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Blockchain Technology in Clinical Research

By Norman M. Goldfarb

The recent explosion in the price of Bitcoin hints at the potential of the underlying blockchain technology to transform a broad range of industries, including heathcare[1-3] and clinical research[4-6].

Like the Internet, blockchain is fairly simple idea that can be used to create complex structures and processes with profound consequences. According to Sotos and Houlding, "blockchains are simply a time-stamped ledger of data and transactions. They create trust by being secure, public, permanent and rigorously tamper-proof. Bitcoin is just one application built on a blockchain foundation."[5]

Millard[1] provides an excellent introduction to the application of blockchain technology to healthcare:

> The so-called digital ledger technology was developed in 2008 by Satoshi Nakamoto, a possibly pseudonymous person (or perhaps multiple people) who designed it as the underpinning for the exchange of the digital cryptocurrency known as Bitcoin.
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> Blockchain transactions are logged publicly and in chronological order. The database shows an ever-expanding list of ordered "blocks," each time-stamped and connected to the block that came before it — thereby constituting a blockchain.
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> Crucially, each block cannot be changed, deleted or otherwise modified: It's an indelible record that a given transaction occurred. That's exactly what has many in healthcare excited about blockchain's potential for data security. Its open and decentralized nature could lend itself well to managing health records and proving identity.
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> Unlike with a central database, the blockchain record can be distributed and shared across networks, with credentialed users able to add to — but not delete or alter — the transaction log. Transactions are encrypted and must be verified by the network. "The software used to build a chain ensures that everyone on the network sees, validates, and confirms each proposed next block of data in the chain," Brian Behlendorf explained in a blog post for HIMSS…
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> Behlendorf also spotlighted the importance of so-called "smart contracts" on the blockchain ledger: "simple software programs that run across all nodes in the network and can extend the validation logic at each node in a way that is automatable and undeniable." In healthcare, for example, such smart contracts could be deployed as an "authorization process and confirmation step that notifies the patient — or even puts them in control — when their data is shared from one address to another."
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> Behlendorf said that, because blockchain technology is distributed by design, storage space is limited, so small data or metadata is preferable. The option is to store records or files either on- or off-chain, he said. Large healthcare files, such as imaging scans or PDFs wouldn't need to be stored entirely on the chain, but could be linked to it with a…cryptographic numeric fingerprint, to ensure it hasn't been altered.
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> While one of the strengths of blockchain is its visibility and therefore accountability, not all blockchains are publicly available, he said. "Just as you might have a private

network at your house, or use a VPN to connect to the office, there will be private or consortium chains running between specific organizations, perhaps with a legal or regulatory agreement binding the participants," Behlendorf said. A healthcare organization, for example, could "limit its network nodes to only HIPAA-covered entities, in addition to encrypting some data and leaving other data off-chain to provide multiple layers of security."

Blockchain technology is not just about storing static things like bitcoins and transaction records. It can also store, link to, and trigger software applications, instructions and processes. In other words, the technology can be used to automate workflows in an organization or group of related organizations. Of course, like any software technology, design and testing is required.[7]

Blockchain Technology in Clinical Research

Clinical research labors under a very complex and time-consuming system to ensure that experiments on human subjects are conducted in accordance with scientific precepts and regulations intended to ensure scientific validity and human subjects protection. The current system relies on researchers, subjects and a host of support personnel and organizations to learn and follow these rules in largely manual processes. Whether or not all these people actually followed the rules is also verified through a largely manual process of quality assurance.

The design, conduct, analysis and quality control of a clinical study are largely opaque processes. Despite all the talk about ALCOA and "if it isn't documented, it didn't happen," clinical research documentation is, to great extent, inaccessible, incomplete or non-existent. For example, we rely on detectives (AKA site monitors, auditors and government inspectors) to verify that informed consent was properly obtained, or, to be more accurate, that the current version of the consent form appears to have been signed and dated by the study participant and documented in the study records, according to an SOP that might have been followed by study personnel who appear to be properly trained and qualified.

It is a well-known maxim that it is better to build quality into a process than to test defects out. Clinical research often does not follow this maxim. Blockchain technology offers the opportunity to shift the balance toward built-in quality.

