A Comprehensive Survey of Digital Twinning Systems for Medical Imaging of Brain Tumors

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***Abstract*—In today's medical environment, quick and accurate diagnosis can make all the difference, and new technologies are pushing the boundaries of what's possible. One exciting development is the combination of AI and digital twin technology to change how we approach brain tumors. This project explores the innovative field of digital twin technology by developing a Digital Twinning System for Medical Imaging—essentially, an intelligent platform that integrates deep learning models with live simulations. Using advanced convolutional neural networks (CNNs) and segmentation tools like U-Net, trained on large datasets from sources like Figshare MRI (Kaggle), BraTS, and TCGA, the system creates personalized virtual models of each patient's brain that update with new clinical data. Instead of just interpreting static MRI scans, this digital twin captures how tumors change over time, allowing doctors to monitor progress continuously, predict tumor stages, and plan treatments more effectively. By combining AI insights with interactive visual tools, clinicians are enabled with a powerful resource for early detection and smarter interventions. More than a tech breakthrough, this approach aims to change patient care into a more responsive, customized experience—where medical decisions are guided not only by images but by energetic, living models of the human brain.**

***Index Terms*—Digital Twin, Brain Tumor Imaging, Medical Imaging, Deep Learning, Convolutional Neural Networks (CNN), U-Net, Tumor Segmentation, MRI Analysis, Personalized Healthcare, AI in Medical Diagnosis, Real-time Simulation, Clinical Decision Support, Image-Based Modeling, Tumor Progression Monitoring, Healthcare Digitalization.**

1. INTRODUCTION

In the last few years, the generative AI domain has witnessed tremendous advancements, specifically in the synthesis of high-quality images from text-based descriptions—a process referred to as text-to-image generation. The growth has come on the back of strong diffusion models like DALL·E, Imagen, and Stable Diffusion that learn intricate patterns between text inputs and visual representations by training over large-scale paired datasets. These models have made it possible for artists, designers, and programmers to generate images by simply telling them what they look like, representing a tremendous advance in human-computer interaction and automation of creativity.

But although text prompts provide expressive control, they do not necessarily encode high-resolution spatial or structural details that the user might want. To answer this, researchers presented ControlNet, an addition to Stable Diffusion, permitting users to condition image creation not only on text but on visual cues such as sketches, edges, or poses. This work takes that capability and combines Stable Diffusion with ControlNet into an interactive Gradio interface. Users can create a sketch and give a textual prompt, marrying the expressiveness of drawing with the descriptiveness of language, to create real images based on both structure and context.

2. LITERATURE REVIEW

1. Organ-Specific Digital Twins for Diagnosis and Monitoring

N. Sasikaladevi et al. [1] proposed a deep learning-based digital twin (DT) system for early diagnosis of chronic kidney disease (CKD) using CT radiography. Leveraging 12,446 abdominal CT scans labeled for normal, cyst, stone, and tumor conditions, they implemented a hypergraph convolutional neural network (HGCNN) for robust feature representation. The model achieved 99.71% validation accuracy, surpassing VGG16, ResNet50, and MobileNet across precision, recall, and F1 score. Their contributions highlight hypergraph-based deep feature learning and DT modeling for clinical decision support in nephrology, addressing diagnostic accuracy gaps and radiologist shortages.

Kaan Sel et al. [2] reviewed the evolution and clinical applications of cardiovascular digital twins (DTs). They emphasized integrating physiological, genomic, sensor, and imaging data into continuously updated heart and vascular models. A five-element framework was proposed to enable real-time prediction of disease progression, treatment optimization, and outcome simulation. Combining AI with mechanistic modeling, DTs were shown to personalize cardiac simulations and forecast risks such as myocardial infarction and heart failure. The review identifies challenges in calibration, hierarchical modeling, and data availability, positioning DTs as a pathway to precision cardiovascular medicine.

Roberta Avanzato et al. [3] presented Lung-DT, an AI-driven digital twin framework integrating IoT devices, deep learning, and microservice architecture for thoracic health monitoring. Using YOLOv8, chest X-rays were classified into five categories (normal, COVID-19, lung opacity, pneumonia, tuberculosis) with 96.8% accuracy, 92% precision, 97% recall, and 94% F1-score. The system supports continuous monitoring through wearables, automated X-ray analysis, and cross-organ data fusion. Unique features include Kubernetes-based deployment, multi-organ diagnostics, and physician decision support. Clinical implications highlight early detection, personalized monitoring, and cost-efficient respiratory care.

