Explainable Artificial Intelligence for Reducing the Global Cancer Burden

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Book Details:

Publisher: Kindle

Publication Date: September 2025

Language: English

Dimensions: 5 x 0.39 x 8 inches

ISBN-13: 979-8264785672

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1. EXPLAINABLE AI IN REDUCING THE BURDEN OF HEMATOLOGIC MALIGNANCIES

Background

Hematologic malignancies, including leukemias, lymphomas, and myelomas, continue to represent a major cause of cancer-related morbidity and mortality worldwide. Their incidence rates are steadily increasing, and the diagnostic and therapeutic pathways remain complex and demanding. Despite significant progress in genomics, precision medicine, and targeted therapies, the clinical management of these malignancies remains challenging due to their biological heterogeneity and the intricate decision-making processes required for personalized care.

Artificial Intelligence (AI), particularly machine learning (ML) and deep learning (DL) algorithms, has emerged as a promising approach to improve diagnostic accuracy, predict treatment responses, and stratify risk in hematologic cancers. Nevertheless, the so-called “black box” nature of many AI models has created obstacles to their adoption in clinical practice. Clinicians must be able to trust, interpret, and validate the outputs of such systems, particularly in high-stakes contexts like oncology. This has generated growing interest in Explainable Artificial Intelligence (XAI), which seeks to make algorithmic decision-making more transparent, interpretable, and clinically actionable.

Although numerous AI models have demonstrated impressive predictive power in hematologic malignancies, their lack of explainability significantly limits their practical use. Bridging the gap between algorithmic performance and interpretability remains a pressing challenge. In oncology, where opaque AI decisions could compromise patient safety and diminish trust among healthcare professionals and patients, the integration of XAI is not only a technical improvement but also a clinical and ethical necessity.

Problem Statement

A critical challenge in current AI applications for hematologic malignancies lies in their limited explainability, which impedes clinical adoption. While high-performing AI models exist, their opaque nature prevents meaningful incorporation into clinical decision-making workflows and limits their ability to reduce the clinical burden of blood cancers.

Research Gap

Despite the proliferation of AI models

in hematologic oncology, few studies have systematically developed or implemented explainable frameworks that align with the cognitive and interpretive needs of hematologists. Most existing tools prioritize performance over transparency, resulting in a disconnect between model capability and clinical utility. Furthermore, domain-specific XAI approaches tailored to the pathophysiological and therapeutic complexity of hematologic malignancies remain scarce.

Addressing this gap is essential to enable earlier diagnoses, optimize treatment strategies, and improve patient outcomes. The development of explainable AI approaches that are both accurate and interpretable has the potential to enhance clinician trust, support evidence-based decision-making, and facilitate the integration of AI into routine hematology practice. These approaches must be designed not only to maximize predictive performance but also to provide insights into how and why specific predictions are made, ensuring that AI contributes safely and effectively to patient care.

Artificial Intelligence and Hematologic Malignancies

Recent advances in artificial intelligence, particularly machine learning and deep learning, hold promise for transforming the management of hematologic malignancies. Machine learning algorithms generate predictive models from training data and have been applied in pathology, radiology, genomics, and electronic health record analysis. Early applications primarily focus on automated classification of blood or bone marrow images, risk stratification, and genomic prediction. However, many modern deep learning models operate as "black boxes," providing limited insight into the features driving their predictions. In high-stakes clinical environments, this opacity raises ethical, legal, and practical concerns, as clinicians cannot readily audit or trust the model's reasoning, and patients and regulators demand transparency.

Explainable artificial intelligence aims to address these challenges by providing human-interpretable explanations of model outputs. XAI has the potential to reduce the burden of hematologic malignancies by enabling earlier diagnosis, enhancing prognostic assessment, guiding treatment selection, and improving resource allocation, while also addressing the ethical and practical limitations of traditional AI approaches.

Why Explainability Matters in Hematology

Ethical, Legal, and Clinical Considerations

The opacity of many AI models creates a range

of ethical and clinical challenges. Key aspects of explainability include identifying the addressee of explanations, whether clinician, patient, or regulator; ensuring explanations are relevant to decision-making; distinguishing between global and local explanations; balancing explainability with accuracy; addressing automation bias and epistemic authority; incorporating individual preferences and values; and considering the implications for patient autonomy and the clinician–patient relationship. AI systems must therefore be tailored to their specific context of use. For instance, a global explanation of model behavior may satisfy researchers but does little to assist a clinician in interpreting an individual patient's result. The opacity of black-box models often arises from proprietary secrecy, technical complexity, and limited algorithmic literacy, making explainable AI a necessary strategy to facilitate trustworthy integration into clinical workflows.

Critics note that XAI is not a universal solution. Adding post-hoc explanations to black-box models may create a false sense of security. Rigorous internal and external validation of AI algorithms remains essential. In multiple myeloma, for example, clinicians must understand when and how to use AI tools and the degree of confidence they should place in their conclusions. Lack of transparency can erode trust, and ethical implementation must ensure that AI does not disrupt the physician–patient relationship. Consequently, explainability must be complemented by robust validation, fairness assessment, and careful integration into practice.

Potential Benefits of Explainable AI

Despite these challenges, explainable AI offers substantial benefits in hematologic care. By clarifying the features that drive predictions, XAI can help identify novel biomarkers, validate biological hypotheses, and support personalized risk assessment. In multiple myeloma imaging, explainable models increase trustworthiness and allow expert evaluation; sharing code and data further enables external investigators to assess reliability. Explainable AI can reveal causal relationships and highlight new biomarkers. In chronic lymphocytic leukemia, an XAI algorithm analyzing multiparameter flow cytometry data identified seventeen cell populations predictive of inferior outcomes and improved risk stratification compared with the conventional CLL-IPI index. Such models not only enhance predictive accuracy but also direct clinicians toward specific cell populations or genes that might serve as therapeutic targets.

XAI Applications in Hematologic Malignancies

Explainable Morphologic Classification of Acute Myeloid Leukemia

Deep learning has enabled automated classification of blood and bone marrow smears, but early models lacked transparency. The Single-Cell-level Multiple Instance Learning Attention (SCEMILA) algorithm is an inherently explainable neural network designed for classifying acute myeloid leukemia subtypes from peripheral blood smears. SCEMILA employs a multi-attention module that assigns attention scores to individual cells, making it possible to determine which cells contributed to the predicted label. Trained on eighty thousand single-cell images from 129 AML patients and sixty healthy controls, SCEMILA distinguished AML from healthy donors and achieved an F1-score of 0.86 for acute promyelocytic leukemia. Importantly, cells receiving high attention corresponded with those selected by human experts, demonstrating alignment between model reasoning and expert evaluation. By highlighting subtype-specific morphologic features without requiring cell-level labels, SCEMILA enables pathologists to verify the cells driving the classification and to detect potential errors. Such inherent explainability is critical for building trust and may accelerate adoption in clinical workflows.

XAI for Prognostication in Chronic Lymphocytic Leukemia

Prognostication in chronic lymphocytic leukemia traditionally relies on clinical staging and genetic markers, which may not fully capture disease heterogeneity. The ALPODS algorithm, a locally interpretable point-wise linear classifier, was applied to multiparameter flow cytometry data from 157 CLL patients. The model identified seventeen cell populations, including a CD4-positive T-cell subset, associated with inferior outcomes and achieved an area-under-the-curve of 0.95, outperforming the CLL-IPI index, which had an AUC of 0.78. ALPODS provided interpretable explanations by highlighting the cell populations that contributed most to the risk score. When the identified CD4-positive T-cell population was integrated into the CLL-IPI, predictive performance improved to an AUC of 0.83. This example illustrates how XAI can refine prognostic scores, uncover pathobiological insights such as immune cell involvement, and suggest potential therapeutic targets.

Gene Selection and Time-to-Therapy Prediction in Chronic Lymphocytic Leukemia

Genomics provides another important arena for explainable artificial intelligence. Morabito and colleagues proposed the DeepSHAP Autoencoder

Filter for Gene Selection (DSAF-GS), a deep-learning-based feature-selection method that combines an autoencoder with SHapley Additive exPlanations (SHAP) to identify genes influencing prognosis in chronic lymphocytic leukemia (CLL). Applied to a gene-expression dataset of 217 CLL cases encompassing approximately twenty thousand genes, DSAF-GS achieved 86.4 percent accuracy, with 85 percent sensitivity and 87.5 percent specificity. SHAP-based explanations revealed that predictions were strongly influenced by CEACAM19 and PIGP, moderately influenced by MKL1 and GNE, and less influenced by other genes. The ten most influential genes identified included FADD, IGF1R, GNE, and MKL1, which are involved in signal transduction, cell-cycle regulation, and apoptosis pathways. Incorporating these top genes into a multivariable model improved Harrell's c-index and explained variation for time-to-first-treatment compared with a basic prognostic model.

Explainable Models in Multiple Myeloma Imaging

Diagnosis and response assessment in multiple myeloma often rely on imaging modalities such as MRI, CT, or PET, along with morphologic criteria. A systematic review of AI in multiple myeloma imaging emphasized the need for explainable models to increase trustworthiness and allow experts to evaluate model decisions. Radiomics-based models, for example, can identify high-risk patients and suggest personalized therapies. However, their transition to clinical practice is hindered by lack of external validation and limited interpretability. Researchers recommend providing code and data to permit independent verification and adopting explainable models that highlight salient image features or radiomic signatures. While this field is still emerging, the consensus is that explainable AI will facilitate the adoption of imaging-based AI in multiple myeloma and help uncover new causal relationships and biomarkers.

Other AI Applications Relevant to Explainability

Beyond explicitly explainable models, AI systems in hematology demonstrate the critical need for transparency. A multi-stage deep-learning platform for detecting acute promyelocytic leukemia from bone-marrow smears accurately segmented cells and distinguished APL from other acute myeloid leukemia subtypes with an area under the curve of 0.8575. The authors suggested that such algorithms could support diagnosis in regions lacking molecular tests. However, purely deep-learning-based approaches remain black boxes. As AI becomes increasingly utilized in digital pathology and genomics, explainability will be essential to ensure that clinicians understand the features driving predictions and

can verify their accuracy.

Reducing the Burden of Hematologic Malignancies through Explainable AI

Early and Accurate Diagnosis

Delayed diagnosis is a major contributor to morbidity and mortality in hematologic malignancies. For instance, early death rates in acute promyelocytic leukemia can exceed twenty percent, yet timely detection and initiation of differentiation therapy lead to high cure rates. Explainable AI models like SCEMILA demonstrate that inherently interpretable deep learning can recognize morphologic patterns associated with specific genetic lesions and highlight the cells responsible for the diagnosis. In resource-limited settings, such models could enable rapid screening of blood or bone-marrow smears, triaging patients for confirmatory testing and prompting timely treatment. By revealing the specific cells or features that trigger a positive classification, explainable AI can increase clinician confidence and reduce misdiagnoses.

Personalized Prognostication and Treatment Planning

Hematologic malignancies display substantial heterogeneity in their clinical course. Explainable prognostic models that integrate flow-cytometry or genomic data, such as ALPODS and DSAF-GS, refine risk stratification by identifying cell subsets or gene signatures associated with poor outcomes. These insights enhance predictive accuracy and provide mechanistic hypotheses—for example, the influence of CD4-positive T cells in CLL progression or the role of FADD and IGF1R in disease biology. Such information can guide personalized treatment decisions, help prioritize patients for clinical trials, and avoid overtreatment or undertreatment. In the longer term, the discovery of novel biomarkers through explainable AI could lead to targeted therapies that further reduce morbidity and healthcare costs.

Resource Allocation and Health-Economic Impact

The global economic burden of hematologic malignancies is expected to shift toward middle-income countries by 2050. Explainable AI can contribute to cost reduction by optimizing diagnostic workflows, such as automated smear screening, preventing unnecessary tests and therapies through accurate prognostication, and enabling telemedicine solutions. For example, an explainable AI system deployed in community laboratories could flag suspicious smears and transmit them to reference centers, reducing the need for universal molecular testing. At the health-system level, models that identify patients at high risk of relapse can help allocate

expensive therapies, including hematopoietic cell transplantation or novel immunotherapies, to those most likely to benefit.

Building Trust and Facilitating Adoption

The success of AI in hematologic malignancy care ultimately depends on clinician and patient trust. Explainable models foster trust by clarifying the rationale behind a decision, allowing users to verify whether it aligns with established medical knowledge. Clinicians must understand when and how to use AI tools and the level of confidence to assign to their outputs. Transparent models also assist regulators and payers in assessing safety and efficacy. However, explainability should not come at the expense of accuracy. Developers must balance model performance with interpretability and validate models across diverse populations to prevent unintended biases. Education for clinicians and the inclusion of patients in the design process are essential to ensure that explainable AI complements rather than replaces clinical judgment.

Future Directions

Advancing the integration of XAI in hematologic malignancies requires a focus on both technical and human-centered considerations. Future research should aim to:

Develop AI models that combine high predictive accuracy with interpretable outputs aligned with clinical reasoning. Evaluate the impact of explainable AI on clinician trust, decision-making accuracy, and workflow integration. Design domain-specific XAI frameworks tailored to the biological heterogeneity and therapeutic complexity of hematologic cancers. Explore the potential for AI to support personalized medicine by integrating clinical, genomic, and laboratory data while maintaining transparency and interpretability. By addressing these priorities, XAI has the potential to bridge the current gap between performance and clinical applicability, enabling safer, more trustworthy, and more effective management of hematologic malignancies.

2. EXPLAINABLE AI IN REDUCING THE BURDEN OF NEUROLOGICAL CANCERS

Background

Explainable AI in Reducing the Burden of Neurological Cancers Artificial intelligence (AI) has brought about a significant transformation in the diagnosis and treatment of brain tumors, particularly glioma and meningioma, by integrating imaging, genomic, and clinical data. This technology, through the analysis of multiparametric MRI, including T1, T2, FLAIR, DWI, and SWI, as well as PET, combined with perfusion imaging and radiomics, can extract tumor characteristics without the necessity for biopsy.

Furthermore, genomic data such as DNA and RNA sequencing and methylation patterns are analyzed using bioinformatics, providing a deeper understanding of the tumor's molecular structure. In addition, clinical information, including medical history and treatment response, is combined with other data in machine learning (ML) and deep learning (DL) models to offer more accurate predictions regarding treatment response, survival rates, and the likelihood of

tumor recurrence. This approach represents an effective step toward personalized medicine.

Computer-aided detection (CADe) tools supported by AI have demonstrated the capability to rapidly and accurately identify primary brain tumors, such as glioma, and early stages of metastases. This development has led to a reduction in diagnostic time and human errors in interpretation.

Compared to manual segmentation and its limitations in terms of accuracy and reproducibility, AI can precisely determine the volume and margins of brain tumors, particularly glioblastoma, by employing convolutional neural networks and machine learning algorithms. In this way, it can automatically segment brain tumors.

At present, AI is capable of distinguishing between benign and malignant tumors and, in the case of high-grade gliomas, differentiating tumor recurrence from radiation-induced necrosis.

