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Review article

HealthCare 5.0: An industry 5.0 perspective for next-generation medical systems with synergistic integration of IoT, AI, and 6G

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ABSTRACT

The rising demand for personalized, reliable, and sustainable health services requires a significant shift beyond current technology barriers. This paper introduces HealthCare 5.0, a transformative vision for next-generation medical systems. It brings the Internet of Things (IoT), Artificial Intelligence (AI), and 6G communications together under the human-centered, sustainable, and resilient principles of Industry 5.0. HealthCare 5.0 showcases the convergence of IoT for continuous health monitoring, AI for intelligent reasoning, and 6G for dependable, low-latency connectivity. These elements work together to provide real-time, personalized, and proactive care. The analysis looks into how this collaboration supports advancements like remote diagnostics, digital twins, federated learning, explainable AI (XAI), and medical large language models (MedLLMs). It also addresses challenges in interoperability, energy efficiency, data privacy, and ethical AI. The framework stresses the importance of digital twins, ambient sensing, and wearable devices in facilitating predictive and patient-centered care. Despite progress, there are still gaps in standardization, clinician adoption, and the ethical use of these technologies. To overcome these issues, we propose a complete approach that combines IoT, AI, and 6G based on Industry 5.0 principles. This closed-loop model of "sense, transmit, reason, act" is backed by key performance indicators, real-world case studies, and a roadmap for compliance and regulatory support. By merging innovation with human values and systemic resilience, HealthCare 5.0 offers a forward-thinking plan for smart, safe, and fair healthcare systems.

1. Introduction

Global healthcare systems are at a critical juncture, facing unprecedented pressures that demand transformative change [1–3]. Factors such as aging populations, the rising prevalence of chronic diseases, escalating healthcare costs, and vulnerabilities exposed by recent pandemics, including COVID-19, underscore the limitations of traditional healthcare models [4–8]. Reactive, hospital-centric approaches are increasingly strained and often fail to deliver timely, personalized care. This convergence of challenges necessitates a fundamental shift toward *HealthCare 5.0*, a proactive, efficient, and patient-focused paradigm, frequently encapsulated by the

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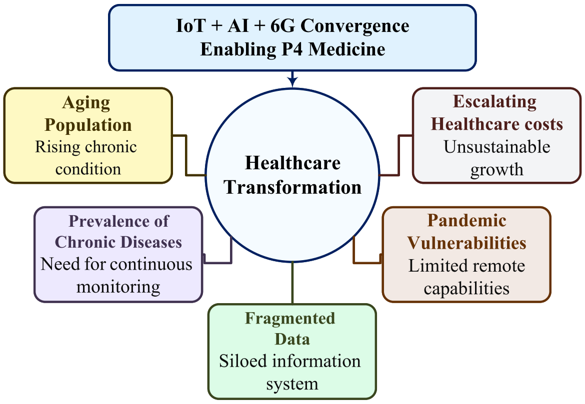

Fig. 1. Healthcare challenges addressed by converging technologies.

vision of Personalized, Preventive, Participatory, and Predictive (P4) medicine [4–6]. Fig. 1 summarizes these systemic pressures and highlights where digital technologies can intervene.

However, achieving this vision requires overcoming significant hurdles related to fragmented data, limited remote capabilities, diagnostic delays, and infrastructural constraints inherent in many current healthcare systems [5,6,9].

1.1. *The promise of converging technologies*

Fortunately, rapid advancements in digital technologies offer powerful tools to address these challenges and catalyze the needed transformation. Three key technological pillars stand out (see Fig. 2):

First, the Internet of Things (IoT) forms the sensory backbone of HealthCare 5.0, encompassing a vast network of interconnected sensors, wearables, smart implants, and ambient devices that enable continuous, real-time collection of physiological, behavioral, and environmental data beyond the clinic and into daily life [10–14]. Modern IoT healthcare architectures are typically organized in three tiers: **(i)** the *perception layer*, consisting of heterogeneous devices (e.g., ECG patches, smart inhalers, implantable glucose monitors) that capture high-resolution biosignals, **(ii)** the *network layer*, which utilizes low-power wide-area networks (LPWAN) such as NB-IoT and LoRaWAN alongside short-range protocols like BLE and IEEE 802.15.6 to transmit data reliably, and **(iii)** the *application layer*, where edge and cloud platforms aggregate, preprocess, and provision data for analytics and decision support [2,15,16].

Second, Artificial Intelligence (AI), particularly Machine Learning (ML) and Deep Learning (DL), provides the reasoning engine that converts raw data streams into actionable clinical insights [17,18]. Modern healthcare AI pipelines typically involve: **(i)** *data preprocessing* at the edge (noise filtering, normalization, compression), **(ii)** *feature extraction* using convolutional and recurrent architectures to capture temporal and spatial patterns in multimodal biosignals, **(iii)** *model training* on federated or centralized datasets leveraging gradient-based optimizers and transfer-learning to adapt general models to specific patient cohorts, and **(iv)** *inference and feedback*, where lightweight models run on-device or at the network edge to deliver real-time alerts and personalized recommendations. In parallel, Medical Large Language Models (MedLLMs) have recently emerged as a transformative paradigm for clinical knowledge retrieval, decision support, and patient engagement [19–23]. By embedding MedLLMs into the edge-cloud continuum, HealthCare 5.0

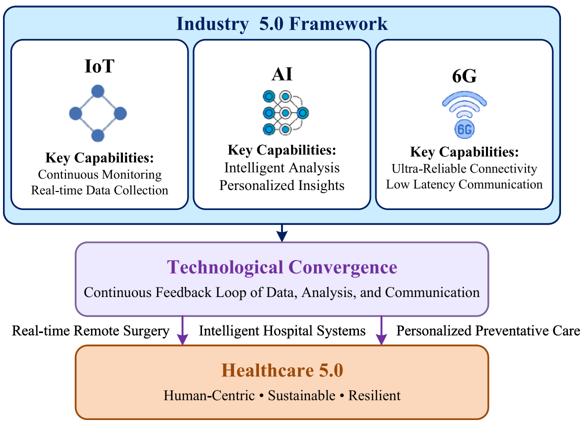

Fig. 2. Technological convergence enabling healthcare 5.0.

Table 1
Comprehensive comparison of survey and framework papers in smart and next-generation healthcare, summarizing each work's core focus, enabling technologies, main challenges, validation or case studies, and identified gaps.

Survey (Short Refs.)	Year	Core Focus	Key Technologies	Main Challenges	Validation / Case Studies	Gaps / Lacks
Foundational IoT Architectures ([21, 28, 29])	2017–2021	End-to-end IoT models; building blocks	Sensors; LPWAN (NB-IoT, LoRa); WSN; middleware; BLE; IEEE 802.15.6	Interoperability; QoS; security/privacy	Conceptual/prototypes; market analyses	No large-scale trials; real deployments; performance data
Wearables Cellular IoT ([30])	2020	Classification of wearable clusters	Wearable sensors; Cellular IoT	Power; connectivity; CIoT uptake	Survey only	No CIoT prototypesor case studies
Edge / Fog / 5G-Enabled Care ([31, 32])	2018–2019	Fog/edge and 5G for low-latency care	Fog nodes; edge AI; 5G small cells; SDN/NFV; mmWave	Interoperability; QoS; latency; energy efficiency	Prototype/simulations	No cross-vendor tests; no user feedback
Industry 4.0 Big-Data ([33, 34])	2020	Mapping Industry 4.0 to healthcare	IoT; fog/cloud; big-data analytics; predictive maintenance	Compliance; data heterogeneity; real-time inference	Case studies; editorials	No cost analyses; performance benchmarks
Federated Learning Privacy ([35, 36])	2022–2025	FL taxonomy; privacy-preserving on-device AI	Federated learning; edge analytics; IoMT	Data heterogeneity; comms. overhead; compute limits	Simulations; COVID-19 case studies	No resource-constrained trials; compliance studies
Blockchain Security ([37, 38])	2022–2023	Blockchain for data sharing; security frameworks	Blockchain; smart contracts; intrusion detection; AI	Scalability; compliance; data tampering; auth	Prototype reviews; framework proposals	No performance metrics; attack evaluations
Explainable AI LLMs ([19, 20])	2022–2023	XAI methods; MedLLM taxonomy	XAI (saliency, counterfactuals); BioBERT; ClinicalBERT; GPT	Interpretability; latency-accuracy; hallucinations; bias	FL case study; benchmarks	No clinician-centric evaluations; multi-center trials
Emerging Next-Gen Paradigms ([39, 40, 41, 42, 43, 44, 45])	2021–2025	Industry 5.0; IoHT; IoMT	integration with 6G	AI; blockchain; robotics; 6G; IoMT; edge computing; IEEE standards	Sustainable models; hybrid AI–IoT–6G; governance; policy integration	Conceptual roadmaps; surveys, No real-world deployments; cost-benefit analyses; stakeholder studies
HealthCare 5.0 (Ours)	2025	Synergistic IoT+AI+6G under Industry 5.0	IoT sensors; AI/ML/DL; 6G; MedLLMs; edge AI	Interoperability; energy; security/privacy; XAI; ethics	Quantitative KPI benchmarks; two real-case trials	

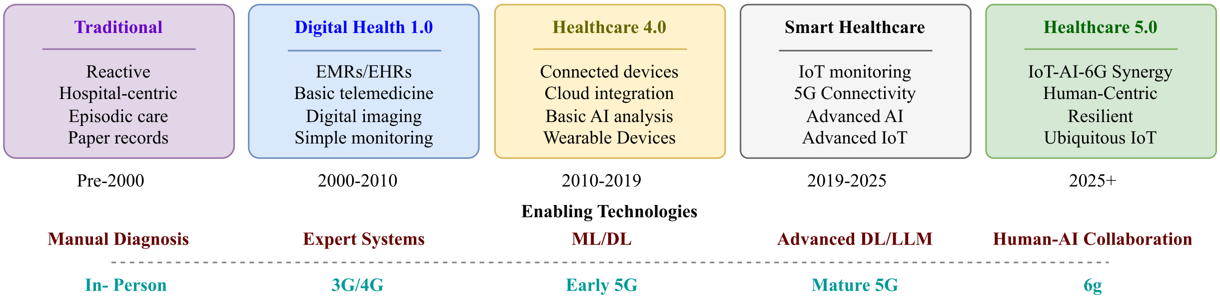

Fig. 3. Evolution from traditional healthcare to healthcare 5.0.

can harness conversational AI agents that support clinicians and empower patients, closing the loop on truly personalized, predictive, and participatory care.

