5G in Healthcare: From COVID-19 to Future Challenges

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***Abstract*—Worldwide up to May 2022 there have been 515 million cases of COVID-19 infection and over 6 million deaths. The World Health Organization estimated that 115,000 healthcare workers died from COVID-19 from January 2020 to May 2021. This toll on human lives prompted this review on 5G based networking primarily on major components of healthcare delivery: diagnosis, patient monitoring, contact tracing, diagnostic imaging tests, vaccines distribution, emergency medical services, telesurgery and robot-assisted tele-ultrasound. The positive impact of 5G as core technology for COVID-19 applications enabled exchange of huge data sets in fangcang (cabin) hospitals and real-time contact tracing, while the low latency enhanced robot-assisted tele-ultrasound, and telementoring during ophthalmic surgery. In other instances, 5G provided a supportive technology for applications related to COVID-19, e.g., patient monitoring. The feasibility of 5G telesurgery was proven, albeit by a few studies on real patients, in very low samples size in most instances. The important future applications of 5G in healthcare include surveillance of elderly people, the immunosuppressed, and nano- oncology for Internet of Nano Things (IoNT). Issues remain and these require resolution before routine clinical adoption. These include infrastructure and coverage; health risks; security and privacy protection of patients' data; 5G implementation with artificial intelligence, blockchain, and IoT; validation, patient acceptance and training of end-users on these technologies.**

***Index Terms*—5G medicine, 5G healthcare, 5G COVID-19, COVID-19 telemedicine.**

Manuscript received 11 December 2021; revised 5 May 2022; accepted 2 June 2022. Date of publication 8 June 2022; date of current version 9 August 2022. *(Corresponding author: Andrea Moglia.)*

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Digital Object Identifier 10.1109/JBHI.2022.3181205

I. Introduction

TELEMEDICINE was made possible by advances in devices and connectivity over the last two centuries [1]. In 1860s during the civil war, the telegraph was used to transmit messages concerning wounded soldiers to remote medical teams [1]. In 1905, William Einthoven developed the first electrocardiogram and successfully transmitted the heart sounds between his laboratory and a hospital, both located in Leiden (Holland) [2]. The first transatlantic transmission of medical data was reported in 1950 when heart sound was transmitted between New York and Europe (Paris and Rome) [3]. The term telemedicine was coined by Bird when in 1974 real-time examination was reported on 1000 patients between the emergency ward at Massachusetts General Hospital and Boston airport by using television and audio-visual circuits [1]. In 2001 the first transatlantic telesurgery was performed by a surgeon in New York on a patient in Strasbourg (France) [4]. The operation was conducted on a Zeus surgical robotic system and lasted 54 minutes. It was possible by virtue of a dedicated 10 megabits per second direct fiberoptic connection. This surgery was later termed 'Lindberg Operation' from the first solo transatlantic flight by Charles Lindberg in 1927 [4]. The advent of smartphones at the end of the first decade of 2000s opened new scenarios of mobile software (called apps) in many fields, including healthcare. Today, the almost ubiquitous availability of wireless connections and the availability of accurate artificial intelligence (AI) models enable the development of novel telemedicine applications, e.g., to boost the efficiency of the triage process of patients with large vessel occlusion who are at high risk of stroke [5].

Consequently, the fifth generation of wireless networks (5G), AI, the Internet of Things (IoT), and blockchain have generated huge interest in the development of new applications in telemedicine [6].

This was further accelerated when the SARS-CoV-2 pandemic broke out in Wuhan (China), where the city's healthcare system was overwhelmed. A disaster response was quickly established, including the new 5G networking telecommunications which, by virtue of its huge bandwidth, reduced significantly the local disruption of pandemic by providing real-time access and 'visibility' to all aspects of healthcare delivery, not possible with 4G [7], [8].

Concurrently, progresses in AI improved disease diagnosis by medical imaging and thermal measurement based on computer vision and infrared technology. AI has been used for COVID-19 situational analysis: tagging, contact tracing and monitoring of

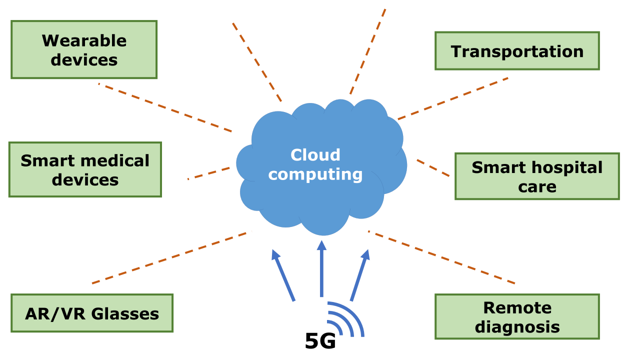

Fig. 1. The 5G ecosystem in healthcare.

personnel movement and infected patients, just-in-time logistics, inventory control, asset tracking and materials allocation.

During the pandemic, telemedicine in addition to delivering medical assistance to remote regions, became a crucial component of healthcare and was adopted worldwide in view of its efficacy and ability for triage of acute patients before arrival to hospitals. Additionally, telemedicine avoids unnecessary visits and reduces exposure risks [1], [9]–[11].

