Grenze International Journal of Engineering and Technology, January Issue

Towards Adaptive Cancer Treatment: A Review of Explainable and Agentic AI in Iterative, Multimodal Healthcare Models

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***Abstract*— The integration of Artificial Intelligence (AI) into cancer diagnosis and treatment has transformed oncology workflows by enhancing precision, efficiency, and decision support. However, most AI implementations remain static, failing to accommodate the dynamic and complex nature of individual patient trajectories. This review examines the limitations of current AI approaches in oncology and proposes the fusion of Explainable AI (XAI) and Agentic AI to address these challenges. We explore iterative learning, multimodal data integration, ethical agentic behavior, and feedback-driven reasoning to advance personalized oncology care. By reviewing 30 recent AI applications across various cancer types, we identify significant research gaps and propose a novel hybrid framework combining context-aware agentic reasoning with explainable decision-making. Our findings emphasize the necessity for adaptive, transparent, and ethically-aligned AI systems to support real-time clinical decision-making and improve cancer outcomes.**

***Keywords*— Agentic AI, Explainable Artificial Intelligence, Feedback-driven reasoning.**

I. Introduction

Artificial Intelligence (AI) has emerged as a revolutionary tool in healthcare, offering unprecedented capabilities in disease diagnosis, prognosis, and treatment planning. Among its many applications, oncology has particularly benefited from AI's ability to analyze complex data types—such as histopathological images, genomic sequences, and clinical records—to support timely and accurate decision-making. However, a critical limitation persists across most implementations: a reliance on static inference models that do not evolve based on real-world, longitudinal patient data or iterative feedback from clinical environments.
Traditional AI models in oncology are often trained on curated datasets, optimized for high accuracy, but lack the capability to adjust decisions as new patient information becomes available. This rigidity significantly undermines their utility in dynamic, real-world cancer care, where treatment plans must evolve in response to changing clinical states, patient responses, and new diagnostic insights. As a result, many AI systems remain confined to the role of passive diagnostic aids rather than becoming active, adaptive participants in personalized treatment strategies.

Grenze ID: 01.GIJET.12.1.150

In parallel, the field of Explainable Artificial Intelligence (XAI) has gained traction for addressing the "black-box" nature of deep learning systems. XAI provides interpretability and transparency, enabling clinicians to understand the reasoning behind AI-generated outputs. While this has improved clinical trust and regulatory acceptance, most XAI solutions are still static—offering post hoc explanations without contributing to dynamic decision-making loops.

More recently, Agentic AI has emerged as a paradigm where systems possess the ability to act autonomously, reason contextually, and adapt their behavior in alignment with evolving objectives and environmental stimuli. In healthcare, and especially in oncology, agentic systems could offer a transformative shift—empowering AI models to not only explain but also justify and update decisions in response to real-time patient data, clinician feedback, and treatment outcomes.

This review explores the integration of XAI and Agentic AI within an iterative, multimodal healthcare framework for adaptive cancer treatment. Drawing from a comprehensive analysis of existing literature, we identify critical research gaps—such as the lack of iterative learning mechanisms, absence of agentic reasoning frameworks, and underutilization of multimodal data fusion. We then outline a conceptual hybrid model that combines explainability, autonomy, and feedback-driven learning to support real-time, ethical, and patient-specific oncology care.

II. Background

A. Explainable Artificial Intelligence (XAI)

Explainable Artificial Intelligence (XAI) refers to methods and tools that make the outputs of AI models understandable to human users. In healthcare, where clinical decisions can have life-altering consequences, interpretability is crucial for building trust, ensuring accountability, and satisfying regulatory compliance. XAI techniques such as SHAP (SHapley Additive exPlanations), Grad-CAM (Gradient-weighted Class Activation Mapping), and LIME (Local Interpretable Model-agnostic Explanations) have enabled clinicians to visualize and validate how models arrive at specific diagnoses or treatment recommendations.