Third, Sixth-Generation (6G) wireless communication systems promise unprecedented performance levels, including ultra-reliable low-latency communication (URLLC), massive device connectivity, terabit-per-second data rates, integrated sensing, and native AI integration, creating a robust communication fabric essential for demanding real-time healthcare applications [2,24–27].

Unlike prior surveys focused on siloed technologies (Table 1)[30,39–43], their true potential lies in synergistic convergence: IoT senses, 6G transmits, and AI reasons forming a closed-loop system aligned with Industry 5.0 principles. This survey takes a broad look at Industry 5.0. It investigates how IoT, AI, and 6G come together in a closed-loop model. The survey includes quantitative KPI comparisons, such as end-to-end latency and reliability across 4G, 5G, and 6G. It also covers energy and bit trajectories. The survey examines real-world case studies, such as 5G telesurgery and the neuro-ICU digital twin. Additionally, it offers a multi-layer standards and compliance map that links capabilities to healthcare regulations. These elements are often absent in earlier reviews of Healthcare 4.0 and 5.0.

1.2. The industry 5.0 lens for healthcare

Simply deploying advanced technology is insufficient. The approach to integration is paramount. Industry 4.0 focused heavily on automation and data exchange for efficiency. However, Industry 5.0 introduces a vital evolution, placing human needs and collaboration back at the center, alongside sustainability and resilience goals [2,5,46–49]. Applied to healthcare, this translates to:

- **Human-Centricity:** Technology should enhance, not replace, human capabilities. This means supporting clinicians in their work, improving the patient experience, and empowering individuals to take control of their health [50]. The synergy of IoT, AI, and 6G enables hyper-personalized medicine at scale. Continuous IoT monitoring provides granular, individualized data. 6G ensures timely transmission, and AI dynamically tailors preventive strategies and treatments, placing individual needs at the center [51–53]. Moreover, 6G's low latency and high bandwidth, potentially combined with AI for enhanced analytics or translation, enable immersive and empathetic remote consultations (e.g., holography), improving access and patient experience [54,55]. In clinical settings, AI decision support systems fed by real-time IoT data over 6G can augment clinicians, reducing cognitive load and improving diagnostic accuracy, fostering effective human-AI collaboration [56–58].
- **Sustainability:** Healthcare systems should use technology to optimize resource usage, whether that involves energy, materials, or staff time [59]. AI algorithms analyzing real-time IoT data (e.g., energy usage, patient flow, asset location) transmitted via 6G can

dynamically optimize energy consumption, staffing schedules, and supply chain logistics [60]. Reliable remote care ecosystems, built on IoT monitoring, AI analysis, and seamless 6G connectivity, reduce the carbon footprint associated with patient and clinician travel [61,62]. The incorporation of ISAC further contributes to sustainability by reducing the need for additional sensing infrastructure, thereby lowering hardware and energy demands [63].

- **Resilience:** Modern healthcare must be prepared to adapt and recover from disruptions such as pandemics, natural disasters, or infrastructure failures [64]. Decentralized care models, heavily reliant on IoT for remote data and 6G for reliable connectivity, reduce dependence on centralized hospital infrastructure [61,65]. Population-level data can be anonymously gathered during public health crises from IoT devices (if ethically implemented) and rapidly analyzed by AI via 6G for early outbreak detection, spread modeling, and optimized resource allocation [66,67]. It is important to highlight that 6G's six-nines reliability and native AI optimization provide an unprecedented safety margin for mission-critical applications such as telesurgery and neuro-ICU digital twins. Such reliability is crucial for ensuring the continuity of essential remote health services during emergencies [68–71].

This Industry 5.0 perspective is uniquely suited for healthcare. It ensures that technological advancements serve core human values and address systemic robustness and long-term viability, moving beyond purely technical optimization. Fig. 3 presents a longitudinal view of how healthcare paradigms have evolved from traditional models toward the holistic HealthCare 5.0 vision.

1.3. Existing surveys

Numerous survey studies have documented the rapid development of smart healthcare technologies, each focusing on different aspects of the IoT, AI, and networking landscape (see Table 1). Early research focused on end-to-end IoT architectures and communication protocols, including BLE, NB-IoT, LoRaWAN, and IEEE 802.15.6, while addressing challenges related to interoperability, quality of service (QoS), and security [21,28,29].

As the field evolved, researchers expanded their focus to include fog, edge computing, and 5G networks. These advancements paved the way for low-latency remote care and smarter, context-aware monitoring systems [31,32,45]. At the same time, ideas from Industry 4.0, such as big data analytics, cloud-fog integration, and predictive maintenance, were adapted to healthcare settings, offering new ways to improve efficiency and patient outcomes [33,34]. More recently, attention has shifted to frameworks that prioritize privacy, trust, and transparency. For instance, federated learning enables privacy-preserving analytics by keeping data on devices rather than centralizing it [35,36]. Blockchain technology has emerged as a tool for secure, tamper-proof data sharing [37,38]. Meanwhile, explainable AI (XAI) and medical large language models (MedLLMs) are helping clinicians better understand and trust AI-driven insights [19,20]. While these studies show the potential of combining IoT, AI, and next-generation networks in healthcare, they often have some shortcomings. Many lack real-world benchmarks, pilot-scale implementations, cost-benefit analyses, and clear regulatory guidance. The HealthCare 5.0 survey fills these gaps by introducing quantitative KPI benchmarks, showcasing several real-world case studies, examining sustainability, and providing a clear compliance roadmap. This framework offers a practical way to improve smart healthcare. The contribution goes beyond technology-specific or pairwise integration surveys by bringing together IoT, AI, and 6G under Industry 5.0, supporting claims with benchmarks, deployed examples, and a compliance roadmap.

1.4. Scope and contribution

This paper presents a survey of how IoT, AI, and 6G can collaborate to transform healthcare. The survey is based on the human-focused, sustainable, and resilient principles of Industry 5.0. Unlike previous surveys on Healthcare 4.0 and 5.0 (see Table 1), this analysis brings all three pillars together and connects them to measurable KPIs, deployments, and governance. The scope goes beyond individual technologies to examine their combined potential and the applications they generate in this new context. A high-level roadmap of the paper is also included for reference, as shown in Fig. 4. Our main contributions lie in the following aspects:

C1) The first integration of IoT, AI, and 6G follows the Industry 5.0 principles of human focus, sustainability, and resilience, as discussed in Section 2. Unlike previous works, as shown in Table 1, the proposed framework outlines a closed-loop "sense, transmit, reason, act" model, which is detailed in Section 3. This model is validated through real-world case studies, like 5G telesurgery and neuro-ICU digital twins, as well as through quantitative benchmarks, including 6G's projected "six-nines" reliability compared to 5G and 4G.

C2) The survey addresses critical gaps in several areas. It proposes cross-layer standards for interoperability to enable seamless integration across different IoT, AI, and 6G systems. For edge intelligence, the focus is on creating lightweight, XAI models that fit the needs of resource-limited medical devices. In the area of 6G optimization, it explores network slicing and Integrated Sensing and Communication to meet healthcare-specific quality-of-service needs.

C3) The survey critically analyzes societal and ethical challenges. It examines strategies to reduce algorithmic bias and tackle the digital divide in 6G-enabled healthcare. Regarding trust, it explores blockchain-based data tracking and clinician-centric XAI for medical large language models (MedLLMs). It also proposes regulatory roadmaps for slice-level safety certification and edge AI compliance.

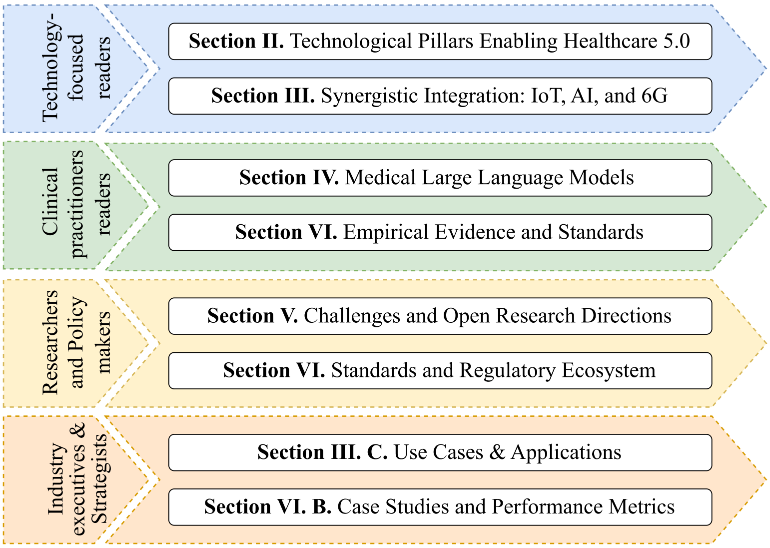

Fig. 4. A text-based visual reading map that helps individuals navigate and comprehend the HealthCare 5.0 paper.