Zofia Rudnicka et al. [4] conducted a systematic review of health digital twins (HDTs) in cardiology, focusing on integration with artificial intelligence (AI) and extended reality (XR). Analyzing 253 studies (2020–2024), they identified AI-powered image segmentation and XR-based 3D visualization as enablers of personalized cardiac care. XR (AR, VR, MR) supports diagnosis, interventional planning, and education, while deep learning enhances semantic segmentation and patient-specific modeling. The study underscores the synergy of AI, XR, and DTs as transformative tools for immersive and precise cardiovascular diagnostics.

Jorge Corral-Acero et al. [5] emphasized the role of digital twins (DTs) in precision cardiology by integrating mechanistic and statistical modeling for patient-specific simulations. They advocated a dual approach combining physics-based models (e.g., bidomain, Navier–Stokes) with data-driven inference (e.g., random forests, Gaussian processes). Clinical applications included non-invasive diagnostics such as CT-based fractional flow reserve and risk prediction in heart failure and arrhythmias. Their work highlights DTs as transformative tools for individualized diagnostics, therapy planning, and outcome forecasting in cardiovascular care.

Phyllis M. Thangaraj et al. [6] explored cardiovascular digital twins in the era of generative AI, emphasizing multimodal integration of genomics, imaging, EHRs, and wearables. These DTs simulate clinical scenarios and predict individualized outcomes, with applications in coronary procedures (e.g., CT-FFR for PCI), electrophysiology (e.g., CRT lead placement), and cardiomyopathies (e.g., geno-digital twins for ARVC). Key challenges include real-time integration, ethical deployment, and federated training. The review envisions adaptive, AI-enabled cardiovascular DTs for lifelong precision health management.

Elisabetta Criseo et al. [7] developed a digital twin (DT) model to assess myocardial blood flow (MBF) for diagnosing perfusion defects. Using AI-based coronary and myocardial segmentation from CT scans, they combined 3D fluid dynamics with a three-compartment Darcy microcirculation model. Blind calibration on six patients and validation on 28 yielded recall of 0.77 and accuracy of 0.72 in classifying MBF < 230 ml/min/100g. As the first DT validated in a large cohort for MBF prediction, this approach demonstrates potential for non-invasive coronary artery disease detection and personalized treatment planning.

Cong Zhou et al. [8] introduced a multi-level digital twin (DT) framework for pulmonary mechanics using 3D CT imaging and 2D chest motion data. A U-Net-based lung segmentation and automated thresholding achieved >95% accuracy. On a dataset of 160 patients, projected 2D lung volume showed strong correlation ($R^2 = 0.73$) with Forced Vital Capacity (FVC). This work validates non-invasive chest motion analysis for regional lung mechanics, offering a clinically viable DT framework for improving ventilation strategies and respiratory disease diagnosis.

Amir Rouhollahi et al. [9] developed CardioVision (CV), an automated deep learning pipeline for generating patient-specific digital twins of aortic stenosis from CT images. The system integrates U-Net aorta segmentation, parametric valve modeling, and calcium quantification, reconstructing 3D geometries and STL outputs for TAVR planning. Using 35 patient scans, CV achieved Dice similarity up to 0.978, validating its segmentation accuracy. By combining CNNs, anatomical reconstruction, and calcification analysis, CV advances scalable digital twin creation for interventional cardiology.

Øystein Bjelland et al. [10] conducted a systematic review on enabling technologies for digital twins (DTs) in arthroscopic knee surgery. Reviewing 80 studies under PRISMA, they analyzed imaging, soft tissue modeling, simulation strategies, and intraoperative data. The review highlighted MRI/CT integration, haptic feedback, real-time deformation, and AI-driven simulations as critical enablers. A macro-level DT system was proposed for surgeon training, preoperative planning, and virtual surgery databases. Their work emphasizes biomechanical realism and transition from rigid VR simulators to dynamic, patient-specific DTs.

David Männle et al. [11] developed an AI-driven digital twin (DT) for quantifying soft tissue shift (TS) in head and neck surgery using pig cadaver models. 3D scans from HoloLens 2 and ArtecEva captured pre/post temperature-induced TS, with AI processing 416 scan datasets. Significant deformations were detected across devices despite mesh density differences. This study demonstrates marker-free, AI-assisted navigation for tissue surgery, enhancing precision in flap reconstruction and intraoperative management.

