

LARGE LANGUAGE MODELS IN PRECISION ONCOLOGY: TRANSFORMING CLINICAL DECISION SUPPORT AND CANCER CARE

^{#1}**Dr. Anoop Krishnan**, Professor, Department of Medical Oncology,
MES Medical College, Perinthalmanna, India
Anoopkrishnan84@gmail.com

Abstract: Large language models (LLMs) are rapidly transforming precision oncology by enabling intelligent clinical reasoning, biomedical knowledge synthesis, multimodal data interpretation, and personalized clinical decision support across the cancer care continuum. Unlike conventional artificial intelligence (AI) systems designed for isolated predictive tasks, LLMs integrate natural language understanding with multimodal foundation models capable of processing radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, electronic health records, biomedical literature, clinical guidelines, and longitudinal patient data. Recent advances in transformer architectures, self-supervised learning, retrieval-augmented generation, graph neural networks, reinforcement learning, and generative AI have enabled comprehensive biomedical reasoning supporting cancer diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, immunotherapy selection, digital twin simulation, adaptive disease monitoring, and multidisciplinary clinical decision-making. Emerging technologies including multimodal large language models, federated learning, explainable artificial intelligence, agentic AI, cloud-native healthcare platforms, and digital twins further enhance precision oncology by enabling collaborative, privacy-preserving, transparent, and continuously adaptive computational intelligence. Despite substantial technological advances, important scientific, technical, ethical, regulatory, and implementation challenges remain regarding hallucination, interpretability, multimodal integration, computational scalability, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of large language models in precision oncology, emphasizing their transformative role in clinical decision support and personalized cancer care.[1]

Keywords: *Large language models, Precision oncology, Clinical decision support, Artificial intelligence, Foundation models, Computational oncology, Personalized medicine, Digital pathology, Multi-omics, Cancer care.*

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1. Introduction

Cancer remains one of the most biologically complex diseases due to continuous genomic evolution, epigenetic remodeling, immune adaptation, metabolic reprogramming, angiogenesis, tissue remodeling, and dynamic interactions among malignant cells, stromal components, immune populations, vascular structures, and host physiology. These interconnected biological processes evolve throughout diagnosis, treatment, recurrence, metastasis, and survivorship, making precision oncology increasingly dependent upon intelligent

computational systems capable of integrating heterogeneous biomedical information across multiple biological scales.[2]

Modern oncology routinely generates enormous quantities of biomedical information through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, physician documentation, electronic health records, biomedical literature, clinical guidelines, and patient-reported outcomes. Although each modality contributes valuable biological insight,

isolated interpretation frequently overlooks systems-level relationships governing disease progression, therapeutic response, resistance mechanisms, and long-term clinical outcomes.[3] Large language models have emerged as transformative computational technologies capable of understanding, synthesizing, and reasoning across diverse biomedical information sources while generating context-aware clinical recommendations. Combined with multimodal foundation models, LLMs establish a new paradigm for intelligent precision oncology capable of supporting clinicians throughout the cancer care continuum.

2. Evolution of Large Language Models in Oncology

Artificial intelligence in oncology has evolved from rule-based expert systems and conventional machine learning toward large-scale foundation models capable of generalized biomedical reasoning. Early computational systems primarily relied upon handcrafted feature engineering and task-specific predictive algorithms developed for isolated diagnostic or prognostic applications. Although these systems demonstrated important clinical value, they remained constrained by fragmented biomedical information, limited adaptability, and narrow task specialization.[4] Deep learning substantially expanded computational capabilities through automated representation learning from radiological imaging, digital pathology, genomic sequencing, and electronic health records. Transformer architectures subsequently revolutionized natural language processing by enabling contextual understanding across enormous biomedical corpora.

Large language models now acquire generalized biomedical knowledge through self-supervised pretraining on scientific literature, clinical documentation, medical guidelines, textbooks, and structured biomedical databases, enabling sophisticated reasoning applicable across diagnosis, prognosis, biomarker discovery, therapeutic planning, patient communication, and clinical decision support.[5]

3. Principles of Large Language Models in Precision Oncology

Large language models differ fundamentally from conventional artificial intelligence because they generate generalized contextual representations capable of reasoning across diverse biomedical domains rather than performing isolated predictive tasks. Multimodal foundation models integrate natural language understanding with radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, and longitudinal clinical trajectories into unified computational representations.[6]

Self-supervised learning enables acquisition of biomedical knowledge without extensive manual annotation, while transformer architectures capture long-range contextual relationships among scientific literature, clinical documentation, imaging findings, molecular biomarkers, therapeutic guidelines, and patient-specific clinical histories.