According to the World Health Organization 115000 health care workers died from COVID-19 from January 2020 to May 2021 [12]. As of May 4, 2022 there have been 515 million cases of COVID-19 infection and over 6 million deaths in the world [13].

The SARS-CoV-2 disease is one of the earliest examples of emergency use of 5G technology for major healthcare crises on a global scale, involving seriously ill patients, not only as a communication tool, but also as a fundamental infrastructure, in providing the necessary systems integration of the multiple informatics technologies. The existing 4G networks were manifestly insufficient in coping with the greatly enhanced communication needs caused by the SARS-CoV-2 pandemic across all activities of modern society: businesses, schooling, research, healthcare and personal/ family communications, as all activities of modern society battled for a share of the limited available bandwidth [12]. In contrast, 5G can reach a speed exceeding one Gb/s with an extremely low latency ($<$ one ms) [14], [15]. However, because 5G transmits at higher frequencies than 4G, signal degradation poses a greater challenge, requiring densely populated ‘base stations’ (approximately every few hundred meters instead of kilometers in the case of 4G) [16].

5G networks are able not only to connect human to humans but also ‘smart devices’, including 14.2 billion of IoT devices, with projections of 25 billion by 2025 and 600 billion by 2030. In addition, there exist currently a massive ongoing data acquisition, continuous monitoring (by micro/nano-sensors) from machines (devices, equipment, systems) or living systems including humans, all linked together by Global Positioning System (GPS) for precise geolocation (Fig. 1).

5G networks have enabled multiple simultaneous connection of devices which one report named ‘Internet of Actions’, thereby providing significantly more intelligent service in a fully automated environment [17], [18]. The authors of such seminal publications conclude that this new era of smart connectivity signifies that cybersecurity has extended to physical space, with life-threatening situations with the potential for mass casualties/ deaths, and quote as a pertinent example, autopilot hacking [17], [18]. Indeed, it is not surprising that the total end-to-end distributed security strategy has been earmarked as one of the key research and development areas requiring multi center R&D collaboration across major countries (especially China and USA) in the 5G and Beyond-5G (B5G) era [19].

The review is divided into several sections: i) applications for COVID-19 with 5G as core technology, ii) applications for COVID-19 with 5G as supportive technology, iii) other applications of 5G, iv) discussion, v) future opportunities, and vi) open challenges.

II. Search Strategy

In October 2021 a literature search was performed on PubMed, Scopus, and IEEE Xplore for published articles in the last five years. It was limited to articles in English language with an abstract and published in peer-reviewed journals. Search was performed by title or abstract, utilizing keywords, subject headings, and Boolean operators. Relevant abstracts and articles were examined to find alternative keywords. Wildcard searches were used to find variations of the search terms. The search was performed as follows: 5G AND (medic∗ OR healthcare OR telemedic∗ OR COVID-19 OR emergency medical service∗ OR telesurg∗ OR telediagnos∗ OR telecardio∗ OR teleconsult∗ OR telemonitor∗ OR teleoperate∗ OR teleradiol∗). The search was supplemented by checking published reviews, and their references. Exclusion criteria were reviews, letters, non-peer reviewed articles, conference abstracts and proceedings. Identified articles were screened by title and abstract, followed by full text review, data extraction, and review of references.

III. Applications for COVID-19 (5G as Core Technology)

A. Fangcang Hospitals

These are large, temporary hospitals built by converting public venues, such as stadiums and exhibition centres into healthcare facilities to treat and isolate patients suffering from COVID-19 and requiring hospital admission. A Fangfang (cabin) hospital is a fast-deploying mobile medical and surgical unit with medical and nursing staff, diagnostic laboratory and imaging facilities [8]. The first Fangcang hospital was established within 29 hours in February 2020 in Wuhan and provided 4000 beds [20]. At the same time, the Chinese government built over 20 such hospitals, all connected by 5G within 48 hours. They were largely engaged in blood testing, mobile computed tomography (CT) scanning, and administration of oral medicines. This effort was characterized by i) a rapid system construction; ii) zero maintenance of network and terminal devices; and iii) reduced risk of cross infection (as the entire communication was electronic and virtually

TABLE I
STUDIES ON 5G FOR COVID-19 APPLICATIONS

Study	Country	Application	Number of patients	Distance	Latency	Speed
Wang et al, 2020 [21]	China	Ultrasound	1	700 km	--	930 and 132 Mbps for the physician and patient sites
Wu et al, 2020 [22]	China	Ultrasound	4	54 km - 1,773 km	23-30 ms	930 Mbps (download) and 130 Mbps (upload)
Yu et al, 2020 [23]	China	Ultrasound	2	700 km	--	--
Ye et al, 2021 [24]	China	Ultrasound	23	560 km	--	930 Mbps (download) and 132 Mbps (upload)
Duan et al, 2021 [25]	China	Ultrasound	32	--	< 200 ms	580 Mbps (download) and 92 Mbps (upload)
Chen et al, 2021 [27]	China	Teleretinal laser surgery	6	1,200 km	20 ms	854 MB/s (download) and 88 MB/s (upload)

paperless), its major benefit was minimal unprotected physical interaction of doctors and nurses with seriously ill patients [8].