C4) The survey shows the potential of HealthCare 5.0 through several innovative applications. These include AI-driven preventive systems, such as personalized coaching with multimodal IoT, holographic telemedicine, which uses 6G to achieve sub-millisecond latency, and self-optimizing hospitals that utilize IoT and AI to improve energy and operational efficiency.

C5) The survey identifies several underexplored research directions. These include THz-band diagnostics, which allow non-invasive sensing through 6G's terahertz frequencies, federated learning at scale, which supports privacy-preserving collaboration among institutions, and human-AI partnerships, which aim to create adaptive interfaces that improve teamwork between clinicians and AI systems.

1.4.0.1. Novelty Statement. To the best of our knowledge, no prior survey simultaneously integrates *all three* pillars IoT, AI, and 6G within an Industry 5.0 perspective, and substantiates the discussion with **(i)** quantitative KPIs, **(ii)** real deployment evidence, and **(iii)** a standards-compliance roadmap. This holistic, empirically grounded approach distinguishes the present work from earlier technology silo or pairwise integration studies, establishing its novel contribution to next-generation medical systems.

1.5. Paper structure

The remainder of this paper is structured as follows: Section 2 explores the three core technologies driving this transformation: IoT, AI, and 6G. In Section 3, an end-to-end convergence framework is introduced. Next, Section 4 delves into the rapidly advancing field of medical large-language models (MedLLMs). Section 5 shifts focus to the challenges ahead. In Section 6, the proposed vision is grounded in real-world data and standards. Finally, Section 7 summarizes the paper by presenting the key findings.

2. Technological pillars enabling healthcare 5.0

The vision of a human-centric, sustainable, and resilient healthcare system, aligned with Industry 5.0 principles, relies heavily on the capabilities offered by converging digital technologies [4–6,72]. This section provides a brief overview of the roles of IoT, AI, and 6G as foundational pillars for this transformation (see Table 2).

2.1. IoT in healthcare: Sensing the human experience

The IoT forms the sensory backbone of modern healthcare, extending monitoring capabilities far beyond traditional clinical environments. Its key components include:

- Wearable devices such as smartwatches, fitness trackers, continuous glucose monitors (CGMs), ECG patches, and specialized sensors provide real-time physiological data (e.g., heart rate, activity levels, blood oxygen, temperature) directly from the patient [91,92].
- Implantable medical devices, including Pacemakers, defibrillators, and emerging smart implants, offer critical monitoring and therapeutic intervention from within the body [93,94].
- Ambient sensing technologies integrated into homes or hospital rooms, these devices monitor environmental factors (temperature, air quality), patient movement (fall detection), or even vital signs passively [95,96].

Table 2
Benefits and limitations of IoT, AI, and 6G in healthcare.

Technology	Benefits	Limitations/Challenges	References
IoT	Continuous, real-time monitoring, Extension of care beyond clinical settings, Early detection of health deterioration, Improved medication adherence tracking , Enhanced patient engagement	Battery life limitations, Data security and privacy concerns, Sensor accuracy and reliability, Integration with legacy systems, Cost barriers for widespread adoption	[9,73–78]
AI	Advanced pattern recognition in complex data, Reduction in diagnostic errors, Personalized treatment recommendations, Operational efficiency improvements, Predictive capabilities for resource planning	“Black box” nature of some algorithms, Training data biases affecting outcomes, Regulatory approval complexities, Clinician adoption barriers, Computational resource requirements	[79–84]
6G	Ultra-reliable low-latency communication, Massive device connectivity, Native AI integration in the network, Integrated sensing capabilities Support for immersive technologies	Early developmental stage, Infrastructure deployment costs, Spectrum allocation challenges, Energy consumption concerns Global standards have yet to be established,	[44,85–90]

- Smart hospital infrastructure, including interconnected medical equipment (infusion pumps, ventilators), asset tracking tags, and smart beds, streamlines hospital operations and improves resource management [16,97].

The primary role of IoT in healthcare is continuous, multi-modal data acquisition, enabling comprehensive remote patient monitoring (RPM), early detection of anomalies, adherence tracking, and efficient clinical/hospital logistics [98–100]. By providing a constant stream of personalized health data, IoT directly contributes to the realization of the Industry 5.0 vision. It enhances the human-centric aspect by enabling personalized insights and care tailored to individual lifestyles and conditions, reducing the need for frequent, burdensome clinic visits. Furthermore, robust RPM capabilities bolster resilience, allowing for care continuity during disruptions (e.g., pandemics, mobility issues), and contribute to sustainability by minimizing patient and clinician travel [101–103].

However, no single radio technology can satisfy the full spectrum of HealthCare 5.0 requirements. Instead, a heterogeneous connectivity fabric covering body links, room networks, campus-scale meshes, and global backhaul is essential. Table 3 summarizes the leading short- and long-range wireless technologies and their representative healthcare use cases [104–120].

2.2. AI in healthcare: Extracting intelligence for action

The vast amount of data generated by IoT and other sources (EHRs, imaging) requires advanced analytical tools to become clinically meaningful. Artificial Intelligence (AI), particularly its subfields, provides these capabilities:

- Machine Learning (ML) and Deep Learning (DL) like algorithms capable of learning patterns from data are used for disease prediction, diagnostic image analysis (radiology, pathology), risk stratification, and identifying subtle changes indicative of health deterioration [79,121,122].
- Natural Language Processing (NLP) and Large Language Models (LLMs) enable advanced analysis of unstructured clinical notes, extraction of information from medical literature, and development of healthcare chatbots or voice assistants. Recent LLMs, such as Med-PaLM 2 and Llama-3-Meditron, have further expanded these capabilities by supporting multi-day EHR summarization, instruction-tuned clinical reasoning, and multilingual applications for low-resource healthcare systems [123–125]. These advancements are discussed in detail in Section 4.
- Computer vision powers the analysis of medical images, observation of patient movement, and robotic assistance in procedures [126–129].

The role of AI is to transform raw data into actionable intelligence (see Fig. 5). This includes supporting clinical decision-making, accelerating drug discovery and development, automating repetitive tasks (e.g., preliminary image screening), personalizing treatment plans based on individual patient profiles, and predicting potential outbreaks or resource needs [130–132]. From an Industry 5.0 perspective, AI significantly enhances human-centricity not by replacing clinicians, but by augmenting their capabilities, reducing diagnostic errors, and freeing up time for complex patient interaction [17,133,134]. AI-driven predictive maintenance of medical equipment, combined with optimized scheduling, contributes to operational efficiency and sustainability. By enabling faster analysis of population health data, AI also improves the resilience of health systems in responding to public health crises [135].

2.3. 6G for healthcare: The ultra-connected nervous system

While 5G provides significant advancements, the full realization of truly immersive, real-time, and massively connected healthcare applications hinges on the anticipated capabilities of Sixth-Generation (6G) wireless communication [97,113,136–139]. Key expected features relevant to healthcare include:

- Extreme Performance refers to the unprecedented capabilities of 6G networks, potentially reaching terabits per second in peak data rates, microseconds in latency, and supporting millions of connected devices per square kilometer [140–142].

Table 3
Comparison of Wireless Communication Technologies for HealthCare 5.0. Abbreviations: BLE = Bluetooth Low Energy; NFC = Near Field Communication; UWB = Ultra-Wideband; Li-Fi = Light Fidelity; LoRaWAN = Long Range Wide Area Network; NB-IoT = Narrowband Internet of Things; LTE-M = LTE for Machines; 5G NR = Fifth Generation New Radio; THz = Terahertz; LEO = Low Earth Orbit; SL = Security Level; DC = Deployment Cost.

Technology	Range	Data Rate	Latency	Use Cases	Pros	Cons	SL	DC
Short-Range Technologies								
Bluetooth / BLE	Up to 10-100 m	1-3 Mbps	Medium	Wearables (ECG, glucose), insulin-pump control, smart inhalers	Easy integration, ubiquity	Range	Medium	Low
Bluetooth LE Audio	Up to 50 m	1-2 Mbps	Low	Hearing aids, audio guidance in rehab, patient notifications	Broadcast audio, low power	Limited support	Medium	Low
Matter (over Thread)	Up to 100 m	250 kbps	Medium	Smart bed occupancy, environmental sensors, asset tracking	Interoperability, secure commissioning	New ecosystem	High	Medium
Wi-Fi 7 (802.11be)	Up to 100 m	30-50 Gbps	Very low	AR/VR therapy, remote diagnostics,high-def video consults	Ultra-high throughput	Power hungry, cost	High	High
Zigbee (IEEE 802.15.4)	Up to 10-100 m	250 kbps	Medium	Infusion pump coordination,smart lighting, nurse-call paging	Mesh networking	Low data rate	Medium	Low
NFC	Up to 10 cm	424 kbps	Very low	Patient ID wristbands, secure drug authentication, device pairing	Secure, instant	Very short range	Very high	Very low
UWB	Up to 50 m	Tens of Mbps	Low	Fall detection, RTLS for equipment, staff localization	Centimeter-scale accuracy	Cost, device availability	High	Medium
Li-Fi	Room-scale	100 Mbps-Gbps	Low	EM-safe data streams in MRI, sterile OR data links, indoor nav	RF-free, secure	Line-of-sight dependence	High	Medium
Long-Range Technologies								
LoRaWAN	Up to 10-15 km	0.3-50 kbps	High	Rural patient monitoring, environmental sensors, asset geo-fencing	Deep coverage	Not real-time	Low	Low
NB-IoT	Up to several km	250 kbps	Medium	In-building vitals patch, wearable geofencing, smart lockers	Indoor penetration	Mobility limits	High	Medium
LTE-M	Up to several km	1 Mbps	Low	Ambulance video, mobile imaging, tele-EMS coordination	Mobility support	Cellular dependency	High	High
5G NR	Up to several km	Up to 10 Gbps	Ultra-low	Remote surgery, digital twin monitoring,massive IoT hubs	Network slicing, QoS	Infrastructure cost	Very high	Very high
6G THz (emerging)	Up to 1 km	100 Gbps-Tbps	Sub-ms	Holographic telehealth, AI-driven imaging backhaul	Ultra-high rate	Immature	Very high	Very high
Satellite (LEO)	Global	100 kbps-Mbps	High	Telepsychiatry, disaster-zone triage, border-clinic links	True global coverage	Latency, cost	Medium	Very high
Sigfox	Up to 30-50 km	100 bps	High	Emergency alerts, sparse vitals logging, fall alarms	Ultra-battery life	Very low rate	Low	Low