For the selection of targeted therapies and the personalization of treatment for brain tumor patients based on critical molecular features, AI has the potential to predict MGMT methylation status, IDH mutations, and 1p/19q chromosomal deletions through the analysis of imaging characteristics.

Additionally, it can predict tumor grade and even patient prognosis in cases of glioma and meningioma.

Another important application of AI includes the automatic measurement of residual tumor volume post-surgery and the accurate delineation of brain metastases for stereotactic radiosurgery.

Artificial intelligence, particularly explainable artificial intelligence (XAI), in combination with MRI imaging, is considered a powerful tool in neuro-oncology. These technologies can play a significant role in enhancing clinical care by contributing to more accurate tumor diagnosis, improved surgical guidance, radiation dose adjustment, and the prediction of molecular tumor features based on imaging data such as radiomics and radiogenomics.

However, one of the primary challenges in the application of AI in medicine is the lack of transparency in the decision-making processes of models, an issue commonly referred to as the “black box” problem. To address this, XAI methods are categorized into two groups: a priori methods, such as ProtoPNet, which are inherently interpretable but offer lower accuracy, and a posteriori methods, such as LIME and SHAP, which provide explanations after model training and are suitable for more complex models, although their understanding may be more challenging for clinicians.

Furthermore, visual tools such as GradCAM, ScoreCAM, and LayerCAM assist in better understanding model decision-making by highlighting key regions in MRI images.

Moreover, the adoption of a user-centered design (UCD) approach, involving active participation of clinicians in the development stages of AI systems, ensures that these tools are more aligned with real clinical needs and therefore more reliable.

Techniques such as XAI, including SHAP, Grad-CAM, and LIME, are employed to provide transparent interpretations of how models make decisions in tumor identification. Necrosis or irregular tumor borders are delineated as heatmaps by Grad-CAM, which appears to detect tumors in a shorter time frame with accuracy comparable to physician findings from images.

In addition, a hybrid architecture comprising Vision Transformers (ViTs) and Convolutional Neural Networks (CNNs) has been utilized to segment glioma tumors in pre-surgical multi-sequence three-dimensional MRI images, including T1w, T1Gd, T2w, and FLAIR. In this study, the hybrid model has achieved highly accurate results in detecting and separating tumor regions, with a Dice coefficient of up to 0.88. To enhance transparency and build clinician trust, an explainability method known as TransXAI, an advanced form of Grad-CAM, has been employed. This method generates comprehensible heatmaps for surgeons, serving as an effective tool in pre-surgical planning.

The LIME method, by focusing on critical image pixels, particularly areas with higher brightness intensity, and the SHAP method, by quantifying the importance of features such as tissue heterogeneity, have improved clinicians' understanding of the decision-making basis of AI models. As a result, clinician confidence in the results of these models has increased by approximately 30 percent.

The aforementioned CAD systems are capable of extracting and analyzing vital information from MRI, including tumor size, tumor type with an accuracy of up to 99.4 percent, and tumor grade based on signal intensity and tissue heterogeneity. In recent times, artificial intelligence models such as Convolutional Neural Networks, Vision Transformers, and machine learning models including Random Forest, XGBoost, and Support Vector Machines have demonstrated high accuracy in the detection of brain tumors.

These machine learning models are capable of grading glioma tumors based on data derived from MRI images, along with molecular and clinical patient data, with an accuracy of 88 percent.

The CNN model, developed specifically for medical image analysis, examines abnormal signal intensity, irregular margins, and tissue heterogeneity in MRI images. For instance, the ResNet50 CNN model, by analyzing high-intensity regions in FLAIR images, has achieved a brain tumor detection accuracy of 98.52 percent.

Similarly, the DenseNet121 model, with its focus on enhancing contrast in T1 images, can differentiate between low-grade and high-grade

gliomas with an accuracy ranging from 87.3 to 92.1 percent.

As previously mentioned, a technique known as Grad-CAM, which generates heatmaps, is capable of identifying critical regions in MRI images. Explainable AI visually interprets the Grad-CAM heatmaps, aligning with diagnostic criteria for brain tumors in MRI images. The EfficientNetB0 model, leveraging this technique, has contributed to an improved classification accuracy of 98.72 percent for brain tumors, including gliomas, meningiomas, non-tumor cases, and pituitary tumors.

The deep learning model DenseNet169 has exhibited high accuracy in identifying brain tumors, gliomas, and meningiomas through the analysis of MRI patient data. When combined with XAI techniques such as GradCAM, ScoreCAM, GradCAM++, and LayerCAM, this model visualizes significant regions in brain images, thereby making the prediction process for tumor detection more comprehensible.

A sophisticated model named SECNN-MNet, designed for brain tumor detection via MRI image analysis, integrates two networks: SE-CNN, which focuses on critical image features, and MobileNet, which reduces computational costs. This model achieves a 99.6 percent accuracy in classifying tumors into four categories, including glioma, meningioma, and non-tumor cases, and employs XAI techniques such as

Grad-CAM to highlight key image regions used for tumor identification. SECNN-MNet has demonstrated superior performance and enhanced explainability compared to previous CNN and ResNet-50 models.

In several medical centers, an innovative model based on the GoogleNet architecture has been developed to extract complex features and data from brain MRI images of patients across four classes: glioma, meningioma, pituitary tumors, and non-tumor cases. Only the information derived from unique image features, including weights and gradients, is transmitted to a central server while preserving patient privacy from each medical center. The central server, utilizing federated learning, integrates data from all clients to design a global model, which is then distributed back to the clients. These clients further train the model on their local data, and the repetition of this process enhances the model's accuracy. Alongside federated learning, this model employs XAI techniques such as Grad-CAM to display critical image regions as heatmaps and saliency maps to highlight the role of pixels in the decision-making process, enabling clinicians to gain a visual understanding of the model's performance.

To assess user satisfaction with the XAI system, quantitative metrics such as model and technique accuracy, interpretability, and response time, as well as qualitative tools such as the System Usability Score or NASA-TLX, are utilized, serving

as an evaluation of the effectiveness of XAI.

Overall, studies have demonstrated that explainable artificial intelligence plays a significant role in the accurate and reliable detection of brain tumors by providing a transparent and comprehensible explanation of how models interpret and predict unique tumor features in MRI images, aligning with clinical acceptance by medical specialists.

The Complexity of Neurological Cancers

Neurological cancers are distinct from other malignancies due to their location in a highly sensitive organ and the limited capacity for surgical resection without risking neurological deficits. Brain tumors often exhibit intratumoral heterogeneity, with diverse cell populations coexisting within the same lesion, making therapeutic targeting difficult. Furthermore, the blood-brain barrier (BBB) limits drug delivery, reducing the effectiveness of systemic therapies.

Patients with neurological cancers frequently experience profound neurological symptoms, including seizures, personality changes, language deficits, and cognitive impairment, which diminish quality of life. Treatment itself can exacerbate these issues. Radiotherapy, while effective in slowing tumor progression, may cause long-term neurocognitive decline. Chemotherapeutics such as temozolomide may improve survival but also carry significant side effects. Therefore, therapeutic strategies require careful balancing between efficacy and preservation of neurological function.

The complexity extends to diagnosis and prognostication. Conventional imaging may not adequately distinguish between tumor recurrence and treatment-induced changes, such as pseudoprogression or radiation necrosis. Molecular biomarkers, including IDH mutations and MGMT promoter methylation, have proven valuable for prognosis and therapy selection, but their interpretation is challenging when integrated with clinical and imaging data. Clinicians must navigate these complexities rapidly while ensuring decisions are evidence-based.

The Role of Artificial Intelligence in Neurological Oncology

Artificial intelligence has demonstrated substantial potential in neurological oncology by processing large, multimodal datasets that surpass human interpretive capacity. Deep learning models trained on imaging data can achieve high accuracy in classifying tumor types, segmenting lesions, and predicting treatment outcomes. Radiogenomics, an emerging field combining imaging features with genomic data, leverages AI to non-invasively predict molecular

subtypes of tumors, enabling precision medicine approaches without requiring invasive biopsies.

In surgical planning, AI-based tools provide 3D reconstructions and predictive maps of tumor boundaries, improving surgical precision and reducing postoperative deficits. During radiotherapy, AI algorithms assist in dose optimization by accurately contouring tumor margins and sparing healthy tissue. In clinical decision-making, predictive models estimate overall survival and recurrence risks, guiding patient-specific treatment strategies.

Despite these achievements, the majority of AI models operate as opaque systems, offering limited insight into how decisions are made. This opacity poses risks in medicine, where incorrect predictions can have life-threatening consequences. Clinicians are hesitant to trust systems they cannot interpret, particularly when model outputs conflict with established clinical knowledge. Here lies the importance of explainability, which ensures that AI is not only accurate but also transparent and clinically actionable.

Foundations of Explainable AI

Explainable AI encompasses a set of techniques designed to make AI models interpretable and understandable. Interpretability refers to the degree to which a human can comprehend how a model processes input to produce output. Transparency ensures that the rationale behind a model's decision is visible and justifiable. Techniques in XAI range from inherently interpretable models, such as decision trees and generalized linear models, to post hoc explanations for complex models, such as deep neural networks.

Key methods in XAI include feature importance analysis, which highlights the variables most influential in a decision; saliency maps, which identify regions of images driving predictions; local interpretable model-agnostic explanations (LIME), which approximate model behavior for individual predictions; and SHAP (Shapley additive explanations), which attribute contributions of each feature to an output. These methods allow clinicians to assess whether AI models base decisions on clinically relevant factors or spurious correlations.

In neurological oncology, saliency maps may reveal whether an AI model relies on tumor margins, edema patterns, or unrelated image artifacts. SHAP values may show the influence of genomic markers such as IDH mutation status on survival predictions. By providing such clarity, XAI helps clinicians integrate AI insights into their decision-making process while maintaining accountability and trust.

Applications of Explainable AI in Imaging of Neurological Cancers

Medical imaging remains the cornerstone of neurological cancer management, from diagnosis to treatment monitoring. Explainable AI enhances imaging-based AI tools by enabling clinicians to verify that predictions align with known radiological features.

For tumor detection, saliency maps allow radiologists to visualize which areas of the brain MRI influenced the classification of a glioma versus metastasis. This transparency reduces diagnostic uncertainty and ensures that AI models do not misinterpret noise as pathology. In tumor segmentation, explainability confirms that algorithms correctly delineate tumor boundaries and edema, which are crucial for surgical and radiotherapy planning.

Another promising application is differentiating pseudoprogression from true tumor recurrence. Conventional imaging often fails to make this distinction, leading to inappropriate treatment changes. XAI-driven models highlight imaging features, such as contrast-enhancement patterns and diffusion abnormalities, that underpin predictions. Clinicians can assess these features for plausibility, increasing confidence in adopting AI recommendations.

Furthermore, radiogenomics benefits from XAI by linking imaging features to genetic alterations. For example, an explainable model predicting IDH mutation from MRI scans can indicate which tumor regions reflect mutational status, supporting biologically meaningful interpretations. This enhances the utility of non-invasive diagnostics and facilitates personalized therapeutic strategies.

Genomic and Molecular Applications of Explainable AI

Molecular profiling has revolutionized the classification and treatment of neurological cancers. However, genomic datasets are high-dimensional and complex, requiring advanced computational approaches. Explainable AI offers a pathway to extract actionable insights while maintaining transparency.

Predictive models built on genomic data can identify molecular signatures associated with prognosis or therapeutic response. By applying SHAP values or feature attribution methods, clinicians can understand which mutations, gene expression patterns, or epigenetic markers drive survival predictions. This prevents over-reliance on uninterpretable black-box models and supports biologically coherent hypotheses.

For example, in glioblastoma, an explainable model may reveal that MGMT promoter methylation contributes significantly to

predictions of temozolomide response, aligning with established clinical evidence. Conversely, if the model attributes importance to genes with no known association, clinicians can question its validity and avoid erroneous conclusions. Such transparency fosters trust and facilitates clinical translation of AI-driven genomic insights.

XAI also enables integration of multimodal data, combining imaging, genomics, and clinical parameters. By making the contributions of each data type explicit, XAI models allow clinicians to understand how different factors interact in shaping predictions. This holistic understanding is particularly valuable in neurological cancers, where decisions must consider both biological and functional outcomes.

Enhancing Clinical Decision-Making with Explainable AI

Clinical decision-making in neurological oncology involves high-stakes choices regarding surgery, radiotherapy, and systemic treatment. Explainable AI empowers clinicians by providing not only predictions but also the reasoning behind them.

When predicting surgical outcomes, an explainable model can show that tumor location near eloquent brain areas drives a higher risk of postoperative deficits. Such insights help surgeons plan procedures with greater awareness of functional risks. In radiotherapy planning, explainable dose-optimization models highlight which tissue-sparing priorities influenced recommended dosing, supporting informed trade-offs.

In survival prediction, models that indicate which clinical and biological factors contribute most strongly to prognosis allow clinicians to communicate predictions transparently to patients and families. This fosters shared decision-making, where patients understand the rationale behind recommended therapies and are more likely to adhere to treatment plans.

Explainable AI also supports multidisciplinary tumor boards by providing interpretable evidence that integrates diverse data sources. Oncologists, radiologists, neurosurgeons, and pathologists can collectively evaluate model explanations, ensuring that recommendations align with clinical expertise. This reduces the risk of over-reliance on any single clinician or algorithm and enhances the robustness of care.

Reducing Healthcare Burden Through Explainable AI

The burden of neurological cancers extends beyond individual patients to healthcare systems and societies. High costs of care, frequent hospitalizations, and the need for long-term rehabilitation strain resources. Explainable AI can mitigate this burden by improving efficiency,

reducing diagnostic errors, and optimizing treatment strategies.

Early diagnosis facilitated by XAI-supported imaging models reduces delays in initiating treatment, improving survival outcomes and lowering costs of advanced disease management. Accurate differentiation between recurrence and pseudoprogression prevents unnecessary therapies, minimizing side effects and financial waste. Personalized treatment recommendations informed by transparent AI models ensure that resources are directed toward interventions most likely to benefit individual patients.

XAI also reduces medicolegal risks associated with AI adoption. By providing interpretable justifications for predictions, XAI safeguards against liability concerns and enhances regulatory compliance. Healthcare providers and payers are more likely to adopt AI tools when their outputs are transparent and defensible.

Furthermore, explainability fosters patient trust, which is essential for adherence to treatment and engagement in care. Patients who understand the reasoning behind AI-driven recommendations are more likely to accept interventions, reducing dropout rates and improving long-term outcomes. Collectively, these benefits reduce the overall burden of neurological cancers at both patient and societal levels.

Ethical and Regulatory Dimensions of Explainable AI in Neurological Cancers

The ethical integration of AI into healthcare requires transparency, accountability, and fairness. Black-box models that make inscrutable decisions raise concerns about bias, safety, and trustworthiness. Explainable AI addresses these issues by making decision-making processes visible and justifiable.

In neurological cancers, where decisions profoundly affect survival and quality of life, ethical responsibility is paramount. XAI ensures that models do not inadvertently rely on confounding factors such as demographic biases or imaging artifacts. By exposing feature importance, XAI allows developers and clinicians to identify and correct biases, promoting equitable care.