B. Radiology: Robot-Assisted Tele-Ultrasound

There has been much interest in robot-assisted tele-ultrasound during COVID-19 pandemic [21]–[24]. Compared with CT, ultrasound has the advantages of absence of ionizing radiation, and ease of use by professional ultrasonographers [23]. The studies on 5G in robot-assisted tele-ultrasound for COVID-19 are summarized in Table I.

Robot-assisted tele-ultrasound showed high image quality score (4.73 out of 5) on 32 patients for examinations of the liver, gallbladder, pancreas, spleen, kidney using MGIUS-R3 robotic tele-echography system by MGI Tech Co, Ltd (Shenzhen, China) [25]. The feasibility of this imaging modality was demonstrated on an 81year old man in Wuhan with the physician operating a MGIUS-R3 robotic tele-echography system from Zhejiang province, some 700 km from the patient [21]. In another study, four patients hospitalized in isolation wards were evaluated by robot-assisted tele-ultrasound enabling expert remote consultation for cardiopulmonary assessment by lung ultrasound, echocardiography, and blood volume assessment [22].

In another report, the diagnosis of COVID-19 by robot-assisted tele-ultrasound in two patients was consistent with that obtained by CT [23]. A recent study on robot-assisted tele-ultrasound system was performed in Wuhan on 23 patients with COVID-19 (12 non-severe and 11 severe disease) by an expert controlling MGIUS-R3 system in in Hangzhou (Zhejiang, China), some 560 km from the patients.

The authors reported that although they obtained excellent results in COVID-19 detection, the 5G robot-assisted remote tele-ultrasound system was still in its infancy, and has several limitations, including restriction of patient positioning during the examination in critically ill patients, limited operating angle of the robotic arm, and use of a single ultrasound probe [24].

C. Contact Tracing

5G has been used also to ensure privacy-preserving contact tracing by a system with decentralized architecture involving users, medical centres, fog nodes, medical organization, and blockchain [26]. The medical centre is responsible for registration and the fog nodes are beside checkpoints for body temperature measurement. Users communicated their encrypted identity and position through their smartphones. This decentralized architecture was tested on multiple users repeatedly, varying from 1000 to 10000, with the contact tracing time ranging from 40 to 50 ms [26].

D. Tele Mentoring for Ophthalmology

Interest in tele-ophthalmology increased during the COVID-19 pandemic. Currently, ophthalmologists must consult with technology experts and data scientists to achieve the desired optimal sustainable ophthalmic services. They need training and continued professional education on this emerging type of ophthalmic healthcare delivery [16]. In a prospective study on six patients with diabetic retinopathy, an expert in Beijing was able to supervise remotely an operation performed by a specialist in Huzhou (Zhejiang, China), some 1200 km away (Table I) [27]. Throughout interventions, the expert supervised the ophthalmologist in Huzhou via videoconferencing to ensure safe real-time synchronization with a mean latency of 20 ms [27].

IV. APPLICATIONS FOR COVID-19 (5G AS SUPPORTIVE TECHNOLOGY)

A. Patient Monitoring Technology

For this purpose, IoT or edge devices were connected by 5G to a cloud in most of the reported studies. An IoT to monitor vital signs (body temperature, heart rate, and peripheral blood oxygen saturation) was developed at the start of the COVID-19 pandemic [28]. In addition to measuring these vital signs, the IoT sends patient data to a smartphone app for display of patients' vital signs and risk factors indicative of progressive disease and alerts users in the event of safe physical distance violation. Data are sent to a cloud server where a machine learning algorithm predicted the risk of spreading the virus [28]. IoT sensing equipment, a wireless router supporting 5G and a cloud server were combined in a platform for monitoring heart rate and body temperature on 2000 patients [29]. A deep learning model, based on recurrent neural networks and auto-encoder, was employed for real-time monitoring, and achieved 96.2% accuracy to classify an increase of body temperature and/or heart rate as being caused by COVID-19 [29].

More recently, a 5G-enabled portable fluorescence sensor for rapid detection and tele-monitoring of COVID-19 patients was developed. It is linked to personal computers and smartphones through Bluetooth which in turn sends the acquired data to a 5G cloud server. This platform, tested on 19 patients, reached a detection time of 10 min [30]. Following the hypothesis that bronchial airflow causes subtle changes in the intrabronchial pressure, which can be detected by sensitive barometric sensors, a solution for sensing of respiratory rate and detection of coughing was designed using a barometric sensor [31]. This was tested on 10 subjects and exhibited a 97.3% accuracy for cough detection with 99.0% specificity for estimation of respiratory rate [31].

A platform for data collection, edge computing, and cloud computing has been reported for screening and diagnosis of COVID-19 [32]. It acquires body temperature, blood pressure, pulse rate, and cough sound via a smartphone app from patients suspected of suffering from COVID-19. A long short-term memory (LSTM) model was developed for analysis of these vital signs and a logistic regression model used to indicate the probability of being infected by COVID-19. If suspected, diagnosis was confirmed by chest X-ray or CT scan. Another deep learning model, based on convolutional neural networks (CNNs), was developed to diagnose COVID-19 in patients with suspect clinical signs and symptoms. When tested on 12420 images, the model exhibited a 97.1% diagnostic accuracy for COVID-19 infection [32].

