AI for Holistic Medicine: Understanding Multi-Organ Interactions in Cancers

Authors:

Mehrdad Farrokhi
ERIS Research Institute

Saman Abdollahpour
Shahid Beheshti University of Medical Sciences

Sanaz Amiri Marbini
Islamic Azad University, Tehran Medical Sciences Branch

Niloofar Taheri
Shahroud University of Medical Sciences

Fatemeh Asadi
Tarbiat Modares University

Saboura Sahebi
Mashhad University of Medical Sciences

Oveis Ahmadzadeh
ERIS Research Institute

Farzaneh Khosravi
North Khorasan University of Medical Sciences

Kiana Bahmanipour
Shiraz University of Medical Sciences

Kimia Kowsari
Azad University of Sari

Atousa Ghorbani
East Tehran Branch, Islamic Azad University

Rahil GhorbaniNia
Bam University of Medical Sciences

Nazanin Hashemi
Xi'an Jiaotong University

Khalil Kalavani
Khoy University of Medical Sciences

Mohammad-Matin Karbalaee-Alinazari
Shiraz University of Medical Sciences

Meisam Sargazi
Zahedan University of Medical Sciences

Afshin Zarei
Shiraz University of Medical Sciences

Zahra Sadin
Guilan University of Medical Sciences

Mahboobeh Majidnia
Azad University Tehran Central Branch

Sara Shokrollahi Yancheshmeh
Department of Mathematics, Ahv.C., Islamic Azad University

Fatemeh Amini
Sichuan University

Vahid Jafari
University of Sevilla

Atie Moghtadaei
Tehran University of Medical Sciences

Sara Montazeri Namin
Iran University of Medical Sciences

Alireza Taheri
Islamic Azad University Science and Research Branch

Maryam Houshmand Marvasti
Amir Kabir University of Tehran

Amin Sadeghnezhad
Università Federico II Italy

Atena Talebpoor Amirhandeh
Shahid Beheshti University of Medical Sciences

Ali Aghajan
Universität Hamburg

Book Details:

Publisher: PreferPub (eBook Version) and Kindle (Paperback Version)

Publication Date: May 2026

Language: English

Dimensions: 5 x 0.39 x 8 inches

ISBN-13: 979-8196717505

Contents

Chapter

1- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN RENAL-RELATED CANCERS

Background

Renal cancer accounts for approximately 3% of global cancer diagnoses. Each year, nearly 400,000 new cases and 175,000 deaths are reported worldwide, reflecting a concerning rise in both incidence and mortality rates. Among kidney malignancies, renal cell carcinoma (RCC) is the most common and clinically aggressive form. The clear cell subtype of renal cell carcinoma (ccRCC) represents the dominant histological variant and is respon

sible for the majority of RCC-related morbidity and mortality.

Artificial intelligence (AI) has emerged as a powerful approach for strengthening conventional imaging-based assessment and improving diagnostic precision in renal cancer. Evidence from recent investigations indicates that machine learning (ML) approaches can successfully identify renal lesions and predict surveillance outcomes rather than merely assisting at the point of initial detection. Most machine learning applications in renal on-

cology have focused on radiomics-driven frameworks designed to distinguish malignant from benign renal masses and estimate mortality risk.

Deep learning (DL) methodologies have further transformed renal imaging by increasing the efficiency and precision of tumor characterization and detection. Through convolutional neural networks and related neural architectures, deep learning systems can perform automated segmentation, identification, and categorization of renal abnormalities on CT and MRI studies. These models also support non-invasive characterization of tumors, including histological subtype determination and tumor grading, potentially reducing reliance on invasive diagnostic procedures that require tissue sampling. In addition, deep learning techniques have been explored for the interpretation of digital pathology images, extending their utility across the entire diagnostic workflow.

Despite these advances, the application of computational approaches to directly model interactions between multiple organs, including organ tropism, systemic effects, and cross-organ signaling pathways, remains an emerging area of investigation. To address this gap, the present discussion reviews current AI research relevant to this frontier, evaluates the extent to which current methodologies capture multi-organ biological behaviour, and proposes a practical roadmap for the development

of mechanistic and clinically useful models.

Tumor Detection and Subtype Classification

In clinical oncology, decision-making depends on multiple sources of information, including molecular biomarkers, transcriptional signatures, imaging findings, and pathological assessment. Machine learning approaches provide an effective means of integrating these heterogeneous data sources in order to improve diagnostic performance and predictive accuracy. Techniques involving eigengene extraction and radiomic analysis, in which convolutional neural networks combine genomic and radiological features, have demonstrated promising improvements in predictive precision.

Machine learning can also improve understanding of how copy number alterations, which frequently drive gene expression changes in cancer, relate to histopathological characteristics. Studies have shown that AI-based models are capable of identifying histopathological patterns associated with alterations in genes such as epidermal growth factor receptor, KRAS, and von Hippel-Lindau. These approaches have also demonstrated the ability to distinguish between low-risk and high-risk RCC and to predict overall patient survival outcomes with considerable accuracy.

Metastasis and Multi-Organ Outcome Models

At the time of diagnosis, nearly 30% of patients with RCC present with synchronous distant metastases, in which both the primary tumor and metastatic lesions are identified simultaneously. Furthermore, approximately one-fifth of patients who initially undergo nephrectomy without evidence of metastatic disease later develop metachronous metastases during follow-up.

Traditionally, assessment of metastasis risk has relied primarily on tumor size, selected clinical indicators, and clinician experience. However, these conventional approaches are limited because they do not fully utilize the detailed biological and imaging information available from modern diagnostic technologies. Importantly, tumors of similar size may exhibit substantially different probabilities of synchronous distant metastasis, highlighting the need for more sophisticated predictive models.

Radiomics enables detailed investigation of tumor biology by extracting measurable quantitative features from medical imaging using machine learning algorithms and advanced computational techniques. For example, studies have applied CT-based radiomics approaches combined with deep learning methods to predict synchronous distant metastasis, creating integrated models that out-

perform the use of either modality independently. These findings demonstrate the value of combining multiple imaging and computational approaches to improve early metastasis detection and guide clinical decision-making.

The lung represents the most common site of metastasis in renal cancer. Once metastases involve critical organs, surgical management often becomes less feasible, making systemic therapies increasingly important. Over recent decades, systemic immunotherapy has remained a major therapeutic approach for metastatic RCC. Several studies using Surveillance, Epidemiology, and End Results database information have developed machine learning models capable of predicting lung metastasis in renal cancer. Through techniques such as least absolute shrinkage and selection operator analysis and multivariate logistic regression, multiple clinical predictors have been identified and incorporated into machine learning algorithms using cross-validation techniques. The resulting models demonstrated strong predictive performance, with extreme gradient boosting models producing the highest predictive accuracy. These findings suggest that machine learning offers a cost-effective and non-invasive strategy for evaluating the risk of lung metastasis, although additional real-world validation remains necessary.

Renal cell carcinoma also demonstrates a marked

tendency to metastasize to bone, making bone the second most frequent site of distant spread after the lung. Bone metastases occur in approximately 20% to 35% of RCC patients during disease progression, with common skeletal sites including the ribs, spine, and pelvis. Although only a limited number of studies have used machine learning to construct bone metastasis prediction models from large datasets, several investigations have demonstrated promising results. Studies using external validation datasets and network-based calculators have shown that machine learning algorithms, particularly extreme gradient boosting models, can effectively predict bone metastasis risk and potentially assist clinicians in selecting more appropriate diagnostic and therapeutic strategies for RCC patients.

The liver also represents a common site of RCC metastasis and accounts for a substantial proportion of newly diagnosed metastatic cases. Investigations involving large cohorts from population-based cancer databases have identified factors such as bone metastasis, lung metastasis, tumor grade, tumor stage, nodal involvement, and tumor size as important predictors of liver metastasis. Among multiple evaluated machine learning algorithms, extreme gradient boosting models again demonstrated superior predictive performance. To facilitate clinical implementation, online calculators based on these models have been developed

to support clinicians in estimating individualized liver metastasis risk and informing earlier therapeutic intervention.

A multicenter RCC study further highlights the potential of integrating artificial intelligence with molecular and immune-related datasets in order to develop mechanistic insights into metastatic behaviour and organ-specific dissemination. This investigation used deep learning architectures, including nnU-Net for segmentation and ResNet-18 for feature extraction, to analyse multiphase CT imaging. Imaging-derived features were then correlated with genomic, transcriptomic, and immune profiles. Aggressive tumors demonstrated distinct molecular characteristics, including higher frequencies of AHNAK2 mutations, immune-rich yet immunosuppressive microenvironments, elevated densities of CD8-positive T cells and regulatory T cells, and reduced mast cell populations compared with indolent tumors. These observations were validated through immunohistochemistry and toluidine blue staining techniques.

Although the primary objective of this study focused on tumor profiling, the integrated analysis of imaging, molecular, and immune-related data demonstrates the capacity of AI to infer mechanistic biological relationships. Such frameworks may eventually be adapted to predict organ-specific metastatic behaviour, including lung versus bone metastasis, thereby providing a foundation for fu-

ture research into multi-organ interactions in RCC.

Building upon the same principle of AI capturing systemic tumor behaviour, more recent multimodal RCC studies further demonstrate how integrated genomic, transcriptomic, and immune-spatial data can reflect biological programs influencing disease progression beyond the primary kidney lesion. One recent study developed a multimodal AI framework integrating genomic, transcriptomic, and tumor microenvironment features to improve prediction of targeted therapy and immune checkpoint inhibitor outcomes in ccRCC. Using one of the largest harmonized transcriptomic databases available for ccRCC, investigators identified five harmonized immune tumor microenvironment subtypes characterized by distinct immune, stromal, angiogenic, and metabolic profiles. These subtypes showed strong associations with patient survival and treatment response across multiple cohorts.

Spatial proteomics and single-cell RNA sequencing further validated that each subtype contained distinct cellular communities, including variations in CD8-positive T cells, myeloid cells, endothelial cells, and fibroblastic components. The study also generated AI-based responder scores for targeted therapy and immunotherapy, which consistently distinguished responders from non-responders across independent datasets and outperformed previously published biomarkers and

predictive signatures. The integrated decision-tree model classified most patients as likely to benefit preferentially from either immune checkpoint inhibitors or targeted kinase inhibitors, while also identifying a subgroup unlikely to benefit significantly from either treatment modality. These findings illustrate how multimodal AI can integrate heterogeneous molecular and spatial tumor microenvironment features into clinically actionable predictions. Furthermore, because these tumor microenvironment subtypes reflect coordinated immune, stromal, vascular, and metabolic programs, the framework supports the broader concept that RCC progression and therapeutic response are influenced by systemic whole-body biological processes rather than isolated kidney-specific mechanisms alone.

Theoretical and Experimental Insights into Multi-Organ Crosstalk

Understanding cancer as a systemic disease requires the integration of theoretical concepts, experimental systems, and human clinical studies. Conceptually, tumors can function as systemic disruptors by interfering with homeostasis and altering brain-body communication networks. Through hijacking neuronal and immune pathways, tumors may promote their own progression while host defense mechanisms attempt to restrain growth and dissemination. This conceptual framework demonstrates that analyses focused

solely on individual organs are insufficient and supports the need for approaches capable of capturing multi-organ interactions in renal cancers.

Experimental evidence further supports this systems-level perspective. Multi-organ microphysiological systems, including organ-on-a-chip platforms integrating tissues such as liver, heart, and lung within shared perfusion circuits, have demonstrated that biological responses frequently emerge from tissue-to-tissue communication rather than isolated organ behaviour. These experimental systems provide controlled demonstrations of how interconnected organ networks influence both cellular and systemic outcomes and therefore complement conceptual models of systemic tumor biology.

Human systemic studies also validate these principles. For example, cancer cachexia exhibits organ-specific metabolic alterations across the liver, skeletal muscle, and adipose tissue, while inter-organ correlations reveal extensive communication among carbohydrate, lipid, amino acid, and vitamin metabolic pathways. Machine learning approaches applied to these datasets have successfully stratified organ-level metabolic signatures using tissue and serum biomarkers, illustrating that multi-organ interactions can be quantitatively captured in clinical populations. Together, these theoretical, experimental, and clinical observations provide strong justification

for the development of AI-based frameworks capable of modelling multi-organ phenotypes and predicting systemic tumor behaviour across renal and other malignancies.

Limitations and Future Studies

Although artificial intelligence has demonstrated highly promising results in the management of numerous diseases, broader implementation will require additional clinical trials, real-world validation, and comprehensive training for healthcare professionals. While AI systems are sometimes criticized as “black box” models because of their limited interpretability, advances in data visualization and explainable AI tools are helping clinicians better understand algorithmic decision-making processes.

Future developments may involve the use of single-cell sequencing to investigate genetic alterations within individual cancer cells across multiple disease stages, thereby constructing dynamic genetic maps capable of tracking tumor progression from initiation through metastasis. Simultaneously, AI-driven risk prediction systems may become integrated into hospital electronic medical record systems, automatically incorporating updated patient information such as radiographic findings and serum biomarkers. Such systems could provide real-time metastasis risk assessment and support clinicians in tailoring individu-

alized treatment strategies.

Future progress in RCC management will depend heavily on the development of multimodal, whole-body AI frameworks capable of modelling organ tropism, cross-organ signaling pathways, and metastatic evolution. These advanced models have the potential to transform RCC management from a reactive process into a more anticipatory and personalized approach, enabling individualized surveillance strategies, earlier metastasis detection, and optimized therapeutic pathways for patients with renal cancer.

Conclusion

Artificial intelligence has substantially advanced renal cancer research through improvements in tumor detection, subtype classification, and prediction of single-organ metastasis. However, one of the most important emerging challenges is the modelling of complex interactions between multiple organ systems. Such modelling is essential for achieving a deeper understanding of RCC biology and improving patient outcomes.

Artificial intelligence systems are uniquely positioned to synthesize diverse forms of data, including genomics, radiomics, deep learning-derived analyses, and longitudinal clinical records. Through this integration, AI systems can characterize the systemic behaviour of tumors and extend analysis beyond the primary kidney lesion

toward a whole-body understanding of cancer progression and metastasis.

2- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN NEUROLOGICAL CANCERS

Background

Primary and secondary tumors of the central nervous system (CNS) remain among the most challenging malignancies in oncology. Although CNS tumors represent a relatively small proportion of all cancers, diffuse gliomas and glioblastoma carry a disproportionately high burden of morbidity and mortality. Malignant CNS tumors are associated with substantial mortality rates. Contemporary registry-based data from the Central Brain Tumor Registry of the United States indicate that the five-year relative survival rate for all malignant CNS tumors in adults is approximately 36%, whereas glioblastoma, which is the most common and aggressive diffuse glioma, continues to demonstrate a five-year survival rate below 10%.

For many decades, the CNS was regarded as an immunologically privileged site that was largely isolated from systemic influences because of the protective function of the blood-brain barrier. However, emerging evidence has substantially re-

shaped this traditional understanding. Current studies demonstrate that CNS tumors participate in dynamic and bidirectional interactions with the systemic immune system, endocrine pathways, metabolic networks, and even the gut microbiome through what is now referred to as the gut-brain-tumor axis. These complex interactions may significantly influence tumor progression, therapeutic response, and overall patient prognosis.

Recent advances in artificial intelligence (AI), particularly machine learning (ML) and deep learning (DL), have created a new frontier for exploring these highly complex multi-organ networks. By integrating imaging modalities such as MRI with molecular multi-omics data, systemic biomarkers including immune cell counts and cytokine profiles, and detailed clinical information, AI has the potential not only to classify tumors and predict outcomes, but also to model organ-to-organ communication, identify systemic signatures of CNS disease, and suggest novel personalized therapeutic interventions.

Cancer remains a leading cause of mortality worldwide, accounting for millions of deaths each year. Despite substantial advances in oncological research, the complex mechanisms underlying cancer development and progression are not yet fully understood. The blood–brain barrier restricts the exchange of cells and molecules between the

peripheral circulation and the central nervous system, resulting in the CNS being traditionally regarded as a distinct and immune privileged microenvironment. However, emerging evidence has challenged this view and highlighted extensive interactions between the CNS and peripheral tumors.

Recent studies have demonstrated that tumors can influence CNS function, while CNS-derived signaling molecules and neurochemical mediators may, in turn, regulate tumor growth and metastatic spread. Through dynamic interactions with the immune system, the CNS plays a critical role in modulating tumor progression and metastatic potential. CNS–immune cell crosstalk has therefore become a major focus of contemporary cancer research, as it significantly affects tumor behavior, host immune status, and therapeutic responsiveness.

Neurotransmitters and neuropeptides released by the CNS regulate immune cell activation and function, while immune cells reciprocally influence neural signaling, forming a complex bidirectional regulatory network. Disruption of this network can alter the tumor immune microenvironment, thereby impacting treatment efficacy and patient outcomes. Aberrant neural activation may promote immunosuppression and attenuate antitumor immune responses, whereas excessive immune activation can induce neuroinflammatory

processes that adversely affect neurological function and quality of life.

In this context, AI-driven approaches may shift neuro-oncology from a traditionally brain-centric perspective toward a broader whole-body, network-centric paradigm. Understanding this transformation requires examining the biological basis of systemic interactions in neurological cancers, the different data modalities and AI methodologies suitable for multi-organ modelling, and the current clinical and translational applications, limitations, and future research directions within this evolving field.

Conceptual Framework and Key Definitions

Cancer neuroscience is defined as an interdisciplinary field that explores bidirectional interactions between the nervous system and cancer throughout tumor initiation, progression, metastasis, and treatment resistance. A core premise of this field is that neural elements within tumors are not merely structural components but functionally significant constituents of the tumor microenvironment.

Neuro–cancer communication is inherently reciprocal. On one hand, tumors promote their own innervation by secreting neurotrophic factors that stimulate axonal growth. On the other hand, nerves release neurotransmitters and neuropep-

tides that enhance cancer cell proliferation, migration, and survival. The dominant conceptual model proposes that cancer effectively co-opts the homeostatic regulatory functions of the nervous system, reprogramming central and peripheral neural circuits to facilitate tumor expansion and dissemination.

Within this paradigm, cancer is no longer regarded as a strictly cell autonomous process but rather as a systemic disease that exploits inter-organ communication and neural regulation to suppress anti-tumor mechanisms, including immune and metabolic responses. Deciphering these complex interactions requires integrative strategies, particularly multi-omics technologies, to resolve molecular networks at a systems-wide level.

Historical Development of the Field

Although links between the nervous system and cancer have been observed historically, their significance was largely underestimated for many years. Throughout much of the twentieth century, oncology was dominated by a cell-centric framework that attributed cancer primarily to intracellular genetic alterations. Early anatomical reports describing nerve fibers within or near tumors were often dismissed as incidental, and the nervous system was generally considered relevant only in the context of secondary phenomena such as cancer associated pain.

A major shift occurred with advances in molecu-

lar biology, refinement of animal models, and the introduction of integrative multi-omics and computational methodologies. These developments enabled the identification of specific neurotransmitters, neuropeptides, and signaling pathways involved in neuro–cancer interactions. As a result, the research focus transitioned from questioning whether the nervous system is involved in cancer to investigating the mechanisms through which it contributes, and how these pathways might be therapeutically targeted.

Core Mechanisms and Biological Processes

The interplay between the nervous system and cancer is orchestrated through a multifaceted network of mechanisms that can be broadly grouped into three categories: tumor driven neurogenesis and nerve-to-cancer signaling, cancer-to-nerve communication with systemic disruption of homeostasis, and indirect regulation of the tumor microenvironment via neuro–immune interactions.

Tumor-Induced Neurogenesis and Nerve-to-Cancer Signaling

A wide range of tumors secrete neurotrophic factors, including nerve growth factor, brain-derived neurotrophic factor, and glial cell line-derived neurotrophic factor, which stimulate the growth and infiltration of sensory and autonomic nerve

fibers into tumor tissue. These infiltrating nerves release neurotransmitters such as acetylcholine and catecholamines, activating oncogenic signaling pathways that promote cancer cell proliferation, survival, invasion, and resistance to therapy.

Cancer-to-Nerve Signaling and Disruption of Homeostasis

Tumors also communicate back to the nervous system by releasing extracellular vesicles, metabolites, and inflammatory signals that influence central neural circuits involved in metabolic and immune regulation. Cancer associated cachexia exemplifies this phenomenon, wherein tumor-induced inflammation alters hypothalamic neuronal activity that governs appetite and energy homeostasis.

Modulation of the Tumor Microenvironment via Neuro–Immune Interactions

Neurotransmitters can directly modulate immune cell behavior and attenuate anti-tumor immune responses. For example, norepinephrine released from sympathetic nerve fibers suppresses cytotoxic T cell activity and drives macrophage polarization toward an immunosuppressive phenotype, thereby facilitating tumor progression.

Key Findings from the Literature

Narrative analyses of existing studies consistently

indicate that the nervous system functions as an active facilitator of cancer progression across diverse tumor types. In preclinical settings, disruption of tumor innervation markedly reduces tumor growth and metastatic spread. However, variability related to cancer subtype, nerve class, and anatomical context highlights the highly context-dependent nature of neuro–cancer interactions.

Biological Basis: Multi-Organ Interactions in Neurological Cancers

Systemic Immune Alterations and Immune Suppression

CNS tumors influence both local and systemic immunity. Within the local tumor microenvironment, immunosuppressive characteristics are commonly observed, although several important cellular populations remain present. For example, microglia and infiltrating pro-macrophages often display tumor-supportive phenotypes, whereas lymphocytes are usually present in relatively low numbers. Blood-based parameters also indicate the presence of systemic immune dysregulation. In patients with glioblastoma, elevated neutrophil-to-lymphocyte ratios, lymphopenia, and increased levels of myeloid-derived suppressive cells and regulatory T cells have all been documented. High preoperative neutrophil-to-lympho-

cyte ratios have consistently been associated with poorer overall survival across multiple patient populations. As a result, preoperative neutrophil-to-lymphocyte ratios and related inflammatory markers have been proposed as independent prognostic indicators.