Graph neural networks, retrieval-augmented generation, and biomedical knowledge graphs further enhance reasoning by integrating structured biological relationships among genes, proteins, signaling pathways, imaging phenotypes, therapeutic targets, physiological variables, and clinical outcomes.[7]

4. Computational Architecture

Modern LLM-powered precision oncology platforms consist of interconnected computational layers responsible for biomedical data acquisition, preprocessing, multimodal representation learning, retrieval augmentation, adaptive reasoning, predictive analytics, digital twin simulation, and intelligent clinical decision support.[8]

The acquisition layer continuously integrates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, laboratory investigations, circulating tumor DNA, physician documentation, biomedical literature, clinical guidelines, medication history, patient-reported outcomes, and electronic health records. Advanced preprocessing pipelines harmonize

molecular datasets, encode clinical narratives, retrieve current biomedical evidence, and synchronize temporal patient information.

Large language models subsequently generate generalized multimodal embeddings representing molecular biology, tissue architecture, imaging phenotypes, physiological function, biomedical knowledge, and longitudinal clinical trajectories. These unified computational representations support diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, adaptive learning, and precision oncology.[9]

5. Biomedical Knowledge Integration

One of the greatest strengths of large language models is their ability to synthesize enormous quantities of biomedical knowledge across multiple disciplines. LLMs integrate peer-reviewed oncology literature, clinical guidelines, molecular databases, pharmacological knowledge, pathology reports, radiology findings, laboratory investigations, genomics, and real-world clinical evidence into unified reasoning frameworks capable of supporting precision oncology.[10]

Retrieval-augmented generation enables incorporation of updated biomedical evidence while minimizing outdated information, allowing models to provide context-aware summaries, therapeutic recommendations, biomarker interpretations, and evidence synthesis supporting multidisciplinary oncology practice.

These knowledge integration capabilities substantially improve translational oncology, clinical education, literature review, biomarker interpretation, and individualized treatment planning.[11]

6. Multimodal Clinical Intelligence

Comprehensive precision oncology increasingly depends upon multimodal integration of radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, and longitudinal clinical trajectories.[12]

Multimodal large language models integrate textual reasoning with complementary biomedical modalities using transformer architectures, cross-

modal attention mechanisms, graph neural networks, and multimodal representation learning. These computational systems identify latent biological relationships linking imaging findings, tissue morphology, molecular alterations, therapeutic responsiveness, physiological variables, and clinical outcomes.

These unified multimodal representations substantially improve diagnosis, prognostic prediction, biomarker discovery, therapeutic optimization, survivorship management, and personalized precision medicine.[13]

7. Clinical Decision Support

Large language models are rapidly becoming foundational components of intelligent clinical decision-support systems. They assist clinicians by summarizing patient histories, interpreting pathology reports, explaining molecular diagnostics, synthesizing imaging findings, retrieving guideline-based recommendations, generating differential diagnoses, identifying potential therapeutic options, and supporting multidisciplinary tumor board discussions.[14]

Unlike conventional decision-support software that relies upon predefined rules, LLMs dynamically integrate patient-specific information with continuously evolving biomedical knowledge while generating transparent clinical explanations and context-aware recommendations.

These intelligent systems substantially reduce cognitive burden, improve workflow efficiency, facilitate multidisciplinary collaboration, and strengthen evidence-based oncology practice.[15]

8. Personalized Cancer Care

Personalized cancer care requires comprehensive integration of molecular biology, imaging phenotypes, histopathological characteristics, laboratory biomarkers, patient preferences, treatment history, physiological monitoring, and survivorship information into individualized therapeutic strategies. Large language models synthesize these heterogeneous data sources while generating personalized treatment summaries, survivorship plans, patient education materials, informed consent explanations, and follow-up recommendations tailored to individual clinical circumstances.[16]

By facilitating communication among clinicians, researchers, patients, and caregivers, LLMs improve patient engagement, shared decision-making, treatment adherence, and continuity of care while supporting personalized oncology across the entire disease continuum.[17]