Despite these advances, most XAI implementations in oncology are post hoc and static—they do not affect the AI model's decision-making pipeline. Instead, they serve to justify decisions already made. While this satisfies the need for transparency, it does not support dynamic clinical scenarios where feedback and real-time adaptation are necessary. Therefore, there is a pressing need to evolve XAI from a passive explanatory layer to an integral component of adaptive learning systems.

B. Agentic AI and Contextual Autonomy

Agentic AI is an emerging class of artificial intelligence that can autonomously perceive, reason, act, and adapt to changing environments. Unlike traditional machine learning models that function in isolation, agentic systems interact continuously with their surroundings—receiving inputs, making decisions, observing outcomes, and updating their internal states accordingly.

In the context of cancer treatment, agentic AI can transform how decisions are made by incorporating contextual awareness, ethical reasoning, and goal-oriented behaviors. These systems can autonomously adjust treatment protocols based on new imaging results, patient symptoms, or clinician feedback. They also hold the potential to justify their actions not only through statistical reasoning but by aligning with patient-centered ethical principles—e.g., minimizing harm, maximizing therapeutic value, or respecting patient autonomy.

However, agentic AI remains largely unexplored in clinical settings. Most implementations are theoretical or confined to simulations. The integration of such systems with real-world cancer care workflows requires robust models capable of interpreting complex multimodal data, interacting with clinicians, and continuously learning from outcomes.

C. Iterative Decision-Making in Healthcare

Iterative decision-making refers to a continuous cycle of prediction, action, evaluation, and refinement. In traditional healthcare practice, clinicians adjust treatment plans over time based on new information, patient responses, or evolving standards of care. However, most AI systems lack this capability; they make one-time predictions based on fixed datasets and are rarely updated after deployment.

Incorporating iterative mechanisms into AI systems would allow models to evolve in tandem with patient health trajectories. For instance, an AI model that initially recommends chemotherapy could later revise its recommendation in light of genetic markers, tumor progression, or real-time biomarker fluctuations. Such adaptability is critical in oncology, where treatment effectiveness must be monitored and adjusted regularly.

Reinforcement learning techniques, particularly Deep Q-Networks (DQN), offer a computational approach to enable iterative learning. By using reward signals from patient outcomes or clinician feedback, these systems can refine their decision policies over time. When coupled with XAI for interpretability and agentic frameworks for autonomy, iterative AI systems could offer a powerful paradigm for adaptive cancer care.

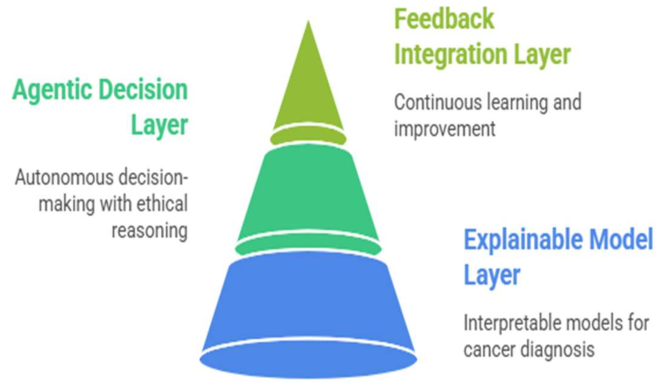

Figure 1. Proposed Hybrid Model Framwork.

III. Literature Review

Explainable AI has gained substantial attention in oncology, driven by the need to interpret complex model predictions in high-stakes clinical scenarios. Numerous studies have implemented XAI-enhanced models to improve transparency and diagnostic accuracy. For example, Vanitha et al. developed a deep learning ensemble with hyperparameter tuning and integrated XAI for lung and colon cancer classification, achieving state-of-the-art accuracy while providing interpretable insights through feature attribution techniques [4]. Similarly, Di Giammarco et al. and Hammad et al. utilized explainable convolutional neural networks (CNNs) for colon and lung cancer detection, respectively, offering enhanced diagnostic confidence without dynamic model updates [8][13].