Alexander M. Zolotarev et al. [12] proposed a deep learning pipeline for predicting atrial fibrillation (AF) treatment outcomes using digital twin (DT)-based simulations. Generating 1000 virtual patients from CT and LGE-MRI fibrosis maps, they integrated biophysical atrial modeling with Siamese neural networks to fuse multimodal features. The pipeline predicted AF termination likelihood across ablation strategies, offering real-time, patient-specific recommendations. This work demonstrates feasibility of combining electrophysiological DTs with deep learning for precision AF therapy planning.

Chengyue Wu et al. [13] developed a patient-specific digital twin (DT) framework for optimizing neoadjuvant chemotherapy (NAC) in triple-negative breast cancer (TNBC). Using longitudinal MRI data from 105 patients in the ARTEMIS trial, they simulated tumor response to 128 regimens. Their DTs predicted pathological complete response (pCR) with AUC of 0.82 and improved pCR rates by up to 24.76% through multi-step, simultaneous, and midway optimization. Predictions were validated against landmark trials (INT C9741, ECOG 1199, SWOG S0221). This study reinforces DTs as reliable, low-risk tools for individualized oncology care.

Anushka Kotnala et al. [14] reviewed the role of digital twins (DTs) in personalized breast cancer management. Highlighting tumor heterogeneity and limitations of population-based models, they emphasized DTs integrating genetic, biochemical, and lifestyle data for individualized care. The review discussed simulation-based decision support for therapy selection and optimization, while noting challenges in data integration, personalization, and validation. DTs are presented as transformative tools enabling real-time, patient-specific breast cancer management.

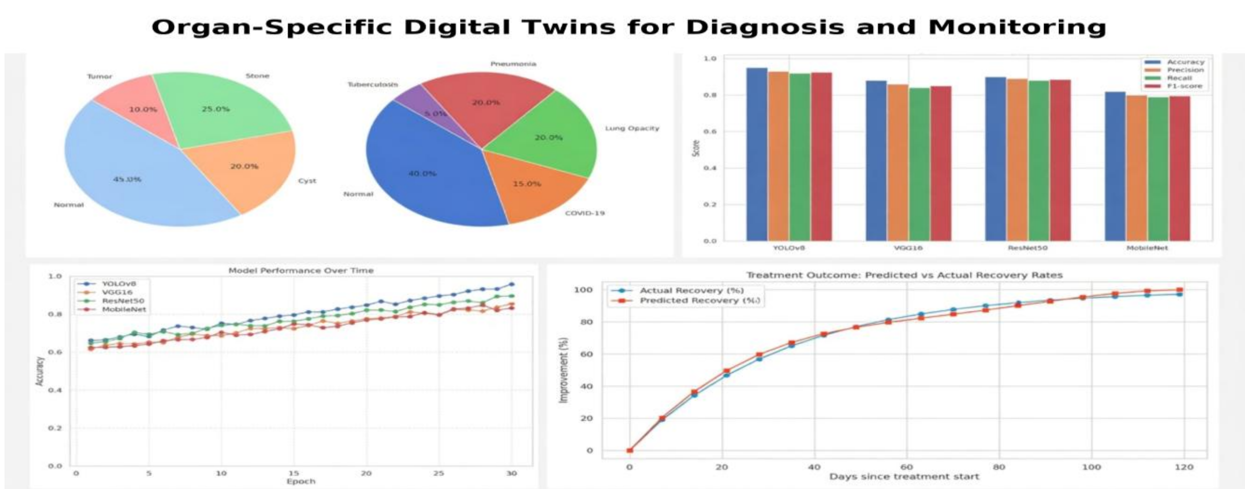

Fig 1: Overview of AI Techniques and Performance Metrics in Organ-Specific Digital Twins for Diagnosis and Monitoring

2. Digital Twins in Cancer Diagnosis, Therapy, and Imaging Analytics

Jun Zhang et al. [15] proposed a cyber-resilient healthcare digital twin (DT) model for lung cancer diagnosis, integrating deep learning to secure and enhance the intelligence of IoT-based medical systems. They introduced "DeepVR," a Bi-LSTM model with self-attention to detect software vulnerabilities in healthcare DTs, trained on real-world and synthetic datasets like SARD and nine open-source C-based IoT projects. Their model utilizes Word2Vec-based code embeddings, captures bi-directional code dependencies, and highlights vulnerability-critical tokens. Experiments showed DeepVR outperformed standard LSTM and tools like Flawfinder with improved F1 scores, ROC-AUC, and top-k precision. The system also supports immersive VR-based lung surgery simulation using Unity and physics-based rendering from CT data. A CNN classifier predicted pulmonary embolism in lung cancer patients with d-dimer and ECG features. With visualized attention maps highlighting real-world code flaws (e.g., CVE-2013-1432), this model provides a scalable, interpretable solution for code security in digital health systems.