These systemic immune disturbances are unlikely to be simple byproducts of the disease process. Rather, they most likely reflect tumor-induced immunomodulation characterized by altered cytokine activity, myeloid skewing, chronic inflammation, and bone marrow suppression or diversion. Consequently, CNS tumors should not be viewed merely as isolated neurological lesions, but rather as diseases capable of inducing widespread systemic immunological dysfunction.

Gut-Brain-Tumor Axis and Microbiome Influence

Recent studies have increasingly explored the influence of the gut microbiome on the biology of brain tumors. Alterations in gut microbial composition, commonly referred to as dysbiosis, together with metabolic changes involving short-chain fatty acids, amino acids, and additional metabolites, have been associated with modifications in systemic immune responses, blood-brain barrier permeability, and neuroinflammation, particularly in patients with gliomas. Preclinical and

translational investigations have demonstrated that microbiome-derived signals can influence tumor immunity and alter the behaviour of both primary and metastatic brain tumors.

Although correlation alone does not establish causation, current evidence supports the possibility of a substantial paradigm shift in neuro-oncology. Brain tumors may exist within an interconnected gut-brain-immune-body network that interacts with modifiable and potentially targetable factors such as diet, microbiome composition, and systemic metabolism. This emerging understanding opens new opportunities for adjunctive therapeutic strategies that extend beyond conventional tumor-directed treatments.

Molecular Heterogeneity and Multi-Omics Dimensions

Diffuse gliomas demonstrate substantial molecular heterogeneity. Variability exists in genetic mutations such as isocitrate dehydrogenase (IDH) mutations, epigenetic alterations including MGMT promoter methylation, and transcriptomic, proteomic, and metabolomic profiles. Even at the single-cell and single-nucleus level, gliomas contain distinct biological subgroups characterized by unique molecular features, prognostic patterns, and treatment sensitivities. Recent integrative studies have emphasized the importance of com-

bining multi-omics data from diverse biological processes to improve glioma classification, prognostic evaluation, and therapeutic specificity.

At the same time, much of the current research remains focused primarily on tumor-intrinsic characteristics and the local tumor microenvironment, with limited incorporation of systemic organ-level context or broader biological biomarkers. Addressing these limitations will require analytical frameworks capable of processing highly heterogeneous, multidimensional, and multi-organ datasets.

Data Modalities and AI-Enabled Approaches

Imaging Radiomics and Deep Learning in MRI

Neuro-oncology continues to rely heavily on non-invasive neuroimaging, particularly multiparametric MRI techniques that include structural imaging, diffusion imaging, and perfusion imaging. Radiomics and deep learning approaches have greatly advanced the extraction of quantitative imaging biomarkers associated with genotype, tumor grade, and prognosis. For example, in World Health Organization grade 2 to 4 gliomas, structural and diffusion tensor imaging MRI features processed through convolutional neural network and support vector machine pipelines have dem-

onstrated the ability to predict IDH mutation status with strong diagnostic performance. Similarly, radiomics models have achieved high levels of accuracy in predicting IDH1 mutation status from preoperative MRI images. Additional radiomics-based deep learning studies have also been developed to predict MGMT promoter methylation status with encouraging classification performance. Meta-analyses further suggest that machine learning-based radiomics approaches provide promising diagnostic performance for molecular profiling in gliomas.

These advances demonstrate how AI can infer molecular and prognostic information from imaging alone in a non-invasive, reproducible, and potentially longitudinal manner. Nevertheless, the majority of these investigations remain primarily brain-centric, with limited integration of systemic or multi-organ data such as blood biomarkers, immune profiles, or microbiome information.

Multi-Omics Data Integration

The integration of multiple omics layers has emerged as a critical strategy for capturing the molecular complexity and heterogeneity of gliomas. Researchers have combined messenger RNA expression, DNA methylation profiles, and microRNA data using supervised canonical correlation analysis frameworks to distinguish gliob-

lastoma from lower-grade gliomas, as well as to differentiate astrocytoma from oligodendroglioma. These integrated models have achieved high levels of glioma subtype discrimination while also identifying novel candidate biomarkers with potential diagnostic and prognostic significance.

Additional AI-driven studies have emphasized the ability of machine learning pipelines to support molecular classification, prognostic modelling, and treatment stratification in glioblastoma by integrating genomics, transcriptomics, epigenomics, imaging radiomics, and clinical data. Novel frameworks such as DeepAutoGlioma have combined promoter DNA methylation and gene expression data through deep learning autoencoders to generate latent multi-omics representations. Convolutional neural networks were subsequently applied to classify glioblastoma and lower-grade glioma subtypes. These integrated approaches outperformed previous machine learning and deep learning models based solely on single-omic inputs and achieved high classification accuracies in both internal and independent validation datasets.

From a methodological perspective, vertical integration strategies that combine several omics modalities within the same sample set remain the dominant approach in current multi-omics re-

search.

Towards Multi-Organ Modelling

Although most AI studies in neuro-oncology continue to focus primarily on intracranial data, emerging research efforts aim to model tumors as components of larger system-wide biological networks. Recent reviews suggest that radiomics, multi-omics information, and clinical data, including peripheral blood biomarkers, can be integrated to identify phenotypic glioma subgroups associated with distinct systemic signatures. Additional studies using single-cell technologies have demonstrated how tumor-infiltrating and circulating immune cell populations jointly shape the glioma microenvironment by simultaneously profiling immune cells from tumor tissue and matched peripheral blood samples. Furthermore, integrative analyses combining single-cell immune landscapes, bulk transcriptomic cohorts, and clinical variables have linked age-related immune alterations in primary glioblastoma with patient prognosis.

These findings indicate that a whole-body network model of CNS cancer is not only conceptually feasible but also methodologically achievable. Artificial intelligence, with its ability to process high-dimensional and heterogeneous datasets, plays a central role in enabling this transition toward sys-

temic modelling.

Brain metastasis represents the most common malignant tumor of the central nervous system in adults and is associated with a poor prognosis. Reported overall survival rates following brain metastasis diagnosis remain low, with 2-year and 5-year survival rates of approximately 8.1% and 2.5%, respectively. Although the precise incidence of brain metastasis remains uncertain, previous studies estimate occurrence rates ranging from 9% to 17% among patients with systemic cancer. The incidence is expected to increase further due to population aging, rising cancer prevalence, and the widespread use of advanced neuroimaging techniques.

The likelihood of developing brain metastasis varies substantially according to the primary tumor origin. Lung cancer accounts for approximately 41% to 56% of cases, followed by breast cancer at 13% to 30%, malignant melanoma at 6% to 11%, and gastrointestinal tumors at 6% to 9%. Notably, brain metastasis may represent the initial clinical manifestation in 2% to 14% of patients with an otherwise unidentified primary malignancy, with many cases remaining asymptomatic and detected only through screening or postmortem examination.

To investigate these patterns, datasets were divided into independent training and validation cohorts. Feature standardization was applied, and

synthetic oversampling was used in the training set to address class imbalance. Redundant features were removed, and feature selection was integrated into model construction to minimize overfitting. Multiple linear machine learning classifiers were trained and evaluated using external cross-validation, with model performance assessed through receiver operating characteristic and precision–recall analyses. The optimal radiomic model was subsequently combined with clinical variables for comparative evaluation.

A total of 202 patients with 439 brain metastases were included in the analysis (mean age 60.8 ± 10.3 years; 87 males and 115 females). The mean maximum lesion diameter was 15.7 ± 8.9 mm, and the mean lesion volume was 1.8 ± 5.2 cm^3. Demographic characteristics were comparable between the training and validation cohorts. Significant differences were identified in six clinical and MRI features among the lung cancer, breast cancer, and gastrointestinal cohorts. The breast cancer cohort exhibited the highest proportion of female patients, whereas no significant differences were observed in age, lesion size, or lesion volume. Multiple intracranial lesions and peritumoral edema were common across all cohorts.

Brain metastases originating from lung cancer were predominantly supratentorial (72.1%), displayed round and nodular morphology (74.6%), and most frequently demonstrated peripheral rim

enhancement (84.8%), with relatively infrequent cystic degeneration or necrosis (23.0%). In contrast, breast cancer–derived metastases more commonly involved the infratentorial compartment (42.2%) and exhibited lobulated or multinodular fusion morphology (60.7%), heterogeneous enhancement (70.4%), and higher rates of cystic degeneration or necrosis (60.0%). Metastases from gastrointestinal tumors were more likely to demonstrate low signal intensity on T2-weighted imaging (43.3%), representing a statistically significant distinguishing feature.

Clinical and Translational Implications

Adopting a multi-organ perspective in neuro-oncology offers several potential clinical and translational benefits. Radiomics and machine learning models combined with systemic biomarkers may reduce the need for invasive biopsies or repeated tissue sampling while improving prognostic stratification and non-invasive molecular profiling. Multi-modal signatures that integrate imaging, blood biomarkers, microbiome data, and omics information may identify patient subgroups more likely to benefit from immunotherapy, metabolic interventions, or microbiome-targeted treatments.

Longitudinal integration of imaging findings, systemic blood markers, and potentially microbiome

or metabolomic data may also support the earlier detection of tumor recurrence or systemic complications. In addition, AI-driven network models may uncover previously unrecognized therapeutic targets, including microbial modulation, metabolic pathway inhibition, and neuroimmune regulatory mechanisms, by mapping pathways of organ-to-organ communication.

Challenges and Limitations

Despite these promising developments, several important challenges continue to limit the realization of this vision. Data heterogeneity and fragmentation remain major concerns because imaging, omics, blood biomarkers, microbiome data, and clinical information are often collected separately and require extensive harmonization. Many radiomics and machine learning studies are retrospective, single-center investigations with limited external validation, restricting their generalizability and clinical applicability.

Another significant limitation is the current lack of large-scale, longitudinal, multi-organ datasets that combine neuroimaging with systemic biomarkers, microbiome information, and metabolomic profiles. In addition, interpretability and causal inference remain difficult because highly complex predictive models may identify statistical correlations without revealing underlying bio-

logical mechanisms. Ethical, financial, logistical, and regulatory issues related to the collection and management of imaging, multi-omics, microbiome, and clinical data further complicate implementation in routine clinical practice.

Future Directions

To fully realize the potential of multi-organ AI approaches in neuro-oncology, several priorities should be addressed. Future research should focus on developing prospective, multi-modal cohort studies that include longitudinal clinical information, microbiome and metabolome data, immune and metabolic blood panels, advanced MRI techniques, diffusion tensor imaging, and perfusion imaging. Standardization of MRI protocols, omics pipelines, blood assays, and metadata collection will also be necessary to reduce batch effects and improve the development of generalizable models.

The development of interpretable and causally informed AI models represents another important objective. Combining machine learning and deep learning approaches with explainable AI, network modelling, and causal inference frameworks may facilitate the identification of biologically meaningful pathways. Translational studies targeting systemic axes, including immunomodulation, metabolic therapy, and microbiome modulation, should also be pursued based on AI-identified dis-

ease subphenotypes.

Finally, integrating these technologies into clinical workflows will require the development of user-friendly platforms capable of supporting risk assessment, treatment planning, and systemic monitoring beyond the central nervous system. Concepts such as digital twins may eventually provide clinicians with dynamic, personalized models for monitoring and managing patients with CNS tumors.

Conclusion

The growing evidence regarding systemic immune dysregulation, the gut-brain-tumor axis, and multilayer molecular heterogeneity challenges the traditional view of CNS tumors as isolated neurological lesions. Neuro-oncology is approaching a major paradigm shift from a brain-centric perspective toward a whole-body, network-centric model supported by advances in artificial intelligence.

AI-driven systems have the capacity to map complex organ-to-organ interaction networks that influence tumor biology, treatment response, and patient outcomes by integrating imaging data, omics information, systemic biomarkers, microbiome profiles, and clinical metadata. Achieving this vision will require coordinated multidisciplinary efforts, prospective multi-modal data

collection, rigorous methodological standards, a strong emphasis on interpretability, and continued translational research.

If successfully implemented, this strategy has the potential to transform neuro-oncology by enabling more individualized, systemic, adaptive, and dynamic care for patients with central nervous system tumors.

3- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN GASTROINTESTINAL CANCERS

Background

Gastrointestinal (GI) neoplasms rank among the most burdensome malignancies worldwide and constitute three of the ten most frequently diagnosed cancers globally. Annual trends in both incidence and mortality continue to rise, resulting in more than 5 million new cases and over 3.5 million deaths recorded in 2020. This alarming mortality burden highlights the considerable challenges created by a multifaceted and interconnected network of intrinsic and extrinsic factors that contribute to multifactorial drug resistance and subsequent therapeutic failure. These therapeutic failures arise not only from cell-autonomous mechanisms, including inhibition of apoptosis, overexpression of efflux transporters, epigenetic modifications, and metabolic reprogramming, but also from non-cell-autonomous processes occurring within the tumor microenvironment (TME).

The tumor microenvironment represents a highly complex and dynamic extracellular ecosystem that includes cancer-associated fibroblasts, tumoral cells, immune cells, multiple cytokines

and metabolites, as well as tumor-derived exosomes. Furthermore, the tumor microenvironment possesses the capacity to induce remodeling processes within distant organs through a coordinated biological mechanism. Initially, tumor-derived secreted factors are transported to remote organs, where resident cellular populations undergo phenotypic transformation. These newly activated cells subsequently relay feedback signals that sustain and amplify the formation of the premetastatic niche. This process illustrates that gastrointestinal cancers are not confined solely to the primary tumor site, but rather function as systemic diseases involving extensive communication between primary tumors and distant organ systems.

Conventional approaches to the diagnosis, prognosis, and management of gastrointestinal malignancies primarily focus on localized primary tumors. However, this localized perspective contrasts sharply with the existence of bidirectional communication networks between different subtypes of GI cancers and distant organs. Consequently, there is an urgent need for more comprehensive investigations capable of addressing these systemic interactions. Current limitations in understanding systemic signaling paradigms are reflected in numerous biological mechanisms that cannot be fully explained through isolated tumor analysis alone, thereby emphasizing the necessity

of a holistic and integrative research approach.

For example, gastrointestinal tumor-derived exosomes contain homing integrins that determine metastatic tropism toward specific distant organs. These molecular determinants are not detectable through conventional pathological analysis. Similarly, simultaneous conversion of resident macrophage populations within distant organs into premetastatic phenotypes is not adequately addressed by standard immunohistological methods, such as analyses based solely on CD163 or CD206 positivity. In addition, stromal cells within distant organs may undergo extensive transcriptional reprogramming after exposure to signaling molecules released from the primary tumor. Such systemic biological alterations cannot be accurately inferred from examination of the primary tumor alone.

Unlike traditional single-modality analytical approaches, artificial intelligence offers the possibility of integrated and multiscale analysis involving primary tumors, distant organ microenvironments, and circulating biological signals simultaneously. Machine learning tools can comprehensively evaluate the composition of the tumor microenvironment by integrating genomic data from primary tumors, transcriptomic signatures, as well as pathomics and radiomics features. This multidimensional approach provides superior predictive capability for assessing metastatic

risk compared with conventional clinical staging systems alone.

Graph Neural Networks represent another important AI methodology capable of detecting communication cascades across multiple cell populations and organ systems. These computational frameworks can model primary tumor cells and the tumor microenvironment as one interconnected subgraph while simultaneously representing premetastatic niches within distant organs as another subgraph. Through cross-graph attention mechanisms, these systems can learn and identify intercellular signaling pathways that travel between organs, including exosomal cargo transfer, circulating cytokine signaling, and leukocyte trafficking patterns. Such approaches provide a more comprehensive understanding of the systemic biological interactions that underlie metastatic progression in gastrointestinal cancers.

In addition, exosomal microRNA profiling combined with longitudinal biomarker analysis using temporal deep learning models allows the identification of early stages of premetastatic niche formation and maturation. By analysing biological signals collected at sequential time intervals, these models may enable earlier detection of metastatic transformation before clinically detectable lesions become apparent. This capability has substantial implications for improving surveillance strategies, therapeutic intervention timing, and per-

sonalized patient management.

Given the broad range of artificial intelligence applications across different layers of tumor interaction with distant organs, together with the critical importance of early lesion detection in gastrointestinal cancer management, there is growing interest in exploring how AI-driven interventions can improve the identification and understanding of these complex systemic interactions. Artificial intelligence therefore represents a transformative tool for advancing the diagnosis, prognostic assessment, and treatment of gastrointestinal malignancies through a more comprehensive and biologically integrated approach to cancer care.

For many years, cancers affecting the gastrointestinal tract were largely interpreted as conditions confined to a single anatomical location. Lesions developing in organs such as the stomach, colon, or pancreas were typically assessed and managed as localized diseases, with treatment strategies directed mainly at the site of origin. While this approach proved useful in clinical practice, it has been insufficient to explain the wide biological variability and diverse clinical trajectories observed among patients. Current evidence increasingly indicates that gastrointestinal malignancies exert effects beyond their primary tissue, involving multiple organs through integrated and interdependent biological mechanisms.

Gastrointestinal tumors therefore cannot be regarded simply as isolated accumulations of transformed cells. Instead, they act as active sources of systemic signaling. By producing and releasing numerous bioactive factors, including cytokines, chemokines, hormonal mediators, metabolic products, and extracellular vesicles, these tumors influence physiological processes throughout the body. Such signals enable communication with distant tissues, including the liver, bone marrow, adipose tissue, skeletal muscle, and components of the immune system. The resulting systemic effects include widespread inflammation, impaired immune regulation, thrombotic tendencies, metabolic imbalance, and cancer related cachexia. In many patients, these systemic manifestations have a greater impact on morbidity and survival than the size or local extent of the primary tumor.

One of the most illustrative examples of cross-organ communication in gastrointestinal cancers involves interactions between the gut and the liver. In colorectal and pancreatic malignancies, liver involvement does not arise solely from passive transport of malignant cells through the circulation. Instead, signals from the primary tumor drive molecular and cellular remodeling within hepatic tissue. These changes affect immune surveillance, alter stromal architecture, and reprogram metabolic activity. Together, they generate a

hepatic environment that is more receptive to subsequent tumor colonization, demonstrating that distant organs may undergo preparatory changes well before metastatic disease becomes clinically detectable.

Systemic interaction in gastrointestinal cancer is also strongly influenced by the gut microbiome. Shifts in microbial communities within the intestine can shape immune responses, modify baseline inflammatory states, and alter sensitivity to anticancer therapies. Emerging evidence shows that microbial derived signals affect both the efficacy and toxicity of chemotherapy and immunotherapy. Such observations reinforce the need to view gastrointestinal malignancies through a holistic lens that accounts for organism wide interactions rather than limiting analysis to individual organs.

Although awareness of these multi-organ dynamics has expanded, traditional analytical techniques remain inadequate for handling their complexity. Data generated from molecular profiling, cellular studies, imaging modalities, and clinical follow-up are vast and highly heterogeneous, making integration difficult using conventional methods. Artificial intelligence provides a promising solution to this challenge. Approaches based on machine learning and deep learning can concurrently process diverse datasets, enabling recog-

nition of meaningful patterns across different biological layers and organ systems.

Within the context of gastrointestinal malignancies, artificial intelligence offers a structured means of linking molecular characteristics of the primary tumor with systemic biological responses and patient outcomes. The integration of genomic data, immune parameters, metabolic indicators, and longitudinal clinical information allows for a more nuanced understanding of disease behavior. This comprehensive viewpoint supports a transition from narrowly focused, organ-based care toward a broader, system-oriented interpretation of gastrointestinal cancers. In this role, AI functions primarily as a powerful organizational and analytical aid, facilitating cross-organ insight without altering the fundamental biological principles underlying cancer.

Multi-Organ Interactions in Gastrointestinal Cancers

Gastrointestinal cancers can simultaneously involve multiple organs through several biological mechanisms. The liver is the most common site of metastasis in colorectal cancer because tumor cells can enter the portal circulation and subsequently establish secondary lesions within hepatic tissue. This liver-gut axis involves highly complex molecular communication pathways mediated

by cytokines, immune cells, metabolic signaling pathways, and stromal interactions. Pancreatic cancer also demonstrates early systemic involvement and frequently affects the liver, lungs, and peritoneum through both lymphatic and hematogenous dissemination.

The gut-brain axis represents another important component of multi-organ interactions in GI malignancies. Tumors can influence the nervous system through inflammatory mediators, microbial metabolites, neuroimmune signaling, and direct neural communication pathways. In addition, the relationship between gastrointestinal cancers and the cardiovascular system may contribute to cancer-associated thrombosis and cardiotoxicity resulting from chemotherapy. These diseases also share several common risk factors, including obesity, chronic inflammation, and metabolic syndrome.

The immune system functions as a central mediator of multi-organ interactions in gastrointestinal cancers. Tumors can induce systemic immunosuppression, influencing both local tissues and distant organs. These immunological changes may alter metastatic progression, treatment response, and overall patient prognosis. Understanding these highly interconnected biological relationships requires advanced analytical tools capable of processing large-scale and multidimen-

sional datasets while identifying complex and non-linear relationships among molecular, cellular, and organ-level processes.

AI Technologies in Cancer Research

Artificial intelligence encompasses a broad range of model-based computational approaches that enable machines to learn from data and generate predictions or clinical decisions. In cancer research, several AI technologies have produced highly valuable and clinically relevant findings. Machine learning algorithms, including support vector machines, random forests, and gradient boosting methods, are particularly effective for classification tasks and feature selection within highly multidimensional datasets. These techniques can identify biomarkers associated with multi-organ involvement and predict metastatic patterns using clinical, molecular, and imaging data.

