International Journal of Emerging Research in Applied Medical Sciences (IJERAMS)

# Federated Foundation Models for Privacy-Preserving Precision Cancer Intelligence Across Healthcare Systems

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## ABSTRACT

Cancer remains one of the leading causes of morbidity and mortality worldwide despite remarkable advances in molecular biology, targeted therapeutics, immunotherapy, and precision medicine. The increasing availability of multimodal biomedical data generated through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory investigations, wearable technologies, and electronic health records has created unprecedented opportunities for artificial intelligence (AI)-driven precision oncology. However, widespread implementation of large-scale AI models is constrained by strict privacy regulations, institutional data silos, heterogeneous healthcare infrastructures, and concerns regarding secure sharing of sensitive patient information. Federated foundation models have emerged as a transformative computational paradigm that combines federated learning with large multimodal foundation models to enable collaborative model development without transferring raw patient data across institutions. These systems facilitate privacy-preserving representation learning while integrating imaging, pathology, multi-omics, clinical documentation, longitudinal patient records, and real-world healthcare data into generalized biomedical intelligence capable of supporting diagnosis, prognostic prediction, therapeutic optimization, clinical decision support, and precision medicine. Advances in transformer architectures, self-supervised learning, multimodal foundation models, graph neural networks, differential privacy, secure aggregation, homomorphic encryption, blockchain technologies, and cloud-native healthcare infrastructure have significantly accelerated development of federated computational oncology ecosystems. Despite remarkable progress, important challenges remain regarding interoperability, communication efficiency, computational scalability, model heterogeneity, explainability, regulatory validation, cybersecurity, and ethical governance. This review presents a comprehensive overview of federated foundation models in precision oncology, highlighting computational principles, clinical opportunities, implementation challenges, and future perspectives for privacy-preserving cancer intelligence across distributed healthcare systems.[1]

**Keywords:** Federated learning, Foundation models, Precision oncology, Artificial intelligence, Privacy-preserving AI, Computational oncology, Multi-omics, Clinical intelligence, Digital pathology, Personalized medicine.

**Article History**

**Received:** 10 December 2025**; Accepted:** 18 December 2025**; Published:** 28 December 2025

**Citation**

Tandon V.,(2025).Federated Foundation Models for Privacy-Preserving Precision Cancer Intelligence Across Healthcare Systems. *International Journal of Emerging Research in Applied Medical Sciences (IJERAMS), 1(5), 85-92.*

**DOI:** https://doi.org/10.65477/ijerams.v1.i5.11

## 1. Introduction

Cancer is a biologically complex disease characterized by genomic instability, epigenetic regulation, transcriptional heterogeneity, metabolic reprogramming, immune diversity, and dynamic interactions between malignant cells and the tumor microenvironment. Although precision oncology has substantially improved patient outcomes through molecular diagnostics and targeted therapeutics, effective individualized cancer management increasingly depends upon analysis of enormous quantities of heterogeneous biomedical information generated across multiple healthcare institutions.[2]

Modern oncology continuously produces multimodal data through computed tomography, magnetic resonance imaging, positron emission tomography, mammography, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable biosensors, and electronic health records. While these datasets collectively provide comprehensive insight into tumor biology, they remain fragmented across hospitals, research centers, diagnostic laboratories, and national healthcare systems because of privacy regulations, institutional policies, and technical interoperability limitations.[3]

Artificial intelligence has emerged as a transformative technology capable of extracting clinically meaningful knowledge from these complex datasets. However, conventional centralized AI training requires aggregation of sensitive patient data into common repositories, creating substantial concerns regarding privacy, cybersecurity, regulatory compliance, and data ownership.[4]

Federated foundation models address these limitations by enabling collaborative learning across geographically distributed healthcare institutions while ensuring that raw patient data remain securely within local environments. This emerging computational paradigm has the potential to transform precision oncology through privacy-preserving, large-scale collaborative intelligence that supports personalized cancer diagnosis, prognostic prediction, therapeutic optimization, and real-world clinical decision-making.[5]

## 2. Evolution of Federated Artificial Intelligence in Oncology

Early artificial intelligence systems within oncology primarily relied on centralized datasets collected from individual academic medical centers or national registries. Although these datasets facilitated important algorithmic advances, model performance was frequently limited by restricted population diversity, institutional bias, and inadequate representation of rare cancers.[6]