Sabaa Ahmed Yahya Al-Galal et al. [16] conducted a systematic review on deep learning (DL) applications for MRI brain tumor analysis, evaluating 427 papers (filtered to 92) from major databases. Focusing on segmentation and classification, the study highlights CNN-based models like U-Net, V-Net, and DeepMedic using the BRATS dataset, achieving up to 96% Dice Similarity Coefficient. Classification tasks employed networks such as VGG19, ResNet, and GoogleNet, with some models reporting near 100% accuracy, especially when combined with data augmentation or transfer learning. Compared to traditional ML methods (e.g., SVM, RF), DL models outperformed in both precision and scalability. The review identifies challenges like limited labeled data and model interpretability, tackled via synthetic data, augmentation, and transfer learning. Concluding, the paper emphasizes CNNs' growing role in automated, accurate MRI-based brain tumor detection, paving the way for enhanced clinical support systems.

Zhibo Wan et al. [17] proposed a brain image fusion diagnostic model combining Semi-Supervised Support Vector Machines (S3VMs) and an improved AlexNet CNN within a Digital Twin (DT) framework to enhance MRI brain tumor analysis. Addressing the abundance of unlabeled MRI data, the system integrates labeled-unlabeled learning via S3VM and feature extraction via CNN, mapping real brain images into virtual space for diagnosis. The improved AlexNet structure includes changes like pooling-before-normalization to speed up convergence and reduce overfitting. Experiments on multi-sequence MRI datasets showed 92.52% feature recognition accuracy, outperforming LSTM, RNN, MLP, CNN, and baseline AlexNet. The model achieved 79.55% Jaccard, 90.43% PPV, 73.09% sensitivity, and 75.58% DSC with minimal time delay and RMSE (4.91%) and MAE (5.59%) values. Suitable for large-scale data with high-speedup indicators, it provides an efficient, accurate alternative for digital diagnosis, though future work may involve tumor grading and volumetric analysis.

Grace M. Thiong'o and James T. Rutka [18] explored the potential of Digital Twin (DT) technology to predict neurological complications in pediatric cancer patients by modeling a virtual replica of the child using EHR data, AI, and machine learning. The paper proposes grey box, surrogate box, and black box DT models to personalize treatment and stratify risk, incorporating data across clinical visits, radiology, and wearables. DTs can complement limited pediatric clinical trials, simulate disease progression, and enhance drug discovery using real-time physiological modeling. Machine learning enables predictive analytics by mining big data to uncover disease patterns, improving early intervention. Additionally, DTs can harmonize differing clinical opinions by synthesizing diverse physician inputs into consensus decisions. Though promising, the approach faces challenges in data privacy, implementation cost, and model explainability. The paper concludes that DTs can revolutionize pediatric oncology by fusing digital models with clinical acumen to foresee and mitigate neurological risks.

Mahsa Arabahmadi et al. [19] conducted a comprehensive survey on deep learning (DL) techniques, especially CNN-based models, for brain tumor detection using MRI in smart healthcare systems. The paper reviews segmentation and classification methods, including U-Net, FCN, DeepMedic, and hybrid techniques like CNN+SVM, emphasizing the role of automated image analysis in improving diagnostic accuracy. It discusses datasets like BRATS, TCIA, OASIS, and ISLES and covers CNN architectures like LeNet, AlexNet, VGGNet, GoogLeNet, and ResNet, comparing their depth, parameters, and performance. Deep learning models show significant advantages in automatic feature extraction, tumor localization, and reducing manual error. The study also highlights CAD systems, transfer learning, GANs, autoencoders, and deep belief networks for enhancing diagnosis. Major challenges include lack of labeled data, interpretability, computational cost, and privacy. The survey concludes that DL, combined with AI and IoT, revolutionizes brain tumor detection, offering scalable, accurate, and automated healthcare solutions.