In another study ECG signals, acquired by wearable sensors and relayed to cloud by 5G, were processed by AI to predict the COVID-19 patients' health risk. CNNs and LSTM models were developed on 47 patients achieving a prediction accuracy of cardiovascular disease to 99.29% [33].

B. Federated Learning for Diagnosis

Due to the need of protecting patients' privacy, most AI models are built on data from single institutions, resulting in poor generalization of the trained model when applied to data from external centres. AI federated learning may solve this issue. It is an approach that enables learning from a shared prediction model, hosted on an external cloud, while keeping the training data in a private network of each hospital, thus decoupling the ability for AI inference in the cloud from secure data storage in each hospital. Federated learning was applied to blood tests of 1013 patients from three different centres to classify different grades of COVID-19 infection severity as low, medium, and high risk [34]. At each center patients' data were sent by 5G to a cloud edge which applied the AI model, hosted in an external cloud, to make the required predictions. The AI model in the cloud receives only the updates (not patients' data) from each edge cloud. This model achieved an accuracy of 95.3%, 79.4%, and 97.7%, respectively from each centre, to classify severity of COVID-19 patients at admittance into hospital [34].

C. Lung Pathology in Patients With COVID-19 Disease

A multi-institutional report evaluated the lungs of 68 autopsies from three institutions in heavily hit areas (two in the USA, and one in Italy) [35]. The findings showed that COVID-19 pneumonia is a heterogeneous disease (tracheobronchitis, diffuse alveolar damage, and vascular injury).

In patients with exacerbations of chronic respiratory disease, remote monitoring during primary care may reduce hospital admissions and healthcare treatment costs. However, previous evidence that telemedicine can help address this emergency was conflicting [36]. A recent report specifically on patients suffering from chronic respiratory disorders, reported excellent results. The system consists of wearable respiratory and activity monitor, an environmental sensor, and a pulse oximeter [36]. All data are streamed to a tablet connected to a 5G infrastructure. The system was tested on 18 healthy volunteers during non-supervised recordings lasting at least 48 hours. The results confirmed that the system provided more complete and clinically relevant real-time information than previously studied telemedicine systems [36].

D. Radiology: Computed Tomography Scan

Given that most hospitals are equipped with CT scans or X-ray radiography, these imaging modalities have been used for screening of COVID-19. The first report on CT scanning during COVID-19 pandemic was performed on 152 patients from Chengdu (Sichuan, China) and other centres in Sichuan province [7]. Subsequently multilayer platforms, based on edge devices or IoT and cloud computing, were proposed [37], [38].

In one study, a 5G framework consisting of CT scans (bottom), edge devices (middle), and cloud computing (top layer) was used for surveillance of 4650 CT scans. This study used blockchain for data security. CNNs were trained in the cloud while explainable AI was used in the edge layer to visualize COVID-19 in CT scans [37]. In another report, IoT devices were used to acquire patient data that were sent directly to a cloud server using 5G networks [38]. Several CNNs models were ensembled to boost performance of COVID-9 diagnosis from CT scans. The ensemble model was trained on 2484 sample CT scan and achieved a 96.6% diagnostic accuracy [38].

E. Vaccines Distribution

Unmanned aerial vehicles (UAVs) can speed up the distribution process of vaccines, including those against COVID-19, due to the shorter round-trip delivery time, and lower shipping costs compared to road transportation. A multilayer architecture was recently proposed for this purpose [39]. It consists of an administration layer (including hospitals, vaccines production warehouses, and pharmacies), a UAVs and 5G and distribution layer for vaccines distribution and registration of intended receivers of the vaccine, with blockchain ensuring data encryption [39]. A simulation study estimated a cost of 0.0229 USD per kg compared with road transportation costs of 0.0546 USD per kg [39].

V. Other Applications

A. Emergency Medical Services

5G can provide new ways to provide emergency medical services, by connecting ambulance, paramedic, patients, and expert doctors in hospitals. In Madrid (Spain) 5G was used for the management of heart attacks [40]. A wearable device, like a smartwatch, sends via 5G an alarm of possible heart attack to a central cloud server which monitors the patient medical records, configures the likely diagnosis, and sends the appropriate team by assessing the location and the required skills. An augmented reality (AR) application was built using Microsoft Hololens v1 holographic glasses (Redmond, WA, United States) and hosted on an edge server close to the emergency site. A 5G smartphone ensures connection between Microsoft Hololens v1 and the edge server. The AR application displays geolocation and health information from the patient. The edge server is connected to guide the emergency team towards the patient location by streaming