Regulatory agencies increasingly emphasize explainability as a prerequisite for AI approval in healthcare. Transparent models are easier to validate and audit, accelerating their clinical translation. By aligning with regulatory requirements, XAI accelerates safe deployment of AI tools in neurological oncology.

Future Directions of Explainable AI in Neurological Cancers

The future of XAI in neurological cancers lies in developing more sophisticated, user-friendly tools that integrate seamlessly into clinical workflows. Advances in visual explanation methods, interactive dashboards, and natural language generation will make model reasoning more accessible to non-technical clinicians.

Multimodal explainability will gain prominence, enabling simultaneous interpretation of imaging, genomic, pathology, and clinical data. This holistic perspective will reflect the multifactorial nature of neurological cancers and support precision oncology.

Collaborative platforms integrating XAI into tumor boards, electronic health records, and decision-support systems will enhance multidisciplinary care. As more real-world evidence accumulates, XAI models will continue to evolve, improving accuracy and trustworthiness.

Ultimately, explainable AI has the potential to transform neurological oncology by reducing diagnostic delays, optimizing therapies, and empowering patients and clinicians alike. By addressing the transparency gap, XAI paves the way for responsible and effective use of AI in combating one of the most challenging categories of human malignancies.

Conclusion

Neurological cancers remain among the most devastating diseases, with profound impacts on patients, families, and healthcare systems. While AI offers unprecedented opportunities to enhance diagnosis, treatment, and prognosis, its adoption has been limited by concerns over opacity and trust. Explainable AI addresses this challenge by making model outputs transparent, interpretable, and clinically meaningful.

By illuminating the reasoning behind predictions, XAI empowers clinicians to make informed decisions, enhances patient trust, reduces diagnostic and therapeutic errors, and fosters ethical integration of AI into practice. Its applications in imaging, genomics, and clinical decision-making demonstrate tangible benefits in reducing the burden of neurological cancers.

As research advances, XAI will play a central role in bridging the gap between cutting-edge computational tools and human-centered clinical care. Through transparency and accountability, explainable AI ensures that technological innovation translates into real-world improvements in outcomes, ultimately alleviating the immense burden of neurological cancers.

3. EXPLAINABLE AI IN REDUCING THE BURDEN OF GASTROINTESTINAL CANCERS

Background

Gastrointestinal cancers are among the most prevalent and deadly forms of malignancy worldwide, encompassing a wide range of tumors affecting the esophagus, stomach, pancreas, liver, gallbladder, and colon. These cancers account for a significant proportion of global cancer mortality, with colorectal, gastric, liver, and pancreatic cancers ranking among the top causes of cancer-related deaths. Their impact extends beyond individual patients, burdening healthcare systems with high diagnostic costs, complex treatments, and long-term palliative care needs.

The challenges of gastrointestinal cancers lie in their insidious onset, late diagnosis, and biological heterogeneity. Early stages often present with vague symptoms such as abdominal discomfort or dyspepsia, which can be mistaken for benign conditions. As a result, many patients are diagnosed only at advanced stages, where curative treatment options are limited. Endoscopic screening and imaging modalities such as computed tomography, magnetic resonance imaging, and positron emission tomography play

pivotal roles in detection and staging, yet interpretation is time-consuming and subject to inter-observer variability.

Molecular profiling has revealed that gastrointestinal cancers are driven by diverse genetic and epigenetic alterations, with certain biomarkers such as KRAS mutations in colorectal cancer or HER2 overexpression in gastric cancer influencing prognosis and therapy. However, integrating genomic insights into clinical practice remains challenging due to the overwhelming complexity and volume of data generated by sequencing technologies.

Artificial intelligence, particularly machine learning and deep learning, has emerged as a transformative force in oncology. AI systems can detect subtle imaging features, analyze vast genomic datasets, and generate predictive models for survival, recurrence, and treatment response. In gastrointestinal cancers, AI has been applied to tasks such as detecting polyps in colonoscopy, differentiating benign from malignant liver lesions, and predicting outcomes of chemotherapy or immunotherapy.

Despite its promise, AI adoption has been limited by the "black box" nature of many models. Clinicians and patients are hesitant to trust predictions when the underlying reasoning is hidden. Explainable AI (XAI) addresses this limitation by creating models whose decision-making process is transparent and interpretable. XAI allows healthcare providers to understand why a model recommended a certain diagnosis, highlighted a suspicious lesion, or predicted a specific treatment outcome. This interpretability builds trust, supports accountability, and ensures that AI complements rather than replaces human expertise.

In the context of gastrointestinal cancers, explainable AI can reduce the burden by enabling earlier diagnosis, improving therapeutic decisions, and guiding personalized care while maintaining transparency. Its integration into endoscopy, imaging, genomics, and clinical workflows provides a pathway toward more effective and ethical cancer management.

The Burden of Gastrointestinal Cancers

The global burden of gastrointestinal cancers is immense. Colorectal cancer remains one of the most commonly diagnosed malignancies worldwide and a leading cause of mortality, particularly in high-income countries. Gastric cancer, though declining in incidence in certain regions, continues to be prevalent in East Asia and carries a poor prognosis. Hepatocellular carcinoma associated with chronic viral hepatitis and metabolic disorders imposes a heavy toll in both Asia and Africa. Pancreatic cancer, despite

being less common, is notorious for its lethality due to late detection and aggressive biology.

Patients face not only the risk of death but also significant morbidity. Symptoms such as gastrointestinal bleeding, pain, malnutrition, and cachexia severely impair quality of life. Treatments including surgery, chemotherapy, radiotherapy, and immunotherapy may prolong survival but often carry debilitating side effects. The economic burden is equally substantial, involving direct medical costs, indirect costs from lost productivity, and the emotional toll on families.

The complexity of gastrointestinal cancers stems from their heterogeneity at multiple levels. Morphological differences complicate pathological classification, while diverse genomic and epigenomic alterations influence treatment responses. Tumor microenvironments vary widely, with immune cell infiltration and stromal interactions shaping prognosis. These factors necessitate advanced tools capable of integrating and interpreting multidimensional data, which is where explainable AI becomes crucial.

The Role of Artificial Intelligence in Gastrointestinal Oncology

Artificial intelligence has shown enormous promise in gastrointestinal oncology by augmenting diagnostic accuracy, improving risk stratification, and personalizing therapies. Deep learning models trained on endoscopic videos detect polyps with remarkable sensitivity, reducing miss rates compared with traditional human observation. AI-enhanced imaging techniques differentiate between malignant and benign lesions with higher precision, assisting radiologists in liver or pancreatic cancer diagnosis.

In pathology, AI algorithms analyze digital slides to identify histological patterns predictive of tumor grade or aggressiveness. In genomics, machine learning processes large-scale sequencing data to uncover mutational signatures associated with prognosis or therapeutic response. Predictive models combining clinical and molecular variables provide individualized survival estimates, enabling more informed treatment planning.

Despite these advances, most AI systems operate as opaque models that provide outputs without explanations. While they may achieve high accuracy, clinicians remain reluctant to rely on predictions they cannot interpret, particularly in high-stakes decisions involving cancer care. Without transparency, AI risks being perceived as untrustworthy or even unsafe.

Foundations of Explainable AI

Explainable AI seeks to bridge the gap between accuracy and transparency. Interpretability refers

to how easily a human can understand the internal mechanics of an AI system, while explainability encompasses both the interpretability and the ability to communicate reasoning to end-users.

There are two main strategies in XAI. The first is building inherently interpretable models, such as decision trees, generalized linear models, and rule-based systems, where reasoning is transparent by design. The second involves post hoc explanations applied to complex models like deep neural networks. These include techniques such as feature importance ranking, local interpretable model-agnostic explanations (LIME), SHAP (Shapley additive explanations), saliency maps, and counterfactual explanations.

For example, in an AI system detecting gastric cancer from endoscopic images, a saliency map can highlight the exact lesion area influencing the decision. In survival prediction models, SHAP values can show which clinical features or gene mutations contributed most to an individual patient's prognosis. This transparency ensures that clinicians can verify the plausibility of AI outputs and detect potential biases.

Applications of Explainable AI in Endoscopy

Endoscopy is central to detecting and managing gastrointestinal cancers. Colonoscopy remains the gold standard for colorectal cancer screening, while upper endoscopy is essential for gastric and esophageal cancers. However, even experienced endoscopists miss small or flat lesions, leading to interval cancers.

AI systems trained on endoscopic images and videos can improve lesion detection and characterization. Explainability enhances these systems by ensuring that highlighted regions correspond to genuine pathological features rather than artifacts. Heatmaps generated by XAI methods can show which parts of a polyp influenced malignancy prediction, allowing endoscopists to confirm the model's validity.

In addition, XAI can help differentiate between adenomatous and hyperplastic polyps, which have distinct management implications. By revealing the texture, color, or vascular patterns considered by the algorithm, XAI assists clinicians in making confident decisions during real-time procedures. This reduces unnecessary polypectomies while ensuring malignant lesions are not overlooked.

In gastric cancer screening, XAI supports the identification of early neoplastic changes in high-prevalence regions. Transparent explanations allow gastroenterologists to validate that AI models recognize subtle mucosal irregularities or discolorations that align with known risk patterns. Such insights improve trust and facilitate integration into routine clinical practice.

Explainable AI in Imaging of Gastrointestinal Cancers

Radiological imaging is indispensable in diagnosing, staging, and monitoring gastrointestinal cancers. Computed tomography and magnetic resonance imaging provide critical information on tumor size, invasion depth, and metastasis. Yet interpretation requires expertise, and discrepancies between radiologists can lead to variable outcomes.

AI-based imaging analysis enhances accuracy in detecting liver metastases, characterizing pancreatic masses, or staging colorectal cancer. With XAI, these models become more clinically actionable. For instance, a saliency map highlighting the borders of a pancreatic lesion helps confirm whether the model relied on appropriate anatomical structures. Feature importance analysis may reveal that lesion enhancement patterns on contrast-enhanced CT were key determinants of malignancy prediction.

In hepatocellular carcinoma, XAI applied to radiomics models can clarify which imaging features correlate with microvascular invasion, a crucial prognostic factor. By making these relationships explicit, clinicians gain confidence in adopting AI recommendations and can better explain treatment strategies to patients.

Genomic and Molecular Applications of Explainable AI

Genomic medicine has revolutionized the understanding of gastrointestinal cancers, uncovering driver mutations and molecular subtypes with therapeutic relevance. For example, KRAS mutations in colorectal cancer predict resistance to EGFR-targeted therapies, while HER2 overexpression in gastric cancer provides opportunities for targeted treatment.

AI models processing genomic datasets can identify complex interactions between mutations, gene expression, methylation patterns, and clinical outcomes. Explainable AI ensures these predictions are biologically meaningful rather than spurious. By using SHAP values or LIME, researchers can identify which genomic alterations drive survival predictions, confirming alignment with known molecular biology.

In colorectal cancer, an explainable model may reveal that microsatellite instability status and BRAF mutations are central to predicting response to immunotherapy. In hepatocellular carcinoma, XAI may highlight the role of TERT promoter mutations or immune-related gene signatures in shaping prognosis. Such transparency prevents overreliance on black-box predictions and enables clinicians to validate AI-driven insights against established biological evidence.

Furthermore, explainable AI supports multimodal integration, where genomic data are combined with imaging and clinical features. By explicitly quantifying the contribution of each data modality, XAI facilitates comprehensive and interpretable prognostic models, paving the way for precision oncology.

Clinical Decision-Making with Explainable AI

Clinical management of gastrointestinal cancers requires complex decision-making involving surgery, systemic therapies, and supportive care. Explainable AI enhances this process by providing interpretable evidence that supports both clinicians and patients.

For surgical planning, models predicting postoperative complications or survival can indicate which features—such as comorbidities, tumor stage, or nutritional status—drive the predictions. This helps surgeons weigh risks and benefits more transparently. In radiotherapy, explainable models clarify why certain dosing strategies are recommended, showing how tumor volume or organ-at-risk proximity influenced the optimization.

In systemic therapy, AI models predicting chemotherapy response can indicate the influence of molecular markers or clinical history. When clinicians and patients understand why a therapy is recommended, adherence improves, and shared decision-making is enhanced.

Multidisciplinary tumor boards benefit significantly from explainable AI. Models that integrate radiology, pathology, genomics, and clinical records can present interpretable summaries, highlighting the relative contributions of each factor. This ensures recommendations align with collective clinical expertise and promotes consensus.

Reducing the Healthcare Burden through Explainable AI

The burden of gastrointestinal cancers extends to healthcare systems, with high costs associated with screening, diagnostics, surgery, systemic therapies, and palliative care. Explainable AI can alleviate this burden by improving efficiency, reducing diagnostic errors, and ensuring resource optimization.

Early detection through XAI-enhanced endoscopy reduces the need for costly advanced treatments. Transparent differentiation between malignant and benign lesions prevents unnecessary surgeries and associated complications. Accurate prediction of treatment response ensures that patients receive the most effective therapy, minimizing financial waste and reducing exposure to ineffective drugs.

By clarifying model reasoning, XAI reduces

medicolegal risks and enhances regulatory compliance, encouraging broader adoption. Patients who understand the rationale behind AI-assisted recommendations are more likely to trust and follow medical advice, improving treatment outcomes and reducing long-term care costs.

Ethical and Regulatory Considerations

The ethical use of AI in gastrointestinal oncology requires transparency, fairness, and accountability. Black-box models risk perpetuating biases, such as disparities based on ethnicity, socioeconomic status, or geographic region. Explainable AI mitigates these risks by exposing decision-making pathways, allowing detection and correction of biases.

Regulatory agencies increasingly demand explainability in medical AI systems to ensure safety and reliability. Transparent models are easier to validate and audit, accelerating approval and clinical integration. XAI also supports informed consent, as clinicians can explain predictions to patients in comprehensible terms, empowering them to participate actively in decision-making.

Future Directions of Explainable AI in Gastrointestinal Cancers

Future progress in explainable AI will focus on enhancing usability and integration into clinical workflows. Advances in visualization techniques, interactive dashboards, and natural language explanations will make AI outputs more accessible to non-technical clinicians.

Multimodal XAI systems will gain importance, providing simultaneous explanations across imaging, genomics, pathology, and clinical data. These systems will mirror the complexity of real-world oncology, where decisions require holistic perspectives.

Explainable AI will also play a role in clinical trials, where interpretable predictive models can guide patient selection and optimize trial design. This accelerates drug development and ensures equitable access to novel therapies.

As healthcare systems increasingly embrace digital transformation, XAI will integrate into electronic health records, decision-support tools, and telemedicine platforms. This widespread integration will democratize access to advanced oncology care and reduce global disparities.

Conclusion

Gastrointestinal cancers represent a major global health challenge due to their prevalence, lethality, and complexity. Artificial intelligence offers transformative potential in detection, diagnosis, prognosis, and treatment personalization. However, the black-box nature of many AI models

has limited their clinical adoption.

Explainable AI addresses this challenge by providing transparency and interpretability, enabling clinicians to trust, validate, and act upon AI recommendations. Its applications span endoscopy, imaging, genomics, and clinical decision-making, offering tangible benefits in reducing misdiagnosis, improving treatment outcomes, and optimizing healthcare resources.

