



Blockchain: chaining digital health to a new era

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Blockchain technology, first known as Bitcoin, is an integration of distributed ledgers, asymmetric encryption, and hash algorithms to achieve decentralization, immutability, security and traceability (1). It eliminates intermediaries, transfers the trust from institutions to hard coding, and is considered the turning point to collapse the monopoly of data by returning control over information to individual owners (2). Ethereum, a symbol for advanced concoction, was empowered by smart contracts (3), which are coding programs that automatically self-execute the exchange of value once specific agreements are triggered. Most of the aforementioned applications are on public chains, which mean that everyone in the community has viewing permission. As the need increases in high-security industries such as pharmacies and healthcare, there has emerged a new type of blockchain, the consortium chain, with inspected members.

Blockchains can be utilized on a large scale in healthcare, where data silos caused by the centralized framework for data storage and the rigorous requirements for data security hinder information sharing, especially when billions of data points are generated by wearable devices and tremendous demands for data storage and utilization are created by artificial intelligence (AI). Furthermore, the advantages of blockchains over verifying the ownership of data and extending the spatial or temporal dimension (4,5) also endow the concept of the blockchain with promising prospects in the healthcare industry. Guardtime partnered with the Estonian government to deploy a nationwide blockchain-based platform to validate patient identities and

secure citizens' health records in a patient-centric way. This system ensured that patients could control their data and determine access permissions and was immune to malicious tampering, even with multiple stakeholders (6).

The involvement and interactions of more parties and nodes of clinical trials far from the main institutions produce the chance of human-induced error, whether accidental or malicious. The prototype designed by Wong *et al.* presented a blockchain-based solution for clinical trials to lock every alteration on the chain involving multiple parties under the inspection of regulators (7). Additionally, applicable scenarios due to immutability or traceability can be extended to pharmaceutical supply chain management, medical professional credentialing and licensing, and health insurance claims management (8,9). Inspired by data monetization solutions to incentivize individual data sharing, companies such as Nebula Genomics have established blockchain-based data marketplaces to enable individuals to sell their biological data, including DNA sequences, to other stakeholders with digital rewards (10-12). Patients not only have control over their data but also have the right to share the profits generated by their data in the digital health ecosystem.

However, in view of the Gartner Hype Cycle, the blockchain is still in the stage between the "peak of inflated expectations" and the "trough of disillusionment" (13). For the healthcare industry, security and privacy are the main concerns. In general, the balance between transparency and confidentiality may be subtle when "everyone can see everything" on public chains, while further applications

might concentrate on specific solutions utilizing consortium chains or private chains. Immutability is also a double-edged sword when patients expect to take their data off the chains. Furthermore, if all medical data are on the blockchain, it will become swollen as it does not fundamentally change how data are stored but rather changes how to retrieve and share data; thus, in most applications, data are stored outside the chains with cryptographic address pointers on the chains (14). Additionally, the application of a blockchain must be subject to elaborate consideration and reproductive testing by professionals. From 2016 to 2019, hackers obtained cryptocurrency of more than 80 million dollars by exploiting the bugs of smart contracts (15). Hence, before their widespread adoption, the feasibility of blockchains in healthcare remains to be tested on a larger scale.

Nevertheless, due to the evolution of technology, not just data can be distributed through blockchains but models and computing power can also be allocated, which implies that the mistrust about putting data on the chain may be decreased. With its fit-for-purpose, a blockchain-based pharmaceutical application, the Machine Learning Ledger Orchestration for Drug Discovery (MELLODDY) project, is expected to train AI models with numerous datasets without altering data storage or sacrificing data ownership. In addition, quantum computing might trigger fundamental changes in underlying cryptography (16), and future encrypted technology will be beyond what we can imagine.

Moreover, breaking down data silos utilizing blockchains might cause “technology silos” when data are locked into various chains without being connected to each other under general standards (8). Therefore, general standards for data sharing across blockchains are essential for releasing blockchains’ dividends and promoting data sharing to the greatest extent. Sophisticated upstream and downstream facilities to back up extensive blockchain applications in healthcare are crucial. As data engines, they ultimately consume data to generate value and promote the development of the blockchain, in turn contributing to forming a closed-loop ecosystem (17). The sounder the standards among different chains and supporting facilities are, the clearer the blueprint of healthcare blockchain-based ecosystems will be realized.

The technology fusion of AI, big data mining, cloud computing, and supercomputers has unleashed the power of big data and technology and presented challenges in fit-for-blockchain scenarios. As mentioned above, in healthcare, the blockchain may be able to blend AI with other techniques to sufficiently address such data in the

near future while breaking down data and technology silos. Although the blockchain is in its infancy, appropriate healthcare applications and research will spur the potential of the blockchain after it is securely tested by professionals and facilitate the establishment of the ecosystem.

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