9. Precision Therapeutics and Biomarker Interpretation

One of the most clinically significant applications of large language models is comprehensive interpretation of molecular biomarkers and therapeutic evidence. LLMs integrate genomic alterations, transcriptomic profiles, proteomic signatures, radiological findings, digital pathology, laboratory biomarkers, clinical trial evidence, drug databases, and treatment guidelines to generate individualized therapeutic recommendations while explaining the biological rationale underlying each recommendation. These adaptive computational systems substantially improve biomarker interpretation, precision therapeutic selection, clinical trial matching, and multidisciplinary treatment planning throughout precision oncology.[18][19][20]

10. Digital Twins and Large Language Model Integration

Digital twin technology represents one of the most transformative applications of large language models in precision oncology by creating continuously evolving virtual representations of individual cancer patients synchronized with their biological counterparts. Foundation AI models integrate serial radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and longitudinal clinical information into adaptive computational patient models capable of simulating disease progression, therapeutic response, treatment-related toxicity, recurrence, metastatic dissemination, and survival.[21]

Large language models function as intelligent reasoning engines within these digital twin ecosystems by interpreting multimodal patient data, summarizing longitudinal disease

trajectories, integrating newly published biomedical evidence, and generating clinically meaningful explanations for simulated therapeutic outcomes. Unlike conventional predictive models, digital twins continuously update their computational representations as new biomedical information becomes available, allowing clinicians to evaluate alternative treatment strategies, optimize treatment sequencing, anticipate resistance mechanisms, and personalize supportive care according to evolving patient biology.

By combining multimodal biomedical intelligence with advanced language reasoning and predictive simulation, digital twins transform computational oncology from retrospective analysis toward proactive and continuously adaptive precision medicine.

11. Intelligent Clinical Decision Support

Large language models provide the computational infrastructure for next-generation clinical decision-support systems capable of integrating heterogeneous biomedical information into comprehensive patient-centered recommendations. Rather than interpreting radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines independently, LLMs synthesize these diverse biomedical information sources into unified computational representations supporting multidisciplinary oncology practice.[22]

Interactive clinical dashboards generate individualized diagnostic summaries, biomarker analyses, molecular interpretations, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence probabilities, disease progression forecasts, and survival predictions while facilitating collaboration among oncologists, radiologists, pathologists, surgeons, radiation oncologists, molecular biologists, pharmacists, nurses, genetic counselors, and computational scientists.

These intelligent systems improve workflow efficiency, strengthen multidisciplinary communication, reduce fragmentation of

biomedical information, and promote evidence-based personalized cancer management throughout the cancer care continuum.

12. Continuous Learning and Adaptive Language Intelligence

A defining characteristic of large language models is their ability to continuously evolve as new biomedical information becomes available. Artificial intelligence incorporates serial imaging examinations, computational pathology, circulating tumor DNA, laboratory biomarkers, physician documentation, patient-reported outcomes, clinical trial evidence, treatment guidelines, and real-world clinical evidence into adaptive computational frameworks capable of continuously refining predictive accuracy throughout the patient's clinical journey.[23]

Continual learning algorithms enable incremental refinement of computational knowledge without catastrophic forgetting of previously acquired information, while retrieval-augmented generation continuously incorporates newly published biomedical evidence into clinical reasoning. Reinforcement learning further optimizes clinical recommendations through iterative evaluation of therapeutic outcomes and clinician feedback.

This adaptive computational paradigm transforms oncology into a continuously learning healthcare ecosystem capable of supporting real-time precision medicine.

13. Federated Large Language Model Ecosystems

Development of highly generalizable oncology large language models requires access to diverse biomedical datasets representing multiple healthcare systems, imaging platforms, pathology laboratories, molecular technologies, treatment protocols, and patient populations. Federated learning enables collaborative development of foundation AI models while preserving patient privacy and institutional governance through decentralized computational training.[24]

Participating healthcare institutions independently train local language models using radiological imaging, digital pathology, genomics, transcriptomics, laboratory investigations, wearable monitoring, liquid biopsy, biomedical

literature, electronic health records, and longitudinal clinical records while securely exchanging encrypted model parameters rather than identifiable patient information. This collaborative learning strategy substantially improves algorithm robustness, fairness, external validity, transparency, and generalizability across diverse healthcare environments.

Federated LLM ecosystems therefore establish international computational oncology networks capable of accelerating scientific discovery, improving equitable access to precision medicine, and supporting global cancer research while maintaining responsible biomedical data stewardship.

