Data privacy & cybersecurity in medicine and healthcare

With the progress of big data and its advancement into medical innovation, there are potential risks to patient data privacy [134]. Healthcare is a prime target for cyberattacks, and even with continued investment in cyber security, critical vulnerabilities remain in many of the medical devices that hospitals relies on to treat patients [135]. Modern healthcare requires advanced solutions that reduce risks due to cyber attacks. Alongside this, the GDPR patient sensitive data also needs to be protected so that privacy of patients is not compromised.

For healthcare organizations, it is extremely important to ensure proper handling of patient data not only according to GDPR but also because it’s crucial for transparency with patients [136]. It can be said that the narrow scope of data privacy laws can be an issue. That can be pointed to the U.S. health-data privacy law (HIPAA), which regulates data between healthcare professionals and patients, but not un-identified data. *e.g.*, the data shared with a fitness trainer, tracking from smartphones, and data from various apps can be considered as unprotected .

However, the relevant laws have become more and more effective in medical data privacy. The European Union’s General Data Protection Regulation passed in 2016 is a good example. The EU law now requires data processors and controllers to provide users with their own data, clearly disclose data collection, set high-privacy defaults, and more.

Healthcare gadgets are not fully unprotected, similar to other IoT devices, and that affects data privacy and even safety of the device. Risks and threats always exist. The trends in the rapid growth of the audience facing cyberattacks, can be explained by the growing usage of electronic medical records andan increase in the number of medical equipment and IoT devices connected to hospital networks. Additionally, the spread of viruses that interfere with the work of not only computers but also medical devices is a continual problem. However, to eliminate such issues, cybersecurity is actively regulated by the healthcare and government-associated organizations, e.g., like FDA [137]. It results in reduced risks of potential cybersecurity threats in legally marketed healthcare devices.

It can be concluded that there is a necessity of regulated procedures to protect patient data [138].

3.4. Big Data Analytics (BDA) in healthcare

BDA in healthcare enables improved diagnostic practice efficiency. Moreover, even the therapeutic treatment based on BDA is much more accurate. It is especially relevant for cases with medical tumor including hard cancer pathologies. The main things of extreme importance in this regard are on-time diagnosis and accurate choice of treatment [50,121,139].

BDA is advantageous for genetic analysis to compute genetic pathology and generating possible problem-oriented knowledge [121,140]. It should be considered that even superfast computers may take hours to do an intense data analysis which can now be accelerated using GPU computing [141].

BDA helps to decrease the rate of medication errors and to predict the future admission rates [50]. It can be concluded that BDA helps to make healthcare more predictive. Predictive analysis about burden on healthcare system and admission loading allows to make services more effective and to optimize resources for active deployment.

It should also be considered, that predictive analysis could help companies to smoothly mobilise the manpower resources by predictively knowing possible outbreaks of colds/flu that could lead to manpower shortage.

Pharmaceutical manufacturers are looking to gain access to patient health data and are therefore striking deals with technical companies knowledgeable in BDA - a tool that opens up new possibilities for understanding how drug works in real life. One recent example is the Roche deal announced in 2018, wherein the company acquired all shares of Flatiron Health, a clinical data collection company for cancer patients, by paying USD 2 billion [142]. Examining real-world evidence allows pharmaceutical manufacturers to prove the usefulness and value of their drugs. The most active research in this area is carried out in the field of oncology, heart disease, and respiratory disorders. Actual drug use data is collected outside of the traditional randomized clinical trials, which are today’s gold standard for drug evaluation. Neural networks is now effectively used for the development of automated drug discovery. Researchers and medicinal chemists are working together to identify problematic issues and create more proficient models for newer drug design [143]. Advances in interdisciplinary field that combine computational and genomic technologies are expected to lead to newer horizons in personalized medicine [121,140,144,145].

In the United States, the Human Microbiome Project was launched simultaneously with the renowned Human Genome Project [146]. During its implementation, a special Data Analysis and Coordination Center was created within the framework of the US National Institutes of Health. A joint Chinese-European project MetaHit is being implemented, where active research is being carried out in this direction.