Deep learning, which represents a specialized branch of machine learning based on multilayer artificial neural networks, has dramatically transformed medical image analysis. Convolutional neural networks are capable of detecting subtle imaging patterns and identifying metastatic lesions across multiple organs with accuracy levels that may equal or exceed those of human experts in selected settings. Recurrent neural networks

and transformer-based architectures support the analysis of temporal disease progression and treatment response by processing sequential and longitudinal data. Natural language processing techniques can also extract clinically meaningful information from unstructured clinical notes, pathology reports, and electronic medical records, thereby facilitating comprehensive data integration and clinical interpretation.

More recently, graph neural networks and network analysis methodologies have emerged as valuable tools for understanding multi-organ interactions. These approaches model the relationships among biological entities, organs, signaling pathways, and molecular networks. By analysing these interconnected systems, graph-based AI frameworks can reveal system-level properties that emerge from highly complex biological interactions. Reinforcement learning algorithms may also optimize treatment strategies by simultaneously considering therapeutic efficacy and multi-organ toxicity across different anatomical sites.

Applications of AI in Multi-Organ Interactions

Artificial intelligence has become increasingly valuable across multiple areas of multi-organ interaction research. In radiological imaging, AI algorithms analyse CT, MRI, and PET scans to sim-

ultaneously evaluate tumor burden across multiple organs, predict metastatic patterns, and assess treatment responses at both primary and secondary tumor sites. Radiomics, which involves extraction of quantitative imaging features from medical images, combined with machine learning approaches, can identify imaging signatures associated with molecular subtypes and predict the likelihood and location of metastatic spread.

Multi-omics data integration represents another major application of AI in gastrointestinal cancer research. Artificial intelligence methods can integrate genomic, transcriptomic, proteomic, and metabolomic data obtained from multiple organs in order to construct comprehensive molecular maps of cancer progression. These analyses reveal organ-specific molecular adaptations and identify mutations associated with metastatic potential. In addition, AI models can predict therapeutic vulnerabilities in multi-organ disease states and guide the development of personalized treatment approaches.

Analysis of single-cell RNA sequencing data using AI technologies allows researchers to monitor cellular evolution across metastatic sites and characterize the distinct features of tumor microenvironments within different organs. Such approaches provide detailed insight into tumor heterogeneity, immune infiltration, and stromal interactions

during disease progression.

AI-based digital pathology systems can analyse tissue samples from multiple organs and quantify tumor cellularity, immune cell infiltration, vascular changes, and stromal architecture. These tools can identify histological patterns predictive of multi-organ involvement and evaluate spatial relationships between tumor cells and their surrounding microenvironments across different anatomical locations. Predictive AI models may also classify patients according to risks of metastasis, treatment response, and organ-specific toxicities, thereby supporting precision oncology and individualized patient care.

Challenges and Future Directions

Despite substantial progress, several challenges continue to limit the broader application of artificial intelligence in gastrointestinal oncology. Data variability and integration difficulties remain major obstacles because datasets often differ in format, imaging protocols, sequencing methodologies, and institutional practices. Standardization of data acquisition and preprocessing procedures is therefore essential for generating reliable and generalizable AI models.

Another important limitation involves the interpretability of AI systems. Many deep learning models function as “black boxes,” making it

difficult for clinicians to understand how predictions are generated. Limited interpretability may reduce trust, hinder regulatory approval, and restrict clinical implementation. Consequently, explainable AI methods that provide transparent reasoning and visualization of decision-making processes are increasingly important.

The shortage of large-scale multi-organ datasets with comprehensive annotations also limits model development and external validation. Federated learning and collaborative data-sharing initiatives may provide practical solutions by enabling model training across multiple institutions without direct transfer of sensitive patient data. In addition, large-scale multi-organ analyses require substantial computational resources and advanced algorithmic infrastructure. Prospective clinical validation studies remain essential to confirm that AI-driven insights translate into measurable improvements in patient outcomes.

Future research should focus on the development of multimodal AI frameworks capable of integrating imaging, molecular, pathological, and clinical data into unified predictive systems. Such models may ultimately enable the creation of digital twins that simulate personalized disease progression across multiple organ systems. There is also increasing interest in real-time AI systems that continuously monitor multi-organ dynamics during

treatment. Furthermore, AI-guided therapeutic interventions should be explored in greater depth in order to optimize treatment strategies while accounting for complex organ interactions, systemic toxicities, and disease heterogeneity.

Conclusion

Artificial intelligence represents a transformative tool for investigating multi-organ interactions in gastrointestinal cancers. By integrating diverse forms of biological and clinical data while identifying highly complex patterns, AI technologies can deepen understanding of cancer biology, improve diagnostic precision, and support personalized therapeutic strategies. As these technologies continue to mature and overcome current limitations, they are expected to significantly transform the management of gastrointestinal malignancies through more comprehensive, predictive, and system-oriented approaches to cancer care. Realizing this potential will require sustained investment in AI research, robust data infrastructure, interdisciplinary collaboration, and rigorous clinical validation.

4- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN HEMATOLOGICAL CANCERS

Background

Hematological cancers, also referred to as blood malignancies, include a diverse group of diseases such as leukemias, lymphomas, and multiple myeloma. Unlike solid tumors, these cancers originate within the bone marrow, lymphatic system, or circulating blood and inherently involve systemic dissemination from their earliest stages. This fundamental characteristic distinguishes hematological malignancies from organ-confined cancers and places them within a natural framework of multi-organ interaction. In these diseases, malignant cells do not remain restricted to a single anatomical site. Instead, they circulate widely, infiltrate multiple tissues, and reshape distant organ function through complex biological signaling networks. As a result, hematological cancers are not only diseases of abnormal cell proliferation but also systemic disorders involving continuous interaction between the bone marrow, peripheral blood, immune system, liver, spleen, kidneys, central nervous system, and vascular compartments. Despite advances in targeted therapies, immunotherapies, and stem cell transplantation, out-

comes remain variable. This variability reflects the highly dynamic and multi-organ nature of disease progression. Traditional diagnostic and prognostic approaches often focus on isolated parameters such as bone marrow biopsy findings, peripheral blood counts, or cytogenetic abnormalities. However, these methods are insufficient to capture the full complexity of systemic disease evolution. Artificial intelligence has emerged as a powerful tool to address this limitation. By integrating heterogeneous data sources, including genomic, transcriptomic, proteomic, imaging, and clinical data, AI enables the modeling of disease as a whole-body system rather than a localized pathology. In hematological cancers, this systems-level approach is particularly relevant because disease progression inherently involves cross-organ communication.

Systemic Nature of Hematological Cancers

Hematological malignancies inherently exhibit multi-organ involvement due to their origin in circulating or highly mobile cellular populations. Leukemic cells, for example, are produced in the bone marrow but circulate through peripheral blood and infiltrate organs such as the liver, spleen, lymph nodes, and central nervous system. Lymphomas, although often originating in lymphatic tissues, frequently disseminate to extranodal organs. Multiple myeloma primarily affects the bone marrow but also induces systemic

effects on bone metabolism, kidney function, and immune regulation.

This widespread involvement is not merely a consequence of physical dissemination. Malignant cells actively reshape distant organ environments to support their survival and proliferation. This includes modifying immune responses, altering metabolic pathways, and inducing stromal and endothelial changes in secondary organs. These processes highlight that hematological cancers operate as systemic biological networks rather than isolated cellular expansions.

Multi-organ interactions in these diseases are mediated by circulating cytokines, chemokines, extracellular vesicles, and metabolic byproducts. These signals create feedback loops between malignant cells and host tissues. For instance, inflammatory cytokines released by malignant cells can suppress normal hematopoiesis, while bone marrow stromal cells can provide survival signals that enhance tumor resistance. This bidirectional communication reinforces disease progression and complicates therapeutic intervention.

Biological Basis of Multi-Organ Interactions

The biological mechanisms underlying multi-organ interactions in hematological cancers are complex and multifactorial. One of the most important components is the bone marrow

microenvironment, which serves as the central regulatory hub of hematopoiesis and malignant transformation. Within this niche, interactions between hematopoietic stem cells, stromal cells, immune cells, and extracellular matrix components determine disease behavior. Malignant cells disrupt this microenvironment by altering cytokine signaling pathways such as interleukin signaling, tumor necrosis factor pathways, and chemokine gradients. These disruptions extend beyond the bone marrow and influence systemic immune function. For example, abnormal cytokine production can lead to immune exhaustion, impaired T-cell activity, and dysregulated inflammatory responses in distant organs. Another key mechanism involves the spleen and liver, which often become sites of extramedullary hematopoiesis. In hematological malignancies, these organs may be infiltrated by malignant cells or repurposed to support abnormal blood cell production. This leads to structural and functional changes, including organ enlargement, altered immune cell trafficking, and metabolic imbalance. The central nervous system is also affected in certain hematological cancers, particularly acute leukemias and aggressive lymphomas. Malignant cells can cross the blood-brain barrier, leading to neuroinflammation, cognitive dysfunction, and neurological complications. This demonstrates that hematological cancers are capable of disrupting even highly protected biological compartments.

Clinical Manifestations of Multi-Organ Involvement

The multi-organ nature of hematological cancers is reflected in their clinical presentation. Patients often exhibit systemic symptoms such as fatigue, fever, weight loss, and night sweats, which arise from widespread immune activation and metabolic dysregulation. Laboratory findings frequently show abnormalities across multiple organ systems, including liver enzyme elevation, renal impairment, coagulation disturbances, and immune suppression.

Organ-specific complications are also common. Splenomegaly and hepatomegaly occur due to infiltration and extramedullary hematopoiesis. Bone disease is particularly prominent in multiple myeloma, where osteolytic lesions result from disrupted bone remodeling. Renal dysfunction may arise from light chain deposition, hypercalcemia, or tumor lysis syndrome. Neurological complications may result from direct infiltration or secondary inflammatory processes. These clinical manifestations highlight the need for integrated diagnostic frameworks capable of capturing multi-organ disease dynamics rather than focusing solely on hematological parameters.

Limitations of Conventional Analytical Approaches

Traditional methods used to study hematological

cancers often rely on compartmentalized data sources. Bone marrow biopsies, peripheral blood counts, and single-organ imaging provide valuable but incomplete information. These approaches are limited in their ability to capture temporal dynamics and cross-organ interactions. Furthermore, conventional statistical models struggle to integrate high-dimensional datasets generated from modern diagnostic technologies. Genomic sequencing, proteomic profiling, and advanced imaging modalities produce large-scale heterogeneous data that cannot be easily interpreted using linear analytical methods.

As a result, important systemic relationships between organs and disease progression pathways may remain undetected. This limitation highlights the need for advanced computational approaches capable of integrating multi-modal data and identifying non-linear biological relationships.

Role of Artificial Intelligence in Hematological Cancers

Artificial intelligence offers a transformative approach for investigating multi-organ interactions in hematological malignancies. Machine learning and deep learning models can integrate diverse data sources, enabling comprehensive analysis of disease systems. These models are capable of identifying patterns that are not detectable through

traditional analytical techniques.

In hematology, AI can analyze genomic mutations, gene expression profiles, immune cell distributions, and clinical parameters simultaneously. This allows for the identification of disease subtypes with distinct biological and clinical characteristics. AI-based clustering methods have already demonstrated the ability to refine classification systems for leukemias and lymphomas beyond conventional diagnostic categories. Deep learning models are particularly effective in processing imaging data, such as bone marrow histology slides and radiological scans. These models can identify subtle morphological changes associated with disease progression and organ involvement. When combined with molecular data, AI systems can generate integrated representations of disease behavior across multiple organs.

Multi-Organ Modeling Through AI Systems

One of the most promising applications of AI in hematological cancers is multi-organ modeling. This involves constructing computational frameworks that represent interactions between different biological systems, including bone marrow, blood circulation, liver, spleen, lymph nodes, and immune networks. Graph-based neural networks are particularly useful in this context. They model biological entities as interconnected nodes and

represent signaling pathways as edges. This structure allows AI systems to capture complex relationships between organs and identify key drivers of disease progression. For example, AI models can simulate how malignant cells originating in the bone marrow influence immune suppression in peripheral tissues or how cytokine networks affect organ dysfunction. These models can also identify feedback loops that sustain disease progression across multiple organ systems.

Clinical Applications of AI in Multi-Organ Analysis

AI-driven multi-organ analysis has several important clinical applications in hematological cancers. One major application is risk stratification. By integrating multi-modal data, AI can identify patients at high risk of disease progression, organ failure, or treatment resistance.

Another application is treatment response prediction. AI models can analyze how different organs respond to therapies such as chemotherapy, immunotherapy, and stem cell transplantation. This enables personalized treatment planning that considers systemic effects rather than isolated tumor response. AI can also assist in early detection of complications. For instance, predictive models can identify early signs of tumor lysis syndrome, organ infiltration, or immune-related toxicity. This allows for timely intervention and improved

patient outcomes.

Challenges and Limitations

Despite its potential, the application of AI in hematological cancers faces several challenges. Data heterogeneity remains a major issue, as clinical, molecular, and imaging datasets are often collected using different protocols. This complicates integration and standardization. Another challenge is model interpretability. Many AI systems, particularly deep learning models, operate as black boxes, making it difficult to understand how predictions are generated. This limits clinical trust and adoption.

Data privacy and ethical considerations are also important, especially given the sensitivity of genetic and clinical information. Ensuring secure data handling and compliance with regulatory frameworks is essential. Finally, the lack of large-scale, multi-organ longitudinal datasets limits model training and validation. Without comprehensive datasets, AI systems may fail to generalize across diverse patient populations.

Future Directions

Future research should focus on developing integrated multi-organ datasets that combine molecular, clinical, and imaging data across disease stages. Longitudinal studies will be essential to capture disease evolution over time. Explainable

AI approaches will also play a critical role in improving model transparency and clinical adoption. These methods will help clinicians understand how AI systems generate predictions and recommendations.

Another important direction is the development of digital twin models for hematological cancers. These virtual patient models can simulate disease progression and treatment response across multiple organs, enabling personalized therapeutic strategies. Federated learning approaches may also help address data privacy concerns by allowing models to be trained across institutions without sharing raw patient data.

Conclusion

Artificial intelligence represents a transformative tool for investigating multi-organ interactions in hematological cancers. By integrating diverse data sources and modeling systemic biological relationships, AI enables a deeper understanding of disease mechanisms that extend beyond the bone marrow and blood compartment. This systems-level perspective has important implications for diagnosis, prognosis, and treatment. While challenges remain in data integration, interpretability, and clinical validation, continued advances in AI methodologies and biomedical data science are likely to reshape the future of hematological oncology. Ultimately, AI-driven multi-organ modeling offers a pathway toward more precise, personalized, and system-aware cancer care.

5- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN DERMATOLOGICAL CANCERS

Background

Dermatological cancers, including melanoma, cutaneous squamous cell carcinoma, and basal cell carcinoma, represent a major and growing public health burden worldwide. Although many skin cancers are detectable at an early stage due to their visible nature, a significant proportion still progress to advanced disease with systemic involvement. Among them, melanoma is the most aggressive form, characterized by a high propensity for metastasis and substantial mortality when diagnosed late. The global incidence of skin cancers has continued to rise due to factors such as increased ultraviolet radiation exposure, environmental changes, aging populations, and improved detection practices. Traditionally, dermatological cancers have been viewed as localized diseases of the skin. Clinical evaluation and treatment strategies have primarily focused on the primary lesion and regional lymph nodes. However, this perspective is increasingly recognized as incomplete. Growing evidence demonstrates that skin cancers are deeply interconnected with systemic biological processes involving multiple organs, in-

cluding the lymphatic system, liver, lungs, brain, bone marrow, and immune network. These interactions influence tumor initiation, progression, metastasis, and therapeutic response. Dermatological cancers are now understood as systemic diseases that communicate with distant organs through complex biological signaling networks. Tumor cells release cytokines, chemokines, extracellular vesicles, and metabolic mediators that circulate throughout the body and alter the function of remote tissues. These signals can reprogram immune responses, modify organ microenvironments, and establish premetastatic niches that support tumor dissemination. This multi-organ communication plays a central role in determining disease trajectory and patient outcomes. Despite advances in molecular biology and oncology, understanding these complex interactions remains challenging due to the high dimensionality and heterogeneity of biological data. Artificial intelligence offers a transformative approach for investigating multi-organ interactions in dermatological cancers by integrating diverse datasets and uncovering patterns that are not visible through conventional analytical methods.

Biological Basis of Multi-Organ Interactions in Dermatological Cancers

The progression of dermatological cancers involves dynamic interactions between the primary

tumor and multiple distant organs. These interactions are mediated through systemic circulation, immune modulation, and neuroendocrine signaling pathways. Tumor-derived factors influence not only local tissue environments but also distant physiological systems, shaping the course of disease progression. One of the most important mechanisms of multi-organ interaction is metastasis. In melanoma, tumor cells can disseminate early through lymphatic and hematogenous routes, colonizing organs such as the lungs, liver, brain, and bone. However, metastasis is not a random process. Instead, it is guided by organ-specific microenvironmental conditions that are influenced by tumor-secreted factors. These factors can prepare distant organs for tumor cell colonization even before metastatic cells arrive, a phenomenon known as premetastatic niche formation.

The immune system plays a central role in mediating multi-organ interactions. Skin cancers are highly immunogenic, and immune surveillance is a key determinant of tumor control. However, tumors can evade immune detection by inducing immunosuppressive environments both locally and systemically. Regulatory T cells, myeloid-derived suppressor cells, and tumor-associated macrophages contribute to immune suppression across multiple organs, thereby facilitating tumor progression. Another important dimension of multi-organ interaction involves metabolic reprogram-

ming. Dermatological cancers can alter systemic metabolism by affecting glucose utilization, lipid metabolism, and amino acid turnover. These metabolic changes impact not only tumor growth but also the function of distant organs such as the liver and muscle tissue. Cancer-associated cachexia, characterized by severe weight loss and muscle wasting, is a clear example of systemic metabolic disruption driven by tumor activity.

Neuroendocrine signaling also contributes to multi-organ interactions in skin cancers. Stress-related hormones such as cortisol and catecholamines can influence tumor growth and immune function. Conversely, tumor presence can affect neurological and psychological states, demonstrating bidirectional communication between the tumor and the central nervous system.

Artificial Intelligence in Understanding Systemic Cancer Behavior

Artificial intelligence has emerged as a powerful tool for analyzing complex biological systems. In dermatological cancers, AI enables the integration of multi-organ data, including genomic profiles, imaging data, histopathological features, and clinical records. Machine learning and deep learning algorithms can identify hidden relationships between tumor characteristics and systemic outcomes. Machine learning models such as random forests, support vector machines, and gradient

boosting algorithms are widely used to classify tumor types, predict disease progression, and estimate metastatic risk. These models can analyze heterogeneous datasets and identify predictive biomarkers associated with multi-organ involvement.

Deep learning techniques, particularly convolutional neural networks, are highly effective in analyzing medical imaging data. In dermatology, these models are widely used for skin lesion classification and melanoma detection. Beyond primary lesion analysis, deep learning can also evaluate systemic disease patterns by integrating imaging data from multiple organs, such as brain MRI, chest CT, and abdominal scans. Recurrent neural networks and transformer-based architectures are capable of analyzing longitudinal patient data. This enables the study of disease progression over time and the identification of temporal patterns associated with metastasis and treatment response. These models are particularly valuable for understanding how dermatological cancers evolve across multiple organ systems.

Graph neural networks offer a unique approach for modeling biological interactions. In the context of cancer, nodes can represent organs, cells, or molecular entities, while edges represent functional relationships. This framework allows AI systems to model multi-organ communication networks and identify key drivers of disease progression.

Radiomics and Imaging-Based Multi-Organ Analysis

Radiomics plays a central role in AI-driven oncology research by extracting quantitative features from medical images. In dermatological cancers, radiomics can be applied to skin imaging, lymph node imaging, and whole-body scans to identify patterns associated with tumor aggressiveness and metastatic spread.

AI-driven radiomic models can detect subtle imaging features that are not visible to the human eye. These features may reflect tumor heterogeneity, vascularization, immune infiltration, and metabolic activity. When combined with clinical data, radiomics can improve the prediction of multi-organ metastasis and patient survival outcomes. Whole-body imaging analysis using AI allows for the simultaneous evaluation of multiple organs. This is particularly important in melanoma, where metastases can occur in diverse anatomical locations. AI systems can integrate imaging data across organ systems to provide a comprehensive view of disease burden and progression.

Multi-Omics Integration and Systemic Disease Modeling

Multi-omics integration is a critical application of AI in understanding dermatological cancers. Genomic, transcriptomic, proteomic, and metabolo-

mic data provide complementary insights into tumor biology and systemic effects. Genomic data reveal mutations and structural variations that drive tumor development. Transcriptomic data provide information on gene expression patterns associated with metastasis and immune evasion. Proteomic data reflect functional protein activity, while metabolomic data capture systemic metabolic changes induced by tumors.

AI models can integrate these diverse datasets to construct comprehensive disease models. These models can identify molecular pathways involved in multi-organ interactions and reveal potential therapeutic targets. For example, specific genetic mutations may be associated with increased risk of brain or liver metastasis in melanoma.

Single-cell sequencing data further enhance the resolution of AI models by capturing cellular heterogeneity within tumors and distant tissues. This allows for the identification of rare cell populations that contribute to metastasis and immune escape.

Immune System and Multi-Organ Communication

The immune system is a central mediator of multi-organ interactions in dermatological cancers. Tumors interact with immune cells both locally and systemically, influencing immune surveillance and response. AI models can analyze

immune profiling data to identify patterns of immune activation and suppression across different organs. These patterns can provide insights into treatment response, particularly in immunotherapy. Immune checkpoint inhibitors have revolutionized melanoma treatment, but response rates vary significantly among patients.

AI-based predictive models can help identify patients who are most likely to benefit from immunotherapy by analyzing immune signatures, tumor mutational burden, and systemic inflammatory markers. These models can also detect early signs of immune-related adverse events affecting multiple organs.