Karen E. Batch et al. [20] developed a Cancer Digital Twin framework that uses NLP and deep learning to detect metastases from over 714,000 consecutive structured radiology reports at MSKCC. The system integrates historical patient data using three models—a simple CNN, an augmented CNN with attention, and a Bi-LSTM—to predict lung, liver, and adrenal metastases. Compared to a baseline TF-IDF ensemble model, multi-report models significantly improved F1 scores (e.g., lung: 0.7815 → 0.8964, liver: 0.8637 → 0.9831). The best performance came from the augmented CNN, showing 99.04–99.68% accuracy in validation. This approach enables automatic, time-efficient labeling of radiology data without manual effort, allowing high-resolution tracking of cancer progression. The study pioneers using multi-report sequential input for metastases detection and emphasizes that such models can enhance real-time digital representations of cancer patients, crucial for precision treatment planning.

Hamza Rafiq Almadhoun and Samy S. Abu Naser [21] developed a deep learning-based brain tumor detection model using a dataset of 10,000 MRI images, comparing a custom CNN with four pretrained models: VGG16, ResNet50, MobileNet, and InceptionV3. Their model architecture included 12 convolutional layers optimized with Adam and trained using Google Colab, achieving 100% training and 98.28% validation accuracy. Data augmentation techniques like rotation, shifts, and flips enhanced robustness. On testing, InceptionV3 and VGG16 outperformed others with 99% accuracy, while MobileNet lagged at 88%. The proposed system used high-resolution preprocessing and image normalization, improving tumor boundary detection. Techniques like SR-FCM, stacked autoencoders, and ELM-based classifiers were explored for enhanced segmentation. The study concluded that deep CNNs—especially when coupled with transfer learning and augmentation—can offer reliable, fast, and accurate brain tumor detection in clinical settings.

Eric A. Stahlberg et al. [22] explored predictive cancer patient digital twins (CPDTs) through five pilot projects initiated by the NCI–DOE collaboration to enhance precision oncology. Projects spanned cancers like pancreatic, melanoma, lung, and breast, leveraging AI, multiscale mechanistic modeling, and HPC. Georgetown simulated 1 million pancreatic cancer patients using subclonal evolution; Indiana created melanoma CPDTs with canine-human immune modeling; Stanford developed adaptive lung cancer twins using multi-modal data and RNA-GANs; South Carolina built patient-specific NSCLC twins integrating pathway exploration; and UMass Amherst's "My Virtual Cancer" used QSP models to simulate breast cancer dynamics. Across projects, challenges included data sparsity, model fitting, and validation. All emphasized community collaboration, trustworthy AI, and transfer learning to scale CPDTs for real-world clinical utility. The paper concludes that CPDTs are advancing from conceptual frameworks to actionable clinical tools.

Shko M. Qader et al. [23] proposed an enhanced brain tumor detection model using a Deep Convolutional Neural Network (DCNN) optimized by a hybrid algorithm called G-HHO, which combines Grey Wolf Optimization (GWO) and Harris Hawks Optimization (HHO). The model incorporates Otsu thresholding for precise tumor segmentation and extracts key features (size, mean, variance) from augmented MRI images. Implemented in Python, the DCNN-G-HHO was validated on 2073 MRI images, achieving 97% accuracy with high precision (0.99), recall (0.95), and F-measure (0.97). Compared to nine existing algorithms—including CNN, SVM, DeepFM, and WHHO-based DeepCNN—the proposed method outperformed all in accuracy, execution time, and memory usage. Its architecture includes three convolutional layers and a novel training optimization process leveraging G-HHO's enhanced explorationexploitation balance. The authors highlight the model's potential for clinical use due to its speed, resource efficiency, and robustness across varied datasets.

Akmalbek B. Abdusalomov et al. [24] proposed an enhanced YOLOv7-based deep learning model for automated brain tumor detection in MRI images, targeting glioma, meningioma, and pituitary tumors. Their model integrates the Convolutional Block Attention Module (CBAM), SPPF+ (Spatial Pyramid Pooling Fast+), BiFPN (Bidirectional Feature Pyramid Network), and a decoupled head for improved multi-scale feature fusion, small tumor detection, and spatial focus. The model was trained on a dataset of 10,288 MRI images (augmented to 51,448), achieving 99.5% accuracy, 99.3% recall, and 99.4% F1-score—outperforming other CNNs like EfficientNet, VGG16, ResNet50, and existing models like YOLOv4 and DenseNet. Ablation studies confirmed the superior performance of CBAM over SE and ECA attention mechanisms, and the combined modules (SPPF+, BiFPN, DP) significantly enhanced the detection of small and complex tumor structures. The study concludes that the optimized YOLOv7 model is highly effective and scalable for clinical brain tumor diagnosis.