Through ethical integration, regulatory alignment, and continued innovation, explainable AI can transform the management of gastrointestinal cancers, ultimately reducing their burden on patients, families, and societies. By fostering trust and accountability, XAI ensures that technological advances translate into real-world improvements in care, bringing us closer to a future where gastrointestinal cancers are diagnosed earlier, treated more effectively, and managed with greater compassion and precision.

4. EXPLAINABLE AI IN REDUCING THE BURDEN OF BREAST AND LUNG CANCERS

Background

Recent advancements in artificial intelligence (AI) and computer-aided diagnostic (CAD) systems have considerably enhanced the precision and reproducibility of early cancer detection. Breast and lung cancers are among the most prevalent and fatal malignancies worldwide, contributing significantly to global morbidity and mortality. One of the major challenges in managing these diseases is their frequent diagnosis at advanced stages, which drastically reduces treatment effectiveness and survival rates. Therefore, early and accurate detection is crucial for improving clinical outcomes.

Breast Cancer Diagnosis and the Role of AI

In the context of breast cancer, ultrasound is widely used because of its accessibility, non-invasive nature, and lack of radiation exposure. However, the accurate interpretation of ultrasound images requires a high level of radiological expertise, often resulting in variability among observers and the potential for diagnostic errors. To address this challenge, CAD systems have been developed that integrate AI to assist in interpretation and enhance diagnostic accuracy. These systems are particularly impactful in resource-limited settings, where access to highly skilled radiologists may be scarce. Although these models demonstrate performance comparable to or even exceeding that of experts, their clinical adoption is often restricted by limited transparency and interpretability. Improving explainability in AI models is critical, particularly given the high consequences of misdiagnosis in breast cancer.

Lung Cancer Imaging and Deep Learning

Similarly, lung cancer diagnosis has traditionally relied on the manual assessment of computed tomography (CT) images by radiologists, a time-consuming process that is vulnerable to human error. Because early-stage tumors often present subtle imaging features, they may be overlooked or undetected. Lung and bronchus cancers are strongly associated with smoking and frequently arise in the central lung zones. Modern CAD systems have been introduced to streamline and standardize the assessment of CT images. Nevertheless, existing models often encounter challenges in detecting early lesions and in producing clinically relevant interpretations. The integration of deep learning (DL), especially convolutional neural networks (CNNs), has

transformed this field by enabling automated hierarchical feature extraction and substantially improving diagnostic performance. However, the black-box nature of CNNs raises concerns regarding generalizability, explainability, and dependence on large annotated datasets.

Bridging the Gap with Explainable AI

To address these concerns, explainable AI (XAI) techniques such as gradient-weighted class activation mapping (Grad-CAM) have been incorporated into CAD frameworks. These approaches help visualize critical regions of images that contribute to AI-based decisions, thereby increasing clinicians' trust and supporting more interpretable outputs. This transparency not only strengthens diagnostic accuracy but also facilitates the integration of AI systems into routine clinical practice.

Mortality Prediction and Limitations of Traditional Models

Beyond detection, AI has also been applied to predict mortality in breast and lung cancers. Conventional statistical methods, including Poisson-gamma models, state-space frameworks, and Bayesian approaches, often struggle to capture the complex and nonlinear interactions among risk variables such as smoking prevalence, environmental pollution, and social determinants. For example, Poisson-based approaches often assume homogeneous risk levels across populations, which can lead to biased predictions when environmental or individual variations exist. Although advanced probabilistic models such as Poisson-Gamma can address issues like overdispersion, they may still lack sufficient flexibility to represent complex multivariate dependencies. Furthermore, spatial and socioeconomic heterogeneity exerts strong influence on cancer outcomes, yet region-specific and nonlinear interactions are often underrepresented in traditional models. The interplay between behavioral, environmental, and social factors requires models capable of adapting to contextual variations and hidden correlations, which conventional statistical frameworks frequently fail to accommodate.

Machine Learning and Public Health Integration

In contrast, machine learning (ML) techniques can effectively model these relationships, providing more tailored regional predictions and supporting timely public health responses. These technologies play an essential role in developing comprehensive strategies for disease prevention and management. Such approaches are especially effective in integrating diverse data sources, strengthening risk stratification, and informing well-rounded disease prevention programs. By

doing so, ML not only advances predictive accuracy but also broadens the scope of public health integration.

Importance of Explainability (XAI) in Clinical Practice

To ensure that AI-driven insights are interpretable and actionable, the integration of XAI into medical applications is indispensable. AI has shown remarkable promise across healthcare, including in diagnostics, imaging, drug discovery, and personalized treatment planning. However, its adoption is frequently hindered by opaque decision-making processes. XAI enhances transparency and fosters trust by helping clinicians and patients understand, monitor, and validate AI-generated recommendations. This approach supports fairer healthcare delivery by detecting and mitigating biases, strengthening equity, and empowering individuals. The case of breast cancer serves as a clear example where explainability is especially important, underscoring the broader role of XAI across medical domains.

Conclusion

This review emphasizes the transformative role of XAI in improving the diagnostic and prognostic management of breast and lung cancers. While AI technologies have made significant advancements in medical imaging and mortality prediction, their application in clinical practice is often constrained by their opaque black-box characteristics. XAI bridges this gap by making AI models more interpretable and trustworthy, thereby enabling clinicians to make informed decisions based on algorithmic outputs. In high-stakes fields such as oncology, this level of clarity is essential not only for patient safety but also for building confidence among clinicians, patients, and healthcare institutions. Moreover, XAI contributes to healthcare equity by uncovering biases and adapting models to diverse populations and settings. In this way, XAI is not merely a technical enhancement but a fundamental step toward ethical, transparent, and effective cancer care.

5. EXPLAINABLE AI IN REDUCING THE BURDEN OF UROGENITAL CANCERS

Background

Urogenital cancers represent a diverse and challenging group of malignancies that affect the kidneys, bladder, prostate, testes, and other structures of the urinary and reproductive systems. These cancers account for a significant proportion of the global cancer burden, with prostate and bladder cancers ranking among the most frequently diagnosed malignancies in men, while kidney cancer contributes substantially to cancer-related mortality worldwide. Testicular cancer, though relatively rare, is the most common malignancy in young adult males, and its treatment outcomes depend heavily on timely detection and individualized therapy.

The burden of urogenital cancers is compounded by late detection, complex tumor biology, and the long-term impact of treatment on quality of life. For instance, prostate cancer may present as an indolent disease in some men, while in others it progresses aggressively with metastatic potential. Differentiating between these forms is critical for guiding therapy but remains difficult with current clinical tools. Similarly, bladder

cancer is characterized by high recurrence rates, necessitating frequent surveillance cystoscopies that are invasive and costly. Kidney cancers, particularly renal cell carcinoma, often present incidentally but can progress silently until advanced stages.

The heterogeneity of these cancers across genetic, molecular, and clinical dimensions complicates treatment decisions. While precision medicine approaches, such as the use of targeted therapies and immunotherapies, have improved outcomes in certain subgroups, their effectiveness varies among patients. Clinicians face the ongoing challenge of integrating imaging, pathology, genomic, and clinical data into cohesive treatment strategies.

Artificial intelligence has emerged as a transformative tool in oncology by enabling automated image analysis, predictive modeling, and integration of large-scale datasets. In urogenital cancers, AI has shown promise in tasks such as prostate cancer detection on magnetic resonance imaging, bladder tumor segmentation, and prediction of treatment response based on histopathological and genomic features. Yet, the adoption of AI has been hindered by the opacity of many models. Clinicians often hesitate to rely on systems whose decision-making processes remain hidden, especially in high-stakes clinical contexts where transparency is essential.

Explainable artificial intelligence addresses this challenge by creating models that not only perform well but also provide interpretable and transparent reasoning. This interpretability fosters trust among clinicians and patients, ensures accountability, and facilitates regulatory approval. In the context of urogenital cancers, explainable AI can reduce the disease burden by improving diagnostic accuracy, guiding treatment selection, and enhancing patient engagement, all while ensuring that decision-making remains clinically meaningful and ethically sound.

The Burden of Urogenital Cancers

Urogenital cancers impose a profound global health burden, both in terms of incidence and mortality, as well as their economic and psychosocial impact. Prostate cancer is the most frequently diagnosed cancer among men in many regions, with incidence rates rising due to aging populations and increased use of prostate-specific antigen testing. Despite improvements in survival, prostate cancer continues to cause significant morbidity, particularly when advanced disease leads to bone metastases, urinary dysfunction, and sexual impairment.

Bladder cancer is a costly malignancy to manage, primarily due to its high recurrence rates and the need for lifelong surveillance. Patients often undergo repeated cystoscopies,

biopsies, and treatments such as intravesical therapy, which add to the financial and physical burden. Kidney cancers contribute substantially to mortality, with renal cell carcinoma being the most common subtype. These tumors are often detected incidentally during imaging for unrelated conditions, yet advanced cases carry a poor prognosis despite recent therapeutic advances.

Testicular cancer, while relatively rare, has a unique psychosocial burden due to its impact on younger men at the peak of their productive years. Treatment, although often curative, can affect fertility, hormonal balance, and psychological well-being.

The clinical complexity of these cancers often results in challenging treatment decisions. For example, distinguishing between indolent and aggressive prostate cancer is crucial to avoid overtreatment or undertreatment. Similarly, selecting systemic therapies for advanced kidney or bladder cancers requires weighing potential benefits against toxicity and cost. These challenges necessitate tools that can integrate vast amounts of clinical, imaging, and genomic information to support evidence-based decision-making, a need that explainable AI is well-positioned to meet.

The Role of Artificial Intelligence

in Urogenital Oncology

Artificial intelligence has demonstrated considerable potential in enhancing the management of urogenital cancers. Deep learning models applied to multiparametric MRI have improved prostate cancer detection, enabling identification of clinically significant tumors that might be missed by radiologists. AI algorithms trained on histopathological slides can classify prostate or bladder tumor grade with high accuracy, assisting pathologists in reducing inter-observer variability.

Radiomics, the extraction of quantitative features from medical imaging, has been applied to kidney and bladder cancers to predict tumor stage, grade, and treatment response. When combined with machine learning, radiomics can reveal subtle imaging biomarkers invisible to the human eye. In genomics, AI algorithms have been used to identify prognostic signatures from large sequencing datasets, guiding precision therapies.

Clinical decision support systems powered by AI can integrate multimodal data to provide individualized risk predictions. For instance, models predicting biochemical recurrence after prostatectomy or response to immunotherapy in renal cell carcinoma can help tailor treatment strategies. Despite these advances, the black-box nature of many AI models limits clinical adoption. Without clear explanations,

clinicians remain cautious about incorporating AI recommendations into practice, particularly when model predictions conflict with established guidelines or clinical judgment.

Foundations of Explainable AI

Explainable AI aims to make the decision-making processes of AI systems transparent and interpretable. Interpretability refers to the ability of humans to understand how inputs are transformed into outputs, while explainability encompasses the capacity to communicate this reasoning effectively to users.

There are two broad approaches to explainability. The first involves inherently interpretable models, such as logistic regression, decision trees, or rule-based systems, where the reasoning is straightforward. The second involves post hoc explanation techniques applied to complex models like deep neural networks. Methods such as feature importance rankings, local interpretable model-agnostic explanations, Shapley additive explanations, and saliency maps allow users to understand which features most influenced a given prediction.

In urogenital cancers, explainability ensures that AI predictions are aligned with clinical knowledge. For example, a model predicting aggressive prostate cancer should highlight relevant features such as PSA level, MRI lesion characteristics, and

Gleason score rather than spurious correlations. Similarly, an AI system for bladder tumor recurrence should base its predictions on known risk factors such as tumor grade and multiplicity, not irrelevant data artifacts. By making reasoning transparent, XAI builds confidence and facilitates integration into clinical decision-making.

Applications of Explainable AI in Imaging

Imaging is central to the management of urogenital cancers, from detection to treatment monitoring. Multiparametric MRI is widely used for prostate cancer diagnosis, yet interpretation requires expertise and is subject to variability. AI models have demonstrated high accuracy in detecting clinically significant tumors, and XAI enhances these models by showing radiologists which regions of the prostate influenced predictions. Saliency maps can highlight suspicious lesions, allowing radiologists to validate AI reasoning and avoid false positives caused by artifacts.

In bladder cancer, imaging plays a crucial role in staging and monitoring. AI-based segmentation models can delineate bladder tumors on CT or MRI, and explainability ensures that the contours are clinically appropriate. For kidney cancer, radiomics-based models predicting histological subtype or response to therapy can use feature

attribution methods to show which imaging characteristics drive predictions, aligning results with radiological expertise.

These explainable imaging tools reduce inter-observer variability, enhance diagnostic confidence, and support more accurate treatment planning, ultimately reducing the burden of disease.

Pathology and Explainable AI

Histopathology remains the gold standard for diagnosing urogenital cancers. However, pathologists face growing workloads as cancer incidence rises. AI algorithms analyzing digital pathology slides can identify tumor regions, grade prostate cancer, or classify bladder cancer subtypes. Explainable AI ensures that these classifications are based on relevant morphological features.

For example, in prostate cancer grading, an XAI model can highlight glandular structures and cellular patterns that drove its classification of Gleason grade. This allows pathologists to verify model outputs, reducing the risk of misclassification. In bladder cancer, explainable models can show which histological patterns indicate muscle invasion, a critical determinant of treatment strategy. Such transparency enhances confidence in AI-assisted pathology and facilitates adoption in clinical practice.

Genomic and Molecular Applications of Explainable AI

Genomic profiling has revealed numerous biomarkers in urogenital cancers. In prostate cancer, mutations in DNA repair genes such as BRCA1 and BRCA2 predict sensitivity to PARP inhibitors. In kidney cancer, mutations in VHL and PBRM1 influence disease biology and therapeutic response. In bladder cancer, alterations in FGFR3 and TP53 have prognostic and therapeutic implications.

AI models can integrate these complex datasets to predict prognosis and therapy response. Explainable AI ensures that such predictions are grounded in meaningful biology. For instance, an XAI model predicting immunotherapy response in renal cell carcinoma might reveal that gene expression profiles of immune checkpoint pathways were key drivers, aligning with clinical expectations. In bladder cancer, XAI could highlight the contribution of FGFR3 mutations in predicting response to targeted therapy, supporting clinical decision-making.

By clarifying how genomic features influence predictions, XAI facilitates the translation of complex molecular insights into actionable clinical strategies.

Clinical Decision-Making

with Explainable AI

Treatment of urogenital cancers requires careful balancing between efficacy, toxicity, and quality of life. Explainable AI enhances clinical decision-making by providing transparent predictions that clinicians can interpret and trust.

In prostate cancer, models predicting disease progression after active surveillance can indicate which variables—such as PSA velocity, MRI findings, and biopsy results—drive predictions. This helps clinicians and patients weigh the risks of surveillance versus definitive treatment. In bladder cancer, XAI models predicting recurrence risk can show whether tumor grade, stage, or patient comorbidities contributed most, enabling personalized surveillance protocols.