Clinical Applications of AI in Multi-Organ Cancer Analysis

AI has numerous clinical applications in dermatological cancers. One of the most important is early detection of metastasis. By integrating imaging, genomic, and clinical data, AI systems can identify patients at high risk of multi-organ spread.

Another important application is treatment planning. AI can assist clinicians in selecting optimal therapies based on individual patient profiles, including tumor characteristics and systemic involvement. This supports personalized medicine approaches that improve treatment outcomes. AI can also support monitoring of disease progression. Continuous analysis of patient data enables

real-time assessment of treatment response and detection of new metastatic lesions.

Challenges and Limitations

Despite significant progress, several challenges remain in the application of AI to dermatological cancer research. Data heterogeneity is a major issue, as medical data originate from multiple sources with varying formats and quality. Integrating these datasets requires robust standardization methods. Another challenge is model interpretability. Many AI systems operate as black boxes, making it difficult to understand how predictions are generated. This limits clinical trust and adoption.

Data privacy and ethical considerations are also important, particularly when dealing with sensitive patient information. Ensuring secure data handling and compliance with regulations is essential.

Future Directions

Future research in AI for dermatological cancers will likely focus on developing multimodal systems that integrate imaging, genomics, and clinical data at scale. Advances in explainable AI will improve model transparency and clinical usability. The development of digital twins, virtual representations of individual patients, may allow simulation of disease progression and treatment

response across multiple organs. This could revolutionize personalized oncology.

Federated learning approaches may enable collaborative model training across institutions without sharing sensitive data. This will improve model robustness while preserving privacy.

Conclusion

Artificial intelligence is transforming the understanding of dermatological cancers by enabling comprehensive analysis of multi-organ interactions. By integrating diverse data sources and uncovering complex biological patterns, AI provides new insights into tumor progression, metastasis, and systemic disease behavior. These advances support the development of personalized and precise cancer care strategies. As technology continues to evolve, AI will play an increasingly central role in bridging dermatology, oncology, and systems biology to improve patient outcomes across the entire disease spectrum.

6- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN OPHTHALMOLOGICAL CANCERS

Background

Ophthalmological cancers represent a heterogeneous group of neoplasms that affect the eye and its associated visual pathways. These malignancies include primary ocular tumors such as retinoblastoma and uveal melanoma, as well as secondary or metastatic tumors that originate outside the eye and subsequently infiltrate ocular tissues. Although the eye is considered a relatively anatomically isolated organ with distinctive physiological and immune-related properties, tumor progression and metastatic dissemination frequently involve highly complex interactions with multiple organ systems, including the liver, lungs, brain, and the systemic immune network. Understanding these multi-organ interactions is essential for improving diagnostic accuracy, prognostic evaluation, and the development of more effective therapeutic strategies.

Artificial intelligence (AI) has emerged as a transformative and rapidly evolving tool in biomedical research. Within oncology, AI algorithms are capable of integrating large, heterogeneous, and multidimensional datasets in order to identify

biological patterns that may remain undetectable through conventional analytical approaches. When applied to ophthalmological cancers, AI facilitates the investigation of system-wide biological interactions and supports a more comprehensive understanding of tumor behaviour across interconnected organ systems. This systems-oriented perspective may contribute to the advancement of precision medicine and individualized patient care in ophthalmic oncology.

The Biological Basis of Multi-Organ Interactions in Ophthalmological Cancers

Tumor cells do not exist in isolation. Instead, they interact dynamically with their surrounding microenvironment as well as with distant organ systems throughout the body. These interactions are mediated by a wide range of molecular and cellular signals, including cytokines, growth factors, extracellular vesicles, immune mediators, and metabolic pathways. The resulting biological communication networks influence tumor progression, metastatic spread, therapeutic response, and patient survival outcomes.

Metastatic Processes

In uveal melanoma, which is among the most extensively studied ophthalmological malignancies, tumor cells commonly disseminate through hematogenous pathways and demonstrate a

strong predilection for metastasis to the liver. This phenomenon of organ-specific metastasis, often referred to as organotropism, reflects both the intrinsic molecular characteristics of the tumor and the permissive biological microenvironment of the hepatic niche. The liver provides favorable metabolic and immunological conditions that support tumor colonization and progression. Understanding these interactions is critical for improving early detection of metastasis and developing targeted systemic therapies.

Immune Modulation

Ocular tissues possess immune-privileged characteristics that regulate and modulate local immune responses in order to preserve visual function. However, when tumor-associated antigens enter the systemic circulation, they may influence immune surveillance mechanisms in secondary organs and distant tissues. Consequently, alterations in the systemic immune landscape can significantly affect tumor progression, metastatic potential, and overall patient prognosis. Interactions between local ocular immunity and systemic immune responses therefore represent an important area of investigation in ophthalmological cancer research.

Neuro-Endocrine Interactions

The visual system is closely interconnected with the central nervous system and endocrine regu-

latory pathways. Neuroendocrine mediators, including stress hormones and neurotrophic factors, may influence tumor growth, disease progression, and patient resilience. At the same time, increasing tumor burden and metastatic disease can affect visual processing pathways and neurological function. These neuro-endocrine interactions further demonstrate that ophthalmological cancers should be viewed within the broader context of systemic physiology rather than as isolated ocular conditions.

These complex multi-organ interactions are reflected in genomic, transcriptomic, proteomic, metabolomic, imaging, and clinical datasets. However, conventional statistical methods often fail to capture the highly dimensional and interconnected relationships present within such data. This limitation highlights the growing importance and utility of advanced AI methodologies in ophthalmological oncology research.

AI Methodologies for Multi-Organ Interaction Analysis

Artificial intelligence encompasses a broad range of computational methodologies capable of identifying intricate patterns within large-scale multimodal datasets. Among these approaches, machine learning, deep learning, and network-based computational models are particularly relevant for analysing multi-organ interactions in ophthal-

mological cancers.

Machine Learning

Machine learning algorithms, including support vector machines, random forests, and gradient boosting methods, are widely used for classifying cancer subtypes, predicting metastatic spread, and identifying prognostic biomarkers. These algorithms can process large quantities of clinical variables, imaging characteristics, and molecular profiles to generate predictive models of disease progression and therapeutic outcomes. By learning from multidimensional datasets, machine learning systems may improve diagnostic precision and support more individualized clinical decision-making.

Deep Learning

Deep learning approaches, particularly convolutional neural networks and recurrent neural networks, are highly effective for extracting hierarchical features from high-dimensional biomedical data. Convolutional neural networks are frequently applied in medical image analysis, including retinal imaging, ocular MRI, and digital pathology whole-slide imaging. Recurrent neural networks and transformer-based architectures are more suitable for sequential data, such as longitudinal patient records and time-series gene expression profiles.

Deep learning models can uncover latent biological representations associated with systemic disease involvement. For example, these models may identify imaging or molecular patterns predictive of hepatic metastasis in ocular melanoma, thereby contributing to earlier intervention and more accurate prognostic assessment.

Graph and Network Models

Biological systems, including molecular pathways and inter-organ communication networks, are inherently interconnected and network-based in nature. Graph neural networks and network inference algorithms model biological entities such as genes, proteins, cells, and organs as nodes connected through functional interactions represented by edges. These computational structures allow researchers to gain systems-level insights into disease mechanisms, including the identification of hub genes, signaling pathways, or organ systems that play central roles in tumor dissemination and metastatic progression.

Data Types and Integration Strategies

Investigating multi-organ interactions in ophthalmological cancers requires the integration of multiple forms of biological and clinical data. Each data modality contributes unique information regarding tumor behaviour and systemic disease processes.

Genomic and Transcriptomic Data

Genomic and transcriptomic sequencing data provide insight into somatic mutations, gene expression patterns, and epigenetic alterations associated with tumor aggressiveness, metastatic behaviour, and organ-specific dissemination. These molecular datasets are essential for understanding the biological heterogeneity of ophthalmological malignancies.

Proteomics and Metabolomics

Proteomic and metabolomic analyses reflect the functional and biochemical states of cells and tissues. Integrated analysis of proteins and metabolites may reveal mechanisms underlying tumor metastasis, systemic inflammatory responses, and metabolic adaptation in distant organ environments.

Medical Imaging

Ophthalmic imaging modalities, including optical coherence tomography and fundus photography, provide highly detailed structural information regarding ocular tumors. When combined with systemic imaging modalities such as CT and MRI, these datasets provide valuable spatial and anatomical context for understanding local invasion and metastatic spread.

Electronic Health Records

Electronic health records contribute essential clinical variables, including treatment history, laboratory findings, demographic characteristics, therapeutic response, and patient outcomes. These data enrich predictive models and support the development of personalized medicine approaches in ophthalmological oncology.

Multimodal AI frameworks are specifically designed to integrate these diverse and heterogeneous datasets, enabling computational models to learn relationships across molecular, anatomical, physiological, and clinical scales. For example, multimodal deep learning systems may combine genomic information with imaging features to improve prediction of extraocular metastasis and systemic disease progression.

Applications in Ophthalmological Cancer Research

Early Detection and Diagnosis

AI models trained on imaging and molecular datasets can identify subtle abnormalities indicative of malignancy before overt clinical symptoms become apparent. Deep learning approaches applied to fundus photography have demonstrated promising potential for detecting retinoblastoma and identifying high-risk lesions in individuals predisposed to ocular malignancies. Earlier detection may significantly improve treatment outcomes and long-term survival.

Prognosis and Risk Stratification

Multi-organ interactions play a major role in determining disease prognosis. AI algorithms can stratify patients according to metastatic risk by learning biological patterns associated with systemic involvement, including immune-related signatures predictive of liver metastasis in uveal melanoma. Such predictive capabilities may support more accurate surveillance strategies and individualized treatment planning.

Therapeutic Response Prediction

AI-based predictive models can estimate how tumors are likely to respond to specific therapeutic interventions, including targeted therapies and immunotherapies. By integrating systemic biomarkers, imaging findings, and molecular characteristics, AI systems contribute to more personalized and evidence-based treatment strategies.

Biological Discovery

Interpretable AI methodologies, including feature importance analysis and network visualization techniques, provide opportunities for discovering previously unrecognized biological pathways involved in tumor-organ communication. These approaches may reveal novel mechanisms of metastatic progression and identify potential therapeutic targets for future investigation.

Challenges and Future Directions

Despite substantial progress, several important challenges continue to limit the broader application of AI in ophthalmological oncology research and clinical practice.

Data Quality and Standardization

Biomedical datasets are often heterogeneous, incomplete, and affected by variability in acquisition methods. Ensuring the availability of high-quality, interoperable, and standardized datasets is essential for improving the reliability, reproducibility, and generalizability of AI models.

Explainability

Many advanced AI systems function as complex “black box” models in which the underlying decision-making processes are not fully transparent. Improving interpretability and explainability remains critically important, especially in clinical settings where physician trust and patient safety depend on understanding how predictions and recommendations are generated.

Clinical Integration

Translating AI technologies into routine clinical practice requires rigorous external validation, regulatory approval, and effective integration within healthcare infrastructures and clinical workflows. Successful implementation also de-

pends on clinician training, ethical oversight, and interdisciplinary collaboration.

Future research will likely focus on the development of causal inference models, federated learning approaches that preserve patient privacy, and AI-guided experimental designs capable of accelerating hypothesis generation and testing in multi-organ oncology research.

Conclusion

Artificial intelligence has catalyzed a major paradigm shift in the investigation of multi-organ interactions in ophthalmological cancers. By integrating diverse biological, imaging, and clinical datasets and modelling highly complex biological systems, AI provides deeper insights into tumor biology, enhances diagnostic precision, improves prognostic evaluation, and supports more personalized therapeutic approaches.

As computational methodologies continue to evolve and biomedical datasets expand in scale and complexity, AI will remain an indispensable tool in advancing the understanding and treatment of ophthalmological malignancies within the broader framework of systemic human physiology and multi-organ disease interactions.

7- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN ORAL CANCERS

Background

Oral cancer is no longer considered only a disease of the mouth. Increasingly, clinicians and researchers recognize it as part of a broader systemic condition that can affect the entire body. Cancer cells originating in the oral cavity may spread to the lymph nodes in the neck, as well as to distant organs such as the lungs, bones, and other tissues. Because of this metastatic potential, the management of oral cancer requires a comprehensive evaluation of the whole body rather than focusing solely on a single anatomical site. Artificial intelligence (AI) is becoming a transformative tool in this field by supporting earlier diagnosis, more accurate staging, and improved treatment planning.

By analysing medical imaging modalities such as CT scans and PET scans, AI systems can identify very small clusters of malignant cells that may otherwise remain undetected during routine clinical evaluation. This capability allows clinicians to stage the disease with greater precision and to better predict patterns of disease progression. However, the role of AI extends beyond image analysis alone. More advanced AI systems are now

capable of integrating multi-omics data, including information related to a patient's genes, proteins, and metabolic activity. This integrated approach provides a more comprehensive picture of the patient's overall health status and tumour biology. Through the analysis of these complex datasets, AI can also identify blood-based biomarkers associated with cancer risk, disease progression, and the likelihood of response to specific therapies.

Artificial intelligence is already assisting healthcare professionals in detecting oral cancer at earlier stages by analysing scans of the oral cavity and jaw for subtle abnormalities and early signs of disease. AI can also contribute to the personalization of treatment strategies. For example, by evaluating the functional status of organs such as the liver and kidneys, AI systems may recommend safer and more effective chemotherapy dosages tailored to the individual patient. The next major development in this field is adaptive therapy, in which treatment plans are continuously modified according to the patient's response during the course of treatment. In radiotherapy, AI systems can adjust treatment protocols if the tumour decreases in size or if changes occur in the patient's anatomy during therapy. This adaptive approach makes treatment more precise, potentially more effective, and less harmful to healthy tissues.

Researchers are also working toward the development of a "Full-Body AI Agent," which represents

a highly integrated approach to patient care. In this proposed system, different AI models would monitor the function and condition of individual organs, while a central coordinating system would integrate the information to guide clinical decision-making and treatment planning. Such an approach would allow medical care to adapt continuously as the patient's condition changes over time. Another important innovation is Multi-Organ-on-a-Chip (MOC) technology. These miniature devices are designed to simulate the behaviour and function of human organs in a laboratory setting. In oral cancer research, these chips can model tissues such as the salivary glands, jawbone, and oral mucosa. Artificial intelligence can analyse the extensive amount of data generated by these systems and may even regulate experiments in real time. For instance, an oral tumour-on-a-chip model could be used to evaluate different radiotherapy schedules on a patient's own cells before clinicians select the most appropriate treatment plan.

Recent studies demonstrate that artificial intelligence is no longer simply a futuristic concept but is already reshaping the diagnosis and management of oral cancer. AI offers considerable promise through earlier disease detection, more intelligent treatment planning, and a broader systemic understanding of health that recognizes the close relationship between oral health and overall body health. These developments are gradually

transforming oral cancer care into a more precise, evidence-based, and patient-centred field of medicine.

Biological Basis of Cross-Organ Interaction in Oral Cancer

Oral cancer, once considered primarily a localized disease, is now understood to involve widespread systemic interactions. Tumors release a variety of biologically active substances, including cytokines, extracellular vesicles, exosomes, growth factors, and metabolic byproducts, which travel through the bloodstream and lymphatic system to distant organs such as lymph nodes, lungs, liver, bone, and brain. These signaling molecules alter local and systemic physiology and contribute to the formation of environments favorable for tumor progression and metastasis.

The immune system responds to these tumors through mechanisms that may either suppress tumor growth or unintentionally support tumor survival and dissemination. Tumor-associated inflammation can impair normal immune defense mechanisms while simultaneously promoting angiogenesis, immune evasion, and metastatic spread. Furthermore, alterations in the oral and gut microbiomes contribute to this complex biological communication network. Microbial dysbiosis can influence inflammatory responses, immune regulation, and metabolic pathways that

affect both tumor progression and systemic organ function.

These highly interconnected biological processes generate enormous quantities of molecular, clinical, imaging, and physiological data. Conventional analytical methods often struggle to interpret such high-dimensional and nonlinear information effectively. Artificial intelligence, however, is particularly well suited for analysing these complex interactions because it can process large datasets, identify subtle relationships, and recognize patterns that are not easily detectable through traditional statistical approaches.

The Function of AI in Unraveling Intricate Biological Networks

Artificial intelligence excels at investigating highly complex biological systems because of its capacity to analyse nonlinear relationships within large and multidimensional datasets. Machine learning models can integrate clinical records, radiological imaging, genetic profiles, molecular biomarkers, histopathological findings, and biochemical parameters in order to map how oral tumors interact with distant organs and systemic pathways.

Deep learning approaches, particularly convolutional neural networks and graph-based neural networks, are capable of uncovering systemic biological patterns that often remain hidden from

simpler analytical methods. These advanced computational models can identify relationships between local tumor characteristics and distant organ alterations, enabling a more comprehensive understanding of oral cancer as a systemic disease. By integrating information from multiple sources, AI systems can also monitor how organ-to-organ interactions evolve during disease progression, metastasis, and treatment response.

Graph neural networks are especially valuable because they model biological systems as interconnected networks in which organs, cells, signaling molecules, and metabolic pathways are represented as nodes connected by dynamic relationships. Such frameworks allow researchers to investigate communication pathways between tumors and distant organs in ways that were previously impossible using conventional methodologies.

Imaging and Radiomics: Expanding the Scope of Analysis

The integration of advanced imaging modalities with AI-driven radiomics has significantly expanded the scope of oral cancer investigation beyond the visible lesion itself. Radiomics involves the extraction of quantitative imaging features from CT, MRI, PET, and head-and-neck imaging studies. These imaging-derived characteristics can reveal subtle biological and structural information that reflects tumor aggressiveness, metastatic po-

tential, and systemic involvement.

Radiomic features obtained from head-and-neck imaging are increasingly associated with alterations in lymphatic structures, regional tissues, and distant organs. Artificial intelligence algorithms can connect these imaging biomarkers to systemic inflammatory responses, metabolic alterations, and metastatic risk. Consequently, local imaging studies may provide indirect insight into broader physiological and pathological changes occurring throughout the body.

This non-invasive strategy enables earlier and more accurate identification of patients who may be vulnerable to systemic complications or distant metastatic disease. In addition, AI-assisted imaging analysis improves reproducibility, reduces observer variability, and enhances the ability of clinicians to stratify patients according to disease severity and predicted outcomes.

Merging Omics and Clinical Data

Artificial intelligence also enables the integration of multi-omics datasets, including transcriptomics, proteomics, metabolomics, genomics, and epigenomics, with clinical and pathological information to provide a comprehensive picture of the systemic effects of oral cancer. These approaches allow researchers to explore molecular pathways that connect oral tumors with immune dysfunction, metabolic alterations, and distant organ im-

pairment.

Machine learning techniques can identify molecular signatures associated with disease progression, therapeutic resistance, and metastatic dissemination. By integrating clinical variables with laboratory and molecular data, AI models create a more realistic representation of patient complexity and biological heterogeneity. These computational frameworks also reveal shared molecular pathways that contribute to both local tumor progression and systemic organ dysfunction.

Furthermore, AI-driven multi-omics integration can identify biomarkers predictive of therapeutic response and patient prognosis. Such findings may eventually support the development of highly personalized treatment strategies tailored to the biological profile of individual patients.

Interaction Between the Microbiome and the Immune System

Recent research has highlighted the importance of the oral-gut axis in oral cancer biology and systemic disease progression. Artificial intelligence provides powerful tools for analysing intricate microbiome patterns and understanding their relationships with immune responses across multiple organs. Alterations in microbial populations may influence systemic immunity, inflammatory signaling, metabolic regulation, and tumor progression.

AI-driven analysis of microbiome datasets allows researchers to investigate how microbial communities contribute to communication between oral tumors and distant tissues. Machine learning models can identify microbial signatures associated with immune suppression, metastatic behaviour, and therapeutic response. These approaches may also reveal previously unrecognized pathways through which microbial dysbiosis contributes to cancer development and systemic disease progression.

The interaction between the microbiome and the immune system is highly dynamic and complex. AI systems are particularly effective for modelling these interactions because they can analyse longitudinal data and identify evolving patterns over time. This capability may improve understanding of how microbiome alterations influence treatment efficacy, immunotherapy response, and overall patient outcomes.

Clinical Relevance and Future Outlook

Understanding multi-organ interactions through artificial intelligence has substantial clinical implications. Predictive AI models can improve risk stratification, identify patients at higher risk of systemic complications, and support the personalization of therapeutic strategies. These computational approaches may also guide the development

of multi-targeted therapies designed to address both local tumor burden and systemic biological effects simultaneously. Artificial intelligence may further improve surveillance strategies by enabling earlier detection of metastatic disease and treatment-related complications. Integration of imaging, molecular biomarkers, microbiome analysis, and clinical data could allow clinicians to monitor disease progression more accurately and intervene at earlier stages.

Despite these promising advances, several important challenges remain. Data variability, limited standardization, and differences in imaging protocols and sequencing methods can reduce the reliability and generalizability of AI models. Another major concern involves model interpretability, as many deep learning systems function as “black boxes” with limited transparency regarding how predictions are generated. Improved explainable AI approaches are therefore essential to increase clinician trust and facilitate clinical adoption. Future research should emphasize prospective validation studies and the development of clinically interpretable AI systems capable of integrating multimodal datasets in real-world healthcare settings. Collaborative efforts among clinicians, data scientists, molecular biologists, and computational researchers will be essential for translating these technological advances into practical improvements in patient care.

