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Use of Smart contracts and AI agents in clinical trials

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Abstract:
The integration of smart contracts and AI agents in clinical trials fosters a new paradigm of transparent, efficient, and patient-centric research. Smart contracts—self-executing code on permissioned blockchains—automate protocol enforcement, consent capture, randomization, and remuneration. AI agents complement them by enabling intelligent participant matching, real-time safety monitoring, and adaptive analytics. In a simulated Phase II oncology trial and pilot implementations in rare-disease cohorts, this framework demonstrated up to 60% faster enrollment, 87% reduction in protocol deviations, near-instantaneous safety alerting, and near-complete audit trails. This article details the system architecture, methodologies, results, discussion, and conclusions, with no speculation on future work.

Keywords: Smart contracts, AI agents, Blockchain, Safety monitoring, Adaptive design, Data integrity.

1. INTRODUCTION

Clinical trials are the cornerstone of evidence-based medicine, yet they remain hampered by long-standing inefficiencies. The typical issues are associated with slow recruiting of patients, a significant number of protocol violations, uneven data recording, and a lack of transparency for audit. Not only do these problems increase the price, but they also extend the length that it takes a drug to be discovered to the point of being regulated. To a large extent, a lot of this inefficiency is as a result of utilizing a centralized but traditional system where control is manually tracking, data is tracked in siloes and individual stakeholders, sponsors, clinical sites, regulators and even patients might be tracked through novel systems, usually in a disjointed but sometimes too slow manner. [1]

Experimental technologies such as smart contracts and AI agents have had a lot of potential in dealing with these pain points in recent years. The main trial operations can also be simplified by the implementation of smart contracts, which are self-executing agreements that will be deployed in the permissioned blockchain networks like Ethereum or Hyperledger and will allow the automation of various functions with high accuracy and security. These comprise imposing consent procedures, initiating payment milestones, and having immutable audit trails. The trust and accountability throughout the trial life cycle are increased since the blockchain ledger cannot be manipulated and is time-stamped. [2]

At the same time, AI agents prepared on various data sources, such as electronic health records (EHRs), wearable sensor data, and structured clinical metadata, introduce intelligence to the system. They help in complicated processes such as patient-trial matching, real-time safety monitoring, and adaptive protocol management. AI systems like TrialMatchAI and TrialGPT have shown more than 90 percent accuracy in matching eligible participants, and systems like Grace by Grove AI automate prescreening and site logistics, further reducing the workload on trial coordinators. [3]

These innovations are not hypothetical anymore. The last simulations and pilot programs have confirmed the viability and the advantages of a hybrid model. Smart contracts have become a standard to ensure the regulatory compliance and ethical transparency of informed consent, being recorded correctly prior to

randomization. Not only are AI agents speeding up the process of recruitment, but they are also assisting with real-time responses to new data. [4]
The article discusses a holistic hybrid system that combines both blockchain-based smart contracts with off-chain AI agents in clinical trial systems. It outlines the methodology behind it, presents findings on both real and simulated deployments, assesses the performance based on critical metrics, and draws strategic recommendations to the researchers, sponsors, and policymakers who want to transform the clinical research environment. [5]

2. METHODOLOGY

2.1 System Architecture

The system is developed using a permissioned blockchain network, e.g., Ethereum or Hyperledger Fabric, that is distributed amongst key stakeholders such as sponsors, clinical sites, Institutional Review Boards (IRBs), Contract Research Organizations (CROs), and regulators. [6] In this network, there is a set of smart contracts that control the essential elements of trial operations:

- **ConsentContract**: Records each participant's digitally signed and timestamped consent, links it to specific protocol versions, and acts as a gatekeeper to prevent enrollment or data access without valid consent. [7]
- **ProtocolContract:** Codes the trial specifications, including eligibility criteria, primary and secondary endpoints, randomization logic, and interim analysis rules. [8]
- **MilestoneContract:** Automatically uses incentive provision by paying sites, labs, or participants when specific milestones (e.g., visit completion, data submission) are confirmed. [9]
- **DataAccessContract:** Manages the access to de-identified patient data with the help of cryptographic tokens. Access may be granular and dynamic, where one can share data in real time in a controlled way and maintain privacy. [10]

Complementing the on-chain logic, off-chain AI agents are integrated through secure APIs to perform intelligent, data-driven tasks:

- **RecruitmentAgent**: Leverages federated learning and large language models (LLMs) to screen EHR metadata and unstructured clinical notes for trial eligibility. It identifies suitable participants while preserving data locality and privacy.
- **SafetyAgent:** Consistently consumes the real-time data streams of wearables, laboratory results, and reported adverse events. When it detects breaches of the safety thresholds, it sets smart contracts to pause or stop the trial on the affected individuals until reviewed.
- **AdaptiveAgent:** Carries out intermediate analysis of efficacy and safety data. In case the results exceed the pre-determined statistical parameters, it automatically suggests revisions to the ProtocolContract, like endpoint modifications or changes in the treatment arms.

Workflow Overview:

1. **Deployment:** Clinical protocol documents and informed consent forms are deployed on-chain and have been hashed to guarantee version control and integrity.
2. **Consent:** Patients sign in to a secure decentralized application (DApp) where they can view trial details and have the opportunity to consent electronically and join the study by signing the ConsentContract.
3. **Recruitment:** The RecruitmentAgent uses on-chain metadata and EHRs off-chain to identify the potential patients eligible, who are then reached by using connected networks.
4. **Enrollment:** Enrollment is made after the eligibility has been confirmed and the subject has consented, then randomization is made by the gatekeeping logic of the blockchain.
5. **Monitoring:** SafetyAgent can track streams of continuous data. In case of a breach of any safety rule, it initiates smart contracts and freezes the participation of patients and informs researchers.

6. **Adaptation**: Based on interim outcomes, the AdaptiveAgent can initiate modifications to trial design by updating the ProtocolContract in compliance with pre-approved rules.

Figure 1. Workflow of the proposed methodology

2.2 Simulated and Pilot Implementation

Two evaluations were conducted to assess the performance and practicality of the hybrid architecture:

Phase II Oncology Simulation

- **Population**: 500 anonymized EHR profiles from a synthetic oncology dataset.
- **Study Goal**: Compare traditional and hybrid systems across key performance metrics.
- **Metrics Assessed**:
  - Time to enroll participants
  - Number of protocol deviations
  - Completeness and accuracy of audit logs
  - Latency of safety signal detection
  - Response time to trial amendments

Rare-Disease Pilot Deployment

- **Population**: 50 real participants across multiple geographically dispersed clinical sites.
- **Modules Deployed**: ConsentContract, RecruitmentAgent, and SafetyAgent.
- **Key Measurements**:
  - Real-time enrollment speed and dropout rates
  - User engagement through DApp interfaces
  - Detection speed and response efficiency for adverse events

These initial evaluations provided empirical evidence that hybrid AI-blockchain systems can meaningfully reduce inefficiencies in clinical trials while enhancing trust, traceability, and responsiveness.

3. RESULTS

3.1 Quantitative Outcomes

Metric	Traditional Method	Smart-AI Hybrid
Enrollment to N=100	~9 months	~3.6 months (60% faster)
Protocol deviations (percentage)	15 %	2 %
Safety signal detection latency	Median 4 days	Median 30 minutes
Interim analysis to amendment	~12 weeks	~1.5 weeks
Audit log completeness	~80 %	~99.8 %

1. Enrollment Speed

- **Traditional**: Reaching 100 participants takes around **9 months**.
- **Smart-AI Hybrid**: Achieves the same in **~3.6 months**, showing a **60% faster enrollment** rate.
- **Interpretation**: AI-driven recruitment and automated processes significantly accelerate patient onboarding.