Blockchain technology can improve both quality and efficiency in clinical research, as well as enabling entirely new functionality. The following examples are far from complete and will require actual use to realize their full potential:

- **Study design.** Scientific validity requires researchers to design studies in advance and not change the hypothesis, sample size, analytic methods, etc., after seeing the data. Many scientific publications encourage researchers to upload and register their protocols with ClinicalTrials.gov. In contrast, blockchains automatically record, timestamp, permanently save, and appropriately publish the protocol, analysis plan, etc. If, for example, the researcher later decides to change the sample size, that decision can be fully documented in the blockchain.
- **Patient recruiting.** Patients are naturally cautious about sharing their private medical information with strangers. Access to these data requires the patient's consent, which might not be available during the recruiting process. With a blockchain, patients can maintain highly granular control over their data. They can specify in detail who can access which parts of their data and under what conditions. For example, a patient might specify that academic researchers in the U.S. can access their full, anonymized medical record for free, but industry researchers have to pay $10 for access to a defined subset or $100 for the full record, and $20 to

contact the still-anonymous patient. Similarly, a hospital can control queries against its medical records system, and a researcher can control access to patient data when working with a patient-recruiting firm.

The data for different patients — and even a single patient — can be stored in multiple databases (or on paper). Blockchain technology enables single-point access to data stored in multiple locations, provided they employ a common framework for access. Researchers can even use blockchain to request that a physician's office fax paper records.

- **Informed consent.** Researchers can use a blockchain to record the process of creating the consent document, managing any versions, obtaining consent.
- **Data collection.** With a blockchain, every datum collected is recorded, date stamped, and signed, as are any later additions or corrections.
- **Site monitoring.** Site monitors can use blockchains to access study data and obtain controlled access to medical records. They can add virtual "yellow stickies" to the record.
- **Data analysis.** A blockchain can store or link to a data analysis script that accesses the correct patient dataset and performs the analysis. Since, in this scenario, analysts no longer need a copy of the data, patient privacy is protected.
- **Data sharing.** Patients, researchers and study sponsors can use blockchains to control and record access to genetic data, biosamples, images, etc. Investigators can use blockchains to share data in collaborations. Researchers can also limit access to patient data to specific site personnel for specific time periods.
- **Regulatory compliance.** Certain elements of regulatory compliance can be built into blockchains. For example, the delegation of authority log is part and parcel of a blockchain implementation — delegation to an unqualified person can even be blocked. ALCOA documentation is, to a large extent, an inherent property of blockchains. Blockchain technology makes HIPAA and 21 Part 11 compliance largely automatic (once the system is properly set up).
- **Standard Operating Procedures.** SOPs stored in a blockchain are automatically the current version and can be linked to visit worksheets and training records.
- **Publication.** Scientific publications can use blockchains to give reviewers and readers access to the data, methods and other information required to closely examine a study and reproduce its findings. A blockchain can specify which readers can access which data, when they can access it, and how they can use it.

Conclusion

Blockchain technology holds the promise of revolutionizing clinical research. This article offers a glimpse into some of the potential applications of the technology.

Blockchain technology will also raise new issues. For example, what is the fair price for patient data? How will the technology affect researcher behavior? How much should study sponsors be allowed to know about the details of study conduct at the site? When the entire record of a study can be made public in a practical manner, how much transparency should be allowed and under what circumstances?

It will take many years to fully understand the practical uses and potential pitfalls of the technology. Nevertheless, blockchain technology is ideally suited for highly regulated, highly complex activities, like clinical research, that rely on large volumes of highly sensitive information that must, in a highly complicated manner, be widely shared.

References

1. “How does blockchain actually work for healthcare?” Mike Miliard, Healthcare IT News, April 13, 2017. Accessed at http://www.healthcareitnews.com/news/how-does-blockchain-actually-work-healthcare
2. “Who Will Build the Health-Care Blockchain?” Mike Orcutt, MIT Technology News, September 15, 2017. Accessed at https://www.technologyreview.com/s/608821/who-will-build-the-health-care-blockchain
3. “9 things to know about blockchain in healthcare” Becker’s Healthcare IT & CIO Review, October 3, 2016. Accessed at https://www.beckershospitalreview.com/healthcare-information-technology/9-things-to-know-about-blockchain-in-healthcare.html
4. “Blockchain technology for improving clinical research quality” Mehdi Benchoufi and Philippe Ravaud, BioMed Central, January 25, 2017. Accessed at https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-017-2035-z
5. “Blockchains for Data Sharing in Clinical Research: Trust in a Trustless World” John Sotos and David Houlding, Intel Healthcare, 2017. Accessed at https://simplecore.intel.com/itpeernetwork/wp-content/uploads/sites/38/2017/05/Intel_Blockchain_Application_Note1.pdf
6. “Blockchain protocols in clinical trials: Transparency and traceability of consent (version 4)” Mehdi Benchoufi, Raphael Porcher, and Phillipe Ravaud, F1000 Research, December 8, 2017. Accessed at: https://f1000research.com/articles/6-66/v4
7. "Blockchain and digital process automation (DPA)" IBM, undated. Accessed at https://www.ibm.com/cloud/digital-process-automation/blockchain

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