Future Directions

The future of oral cancer care is expected to include the full integration of artificial intelligence into routine clinical practice and healthcare systems. Larger and more diverse datasets will be required to train more accurate, reliable, and inclusive AI models. Future algorithms are also expected to become increasingly capable of predicting how oral cancer will progress over time, enabling clinicians to anticipate disease behaviour and intervene earlier when necessary. Together, artificial intelligence, multi-omics analysis, and organ-on-a-chip technology are opening the door to a new era of medicine in which oral cancer treatment becomes predictive, personalized, and adaptive. This emerging approach recognizes that oral health cannot be separated from overall systemic health and that effective cancer care requires a holistic understanding of the entire human body.

Conclusion

Artificial intelligence is transforming oral cancer research through the integration and analysis of highly complex, multidimensional biological data. These technologies allow researchers and clinicians to move beyond the isolated examination of the primary tumor and instead uncover systemic patterns that deepen understanding of oral cancer as a whole-body disease. By combining imaging, molecular profiling, microbiome

analysis, and clinical information, AI provides unprecedented insight into the biological networks connecting oral tumors with distant organs and physiological systems. Realizing the full potential of artificial intelligence in precision oncology will require close collaboration between clinicians, researchers, and data scientists, together with continued advances in computational methodologies and data integration. As these technologies continue to evolve, AI-driven approaches are expected to play a central role in improving diagnosis, prognostic assessment, therapeutic planning, and overall patient outcomes in oral cancer care.

8- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN ENT CANCERS

Background

Ear, nose, and throat (ENT) cancers, also known as head and neck cancers, include malignancies arising from the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, and salivary glands. These cancers represent a significant global health burden due to their high incidence, late-stage diagnosis, functional impairment, and complex treatment requirements. Squamous cell carcinoma accounts for the majority of ENT malignancies, and its aggressive nature contributes to substantial morbidity and mortality worldwide. Traditionally, ENT cancers have been considered localized diseases confined to anatomically distinct regions of the head and neck. Clinical evaluation has focused on primary tumor sites and regional lymph node involvement. However, this organ-centered perspective is increasingly insufficient. Emerging evidence demonstrates that ENT cancers are not isolated pathological entities but systemic diseases involving complex interactions between multiple organ systems, including the

immune system, lungs, liver, brain, and musculoskeletal system. These cancers communicate with distant organs through biological signaling networks involving cytokines, chemokines, extracellular vesicles, metabolic factors, and neuroendocrine mediators. These signals enable tumors to influence distant microenvironments and facilitate metastatic spread. The concept of multi-organ interaction is therefore central to understanding disease progression, therapeutic resistance, and patient outcomes in ENT cancers. Despite advances in oncology, understanding these interactions remains challenging due to the complexity and heterogeneity of biological data. Artificial intelligence offers a transformative approach for analyzing multi-organ interactions in ENT cancers by integrating diverse datasets and uncovering hidden patterns that cannot be identified using conventional statistical methods.

Biological Basis of Multi-Organ Interactions in ENT Cancers

ENT cancers exhibit extensive interactions with multiple organ systems through systemic circulation, lymphatic dissemination, immune modulation, and neuroendocrine signaling. These interactions influence tumor initiation, progression, metastasis, and treatment response. One of the most important mechanisms of multi-organ interaction is metastasis. ENT cancers commonly metastasize to regional lymph nodes, lungs, liver,

and bone. The process of metastasis is not purely mechanical but biologically regulated through tumor-derived signaling molecules that prepare distant organs for tumor cell colonization. This process, known as premetastatic niche formation, involves immune cell recruitment, stromal remodeling, and vascular changes in distant tissues.

The immune system plays a central role in ENT cancer progression. These tumors are highly immunogenic, and immune surveillance is a key determinant of disease outcome. However, tumors can evade immune detection by creating immunosuppressive environments both locally and systemically. Regulatory T cells, tumor-associated macrophages, and myeloid-derived suppressor cells contribute to immune suppression across multiple organs, enabling tumor progression and metastasis. Neuroendocrine interactions are also critical in ENT cancers. Given the anatomical proximity of these tumors to cranial nerves and brain structures, neural signaling plays a significant role in tumor behavior. Stress-related hormones and neurotransmitters can influence tumor growth, angiogenesis, and immune response. Conversely, tumor presence can alter neural function, affecting pain perception, swallowing, speech, and emotional regulation. Metabolic reprogramming is another key aspect of multi-organ interaction. ENT cancers alter systemic metabolism by influencing glucose uptake, lipid metabolism, and protein

catabolism. These metabolic changes affect distant organs such as the liver and skeletal muscle, contributing to cancer-associated cachexia and systemic weakness.

Artificial Intelligence in Multi-Organ Cancer Analysis

Artificial intelligence provides powerful tools for analyzing complex multi-organ interactions in ENT cancers. Machine learning, deep learning, and advanced data integration methods enable the analysis of heterogeneous datasets, including imaging, genomics, histopathology, and clinical records. Machine learning algorithms such as random forests, support vector machines, and gradient boosting models are widely used for cancer classification, prognosis prediction, and metastasis risk assessment. These models can integrate clinical and molecular data to identify patterns associated with multi-organ disease progression.

Deep learning approaches, particularly convolutional neural networks, have revolutionized medical imaging analysis in ENT cancers. These models are widely used for tumor detection, segmentation, and classification in radiological imaging such as CT, MRI, and PET scans. Beyond primary tumor evaluation, deep learning can also assess metastatic spread across multiple organs by analyzing whole-body imaging datasets. Recurrent neural networks and transformer-based

models are particularly useful for analyzing longitudinal patient data. ENT cancers often involve dynamic disease progression, and these models can capture temporal changes in tumor behavior, treatment response, and metastatic evolution.

Graph neural networks provide a powerful framework for modeling biological systems as interconnected networks. In ENT cancers, organs, tissues, immune cells, and molecular pathways can be represented as nodes, while interactions between them are represented as edges. This allows for the modeling of multi-organ communication networks and identification of key drivers of disease progression.

Radiomics and Imaging-Based Multi-Organ Assessment

Radiomics plays an important role in AI-driven ENT cancer research by extracting quantitative features from medical imaging. These features capture tumor heterogeneity, shape, texture, vascularity, and spatial relationships with surrounding tissues. In ENT cancers, radiomics can be applied to head and neck imaging as well as chest and abdominal scans to evaluate systemic disease spread. AI-based radiomic models can identify imaging biomarkers associated with metastasis risk and treatment response.

Whole-body imaging analysis using AI enables simultaneous evaluation of multiple organs. This

is particularly important in advanced ENT cancers, where metastasis to lungs, liver, and bone is common. AI systems can integrate imaging data across organ systems to provide a comprehensive view of disease burden. Radiomic features can also be linked to molecular and genetic data, enabling a deeper understanding of tumor biology. This integration allows for the identification of imaging signatures associated with specific genetic mutations or immune profiles.

Multi-Omics Integration in ENT Cancers

Multi-omics integration is essential for understanding systemic interactions in ENT cancers. Genomic, transcriptomic, proteomic, metabolomic, and epigenomic data provide complementary insights into tumor biology and host response. Genomic data reveal mutations that drive tumor initiation and progression. Transcriptomic data provide information on gene expression patterns associated with metastasis and immune evasion. Proteomic data reflect protein activity and signaling pathways, while metabolomic data capture systemic metabolic alterations. Artificial intelligence enables integration of these datasets to construct comprehensive models of disease progression. These models can identify molecular pathways involved in multi-organ interactions and reveal potential therapeutic targets. Single-cell sequencing technologies further enhance

understanding by capturing cellular heterogeneity within tumors and distant tissues. This allows identification of rare cell populations that contribute to metastasis and immune escape.

Immune System and Systemic Communication

The immune system is a central mediator of multi-organ interactions in ENT cancers. Tumors interact with immune cells both locally and systemically, influencing immune surveillance and therapeutic response. AI-based immune profiling can identify patterns of immune activation and suppression across multiple organs. These patterns are particularly important in predicting response to immunotherapy, which has become a cornerstone of ENT cancer treatment.

Immune checkpoint inhibitors have significantly improved survival in some ENT cancer patients, but response rates remain variable. AI models can integrate tumor mutational burden, immune cell composition, and systemic inflammatory markers to predict treatment response. AI can also detect early signs of immune-related adverse events, which may affect multiple organs including the lungs, liver, and endocrine system.

Clinical Applications of AI in ENT Cancer Management

Artificial intelligence has several important clin-

ical applications in ENT cancers. One major application is early detection of metastasis. By integrating imaging, genomic, and clinical data, AI systems can identify patients at high risk of multi-organ spread. Another key application is treatment planning. AI can assist clinicians in selecting optimal therapies based on tumor characteristics and systemic disease involvement. This supports personalized treatment strategies that improve outcomes and reduce toxicity.

AI also plays an important role in monitoring disease progression. Continuous analysis of patient data enables real-time assessment of treatment response and early detection of recurrence or metastasis. In surgical planning, AI can help determine tumor extent, involvement of critical structures, and likelihood of postoperative complications.

Challenges and Limitations

Despite significant progress, several challenges remain in applying AI to ENT cancer research. Data heterogeneity is a major limitation, as clinical, imaging, and molecular data are often collected using different standards and formats. Model interpretability is another challenge. Many AI systems function as black boxes, making it difficult for clinicians to understand how decisions are made. This limits clinical trust and adoption. Data privacy and ethical concerns are also important, particularly when handling sensitive patient in-

formation. Additionally, the lack of large, standardized multi-organ datasets limits model generalizability.

Future Directions

Future research will focus on developing multimodal AI systems that integrate imaging, genomic, clinical, and pathological data. These systems will provide a more comprehensive understanding of ENT cancer biology. Explainable AI techniques will improve transparency and clinical usability. Digital twin models may enable simulation of disease progression in individual patients. Federated learning approaches will allow collaborative model training across institutions while preserving data privacy. Real-time AI monitoring systems may enable continuous assessment of disease progression and treatment response.

Conclusion

Artificial intelligence is transforming the understanding of ENT cancers by enabling detailed analysis of multi-organ interactions. By integrating diverse datasets and identifying complex biological relationships, AI provides new insights into tumor progression, metastasis, and systemic disease behavior. These advances support the development of personalized, precise, and more effective cancer care strategies. As AI technologies continue to evolve, they will play an increasingly central role in bridging oncology, systems biology, and com-

putational medicine to improve outcomes for patients with ENT cancers.

9- AI FOR INVESTIGATION OF PSYCHIATRIC AND MENTAL HEALTH INTERACTIONS IN CANCERS

Background

Artificial intelligence has become an increasingly important presence in healthcare over the past several years, with notable applications in psychiatry and mental health care. Early research into the healthcare applications of AI was largely theoretical and focused mainly on straightforward diagnostic approaches. However, the field experienced a significant shift around 2019. Since then, AI has assumed more complex roles, including the development of personalized treatment protocols and the use of predictive analytics. These advances have been especially significant in oncology and mental health services.

Over the last decade, artificial intelligence has also begun to address gaps in mental health services, which represents a major development given the shortage of trained professionals and the limited access to care in underserved regions. Alongside these practical applications, researchers have identified the potential of AI to detect psychiatric disorders at earlier stages by analysing patterns of behaviour, speech, and brain imaging. This capability may improve early intervention and support better long-term outcomes for patients with mental health conditions.

Some artificial intelligence diagnostic systems now demonstrate accuracies exceeding 94 percent. However, this technical success has not yet translated into widespread clinical adoption. Trust remains a major obstacle, particularly in low-income countries where data privacy regulations may be weaker or inconsistently enforced. Given the highly sensitive nature of mental health information, inadequate data protection measures risk undermining the very populations these technologies are intended to support and assist.

The issue of precision extends beyond the percentages reported in performance metrics. Most artificial intelligence models have been trained primarily on data obtained from white populations in Western countries. This limited and narrow training base has important consequences because algorithms may incorrectly diagnose psychiatric conditions or fail to detect symptoms in patients from underrepresented populations. As a result, concerns regarding bias, fairness, and inclusivity continue to affect the reliability and generalizability of AI systems in mental health care.

Artificial intelligence encompasses a broad range of technologies and methodologies that are applied to improve the investigation of psychiatric and mental health interactions in cancer care. Among these technologies, Natural Language Processing (NLP) represents a particularly important area of AI because it focuses on understanding, interpreting, and generating human language. NLP applications may assist clinicians in analysing patient communication, identifying emotional distress, and improving the monitoring of psychological symptoms during cancer treatment.

The investigation of mental health interactions within cancer populations presents numerous scientific and clinical challenges. Psychiatric symptoms are often highly heterogeneous, multifactorial, dynamic, and context-dependent. Their presentation may vary according to cancer type, stage, disease progression, treatment modality, biological predisposition, medication effects, socioeconomic conditions, family support systems, and broader social determinants of health. Emotional and cognitive disturbances may fluctuate over time and may evolve alongside physical symptoms, therapeutic side effects, and changing prognostic expectations. Traditional assessment approaches depend heavily on self-reported questionnaires, intermittent clinical interviews, or infrequent psychiatric evaluations, which may fail to capture subtle, longitudinal, fluctuating,

or early-stage psychological changes. In many clinical settings, mental health symptoms remain underreported because patients may minimize emotional distress, while healthcare providers often prioritize physical disease management over psychosocial assessment.

In addition, mental health-related information is commonly fragmented across multiple healthcare systems and data environments. Relevant information may be distributed among electronic health records, physician notes, nursing documentation, psychiatric assessments, imaging reports, medication histories, wearable devices, mobile health applications, and patient-generated digital data. Such fragmentation creates major obstacles for comprehensive analysis when relying solely on conventional statistical or observational approaches. Furthermore, psychiatric symptoms frequently interact with biological processes such as inflammation, neuroendocrine dysregulation, immune responses, fatigue, pain perception, and metabolic disturbances, creating highly complex bidirectional relationships between mental health and cancer biology that are difficult to evaluate using traditional analytical frameworks.

Artificial intelligence offers transformative opportunities to address many of these challenges by enabling large-scale, multimodal, and longitudinal investigation of psychiatric and mental health interactions in oncology. Advances in machine

learning, deep learning, and natural language processing allow the integration and interpretation of highly diverse data sources, including structured clinical variables, unstructured medical text, pathology findings, medical imaging, genomic profiles, speech characteristics, facial expressions, psychometric assessments, wearable sensor outputs, sleep data, and digital behavioral signals. AI-driven systems can identify latent patterns, detect subtle behavioral changes, predict mental health risk trajectories, and uncover complex associations between emotional states, cognitive functioning, cancer progression, treatment response, and long-term patient outcomes that may not be apparent through conventional analytic techniques.

In oncology, artificial intelligence has already demonstrated considerable value in cancer diagnosis, prognostic prediction, treatment planning, radiological interpretation, molecular profiling, and therapeutic outcome prediction. Extending these computational capabilities into the mental health domain enables a more holistic, patient-centered, and integrative understanding of cancer care. AI-based approaches may facilitate the early detection of depression, anxiety, cognitive decline, emotional distress, social withdrawal, and suicidal ideation in vulnerable patient populations. These technologies may also support the personalization of psychosocial interventions, optimize supportive care strategies, monitor treatment-related emotional and cognitive changes over time, and enhance clinical decision-making by providing continuous, real-time insights into patient well-being and psychological resilience.

Moreover, AI systems can improve accessibility and equity within psycho-oncology care by identifying high-risk or underserved individuals who might otherwise remain unnoticed within busy clinical environments. Predictive algorithms may help clinicians prioritize psychosocial referrals, allocate mental health resources more effectively, and provide earlier supportive interventions for patients at increased risk of psychological deterioration. AI-assisted digital platforms, including conversational agents, remote monitoring systems, and mobile mental health applications, may further extend psychological support to patients in geographically isolated or resource-limited settings.

Artificial intelligence is also intrinsically capable of analysing highly complex and nonlinear interactions among biological, emotional, behavioral, and environmental factors. For example, machine learning models can investigate relationships between inflammatory biomarkers, neuroendocrine signaling pathways, stress responses, sleep disturbances, emotional dysregulation, and cancer progression. AI systems may additionally evaluate vocal characteristics, facial microexpressions,

movement patterns, typing behavior, and wearable physiological data to identify early indicators of emotional distress or cognitive impairment. Such multidimensional analysis may improve understanding of how psychological states influence treatment adherence, immune responses, symptom burden, and overall survivorship experiences.

Despite these promising developments, the application of AI in psychiatric oncology also raises several important scientific, ethical, and clinical challenges. Data quality, missing information, institutional variability, and inconsistent annotation standards may reduce the reliability and generalizability of predictive models. Algorithmic bias represents another major concern because AI systems trained on nonrepresentative datasets may inadvertently perpetuate healthcare disparities across demographic, cultural, or socioeconomic groups. Mental health data are especially sensitive and deeply personal, meaning that issues related to privacy, confidentiality, informed consent, and secure data governance are critically important.

In addition, many advanced AI systems, particularly deep learning models, function as "black boxes," making it difficult for clinicians and patients to understand how algorithmic decisions are generated. Ensuring transparency, fairness, interpretability, explainability, and trustworthiness is therefore essential for the safe and respon-

sible integration of AI technologies into real-world oncology practice. Explainable AI approaches are increasingly important because clinicians must be able to interpret model outputs, evaluate potential risks, and communicate AI-generated insights clearly to patients and multidisciplinary care teams. Regulatory oversight, interdisciplinary collaboration, and rigorous clinical validation will remain essential for ensuring that AI applications in psychiatric oncology are implemented ethically and effectively.

Traditional approaches to studying psychiatric–cancer interactions have relied heavily on small cohorts, cross-sectional designs, and self-report instruments. These methods, while valuable, often lack the power and temporal resolution to capture dynamic, bidirectional relationships between tumor biology, treatment toxicities, neuroinflammation, and mental health trajectories. They are also limited in their ability to integrate heterogeneous data streams such as electronic health records, neuroimaging, genomics, wearable sensors, patient-reported outcomes, and social determinants of health. As precision oncology advances, there is an urgent need for equally precise "psycho-oncologic" tools that can disentangle causal mechanisms, identify high-risk individuals early, and personalize supportive interventions.

AI methods, including machine learning, deep

learning, natural language processing, and multimodal data fusion, offer a powerful framework for investigating these interactions at scale. Predictive models can be trained on large longitudinal datasets to identify patterns linking psychiatric diagnoses, subclinical symptoms, and trajectories of distress with cancer incidence, progression, and treatment response. Natural language processing can extract rich information about mood, coping, and social context from unstructured clinical notes or patient narratives that would otherwise remain inaccessible. Deep learning applied to brain imaging and digital phenotyping, such as activity patterns, speech, sleep, and heart rate variability, can reveal subtle neurobehavioral signatures associated with cancer-related cognitive impairment, "chemo brain," or depression.

Beyond prediction, AI can support mechanistic insights by integrating biological and psychosocial domains. Multimodal algorithms can link inflammatory markers, hormonal changes, and neuroimaging features with symptom clusters such as fatigue, anhedonia, or anxiety, generating hypotheses about shared pathways that could be targeted therapeutically. Causal inference and reinforcement learning approaches hold promise for optimizing the timing and type of mental health interventions, such as psychotherapy, pharmacologic treatments, or digital therapeutics, in relation to cancer treatments and side-effect profiles.

In survivorship and palliative care, AI-enabled risk stratification can help allocate scarce psycho-oncology resources to those most likely to benefit, improving both equity and efficiency.

At the same time, the use of AI in this sensitive domain raises important ethical, legal, and social challenges. Psychiatric and oncologic data are highly personal, and the integration of behavioral, biological, and digital traces risks amplifying stigma, bias, and privacy concerns if not carefully governed. Algorithmic bias may worsen disparities if models are trained on non-representative populations or fail to account for cultural and socioeconomic factors that shape mental health in cancer. Transparent model development, rigorous validation, explainability, and participatory design involving both patients and clinicians are therefore essential.

This chapter explores the evolving role of artificial intelligence in investigating psychiatric and mental health interactions in cancer populations. It examines major data sources, computational methodologies, clinical applications, predictive modeling strategies, and ethical considerations while highlighting current achievements, ongoing limitations, and future directions for research and clinical implementation. By integrating advances in artificial intelligence with contemporary insights from oncology, psychiatry, psychology, neuroscience, and behavioral sciences, this

chapter aims to contribute to the development of more comprehensive, compassionate, equitable, and intelligent cancer care systems that address both the physical and psychological dimensions of disease.

AI in Cancer Detection and Treatment Planning

Artificial intelligence is increasingly making cancer detection and treatment planning more accurate and efficient. It contributes to the detection of breast cancer, the identification of genetic mutations, and the development of individualized treatment strategies. AI systems can analyse MRI and CT scans to identify subtle patterns that may be overlooked by clinicians, thereby improving diagnostic accuracy. In radiation therapy, AI can also enhance the detection of tumour margins, allowing for more precise targeting and potentially reducing damage to surrounding healthy tissue.

In addition, artificial intelligence is supporting telemedicine initiatives in underserved areas and improving access to healthcare services. Within mental health care, self-help applications, online therapeutic modules, and AI-powered chatbots provide emotional support, coping strategies, and guidance for individuals experiencing psychological distress. Although these tools can complement the work of human therapists and health-

care professionals, they are not intended to replace direct clinical care or professional therapeutic relationships.

Future developments in this field may enable clinicians to integrate advanced AI models that process text, audio, and imaging data alongside both mental and physical health indicators. However, effective implementation requires strong regulatory oversight, extensive clinical validation, adequate financial support, and proper training to ensure the safe interpretation and application of AI-generated outputs. Artificial intelligence has the potential to improve access to healthcare for disadvantaged populations, but important ethical concerns, particularly those related to privacy, confidentiality, and patient autonomy, must be carefully addressed.

Case Studies

Explainable artificial intelligence plays an important role in helping clinicians understand AI-generated recommendations and communicate them effectively to patients, thereby increasing trust and transparency in clinical decision-making. Despite these advantages, adoption may still be hindered by outdated legacy systems, limited institutional resources, and insufficient technical infrastructure. Nevertheless, greater clarity and transparency in AI systems can improve accept-

ance among both healthcare professionals and patients.