TABLE II
STUDIES ON 5G IN TELESURGERY

Study	Country	Type of telesurgery	Device	Application	Distance	Latency	Speed
Zheng et al, 2020 [46]	China	Robot-assisted surgery	MicroHand by WEGO Group (China)	Animal model	1,768 km	264 ms	1 Gb/s
Jell et al, 2019 [47]	Germany	Robot-assistance system to hold the laparoscope	SoloAssist by AKTORmed (Germany)	Phantom model	--	60 ms	From 7.2 to 8 MB/s
Tian et al, 2020 [48]	China	Spinal surgery	TiRobot by TINAVI Medical Tehncologies (China)	Patients (n=12)	70 – 112 km	--	--
Madder et al, 2020 [49]	United States	Coronary surgery (simulated)	CorPath GRX by Corindus (United States) and ANGIO Mentor simulator by Simbionix – Surgical Science (Sweden)	Virtual model (n=2)	331.5 – 4,965 km	From 86.8 ms to 162.5 ms	
Lacy et al, 2019 [50]	Spain	Laparoscopy (telementoring)	Laparoscope by Olympus (Japan)	Patients (n=2)	4 and 6.1 km	From 146 ms to 202 ms	98-101 Mb/s for both download and upload
Xie et al 2021 [51]	China	Cardiac surgery (telementoring)	--	Patient (n=1)	400 km	30 ms	25 Mb/s
Lu et al 2021 [52]	China	Ophthalmic surgery (telementoring)	NGENU- ITY by Alcon (United States)	Patients (n=2)	1,4 km	250 ms	8-20 Mb/s --

an AR pathway to the doctor wearing Microsoft Hololens v1 [40]. In China 5G was employed to build an intensive care unit at Zhejiang University School of Medicine for intelligent assistance of remote monitoring, remote ward rounds, remote consultation and family visit [41]. In the U.K. the first remote diagnosis was performed thanks to the collaboration between Ericsson, University Hospital Birmingham NHS Foundation Trust and King's College London [42]. A video from an ultrasound was sent from the ambulance to the expert doctor wearing a virtual reality (VR) headset and maneuvering a joystick, and able to guide the paramedic, wearing a haptic glove, to execute the ultrasound scan [42], [43]. 5G was also employed to help treat stroke patients more quickly and effectively [43].

B. Telesurgery

The main applications of telesurgery are remote surgical operations and/or extreme conditions, e.g., the battlefield or during space missions. Telesurgery entails the use of master-slave robotic surgical systems. For the successful implementation of telesurgery, latency between master and slave is critical. Ideally it should be lower than 100 ms and problems such as inaccurate manipulation could arise if higher than 300 ms [44].

Anvari et al reported the largest patient series with more than 30 telesurgeries between Hamilton (ON, Canada) and North Bay (ON, Canada), approximately 400 km apart [45]. An average latency of 140 ms was reported and noticeable by the surgeon, who automatically compensated for the delay.

The studies on 5G in telesurgery are summarized in Table II. The feasibility of tele robot-assisted surgery using 5G was demonstrated on four operations (nephrectomy, partial hepatectomy, cholecystectomy, and cystectomy) on swine model using MicroHand robot by Wego Group (Weihai, Shandong, China), connecting the master in Qingdao (Shandong, China) and the slave in Anshun (Guizhoun, China) at a distance of over 2000 kilometers [46]. The delay of 5G was of 264 ms, compared with 206 ms over a cable network [46]. In another study on phantom model a latency up to 60 ms was reported [47].

C. Telerobotic Spinal Surgery

Most all orthopedic and neurosurgery applications are not true tele-surgery, rather they are stereotactic guided surgery. 5G telerobotic spinal surgeries on 12 patients were performed by connecting the first operator controlling the robot in Beijing (China) with five other Chinese centres [48]. The network latency was 28 ms (Table II). The authors also explored the new pattern of "one-to-many" remote surgery. Under this mode of remote surgery, one expert surgeon can simultaneously provide surgical care to more than one remotely located hospitals, something which previously was significantly restricted by the limit of network bandwidth. A "one-to-three" telerobotic surgery was successfully performed during this study, and it is believed that even more simultaneous multicenter remote surgery is possible, due to the vast capacity of the 5G network [48].

D. Tele-Endovascular Catheter Manipulation

Robot-assisted telestenting, where coronary stent procedures are executed on remote patients, was not performed over long distances [49]. In a recent study, telestenting was executed by an expert interventional cardiologist in Boston who controlled through 5G network CorPath GRX, a robot for vascular surgery by Corindus (Waltham, MA, Unite States). The robot arm controlled Angio Mentor by Simbionix-Surgical Science (Gothenburg, Sweden), a VR simulator for endovascular surgery offering several simulated procedures, e.g., carotid artery stenting and coronary. For the tests the robot and VR simulator were located in New York and San Francisco, respectively 206 and 3085 miles from the interventional cardiologist in Boston (Table II). In each case, a bedside technician at the simulator manually advanced the guide catheter into the ascending aorta, positioned a coronary guidewire at the tip of the guide catheter, and loaded the guidewire and a coronary balloon catheter onto the bedside robotic drive. 5G latencies were perceived as imperceptible, 162.5 ± 1.1 ms (from Boston to San Francisco) vs. 86.6 ± 0.6 ms (from Boston to New York) [49]. The results showed that telestenting could be mature enough to be used in procedures on real patients from long distances. The system could be adapted to treat critical limb ischemia and stroke remotely [49].