- Native AI Integration involves embedding artificial intelligence and machine learning (AI/ML) within the network core and air interface to enable intelligent resource allocation, autonomous optimization, and improved service quality [143,144].
- Integrated Sensing and Communication (ISAC) describes the ability of 6G networks to use communication signals for high-resolution sensing tasks such as localization, imaging, and activity recognition without requiring dedicated sensors [145–151].
- Holographic Communication and Extended Reality (XR) represent the next generation of immersive technologies, enabling ultra-realistic remote consultations, advanced medical training, and real-time surgical planning or assistance through high-fidelity holographic and XR experiences [152–154].
- Enhanced Reliability and Security highlight the evolution of ultra-reliable low-latency communications (URLLC) and new security mechanisms to safeguard mission-critical healthcare services and sensitive patient data in 6G-enabled environments [155–157].
- Terahertz (THz)-band Diagnostics introduce novel possibilities for non-invasive biomedical imaging and sensing, exploiting 6G's THz spectrum to enable early disease detection and high-resolution physiological monitoring [158,159].

The anticipated role of 6G is to serve as the near-instantaneous, ultra-reliable communication fabric connecting patients, clinicians, AI algorithms, and massive numbers of IoT devices seamlessly [160–162]. It will enable applications currently infeasible,

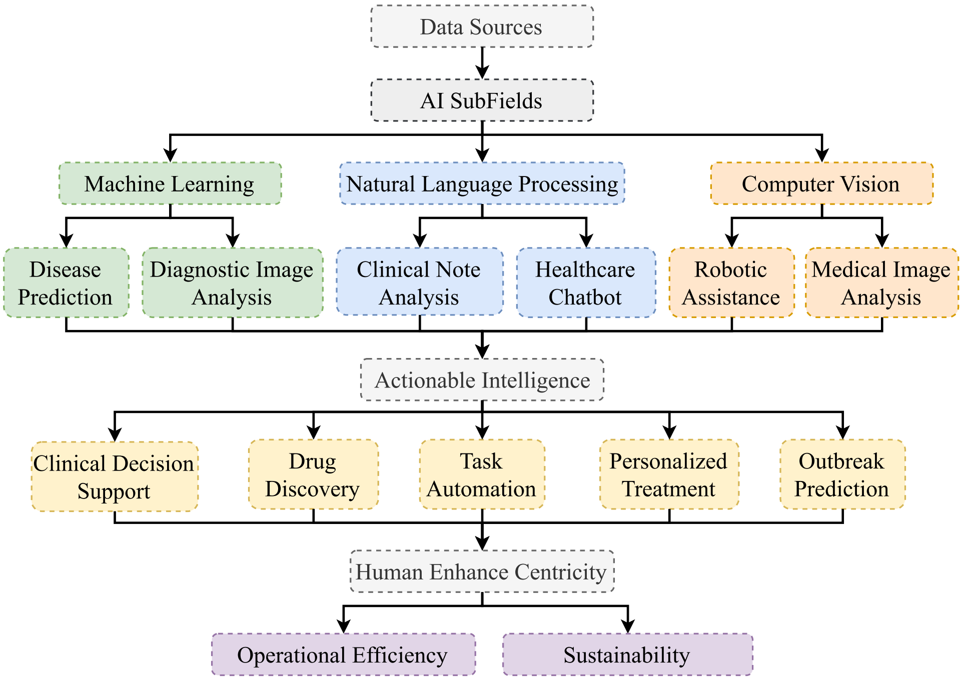

Fig. 5. Hierarchical schematic illustrating the progressive translation of heterogeneous healthcare data sources into clinically actionable intelligence.

such as widespread real-time robotic telesurgery, high-fidelity holographic consultations feeling truly "present," hyper-personalized preventative care based on massive real-time data streams, and city-wide health monitoring using ISAC [163]. In addition, features such as ISAC-driven contactless monitoring and THz diagnostics extend healthcare capabilities beyond connectivity, creating entirely new diagnostic and therapeutic modalities. In Industry 5.0, 6G is a key enabler for human-centricity through immersive interaction and equitable access to remote expertise [164–168]. Its inherent design for massive connectivity and AI-driven optimization supports sustainability in large-scale deployments. Most critically, its focus on ultra-reliability and potential integration with sensing creates a foundation for a highly resilient healthcare infrastructure capable of supporting critical services ubiquitously and adaptively [169–172].

These three pillars of IoT, providing the data, AI providing the intelligence, and 6G providing the connectivity, form the technological foundation upon which the next generation of healthcare, guided by Industry 5.0 principles, can be built. Their true power, however, emerges from their synergistic integration, which is explored in the next section.

3. Synergistic integration: IoT, AI, and 6G for industry 5.0 healthcare

While IoT, AI, and 6G each offer significant advancements, their true transformative power for healthcare emerges from their synergistic integration. This convergence creates a powerful ecosystem that drives the human-centric, sustainable, and resilient healthcare vision aligned with Industry 5.0. This section explores this synergy, its alignment with Industry 5.0 principles, and highlights key enabling applications.

3.1. *The convergence framework: Data, connectivity, and intelligence*

The integration is modeled as a four-stage sense-transmit-reason-act paradigm that connects data collection with clinical action. The core of the synergy lies in a continuous, dynamic feedback loop encompassing data generation, transmission, analysis, and action:

- **IoT Data Generation (Sense)**: A diverse array of IoT sensors (wearables, ambient, in-hospital) continuously generates massive volumes of heterogeneous health and contextual data, providing an unprecedented real-time view of patient status and environment [173–176].
- **6G Data Transmission (Transmit)**: The anticipated capabilities of 6G provide the essential communication fabric. Its ultra-high bandwidth, massive connectivity, and ultra-reliable low latency ensure that data from potentially millions of IoT devices can be transmitted efficiently and reliably, even for mission-critical applications that require near-instantaneous responses. 6G's native AI integration can further optimize data routing and prioritization for healthcare traffic [177–180].
- **AI Data Analysis (Reason)**: AI algorithms, operating potentially at the network edge (enabled by 6G's distributed intelligence) or in the cloud, process the incoming data streams. They perform tasks ranging from anomaly detection, predictive diagnostics, and risk stratification to treatment recommendation and automated system adjustments [181–183].

- **Feedback Loop (Act)**: The insights and decisions generated by AI can then be used to dynamically adapt the system. This could involve triggering alerts, providing personalized feedback to patients via connected devices, guiding clinical interventions, or even adjusting the sensing parameters of IoT devices, creating a closed-loop system for optimized care [184–186].

This sense, transmit, reason, act framework not only organizes the synergy conceptually but also connects directly to practical uses like telesurgery, ICU digital twins, and AI-driven preventive systems (Sections 4 and 5.2). It transforms fragmented data points into a cohesive, intelligent system capable of delivering proactive and personalized healthcare.

3.2. Use cases and applications

The convergence of IoT, AI, and 6G unlocks numerous transformative healthcare applications. A few key examples are highlighted below:

- **Real-time Remote Robotic Surgery.** This demanding application requires high-resolution video feeds, control signals, and haptic feedback transmitted with minimal latency and maximum reliability. IoT sensors on surgical instruments and the patient provide real-time data. AI can offer guidance, tremor stabilization, and image enhancement. 6G's URLLC and high bandwidth are critical to bridge the geographical gap between surgeon and patient, making complex remote procedures feasible and safe [187,188].
- **AI-driven Personalized Preventive Healthcare Ecosystems**: Imagine individuals with multi-modal IoT wearables continuously monitoring vital signs, activity, and environmental exposure. This data is transmitted seamlessly via 6G to personalized AI models that analyze long-term trends, predict potential health risks (e.g., cardiac events, diabetic complications), and provide actionable, customized coaching or alerts for preemptive intervention, often via connected devices or telehealth facilitated by 6G [79,189–191].
- **Intelligent/Smart Hospitals**: IoT sensors track patients, staff, assets (e.g., infusion pumps), and real-time environmental conditions within hospital walls. This data flows over a reliable internal network (potentially private 5G/6G) to AI platforms that optimize patient flow, predict staffing needs, manage inventory automatically, enhance diagnostic workflows (e.g., prioritizing radiology reads), and improve overall operational efficiency and patient safety [72,192,193].
- **Advanced Self-Optimizing Hospital Applications**: Building upon the intelligent hospital concept, four novel applications are identified that demonstrate significant operational efficiency and sustainability improvements:
  (a) **Predictive Resource Orchestration Systems:** AI algorithms analyzing real-time IoT sensor data (patient flow, equipment utilization, environmental conditions) transmitted via 6G networks can predict resource bottlenecks 2–4 hours in advance [194]. For example, when ICU occupancy sensors and patient monitoring data show a possible bed shortage, the system coordinates with discharge planning, ambulatory services, and supply chain management to improve patient flow while ensuring quality care [194].
  (b) **Intelligent Maintenance and Asset Optimization:** Utilizing IoT sensor networks in conjunction with AI-driven predictive maintenance can prevent equipment failures before they occur [195]. Digital twins of essential medical equipment, such as MRI machines, ventilators, and surgical robots, continuously track performance metrics and forecast maintenance needs [196,197].
  (c) **Automated Infection Control and Environmental Safety:** Real-time air quality monitoring, surface contamination detection, and human movement tracking through IoT sensors can enable dynamic infection control protocols. AI systems can automatically adjust ventilation patterns, trigger cleaning protocols, and even modify patient placement strategies to minimize infection transmission risks while optimizing resource utilization [198].
- **Holographic Telemedicine and Training**: To address scalability and sub-millisecond latency requirements, it is important to note that widespread use depends on a system-level design that includes 6G network slicing for URLLC priority, AI-driven lightweight 3D compression, and ISAC for environmental sensing, and 6G alone is not enough [199,200]. Initial deployments (e.g., inter-hospital consults) will operate with low single-digit millisecond latency, with sub-millisecond latency as a long-term target, supported by native AI optimization and edge rendering. This is consistent with our 5G telesurgery case study (Section 6.2), which achieved 12ms latency, suggesting sub-ms is aspirational for consumer-grade systems in the near term [201,202]. Leveraging 6G's high bandwidth and low latency, combined with advanced AI for rendering and interaction, clinicians could consult with patients or specialists via realistic holographic projections, enhancing diagnostic accuracy and empathy in remote settings. Similar technology could provide immersive, interactive training for medical professionals, overlaying AI-generated insights onto holographic anatomical models fed by real-time IoT data if applicable [203,204].

These examples illustrate how the combination of ubiquitous sensing (IoT), intelligent analysis (AI), and seamless, high-performance connectivity (6G) creates possibilities far exceeding the sum of their parts, paving the way for a truly transformed healthcare landscape aligned with Industry 5.0 values.

4. Medical large-language models (medLLMs)

Large Language Model (LLM) research in medicine has evolved through three major waves, each marked by significant advancements in model size, data diversity, and accessibility (See Figs. 6 and 7 and Table 4) . These waves reflect the rapid progress in applying AI to complex medical challenges. Table 5 provides an overview of the key models from each wave.

Wave 1: *Domain-specific BERT derivatives (2019-2021).* The first wave of medical LLMs focused on adapting existing transformer models, such as BERT, to biomedical tasks. Early biomedical transformer models such as BioBERT [221] and ClinicalBERT [220]

Table 4
Overview of recent domain-specific large language models for biomedical and clinical tasks from 2019 to 2025.

Model Name	Key Features	Primary Use Case	Base Model	Year	Access	Parameters
Med-PaLM 2 [205,206]	High accuracy on medical exams (MedQA), summarizes info, generates clinical text.	Clinical QA and Summarization	PaLM 2	2023	Closed	70B
AMIE [207]	Engages in diagnostic dialogue; shown to exceed PCP accuracy in a study.	Diagnostic Dialogue	Gemini	2024	Closed	Undisclosed
Gemini (MedLM) [208]	Family of models fine-tuned for healthcare, including summarization and insights from unstructured data.	General Clinical Tasks	Gemini	2023	Closed	Undisclosed
Med-PaLM M [209]	Multimodal; integrates and interprets text, imaging (X-rays), and genomics.	Multimodal Analysis	PaLM-E	2023	Closed	Undisclosed
Med42 [210–212]	High-performing on medical benchmarks, designed for clinical reasoning.	Clinical Reasoning	MPT	2023	Open (for non-commercial)	70B
BioMistral[213, 214]	Further pre-trained on PubMed Central; strong performance on biomedical benchmarks.	Biomedical QA and Research	Mistral	2024	Open	7B
MedGemma [215]	Further pre-trained and instruction-tuned for general medical tasks.	Medical QA & Text Processing	Gemma	2025	Open	7B
GatorTron [216]	Trained on 82B+ words of clinical notes and biomedical text for concept extraction.	Clinical NLP De-identification	BERT	2021	Open	345M - 5B
BioGPT [217]	Generative model for biomedical text generation and literature mining.	Text Generation Mining	GPT-2	2022	Open	1.5B
PubMed-BERT [218]	BERT model pre-trained from scratch on PubMed abstracts and full-text articles.	Biomedical Text Mining	BERT	2021	Open	340M
ClinicalT5 [219]	Encoder-decoder model for clinical text summarization and NLI tasks on MIMIC data.	Clinical Summarization NLI	T5	2022	Open (Credentialed)	220M - 770M
Clinical-BERT [220]	Pre-trained on MIMIC-III clinical notes for tasks like patient outcome prediction.	Clinical Prediction	BERT	2019	Open	110M
BioBERT [221]	Pre-trained on large-scale biomedical corpora (PubMed) for NER and relation extraction.	Biomedical NER	BERT	2019	Open	340M
PMC-LLaMA [222]	Instruction-tuned LLaMA for medicine, using 4.8M biomedical academic papers.	Medical Instruction Following	LLaMA	2023	Open	13B
ChatDoctor [223]	LLaMA fine-tuned on real doctor-patient conversations from an online					
medical consultation platform.	Medical Chat/Consultation	LLaMA	2023	Open	7B	
MedAlpaca [224]	Instruction-following model fine-tuned on a high-quality medical conversational dataset.	Medical QA	LLaMA	2023	Open	7B, 13B
HuatuoGPT-II [225]	Advanced model trained on a massive Chinese medical knowledge graph and dialogues.	Chinese Medical Consultation	Baichuan	2024	Open	13B
EHRAgent [226]	LLM agent that autonomously generates and executes code to query and analyze EHRs.	EHR Tabular Reasoning	GPT-4	2024	Research	Undisclosed
EHRMamba [227]	A Mamba-based foundation model for EHRs that handles very long patient sequences efficiently.	EHR Forecasting Analysis	Mamba	2024	Open	Undisclosed
BMRetriever [228]	Dense retriever models optimized for searching and retrieving biomedical information.	Biomedical Information Retrieval	T5	2024	Open	410M, 2B
DR-BERT [229]	Protein language model specifically trained to annotate intrinsically disordered regions in proteins.	Protein Structure Analysis	BERT	2021	Open	15M
ADAM-1 [230]	Multi-agent framework that integrates microbiome and clinical data for Alzheimer's detection.	Alzheimer's Research and Detection	GPT-4o	2025 (Announced)	Research	Undisclosed
BioAgents [231]	Multi-agent system using smaller, specialized LLMs to democratize complex bioinformatics analysis.	Bioinformatics Workflows	Phi-3	2025 (Announced)	Research	Undisclosed
CliniQ [232]	Not a model, but a benchmark for evaluating EHR retrieval models with a focus on semantic matching.	EHR Retrieval (Benchmark)	N/A	2025 (Announced)	Open	N/A
Radiology-Llama [233]	Llama 2 fine-tuned on radiology reports or automated report generation and analysis.	Radiology Report Generation	Llama 2	2023	Open	13B
PULSE [234]	Fine-tuned on a vast dataset of clinical notes and chest X-ray reports for multimodal tasks.	Multimodal Clinical Analysis	Undisclosed	2023	Closed	Undisclosed

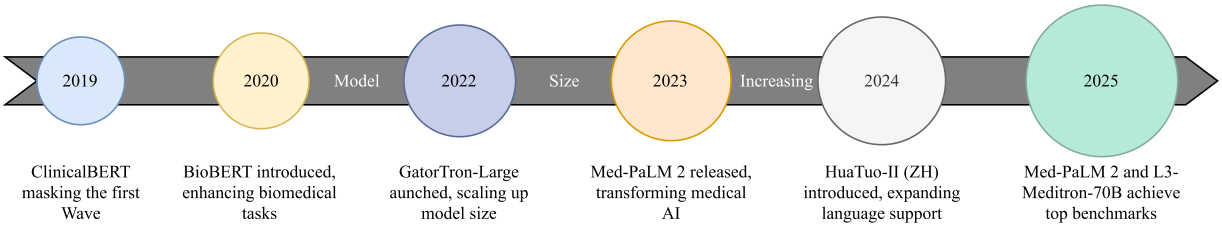

Fig. 6. Evolution of Medical Language Models (2019–2025). The timeline highlights key architectural advancements and performance milestones in clinical natural language processing, from early domain-specific BERT variants to contemporary large-scale generative models.

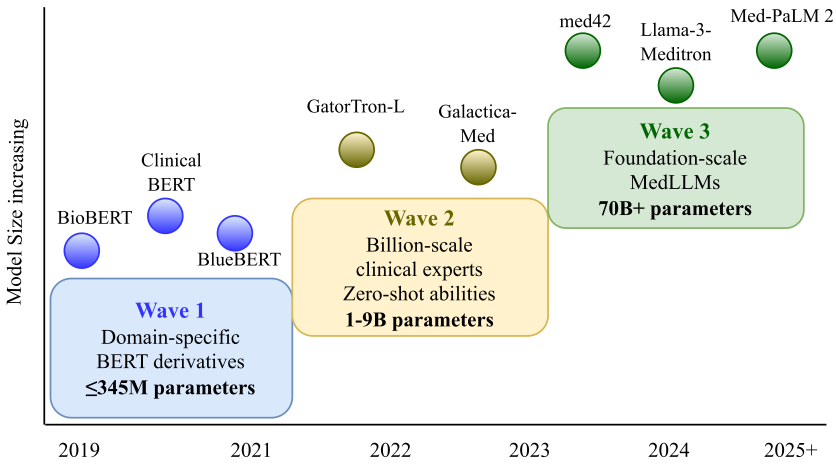

Fig. 7. Progression of medical language model capabilities across three developmental waves.