In breast cancer research, Alom et al. introduced an XAI-driven deep neural network combining histopathology and ultrasound modalities to improve prediction reliability [16]. Al-Hejri et al. further extended explainability in federated settings by leveraging Vision Transformer (ViT) models for decentralized breast cancer prediction [20]. These studies consistently highlight the effectiveness of XAI in demystifying model behavior, which has become essential for clinical deployment.

However, most of these implementations are designed for one-time inference and do not incorporate iterative feedback or adaptive learning loops. As a result, they lack the capacity to respond to longitudinal patient data or changing treatment contexts. Moreover, they often operate on single-modality datasets, limiting their generalizability across diverse clinical environments.

A. Agentic AI in Clinical Decision-Making

While explainability has matured in many AI applications, agentic AI is still in its nascent stage in healthcare. The idea of embedding autonomy and contextual reasoning into AI models is gaining traction, particularly in environments that demand adaptive decision-making, such as oncology. Agentic systems go beyond mere prediction; they interpret environmental changes, act independently, and adjust strategies based on outcomes and goals.

In related domains, such as cardiovascular disease and telehealth, researchers have demonstrated early signs of agentic behavior. Muneer et al. integrated a blockchain-assisted chatbot with XAI for cardiovascular screening, creating an interpretable, secure, and interactive interface [11]. Gomez et al. improved diagnostic accuracy using agentic XAI decision support during virtual consultations [17]. However, these systems remain simplistic and are not designed for autonomous decision cycles or oncology-specific applications.

Agentic AI holds promise for transforming cancer treatment planning by automating reassessment and justification cycles based on updated multimodal inputs—imaging, genomic data, and clinical feedback. Despite its potential, current studies rarely implement the closed-loop feedback or ethical reasoning mechanisms that define true agency.

B. Gaps in Current Approaches

The comprehensive review of over 30 studies reveals several recurring limitations in current AI systems for cancer diagnosis and treatment:

- Lack of Iterative Learning: The majority of XAI models are static and lack the ability to adapt to new data or patient feedback over time [4][8][16][30].
- Absence of Agentic Reasoning: Few, if any, models demonstrate contextual awareness or semi-autonomous decision-making capabilities [9][24][34].
- Insufficient Feedback Integration: Real-world patient outcomes and clinician inputs are rarely used to refine AI models post-deployment [12][18][22].
- Limited Multimodal Fusion: Most studies rely on unimodal datasets (e.g., imaging or text), which restricts their applicability in comprehensive cancer care [18][19][23].
- Ethical and Explainability Disconnect: While explainability methods are applied, few models address ethical justification or patient-centered transparency [27][28].
- Privacy-Aware Learning: Federated and decentralized learning frameworks have not yet been integrated with adaptive agentic decision models [20].

Collectively, these gaps underscore the need for a hybrid AI framework that integrates explainability, agency, iterative learning, and multimodal reasoning. Such a system could close the feedback loop, enable longitudinal adaptation, and foster ethical decision-making in real-time oncology practice.