Federated learning emerged as a distributed computational framework that enabled multiple institutions to collaboratively train machine learning models without directly exchanging sensitive patient information. Instead of transmitting raw clinical data, participating institutions independently train local models while sharing encrypted model parameters that are securely aggregated into a continuously improving global model.[7]

The emergence of foundation models has further expanded these capabilities through large-scale self-supervised representation learning across multimodal biomedical information. Integration of federated learning with multimodal foundation models has created federated foundation models capable of learning generalized biomedical intelligence from diverse healthcare environments while preserving patient privacy.

These advances represent an important milestone toward collaborative precision oncology that combines large-scale artificial intelligence with responsible data governance across international healthcare systems.[8]

## 3. Principles of Federated Foundation Models

Federated foundation models combine two complementary computational paradigms: foundation model pretraining and federated distributed learning. Foundation models learn generalized representations from large-scale biomedical datasets using self-supervised learning, whereas federated learning enables collaborative optimization without centralizing sensitive patient information.[9]

Within federated healthcare environments, participating hospitals locally train multimodal foundation models using institutional imaging archives, pathology repositories, genomic databases, laboratory investigations, electronic health records, and longitudinal patient information. Rather than transferring raw clinical data, each institution securely transmits encrypted model parameters or gradient updates to a federated aggregation server.

Secure aggregation algorithms combine these local updates into an improved global model that is subsequently redistributed to participating institutions for additional training. Through repeated collaborative learning cycles, federated foundation models progressively improve generalized biomedical representations while preserving patient confidentiality throughout the training process.[10]

## 4. Computational Architecture of Federated Oncology Systems

Federated precision oncology ecosystems consist of multiple interconnected computational components that coordinate secure collaborative learning across geographically distributed healthcare institutions.[11]

The local institutional layer acquires multimodal biomedical information from radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, laboratory biomarkers, wearable technologies, medication history, and electronic health records. Advanced preprocessing pipelines standardize heterogeneous datasets through image normalization, molecular harmonization, natural language processing, feature extraction, and multimodal encoding.

Local foundation models independently learn patient-specific biomedical representations before securely transmitting encrypted parameter updates to centralized aggregation servers. Secure federated optimization algorithms integrate these updates into globally optimized models without accessing underlying patient data.

Continuous iterative communication among participating institutions enables collaborative improvement of multimodal representations while preserving institutional autonomy, regulatory compliance, and patient privacy throughout the computational workflow.[12]

## 5. Privacy-Preserving Artificial Intelligence

Privacy preservation represents the defining characteristic of federated foundation models. Unlike conventional centralized artificial intelligence systems that require direct sharing of patient information, federated learning ensures that sensitive biomedical data remain securely stored within institutional infrastructures.[13]

Multiple complementary privacy-preserving technologies strengthen federated oncology systems. Differential privacy introduces carefully calibrated statistical noise that prevents identification of individual patient information while preserving model utility. Homomorphic encryption enables secure computation on encrypted model parameters without exposing underlying data.

Secure multi-party computation allows collaborative model optimization without revealing sensitive information to participating institutions, whereas blockchain technology provides transparent audit trails that strengthen accountability, integrity, and regulatory compliance.

Collectively, these technologies create robust computational environments capable of supporting collaborative biomedical intelligence while satisfying increasingly stringent international privacy regulations governing healthcare information.[14]

## 6. Multimodal Learning Across Healthcare Networks

Federated foundation models enable collaborative learning across diverse biomedical modalities distributed among multiple healthcare institutions. Radiological imaging contributes anatomical and functional information regarding tumor morphology, vascularity, metabolism, and treatment response, whereas digital pathology provides microscopic characterization of tissue architecture, immune infiltration, stromal remodeling, and tumor heterogeneity.[15]

Genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable devices, and longitudinal clinical documentation provide complementary molecular and physiological information describing individual patient trajectories.

Multimodal transformer architectures harmonize these heterogeneous datasets into unified computational representations while federated optimization enables generalized learning across geographically distributed patient populations. These collaborative representations substantially improve diagnostic accuracy, prognostic prediction, therapeutic selection, and precision medicine while maintaining institutional privacy.