Table 5
Evolution of purpose-built Medical LLMs (2019-2025). "Wave" corresponds to the chronology described in the text.

Wave	Model	Year	Params	Tokens (b)	Licence	Context	Primary Benchmark	Ref.
1	BioBERT	2020	345 M	4.5	BSD-3	512	NER/RE	[221]
	ClinicalBERT	2019	110 M	0.8	MIT	512	MedNLI	[220]
2	GatorTron-Large	2022	8.9 B	82	NGC-EULA	2 048	MedNLI	[235]
	Galactica-Med	2022	6.7 B	106	CC-BY-NC	2 048	PubMedQA	[236]
3	Med-PaLM 2	2023	70 B	8.9	Proprietary	32 k	MedQA 86.5 %	[205]
	L3-Meditron-70B	2023	70 B	5.6	Apache-2.0	64 k	MedQA 88.2 %†	[237,238]
	HuaTuo-II (ZH)	2024	13 B	4.7	CC-BY-4.0	32 k	MedBench 72.4 %	[225]

were relatively small, with up to $\leq$ 345M parameters, small by today's standards. However, they were groundbreaking at the time. By fine-tuning on specialized datasets, such as PubMed abstracts and de-identified electronic health records (EHRs), these models achieved significant improvements in tasks like named-entity recognition (NER) and relation extraction. This wave demonstrated that even modestly sized models could deliver meaningful results when tailored to the medical domain.

Wave 2: *Billion-scale "clinical experts" (2021-2023).* The second wave saw a leap in scale, with models exceeding one billion parameters. This increase unlocked new capabilities, such as zero-shot reasoning (for solving tasks without specific training) and chain-of-thought reasoning (for breaking down complex problems step-by-step). Models like GatorTron-Large with 8.9 billion parameters [235] and Galactica-Med with 6.7 billion parameters [236] achieved document-level reasoning, outperforming earlier models like BioBERT on benchmarks such as MedNLI by a significant margin. Despite their size, these models were optimized for efficiency, enabling deployment on single-GPU servers using techniques such as FP16 inference. However, most of these models were restricted by licensing due to the sensitive nature of their training data, such as HIPAA-protected health information.

Wave 3: *Foundation-scale MedLLMs (2023-present).* The third wave represents a turning point in medical AI, marked by the emergence of foundation-scale models, such as Med-PaLM 2 (70 billion parameters) [205] and Llama-3-Meditron (70 billion parameters) [237,238]. These models introduced several transformative features:

- **Context windows:** These expanded from 4 096 to 64 k+ tokens, enabling summarisation of multi-day EHR episodes.
- **Instruction Tuning and RLHF:** These models improved their factual accuracy and relevance in clinical settings by combining large-scale instruction tuning with Reinforcement Learning from Human Feedback (RLHF).

Table 6
Representative text-only MedLLMs (snapshot: June 2025). ‡Tree-of-thought decoding.

Model	Params	Licence	Corpus (B tokens)	Year	Key Benchmark	Score
Med-PaLM 2	70 B	Proprietary	8.9	2025	MedQA	86.5 %
L3-Meditron-70B	70 B	Apache-2.0	5.6	2025	MedQA‡	88.2 %
GatorTron-Large	8.9 B	NGC EULA	82	2022	MedNLI	90.2 % acc.
BioGPT-Large	1.5 B	MIT	15.2	2022	PubMedQA	81.0 %
HuaTuo-XL (ZH)	13 B	CC-BY-4.0	4.7	2024	MedBench	72.4 %

- **Diverse Licensing:** Med-PaLM 2 remains proprietary. However, open-weight models like Llama-3-Meditron (Apache-2.0) and HuaTuo-II (CC-BY-4.0) have enabled local fine-tuning, particularly in low-resource languages.

This wave highlights a growing divide in the field. Larger models (over 40 billion parameters), such as Med-PaLM 2, BM-Jedi, tend to be closed-source due to high computational costs and legal constraints. In comparison, smaller models (with 13 billion parameters or less), such as BioGPT-L, HuaTuo-XL, and AfroClin-13B, are often open-source, which fosters innovation in diverse settings. However, it is important to note that, alongside these rapid advances, MedLLMs also introduce significant risks related to hallucination, bias, explainability, and regulatory compliance. A detailed discussion of these challenges and their implications for clinical deployment is provided in Section 5.

However, while large-scale MedLLMs remain impractical for direct deployment on constrained medical devices, lightweight variants (e.g., ClinicalBERT, BioGPT, PubMedBERT) and compressed versions of larger models provide a viable path forward. By employing distillation, pruning, and edge-compatible fine-tuning, these smaller models can deliver explainability and clinical utility even under strict resource limitations [239–242].

Table 6 contrasts *clinical-note specialists* such as GatorTron with *broad foundation models* such as Llama-3-Meditron.

5. Challenges and open research directions

Despite the immense potential, realizing the vision of healthcare transformed by the synergy of IoT, AI, and 6G within an Industry 5.0 framework faces significant hurdles. Addressing these challenges and pursuing targeted research are critical for successful implementation and adoption.

5.1. Technical challenges

Integrating these complex technologies into cohesive, reliable healthcare systems presents substantial technical difficulties:

- **Integration Complexity and Standardization:** Seamlessly merging diverse IoT devices, sophisticated AI algorithms, and nascent 6G network functions is non-trivial. The lack of standardized data formats, APIs, and vendor communication protocols hinders interoperability and creates integration bottlenecks [243–245].
- **Big Data Management:** The sheer volume, velocity, variety, and veracity of data generated by massive IoT deployments pose significant challenges for storage, processing, real-time analysis, and ensuring data quality. Efficiently handling this data deluge, especially within the latency constraints of 6G, remains a key issue [246,247].
- **Energy Efficiency:** Powering potentially billions of IoT health sensors, many of which are wearable or implantable with limited battery capacity, is a major concern [248]. Furthermore, computationally intensive AI algorithms, whether run centrally or at the edge, require significant energy, which impacts sustainability and device longevity [249–251].
- **6G Performance Guarantees:** While 6G promises extreme performance, consistently delivering guaranteed ultra-low latency (sub-ms), high reliability (e.g., 99.9999 %), and massive connectivity specifically tailored for diverse and critical healthcare applications (from routine monitoring to telesurgery) requires significant network architecture innovation and validation [179,252,253]. Furthermore, ensuring deterministic performance across heterogeneous healthcare environments (urban hospitals, rural clinics, mobile emergency units) is particularly challenging, since real-world settings are more unpredictable than lab conditions [254]. The lack of reference benchmarks for clinical validation also creates uncertainty in translating 6G promises into measurable patient outcomes. Another barrier is the interoperability of guarantees across multi-vendor infrastructures and cross-border deployments, as a telesurgery session or remote patient monitoring system may depend on multiple operators' slices functioning seamlessly together [51,85,254,255]. Without uniform service-level agreements and cross-domain coordination, end-to-end reliability remains fragile. From a clinical standpoint, performance guarantees are not only technical promises but medico-legal commitments: if a 6G-enabled surgery fails due to latency spikes, liability assignment between network providers, device manufacturers, and clinicians becomes ambiguous. This uncertainty may slow adoption until clear accountability frameworks are established [51,85,256].
- **Integrated Sensing and Communication (ISAC):** Employing 6G signals for sensing in healthcare offers exciting possibilities (e.g., contactless vital sign monitoring) but raises challenges in achieving sufficient accuracy, dealing with interference, ensuring privacy, and developing applications that effectively utilize this dual capability [257,258]. Moreover, ISAC raises fundamental questions about medical liability: if sensing data embedded within a communication channel misguides a diagnosis or therapeutic intervention, it is unclear whether responsibility lies with device manufacturers, network operators, or healthcare providers [51,

85]. Addressing these medico-legal uncertainties will be critical before ISAC can move from prototypes into regulated healthcare practice.

- **Lightweight Explainable AI (XAI) for Constrained Devices:** A critical technical challenge lies in optimizing XAI methods so they can operate efficiently on resource-constrained healthcare devices, such as wearables, implantables, and bedside IoT sensors. Conventional XAI frameworks often require substantial computational overhead, limiting their applicability in these settings [79,259]. To address this, techniques such as model compression [259], pruning [260], and knowledge distillation [261] can reduce model size while maintaining interpretability. In parallel, parameter-efficient fine-tuning strategies (e.g., adapters, low-rank factorization) allow models to be updated with minimal added memory costs [262]. Finally, edge-compatible deployment and federated learning ensure that explainability can be achieved locally, lowering latency and preserving patient privacy. Together, these approaches enable interpretable AI in environments with strict energy and memory constraints, thereby expanding the reach of HealthCare 5.0 into real-world clinical and home-care scenarios.
- **Risks and Challenges of MedLLMs:** While MedLLMs show great potential in clinical reasoning, diagnostic conversations, and integrating different types of data, they also come with significant risks that need careful attention. First, these models often experience hallucination, which leads to the generation of fluent but incorrect or unsafe medical statements [263–265]. In critical areas like diagnosis or prescription writing, these errors could threaten patient safety if not supervised by a human [266]. For instance, even sophisticated models like Med-PaLM 2 have been known to suggest harmful treatment options with certain prompts, highlighting the need for human review. Second, the training data for MedLLMs often reflect existing biases, such as the underrepresentation of certain demographic groups, variations in regional health practices, or obscure diseases [266,267]. This can result in models that perform unevenly across different populations. Third, regulatory and ethical guidelines for validating and certifying MedLLMs are still developing. Currently, there is no widely accepted method to evaluate model safety, reliability, or accountability, leading to unresolved issues related to liability, informed consent, and compliance with privacy laws like HIPAA or GDPR. Without strong governance, there is a risk of these systems being used in clinical practice too early or unsafely. Finally, the computational and energy costs of large-scale MedLLMs limit their fair deployment [267]. Training and using models with billions of parameters require special infrastructure that many hospitals and research centers, especially in low-resource or rural areas, cannot access. This leads to a digital divide, where only well-funded institutions can use advanced MedLLM-based services, increasing global disparities in access to medical AI. The need for clinician oversight, bias checks, clear evaluations, and teamwork with regulators is important. Research into efficient and adaptable models is also essential to ensure fairer use in different healthcare settings.