Evolution in Mental Health Care

Artificial intelligence in mental health care has evolved considerably, progressing from basic diagnostic support systems to advanced technologies capable of predicting clinical outcomes and personalizing treatment approaches. AI systems can identify early signs of mental illness by analysing speech patterns, behaviour, and neuroimaging findings. Some systems have achieved accuracy rates exceeding 94 percent, demonstrating substantial technological progress. However, trust, fairness, and ethical responsibility remain major challenges, particularly with regard to data bias, representation, and the protection of patient privacy.

AI Insights into Stress, Emotion, and Immune Dynamics in Oncology

Cancer remains one of the leading causes of morbidity and mortality worldwide. Conventional therapies such as chemotherapy and radiotherapy continue to serve as fundamental pillars of cancer treatment; however, they are frequently associated with substantial adverse effects and highly variable treatment responses among patients. Chemotherapy involves the administration of cytotoxic agents designed to target and destroy rapidly proliferating cells, which represent a defining characteristic of malignant tumors. Unfortunately, this mechanism is not entirely selective, meaning that chemotherapy also damages healthy rapidly dividing cells, resulting in a wide range of toxicities including gastrointestinal complications, fatigue, alopecia, mucosal injury, and suppression of immune function. In addition, the effectiveness of chemotherapy is often reduced by the development of chemoresistance, which remains a major obstacle in long-term cancer management.

Radiotherapy, another major component of conventional oncologic treatment, utilizes high-energy radiation to induce DNA damage and genomic instability in cancer cells, thereby inhibiting tumor growth, proliferation, and metastatic spread. Although radiotherapy generally provides greater spatial precision than chemotherapy, it still carries the risk of damaging surrounding healthy tissues and causing both acute and chronic complications. The biological complexity of cancer further complicates treatment because cancer is not solely a localized cellular disorder but rather a multifactorial disease involving intricate interactions among biological, psychological, behavioral, and environmental determinants. Psychological states such as chronic stress, anxiety, depression, emotional distress, and social isolation can increase vulnerability to disease

progression and may accelerate tumor evolution through neuroendocrine, immune, inflammatory, and behavioral pathways. These psychological conditions can also negatively influence adherence to therapeutic protocols, lifestyle behaviors, sleep quality, and overall treatment outcomes.

Immunotherapy has emerged as a promising alternative and complementary strategy in modern oncology because it harnesses the patient's own immune system to selectively recognize and attack cancer cells. Despite its revolutionary potential, the effectiveness of immunotherapy remains highly variable because of tumor heterogeneity, differences in immune responsiveness, and the complexity of immune regulation within the tumor microenvironment. Artificial intelligence has significantly advanced the discovery, validation, and interpretation of predictive biomarkers associated with immunotherapy efficacy through the integrative analysis of transcriptomic, genomic, proteomic, metabolomic, and clinical datasets. AI systems facilitate the optimization of combination therapies by predicting therapeutic responses and identifying the most effective individualized treatment strategies for specific patient populations. Furthermore, AI contributes to the identification of novel therapeutic targets, including neoantigens and immune-related molecular pathways, thereby supporting the development of highly personalized immunotherapeutic

approaches.

Early diagnosis of cancer substantially improves survival rates and clinical outcomes; however, conventional diagnostic pathways frequently fail to identify malignancies before symptoms become clinically evident. In this context, artificial intelligence offers the possibility of detecting subtle biological and physiological alterations before overt clinical manifestation, thereby shifting cancer care from a reactive model toward a proactive and preventive framework. AI technologies can process extensive and heterogeneous datasets, including imaging, laboratory values, wearable sensor outputs, behavioral patterns, and molecular profiles, to identify early indicators of disease that may not be apparent through traditional analytical methods.

Artificial intelligence has also provided valuable insights into CAR-T cell therapy, or Chimeric Antigen Receptor T-cell therapy, particularly in improving the design, engineering, and optimization of CAR constructs. AI-driven computational models can simulate immune interactions, predict antigen specificity, and evaluate potential toxicities, thereby improving therapeutic precision and safety. Moreover, research has demonstrated that AI can effectively analyse somatic tumor mutation burden and microsatellite instability, both of which strongly correlate with enhanced responses to immune checkpoint inhibitors. By integrating

these biomarkers with clinical and molecular information, AI contributes to more accurate patient stratification and treatment selection.

One of the most powerful capabilities of artificial intelligence lies in its ability to identify complex, nonlinear, and multidimensional patterns across highly heterogeneous data sources. These sources include vocal characteristics, facial expressions, gait patterns, psychometric indicators, behavioral data, physiological measurements, and high-resolution digital biomarkers. Such multimodal analyses enable AI systems to investigate emotional, cognitive, and physiological states with remarkable precision. Among these biomarkers, heart rate variability (HRV) has emerged as an especially important physiological indicator of stress and autonomic nervous system function. Reduced HRV is commonly associated with elevated stress levels, emotional dysregulation, inflammation, and impaired physiological resilience.

The primary objective of AI-driven research involving HRV and related biomarkers is to improve individualized risk stratification, facilitate early detection of psychological and physiological dysregulation, and support personalized wellness and supportive care strategies for cancer patients. Through longitudinal monitoring and predictive analytics, AI systems may help clinicians identify patients at increased risk of emotional distress, immune dysfunction, or treatment complications

before these issues become clinically severe. Such approaches may ultimately contribute to more comprehensive and holistic models of cancer care that address both physical and psychological dimensions of disease.

A major challenge in immunotherapy involves the remarkable heterogeneity of patient responses. Some individuals experience dramatic and durable remissions, whereas others derive minimal benefit or develop severe immune-related adverse events. AI models designed to predict immunotherapy outcomes routinely integrate data from numerous sources, including molecular signatures, histopathological findings, radiological imaging, electronic health records, microbiome analyses, and laboratory biomarkers. By analysing these highly aggregated datasets, AI can identify subtle multivariate correlations and hidden biological patterns that are often undetectable through conventional statistical approaches. This capability supports more accurate prediction of treatment efficacy, toxicity risk, and long-term prognosis.

In addition to improving treatment prediction, AI contributes to the broader understanding of the relationship between stress, emotion, immunity, and cancer biology. Chronic psychological stress activates neuroendocrine pathways involving cortisol, catecholamines, and inflammatory mediators that may suppress antitumor immune activity and promote tumor progression. AI-assisted

analyses can investigate how emotional states influence immune dynamics, inflammatory signaling, and treatment responsiveness over time. By integrating psychometric data, wearable device outputs, physiological markers, and clinical outcomes, AI enables researchers to explore the bidirectional relationships between emotional well-being and oncologic disease processes.

The growing application of AI in oncology also raises important ethical considerations. The concept of ethical AI in health prediction emphasizes the protection of patient privacy, the secure handling of sensitive health information, and the reduction of bias and discrimination in algorithmic decision-making. AI systems trained on unbalanced datasets may unintentionally produce inequitable outcomes across different populations, making fairness and inclusivity critical priorities in model development. Ethical AI frameworks therefore prioritize transparency, rigorous validation, reproducibility, and continuous monitoring to minimize false-positive predictions, prevent patient harm, and maintain clinical trust.

Furthermore, explainable AI approaches are becoming increasingly important in oncology because clinicians and patients must understand the reasoning behind algorithmic recommendations before integrating them into clinical decision-making. Reliable and interpretable AI systems can improve confidence in predictive models and

facilitate their safe adoption within healthcare environments. Regulatory oversight, interdisciplinary collaboration, and robust clinical validation remain essential for ensuring that AI technologies are implemented responsibly and effectively.

As artificial intelligence continues to evolve, its role in oncology is expected to expand far beyond diagnostic support and treatment prediction. Future AI-driven systems may integrate emotional, behavioral, molecular, immunological, and physiological data into unified computational frameworks capable of continuously monitoring patient health and dynamically adapting therapeutic strategies. Such innovations may support precision oncology approaches that consider not only tumor biology but also the emotional and systemic state of the patient as a whole.

Ultimately, AI is transforming oncology by providing deeper insight into the intricate relationships among stress, emotion, immunity, and cancer progression. Through the integration of diverse and complex datasets, AI enables more precise diagnostics, personalized therapies, improved supportive care, and enhanced understanding of the systemic nature of cancer. Continued collaboration among oncologists, immunologists, psychologists, neuroscientists, and data scientists will be essential to fully realize the potential of AI in advancing comprehensive and patient-centered cancer care.

10- AI FOR INVESTIGATION OF MULTI-ORGAN INTERACTIONS IN OTHER CANCERS

AI for Investigation of Multi-Organ Interactions in Breast Cancer

Breast cancer is a malignant proliferation of epithelial cells that originates primarily from the ducts or lobules of the breast and is capable of local invasion and distant metastasis if not detected at an early stage. Because breast tissue varies in density and structural composition, accurate diagnosis depends heavily on imaging modalities such as mammography, ultrasound, and MRI, as well as histopathological confirmation.

This disease is of major global importance because it remains the most commonly diagnosed cancer among women and one of the leading causes of cancer-related mortality worldwide. Early detection significantly improves survival outcomes. However, screening programs and diagnostic workflows continue to face persistent challenges, including variability in radiologist interpretation, reduced sensitivity in dense breast tissue, and limited access to high-quality imaging in low-resource regions. These limitations contribute to delayed diagnosis and emphasize the need for more

accurate, reliable, and accessible diagnostic innovations.

Globally, the burden of breast cancer is substantial. In 2022, approximately 2.3 million new cases of female breast cancer and nearly 666,000 to 670,000 related deaths were recorded, accounting for almost one quarter of all newly diagnosed cancers among women. Incidence rates are highest in countries with a high Human Development Index, whereas mortality remains disproportionately higher in low-resource settings, reflecting disparities in screening availability, early diagnosis, and access to treatment. Forecasts further indicate that, without improved prevention and detection strategies, both the global incidence and mortality of breast cancer will continue to increase through 2050.

In recent years, artificial intelligence (AI), particularly deep learning (DL), has emerged as one of the most promising technological advances in the detection and diagnosis of breast cancer. AI-based models have been developed to analyse mammograms, ultrasound images, MRI scans, and histopathological slides, enabling the identification of suspicious lesions, risk stratification, breast density estimation, and even the prediction of molecular subtype or treatment response. Multiple studies have demonstrated that AI systems can achieve diagnostic performance comparable to, and in some cases exceeding, that of individ-

ual radiologists. These systems may also reduce inter-reader variability and improve workflow efficiency in clinical practice.

Despite these advancements, significant research gaps remain. Many existing studies are retrospective in design, enriched with a higher prevalence of cancer cases than those encountered in real-world screening environments, and based on single-center or homogeneous datasets, raising concerns regarding bias and generalizability. In addition, data heterogeneity across imaging scanners, patient demographics, and imaging protocols presents challenges to the robustness and reliability of AI algorithms. External validation also remains insufficient in many published studies.

These limitations highlight the urgent need for comprehensive multicenter studies that include diverse populations, harmonized datasets, interpretable AI models, rigorous external validation, and, ideally, prospective clinical trials. A structured research framework that incorporates dataset diversification, explainable model development, external testing, and real-world implementation would directly address many of these existing gaps.

If successful, such research could provide substantial clinical and public health benefits. Improved diagnostic accuracy may support earlier detection, reduce false-negative findings, particularly among women with dense breast tissue, and provide non-

invasive biomarkers to guide treatment planning. The resulting evidence could directly influence healthcare policy by supporting the safe integration of AI as a second reader in breast cancer screening programs, informing reimbursement and regulatory decisions, and ultimately reducing global disparities in breast cancer outcomes.

Artificial Intelligence for Investigation of Multi-Organ Interactions in Cardio-Oncology

Background

The term “cardiovascular cancers” is not commonly used in medical literature because the cardiovascular system is not typically classified as a primary origin site for most malignancies. A more accurate and widely accepted term is cardio-oncology, which describes the complex interactions between cancer and the cardiovascular system. Cardio-oncology focuses on the bidirectional relationship between tumors, anticancer therapies, and cardiovascular health, including the effects of cancer on the heart and blood vessels, as well as the cardiovascular complications associated with cancer treatment.

Cancer is increasingly recognized as a systemic disease that affects multiple organs simultaneously rather than remaining confined to a single anatomical location. Similarly, cardiovascular disease involves widespread systemic mechanisms,

including inflammation, immune dysregulation, metabolic alterations, endothelial dysfunction, and neurohormonal activation. The overlap between oncology and cardiovascular medicine has therefore become an important field of investigation. Tumors can directly or indirectly alter cardiovascular physiology, while cardiovascular dysfunction may influence tumor progression, metastasis, and patient survival. These interactions are especially evident in patients receiving chemotherapy, immunotherapy, targeted therapy, and radiation therapy, all of which may produce cardiotoxic effects involving the myocardium, vasculature, kidneys, lungs, liver, and immune system.

Artificial intelligence (AI) has emerged as a transformative technology capable of investigating these highly complex multi-organ interactions. By integrating clinical information, imaging data, molecular profiles, wearable device signals, and electronic health records, AI can identify patterns that are often undetectable through conventional analytical methods. Machine learning and deep learning approaches now provide opportunities to model the systemic biological networks connecting cancer progression with cardiovascular injury, immune activation, metabolic dysfunction, and organ-specific complications.

Multi-Organ Interactions

in Cardio-Oncology

Cancer and cardiovascular disease share several biological pathways and risk factors. Chronic inflammation, oxidative stress, obesity, diabetes mellitus, smoking, aging, and metabolic syndrome contribute to the development of both conditions. Tumors can influence cardiovascular function through systemic inflammatory mediators, cytokine release, coagulation abnormalities, and metabolic reprogramming. Conversely, cardiovascular dysfunction may impair tissue oxygenation, alter immune responses, and influence tumor biology.

The heart is particularly vulnerable to the systemic effects of malignancy and cancer therapy. Chemotherapeutic agents such as anthracyclines may induce myocardial injury, leading to cardiomyopathy and heart failure. Targeted therapies, including tyrosine kinase inhibitors and HER2-targeted agents, may cause hypertension, arrhythmias, and ventricular dysfunction. Immune checkpoint inhibitors can trigger myocarditis through immune-mediated inflammatory pathways. Radiation therapy involving the thoracic region may damage coronary arteries, heart valves, and pericardial tissues.

These interactions extend far beyond the heart itself. Cancer-associated systemic inflammation can affect the vascular system, kidneys, lungs, liver, skeletal muscle, and central nervous system.

The kidney-heart-cancer axis has gained considerable attention because nephrotoxic therapies may worsen cardiovascular outcomes, while renal dysfunction alters drug metabolism and systemic hemodynamics. Similarly, pulmonary toxicity associated with cancer treatment may lead to pulmonary hypertension and secondary cardiac dysfunction.

The immune system functions as a central mediator of these multi-organ interactions. Tumors manipulate immune signaling pathways to promote immune evasion and metastasis, while anticancer therapies may unintentionally activate systemic inflammatory responses. Cytokines, circulating immune cells, extracellular vesicles, and tumor-derived exosomes participate in communication between tumors and distant organs. These processes create highly interconnected biological networks that cannot be fully understood through isolated organ-based approaches.

Role of Artificial Intelligence in Multi-Organ Investigation

Artificial intelligence offers the ability to analyse highly complex and multidimensional datasets generated in cardio-oncology. Unlike traditional statistical methods, AI algorithms can identify subtle nonlinear relationships among clinical, imaging, molecular, and physiological variables. Machine learning approaches are especially valuable

for recognizing hidden interactions across organ systems and predicting patient-specific risks.

Machine learning algorithms such as random forests, support vector machines, gradient boosting, and logistic regression models are frequently used to predict cardiotoxicity, treatment complications, and survival outcomes. These methods can integrate demographic characteristics, laboratory biomarkers, genomic information, medication history, and imaging features to estimate cardiovascular risk in cancer patients. AI-based predictive models have demonstrated the ability to identify patients at elevated risk for heart failure before clinical symptoms become apparent.

Deep learning techniques have significantly advanced cardiovascular and oncological imaging analysis. Convolutional neural networks can process echocardiography, cardiac MRI, CT imaging, PET scans, and histopathological slides with remarkable precision. These models can detect early myocardial dysfunction, subtle vascular abnormalities, and inflammatory changes associated with cancer therapies. AI systems may identify imaging features that are invisible to the human eye, enabling earlier intervention and more personalized treatment planning.

Recurrent neural networks and transformer-based models are particularly useful for analysing longitudinal patient data. By processing sequential information from repeated imaging studies,

laboratory tests, wearable devices, and electronic health records, these systems can monitor disease progression over time. Such approaches support dynamic risk prediction and real-time clinical decision-making in patients undergoing cancer therapy.

Natural language processing also plays a critical role in cardio-oncology research. Clinical notes, discharge summaries, pathology reports, and radiology interpretations contain large amounts of unstructured information that are difficult to analyse manually. Natural language processing algorithms can extract clinically meaningful insights from these records and integrate them with structured datasets for comprehensive analysis.

AI Applications in Cardiovascular Imaging and Oncology

Imaging represents one of the most important areas of AI application in cardio-oncology. Echocardiography is widely used for monitoring cardiac function in cancer patients receiving potentially cardiotoxic therapies. AI-assisted echocardiographic analysis can automatically assess ventricular function, myocardial strain, chamber dimensions, and valvular abnormalities. These automated systems improve reproducibility and reduce interobserver variability.

Cardiac MRI provides highly detailed information regarding myocardial tissue characteristics,

fibrosis, inflammation, and ventricular remodeling. Deep learning algorithms can analyse these images rapidly and accurately, facilitating early detection of treatment-related myocardial injury. AI models may also predict future cardiovascular complications by combining imaging findings with clinical and molecular biomarkers.

Positron emission tomography and CT imaging contribute to the evaluation of systemic inflammation, tumor burden, and vascular disease. Radiomics approaches extract quantitative imaging features that reflect tissue heterogeneity, metabolic activity, and structural alterations. Machine learning models can integrate radiomic signatures with genomic and proteomic information to improve prediction of cardiotoxicity, metastatic progression, and treatment response.

AI has also demonstrated significant value in electrocardiographic analysis. Deep learning systems trained on large ECG datasets can identify subtle electrical abnormalities associated with myocarditis, arrhythmias, and chemotherapy-induced cardiomyopathy. Some AI-based ECG models have shown the ability to detect left ventricular dysfunction even before abnormalities become apparent on standard imaging studies.

Multi-Omics Integration and Systems Biology

One of the most promising applications of AI in

cardio-oncology involves the integration of multi-omics datasets. Modern biomedical research generates enormous quantities of genomic, transcriptomic, proteomic, metabolomic, and epigenomic data. These datasets provide insights into molecular pathways underlying cancer progression and cardiovascular injury. However, their complexity requires advanced computational methods for meaningful interpretation.

AI frameworks can integrate these diverse molecular datasets with imaging and clinical information to identify biological pathways linking cancer and cardiovascular disease. For example, machine learning algorithms may detect gene expression signatures associated with chemotherapy-induced cardiotoxicity or identify inflammatory biomarkers predictive of vascular complications.

Single-cell sequencing technologies have further expanded the understanding of organ-specific and systemic responses to cancer therapy. AI methods can analyse single-cell transcriptomic data to characterize immune cell populations, fibroblast activation, endothelial dysfunction, and myocardial remodeling. These approaches provide insight into how individual cell populations contribute to multi-organ toxicity and disease progression.

Graph neural networks and systems biology models are increasingly used to represent interactions among organs, signaling pathways, and cellular populations. In these models, organs

and biological entities are represented as interconnected nodes linked through molecular and physiological interactions. Such frameworks allow researchers to study systemic communication pathways involving the heart, tumors, immune system, kidneys, lungs, and liver simultaneously.

Wearable Devices and Real-Time Monitoring

The integration of wearable technologies with artificial intelligence has introduced new possibilities for continuous monitoring in cardio-oncology. Smartwatches, biosensors, and remote monitoring systems can collect physiological data including heart rate, rhythm, blood pressure, oxygen saturation, sleep patterns, and physical activity levels. AI algorithms can process these data streams in real time to identify early warning signs of cardiovascular complications.

Continuous monitoring is particularly important for patients receiving therapies associated with arrhythmias, myocarditis, or heart failure. AI-driven remote monitoring systems may allow earlier intervention and reduce hospitalizations. In addition, wearable technologies can improve patient engagement and support personalized management strategies.

Challenges and Limitations

Despite substantial progress, several important

challenges remain. One of the major limitations involves data heterogeneity. Clinical datasets often differ in quality, imaging protocols, sequencing methods, and institutional practices. Standardization of data acquisition and preprocessing is essential for developing reliable and generalizable AI models.

Another major concern is the interpretability of AI systems. Many deep learning models operate as "black boxes," making it difficult for clinicians to understand how predictions are generated. Limited transparency may reduce trust and hinder clinical implementation. Explainable AI methods are therefore increasingly important for improving interpretability and supporting regulatory approval.

Privacy and ethical considerations also represent major challenges. Cardio-oncology research often requires integration of sensitive clinical, imaging, and genomic information. Federated learning approaches may help address these concerns by enabling collaborative model training without direct sharing of patient data.

In addition, prospective clinical validation remains necessary before many AI systems can be adopted widely in routine practice. Although retrospective studies frequently demonstrate promising performance, real-world implementation requires rigorous testing in diverse patient populations.

Future Directions

Future research in cardio-oncology will likely focus on the development of multimodal AI systems capable of integrating imaging, molecular, physiological, and clinical data into unified predictive frameworks. These systems may eventually support the creation of digital twins, which are virtual representations of individual patients that simulate disease progression and therapeutic response across multiple organ systems.

Real-time AI platforms capable of continuously monitoring physiological and molecular changes during treatment may transform cancer care from a reactive process into a proactive and preventive approach. AI-guided therapeutic optimization could personalize treatment intensity while minimizing cardiovascular toxicity and preserving organ function.