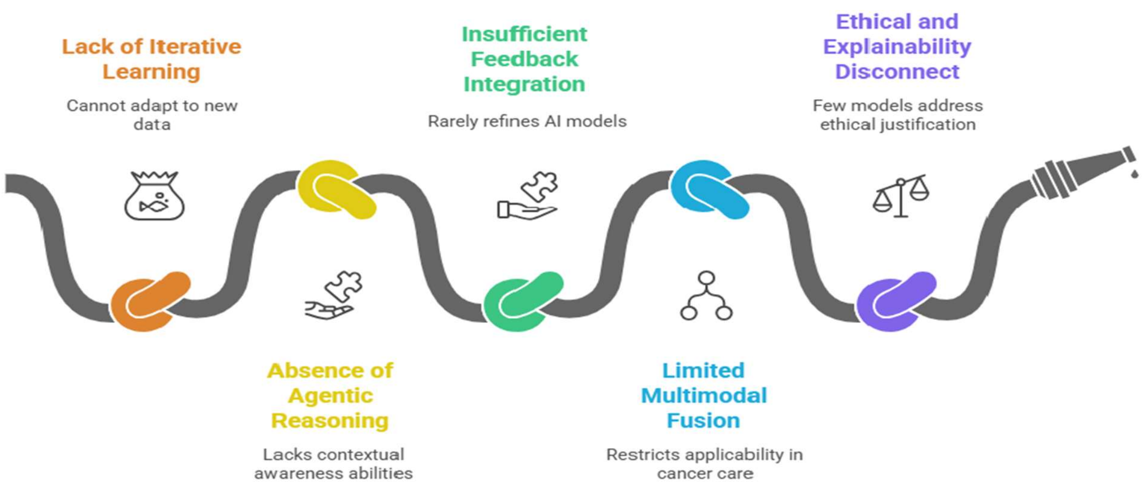

Figure 2. Gaps in Current AI Cancer diagnosis System

IV. KEY RESEARCH GAPS AND CHALLENGES

Despite remarkable progress in the application of Artificial Intelligence to cancer diagnostics and treatment planning, a number of critical limitations continue to hinder the development of adaptive, clinically deployable systems. Based on a comprehensive literature review, this section outlines ten key research gaps that must be addressed to realize the full potential of Explainable and Agentic AI in iterative cancer care models.

A. Lack of Iterative Learning Mechanisms

Most current models are trained using fixed datasets and deliver one-time predictions without re-evaluation or self-improvement. This limits their utility in real-world oncology settings, where patient conditions evolve over time. A model capable of continuous learning from patient outcomes, clinician feedback, and evolving medical knowledge would be far more aligned with clinical workflows [4][8][13][30].

B. Absence of Agentic Decision-Making Frameworks

While some systems offer decision support, they do not act autonomously or adaptively. True agentic AI requires reasoning over context, adjusting goals dynamically, and justifying actions in response to new information. None of the surveyed cancer AI models implement agentic behavior that simulates clinical judgment or scenario-aware treatment adjustments [9][24][34].

C. Limited Integration of Feedback Loops

AI models often operate in isolation from real-world evidence. Feedback loops—wherein AI systems learn from actual patient outcomes and clinician evaluations—are essential for iterative refinement. Their absence results in stagnation and reduces clinical relevance [12][16][22].

D. Domain-Specific but Non-Generalizable Models

Many models are narrowly tailored to specific cancers, such as breast or lung, using domain-specific data and features. This hinders transferability and scalability across cancer types or hospital systems. A generalized, modular design that supports adaptation to diverse cancer contexts is needed [10][16][33].

E. Disconnection Between Explainability and Clinical Utility

Although XAI improves model transparency, its integration into clinical decision-making is often superficial. Explanations tend to be generic and not aligned with actionable clinical insights. Bridging this disconnect requires explainability that informs, justifies, and adapts clinical decisions in real-time [7][18][25].

F. Lack of Ethical and Justified Agentic Interactions

Ethical considerations—such as informed consent, fairness, and patient autonomy—are typically addressed in theory, but not embedded into AI behavior. For agentic systems that can take semi-autonomous actions, ethical reasoning modules must be integrated to guide acceptable and justified behaviors [27][28].

G. Limited Use of Real-World Longitudinal Datasets

The effectiveness of iterative and agentic systems depends on longitudinal data spanning multiple patient encounters. Most existing studies rely on static benchmark datasets that lack temporal depth, limiting real-world adaptability [18][29].

H. Underutilization of Multimodal and Context-Aware Data Fusion

Combining imaging, genomics, clinical records, and behavioral data is crucial for personalized cancer care. However, few models fuse such diverse modalities effectively, restricting their ability to reason contextually or deliver holistic recommendations [19][23][30].

I. Federated and Privacy-Aware Agentic Models Not Explored

While federated learning ensures patient data privacy by distributing training across decentralized systems, it has not yet been integrated with agentic behaviors that adapt based on local and global data trends. This presents an untapped opportunity for scalable, secure, and adaptive cancer care [20].