3.5. Augmented Reality and Virtual Reality (AR &VR)

Smart glasses with the AR-function allow warehouse workers to achieve a higher level of accuracy. For critical-life applications like aircraft-making, AR helps manufacturers to precisely assemble and repair planes and to achieve improved reliability during repairs [147]. VR is transforming the healthcare and changing the way patients are being treated. For millions of people suffering from chronic pain, VR is a working alternative to drug medication. VR is a safe and efficient treatment for pain, and powerful rehabilitation instrument for anxiety, post-traumatic syndrome, stress and stroke [54]. Healthcare professionals and medical students use VR simulations for improving their skills and for complex surgery planning. The global virtual and augmented reality healthcare market is expected to reach USD 5.1 billion by 2025 [148]. Recently, Nevada Spine Clinic surgeons performed a posterior lumbar fusion procedure using a Medtronic Mazor X robotic platform and an xvision augmented reality headset [149]. This is usually a rather invasive and time-consuming operation, lasting six to seven hours, but in this case, using the xvision headset in tandem with Mazor X robotic platform, the surgery took less than two hours. Xvision headset allows the surgeon and his team to locate implants more accurately which would have otherwise taken longer time. Before the procedure, the orthopedic surgeon and neurological surgeon used a robotic platform to carefully plan the exact placement of the implant and screw system. During surgery, an augmented reality headset allows the surgeon to refer to a 3D anatomical plan that has been previously created. As a result, the entire process becomes minimally invasive and much more efficient. The incidence of complications and the recovery time of patients reduced sharply due to the reduction in the time spent in the operation theatre, as well as the minor damage to soft tissues compared to that with the open access.

In late September 2021, Kinomatic launched a virtual reality-based scaffolding platform that allows surgeons to develop customized plans for knee and hip arthroplasty [150]. This platform can work with any implant system and can be adapted for a variety of surgical techniques and surgical approaches. The company's patented VR app allows surgeons to view and manipulate surgical plans in unparalleled details. The platform supports pre-operative modeling for knee and hip arthroplasty using preferred implants, surgical technique and specifications. Patients receive high-resolution computed tomography, which is then converted into an accurate 3D model of the patient's joint, after completion of the simulation. The surgeon can determine the exact size and orientation of the implant, which will most accurately recreate the natural anatomy of the joint.

VR headsets are used for sports and fitness promotion, and these helps children with autism to learn how to orient in the real world [151]. Application of VR training for patients with autism results in improvement of daily living skills [151]. VR and AR possess the potential to help older adults to overcome mobility issues, cognitive ability and socialization limitations [124]. It was recently showed as to how translational potential of VR can be used to reduce suicide risks [148]. The VR factors like dissociation and derealization allowed to simulate the experience of a suicide opportunity and to reduce this risk. Virtual reality not only helps humans but also enables investigation of the behavior and environment of animals [55].

3.6. VR experiments

Development in computational technologies have led to new ways of supporting research and development work which are now also regarded as “Virtual Experiments”. They are fastly emerging and rapidly developing tools within different applications of virtual reality (VR) including medicine [153]. One can briefly define “VR experiment” (VRE) as an advanced tool of computer modelling. Due to the advantages of modern technology in computation and visualization, VRE has already started to play significant role in cases where real experiments are extremely dangerous or prohibitively costly. One such case is related to research in safety, medicine and healthcare. In that aspect, VR experiments can be regarded as non-intrusive and non-invasive. This method is based on the development and utilisation of complex, advanced models of human body and its parts. These models are further used for testing various “what if” scenarios in both static and dynamic cases, making predictions about, how the system called “human body” will react to different situations, and how various equipments designed to prevent injuries, or help with surgical invasions will work. Today such models have become so sophisticated that one can speak about “digital twins” [154,155], and the results of modelling are coming close to experimentation. One of the examples of true success stories in the developments of advanced digital twins and virtual experimentation in medical and safety research is modern achievement in the studies of traumatic brain injuries, and in the development of modern protection helmets [156–160].