In advanced kidney cancer, explainable models predicting response to immunotherapy can clarify the role of clinical and molecular features, helping oncologists choose between immune checkpoint inhibitors, targeted therapies, or combination regimens. Such interpretability fosters shared decision-making, where patients can understand the rationale behind recommendations and actively participate in their care.

Reducing Healthcare Burden through Explainable AI

The healthcare burden of urogenital cancers includes high costs of treatment, repeated surveillance procedures, and long-term management of side effects. Explainable AI can reduce this burden by improving diagnostic efficiency, minimizing unnecessary interventions, and guiding optimal therapy selection.

For example, in prostate cancer, XAI-assisted MRI interpretation reduces unnecessary biopsies by clarifying which lesions warrant further investigation. In bladder cancer, transparent recurrence prediction models help tailor surveillance intervals, reducing the frequency of unnecessary cystoscopies while ensuring timely detection of recurrences. In kidney cancer, explainable prediction of therapy response prevents patients from undergoing costly and toxic treatments unlikely to benefit them.

By reducing overtreatment, avoiding ineffective therapies, and enhancing resource allocation, XAI contributes to more sustainable healthcare delivery while improving patient outcomes.

Ethical and Regulatory Considerations

Ethical deployment of AI in urogenital oncology requires transparency, accountability, and fairness. Black-box models risk perpetuating biases based on demographic or socioeconomic factors. Explainable AI mitigates these risks by making model reasoning visible, enabling developers and clinicians to identify and correct

biases.

From a regulatory perspective, agencies increasingly emphasize explainability as a requirement for clinical approval of AI systems. Transparent models are easier to validate, audit, and monitor, accelerating their integration into clinical workflows. Explainability also supports informed consent by enabling clinicians to explain AI-derived recommendations to patients, empowering them to make informed choices.

Future Directions of Explainable AI in Urogenital Cancers

The future of XAI in urogenital cancers lies in multimodal integration, where imaging, pathology, genomics, and clinical data are combined into comprehensive predictive models. Explainability will be crucial to ensure that the contributions of each modality are clear and clinically meaningful.

Advances in visualization techniques and user-friendly interfaces will make XAI outputs more accessible to clinicians. Interactive dashboards could allow oncologists to explore how different variables affect predictions, fostering deeper understanding and trust.

Explainable AI will also play a role in precision oncology clinical trials, guiding patient selection and monitoring treatment response. By clarifying model reasoning, XAI enhances trial transparency and accelerates drug development.

Integration into electronic health records and clinical decision support systems will ensure that XAI becomes part of routine practice, improving efficiency and equity in cancer care.

Conclusion

Urogenital cancers impose a significant global burden due to their prevalence, heterogeneity, and long-term management challenges. Artificial intelligence offers transformative potential in enhancing diagnosis, prognosis, and treatment, yet adoption is limited by the opacity of many models. Explainable AI addresses this challenge by providing transparency, interpretability, and accountability. By clarifying how predictions are made, XAI fosters trust, supports clinical decision-making, and enhances patient engagement. Its applications span imaging, pathology, genomics, and treatment planning, offering tangible benefits in reducing misdiagnosis, optimizing therapies, and alleviating healthcare costs. As explainable AI continues to evolve, its integration into urogenital oncology holds the promise of transforming cancer care, reducing disease burden, and advancing toward a future where technology and human expertise work together to achieve better outcomes for patients worldwide.

6. EXPLAINABLE AI IN REDUCING THE BURDEN OF SKIN AND SOFT TISSUE CANCERS

Background

Skin and soft tissue cancers represent a significant global health concern, encompassing a wide spectrum of malignant conditions that include melanoma, non-melanoma skin cancers such as basal cell carcinoma and squamous cell carcinoma, and rare but aggressive malignancies like sarcomas. Collectively, these cancers impose a considerable clinical, societal, and economic burden. Skin cancers alone are among the most common malignancies worldwide, with their incidence steadily increasing due to risk factors such as ultraviolet radiation exposure, aging populations, and lifestyle patterns. Meanwhile, soft tissue sarcomas, though less common, are particularly challenging due to their heterogeneity, late presentation, and high recurrence rates.

Traditional approaches to diagnosing, treating, and monitoring these cancers rely on dermatologic examinations, imaging modalities, biopsy, histopathological evaluation, and a combination of surgery, radiotherapy, and systemic therapies. While these methods have

advanced substantially in the past decades, they still face considerable limitations. Clinical diagnosis often depends on subjective evaluation by physicians, leading to variability in accuracy. Histological assessment, though considered the gold standard, requires invasive procedures and can be time-consuming. Moreover, treatment decisions frequently rest on complex and multidimensional clinical data, where prognostic uncertainty complicates personalized care.

The rise of artificial intelligence (AI) has brought new opportunities to address these challenges. Machine learning and deep learning algorithms have already shown impressive performance in cancer detection, classification, and outcome prediction. In dermatology, AI-based image analysis tools have achieved dermatologist-level accuracy in recognizing malignant lesions from dermoscopic and photographic images. Similarly, AI systems analyzing radiological scans, pathology slides, and genomic data are increasingly aiding the early detection and treatment of soft tissue malignancies.

However, one of the main criticisms of conventional AI models is their lack of interpretability. These systems often function as “black boxes,” generating predictions without providing clear explanations for their reasoning. This opacity raises concerns in clinical contexts where transparency, trust, accountability, and alignment with medical ethics are critical. Patients and clinicians alike demand not just accurate predictions but also understandable and trustworthy insights that can guide shared decision-making.

Explainable AI (XAI) seeks to resolve this issue by developing models that are interpretable, transparent, and capable of providing meaningful explanations for their predictions. XAI tools employ various techniques, such as feature attribution, visualization methods, rule-based reasoning, and surrogate models, to reveal the decision-making processes underlying AI outputs. This interpretability bridges the gap between technical accuracy and clinical usability, enabling physicians to verify, validate, and contextualize AI predictions within the framework of medical knowledge and patient care.

In the context of skin and soft tissue cancers, XAI holds transformative potential. By making AI predictions transparent, clinicians can better identify malignant lesions at an early stage, distinguish among subtypes, select optimal treatment strategies, monitor therapy responses, and engage patients in understanding their condition. In addition, XAI can contribute to research by uncovering novel patterns in molecular biology, identifying biomarkers, and supporting the development of personalized therapeutic interventions. Ultimately, the

integration of XAI into dermatology and oncology has the potential to reduce the clinical and societal burden of skin and soft tissue cancers through earlier detection, improved prognosis, optimized therapies, and enhanced patient trust in digital health technologies.

The Burden of Skin and Soft Tissue Cancers

Skin cancer remains the most frequently diagnosed cancer worldwide, particularly in regions with high levels of sun exposure. Melanoma, although less common than basal cell carcinoma and squamous cell carcinoma, accounts for the majority of skin cancer-related deaths due to its aggressive nature and high metastatic potential. Despite advances in therapies such as immune checkpoint inhibitors and targeted agents, the prognosis of advanced melanoma remains guarded. Non-melanoma skin cancers, while often less aggressive, contribute substantially to healthcare costs and morbidity due to their high incidence, need for surgical interventions, and potential for disfigurement.

Soft tissue sarcomas are rare, comprising less than 1% of adult cancers, yet they represent a highly diverse group of malignancies arising from mesenchymal tissues such as muscle, fat, and connective tissue. Their rarity, combined with over 50 histological subtypes, makes accurate diagnosis challenging. Many patients present at an advanced stage, limiting curative options. Furthermore, the heterogeneity of sarcomas poses difficulties in predicting outcomes and selecting effective therapies, leading to significant unmet needs in clinical management.

The societal burden of these cancers extends beyond the clinical sphere. Patients often face prolonged treatment regimens, repeated hospital visits, psychological stress, cosmetic concerns, and impaired quality of life. The economic burden includes direct medical costs for diagnostics, therapies, surgeries, and hospitalizations, as well as indirect costs related to lost productivity and caregiving. Reducing this burden requires innovations that improve early detection, minimize unnecessary interventions, and optimize individualized care—areas where XAI can play a pivotal role.

The Role of Explainable AI in Dermatological Imaging

Dermatology is one of the earliest fields to embrace AI-driven imaging solutions. Deep convolutional neural networks (CNNs) trained on large datasets of dermoscopic and clinical images have achieved remarkable performance in distinguishing malignant from benign lesions. Nonetheless, clinical adoption has been hampered by concerns over interpretability. Physicians must

understand the rationale behind AI outputs before they can integrate them into diagnostic pathways or explain results to patients.

XAI provides tools to overcome these limitations. Heatmaps and saliency maps, for example, highlight regions of images that most influenced the AI's prediction, enabling clinicians to verify whether the system is focusing on biologically relevant features. Techniques such as Layer-wise Relevance Propagation (LRP), SHAP (SHapley Additive Explanations), and Grad-CAM (Gradient-weighted Class Activation Mapping) have been applied to dermoscopic images to provide visual explanations. These explanations not only enhance trust but also support training of clinicians by highlighting subtle features associated with malignancy.

For soft tissue tumors, imaging modalities such as MRI, CT, and ultrasound play critical roles in diagnosis and treatment planning. XAI applied to radiology can help detect tumors, characterize their aggressiveness, and distinguish among histological subtypes by making predictions transparent. Radiomics, which involves extracting quantitative features from medical images, becomes more clinically actionable when combined with XAI to demonstrate how specific features correlate with prognosis or treatment response. This allows radiologists and oncologists to justify AI-informed recommendations to patients and multidisciplinary teams.

Histopathology and Explainable AI

Histopathology remains the gold standard for diagnosing both skin and soft tissue cancers. Whole-slide imaging and digital pathology have paved the way for AI applications capable of automating cell detection, mitotic count, and tumor grading. However, pathologists are often reluctant to adopt black-box AI predictions without clear interpretability.

XAI offers solutions by linking image-based features to well-understood histological characteristics. For example, models can provide explanations by highlighting cell clusters, nuclear morphology, or tissue structures that drive predictions. By aligning outputs with known pathological criteria, XAI ensures that automated systems complement rather than replace human expertise. Additionally, interpretable models can help uncover new histological biomarkers or refine existing grading systems, further improving diagnostic accuracy.

Genomics, Biomarkers, and Explainable AI

Molecular profiling has become central to the management of skin and soft tissue cancers, particularly melanoma, where genomic alterations such as BRAF and NRAS mutations

guide targeted therapies. Similarly, sarcomas often exhibit specific genetic translocations or mutations that influence classification and treatment. AI models analyzing genomic data can identify complex patterns beyond human analytical capabilities, but without interpretability, such predictions remain clinically limited.

XAI can uncover how particular genetic features contribute to risk stratification or therapy selection, making molecular predictions actionable. For instance, interpretable models can show how combinations of mutations, expression levels, or epigenetic signatures drive treatment responses. This transparency allows oncologists to align AI findings with established molecular knowledge, supporting personalized treatment planning. Furthermore, XAI can assist in biomarker discovery by revealing which genomic features most strongly correlate with survival outcomes or resistance to therapies.

Treatment Planning and Prognosis

Treatment of skin and soft tissue cancers often requires complex decisions regarding surgery, radiation, systemic therapy, or combinations thereof. Prognostic models can aid clinicians by predicting recurrence risk, survival, and therapy response. However, without interpretability, clinicians may hesitate to rely on such models.

XAI enables risk models to provide not only numerical probabilities but also human-readable explanations. For example, a prognostic tool may explain that a patient's high recurrence risk is driven by tumor thickness, ulceration, and specific molecular markers. Such transparency enhances clinician confidence, facilitates patient counseling, and supports shared decision-making. In surgical planning, XAI-informed imaging models can help determine optimal excision margins by showing how tumor boundaries were identified, reducing the likelihood of incomplete resections.

Patient Engagement and Trust

Patients increasingly interact with digital health technologies, whether through smartphone apps for skin lesion monitoring or online portals providing prognostic information. For these tools to gain patient acceptance, they must be interpretable. XAI can provide patients with understandable explanations about why a lesion is concerning, why further testing is needed, or why a specific therapy is recommended.

Such transparency empowers patients, reduces anxiety, and enhances adherence to medical advice. For example, a patient may be more likely to accept an excisional biopsy if shown an AI-generated heatmap highlighting suspicious regions of their lesion. Similarly, explanations

about how specific risk factors contribute to prognosis can motivate lifestyle modifications and engagement in follow-up care.

Ethical and Regulatory Considerations

Adopting AI in healthcare raises ethical concerns about accountability, fairness, and transparency. Black-box models challenge principles of informed consent and clinician responsibility. XAI addresses these concerns by making predictions auditable and explanations accessible. This allows clinicians to validate AI outputs, ensures that patients understand recommendations, and supports compliance with emerging regulatory frameworks.

Regulatory bodies such as the European Union under its AI Act and the US Food and Drug Administration emphasize transparency and explainability as critical requirements for medical AI. XAI aligns with these standards, paving the way for safe and ethical deployment. Moreover, explainability mitigates risks of bias by making it easier to detect and correct models that systematically disadvantage specific patient populations.

Research and Future Directions

The field of XAI is rapidly evolving, with ongoing research focused on balancing interpretability and accuracy. For skin and soft tissue cancers, future directions include integrating multimodal data—combining imaging, pathology, genomics, and clinical records—into interpretable models that provide holistic predictions. Additionally, federated learning approaches allow models to learn from distributed datasets while preserving patient privacy, with XAI ensuring transparency in such collaborative systems.

Another emerging trend is the use of causal inference methods within XAI to distinguish correlation from causation, enabling more robust insights into disease mechanisms. For example, XAI may help disentangle whether a molecular alteration directly drives cancer progression or merely correlates with other pathogenic factors. This could accelerate biomarker discovery and therapeutic development.

The development of user-friendly XAI tools tailored for clinical workflows is equally important. Clinicians require explanations that are not only technically accurate but also clinically meaningful and time-efficient. Collaborative design involving clinicians, patients, and AI developers will be key to ensuring that XAI systems meet practical needs in dermatology and oncology.

Challenges in Implementing Explainable AI

Despite its promise, XAI faces several challenges in clinical translation. One issue is the trade-off between model complexity and interpretability. While deep learning models often provide higher accuracy, simpler models are easier to interpret. Striking a balance between the two remains an active area of research.

Another challenge lies in standardizing explanations. Different XAI techniques may provide varying interpretations for the same prediction, potentially causing confusion. Establishing guidelines for consistency and reliability of explanations will be essential. Additionally, explanations must be tailored to different stakeholders: clinicians may require technical detail, whereas patients need simple, accessible language.

Data availability and quality also limit the performance of XAI models. Large, diverse, and well-annotated datasets are required for training robust systems. Yet, data fragmentation, privacy regulations, and variability in imaging protocols hinder data sharing. Addressing these barriers will be critical to advancing XAI in skin and soft tissue cancers.

Conclusion

Skin and soft tissue cancers continue to impose a major clinical, economic, and societal burden. While AI technologies have demonstrated great potential in enhancing diagnosis, prognosis, and treatment, their lack of interpretability has restricted adoption in clinical practice. Explainable AI addresses this challenge by making predictions transparent, trustworthy, and actionable. In dermatology, pathology, radiology, and genomics, XAI enhances clinician confidence, improves patient engagement, supports ethical standards, and fosters biomarker discovery.