J. Static Decision Support without Contextual Reassessment

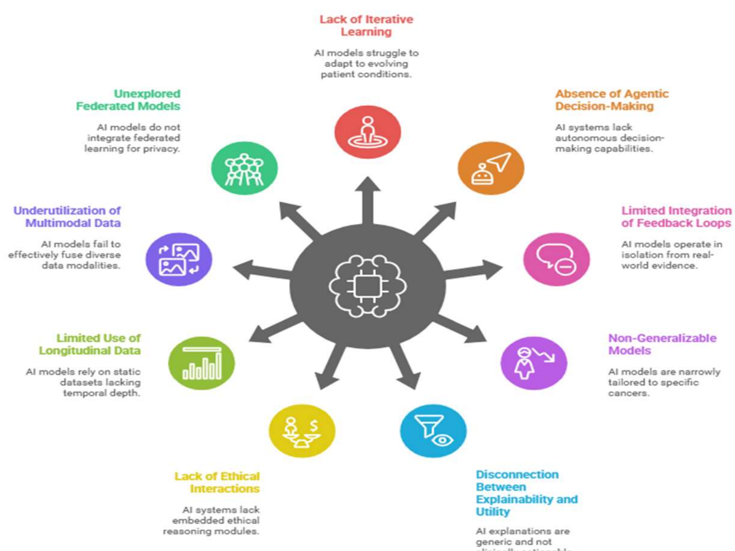

Figure 3. Key Research Gaps and Challenges

Static models do not reassess decisions when new clinical information becomes available. In cancer care, where treatment must evolve with patient response, context-aware reassessment is vital. Systems must be designed to re-evaluate and justify their recommendations dynamically [14][16][34].

These challenges underscore the need for a paradigm shift toward AI systems that are not only explainable and interpretable, but also adaptive, context-aware, and ethically guided. The next section proposes a hybrid framework that addresses these gaps through a layered integration of XAI, agentic AI, and iterative learning mechanisms.

V. Proposed Hybrid Model Framework

To overcome the limitations identified in current AI models for oncology, we propose a novel hybrid healthcare framework that integrates Explainable AI (XAI) with Agentic AI within an iterative learning architecture. This system is designed to provide real-time, personalized, and ethically guided decision support across the entire cancer care continuum. The framework comprises three modular layers: (1) the Explainable Model Layer, (2) the Agentic Decision Layer, and (3) the Feedback Integration Layer.

A. Explainable Model Layer

The base layer of the framework consists of interpretable machine learning models tailored for cancer diagnosis and prognosis. These models incorporate state-of-the-art XAI tools such as:

- SHAP for feature-level attribution and global model understanding
- Grad-CAM for visual explanation in medical imaging tasks
- LIME for local interpretability across diverse data types

This layer ensures that every AI prediction is accompanied by a human-understandable justification, enhancing trust and transparency. In addition, it supports multi-modality, handling inputs from histopathology images, radiology scans, clinical notes, and genomic profiles.

B. Agentic Decision Layer

The agentic layer introduces autonomy and context-awareness into the decision-making process. It is responsible for:

- Contextual reasoning using transformer-based models and semantic ontologies
- Action selection through reinforcement learning mechanisms like Deep Q-Networks (DQN)
- Ethical justification using rule-based or learned ethical reasoning frameworks (e.g., Ethical Decision Trees)

This layer transforms the system from a passive diagnostic tool into an active participant capable of Recommending personalized treatment strategies, revising previous decisions based on new patient data, interacting with clinicians and patients to align decisions with medical and ethical standards

C. Feedback Integration Layer

True adaptiveness requires the ability to learn from real-world interactions. The feedback layer continuously updates the model using:

- Clinician input from human-in-the-loop interfaces
- Patient-specific outcomes such as tumor progression, response to treatment, and biomarker changes
- External knowledge updates from emerging clinical guidelines and literature

This layer implements online learning techniques and reinforcement signals to improve performance iteratively. Feedback is not only used to retrain models periodically but also to recalibrate immediate decisions in real time.