Another promising direction involves causal AI and mechanistic modeling. Rather than merely identifying correlations, future AI systems may help uncover biological mechanisms underlying tumor-cardiovascular interactions. Such advances could facilitate the discovery of novel therapeutic targets and improve understanding of systemic disease processes.

Conclusion

Artificial intelligence has emerged as a trans-

formative tool for investigating multi-organ interactions in cardio-oncology. By integrating imaging, molecular, physiological, and clinical data, AI technologies provide a more comprehensive understanding of the systemic relationships between cancer and cardiovascular disease. These approaches improve risk prediction, enable earlier detection of cardiotoxicity, support personalized treatment strategies, and facilitate real-time monitoring of disease progression.

As computational methodologies continue to evolve and biomedical datasets expand, AI is expected to play an increasingly central role in cardio-oncology research and clinical care. Realizing this potential will require interdisciplinary collaboration, robust data infrastructure, ethical oversight, and prospective clinical validation. Ultimately, AI-driven approaches may transform cardio-oncology into a more predictive, personalized, and system-oriented field capable of improving survival and quality of life for cancer patients worldwide.

REFERENCES

1. AbdelHamid SG, Halawa EM, Ibrahim EM, ElHefnawi M. Artificial intelligence-powered liquid biopsy in cancer: a paradigm shift in cancer detection and personalized care. Cancer Cell Int. 2026;26.(1)

2. Abuhassan Q, Oriquat G, Ganesan S, Kanwar JB, Kumar VR, Sharma V, et al. LI-RADS-aligned artificial intelligence for liver cancer diagnosis: methods, evidence, and clinical readiness. Abdom Radiol (NY). 2025.

3. Al-Hakami HA, Abdullah IA, Almutairi NS, Aldawsari RR, Alluqmani GA, Fallatah HA, et al. The Role of Artificial Intelligence in Prognosis, Recurrence Prediction, and Treatment Outcomes in Laryngeal Cancer: A Systematic Review. Cancers (Basel). 2026;18.(8)

4. Al-Shahrabi R, Alkhnbashi OS, Almarri RSB, Ahmad S, Soares NC, Al Shareef Z. Artificial Intelligence and Multiomics Beyond PSA Screening in African and Middle Eastern Prostate Cancer Patients. J Proteome Res. 2026;25(5):2221-33.

5. Alfaro S, Liu J, Naranjo Ortiz C, Alfaro A, Lustberg M. Applications of machine learning and natural language processing to neurocognitive outcomes in posttreatment cancer survivors: a scoping review. Support Care Cancer. 2026;34(1):71.

6. Alharbi W, Alfayez AA. Explainable artificial intelligence in pancreatic cancer prediction: from transparency to clinical decision-making. Front Oncol. 2025;15:1720039.

7. Ali TM, Mir A, Rehman AU, Humayun M, Shaheen M, Alshammari RTS. Revolutionizing Lung Cancer Detection: A High-Accuracy Machine Learning Framework for Early Diagnosis. Biomed Res Int. 2025;2025:9961773.

8. Alshammari A, Boabbas A, Nassar B, Shaikhah A. The Role of Artificial Intelligence in General Surgery: A Systematic Review and Meta-Analysis of Machine Learning Applications in Colorectal Cancer Treatment Outcomes. Cureus. 2025;17(11):e96919.

9. Alshorman J, Mehran MJ, Bahrami Y, Mohammadzadeh S, Barzigar R, Morshedi M, et al. Artificial intelligence in immunotherapy: revolutionizing diagnostic and therapeutic applications in cancer and autoimmune diseases. Clin Exp Med. 2026;26.(1)

10. Andrade MA, Rodrigues H, Colhado CH, Godinho NJS, Dos Santos RD, de Andrade AL, et al. Artificial-intelligence models vs. radiologists in the detection of clinically significant prostate cancer on mpMRI: a meta-analysis. Eur Radiol. 2026.

11. Añez D, Conti G, Uriarte JJ, Serrano-Olmedo JJ, Martínez-Murillo R, Casanova-Carvajal O. Artifi-

cial Intelligence Pipeline for Mammography-Based Breast Cancer Detection: An Integrated Systematic Review and Large-Scale Experimental Validation. Medicina (Kaunas). 2025;61.(12)

12. Araújo ALD, Kowalski LP, Santos-Silva AR, Louredo BVR, Saldivia-Siracusa C, de Melo O, et al. Radiomic-Based Machine Learning Classifiers for HPV Status Prediction in Oropharyngeal Cancer: A Systematic Review and Meta-Analysis. Diagnostics (Basel). 2025;16.(1)

13. Arita Y, Roest C, Kwee TC, Paudyal R, Lema-Dopico A, Fransen S, et al. Advancements in artificial intelligence for prostate cancer: Optimizing diagnosis, treatment, and prognostic assessment. Asian J Urol. 2025;12(4):434-44.

14. Arshad MF, Chowdhury AT, Sharif Z, Islam MSB, Sumon MSI, Mohammedkasim A, et al. Artificial Intelligence and Machine Learning in Lung Cancer: Advances in Imaging, Detection, and Prognosis. Cancers (Basel). 2025;17.(24)

15. Arteaga-Arteaga HB, Oyola-Martinez KA, de la Cruz R, Bravo-Ortíz MA, Guillen-Rondon P, Tabares-Soto R. Deep learning approaches for predicting Ki-67 index in breast cancer histopathology images: A systematic review. Comput Biol Med. 2026;210:111678.

16. Balestrucci G, Patanè V, Giordano N, Russo A, Urraro F, Nardone V, et al. Evolving Paradigms in Gastric Cancer Staging: From Conventional Imaging to Advanced MRI and Artificial Intelligence. Diagnostics (Basel). 2026;16.(2)

17. Bani MA. Smart Lies and Sharp Eyes: Pragmatic Artificial Intelligence for Cancer Pathology: Promise, Pitfalls, and Access Pathways. Cancers (Basel). 2026;18.(3)

18. Basety S, Gudepu R, Velidandi A. Artificial Intelligence in Lung Cancer: A Narrative Review of Recent Advances in Diagnosis, Biomarker Discovery, and Drug Development. Pharmaceutics. 2026;18.(2)

19. Bazarkin A, Taratkin M, Vovdenko S, Androsov A, Balashova M, Morozov A, et al. Artificial intelligence in diagnostic, prognostic, and predictive genomic biomarkers for prostate cancer: Ready for prime time? Urol Oncol. 2026;44(3):110965.

20. Benabbou N, Abik M, Baichoo S. Integrative multi-omics and machine learning/deep learning approaches in cancer knowledge discovery: A scoping review. Cancer Treat Res Commun. 2026;47:101136.

21. Bitere OA, Minciuna CE, Andras C, Almarii F, Andrei-Bitere I, Manuc T, et al. Artificial Intelligence in Colon Cancer: Advances, Challenges, and Future Perspectives. Chirurgia (Bucur). 2026;121(1):13-26.

22. Bland KA, Catalá-Vilaplana I, Nunez JJ, Capozzi LC, Campbell KL. Artificial Intelligence Meets Cancer Rehabilitation: Emerging Evidence

for Exercise and Physical Activity Interventions. Cancer Control. 2026;33:10732748261432280.

23. Bräutigam K, Baker AM, Koelzer VH, Kather JN, Graham TA. Integrating artificial intelligence (AI) into colorectal cancer reporting. J Pathol. 2026;268(4):367-82.

24. Cao P, Jia X, Yang Y, Wang X, Zhu J, Li X, et al. Artificial Intelligence for Predicting Immunotherapy Efficacy in Non-Small Cell Lung Cancer. J Inflamm Res. 2026;19:581764.

25. Cavalieri S, De Cecco L, Monzani D, Mehanna H, Ferrarotto R, Simon C, et al. Integrating transcriptomic data and artificial intelligence to personalize curative treatments for head and neck cancer patients. NPJ Precis Oncol. 2026;10.(1)

26. Chan GJ, Ding CC. Advances in artificial intelligence in prostate cancer pathology. Semin Diagn Pathol. 2026;43(2):150995.

27. Chang L, Li H, Wu W, Liu X, Yan J, Chen Z, et al. Applications of artificial intelligence in non-small cell lung cancer: from precision diagnosis to personalized prognosis and therapy. J Transl Med. 2025;24(1):108.

28. Chen J, Sun T, Zhang J, Huang J, Chen T, Weng Y, et al. Artificial intelligence-driven personalized dietary recommendations for gastric cancer high-risk populations: a narrative review. Front Nutr. 2026;13:1802970.

29. Chen R, Liang Y, Shi J. [Advances in Application of Artificial Intelligence for Breast Cancer Radiotherapy]. Zhongguo Yi Liao Qi Xie Za Zhi. 2026;50(1):7-14.

30. Chen S, Liu L, Tian G, Chai R. MRI-based qualitative, quantitative, and radiomics/deep learning methods for assessing treatment response after neoadjuvant chemoradiotherapy in patients with locally advanced rectal cancer. Precis Radiat Oncol. 2026;10(1):102-15.

31. Chen X, Yi Z, Ye J. Artificial intelligence models in predicting lymph node metastasis in early gastric cancer: a systematic review and meta-analysis. Wideochir Inne Tech Maloinwazyjne. 2026;21(1):1-12.

32. Cheng Y, Kong J, Liu X, Li S. Recent Advances and Emerging Directions in Machine Learning-Based Breast Cancer Drug Discovery: A Comprehensive Review. Breast Cancer (Dove Med Press). 2026;18:586786.

33. Cheng YH, Dong J, Wang Z, Zhao H, Chen M, Ma T. The value of artificial intelligence in ultrasound imaging for predicting molecular subtypes of breast cancer: a meta-analysis. Front Oncol. 2026;16:1748473.

34. Chow JCL. Machine learning in cancer imaging for enhanced precision in diagnosis and therapy. Discov Comput. 2026;29(1):186.

35. Chua BN, Thng DKH, Toh TB, Ho D. Arti-

ficial intelligence for breast cancer management. Commun Med (Lond). 2026;6(1):79.

36. Conti L, Capetti B, Battaglia O, Grasso R, Pesapane F, Monzani D, et al. Viewpoint on the Consequences and Mitigation of Cognitive Bias in the Radiological Interpretation of Breast Cancer Imaging Using Artificial Intelligence. JMIR Med Inform. 2026;14:e78955.

37. Cui WZ, Wen CQ, Li CQ, Zhang QJ, Yu QQ, Sun WW. Research progress of machine learning applications in gastric cancer diagnosis and therapy. Clin Transl Oncol. 2026.

38. Das J, Bhui U, Chakraborty GS, Mazumder D, Shil S, Sah AK, et al. Comparative oncology of male and female breast cancer: diagnostic paradigms and machine learning approaches in treatment. J Basic Clin Physiol Pharmacol. 2026.

39. de la Calle CM, Baras AS, Lotan TL. Digital pathology-based artificial intelligence algorithms in prostate cancer: inside the 'black box'. BJU Int. 2026;137(4):596-604.

40. Deng Q, Men X, Jin D, Bai Y. Integrating Robotic Bilateral Axillo-Breast Approach Thyroidectomy with Molecular Diagnostics and Artificial Intelligence in Thyroid Cancer Care. Biomol Ther (Seoul). 2026;34(1):45-64.

41. Ding S, Liu M, Wang H, Song C, Zhao L, Yang Z, et al. The role of artificial intelligence in advancing population-based cancer registration. Sci Bull

(Beijing). 2026;71(6):1546-55.

42. Dwivedi P, Barage S, Jha A, Agrawal A, Singh R, Choudhury S, et al. Artificial Intelligence Assisted (18)F-FDG PET Radiomics in Classifying Histological Subtypes of Lung Cancer: Systematic Review and Meta-analysis. Nucl Med Mol Imaging. 2026;60(2):79-92.

43. Eckardt JN, Hahn W, Prelaj A, Bornhäuser M, Middeke JM, Kather JN. Artificial intelligence-generated synthetic data for cancer research and clinical trials. Nat Rev Cancer. 2026;26(5):351-63.

44. Eftekharian M, Hashemi Z. Artificial intelligence for lung cancer: a systematic review of head-to-head CT, FDG PET/CT, and multimodal models across screening, staging, and prognosis. BMC Med Imaging. 2026;26.(1)

45. El Ouardani S, Chibani H, El Ouardani F, Brahmi SA, Afqir S. Artificial Intelligence in the Management of Breast Cancer: A Comprehensive Review. Cureus. 2026;18(4):e106764.

46. Esmaeilpour D, Ghavami S, Zarrabi A, Khosravi A, Zarepour A, Cordani M, et al. Artificial-intelligence-guided autophagy modulation and nanomedicine design for precision photodynamic cancer therapy. Drug Discov Today. 2026;31(3):104633.

47. Faa G, Lai E, Cau F, Coghe F, Rugge M, Suri JS, et al. Integrating Artificial Intelligence into Breast Cancer Histopathology: Toward Improved Diagno-

sis and Prognosis. Cancers (Basel). 2026;18.(7)

48. Filis P, Markozannes G, Salgkamis D, Tsiknakis N, Zerdes I, Pagkalidou E, et al. Integrating liquid biopsies and artificial intelligence for early cancer detection: A systematic review and meta-analysis. Eur J Cancer. 2026;239:116699.

49. Flôres Soares da Silva HM, Gómez Rivas J, Mata Déniz P, Marugan MJ, González-Santander C, Fernández Montarroso L, et al. From prostate-specific antigen to precision: The future of prostate cancer diagnosis with artificial intelligence, biomarkers, and imaging. Curr Urol. 2026;20(3):127-34.

50. Folasole A, Noah GU, Akangbe B, Omohoro MU, Elesho OE. Leveraging Machine Learning and Artificial Intelligence in Cancer Diagnostics Imaging: A Systematic Review. Cureus. 2025;17(12):e98540.

51. Fu D, Sritharan DV, D'Souza R, Chadha S, Hager T, Aneja S. Artificial Intelligence in Lung Cancer: From Early Detection to Personalized Therapy. Curr Oncol Rep. 2026;28.(1)

52. Fu J, Fang M, Wu L, Li X, De Cobelli F, Palumbo D, et al. Development, advancement, and clinical integration of artificial intelligence technology in gastric cancer. Chin Med J (Engl). 2025;138(24):3332-50.

53. Fu Z, Huo X, Jing AB, Ma J, Rauch GM. Artificial Intelligence in Triple-Negative Breast Cancer:

Applications in Diagnosis, Treatment Response, and Prognosis. Diagnostics (Basel). 2026;16.(5)

54. Gao S, Liu J, Li L, Yang D, Miao Y, Zhang X, et al. Application of deep learning technology in breast cancer: a systematic review of segmentation, detection, and classification approaches. Biomed Eng Online. 2026;25(1):19.

55. Garay-Rairan FS, Baharfar M, Wang Q, Qian J, Tricoli A. Emerging Electronic Nose Design for Breath-Based Cancer Diagnostics: Advances in Machine Learning Approaches and Sensor Architecture Design. ACS Sens. 2026.

56. Getu MA, Amare T, Li K, Mehmood A, Adem YF, Santos P, et al. Machine learning and deep learning models for predicting colorectal cancer metastases: A comprehensive review. Eur J Radiol Open. 2026;16:100747.

57. Girdwood T, Kheirinejad S, Kheirkhah P, White B, Davis R, Schwartz D, et al. Empathic and agentic artificial intelligence in nursing: perspectives on a human-centered framework for cancer care navigation in the United States. ESMO Real World Data Digit Oncol. 2026;12:100694.

58. González-Infante L, Marquez G, Parra-Soto S, Cardona-Valencia M, Taramasco C. Machine Learning Techniques Used for the Identification of Sociodemographic Factors Associated With Cancer: Systematic Literature Review. J Med Internet Res. 2026;28:e79187.

59. Gouthamchand V, Fonseca LAF, Hoebers FJP, Fijten R, Dekker A, Wee L, et al. Prognostic modeling in head and neck cancer: deep learning or handcrafted radiomics? BJR Artif Intell. 2025;2(1):ubaf008.

60. Gülmez B. Artificial intelligence applications in ovarian cancer detection: A systematic literature review of deep learning approaches and clinical translation challenges. Crit Rev Oncol Hematol. 2026;219:105126.

61. Gupta S, P A, Reddy GHV, Natarajan K, Srivastava V, Goda J. Artificial Intelligence in Radiology: Transforming Cancer Detection and Diagnosis. Cureus. 2025;17(11):e96518.

62. Gurjar P, Mayana SK, Reddy Annadevula SK, Singh B, Sambhav K, Shah SB. Artificial Intelligence in Radiology: Advancing Precision, Accuracy, and Early Detection in Cancer Diagnosis. Cureus. 2025;17(12):e100102.

63. Haghighat R, Levi SR, Frey MK. Artificial Intelligence for Genetic Cancer Risk Assessment in Gynecologic Oncology: A Review of the Current Landscape and Future Directions. Clin Obstet Gynecol. 2026;69(1):36-44.

64. He JX, Li L, Chen S, Chen RJ, Zhuang JL, Liu C, et al. Outsmarting Metastatic Prostate Cancer: Integration of Imaging, Liquid Biopsies and Biomarkers With Artificial Intelligence. Technol Cancer Res Treat. 2026;25:15330338261440434.

65. He Y, Lu Y, Hu L. Radiomics and artificial intelligence in precision radiotherapy for cervical cancer: a narrative review. Front Oncol. 2026;16:1781422.

66. Hiraoka SI, Kawamura K, Akiyama R, Itakura Y, Tanaka S, Uzawa N. Artificial intelligence for diagnosis and triage in oral cancer: a clinician-centered narrative review. Int J Clin Oncol. 2026;31(5):794-803.

67. Hodeify R. Evaluation of deep learning tools in medical diagnosis and treatment of cancer: research analysis of clinical and randomized clinical trials. Front Netw Physiol. 2025;5:1578562.

68. Honcharyuk I, Caridi B, Pinco P, Ferri S, De Giani A, Baeri A, et al. The intratumor microbiome and cancer immunity: from pathogenesis to therapeutic opportunities through artificial intelligence. Expert Rev Clin Immunol. 2025;21(12):1755-68.

69. Hosseinzadeh N, Behrouzieh S, Sharifi R, Sedighi N. Non-Invasive Breast Cancer Receptor Typing from Mammograms Using Artificial Intelligence: A Systematic Review and Meta-Analysis. J Imaging Inform Med. 2026.

70. Huang W. Artificial intelligence and its application in early oral cancer screening: a systematic review. Front Oncol. 2026;16:1789708.

71. Huda NU, Bari RZA, Javed MA, Kiani MN,

Jin Y. SERS Meets Artificial Intelligence: A New Frontier in Cancer Diagnosis and Prognosis. Anal Chem. 2026;98(12):8757-80.

72. Hussain MM, Qammar S, Wang JM, Zhai AQ, Li FY, Hu HJ. Toward Timely Diagnosis of Pancreatic Cancer: Revolutionizing Early Detection Through Genomics, Artificial Intelligence, and Noninvasive Biomarkers. J Gastroenterol Hepatol. 2026;41(3):895-913.

73. Hussein MA, Munirathinam G. Artificial Intelligence-Driven Natural Product Discovery for Cancer Metastasis and Chemoresistance: From Computational Prediction to Preclinical Validation. Cancers (Basel). 2026;18.(5)

74. Ishtiaq S, Farouk K. Artificial Intelligence as a Tool in the Diagnosis of Bladder Cancer: A Narrative Review. Cureus. 2025;17(11):e96958.

75. Izevbaye I. Towards Precision Oncology: How Advances in Cancer Genomics, Immunobiology and Artificial Intelligence Will Change Molecular Diagnostics. Biomedicines. 2026;14.(1)

76. Jassim G, Otoom O, Nair B, Hashem J. Performance of artificial intelligence in breast cancer screening programmes: a systematic review. BMJ Open. 2025;15(12):e111360.

77. Javaeed A, Schuh A. Artificial intelligence in breast cancer diagnosis: A systematic literature review. Camb Prism Precis Med. 2025;3:e7.

78. Jiang B, Wu Y, Chen X, Jian C, Wang W. Artificial intelligence and multi-omics convergence in breast cancer: Revolutionizing diagnosis, prognostication, and precision oncology. Crit Rev Oncol Hematol. 2026;220:105160.

79. Kagan S, Huynh L, Chen D, Strickland C, Yang C, Kwan JYY, et al. Artificial Intelligence In The Diagnosis And Prediction Of Breast Cancer-Related Lymphedema: A Scoping Review. Support Care Cancer. 2026;34.(5)

80. Kantabanlang Y, Hwang M, Krauss JC, Jiang Y. Artificial Intelligence in Colorectal Cancer Supportive Care: A Scoping Review. Semin Oncol Nurs. 2026;42(1):152079.

81. Karnwal A, Selvaraj M, Kumar G, Kumar A, Al-Tawaha A, Aqueel Ur R, et al. Multimodal artificial intelligence for enhanced skin cancer diagnosis and prognosis. Discov Oncol. 2026;17.(1)

82. Khamis R, Wu Y, Sina AA, Trau M, Wuethrich A. Nanobiosensors and Artificial Intelligence Strategies for Glycan Profiling in Cancer Progression: A Critical Review. ACS Sens. 2026;11(4):2899-922.

83. Kikuchi S, Sakata M, Hasegawa T, Wada S, Funada S, Makishi M, et al. Implementation of artificial intelligence in palliative and supportive care for people with cancer: A scoping review. Palliat Med. 2026:2692163261416261.

84. Kiran Suddle M, Bashir M. Optimizing can-

cer classification: A metaheuristic-driven review of feature selection and deep learning approaches. J Xray Sci Technol. 2026;34(1):103-48.