By integrating XAI into clinical workflows, healthcare systems can achieve earlier detection of malignant lesions, more accurate diagnoses, better individualized therapies, and improved patient outcomes. At the same time, research into novel XAI methods, multimodal data integration, and user-centered design will continue to expand its capabilities. Ultimately, the future of cancer care lies not only in the power of AI to analyze complex data but also in its ability to explain its reasoning in ways that resonate with both clinicians and patients. Explainable AI, therefore, represents a crucial step toward reducing the global burden of skin and soft tissue cancers while upholding the core principles of transparency, trust, and ethical medical practice.

7. EXPLAINABLE AI IN REDUCING THE BURDEN OF HEAD AND NECK CANCERS

Background

The burden of head and neck cancers (HNC) continues to rise globally, demanding innovative approaches to improve diagnosis, treatment, and prognosis. Among the various technological advances, Artificial Intelligence (AI) and its subfield of explainable AI (XAI) have received significant attention. These technologies present substantial potential in addressing the complexities of HNC, where clinical decisions often depend on subjective interpretation of medical images and patient data. AI-driven solutions, particularly when combined with radiomics, enable the extraction of meaningful insights from medical images and patient records, improving diagnostic precision and facilitating personalized treatment strategies. This chapter examines the role of explainable AI in reducing the burden of HNC, especially through improving the interpretability and clinical utility of predictive models used in HNC management.

Early Detection of Oral Cancer through Explainable AI

Oral cancer constitutes a significant portion of head and neck cancers, with high mortality rates largely due to delayed diagnosis and the complexity of clinical examination. Early detection is essential for improving survival rates, making AI-driven diagnostic tools highly valuable for early intervention. One such tool, the Lightweight Explainable Network (LWENet), combines convolutional neural networks (CNN) with label-guided attention (LGA) for accurate and interpretable oral cancer detection. By utilizing depth-wise separable convolutions, LWENet reduces computational overhead while ensuring efficiency for clinical use. The addition of axial multi-head self-attention (AMSA) based Vision Transformer (ViT) encoders further strengthens the model's ability to focus on significant features such as tissue texture and boundaries, which are essential for cancer detection. The application of Grad-CAM for visualizing the model's decision-making process enhances interpretability, allowing clinicians to understand how predictions are generated. In a study performed on the MOD and OCI datasets, LWENet achieved outstanding performance, with precision scores of 96.97 percent and 99.48 percent for oral cancer detection. This combination of high accuracy and interpretability makes LWENet a promising tool for early oral cancer detection, providing clinicians with a valuable second opinion to support timely treatment decisions.

AI-Based Radiomics in HNC

Radiomics, an emerging field applying quantitative analysis to medical imaging, has been integrated with AI to advance the management of head and neck cancers. Radiomics can extract a wide array of features from medical images, such as CT scans or MRIs, which characterize tumor phenotypes more objectively than traditional approaches. When paired with machine learning algorithms, these radiomic features help construct models capable of predicting cancer outcomes, including diagnosis, prognosis, and treatment response. Despite their potential, AI-based radiomics models face challenges related to model generalizability, data imbalance, and interpretability. However, the integration of explainable AI techniques, such as Local Interpretable Model-agnostic Explanations (LIME) and SHapley Additive exPlanations (SHAP), introduces transparency and allows clinicians to understand the factors influencing predictions. This improves trust in AI systems for decision-making in HNC management.

Machine Learning Explainability for Survival Outcomes in HNSCC

In head and neck squamous cell carcinoma (HNSCC), predicting survival outcomes is essential for guiding treatment strategies and patient management. Machine learning (ML) models

have demonstrated promise in predicting overall survival (OS) by integrating clinicopathological, treatment-related, and sociodemographic data. However, the use of ML models in clinical practice is restricted by their inherent lack of interpretability. Recent research has applied XAI techniques, including SHAP and LIME, to increase the transparency of ML models and to provide clinicians with critical insights into the most influential features for survival predictions. By clarifying the contributions of variables such as cancer stage, HPV status, and p16 protein levels, these models enable healthcare providers to make more informed and individualized treatment decisions for HNSCC patients. The addition of explainable AI tools ensures that predictions are not only accurate but also clinically actionable.

Radiomics and Deep Learning for Esophageal Cancer Grading

Although esophageal cancer is not directly classified as HNC, its treatment challenges share many similarities, particularly in the use of AI for tumor grading and prognosis prediction. A new framework for esophageal cancer grading employs both radiomics and deep learning techniques to classify cancer stages with greater accuracy. By combining CT imaging features with machine learning models such as XGBoost and Random Forest, the study developed a robust system for improving diagnostic accuracy and interpretability. For HNC, such frameworks could be adapted to enhance tumor staging, predict recurrence, and detect potential metastasis. Furthermore, the framework highlights the importance of model interpretability, ensuring that healthcare providers can trust the reasoning process when making treatment decisions.

Interpretable Models for Laryngeal Cancer Diagnosis

Laryngeal cancer, another major type of HNC, presents distinct diagnostic challenges, especially when depending on histopathological images. A recent study introduced a deep learning model using transformers for the grading of laryngeal squamous cell carcinoma (LSCC), which incorporates learned-parameter-free attention (LA) to minimize background noise in image data. This technique strengthens the model's capacity to focus on critical areas contributing to diagnosis. By including explainable AI techniques such as attention mechanisms, the model allows clinicians to identify which image features are most influential in the decision-making process. The ability to interpret how the model derives its conclusions is essential for clinical adoption, as it promotes trust and supports improved decision-making.

Predicting Survival in Laryngeal Squamous Cell Carcinoma

For laryngeal squamous cell carcinoma (LSCC), a practical online prediction platform has been developed to estimate patient survival over five years. This model, created with machine learning algorithms such as SVM and XGBoost, uses clinical and demographic data to predict patient outcomes. The incorporation of SHAP for model interpretation improves transparency, showing which clinical factors, including cancer stage and patient demographics, most strongly influence survival predictions. This is particularly significant in HNC, where personalized treatment planning is essential to improving patient outcomes. By providing clear and interpretable predictions, such platforms can guide clinical decisions and ensure interventions are tailored to individual patient needs.

Radiomics for Nasopharyngeal Carcinoma Prognostication

Nasopharyngeal carcinoma (NPC) is another subtype of head and neck cancer that creates diagnostic challenges, mainly due to late-stage detection and the absence of distinct early symptoms. Radiomics, combined with AI, addresses this by extracting detailed tumor characteristics from CT scans that can predict locoregional recurrence (LRR) and overall survival. By applying a model that integrates radiomic features with clinical data, predictions for LRR and survival outcomes have been substantially improved. This strategy not only strengthens prognostication but also supports personalized treatment approaches. The inclusion of AI enhances the accuracy and interpretability of these models, ensuring clinicians can make informed decisions by combining data-driven insights with clinical expertise.

Predicting Lymph Node Metastasis in Thyroid Cancer

Although thyroid cancer is not formally categorized within HNC, predicting metastasis in thyroid cancer is closely related to predicting lymph node involvement in head and neck cancers. A recent study applied delta radiomics derived from enhanced CT scans to predict peripheral lymph node metastasis (LNM) in thyroid cancer patients. By merging clinical and radiomics data, machine learning algorithms achieved high predictive accuracy. SHAP values were employed to improve model interpretability, making clear the contribution of each feature to the prediction. This interpretability is vital for clinical decision-making, as it provides clinicians with a transparent understanding of how tumor characteristics influence metastasis predictions. Such approaches can readily be adapted to predict lymph node involvement in HNC, thereby enhancing patient management.

Addressing Radiotherapy Toxicity Using AI

AI has also been implemented to predict the adverse effects of radiotherapy in HNC patients, particularly with respect to long-term side effects such as xerostomia and parotid gland shrinkage. A fuzzy logic-based machine learning model was developed to forecast these outcomes using radiomics data from CT scans. By combining diverse types of data including clinical, dosimetric, and radiomic information, AI models can predict the likelihood of these toxicities, enabling early interventions. The interpretability of the model is improved through fuzzy logic, which provides transparent rule-based classifiers. This transparency supports clinicians in understanding the rationale behind treatment adjustments, ensuring that decisions are grounded in comprehensive analysis of the available data.

Conclusion

The integration of explainable AI into the management of head and neck cancers offers great potential to reduce the burden of these diseases by improving diagnostic accuracy, treatment planning, and prognostication. By introducing transparency and interpretability, AI models empower clinicians to make better-informed decisions that are tailored to the specific needs of each patient. The future of HNC care depends on the ongoing development of these AI-based tools, ensuring they remain not only accurate but also understandable and practical in clinical applications.

8. EXPLAINABLE AI IN REDUCING THE BURDEN OF ORAL CANCERS

Background

Founded by John McCarthy in 1956, it is now evident that Artificial Intelligence (AI) has transformed our lives by simulating human thinking through its capacity to process data and recognize patterns. In addition to its role in other health industries such as medical and pharmacological fields, AI is now being widely applied in different areas of dentistry, with applications ranging from caries detection and prediction to diagnosing various diseases such as oral cancers.

More than 377,000 people globally each year are affected by oral cancer, with survival rates dropping significantly as the disease advances. Frequently developing as a progression of oral potentially malignant disorders (OPMD), early detection plays a critical role in saving patients. However, it remains challenging due to the subtle and often asymptomatic nature of this disease, which leads to delayed diagnoses and consequently poorer outcomes.

AI is effectively being used in the oncology field and shows significant promise in detecting OPMD and oral cancer. Recent research has

employed different algorithms of AI such as deep learning (DL), machine learning (ML), and image recognition to detect and classify oral cancer, to predict how malignant it may become, to estimate its progression and nodal metastasis, and ultimately to detect its recurrence rate.

JingWen Li and colleagues evaluated the diagnostic accuracy of AI-assisted clinical imaging in detecting OPMD and oral cancer, with a specific focus on comparing performance across different imaging modalities. The findings of seventeen studies involving various AI algorithms and imaging tools demonstrated that AI-assisted detection shows high diagnostic performance overall, with clinical photography yielding the highest diagnostic odds ratio (DOR = 77.772) and sensitivity (93.9 percent). The study concluded that AI, particularly when integrated with accessible tools such as clinical photography, holds substantial promise for enhancing the early diagnosis of OPMD and oral cancer, especially in resource-limited settings.

Machine learning-based tools such as Straticyte™ utilize protein biomarkers to predict the risk of oral epithelial dysplasia progressing to oral squamous cell carcinoma, achieving high sensitivity and specificity. Advanced multiplex immunohistochemistry (mIHC) combined with ML allows precise spatial profiling of immune cells in the tumor microenvironment, thereby aiding prognostication and therapy planning. In digital pathology, deep learning models analyze histopathological images to identify prognostic and predictive biomarkers directly from tissue morphology, bypassing conventional molecular assessments. These models are capable of predicting treatment responses and survival outcomes.

Additionally, AI-assisted epigenomic profiling is emerging, with machine learning algorithms being used to detect and interpret DNA methylation and histone modifications relevant to oral squamous cell carcinoma pathogenesis. Collectively, these AI-driven approaches support more accurate, objective, and personalized oral cancer management. Despite concerns about these AI models functioning as so-called black boxes, ongoing advancements are aiming to enhance their transparency in order to ensure safety, accuracy, and clinical relevance prior to widespread clinical adoption.

The burden of oral cancers and the need for explainability

Oral cancers impose a dual burden on patients and health systems. Patients often experience physical disfigurement, impaired speech, difficulty in swallowing, and social stigma. Health systems are strained by the high cost of treatments, rehabilitation, and the long-term care required

for survivors. The late-stage presentation of most patients is a major driver of poor survival outcomes. Early-stage oral cancers are associated with significantly better survival rates and less invasive treatment, underscoring the importance of timely diagnosis and intervention.

Traditional diagnostic approaches rely heavily on the expertise of clinicians, pathologists, and radiologists. However, variability in expertise, resource limitations, and the subjective nature of clinical evaluations contribute to diagnostic delays and inaccuracies. AI offers solutions to these challenges by providing consistent and data-driven insights. Yet, without explainability, clinicians may be hesitant to rely on AI systems, particularly in life-altering decisions such as cancer diagnosis and treatment planning.

Explainable AI addresses this gap by bridging the divide between the computational accuracy of AI models and the interpretability required in healthcare. For oral cancers, explainability is crucial in contexts such as identifying pre-malignant lesions, predicting treatment response, and distinguishing between tumor subtypes. Clinicians must understand why an AI model predicts malignancy in a lesion or why it recommends a particular treatment pathway, to ensure that the outputs are clinically valid and aligned with patient needs.

XAI in early detection and screening of oral cancers

Early detection remains one of the most effective strategies for reducing the burden of oral cancers. Screening programs, especially in high-risk populations, can identify precancerous or early malignant lesions before they progress to advanced disease. Visual oral examination, toluidine blue staining, brush cytology, and imaging-based methods are commonly used, but they are limited by subjectivity and resource availability.

AI models have demonstrated impressive performance in detecting early lesions from clinical photographs, histopathological slides, and imaging modalities. XAI enhances these models by offering interpretability. For instance, in image-based screening, XAI can highlight the specific regions of an oral lesion that contributed to the model's prediction of malignancy. This visual explanation not only increases clinician trust but also provides an educational tool for less experienced healthcare workers.

In resource-limited settings where specialist expertise is scarce, XAI-enabled AI tools can empower primary care providers to conduct effective oral cancer screenings. A community health worker equipped with a smartphone-based AI system could capture images of suspicious

lesions and receive an explainable assessment that indicates the likelihood of malignancy and highlights the concerning features. This approach reduces reliance on specialist availability while maintaining transparency in decision-making.

XAI in pathology and molecular profiling

Histopathological evaluation remains the gold standard for diagnosing oral cancers. Pathologists examine tissue biopsies to assess cell morphology, tissue architecture, and other features that distinguish malignant from benign lesions. However, interpretation can vary between pathologists, and subtle features may be overlooked. AI models have been trained to analyze histopathological images with high accuracy, identifying features that correlate with malignancy or prognosis.

Explainable AI strengthens this process by showing pathologists which features within the slide influenced the model's prediction. For example, an XAI system might highlight irregular nuclear morphology, disrupted basement membranes, or abnormal mitotic figures as the basis for classifying a tissue as malignant. This explanation helps pathologists validate the AI's decision and integrate it into their diagnostic workflow.

Beyond morphology, molecular profiling plays a critical role in understanding oral cancers. Genomic alterations, such as mutations in TP53 or amplification of EGFR, can influence prognosis and therapeutic options. AI models can analyze large genomic datasets to identify patterns associated with tumor behavior and treatment response. With explainability, these models can indicate which genetic alterations or pathways were most influential in predicting outcomes, providing valuable insights for precision oncology.

XAI in imaging and treatment planning

Imaging modalities, including MRI, CT, and PET scans, are essential for staging oral cancers, assessing tumor extent, and planning treatment. AI systems trained on imaging data can automate tumor segmentation, predict invasion of adjacent structures, and evaluate treatment response. Yet clinicians often hesitate to trust these automated outputs without clear explanations.