D. System Characteristics

The integration of these layers enables the following key system features:

- Iterative Learning: The model evolves continuously with longitudinal data inputs
- Multimodal Fusion: Simultaneous interpretation of diverse data streams for holistic understanding
- Agentic Behavior: Contextual autonomy and decision reassessment in dynamic care settings
- Explainability: Transparent decision logic to support clinician oversight and patient communication
- Ethical Alignment: Justified and patient-centered recommendations that align with healthcare principles

E. Conceptual Workflow

- Input: Multimodal patient data is ingested (imaging, genomics, lab results, clinical notes).
- Initial Decision: The explainable model makes a diagnostic or treatment recommendation.

- ➢ Reasoning & Contextualization: The agentic layer evaluates context, revises decisions if needed, and justifies them.
- ➢ Feedback Loop: Outcomes and clinician feedback are fed into the feedback layer.
- ➢ Model Update: Based on reinforcement and continual learning, the system adapts future decisions.

This closed-loop, modular system bridges the gap between AI performance and clinical practicality, paving the way for real-world, iterative, and personalized cancer care.

VI. Implications and Applications

The integration of Explainable AI (XAI) and Agentic AI into a dynamic, iterative healthcare framework introduces a new paradigm for adaptive oncology. This hybrid model has wide-ranging implications, both theoretical and practical, that directly address long-standing challenges in cancer care.

A. Enhancing Personalization in Oncology

Cancer is a heterogeneous disease, and treatment effectiveness varies significantly among patients. Traditional AI models, though accurate, are often designed for population-level inference and fail to accommodate intra-patient variation over time. The proposed hybrid system enables personalized treatment planning through Iterative updates based on longitudinal data (e.g., tumor progression, genetic markers), Integration of individual patient preferences and comorbidities, Adaptive dosing, imaging follow-up, or modality switching based on real-time feedback by embedding continual learning, the system aligns better with precision oncology goals, improving therapeutic outcomes and reducing adverse effects.

B. Bridging the Explainability Gap for Clinical Trust

Lack of interpretability is one of the main barriers to AI adoption in clinical environments. The integration of XAI throughout the decision pipeline builds transparency and trust by providing visual and feature-level explanations for model predictions, justifying agentic actions in a human-understandable format, Supporting clinician-AI collaboration through explainable interfaces. This fosters a cooperative human-AI ecosystem, where clinicians retain control and oversight while benefiting from AI-assisted insights.

C. Enabling Real-Time Clinical Decision Support

Static decision-support systems are ill-suited to the dynamic nature of oncology workflows. The proposed model enables real-time decision-making that evolves with patient status, institutional guidelines, and contextual constraints. Applications include Dynamic treatment planning (e.g., chemotherapy regimens), Reassessment of diagnostic categories based on new scans or tests, Alerts and decision support for acute care interventions or complications. Such real-time adaptability ensures that the system remains clinically relevant, timely, and aligned with evolving standards of care.

D. Ethical and Responsible AI in Practice

Agentic behavior raises ethical concerns, particularly around autonomy, bias, and accountability. The framework addresses these concerns by Embedding ethical decision trees that explain why specific actions are taken Supporting transparency in goal selection and prioritization (e.g., risk minimization vs. survival maximization), Allowing patients and clinicians to intervene in the decision loop. This ensures alignment with responsible AI principles, including fairness, explainability, and patient-centered care.

E. Applications Across the Cancer Care Continuum

The proposed system is applicable at multiple stages of cancer care, including:

- ➢ Screening and early detection: Risk stratification from imaging and genomics.
- ➢ Diagnosis: Multimodal classification of tumor types and grades.
- ➢ Treatment planning: Dynamic selection of therapies based on evolving conditions.
- ➢ Follow-up care: Monitoring and personalized recurrence prediction.
- ➢ Palliative care: Ethical balancing of quality of life and treatment burden.

The extensibility of the model allows it to serve as a foundation for AI-driven decision support across oncology subdomains, from surgical oncology to immunotherapy.

VII. Future Directions

The convergence of Explainable and Agentic AI presents a powerful yet underexplored frontier in medical AI. While the proposed hybrid framework addresses many existing limitations in oncology decision-making, further research and development are essential to scale its clinical impact. This section outlines key future directions that will refine, extend, and ethically anchor this paradigm.