E. Tele Mentoring

The studies on 5G for tele mentoring are reported in Table II. Tele-mentored laparoscopic surgery was shown on two patients where the mentee surgeon and the mentor communicated in real time through an audiovisual system. The mentor was able to draw on the screen of a laptop (telestration), which the mentees visualize on their screens [50].

In 2019, tele mentoring was used to assist a surgeon in Gaozhou (China) with guidance from an expert in Guangdong province (China) 250 miles away to operate a 41 years old patient suffering from congenital heart disease. The anatomy of the patient was reconstructed from CT scan using AI and sent to the location of the expert. Using the real-time view of the surgeon in the operating room and the corresponding VR scene, the mentor could easily give immediate guidance through real-time audio streaming using 5G, maintaining a transmission rate at 25 Mbps with a latency of 30 ms [51].

Telementoring was also applied to 3D vitreoretinal surgery, with a bitrate ranging from 8 to 20 Mbps and a latency of 250 ms ensured by 5G connection [52].

F. Obstetrics

Cardiotocogram is used in medical care clinics only, and there are few reports attempting to send cardiotocogram data via a mobile network from home or from an ambulance to a medical institution. With the deployment of 5G this solution could be implemented as described in a recent publication, where the authors simulated the feasibility to concomitantly transmit not only cardiotocogram but also real time foetus ultrasound videos with excellent results [53]. The images during ultrasound examinations were high-quality videos on patient actors, which were transmitted without problems [53]. Thus, home monitoring of a fetus with the 5G system is a particularly useful application, which could create a new future for obstetric care.

G. Spinal Cord Stimulation

In a multicenter study on 64 patients a wireless device for spinal cord stimulation by PINS Medical (Beijing) was tested for the treatment of Parkinson's disease [54]. The device is connected to the smartphone of patients through an app to assist them in contacting physicians and managing symptoms and send data to a server which is connected to the physician smartphone. The doctor is able to adjust by remotely parameters and check battery status of the device for spinal cord stimulation inside the patients using a 5G connection. The system allows patients from rural areas to avoid expensive journey in terms of time and money to physician office [54].

VI. Discussion

The new 5G communication is a truly disruptive technology which can make key contributions towards the provision of high quality, sustainable healthcare to all patients. The growing telecommunications technologies along with AI, IoT, edge devices, and blockchain will clearly transform the delivery of healthcare in the immediate future. As these new technologies are being introduced into healthcare, the potential for reliably linked machines and algorithms to improve healthcare service delivery is significant and is likely to become more prevalent as the 5G network coverage and edge computing grow, enabling a more mature internet of medical things (IoMT) and other data acquisition sources to increase.

This myriad of innovations has also created a milieu ripe for telemedicine to thrive, as evidenced by the response to the COVID-19 pandemic, which has significantly hastened the development and use of telemedicine. The pandemic accelerated the deployment of 5G infrastructures in China, the creation of new facilities like Fangcang hospitals, and 5G applications including patient monitoring, contact tracing, tele-radiology (CT scan and ultrasound), and vaccines distribution. Moreover, there are applications related to COVID-19 where 5G functioned in reality as a core technology by virtue of its low latency and ability to handle large quantity of data. In contrast, for other applications 5G served as a supportive technology. The high speed and low latency of 5G were instrumental for the management of the massive quantity of data generated by Fancgang hospitals and for real-time detection during contact tracing [20], [26]. 5G assured stable connections during tele robot-assisted ultrasound and surgery performed on patients with diabetic retinopathy [21]–[25], [27]. Although latency was not reported in all the reported studies, it remained low, ranging from 20 to less than 200 ms [22], [27]. This review reported that published studies on patient monitoring, involving large datasets (thousands of samples), confirmed that 5G appeared to function more as a supportive than a core technology, e.g., to track heart rate, and body temperature or to automatically reconstruct radiological images using deep learning [29], [32]. In other instances, the use of 5G exhibited no advantage over 4G, e.g., monitoring cough rate in a small study on 10 patients [31].

There has been 7 published reports [46]–[52] on telesurgery not related to COVID-19 in which 5G was used. These confirmed the feasibility in real patients of tele mentoring for laparoscopic surgery (latency from 146 to 202 ms), cardiac surgery (latency of 30 ms), ophthalmic surgery (latency of 250 ms), and spinal surgery [48], [50]–[52]. However, the small samples size of these studies (ranging from 2 to 12 patients) does not allow valid assessment of the reliability of 5G in telesurgery on real patients at this stage. The other studies were on large animals (robot-assisted operations), on phantom model with a robotic system holding the laparoscope, and VR simulation for stenting surgery [46], [47], [49].

5G was also applied in the management of critical conditions, e.g., stroke or cardiac arrest [40], [43]. In a study on the management of heart attacks, 5G was instrumental in pushing the frame rate up to 60 fps (higher than 50 fps with 4G) to handle smoothly the AR application to display geolocation and health information from the patient [40].

In such highly risky instances, the time needed to detect and manage the emergency, select the best medical team, and send it to the right location can be largely reduced by enabling an automatic and customized emergency detection system by 5G, thereby increasing significantly the patient's chances of survival [40]. In addition to preventing cardiac arrests through constant monitoring, reduction of emergency team's response time to obtain the exact patient's location undoubtedly saves more lives [40].