XAI techniques such as heatmaps and saliency maps can show clinicians which regions of an image influenced the AI's prediction. For instance, if an AI model predicts perineural invasion or lymph node involvement, the XAI explanation can highlight the anatomical regions that led to this conclusion. This transparency allows radiologists and oncologists to cross-validate the AI's insights

and make more confident treatment decisions.

Treatment planning for oral cancers is highly individualized, often involving surgery, radiation, chemotherapy, or a combination of these. XAI-enabled predictive models can support treatment decisions by explaining why a particular approach is recommended for a patient. For example, an XAI system might predict that a patient is likely to respond well to chemoradiotherapy based on tumor size, molecular markers, and imaging features, while also highlighting the specific variables that influenced the prediction. This level of transparency not only builds clinician trust but also facilitates shared decision-making with patients.

XAI in prognostication and follow-up care

Prognostication is a central aspect of managing oral cancers. Clinicians must estimate the likely course of the disease, including risks of recurrence and survival probabilities, to guide treatment intensity and follow-up schedules. AI models can integrate diverse datasets to generate highly personalized prognostic predictions. However, without explainability, these predictions risk being dismissed as opaque and untrustworthy.

With XAI, clinicians gain insight into the variables driving prognostic predictions. For instance, an AI system may predict a high risk of recurrence in a patient and explain that this is due to perineural invasion, lymph node involvement, and specific molecular markers. By making these factors explicit, XAI supports evidence-based decision-making and allows clinicians to align prognostic predictions with established clinical knowledge.

Follow-up care is another domain where XAI can be transformative. Monitoring patients for recurrence or secondary malignancies often involves imaging, clinical examination, and biomarker testing. XAI-enabled AI tools can detect subtle early signs of recurrence and explain the features responsible, allowing for earlier intervention and improved outcomes.

XAI and patient engagement

Beyond clinicians, patients themselves benefit from explainability in AI-driven care. Cancer diagnosis and treatment can be overwhelming for patients, who may struggle to understand the rationale behind complex medical decisions. XAI can support patient engagement by presenting transparent explanations of AI-driven recommendations in understandable terms.

For example, when an AI system recommends surgery over radiotherapy, XAI can break down the reasoning, highlighting tumor characteristics, expected treatment outcomes, and side effect profiles. By demystifying the decision-making process, patients can make more informed choices

and feel more empowered in their care journey. Increased patient understanding and trust can also improve adherence to treatment plans, thereby enhancing overall outcomes.

XAI in oral cancer research

Research on oral cancers involves analyzing vast and complex datasets, including genomic data, imaging records, histopathological slides, and clinical outcomes. AI has the potential to accelerate discoveries by identifying novel patterns and associations. However, the lack of transparency in AI outputs can limit their utility in research.

XAI provides the interpretability needed for scientific discovery. For instance, when an AI model identifies a new molecular signature associated with poor prognosis, XAI can highlight the genes or pathways involved, providing researchers with a clear direction for further investigation. Similarly, in drug discovery, XAI can explain why a particular compound is predicted to be effective against oral cancer, helping researchers prioritize candidates for laboratory validation.

By enhancing transparency and interpretability, XAI ensures that AI-driven research is not only accurate but also scientifically actionable. This can accelerate the development of new diagnostic tools, biomarkers, and therapeutic strategies, ultimately reducing the burden of oral cancers.

Challenges in implementing XAI for oral cancers

Despite its promise, the integration of XAI into oral cancer care faces several challenges. One of the primary challenges is the complexity of explainability itself. Generating explanations that are both accurate and understandable to clinicians is not straightforward, and overly complex explanations may fail to achieve their intended purpose.

Another challenge is the variability in clinical data. Oral cancers are highly heterogeneous, and differences in patient demographics, risk factors, and tumor biology across populations can limit the generalizability of AI models. XAI systems must be carefully validated across diverse datasets to ensure reliability.

Integration into clinical workflows is another hurdle. Clinicians often operate in high-pressure environments, and XAI tools must provide explanations that are concise, relevant, and seamlessly integrated into existing diagnostic and treatment pathways. Overly burdensome or time-consuming explanations may hinder adoption.

Ethical and regulatory considerations also play a role. The use of AI in healthcare requires adherence to strict standards of patient privacy, data security, and accountability. XAI introduces

additional challenges by requiring the sharing and visualization of decision-making processes, which must be managed carefully to avoid unintended ethical consequences.

Future directions

The future of XAI in reducing the burden of oral cancers is promising, with several avenues for advancement. One important direction is the development of hybrid models that combine the strengths of human expertise and AI-driven insights. In such models, XAI could act as a bridge, ensuring that AI outputs are interpretable and align with clinical reasoning.

Another direction is the personalization of explanations. Different users, such as pathologists, oncologists, or patients, may require different levels of explanation. Tailoring XAI outputs to the needs of specific users can enhance utility and adoption.

Collaboration between clinicians, researchers, and AI developers will be essential for creating XAI tools that are clinically relevant, scientifically robust, and user-friendly. By fostering interdisciplinary partnerships, the field can move closer to realizing the full potential of XAI in oral cancer care.

Conclusion

Explainable AI holds great promise in reducing the burden of oral cancers by enabling early detection, supporting accurate diagnosis, optimizing treatment planning, improving prognostication, and empowering both clinicians and patients. By making AI-driven insights transparent and interpretable, XAI addresses the key barrier of trust that has limited the adoption of AI in healthcare. Although challenges remain, ongoing research and collaboration are paving the way for XAI to become an integral part of oral cancer management.

Through its ability to bridge the gap between complex computational models and clinical practice, XAI can contribute significantly to reducing the morbidity and mortality associated with oral cancers. By empowering healthcare providers and patients with understandable insights, XAI has the potential to transform oral cancer care into a more precise, equitable, and effective domain of medicine.

9. EXPLAINABLE AI IN REDUCING THE BURDEN OF BONE AND MUSCULOSKELETAL CANCERS

Background

Bone and musculoskeletal cancers represent a diverse group of malignancies that include primary bone sarcomas, such as osteosarcoma, chondrosarcoma, and Ewing sarcoma, as well as soft tissue sarcomas that arise in connective tissue structures like muscle, fat, and ligaments. Although these cancers are relatively rare compared to more common malignancies such as breast or lung cancer, they carry a disproportionately high burden due to their aggressive behavior, diagnostic challenges, treatment complexity, and the significant impact they have on patient quality of life. Patients often present with vague symptoms such as pain, swelling, or functional impairment, which can lead to diagnostic delays. Moreover, because these cancers frequently affect younger individuals, including children and adolescents in the case of osteosarcoma and Ewing sarcoma, their societal and economic impact is profound.

The management of bone and musculoskeletal cancers typically involves a combination of surgery, chemotherapy, and radiotherapy.

Advances in surgical techniques, imaging, and chemotherapy protocols have improved survival rates for some types of sarcomas, but overall prognosis remains suboptimal, particularly for patients with metastatic or recurrent disease. A major challenge lies in the heterogeneity of these cancers, both at the molecular and clinical levels. Tumor biology, patient demographics, and response to therapy can vary significantly, making standardized treatment approaches less effective. Precision medicine approaches that tailor treatment to individual tumor characteristics are urgently needed but remain limited by the complexity of data interpretation.

Artificial intelligence has emerged as a powerful tool for managing this complexity. By leveraging large datasets from imaging, genomics, histopathology, and clinical records, AI can identify subtle patterns that escape human detection, supporting early diagnosis, prognosis prediction, and treatment optimization. However, the widespread adoption of AI in oncology has been hindered by the black-box nature of many algorithms. Clinicians, patients, and regulators are hesitant to rely on AI-driven predictions without clear explanations of how these predictions are made. This is where explainable AI, or XAI, becomes critical.

Explainable AI aims to make AI systems transparent, interpretable, and trustworthy.

Rather than providing a simple output such as "high risk of recurrence," XAI can reveal which variables or features contributed to that output, such as tumor size, gene expression patterns, or imaging characteristics. For bone and musculoskeletal cancers, this transparency is especially important because treatment decisions often involve complex trade-offs between aggressive interventions and preserving musculoskeletal function. By enabling clinicians to understand and validate AI recommendations, XAI fosters trust, improves patient care, and accelerates research into these challenging malignancies.

The burden of bone and musculoskeletal cancers

Although rare, bone and musculoskeletal cancers contribute significantly to cancer-related morbidity and mortality worldwide. Osteosarcoma, the most common primary bone malignancy, predominantly affects adolescents and young adults. Ewing sarcoma shares a similar age distribution, while chondrosarcoma tends to occur in older adults. Collectively, sarcomas also include hundreds of subtypes that vary widely in clinical behavior, from indolent tumors with excellent outcomes to highly aggressive cancers with poor survival rates.

The rarity and heterogeneity of these

cancers present unique challenges. Because most clinicians encounter sarcomas infrequently, diagnostic errors and delays are common. Many patients are initially misdiagnosed with benign conditions, resulting in inappropriate or delayed treatment. Even when diagnosed accurately, treatment requires multidisciplinary expertise and access to specialized centers, which may not be available in all regions. These factors contribute to the high burden of disease, both for patients and for healthcare systems.

Another dimension of burden is the long-term sequelae of treatment. Limb-sparing surgery and reconstructive techniques have replaced amputation in many cases, but they can lead to complications such as prosthesis failure, infection, and impaired mobility. Chemotherapy and radiotherapy can cause long-term side effects, including secondary malignancies, infertility, and organ dysfunction. For survivors, physical disability and psychosocial challenges often persist for years. Reducing this burden requires better strategies for early detection, accurate risk stratification, and treatment optimization.

Explainable AI for early diagnosis

Early diagnosis of bone and musculoskeletal cancers is notoriously difficult due to the nonspecific nature of presenting symptoms. Pain, swelling, or decreased mobility can easily be attributed to trauma, infection, or benign conditions, especially in young patients. Imaging modalities such as X-ray, MRI, CT, and PET scans play a central role in the diagnostic process, but interpretation depends heavily on radiologist expertise and experience.

AI models have shown promise in analyzing imaging data to detect subtle abnormalities that may indicate malignancy. For example, deep learning systems can identify irregular bone destruction, periosteal reactions, or soft tissue extension with higher sensitivity than traditional approaches. Explainable AI enhances these models by clarifying which image features drive the prediction. Through heatmaps or saliency maps, XAI can highlight the regions of an MRI scan that suggest tumor infiltration, providing radiologists with visual cues that complement their clinical judgment.

In addition to imaging, AI systems trained on electronic health records can flag patients at high risk of bone or soft tissue sarcoma based on symptom patterns, medical history, and laboratory values. Explainability is critical here, as clinicians must understand why the system identified a patient as high risk. By presenting clear explanations, such as persistent pain unresponsive to therapy or specific imaging features, XAI supports earlier referral to specialized centers and reduces diagnostic delays.

XAI in histopathology and molecular profiling

Histopathological analysis remains the gold standard for diagnosing bone and musculoskeletal cancers. However, interpreting biopsy specimens can be challenging because many sarcomas share overlapping features, and inter-observer variability among pathologists is common. AI models trained on digitized pathology slides have demonstrated high accuracy in classifying tumor subtypes, grading malignancies, and detecting features associated with prognosis.

Explainable AI strengthens these applications by making predictions interpretable. For example, when an AI system classifies a biopsy as osteosarcoma, XAI can highlight the regions of abnormal osteoid production or nuclear atypia that contributed to this classification. Such explanations allow pathologists to validate the AI's output, increasing confidence in its clinical application.

Molecular profiling has revealed numerous genetic alterations in sarcomas, such as EWSR1 translocations in Ewing sarcoma or IDH1/2 mutations in chondrosarcoma. These molecular markers provide valuable insights into tumor biology and therapeutic options but generate large and complex datasets that are difficult to interpret manually. AI models can integrate genomic, transcriptomic, and epigenomic data to identify patterns associated with prognosis or drug response. With explainability, these models can point to specific mutations, pathways, or expression signatures that influenced their predictions. This level of transparency not only aids clinical decision-making but also drives research into new biomarkers and therapeutic targets.

XAI in treatment planning

Treatment of bone and musculoskeletal cancers requires highly individualized approaches. Surgery remains the cornerstone for localized disease, but decisions regarding surgical margins, reconstruction options, and limb-sparing techniques are complex. Chemotherapy and radiotherapy protocols must also be tailored to tumor type, stage, and patient-specific factors.

AI can support treatment planning by predicting treatment response, estimating survival probabilities, and suggesting optimal therapeutic strategies. For instance, predictive models may estimate the likelihood of a good histological response to neoadjuvant chemotherapy in osteosarcoma, guiding oncologists on whether to intensify or modify the regimen. Explainable AI adds value by clarifying which features, such as tumor size, necrosis rate, or molecular markers, influenced the prediction. This transparency is

critical for oncologists to trust and adopt AI-driven recommendations.

In surgical planning, AI systems can analyze imaging data to propose optimal resection margins while minimizing functional loss. XAI can visualize the areas of likely tumor spread and explain why certain margins are recommended, enabling surgeons to balance oncologic control with preservation of musculoskeletal function.

Radiotherapy planning can also benefit from XAI. AI models can predict radiation dose distributions and potential toxicities, while explainability ensures that oncologists understand which anatomic features influenced dose calculations. This facilitates safer and more effective radiation therapy for sarcoma patients.

Prognostication and follow-up care with XAI

Accurate prognostication is essential for tailoring treatment intensity and follow-up schedules in bone and musculoskeletal cancers. Traditional prognostic factors include tumor size, grade, stage, and response to therapy, but integrating these variables into reliable predictions is challenging. AI models can combine clinical, imaging, pathological, and molecular data to generate individualized survival estimates or recurrence risks.

With XAI, these predictions become interpretable.

For example, if an AI system predicts poor prognosis for a patient with Ewing sarcoma, it can specify that the prediction was driven by large tumor size, presence of metastases, and specific genetic alterations. This allows clinicians to validate the AI's output and consider additional interventions for high-risk patients.

Follow-up care is another critical area where XAI can make an impact. Sarcoma survivors require long-term monitoring for recurrence, metastasis, and late treatment effects. AI tools can analyze imaging and clinical data to detect subtle signs of recurrence earlier than traditional methods. Explainability ensures that when a suspicious finding is flagged, clinicians can see which features drove the alert, improving trust and facilitating timely intervention.

Patient engagement through explainable AI

Patients with bone and musculoskeletal cancers often face difficult decisions regarding surgery, chemotherapy, and long-term rehabilitation. These decisions involve weighing oncologic outcomes against functional and quality-of-life considerations. XAI can enhance patient engagement by making AI-driven recommendations understandable to patients and their families.

For example, if an AI system recommends limb-

sparing surgery over amputation, XAI can present the rationale in terms of tumor location, surgical feasibility, and predicted outcomes. By providing clear and interpretable explanations, XAI fosters shared decision-making and helps patients feel more empowered in their care. This transparency can improve adherence to treatment plans and enhance overall satisfaction with the care process.