Unfortunately, computer modelling in general, and virtual experimentation as its part are not free of problems. One of them is that a model cannot be tested from within a model. Further developments in this area are represented by “surrogate twins”. These are body part surrogates (physical models) manufactured using additive manufacturing, another modern technology enabled by digitization [57,58,161]. Such surrogates can have the same shapes and outlines as their digital counterparts as they use same CAD files (see Fig. 5). Properties of materials used in the surrogate mimic soft human tissues and bones, and can be exactly characterized. Surrogates often have encapsulated sensors and experiments in realistic conditions are performed with them. Experiments with surrogate twins are also performed without endangering humans, and collected data are equally useful for both research and development, and for cross-validation of both digital and physical models. Significant progress in the application of surrogate twins is achieved in the area of safety research and studies of the injury mechanisms [57,58,160,161].

Figure 5. Example of body-part surrogate for VRE. Photo courtesy of Prof. A. Koptyug, SportsTech Research Center, Mid Sweden University, Sweden

These methods harness the power of digitization - from scanning the shapes to making surrogates of different complexity with embedded sensors using additive manufacturing and synthetic materials mimicking different tissues. Such an innovative approach allows to design of new devices with a high degree of efficacy. The application of surrogate twins is helpful in both civil and military areas.

3.7. Wearable medical devices

Wearable medical devices are modern trends in healthcare. They help to collect health data to monitor patients health. These devices provide day to day health data which is an active monitoring tool compared to once-a-year or once-a-month clinical checkup.

Medical companies are investing in wearable smart devices that can provide up-to-date monitoring of high-risk patients, preventing a major health episode. According to a recent report, the wearable medical device market is expected to reach to USD 46.6 million by 2025, a spectacular jump from almost USD 8 million in 2017 [162].Some of the most common of devices include:

- Smart watches with heart rate sensors and exercise tracking.
- Sweat meters – used for diabetics to monitor blood sugar levels.
- Smart patches to measure hydration levels, body temperature, heart rate, and other biometric parameters.
- Oximeters measures the amount of oxygen in the blood, which is relevant to patients with respiratory illnesses *e.g.,* asthma.
- Headphones to monitor blood pressure.
- Biosensors in modern devices are able to not only read pulse, steps and calories, but it can also measure hydration, electrolyte levels, blood pressure, and obtain electrocardiogram (ECG), determine muscle load, human strength and fatigue level.

There are many tangible benefits for healthcare companies in spreading the use of wearable devices.

- These devices make patients themselves responsible to monitor their action leading to a certain health state.
- People are attracted to do more sports and remain fit by active monitoring of their results thus setting new goals. Such practice decreases the risks of obesity and reduces the burden on the healthcare system.
- The relevant medical information is on demand for insurance companies to assess the real risks for patients health.
- Patients who uses technologies for preventive treatment and monitoring, are even offered discounts in their health insurance.

3.8. 3D imaging and prototyping

The whole complex of assisted three-dimensional techniques is used in 3D prototyping as described below:

- 3D visualization / medical image processing of a medical problem using medical computed tomography, MRI, and X-ray examination tools [120,139]. Machine learning can be used for medical image processing. After the required features from a particular medical case are extracted, this data can be processed for accurate decision-making [99];
- 3D-modelling using modern digital tools like Magics by Materialise and analogs. The complex model of a damaged area could be realized for further surgical planning. It is especially relevant for complex cancer cases where a surgeon needs to try resection from different sides of a tumor.
- 3D-planning digital systems enable online communication between surgeon and engineer responsible for 3D printing of the implant;
- 3D-prototyping using polymer printers improves accuracy of custom designed metal implants [26,100,146];
- 3D-printing of organs and tissues also called bio-printing is a rapidly developing application for meeting the demands of modern transplantology [163,164].