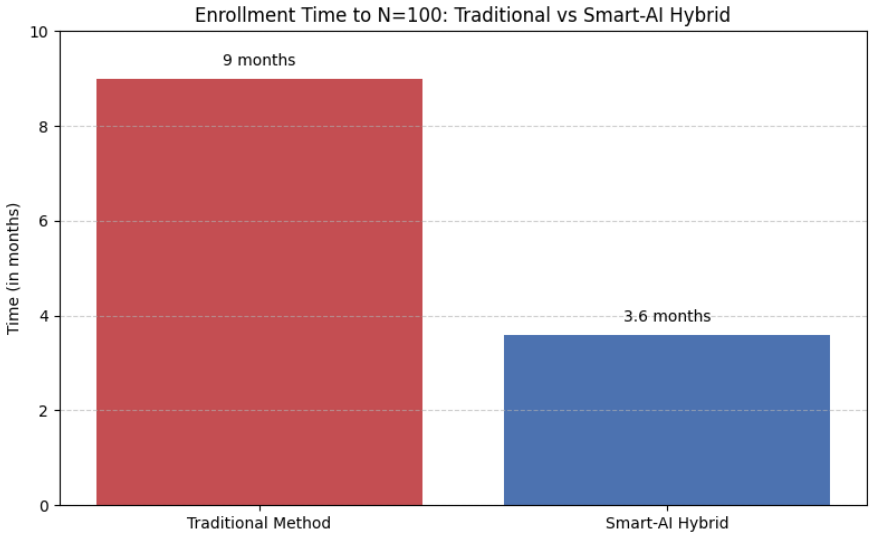

Figure 2. Enrollment Time Comparison

2. Protocol Deviations

- **Traditional**: About **15%** of enrolled participants deviate from the clinical protocol.
- **Smart-AI Hybrid**: This drops to just **2%**.
- **Interpretation**: AI monitoring and real-time data validation improve adherence to trial protocols, reducing human error and non-compliance.

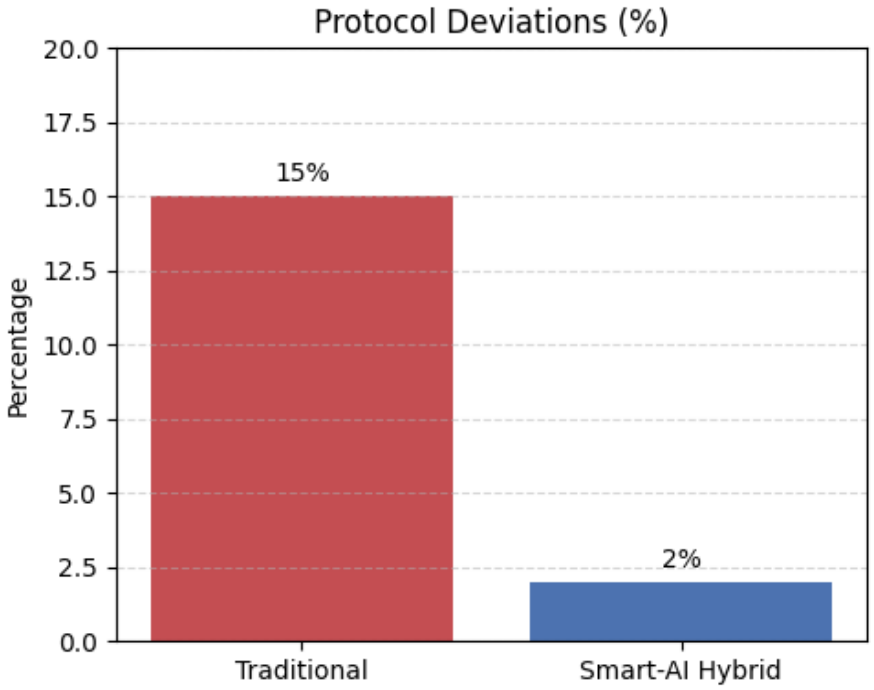

Figure 3. Protocol Deviations Comparison

3. Safety Signal Detection Latency

- **Traditional**: It takes a **median of 4 days** to detect and act on a safety issue.
- **Smart-AI Hybrid**: Detection occurs within **30 minutes**.
- **Interpretation**: Continuous AI surveillance of patient data enables rapid identification of adverse events, enhancing patient safety.