For those applications requiring lower latency and higher speed like telesurgery, or higher fps like those based on AR the next generations of mobile networks (first 6G and then 7G operating, respectively, at 1-3 terahertz and 2-8 petahertz) are expected to provide superior performances to 5G. The telecommunication industry is making rapidly extraordinary progress, and 6G has been demonstrated in the laboratory. China, Finland, Norway and Japan are currently competing for first implementation [55].

Overall, the applications reviewed in this review are not regulated by authorities like Food and Drug Administration (FDA). Studies have proven that the lack of approval from regulatory organizations may hinder market adoption [56]. Unfortunately, many countries do not have regulatory rules for medical devices.

VII. Future Opportunities

A. Assistance to the Elderly

In an ageing population, care of the elderly is of major importance in any healthcare system. Many remote monitoring devices and systems have been developed in recent years, ranging from fall detectors to movement recorders, or monitors of electricity usage. Use of these IoT devices will enable healthcare providers to monitor patients and gather data to improve personalized and preventive care. 5G can improve the monitoring and care of patients at home and in primary care clinics, enabling improved efficacy of general practitioners.

Remote monitoring technology usage is limited by the capacity of the network to handle the data. Implementation of 5G technology in homes, with lower latency and higher capacity, will ensure that home healthcare providers (e.g, visiting nurses) will receive the data they need in real time to enable high levels of care for the elderly, with the added benefit of patients remaining in their homes for as long as possible provided the data connection and network are rapid, broad, reliable and secure. The first 5G system for user sensing was recently reported, using CNNs to classify different activities (sitting, standing, walking) in four subjects [57].

B. Internet of Nano Things (IoNT)

It is indeed surprising that the search for this review failed to identify involvement of 5G networking in the development of nano electromechanical systems (NEMS) for medical applications, with particular emphasis on drug delivery for nano-oncology, and how the potentially huge data sets could be monitored in real time by AI to adjust dosage. These NEMS can be connected to external devices (wearable devices, smartphones, other NEMS, etc…) by 5G, creating new Internet of Nano Thongs (IoNT) applications.

Nano-oncology has the potential to transform clinical oncology by enhancing the efficacy of cancer chemotherapy for a wide spectrum of invasive solid cancers. Nano-oncology achieves this by enabling novel drug delivery systems which target the tumour site with several functional molecules, including tumour-specific ligands, antibodies, cytotoxic agents, and imaging probes simultaneously thereby improving tumour response rates in addition to significant reduction of the systemic toxicity associated with current chemotherapy regimens. Several therapeutic nano-carriers have been approved for clinical use and others are undergoing phase II and III clinical trials [58]. Cell-division (mitosis) is a fundamental process that ensures accurate cell division into daughter cells. It is coordinated by the mitotic spindle made up of microtubules and has been established validated chemotherapeutic target for several years. Microtubules (MT) are dynamic polymers present at sites where chromosomes attach and segregate on mitotic spindle during mitosis. Antimitotic drugs disrupt this by suppressing MT dynamics, thereby producing abnormal chromosome arrangement. Consequently, spindle assembly check points are activated that trigger cancer cell death via mitotic arrest [59]. Because they are responsible for driving bipolar spindle and subsequent chromosome separation, kinesins constitute a new class of highly specific anticancer chemotherapeutic agents that may overcome resistance along with reduced side effects, in currently incurable cancers, e.g., ductal pancreatic adenocarcinoma, which causes death within 12 months of diagnosis. The key intracellular function they perform includes microtubule re-modelling, mitotic spindle assembly, and chromosome segregation in dividing cells [60]. As the human kinesins contribute significantly in cancer development, progression and drug resistance, demonstrated by their elevated expression in various solid cancers, they are considered as potential targets for novel cytotoxic agents against solid cancers.

VIII. Open Challenges

A. Infrastructure and Coverage Issues

5G mid bandwidth varies from 50 MHz to 100 MHz, while 5G high bandwidth can reach 40 GHz [61]. The better performances of 5G over 4G (higher bands and lower latency) are mitigated by an increase in the propagation loss, which can be overcome by installing new small cells every 100 m, compared to large 4G cells which exhibit several km in radii [61]. 5G performance suffers from inaccurate coverage estimation. Underestimation of the coverage can lead to overlapping coverage with neighboring cells causing interference. Conversely, overestimating of coverage can lead to weak received signal below the required level. For this reason, cells site locations need accurate and well planned sites by considering several factors: costs involved for site location, availability of neighboring cell sites to maintain uniform coverage. In addition, purchase of cell site locations require approval from private owners or local governments [61]. Furthermore, since all 5G operators will seek to develop their infrastructures to dominate the market, the number of new cells will increase exponentially [61]. Since different stakeholders are involved in 5G deployment (mobile operators, private owners, approval from local land owners and national government) specific regulations will be needed.

Energy consumption will be another crucial consideration as the 5G cell site requires more energy than 4G (11.5 kW vs. 6.8 kW). Additionally, the boost of energy cost will cause an increase of total 5G costs for the subscribers of services. For this reason, scientists should focus on alternative and cheaper energy sources to develop sustainable 5G infrastructures. Another solution may be reducing the static power consumption in absence of traffic [61].