3D printing is used for additive manufacturing of patient-specific metal/ceramics implants; for stereolithography of drug delivery systems; polymer/metal-based individual prosthesis; and individual surgeon tools design [121].

3.9. Machine learning & deep learning

In biomedicine, machine learning and deep learning are used to simulate human knowledge and for complex analysis of special medical data, and biomedical and biophysical processes in the human body [15]. Here AI works for the systematization of assisted behavioral processes using complex machine learning computing (see Table 4).

Table 4. Areas leveraging AI in medicine

Goals	Effect
Analysis (including cross-sectional) of population data, registration data, omix data, social networks	New correlations for further scientific research and medical applications
Analysis of medical images, creation of a system with an automatic initial level of description and interpretation of results	Improving the speed and quality of medical decision-making
Smart scripts for patient survey	
Clinical decision support system (CDSS), platforms for organizing CDSS as services	
Operational quality control and intelligent benchmarking of healthcare delivery in an institution	Improving the speed and quality of control and expert work
Control of long-term consequences of medical care	Changing the system for assessing and analysing the provision of medical care

Goals	Effect
Systems for increasing adherence of healthy lifestyle citizens and patients to prescribed treatment	Reducing morbidity and improving the effectiveness of treatment
Modelling the activities of a medical organization	Improving the quality of management, optimizing costs
Wearable and other mobile medical devices for remote monitoring	Online / regular monitoring of health indicators
Smart training medical simulators	Improving the quality of training of medical workers
Medical data visualization, including smart navigation during surgical interventions	Improving the speed and quality of medical decision-making, medical care

The main goal of AI in biomedicine is to establish relationships between patient's health, diagnostics, selected treatment program, and follow-up outcomes. Due to AI, the effectiveness of diagnostics and selected therapeutic treatment could be radically improved [25]. Machine learning for such diagnostic tools as electrocardiography (ECG) and electroencephalography (EEG) supports doctors in screening and recognition of the disease, and possible risks reduction [165]. The use of machine learning enables processing of the extracted data, like heart rate, pulse, intervals, and variability from ECG/EEG data, etc. A combination of these parameters can help to identify the existence of heart-related diseases [166].

The diagnosis of cancerous tumors by applying AI (deep learning, image classification, object recognition) to the MRI images is not inferior to the conclusions of highly qualified radiologists in terms of accuracy. The AI algorithms are also an effective solution for proper patient-oriented and patient-specific drug selection.

The implementation of novel digital tools are sometimes united by the concept of "hospital 4.0" emphasizing the digital character of the progress in medicine [50,51,121]. Areas of using AI in medicine can be specified as follows:

- At the design level: predicting diseases, identifying groups of patients with high risk of diseases, organizing preventive measures.
- At the production level: automation and optimization of processes in hospitals, automation and improvement of diagnostic accuracy.
- At the promotion level: price management, risk reduction for patients.
- At the level of service delivery: adaptation of therapy and the composition of drugs for each individual patient, the use of virtual assistants for planning a patient's route in a polyclinic or hospital.

However, at present, the healthcare community has no unanimous opinion if digitalisation in medicine is necessary and helpful for all healthcare industries, or it is being forced on the medical community just because of the general trends. It means that deep academic research on this topic is on demand by health care specialists [51]. The limitations of digitisation stems from the massive requirements of hardware upgradation. Traditionally, mechanical parts such as bolts and nuts of an instrument can simply be taken off and replaced with new, but with electronics this is not the case. Hardwares now very quickly get obsolete, and their software or firmware updates are no more available after their intended design period. Moreover, the electronic circuits themselves become dated as they can no longer function at the same speeds as what a hardware available after a certain period of time can do. Consequently, despite having the so called “right to repair” the repairs of digital hardware’s is almost impossible and is not cost-effective even if pursued. This grim situation is leading the accelerated generatin of electronic waste and these aspects needs serious considerations in view of the growing focus over “net zero” economy.