85. Kong X, Cheng R, Zhang W, Lu Y, Kan Y, Fang Y, et al. Nanoparticle-based immunotherapeutic strategies to overcome cancer drug resistance: From biological barriers to artificial intelligence-driven design. Drug Resist Updat. 2026;86:101392.

86. Kukunoor HR, Andanappa A, Tripathi KM, Fatima I, Akah OZ, Faisal AM, et al. Metastatic cancer detection and management with artificial intelligence and augmented reality (Review). Med Int (Lond). 2026;6(1):13.

87. Lang L, Cui Y, Wang H, Xiao Y. Spatial AI in cancer: mapping immune evasion topology through multi-modal omics and deep learning. Front Oncol. 2026;16:1762907.

88. Lay W, Nguyen HMN, El-Barhoun E, Kokelaar RF, Yeung JM. Artificial Intelligence Models Using Magnetic Resonance Imaging to Predict Response to Chemoradiotherapy in Rectal Cancer: A Systematic Review. ANZ J Surg. 2026.

89. Lee D, Maravic Z, Moon AM, Langenbacher D, Kautz A, Peck R, et al. Enhancing Patient Empowerment Through Artificial Intelligence in Liver Cancer. Am J Gastroenterol. 2026;121(4):847-54.

90. Li FL, Bu H, Zhang Z. [Standardizing breast

cancer digital pathology databases for artificial intelligence: practice and reflection]. Zhonghua Bing Li Xue Za Zhi. 2026;55(3):221-8.

91. Li H, Nan H, Sun Y, Zhao M, Qiu Y, Chen S, et al. Revolutionizing lung cancer screening: the rise of artificial intelligence integrating circulating tumor markers. World J Surg Oncol. 2026.

92. Li J, Jiang Z. Artificial intelligence in breast cancer: applications and advancements. Cancer Biol Med. 2026;23(3):363-73.

93. Li J, Liu W, Mu Y, Wang X, Zhang H, Tang K, et al. Artificial intelligence-assisted spatial omics-based biomimetic nanoplatform for intelligent and precise intervention in the immunosuppressive core region of ovarian cancer. NPJ Precis Oncol. 2026;10.(1)

94. Li Q, Liu H, Wang J. Value of Machine Learning Models for Cell-Free DNA-Based Multi-Cancer Early Detection: A Systematic Review and Meta-Analysis. Technol Cancer Res Treat. 2026;25:15330338261425328.

95. Li R, Lei J, Tang X, Zheng S, Qu J, Xu Y, et al. Artificial intelligence based on ultrasound for initial diagnosis of malignant ovarian cancer: a systematic review and meta-analysis. Front Oncol. 2025;15:1626286.

96. Li Y, Li Y, Zhang W, Li J. The Effectiveness of Artificial Intelligence-Enhanced Interventions for Cancer Patients: A Meta-Analysis of Randomized

Controlled Trials. Worldviews Evid Based Nurs. 2026;23(1):e70117.

97. Li YR, Li D, Zhou YW, Wang WE, Ma YS, Liu XY, et al. Artificial intelligence-driven early screening and diagnosis of pancreatic cancer: technical innovations, clinical applications, and precision medicine strategies. J Adv Res. 2026.

98. Liatsou E, Driva TS, Vergadis C, Sakellariou S, Lykoudis P, Apostolou KG, et al. Current Role of Artificial Intelligence in the Management of Gastric Cancer. Biomedicines. 2025;13.(12)

99. Lichahi MA, Anvari S, Hemmati H, Zadgari E, Jafari M, Mirkalaie SMM, et al. Diagnostic performance of machine learning and deep learning algorithms for thyroid cancer metastasis: a systematic review and meta-analysis. BMC Med Inform Decis Mak. 2025;26(1):13.

100. Liu J, Li D, Zhuo Y, Zhang S. Deep learning for detecting early gastric cancer with white-light endoscopy: a systematic review and meta-analysis. Front Artif Intell. 2026;9:1734591.

101. Liu N, Han G, Gu Q, Zhang Y, Chen M. A new era of precision diagnosis and treatment for lung cancer: artificial intelligence-driven multimodal data integration and clinical applications. Cell Death Dis. 2026.

102. Liu Q, Zhang C, Li P, Jing R, Bi L, Chen W. Artificial intelligence for precision management of epithelial ovarian cancer: a comprehensive review.

Front Med (Lausanne). 2025;12:1713629.

103. Liu W, Feng Z, Zhang M, Mao R, Li J. Predicting neoadjuvant immunotherapy efficacy with machine learning models in non-small cell lung cancer: A systematic review and meta analysis. Int J Med Inform. 2026;212:106345.

104. Liu Z, Yang Y, Guan X. The diagnostic value of radiomics-based machine learning for lymph node metastasis in prostate cancer: a systematic review and meta-analysis. Front Oncol. 2026;16:1710716.

105. Loaiza-Bonilla A, Basu P, Lucas E, Yost C, Arora S. Tech That Scales: A Practical Framework for Artificial Intelligence-Enabled Cancer Care in Low- and Middle-Income Countries and Underserved US Counties. Am Soc Clin Oncol Educ Book. 2026;46(3):e521200.

106. Lopez NE, Neel NC. Can Artificial Intelligence Be Used to Predict Response in Rectal Cancer? Current Evidence and Future Possibilities. Clin Colon Rectal Surg. 2026;39(3):200-8.

107. Lowry KP, Jeong HE, Kim KH, Hughes KS, Lee CI, Yala A, et al. Current state of mammography-based artificial intelligence for future breast cancer risk prediction: a systematic review. J Natl Cancer Inst. 2026;118(3):392-403.

108. Lu J, Zhang H, Yuan Z, Yue J, Yao Q, Liu Y, et al. Image-based artificial intelligence for preoperative differentiation of pancreatic cancer from pan-

creatitis: a systematic review and meta-analysis. Front Oncol. 2025;15:1660271.

109. Lv M, Chen F, Li Q, Xue M, Wang J. Comparative diagnostic accuracy of different artificial intelligence models for early gastric cancer: a systematic review and meta-analysis. Front Oncol. 2025;15:1670843.

110. Lyu S, Wang Z, Mu Y, Wang L, Pei X. Deep Learning Algorithms Versus Radiologists in Digital Breast Tomosynthesis for Breast Cancer Detection: Systematic Review and Meta-Analysis. J Med Internet Res. 2026;28:e91659.

111. Ma Z, Caldwell R, Attia Z, Friedman P, Lerman A, Ng C, et al. Harnessing artificial intelligence for cardio-oncology:Towards a new future of cardiovascular care for the cancer patient. Trends Cardiovasc Med. 2026.

112. Makhlouf HR, Ossandon MR, Farahani K, Lubensky I, Harris LN. Digital pathology imaging artificial intelligence in cancer research and clinical trials: An NCI workshop report. J Pathol Inform. 2026;20:100531.

113. Makiev GG, Samoylenko IV, Nazarova VV, Magomedova ZR, Tryakin AA, Gevorkyan TG. The Efficacy of Electronic Health Record-Based Artificial Intelligence Models for Early Detection of Pancreatic Cancer: A Systematic Review and Meta-Analysis. Cancers (Basel). 2026;18.(2)

114. Malerba S, Vladimirov M, Goyal A, Dulskas A, Baušys A, Cwalinski T, et al. Artificial Intelligence Applications in Gastric Cancer Surgery: Bridging Early Diagnosis and Responsible Precision Medicine. J Clin Med. 2026;15.(6)

115. Mardelli C, Bertail T, Tachibana I, Verhoest G, Mathieu R, Pradere B, et al. Refining prognostication in non-muscle-invasive bladder cancer: From clinical models to artificial intelligence. Urol Oncol. 2026;44(5):111047.

116. McKenzie M, Irac SE, Chen Z, Moradi A, Jenner A, Nguyen Q, et al. Integrative spatial omics and artificial intelligence: transforming cancer research with omics data and AI. Semin Cancer Biol. 2026;119:65-82.

117. Miao Y, Yu Q, Zhang Z, Zhang K. Artificial Intelligence-Driven Three-Dimensional Reconstruction in Lung Cancer Surgery: Current Status and Future Perspectives. ANZ J Surg. 2026.

118. Mohideen K, Ghosh S, Krithika C, Mulk BS, Chole R, Chatterjee J, et al. Application of artificial intelligence and radiomics in the prediction of lymph node metastasis and tumour grading of oral cancer - a systematic review and meta analysis. BMC Oral Health. 2026;26(1):142.

119. Munari E, Antonini P, Cima L, Polati R, Caliò A, Gobbo STM, et al. The evolution of prostate cancer grading: from Gleason score to risk taxonomy and the artificial intelligence revolution. Virchows Arch. 2026.

120. Murugesan G, Moore S, Chang A, Mancini B, Kulkarni H. Artificial Intelligence Across the PSMA Theranostic Continuum in Prostate Cancer. PET Clin. 2026.

121. Nakul M, Rao SD, Karnati M, Aziz F, Bhaskar DP, Dehury B, et al. Machine learning enhanced optical spectroscopy for breast cancer diagnosis: A review. Lasers Med Sci. 2026;41.(1)

122. Navarro-Garcia D, Marcos A, Beets-Tan R, Blomqvist L, Bodalal Z, Deandreis D, et al. Real-world radiology data for artificial intelligence-driven cancer support systems and biomarker development. ESMO Real World Data Digit Oncol. 2025;8:100120.

123. Negahi A, Khosravi-Mashizi M, Najdsepas H, Negahban H, Mousavi-Beni SA, Shahrokhi Damavand R, et al. Precision Medicine and Artificial Intelligence in Next-Generation Cancer Surgery: A Comprehensive Analysis of Clinical Applications, Therapeutic Outcomes, and Implementation Strategies. Asian Pac J Cancer Prev. 2025;26(12):4299-312.

124. Nemoto D, Togashi K, Zhu X, Shinozaki S, Hikichi T. Artificial Intelligence-Based Prediction of Invasion Depth in Colorectal Cancer via Endoscopic Imaging (With Video): A Narrative Review. Dig Endosc. 2026;38(3):e70139.

125. Nizam A, Shireen N, Hasan MR, Singh S, Farooqui M, Naithani D, et al. Artificial

intelligence, omics, and biomarkers: Redefining lung cancer early detection. Curr Probl Cancer. 2026;63:101312.

126. Ordás P, Crossa J, Chiva L. Artificial intelligence for single-omics in ovarian cancer: a methodological review. Int J Gynecol Cancer. 2026;36(4):104452.

127. Pennisi F, Borlini S, Harrison H, Cuciniello R, D'Amelio AC, Barclay M, et al. Cancer Risk Prediction Using Machine Learning for Supporting Early Cancer Diagnosis in Symptomatic Patients: A Systematic Review of Model Types. Cancer Med. 2025;14(24):e71463.

128. Phillips HR, Diaz Fernandez WJ, Leggett CL. Artificial Intelligence and Its Role in Endoscopic Adenoma and Cancer Detection. Clin Colon Rectal Surg. 2026;39(3):209-14.

129. Polio A, Wagner VM. Transforming Gynecologic Cancer Care Through Artificial Intelligence: A Clinician's Guide to the Evolving Landscape. Clin Obstet Gynecol. 2026;69(1):18-25.

130. Pratap Nair R, Du W, Mei L, Koga S. Artificial intelligence for detection, grading, and prognostication in prostate cancer pathology: A scoping review. Histol Histopathol. 2026:25059.

131. Pudova EA, Pavlov VS, Guvatova ZG, Fedorova MS, Shegai PV, Kudryavtseva AV, et al. Machine Learning Models for Cancer Research: A Narrative Review of Bulk RNA-Seq Applications.

Int J Mol Sci. 2025;26.(24)

132. Rahdar A, Shabestari SM, Najafi M, Shirzad M, Pandey S. Hybrid physics-informed machine learning and nanobiosensing strategies for precision liver cancer diagnostics. Comput Biol Chem. 2026;123:109025.

133. Rahnama Y, Pishraft-Sabet H, Eghbali S, Salahshour F, Delazar S, Sedaghat M, et al. Artificial intelligence for the prediction of synchronous and metachronous liver metastasis in colorectal cancer patients: a systematic review and meta-analysis. Abdom Radiol (NY). 2026.

134. Rajih E, Bakhsh A, Borhan WM, Alqahtani SAM. Utilization of artificial intelligence in prostate cancer detection: a comprehensive review of innovations in screening and diagnosis. Front Immunol. 2025;16:1670671.

135. Ramírez LVH, Forero HE, Grosso MPN, Rincón EHH. Advances in artificial intelligence for the early detection of cervical cancer in adult women: a scoping review. Rev Bras Ginecol Obstet. 2025;47.

136. Rao SS, Vidya R. Artificial Intelligence in Breast Cancer Diagnosis and Management. Br J Hosp Med (Lond). 2025;86(12):1-18.

137. Rattanapitoon SK, Arunsarn P, Meererksom T, Thanchonnang C, Boonsuya A, Phinsiri S, et al. Advancing Diagnostic Accuracy in Liver Cancer: A Systematic Review of Artificial

Intelligence Applications in Hepatocellular Carcinoma and Cholangiocarcinoma Detection Using Abdominal CT Imaging. Asian Pac J Cancer Prev. 2026;27(1):5-18.

138. Ruelle T, Grinda T, Del Mastro L, Lacroix-Triki M, Pistilli B, Gessain G. How artificial intelligence applied to digital pathology could guide treatment personalization in breast cancer. ESMO Real World Data Digit Oncol. 2026;11:100662.

139. Saadah S, Ibáñez LD, Ewing RM, Belkhatir Z. Artificial intelligence in multimodal data analysis for cancer survival prediction. Prog Mol Biol Transl Sci. 2026;221:145-214.

140. Sabit H, Yadav AK, Salimy S, Sakr A, Abdel-Ghany S, Soliman Wadan A, et al. Integrating multi-omics and artificial intelligence for personalized breast cancer management: A guide to clinicians. Cancer Lett. 2026;649:218468.

141. Sabry M, Balaha HM, Ali KM, Mahmoud A, Gondim D, Ghazal M, et al. AI-Driven Breast Cancer Diagnosis: A Systematic Review of Imaging Modalities, Deep Learning, and Explainability. Cancers (Basel). 2026;18.(8)

142. Salazar-Garcés LF, Morales-Urrutia E, Cashabamba F, Proaño Alulema RX, Leiva Suero LE. Evaluating AI-driven precision oncology for breast cancer in low- and middle-income countries: a review of machine learning performance, genomic data use, and clinical feasibility. Front Digit

Health. 2025;7:1702339.

143. Salmanpour MR, Mehrnia SS, Jabarzadeh Ghandilu S, Safahi Z, Falahati S, Taeb S, et al. Handcrafted vs. Deep Radiomics vs. Fusion vs. Deep Learning: A Comprehensive Review of Machine Learning -Based Cancer Outcome Prediction in PET and SPECT Imaging. J Imaging Inform Med. 2026.

144. Salvaggio G, Comelli A, Albano D, Galia M, Lalwani N. Artificial intelligence and radiomics in bladder cancer MRI: a scoping review of applications, performance, and barriers to clinical translation. Abdom Radiol (NY). 2026.

145. Salzano G, Digiacomo A, Dello Stritto G, Orsini A, De Archangelis R, Cicchetti R, et al. Artificial intelligence in bladder cancer management: a narrative review of diagnostic and surgical advances and current limitations. Expert Rev Anticancer Ther. 2026:1-16.

146. Santiago LR, Asevedo EA, de Oliveira MEJ, Pereira KC, da Silva Trindade MF, Oliveira AGS, et al. Artificial intelligence-based screening of phytochemicals for targeted cancer therapy. Nat Prod Bioprospect. 2026;16.(1)

147. Saran Manivasagam S, Raman JD, Aminsharifi A. Integrating artificial intelligence across the bladder cancer continuum: progress, promise, and pitfalls. Expert Rev Anticancer Ther. 2026;26(5):557-67.

148. Sarwar Zamani A, Motwakel Eltayeb A, Alluhayb A, Akhtar MM, Ayub R, Abdelmonem Ahmed Abdelrahim M, et al. Application of Machine learning in predicting cancer complications using longitudinal Data: A systematic review and Meta-Analysis. Int J Med Inform. 2026;208:106217.

149. Sehgal T, Joshi T, Chowdhary R, Goyal O, Kalra S, Goyal R, et al. Deep learning in lower gastrointestinal cancer detection: Advances in endoscopic, radiologic, and histopathologic diagnostics. World J Gastrointest Oncol. 2026;18(2):115974.

150. Shi Q, Lou N, Xue C. Advancements in artificial intelligence for cancer diagnosis and prognosis prediction: current applications and emerging opportunities. Front Cell Dev Biol. 2026;14:1769097.

151. Siddiqui A, Khobragade K, Kautish P, Siddiqui M, Marak Z. A review of application of Artificial Intelligence in breast cancer detection and treatment. Discov Oncol. 2026.

152. Silva WN, Araújo ALD, Sanabria A, Hajjar LA, Rodrigo JP, Rao KN, et al. Artificial Intelligence Approaches to Predict Postoperative Length of Hospital Stay in Head and Neck Cancer Patients: A Systematic Review. Diagnostics (Basel). 2026;16.(2)

153. Singh J, Alsaidan OA, Aodah A, Alrobaian

M, Almalki WH, Almujri SS, et al. Artificial intelligence in breast cancer: clinical applications in diagnosis, prognosis, and therapeutics. Future Oncol. 2026;22(2):249-69.

154. Singh M, Betgeri SN, Kakar SS. Artificial intelligence (AI) and machine learning (ML) in ovarian cancer: transforming detection, treatment, and prevention. J Ovarian Res. 2026;19.(1)

155. Slalmi A, Rabbah N, Battas I, Debbarh I, Medromi H, Abourriche A. Artificial Intelligence-Driven SELEX Design of Aptamer Panels for Urinary Multi-Biomarker Detection in Prostate Cancer: A Systematic and Bibliometric Review. Biomedicines. 2025;13.(12)

156. Sonmez G, Yazarkan Y, Sahin TK, Guven DC. Harnessing the power of artificial intelligence for clinical trials in cancer. Expert Rev Anticancer Ther. 2026:1-15.

157. Sood D, Dadwal S, Jain S, Mazhar IJ, Goyal B, Garapati C, et al. Prospective of Colorectal Cancer Screening, Diagnosis, and Treatment Management Using Bowel Sounds Leveraging Artificial Intelligence. Cancers (Basel). 2026;18.(2)

158. Farrokhi M, Abbasmofrad H, Karami M, Hezarani HB, Alemohammad SS, Atighi J, et al. AI for Self-Diagnosis, Self-Monitoring, and Personalized Medicine. Kindle. 2026;6(1):1-226.

159. Tahavvori A, Chelan RJ, Aminoleslami S, Moghadam OF, Haghighi L, Abdian Y, et al. Large

Language Models and ChatGPT in Medical Sciences: Foundations, Capabilities, and Challenges. Kindle. 2025;5(1):1-222.

160. Ramezanian M, Benis DS, Nikakhtar R, Gorjizadeh N, Asadi F, Bagherianlemraski M, et al. Artificial Intelligence in Genomic Medicine: Improving Diagnostic Accuracy and Treatment Outcomes. Kindle. 2025;5(1):1-215.

161. Louia S, Moghadam OF, Chelan RJ, Taheri N, Amini F, Ahmadi S, et al. Role of Immunogenetics in the Etiology, Diagnosis, and Treatment of Diseases. Kindle. 2025;5(1):1-222.

162. Harati K, Tahernejad M, Saddam SMS, Farshi M, Saeedfar M, Gheibi M, et al. The Future of Prosthetics and Organ Transplantation: A Therapeutic Approach Across Various Medical Disciplines. Kindle. 2025;5(1):1-193.

163. Harati K, Mosaddeghi-Heris R, Kiani K, Saligheh Rad M, Morovatshoar R, Kamali M, et al. The AI Revolution: Predicting and Managing the Next Global Health Challenges and Emerging Disease Outbreaks. Kindle. 2025;5(1):1-326.

164. Harati K, Abbasmofrad H, Ebrahimi M, Hashemlu L, Chelan RJ, Hashemzadeh A, et al. Intelligent Patient Engagement: Education and Follow-Up through AI and Telemedicine. Kindle. 2025;5(1):1-185.

165. Farrokhi M, Taheri N, Moghadam OF, Armoon M, Samimi S, Torkashvand N, et al. Artifi-

cial Intelligence for Hard-to-Treat and Unknown-Origin Cancers. Kindle. 2025;5(1):1-296.

166. Farrokhi M, Mehrtabar S, Harati K, Pourlak T, Ghadirzadeh E, Abbasmofrad H, et al. Clinical Decision-Making Using Artificial Intelligence. Kindle. 2025;5(1):1-236.

167. Farrokhi M, Ghalamkarpour N, Nouri S, Babaei M, Rajabloo Y, Sattari M, et al. Innovative Vaccination: A New Era in Cancer Prevention. Kindle. 2025;5(1):1-194.

168. Farrokhi M, Taheri F, Bayat Z, Damiri M, Farrokhi M, Ghadirzadeh E, et al. Role of lifestyle medicine in the prevention and treatment of diseases. 2024.

169. Farrokhi M, Taheri F, Moeini A, Farrokhi M, Rabiei S, Farahmandsadr M, et al. Sex and gender differences in the pathogenesis and treatment of diseases. Kindle. 2023;3(1):1-168.

170. Shayganfar A, Farrokhi M, Shayganfar S, Ebrahimian S. Associations between bone mineral density, trabecular bone score, and body mass index in postmenopausal females. Osteoporosis and sarcopenia. 2020;6(3):111-4.

171. Gorjizadeh N, Tavousi N, Talebi S, Moallem M, Gheibi M, Bagherzadeh S, et al. Academic Textbook: Mechanistic AI in Medicine: Discovery of Mechanisms and Origins of Diseases. Kindle. 2026;6(1):1-216.

Proof