5.2. Security, privacy, and trust

The highly sensitive nature of health data, combined with hyper-connectivity, creates a complex threat landscape:

- **End-to-End Security**: Securing the entire data pipeline from resource-constrained IoT sensors, across 6G networks, to edge/cloud AI platforms and clinical interfaces against diverse cyber threats (e.g., data breaches, manipulation, denial-of-service) is paramount and requires holistic security frameworks [268–273]. The expanded attack surface is a major vulnerability.
- **Patient Data Privacy**: Protecting patient confidentiality while enabling data-driven insights is crucial. Techniques like Federated Learning (FL), Differential Privacy, Homomorphic Encryption, and Secure Multi-Party Computation are promising but require further development for efficient implementation at scale within the IoT-AI-6G ecosystem. Balancing data utility and privacy remains a delicate act [274–277].
- **Trust in AI**: For clinical adoption, both patients and healthcare professionals must trust AI-driven recommendations. This necessitates the development of explainable AI (XAI) methods that can provide transparent justifications for diagnoses or treatment suggestions, especially in high-stakes situations. Overcoming the "black box" problem is essential for building confidence [25,278–280]. Blockchain-based Trust Frameworks: Recently, there has been a growing interest in integrating smart contracts and distributed ledger technologies (DLTs) into the IoT-AI-6G healthcare pipeline. The goal of this convergence is to improve data governance by enabling fine-grained access control policies, tamper-resistant audit trails, and immutable provenance tracking [245,281–283]. For instance, blockchain-based secure data architectures have been proposed wherein patient-generated physiological measurements are cryptographically anchored into a decentralized ledger prior to their transmission via 6G networks. Such an approach ensures end-to-end data integrity and non-repudiation, critical for high-stakes clinical decision-making. In addition to anchoring raw measurements, smart contract-driven consent management enables dynamic provenance tracking across multiple stakeholders, ensuring that every access request and modification is logged transparently for auditability. Furthermore, decentralized edge computing paradigms such as Bedge-health [65,284–286] illustrate how lightweight consensus mechanisms can be adapted for resource-constrained Fog/edge nodes. These architectures facilitate real-time ingestion and logging of sensor data streams while maintaining secure aggregation protocols that minimize computational burden on low-power medical devices. Despite these advancements, integrating such blockchain frameworks with established Fog computing platforms like FogBus [287,288] presents a significant area of ongoing research. To illustrate in a simulation environment, integration with FogBus allows provenance records to be automatically synchronized between IoT devices and hospital servers, providing clinicians with verifiable assurance of data lineage during diagnosis and treatment.

In this context, several critical challenges remain unresolved. Paramount among them are the optimization of consensus algorithms to support sub-second response times required in time-sensitive healthcare applications, the mitigation of energy and processing

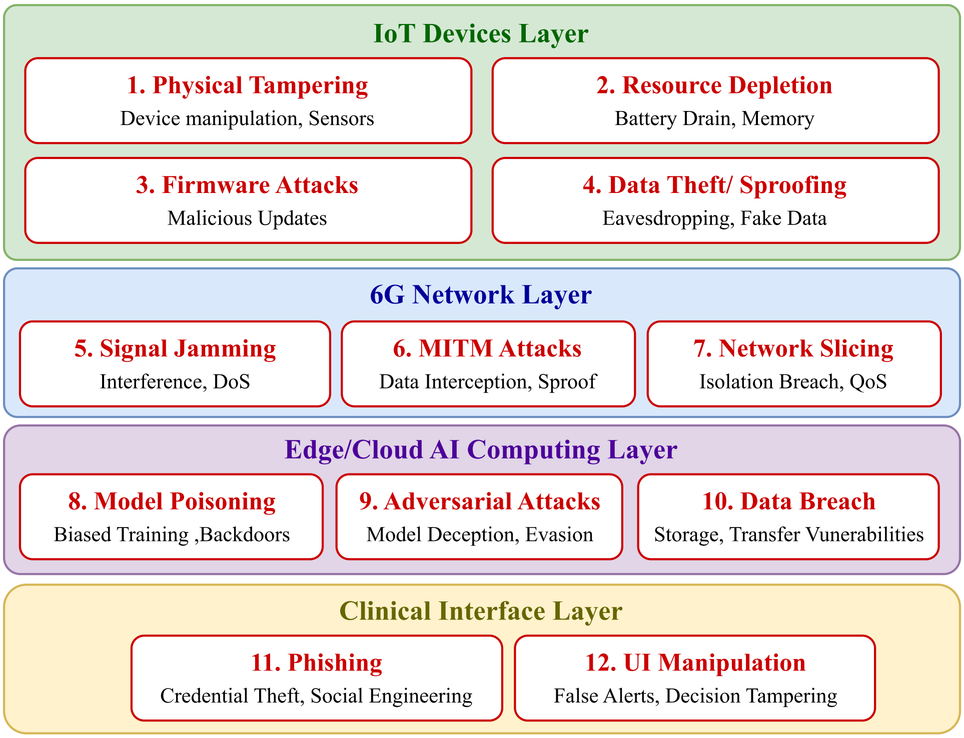

Fig. 8. Healthcare IoT-AI-6G ecosystem threat landscape.

overheads at the network edge, and the development of interoperable interfaces between blockchain layers and smart contract-driven consent management systems [289]. Addressing these issues is essential to realizing scalable, secure, and efficient next-generation healthcare infrastructures.

5.3. Ethical and societal considerations

Beyond technical and security issues, broader societal implications must be addressed (see Fig. 8):

- **Algorithmic Bias:** AI models trained on biased data can perpetuate or even amplify existing health disparities related to race, gender, or socioeconomic status. Ensuring fairness, equity, and rigorous bias auditing in healthcare AI is an ongoing ethical imperative [290,291].
- **Digital Divide and Access:** Unequal access to enabling technologies (smart devices, reliable high-speed internet like 6G) could exacerbate health inequities, creating a divide between those who benefit from advanced digital health and those who do not [72,292]. Ensuring equitable deployment and affordability is crucial. In the near term, 6G rollouts are likely to favor urban, high-income regions due to cost and infrastructure density, potentially excluding rural and resource-constrained areas [293]. This may lead to a two-tier healthcare system, where only certain populations gain access to immersive telemedicine, digital twins, or ultra-reliable telesurgery [256,294]. Policy measures will therefore be required to ensure inclusivity. In this regard, blockchain-based provenance frameworks could support fairness by offering decentralized consent management, allowing under-served populations to retain control over their health data while still participating in collaborative healthcare networks [295]. This provides a governance mechanism that complements infrastructure investments.
- **Impact on Healthcare Workforce:** Integrating AI and automation will inevitably change the roles and required skills of healthcare professionals [296,297]. Proactive strategies for workforce training, adaptation, and addressing concerns about job displacement are needed to ensure a smooth transition that focuses on human-AI collaboration [17,296–298].
- **Regulatory and Approval Processes:** Current regulatory frameworks (e.g., for medical devices, data privacy) often lag behind the rapid pace of technological development, particularly for complex systems combining IoT, AI, and advanced communications. Clearer, agile regulatory pathways are needed to validate the safety and efficacy of these integrated solutions [298]. At present, no clinical-grade certification process exists for 6G-enabled end-to-end healthcare workflows (e.g., a telesurgery operation that integrates IoT sensors, AI guidance, and URLLC communication). Without a pathway for multi-stakeholder approval (clinicians, telecom operators, device manufacturers, and regulators), adoption will remain fragmented and confined to pilot studies [294].

Table 7
End-to-end network KPIs for representative cellular generations in healthcare scenarios.

Generation	Example 3GPP Release/Profile	Latency (ms)	Reliability	Peak Throughput (Gbps)	Healthcare Use-cases
4G LTE-A	Rel-14 eMTC (Cat-M1)	30-70	99 %	0.3	Remote patient monitoring, mHealth apps[311]
5G NR URLLC	Rel-17 SA slice	< 1	99.999 %	10	Robotic telesurgery, AR guidance[115]
6G (target)	IMT-2030/Rel-20 +	0.05-0.1	99.999999 %	≥ 100	Haptic internet, clinical digital twins[312,313]

Table 8
Energy-efficiency outlook for cellular generations (*vs.* 4G baseline).