## 7. Federated Foundation Models in Cancer Diagnosis

Accurate diagnosis represents one of the most important clinical applications of federated foundation models. Large collaborative imaging repositories distributed across multiple hospitals enable artificial intelligence to learn generalized representations that improve tumor detection, lesion segmentation, disease classification, and radiological interpretation across diverse patient populations.[16]

Digital pathology repositories further strengthen diagnostic capability by enabling collaborative learning from millions of whole-slide tissue images collected across geographically distributed pathology laboratories. Artificial intelligence identifies histomorphological biomarkers associated with tumor subtype, immune infiltration, metastatic potential, and molecular characteristics while improving diagnostic reproducibility.

Integration of imaging, pathology, genomics, laboratory biomarkers, and clinical documentation through federated multimodal learning enables increasingly comprehensive diagnostic reasoning while preserving institutional privacy and regulatory compliance.[17]

## 8. Multi-Omics and Precision Medicine

Precision oncology increasingly depends upon integration of genomics, transcriptomics, proteomics, metabolomics, immunomics, and additional molecular datasets that collectively characterize tumor biology across multiple biological layers. Federated foundation models enable collaborative learning from distributed multi-omics repositories without requiring centralized storage of sensitive genomic information.[18]

Artificial intelligence identifies clinically actionable mutations, molecular subtypes, signaling pathways, therapeutic targets, resistance mechanisms, and prognostic biomarkers by integrating heterogeneous omics information across multiple institutions. These collaborative computational representations improve biomarker discovery, molecular classification, treatment prediction, and systems biology research while preserving genomic privacy.

By learning generalized molecular representations from diverse patient populations, federated foundation models substantially strengthen precision medicine while reducing institutional bias and improving generalizability across healthcare systems.[19]

## 9. Federated Foundation Models for Personalized Cancer Therapy

Personalized therapy represents one of the most important clinical applications of federated foundation models. These systems integrate radiological imaging, digital pathology, multi-omics, laboratory biomarkers, medication history, treatment response, and longitudinal clinical information from multiple healthcare institutions to generate individualized therapeutic recommendations while preserving patient privacy.[20]

Artificial intelligence estimates treatment response, recurrence probability, progression-free survival, overall survival, treatment-related toxicity, and mechanisms of therapeutic resistance across chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations.

Because federated learning continuously incorporates diverse clinical experience from geographically distributed healthcare systems, therapeutic recommendations become increasingly robust and generalizable while minimizing institutional bias and preserving confidentiality.

## 10. Clinical Decision Support Across Distributed Healthcare Systems

Federated foundation models enable collaborative clinical decision support by connecting hospitals, diagnostic laboratories, cancer centers, and research institutions through secure distributed artificial intelligence networks. Rather than exchanging patient records, participating institutions share encrypted model updates that continuously improve global clinical intelligence.[21]

Artificial intelligence integrates pathology reports, radiological findings, genomic sequencing, laboratory investigations, medication histories, wearable sensor data, and longitudinal electronic health records into comprehensive patient-specific computational representations.

Interactive clinical dashboards provide individualized diagnostic assessments, therapeutic recommendations, toxicity predictions, recurrence risk, survival estimates, and guideline-supported treatment pathways while maintaining institutional data sovereignty and physician oversight.

This distributed intelligence substantially improves multidisciplinary collaboration and supports evidence-based precision oncology across diverse healthcare environments.

## 11. Drug Discovery and Collaborative Clinical Research

Federated foundation models have the potential to transform oncology drug discovery by enabling secure collaborative learning across pharmaceutical companies, academic medical centers, biotechnology organizations, and clinical research networks. Artificial intelligence integrates molecular biology, systems pharmacology, genomics, proteomics, metabolomics, clinical outcomes, and real-world healthcare data without requiring centralized patient databases.[22]

Generative AI supports molecular design, drug-target prediction, toxicity estimation, protein interaction modeling, and identification of novel therapeutic candidates while federated learning enables validation across diverse patient populations.

Clinical research also benefits through secure multicenter patient stratification, molecular eligibility assessment, adaptive clinical trial optimization, outcome prediction, and collaborative biomarker discovery while preserving institutional autonomy and patient confidentiality.