A. Federated Agentic AI for Privacy-Preserving Adaptation

One of the main challenges in medical AI is the scarcity of large, diverse, and ethically accessible datasets. Federated learning enables decentralized training of models across multiple hospitals or regions without sharing raw patient data. Extending this to include agentic adaptation allows each local model to Autonomously fine-tune decisions based on local patient populations, Share abstracted insights with global models to improve generalization, retain patient privacy while enabling continuous learning. This approach could democratize access to adaptive cancer care models across institutions, especially in under-resourced healthcare settings.

B. Integration of Real-World Evidence and Longitudinal Datasets

Many AI systems fail in clinical deployment due to over-reliance on curated, static datasets. Future research should prioritize the use of real-world evidence (RWE) and longitudinal datasets, such as Electronic Health Records (EHRs) with temporal markers, Radiological image series and genomic time-series data, post-treatment follow-up data. This will improve model robustness and support continual validation of agentic decision policies over time.

C. Deep Integration with Clinical Workflows

For the hybrid system to be impactful, it must seamlessly integrate into clinical ecosystems via EHR and PACS system compatibility, Clinician-in-the-loop dashboards for visualization and overrides, Real-time alerts and adaptive care pathways based on patient trajectories. Future development should focus on co-design with healthcare professionals to ensure usability and adoption.

D. Explainability Metrics and Evaluation Frameworks

While explainability is often claimed, it remains poorly quantified. There is a need for standardized explainability metrics that assess Clinician comprehension, Time-to-decision improvements, Reduction in diagnostic error or uncertainty, establishing benchmarks for explainability, along with usability studies, will help validate and refine XAI components in clinical environments.

E. Ethical Governance and Regulatory Compliance

As agentic AI systems begin to influence real patient care, their ethical grounding becomes critical. Future directions must explore Regulatory sandboxes for testing agentic AI in clinical trials, Ethical oversight frameworks integrating bioethics, law, and patient rights, Justification standards for semi-autonomous medical systems. This will ensure compliance with evolving guidelines from regulatory bodies such as the FDA, EMA, and WHO.

F. Domain Extension Beyond Oncology

While this framework is optimized for oncology, its underlying architecture can be extended to Chronic disease management (e.g., diabetes, heart failure), Intensive care unit (ICU) triage and decision support, Preventive medicine and risk prediction. These extensions would require domain-specific retraining but could leverage the same modular structure for adaptive, explainable, and agentic decision-making.

VIII. Conclusion

The evolution of artificial intelligence in healthcare has brought significant advancements in the early detection, diagnosis, and management of cancer. However, the current generation of AI models largely operates within static, one-time decision-making frameworks that fail to reflect the complexity and dynamism of real-world oncology.

As patient data accumulates and clinical contexts shift over time, the need for systems that can adapt, explain, and reason in context becomes increasingly critical.

This review highlights the transformative potential of integrating Explainable AI (XAI) and Agentic AI into a unified, iterative framework for cancer treatment. By enabling interpretability, autonomy, and feedback-driven adaptation, the proposed hybrid model addresses key limitations in existing approaches—such as lack of real-time learning, limited multimodal integration, and ethical opacity. It introduces a closed-loop system where AI decisions are not only transparent but are dynamically reassessed and improved based on longitudinal patient data and clinician input.

Through a detailed literature analysis, we have identified significant research gaps and proposed a modular architecture that fuses diagnostic accuracy with contextual reasoning and ethical decision support. The model leverages cutting-edge tools including reinforcement learning, transformers for multimodal fusion, and semantic ontologies, supported by privacy-preserving federated learning and clinician-in-the-loop mechanisms.

Looking ahead, the development and clinical deployment of such systems will depend on the availability of longitudinal datasets, deeper ethical integration, standardization of explainability metrics, and compliance with global regulatory frameworks. Ultimately, this hybrid AI model offers a pathway toward truly personalized, adaptive, and trustworthy oncology care—where technology augments human expertise to deliver better outcomes and improved patient experiences.

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