Generation	Energy/bit	RAN Power-saving Features	Notes	Sources
4G LTE	100 %	Carrier shut-down, C-DRX	Baseline	–
5G NR	↓ 90 %	Massive-MIMO deep-sleep, AI RAN metering	Commercial demos	[320]
6G (proj.)	↓ 99 %	Cell-free mMIMO, RIS joint comm-compute	ITU-R study cycle	[319]

5.4. Open research directions

Addressing the challenges requires focused research efforts, particularly at the intersection of these technologies:

- **Healthcare-Optimized 6G Architectures:** How can 6G network slicing, edge computing, and AI-native capabilities be specifically designed and optimized to meet the diverse QoS requirements (latency, reliability, bandwidth, connection density) of concurrent healthcare applications? [180,271,299]. This includes designing slice-level safety certification for mission-critical services like holographic telemedicine, where deterministic performance must be guaranteed end-to-end across multi-vendor infrastructure.
- **Lightweight, Secure, and Explainable Edge AI:** Developing energy-efficient, robust AI/ML models capable of running securely on resource-constrained health IoT devices, while also providing explainability for critical health inferences [277,300–304].
- **Trustworthy Human-AI Collaboration Frameworks:** Creating verifiable methods and interfaces that foster effective and trusted collaboration between clinicians and AI systems in complex diagnostic and therapeutic scenarios within the Industry 5.0 paradigm [303,305,306].
- **Energy-Autonomous Health Monitoring:** Research into ultra-low-power IoT communication protocols (possibly leveraging 6G features) and energy harvesting techniques to enable long-term, unobtrusive, "deploy-and-forget" health sensors [307,308].
- **Novel Health Applications of 6G Features:** Exploring and validating new diagnostic or therapeutic possibilities unlocked by unique 6G capabilities like Terahertz imaging/spectroscopy for non-invasive sensing or advanced ISAC for fine-grained activity recognition and vital sign monitoring [165,166,309].
- **Privacy-Preserving Distributed Learning at Scale:** Advancing scalable and efficient FL or other distributed privacy techniques that work effectively over 6G networks with heterogeneous IoT data sources for collaborative health intelligence without compromising patient confidentiality [276,277,310].

Targeted research in these areas is crucial to overcoming the identified barriers and unlocking the full potential of this technological synergy for a future human-centric, sustainable, and resilient healthcare system.

6. Empirical evidence and standards

6.1. Quantitative performance comparison

Table 7 contrasts the headline *network-centric* KPIs end-to-end latency, reliability, and peak user throughput across 4G LTE, 5G NR, and the projected 6G IMT-2030 targets. Two observations stand out: **(i)** the three-orders-of-magnitude reliability increase from 4G (99 %) to 6G (“six nines”) is even more dramatic than the latency improvement, underscoring the centrality of ultra-reliability for mission-critical tele-interventions, **(ii)** peak throughput, while impressive, is *not* the primary bottleneck for most health workloads, which are dominated by small haptic control packets rather than high-rate video streams [115,311–315].

To complement the network view, Table 8 summarises the *energy-per-bit* trajectory and the RAN power-saving mechanisms that enable it. The 90 % reduction already demonstrated in commercial 5G deployments provides an empirical baseline for the more aspirational 99 % target now being discussed in Hexa-X II white papers [316–319]. Finally, the bibliometric snapshot in Table 9 reveals a steep rise in peer-reviewed 5G healthcare publications between 2018 and 2024, alongside a non-trivial increase in registered Phase I/II clinical trials [115,311,315]. The data confirm that the technology moves beyond concept demonstrations toward regulated clinical evaluation.

6.2. Case studies

Two representative deployments were examined to ground the KPI analysis in operational reality.

Table 9
Bibliometric trend for "5G AND healthcare" (PubMed query, April 2025).

Year	Publications	Phase I/II Trials	Notable milestones
2018	7	0	Concept papers dominate
2021	42	4	First human-in-the-loop 5G telesurgery
2024	118	13	Multi-site AI-assisted remote ultrasound trials

Table 10
Layered mapping of interoperability, safety, and security standards relevant to IoT-AI-6G healthcare.

Stack layer	Interoperability	Safety / Quality	Security & Privacy	Governing bodies	Key gaps
Device	IEEE 11073-1070x; HL7 FHIR R5	IEC 60601-1; IEC 80601-2-77	NIST 800-53 IoT; ISO/IEC 27,001	IEEE, ISO, HL7	Wearable AI sensor conformity
Network	3GPP Rel-18/19 URLLC; IETF DetNet; ETSI MEC 016	ITU-T Y.3107 QoS	3GPP SA3 33.531	3GPP, IETF, ETSI	Slice-level safety certification
Edge / Cloud	ISO/IEC 23,894 AI risk; ETSI MEC IEG	IEC 62304-Amd2 (SaMD)	CSA STAR; PCI DSS 4.0	ISO, IEC, CSA	Harmonised edge-AI lifecycle
Data and AI svc.	ISO/IEC 5338; IMDRF SaMD N41; EU AI Act (HR)	AMA Digital Health	GDPR; HIPAA; ISO/IEC 27,701	EC, FDA, IEEE	Global AI conformity reciprocity
Human Factors	IEC 62366-1; ISO 9241-210; WHO Ethics 2023	–	–	IEC, WHO	Integration in agile dev cycles

Case Study 1 – 5G-enabled Robotic Telesurgery [321,322]. As detailed in the narrative that precedes Table 7, a surgeon located in New York performed four laparoscopic tasks on a porcine model in Barcelona through a standalone 5G URLLC slice with a median round-trip latency of 12 ms and zero packet loss [321]. This latency is an order of magnitude lower than that reported in the earliest 4G tele-operation pilots [323], and well within the 20-ms upper bound identified by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES).

Case Study 2 – Neuro-ICU Digital Twin [292,324,325]. The University of Florida’s real-time digital twin ingests data from over 400 heterogeneous IoT sensors over a private 5G band-n77 RAN. Early results show an AUROC of 0.91 for sepsis prediction 3h in advance and an 18 % reduction in nurse walking distance, evidence that edge-resident graph neural networks can translate network KPIs into measurable clinical outcomes.

These examples illustrate that the leap from 5G to 6G is not merely about faster radio links, but about enabling *system-level co-design*, where network slicing, edge AI, and clinical workflows are jointly optimized.

6.3. Standards and regulatory ecosystem

Table 10 maps the multi-layered standards landscape from the physical device tier to human-factor governance. Three insights emerge:

1. **Convergence, not silos**: 3GPP Rel-18 URLLC specifications reference security artefacts from ISO/IEC 27,001 and risk-management processes from IEC 62304, signalling increasing cross-forum alignment [326–328]. At the data layer, HL7 FHIR [329] has emerged as the primary cross-platform healthcare data exchange standard, complemented by semantic ontologies such as SNOMED CT and LOINC for clinical reasoning. At the network layer, 3GPP 6G proposals, IETF Deterministic Networking [330,331], and IEEE 802.1 TSN [332] provide interoperability foundations for mission-critical latency and reliability. At the application layer, openEHR and IMDRF SaMD frameworks ensure clinical interpretability, while security and privacy are underpinned by ISO/IEC 27,001 and ETSI ISG PDL for distributed ledger interoperability.
2. **Edge-AI regulatory vacuum:** While FDA’s “Good Machine Learning Practice” guidance addresses software as a medical device (SaMD) in the cloud, no equivalent framework yet covers deterministic execution on *on-premise* MEC nodes [333–335]. This gap shows the need for harmonized AI lifecycle standards (e.g., ISO/IEC 23894, ISO/IEC 5338) that explicitly account for edge deployment scenarios in healthcare.
3. **Slice-level safety certification:** Existing safety standards (e.g., IEC 60601-1) apply to individual devices, whereas a URLLC slice supporting telesurgery constitutes a *system-of-systems*. The lack of a certification pathway here is poised to become a primary bottleneck for the large-scale adoption of 6G in clinical settings. This limitation becomes more significant because traditional device-level certification does not consider the changing behavior of network slices. Their reliability can vary based on load and context. Therefore, it is crucial to create a new type of system-level safety certification that covers devices, AI algorithms, and network layers. Clinicians and hospitals need this certification to trust the 6G infrastructure for life-critical interventions.

Finally, it is important to point out that while current standards offer strong foundations for interoperability, further integration between healthcare-specific frameworks, such as HL7 FHIR and openEHR, and new 6G network functions, like the Network Data Analytics Function in the 6G core, remains a significant challenge.

By situating earlier KPI and case-study findings within this standards matrix, practitioners are provided with a navigational chart that links technological capability to compliance obligations and, crucially, to the open gaps that motivate the research agenda laid out in Section 5.

7. Conclusion

This study outlines the first comprehensive roadmap for HealthCare 5.0 by combining the latest advancements in IoT, AI, and 6G. The integration of these technologies has the potential to transform remote monitoring, predictive analytics, autonomous diagnostics, and personalized treatment planning. The study highlights the need for teamwork across different fields, data privacy, and clear AI to build trust and encourage use in clinical settings. It also points out four research areas that must be explored to unlock the full potential of HealthCare 5.0: **(i)** health-optimized 6G RAN designs with slice-level safety certification, **(ii)** lightweight, clear edge-AI for real-time decision support, **(iii)** privacy-preserving federated learning on a global 6G scale, and **(iv)** energy-autonomous sensing to maintain constant monitoring without needing battery changes. By tackling these issues, HealthCare 5.0 aims to provide sustainable, efficient, and patient-centered care systems in line with Industry 5.0 principles.

CRediT authorship contribution statement

Abolfazl Younesi: Writing – review & editing, Writing – original draft, Investigation; **Elyas Oustad:** Writing – review & editing; **Mohsen Ansari:** Writing – review & editing; **Thomas Fahringer:** Writing – review & editing; **Rajkumar Buyya:** Writing – review & editing.

Data availability

No data was used for the research described in the article.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT mainly for two purposes: first, to improve the fluency and readability of the English text, and second, to help organize and segment sections of the manuscript. It is important to emphasize that all data organization, interpretation of results, conceptual contributions, and domain-specific analyses were done entirely by the authors. After AI assistance, the authors thoroughly reviewed, validated, and corrected all outputs to ensure technical accuracy and scholarly integrity. The authors take full responsibility for the final content of the article.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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