## 12. Explainable Artificial Intelligence and Trustworthy Federated Models

Clinical implementation of federated foundation models requires transparency, reliability, and physician confidence. Explainable artificial intelligence (XAI) enables clinicians to understand how distributed models generate recommendations through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, and counterfactual reasoning.[23]

Explainability is particularly important within federated systems because training occurs across multiple institutions using heterogeneous patient populations and diverse biomedical datasets. Transparent computational reasoning facilitates multidisciplinary interpretation while improving clinician acceptance and regulatory confidence.

Trustworthy federated AI further requires robust validation across diverse healthcare environments to ensure consistent performance, fairness, and clinical reliability before routine implementation.

## 13. Cybersecurity, Ethics, and Regulatory Considerations

Although federated learning substantially improves privacy protection, several important challenges remain regarding cybersecurity, governance, and regulatory implementation. Distributed artificial intelligence systems must protect against model inversion attacks, gradient leakage, adversarial manipulation, unauthorized access, and communication vulnerabilities.[24]

Robust authentication protocols, encrypted communication channels, differential privacy, homomorphic encryption, blockchain audit systems, secure aggregation, and continuous threat monitoring are essential for maintaining trustworthy federated healthcare ecosystems.

Additional ethical considerations include informed consent, data ownership, algorithmic bias, accountability, transparency, equitable access, cross-border data governance, and compliance with international healthcare regulations. Addressing these issues will require harmonized regulatory frameworks, standardized validation methodologies, and multidisciplinary collaboration among clinicians, engineers, legal experts, policymakers, and healthcare organizations.

## 14. Emerging Innovations and Future Perspectives

Rapid advances in artificial intelligence continue to expand the capabilities of federated foundation models. Multimodal foundation models, agentic AI, digital twins, reinforcement learning, retrieval-augmented generation, quantum computing, spatial multi-omics, liquid biopsy, wearable biosensors, cloud-native healthcare infrastructure, and Internet of Medical Things (IoMT) technologies are expected to further strengthen distributed precision oncology ecosystems.[25]

Future federated healthcare networks may function as continuously learning international oncology platforms capable of integrating imaging, pathology, genomics, laboratory medicine, pharmacy, surgery, radiation oncology, and survivorship care while preserving patient privacy across participating institutions.

These intelligent systems have the potential to democratize access to advanced computational oncology by enabling collaborative learning among hospitals with varying patient populations, technological resources, and clinical expertise.

## 15. Discussion

Federated foundation models represent one of the most significant advances in privacy-preserving computational oncology by combining large-scale multimodal representation learning with secure distributed artificial intelligence. Unlike conventional centralized AI systems that require aggregation of sensitive patient information, federated models enable collaborative biomedical intelligence while maintaining institutional autonomy and patient confidentiality.[26]

Applications spanning diagnostic imaging, digital pathology, multi-omics, precision therapeutics, drug discovery, clinical decision support, and collaborative research demonstrate the extraordinary potential of these technologies for improving precision medicine across diverse healthcare systems.

Nevertheless, successful implementation depends upon overcoming computational, technical, ethical, regulatory, and organizational challenges through standardized interoperability, explainable artificial intelligence, robust cybersecurity, prospective clinical validation, and international collaboration among healthcare institutions.

## 16. Conclusion

Federated foundation models are redefining precision oncology by enabling collaborative artificial intelligence across distributed healthcare systems without compromising patient privacy. Through secure integration of radiological imaging, digital pathology, multi-omics, laboratory biomarkers, electronic health records, wearable technologies, and longitudinal clinical information, these systems support comprehensive precision cancer intelligence while preserving regulatory compliance and institutional data sovereignty.[27]

Advances in multimodal foundation models, self-supervised learning, graph neural networks, agentic artificial intelligence, digital twins, federated optimization, cloud computing, and generative AI are expected to further strengthen privacy-preserving computational oncology while improving scalability, robustness, and clinical applicability.

Although important scientific, technical, ethical, and regulatory challenges remain, continued interdisciplinary collaboration among clinicians, computer scientists, biomedical engineers, cybersecurity specialists, regulatory agencies, and healthcare organizations will accelerate responsible implementation of federated foundation models, ultimately improving cancer diagnosis, therapeutic precision, clinical research, and patient outcomes worldwide.[28][29][30]

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