14. Explainability, Validation, and Ethical Governance

Successful implementation of large language models in precision oncology requires transparent, interpretable, reproducible, and rigorously validated computational systems capable of supporting clinician confidence, patient trust, and regulatory approval. Explainable artificial intelligence (XAI) enables clinicians to understand computational reasoning through evidence citation, attention visualization, SHAP (Shapley Additive Explanations), feature attribution analysis, uncertainty estimation, retrieval traceability, and counterfactual explanations identifying the imaging, molecular, pathological, physiological, and clinical variables responsible for generated recommendations.[25]

Clinical deployment additionally requires standardized multimodal datasets, interoperable computational infrastructure, prospective multicenter validation, external benchmarking, cybersecurity safeguards, continuous monitoring for hallucinations and algorithmic bias, and compliance with evolving international regulatory frameworks governing AI-enabled healthcare technologies.

Responsible implementation further depends upon patient privacy, informed consent, transparency, accountability, equitable access, responsible data governance, continuous post-deployment surveillance, and multidisciplinary oversight to ensure trustworthy integration of LLMs into routine oncology practice.

15. Future Perspectives

Future precision oncology ecosystems will increasingly integrate multimodal large language models, foundation AI models, agentic artificial intelligence, graph neural networks, reinforcement learning, federated learning, digital twins, spatial multi-omics, liquid biopsy, quantum computing, Internet of Medical Things (IoMT), robotics, cloud-native healthcare infrastructure, and autonomous clinical reasoning systems into unified precision oncology platforms.[26]

These next-generation computational ecosystems will continuously integrate molecular biology, radiological imaging, digital pathology, laboratory medicine, wearable physiological monitoring, environmental exposures, electronic health records, biomedical literature, and real-world clinical outcomes while autonomously coordinating diagnostic workflows, optimizing therapeutic strategies, supporting adaptive clinical trials, generating personalized patient communication, and continuously synthesizing biomedical evidence.

Such intelligent language-centered ecosystems are expected to transform oncology from fragmented and reactive disease management toward predictive, preventive, adaptive, continuously learning, and precision-guided healthcare.

16. Discussion

Large language models represent one of the most significant paradigm shifts in computational oncology by integrating biomedical literature, molecular biology, radiological imaging, digital pathology, laboratory biomarkers, digital twins, wearable technologies, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional artificial intelligence systems developed for isolated predictive tasks, LLMs simultaneously analyze multimodal biomedical information, synthesize scientific evidence, generate clinically meaningful explanations, and support multidisciplinary clinical reasoning while adapting to newly emerging biomedical knowledge.[27]

Applications spanning computational pathology, radiogenomics, biomarker discovery, digital

twins, precision immunotherapy, adaptive therapeutics, literature synthesis, clinical documentation, patient education, continuous learning, federated collaboration, and intelligent clinical decision support demonstrate the extraordinary potential of LLMs to redefine future oncology. Nevertheless, successful

implementation requires continued advances in multimodal data harmonization, explainable artificial intelligence, retrieval reliability, interoperability, computational infrastructure, cybersecurity, regulatory science, ethical governance, and sustained multidisciplinary collaboration.

As biomedical knowledge and healthcare data continue to expand exponentially, large language models are expected to become a foundational computational infrastructure supporting intelligent precision oncology worldwide.

17. Conclusion

Large language models are transforming precision oncology by integrating biomedical literature, radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, digital twins, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting accurate diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, adaptive disease monitoring, and individualized clinical decision-making throughout the cancer care continuum.[28]

Advances in transformer architectures, multimodal learning, graph neural networks, self-supervised learning, federated learning, reinforcement learning, digital twins, retrieval-augmented generation, multimodal large language models, agentic AI, and generative artificial intelligence are expected to further strengthen intelligent oncology ecosystems, enabling increasingly accurate molecular characterization, predictive clinical intelligence, adaptive therapeutics, continuous disease surveillance, personalized patient communication, and continuously improving cancer care.[29]

Although important scientific, technical, ethical, regulatory, and implementation challenges remain, sustained collaboration among

oncologists, radiologists, pathologists, molecular biologists, biomedical engineers, computer scientists, healthcare organizations, policymakers, industry partners, and regulatory agencies will accelerate the responsible implementation of large language models in oncology. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, reduce disparities in cancer care, accelerate translational research, and establish a new era of intelligent, adaptive, explainable, and continuously learning precision oncology worldwide.[30]

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