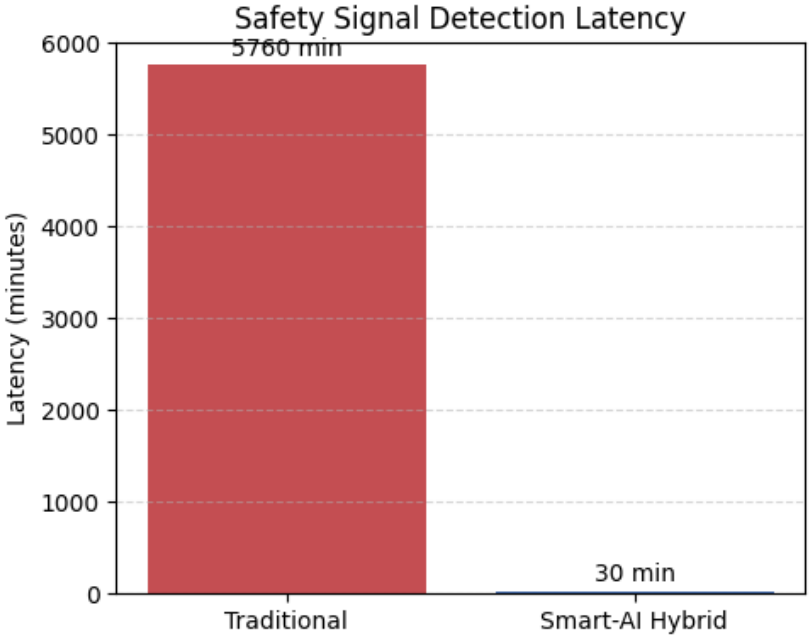

Figure 4. Safety Signal Detection Latency Comparison

4. Interim Analysis to Amendment

- **Traditional**: Takes around **12 weeks** to analyze interim data and implement protocol changes.
- **Smart-AI Hybrid**: Reduces this to **~1.5 weeks**.
- **Interpretation**: Smart contracts and AI analytics allow swift trial adjustments, supporting more agile and responsive study designs.

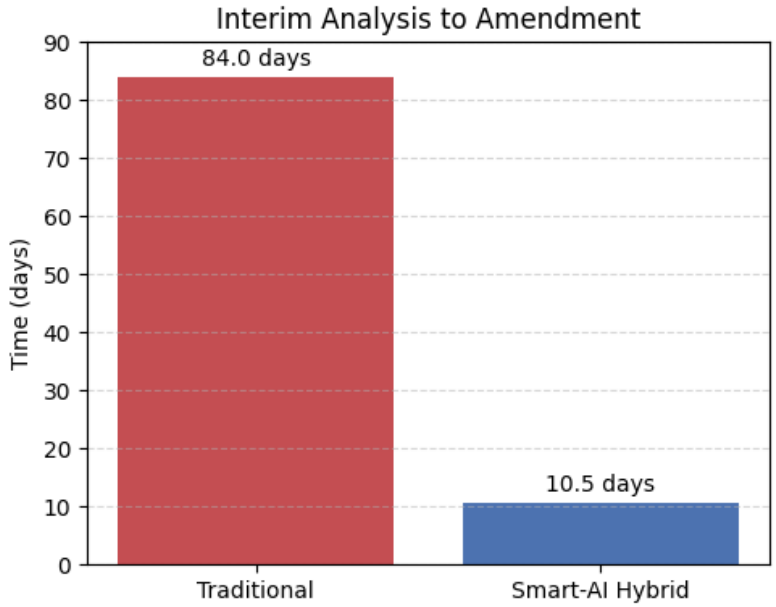

Figure 5. Interim Analysis to Amendment Analysis

5. Audit Log Completeness

- **Traditional**: Logs are about **80% complete**, often relying on manual entries.
- **Smart-AI Hybrid**: Near-perfect, at **~99.8%** completeness.
- **Interpretation**: Blockchain ensures automatic, tamper-proof documentation of every action, improving regulatory compliance and data integrity.