5. Summary

In the post era of the 4th Industrial Revolution, the term "5th Industrial Revolution" started to be used in scientific reported data [167]. In healthcare, the terms "hospital 4.0" and "medicine 4.0" are gaining popularity by highlighting new era in medicine and healthcare assisted spheres.The main trends in technological and economic development that can be observed are that the advent of Industrial Internet of Things is a very specific economic and technological evolution that requires new actions and will enable incredible development. Now the business strategy and administration need to be customer-oriented through new relationships provided by IIoT. It is also noteworthy that Artificial intelligence, Big Data Analytics, and robotics will be enabling the very fibre of everyday's life, and especially in safety-critical applications. Besides, "Virtual Experiments" and experiments with body part surrogates applied for medicine and healthcare represent true power of digitization - from scanning the shapes to making surrogates of different complexity with embedded sensors using additive manufacturing and synthetic materials, mimicking different tissues. With the use of finite element modeling, "Virtual Experiments" can achieve newer horizon, hitherto, not realized.

In the time to come, newer forms of prescription will become the most exciting medical advances. The tablets with support of microscopic sensors can provide doctors with the best information about the condition of patient's internal organs. In this regard, digital techniques will pave the way for patient-specific, need-oriented, and predictive/provision-based approaches for all spectra of the medical industry. 3D printing and digital health devices (IoT). BDA will lead various areas of medical digitalisation, having a significant influence on the healthcare industry evolution and development. According to analysts' forecast, the market volume of the Internet of Things in medicine by 2022 will exceed USD 158 billion. The average market growth rate (CAGR) in the period from 2016 to 2022 was estimated by Market Research Engine experts will be 30.8% [168]. This review maps the breakthrough technologies of digitalised healthcare as important ingredients.

In the area of Big Data and modern modelling, the medical industry would benefit from digital tools tailoring existing technology to the needs of the industry, healthcare professionals, and patients.

Among the factors contributing to the increase in medical IoT costs on a global scale are the growing number of chronic diseases, the introduction of favourable initiatives by governments in various countries and the evolution of artificial intelligence technologies. The current assessments suggest that further integration of digital instruments and technologies will improve the efficiency of healthcare system, development of patient-oriented innovations, the transformation of business models, and workspace new organization.

It is necessary to note that the digital technologies discussed in this paper relates to the most successful industrial application up to now. However, both international cooperation and organizational efforts are required for deeper research and further digitalisation. Moreover, it is important to mention that higher awareness from society on digitalisation and Industry 4.0 technologies through improved education and development of "digital" professionals will be of great importance.

Future research directions will cover the aforementioned technologies related to digitalisation in medicine and healthcare, including virtual and VR experiments, biological additive manufacturing progress, development of cybersecurity, and pandemic predictive Big Data analysis.

Author Contributions: Conceptualization and methodology, V.P., E.V.K. and S.G.; resources, V.P, E.V.K., A.S., and S.G.; writing—original draft preparation, V.P., E.V.K., N.K.K., A.S., S.I.S., and S.G.; writing—review and editing, V.P., N.K.K., and S.G.; visualization, V.P., N.K.K., S.G.; supervision, V.P., E.V.K., S.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Not applicable.

Acknowledgments: SG greatly acknowledge the financial support provided by the UKRI via Grants No. EP/L016567/1, EP/S013652/1, EP/S036180/1, EP/T001100/1 and EP/T024607/1, Transformation Foundation Industries NetworkPlus feasibility study award to LSBU (EP/V026402/1), the Royal Academy of Engineering via Grants No. IAPP18-19\295 and TSP1332, EURAMET EMPIR A185 (2018), the EU Cost Action (CA15102, CA18125, CA18224 and CA16235) and the Newton Fellowship award from the Royal Society (NIF\R1\191571). Wherever applicable, the work made use of Isambard Bristol, UK supercomputing service accessed by a Resource Allocation Panel (RAP) grant as well as ARCHER resources (Project e648).

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

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