B. Health Risks

In 2011, the International Agency for Research on Cancer at the World Health Organization (WHO) classified radiation in the frequency from 30 kHz to 300 GHz to be a 'possible' human carcinogen [62]. 5G frequency falls within this spectrum, with a band over 28 GHz in United States and 26 GHz in European Union [63]. Some studies have shown weak evidence for an association between radiofrequency (RF) radiation and cancer [64]. A more recent study found no significant association between cell phone use and thyroid cancer [65].

It is worth noting that the guidelines on exposure of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) have been solely based on thermal effects from the first release in 1998 to the latest in 2020, repeatedly ignoring scientific evidence on adverse effects of RF radiation to humans and the environment [62]. Conflicts of interest and ties to the industry seem to have contributed to biased reporting [62]. For this reason, they must be interpreted with caution when used to assess the effects of 5G on health.

In many countries, the deployment of 5G is of major concern with groups of citizens trying to implement a moratorium until thorough research studies on adverse effects of 5G on human health and environment have been conducted [62]. Additionally, the question about whether children absorb more RF energy than adults when using a smartphone is still unsolved [63]. Specific absorption rate (SAR) is a common parameter used to evaluate the degree of absorbed RF in human brain and body. A recent study on two adults and two children found a significant local SAR peak value in localized superficial points [63]. However, they found that at 28 GHz, a frequency typical of 5G, the reduction of SAR from the surface to the innermost tissues is much more sudden than 4G [63]. Another published study showed a very low penetration of RF radiation into the ear at 30 GHz [66]. Further investigations are required to shed light on the role of RF absorption, especially now that the adoption of 5G devices and time spent by humans with them is constantly increasing. In fact, developing 5G applications for telemedicine to provide better care, but exposing patients to unwanted and harmful doses of radiations would represent a highly dangerous situation that must be prevented at all costs.

C. Cybersecurity Issues

As indicated in the introduction, security and privacy of 5G and its future evolutions remain crucial, because in essence 5G has invaded the physical domain. 5G medical devices will involve a massive number of connected devices of different types (wearable devices, smartphones, edge devices, cloud servers, and IT infrastructures at hospitals/ medical centers). Since cybersecurity threats have the potential to exploit one or more vulnerabilities in each of them, resulting in possible patient harm, cybersecurity is of paramount importance and should be given the highest priority possible with constant monitoring against breaches and hacking, especially with the successful and increased adoption of 5G devices in healthcare [67]. Moreover, cybersecurity risks evolve over time and consequently the effectiveness of cybersecurity controls may degrade as new risks, threats, and attack methods arise.

A traditional single-server architecture requires to store a massive number of identities and passwords, which imposes a significant database cost [68]. A multi-server e-health architecture exploiting biometrics, passwords, and smart cards was recently proposed. It reduced network load and database cost [68]. Blockchain has considerable potential to secure data for applications in COVID-19 and other areas of healthcare, although at present the translation of blockchain into clinical use is limited [69]. Blockchain was used for COVID-19 applications for encryption of data transmitted by 5G for contact tracing, reconstruction of CT scans, and transportation of vaccines [26], [37], [39], whereas federated learning was explored in AI predictive models of COVID-19 [34].

The FDA requires manufacturers to address cybersecurity risks as part of design controls, and to provide security in terms of: authenticity; authorization; cryptography; code, data, and execution integrity; confidentiality; event detection and logging; resilience and recovery; and updatability [67]. Additionally, a lack of information to users to maintain the cybersecurity of devices over their lifecycle has the potential to affect the safety and effectiveness of the device itself. FDA currently recommends that manufacturers conduct a safety risk assessment according to ISO 14971:2019 and a security risk assessment to guarantee a comprehensive identification and management of patient safety risks. Manufacturers are responsible for identifying cybersecurity risks in their devices and the systems in which they expect those devices to operate, and for implementing the appropriate controls to mitigate those risks [67]. A similar initiative on cybersecurity was undertaken by European Union [70].

The majority of experts in 5G networking consider that solutions to the major problem of security by virtue of its negative worldwide impact and use lies through quantum computing. In this respect a recent publication has made a significant impact on 5G and its future successors (e.g., 6G) on the importance of quantum computing - based 5G security [17]. The realization of a defined quantum-resistant security is increasingly becoming a top priority for the 5G-oriented infrastructure network for both owners and operators. Essentially, the proposed security systems rely on Post-Quantum Cryptography (PQC), which are considered as unbreakable [71]. In addition, the exploitation of Quantum Key Distribution (QKD) is fully compatible with the current existing cryptographic infrastructure. However, its continued security against known and future quantum attacks cannot be guaranteed [72]. In contrast, the unconditional security of QKD has been enhanced through several demonstrations' encryption across quantum networks. The established limitation of QKD is that it cannot replicate all the functionalities of public-key cryptography. This can be overcome by a joint PQC/QKD encryption in which, quantum-resistant algorithms can access the secure shared key material from QKD has been confirmed [73].

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