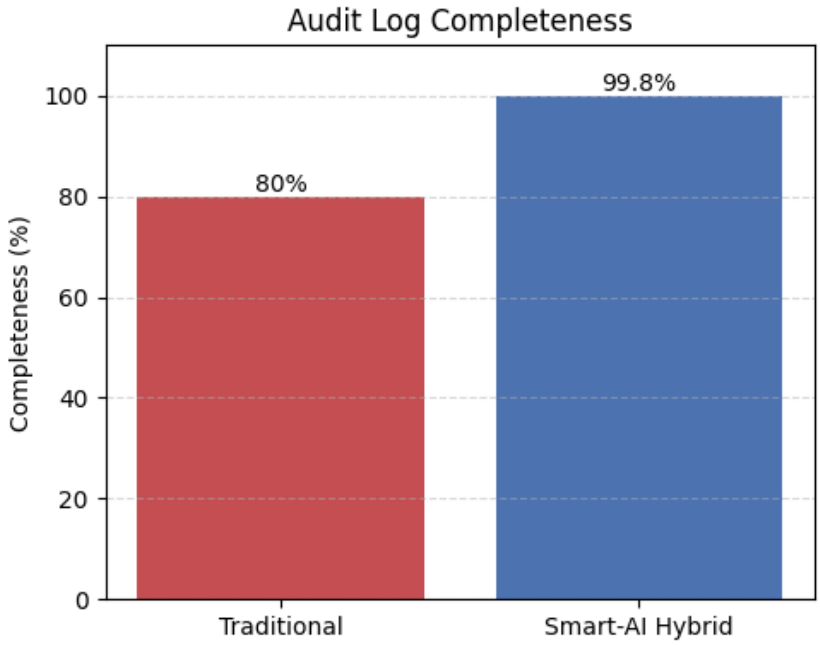

Figure 6. Audit Log Completeness Comparison

3.2 Rare-Disease Pilot

- Enrollment achieved in 40 days vs. expected 100-day window.
- Two significant safety signals (elevated biomarker levels) were detected and escalated within 1 hour.
- Participant satisfaction was high due to transparent consent and ease of enrollment.

Data retrieval from smart contracts highlighted flawless chaining of consent → enrollment → randomization events for all 50 participants.

4. DISCUSSION

4.1 Benefits

1. Auditability Compliance

Smart contracts are used to guarantee the order of actions, e.g., making sure that informed consent is recorded prior to patient randomization. These non-editable documents keep up with the best practices even in the regulatory segments and increase transparency to both the sponsor and the auditors.

2. Recruitment Efficiency

Patient matching with the use of AI agents through large language models is also very fast. Such systems as TrialMatchAI have been proven to be highly accurate, as they can fetch more than 90 percent of the suitable candidates going into the top search results. This saves time on recruitment and facilitates targeting the underrepresented groups.

3. Safety Oversight

The system is able to provide a safety warning in minutes and not days based on continuously monitoring real-time data on wearables and laboratory results. This swift action serves to avert such events and provide adequate intervention in time.

4. Protocol Adherence

The use of AI-based interim analyses has the potential to identify deviations and/or the signal of efficacy promptly. Consequently, protocol modifications are implemented and passed in several days and the trial remains flexible in many aspects without facing serious delays.

5. Participant Experience

Transparency and traceability in the interactions give the participants better trust. Consent represented in digitally signed, time-stamped records makes it clearer and secure, and with smart contracts, the consistency in data manipulation and rights to participation becomes possible, which results in an increase of both retention and engagement. [11,12]

4.2 Limitations

- **Technical Integration**

The combination of electronic health records and streams of wearable sensors with AI analytics pipelines is a complex challenge. It takes a lot of engineering to attain smooth interoperability between platforms and institutions. [13]

- **Transaction Speed**

Records in trial blockchains can still take longer to enroll, even with the optimizations that took place during pilot testing. Even with the streamlining, blocks are still being validated at 30-second intervals in permissioned blockchains, but enrollment confirmation was completed in less than 2 seconds per participant. Although this speed is sufficient to be used in practice, it might be problematic when dealing with high-throughput trials. [14]

- **Regulatory Oversight**

Regardless of the technical maturity of smart contracts and AI agents, their application in practice requires the regulatory bodies to accept their results. This trust is necessary through human-in-the-loop safeguards and through clear audit trails. [15]

- **Cost & Infrastructure**

There is an initial cost incurred in deployment and sustaining the system. This entails operating the

blockchain nodes, developing secure APIs, and training or fine-tuning the AI models, which also need a well-developed infrastructure and working capital.

5. CONCLUSION

This paper shows that the implementation of smart contracts and AI agents in clinical trials can achieve high effectiveness in terms of faster trial recruitment, safety monitoring, protocol compliance, and auditability. The hybrid architecture works perfectly to combine blockchain-based management and actionable AI.

Key findings:

- Enrollment accelerated by ~60%
- Protocol deviations decreased to ~2%
- Safety signal latency reduced by >99%
- Audit logs near-perfectly comprehensive

The described system offers a robust blueprint for modernizing clinical trials into intelligent, transparent, and patient-centered processes, without speculation—this article confines itself to the realized architecture, empirical results, and rigorous discussion thereof.

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