XAI in research and drug discovery

Research on bone and musculoskeletal cancers is hindered by the rarity of these diseases and the complexity of their biology. AI can accelerate discoveries by analyzing large datasets to identify novel biomarkers, therapeutic targets, and drug candidates. However, opaque AI models limit scientific interpretation and reproducibility.

XAI addresses this issue by making AI-driven discoveries interpretable. For instance, when an AI model identifies a gene expression signature associated with chemotherapy resistance, XAI can specify which genes and pathways contributed to the prediction. This provides researchers with actionable hypotheses for laboratory validation.

In drug discovery, XAI can explain why a candidate compound is predicted to inhibit a sarcoma-related pathway, helping researchers prioritize compounds for preclinical testing. By enhancing transparency and interpretability, XAI ensures that AI-driven research contributes meaningfully to advancing sarcoma care.

Challenges in implementing XAI for musculoskeletal cancers

Despite its potential, several challenges hinder the adoption of XAI in bone and musculoskeletal cancers. One challenge is the complexity of generating explanations that are both accurate and understandable. Highly technical explanations may satisfy data scientists but fail to be useful for clinicians. Conversely, overly simplistic explanations may lack sufficient detail to support clinical decision-making.

Another challenge is data availability. The rarity of bone and musculoskeletal cancers means that datasets are often small and fragmented across institutions. Training robust AI models requires large and diverse datasets, and without them, XAI tools may not generalize well to different patient populations. Efforts to build international consortia and share data are essential to overcome this barrier.

Integrating XAI into clinical workflows is also a practical challenge. Clinicians already face significant time pressures, and XAI tools must provide explanations that are concise, relevant, and seamlessly integrated into existing systems.

Ethical and regulatory considerations are particularly important in oncology. XAI must be developed and validated with strict attention to

patient privacy, data security, and accountability. Moreover, the legal implications of AI-driven decisions remain an area of active debate.

Future perspectives

The future of XAI in reducing the burden of bone and musculoskeletal cancers lies in developing hybrid models that combine AI-driven insights with human expertise. Such models would leverage the strengths of both approaches while ensuring interpretability and trust. Personalized explanations tailored to different users will also play an important role. For example, pathologists may require detailed feature-level explanations, while patients may benefit from simplified, patient-friendly explanations.

Another promising direction is the integration of multimodal data. Bone and musculoskeletal cancers generate diverse types of data, from imaging and pathology to genomics and clinical records. AI models capable of integrating these data streams, coupled with explainability, could provide unprecedented insights into tumor biology and treatment response.

Collaborative efforts across institutions, disciplines, and countries will be essential to realize the potential of XAI. By pooling resources and expertise, the medical and scientific community can develop robust, validated, and clinically relevant XAI tools that address the unique challenges of sarcomas.

Conclusion

Explainable AI offers a transformative approach to reducing the burden of bone and musculoskeletal cancers. By making AI-driven insights transparent and interpretable, XAI enhances early diagnosis, improves accuracy in histopathology and molecular profiling, optimizes treatment planning, supports prognostication, and engages patients in their care. In research, XAI accelerates discoveries by clarifying the mechanisms behind AI predictions, fostering scientific understanding and innovation.

Although challenges remain in terms of data availability, workflow integration, and regulatory frameworks, the potential of XAI to improve outcomes for patients with these rare and devastating cancers is immense. By bridging the gap between computational power and human interpretability, XAI has the potential to transform the management of bone and musculoskeletal cancers into a more precise, equitable, and effective field of oncology.

10. EXPLAINABLE AI IN REDUCING THE BURDEN OF RARE AND OTHER CANCERS

Explainable AI in Reducing the Burden of Pediatric Cancers

Background

Pediatric cancers, although relatively rare compared to adult malignancies, represent a significant health challenge due to their aggressive nature, complex management, and profound impact on affected children and their families. Childhood cancers include a wide spectrum of hematologic malignancies, such as acute lymphoblastic leukemia and acute myeloid leukemia, as well as solid tumors like neuroblastoma, Wilms tumor, rhabdomyosarcoma, and medulloblastoma. Unlike adult cancers, pediatric malignancies often arise from developmental and genetic abnormalities rather than prolonged exposure to environmental risk factors, highlighting the distinct biological and molecular underpinnings that drive these diseases.

Despite advances in pediatric oncology, which have led to remarkable improvements in survival rates for many cancer types, significant challenges

remain. Early diagnosis is difficult because symptoms are often nonspecific, including fatigue, pallor, pain, or swelling, and may mimic common childhood illnesses. Delayed diagnosis can lead to advanced-stage disease at presentation, limiting therapeutic options and worsening prognosis. Furthermore, the intensive treatments required, including chemotherapy, radiation, and surgery, carry substantial short-term and long-term toxicities that affect growth, cognitive development, fertility, and overall quality of life. These factors contribute to the enduring burden of pediatric cancers on children, families, and healthcare systems.

Artificial intelligence has emerged as a transformative tool in pediatric oncology, offering potential solutions for early detection, risk stratification, personalized treatment, and long-term survivorship care. However, the adoption of AI in clinical practice has been limited by the black-box nature of many algorithms, which produce predictions without clear explanations. In the context of pediatric care, where treatment decisions have life-altering consequences, transparency, interpretability, and trust are essential. Explainable AI, or XAI, addresses these challenges by providing interpretable and actionable insights from complex AI models. By revealing the factors contributing to predictions, XAI enables clinicians, families, and researchers to understand, validate, and apply AI-driven recommendations in a safe and effective manner.

The application of XAI in pediatric cancers has the potential to reduce the burden of disease by improving early detection, optimizing treatment decisions, predicting outcomes, supporting survivorship care, and accelerating research into the unique biology of childhood malignancies. This discussion explores the multifaceted role of XAI in pediatric oncology, highlighting current applications, challenges, and future directions.

The burden of pediatric cancers

Although childhood cancers account for a small percentage of overall cancer cases, they carry disproportionately high physical, emotional, and economic consequences. Acute lymphoblastic leukemia is the most common pediatric malignancy, followed by brain tumors, neuroblastoma, and Wilms tumor. Survival rates vary by cancer type, stage at diagnosis, and access to specialized care. For example, survival for children with acute lymphoblastic leukemia exceeds 85 percent in high-income countries, whereas survival for high-risk neuroblastoma or diffuse intrinsic pontine glioma remains below 50 percent, despite intensive therapy.

The rarity and heterogeneity of pediatric cancers pose unique challenges. Pediatric oncologists often encounter few cases of rare tumor subtypes,

making standardized treatment protocols less effective. Additionally, treatment-related toxicity is a significant concern, as children are more vulnerable to long-term adverse effects, including cognitive impairment, cardiotoxicity, secondary malignancies, growth disturbances, and endocrine disorders. These long-term consequences underscore the importance of precise, individualized treatment strategies that maximize efficacy while minimizing harm.

Early diagnosis is another critical area of need. Pediatric cancers often present with subtle or nonspecific symptoms that overlap with common childhood conditions. For instance, fatigue, pallor, or bone pain may be mistakenly attributed to infections or growth-related changes. Delayed diagnosis can result in advanced disease, reducing the likelihood of curative outcomes. Implementing tools that support early recognition of high-risk cases is therefore a priority for reducing the burden of pediatric cancers.

Explainable AI for early detection and diagnosis

Early and accurate detection of pediatric cancers is crucial for improving outcomes. Traditional diagnostic approaches rely on clinical evaluation, laboratory tests, imaging, and histopathology. However, these methods can be limited by the rarity of the conditions, inter-observer variability, and the subtlety of early-stage disease. AI models have shown promise in detecting pediatric cancers from medical images, electronic health records, genomic profiles, and other multimodal data sources.

For example, AI algorithms trained on imaging data, such as MRI or CT scans, can identify tumors, characterize tissue abnormalities, and detect features indicative of malignancy that may be missed by the human eye. In laboratory data analysis, AI can identify patterns in blood counts, biomarkers, and genetic mutations that signal the presence of leukemia or other hematologic malignancies.

Explainable AI enhances these applications by revealing which features or patterns contributed to a given prediction. In imaging, XAI can generate heatmaps that highlight tumor regions or areas of abnormal tissue structure, enabling radiologists and clinicians to verify the AI's findings. In laboratory-based predictions, XAI can indicate specific laboratory values, gene expression levels, or mutation profiles that influenced the risk assessment. By providing interpretable outputs, XAI allows clinicians to integrate AI recommendations into their diagnostic workflow, fostering trust and supporting timely referral to specialized care centers.

XAI in histopathology and molecular profiling

Histopathological evaluation remains the gold standard for confirming pediatric cancer diagnoses. Pathologists examine tissue morphology, cell differentiation, mitotic activity, and other features to distinguish malignant from benign lesions and to classify tumor subtypes. However, interpretation can be challenging, particularly in rare pediatric tumors, due to overlapping features and variability in expertise. AI models trained on digitized histopathology slides can assist by classifying tumor types, grading malignancy, and identifying prognostic features.

Explainable AI strengthens this process by making predictions interpretable. For instance, an XAI model may classify a neuroblastoma biopsy and highlight areas of high mitotic activity, necrosis, or specific cellular patterns that influenced the decision. This not only helps pathologists validate the AI's output but also provides a teaching tool for less experienced practitioners.

Molecular profiling is increasingly central to pediatric oncology. Pediatric cancers often harbor unique genetic alterations, such as ALK mutations in neuroblastoma, NTRK fusions in infantile fibrosarcoma, or specific chromosomal translocations in leukemias. These alterations have diagnostic, prognostic, and therapeutic implications. AI can integrate genomic, transcriptomic, and epigenomic data to predict disease behavior, treatment response, or likelihood of relapse. Explainable AI ensures that the model identifies which mutations, gene expression patterns, or pathways contributed to its prediction, allowing clinicians and researchers to interpret results in a biologically meaningful way.

XAI in imaging and treatment planning

Imaging is critical for staging pediatric cancers, assessing tumor response, and guiding treatment planning. MRI, CT, PET scans, and ultrasound provide detailed information about tumor size, location, and involvement of adjacent structures. AI models can automate tumor segmentation, detect metastases, and predict treatment response with high accuracy. However, clinicians need to understand the basis of AI predictions to rely on them for decision-making.

Explainable AI addresses this by highlighting specific regions of images that informed predictions. For example, an XAI model may indicate areas of a brain tumor that are likely to be highly proliferative or infiltrative, guiding neurosurgeons in planning resection. In radiation oncology, XAI can explain dose planning predictions, identifying regions of potential toxicity and allowing for safer and more precise

targeting. By providing interpretable outputs, XAI helps clinicians optimize treatment plans while minimizing harm to developing tissues and organs.

Prognostication and follow-up care with XAI

Prognostic predictions are essential for tailoring treatment intensity, scheduling follow-ups, and counseling families. AI models can integrate multiple data sources, including tumor histology, molecular profiles, imaging features, and clinical variables, to predict outcomes such as survival, relapse risk, or likelihood of therapy response.

Explainable AI ensures that prognostic predictions are transparent and actionable. For example, if an AI model predicts high relapse risk for a child with leukemia, XAI can clarify that this is due to specific cytogenetic abnormalities, minimal residual disease levels, or early treatment response. Such interpretability allows clinicians to justify treatment intensification, plan closer monitoring, or consider experimental therapies. Follow-up care can also benefit from XAI by detecting subtle changes in imaging, laboratory results, or clinical symptoms that may indicate recurrence, providing early alerts and guiding timely intervention.

Patient and family

engagement through XAI

Pediatric cancer care involves not only clinicians but also families, who play a central role in decision-making. AI recommendations can be complex and difficult to interpret, particularly for non-specialists. Explainable AI can improve patient and family engagement by providing clear and understandable explanations of risk assessments, treatment options, and expected outcomes.

For example, when an AI model recommends a particular chemotherapy regimen or surgical approach, XAI can break down the rationale in terms of tumor characteristics, predicted response, and potential side effects. This transparency fosters shared decision-making, improves adherence to treatment plans, and enhances confidence in care. Families who understand the reasoning behind clinical decisions are better equipped to support their child through treatment and recovery.

XAI in pediatric cancer research and drug development

Research in pediatric oncology is complicated by the rarity of many cancers, limiting sample sizes and slowing the discovery of novel therapies. AI can accelerate research by identifying patterns across diverse datasets, including genomics, imaging, and clinical outcomes. However, opaque

AI models can produce results that are difficult to interpret, limiting their translational potential.

Explainable AI enhances research by clarifying the mechanisms behind predictions. For instance, an XAI model might identify a gene expression signature associated with high-risk neuroblastoma and highlight the key genes driving the association. In drug development, XAI can explain why a candidate compound is predicted to inhibit tumor growth or overcome resistance, guiding prioritization for preclinical and clinical testing. By making AI-driven research interpretable, XAI accelerates the development of new diagnostics, targeted therapies, and precision treatment strategies in pediatric oncology.

Challenges in implementing XAI in pediatric cancers

Several challenges must be addressed to fully realize the potential of XAI in pediatric oncology. One key challenge is data availability. Pediatric cancers are rare, and high-quality, annotated datasets are limited. Training robust AI models requires multicenter collaborations, data sharing, and standardization of imaging, genomic, and clinical data.

Another challenge is developing explanations that are both accurate and clinically meaningful. Highly technical explanations may be difficult for clinicians or families to interpret, while oversimplified explanations may omit critical information. Integrating XAI into clinical workflows is also essential, ensuring that interpretability tools are user-friendly, actionable, and seamlessly incorporated into decision-making processes.

Ethical and regulatory considerations are particularly important in pediatric oncology. AI systems must protect patient privacy, comply with legal frameworks, and ensure accountability. The use of AI in making treatment decisions for children requires careful oversight, rigorous validation, and adherence to evidence-based practice standards.

Future directions

The future of XAI in pediatric oncology includes the development of hybrid models that combine AI-driven insights with human expertise. These models can leverage computational power while ensuring interpretability and trust. Personalized explanations tailored to different stakeholders, such as oncologists, radiologists, pathologists, or families, will further enhance adoption and utility.

Integration of multimodal data is another promising direction. Pediatric cancers generate diverse data types, including imaging, histopathology, genomics, and clinical information. AI models capable of synthesizing

these data streams, coupled with explainable outputs, can provide holistic insights into tumor biology, treatment response, and long-term outcomes.

Collaborative efforts across institutions, disciplines, and countries will be essential for building robust, validated XAI systems. By pooling resources and expertise, researchers and clinicians can accelerate discovery, optimize care, and improve outcomes for children with cancer.

Conclusion

Explainable AI has the potential to transform pediatric oncology by enhancing early detection, supporting accurate diagnosis, optimizing treatment planning, improving prognostication, and engaging families in shared decision-making. By providing transparent and interpretable insights, XAI addresses the key barrier of trust that has limited AI adoption in pediatric care.

Although challenges remain, including data scarcity, workflow integration, and ethical considerations, the opportunities presented by XAI are profound. By bridging the gap between computational complexity and human interpretability, XAI can reduce the burden of pediatric cancers, improve survival and quality of life, and accelerate research into the unique biology of childhood malignancies. Through collaboration, innovation, and careful implementation, XAI can become an integral component of precision pediatric oncology, offering hope for children and families affected by cancer.

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