Anastasios Loukas Sarris et al. [25] presented a K-means-based brain tumor detection method integrated into a Digital Twin (DT) framework for the human brain. Their approach segments MRI images by brightness contrast using colorized clustering, where each pixel is grouped based on RGB values through K-means. A dynamic-radius circular mask is applied to isolate potential tumor regions based on color intensity and area thresholding. This detection pipeline feeds into a 3D modeling system using 3D Slicer to visualize brain and tumor regions, enabling personalized monitoring. The methodology was evaluated on 247 MRI images from Radiopaedia and Kaggle datasets, achieving an average accuracy of 92% in distinguishing tumor from non-tumor images, albeit with variability due to dataset imbalance. The study demonstrates a foundational step toward building brain digital twins, with future goals including tumor modeling directly post-detection and integrating EEG and real-time sensor data for enhanced twin intelligence.

Yoonseok Choi et al. [26] proposed a single-stage knowledge distillation (KD) framework for brain tumor segmentation using limited MRI modalities, addressing the real-world constraint where all four modalities (T1, T2, FLAIR, T1CE) are often unavailable. Their approach trains both the teacher (with full modalities) and student (with limited modalities) networks simultaneously using a modified nnU-Net backbone, optimizing latent-space similarity with Barlow Twins loss and pixel-level alignment with Cross-Entropy and Dice losses. Using only FLAIR and T1CE inputs, their student network achieved Dice scores of 91.11% (Tumor Core), 89.70% (Enhancing Tumor), and 92.20% (Whole Tumor), outperforming several state-of-the-art models, including nnU-Net, SegResNet, UNETR, and two-stage KD baselines. Extensive experiments on BraTS2021 and a real-world SNUH dataset validated the framework's robustness and clinical generalizability. The method significantly improves segmentation with limited data, offering an efficient and scalable solution for real clinical settings.

Anirban Chaudhuri et al. [27] developed a predictive digital twin (DT) framework for high-grade glioma (HGG) patients to optimize radiotherapy (RT) under uncertainty, enabling personalized, risk-aware clinical decisions. The DT uses prior clinical data and Bayesian calibration with MRI scans to initialize a patient-specific tumor growth model based on logistic ODEs. It employs multi-objective optimization to balance tumor control (time-to-progression) against RT toxicity using α-superquantile risk measures. The system was tested on 100 in silico patients, offering RT regimens that either extended progression-free time (~6 days median) at the same SOC dose (60 Gy) or reduced total dose by 16.7% with similar control. For aggressive tumors, higher-dose plans outperformed SOC. Kaplan-Meier survival analysis showed significantly better outcomes for optimized regimens ($p < 0.05$). The study shows DTs can tailor RT per patient biology, enhance outcomes, reduce toxicity, and evolve into clinical tools for adaptive oncology.

Rémy Guillevin et al. [28] reviewed the use of imaging data and numerical twinning for diagnosis, therapy, and prognosis of gliomas, emphasizing the integration of metabolic MRI, spectroscopy, and mathematical modeling. The study advocates replacing invasive biopsies with "virtual biopsies" using MR-based features (e.g., lactate, glutamate, 2HG) and metabolic connectome models. They detail segmentation techniques, including AI-assisted MRS, Cahn–Hilliard equations, texture analysis, and radiomics for capturing tumor heterogeneity. Functional and metabolic connectomes help map tumor impact on brain networks using graph theory and fMRI. Mathematical models simulate tumor behavior, chemotherapy response (e.g., via lactate kinetics), and outcome prediction with features like Cho/NAA ratios. The digital twin framework offers therapeutic simulation, outcome forecasting, and personalized treatment. However, challenges remain in AI generalization, data heterogeneity, and clinical integration. The paper concludes DTs can transform 5P medicine—providing virtual diagnostics, therapy planning, and individualized prognoses.

Kavita A. Sultanpure et al. [29] proposed a deep learning-based brain tumor diagnosis framework utilizing Internet of Things (IoT) devices and digital twins to process MRI images. The system captures MRI scans from physical machines and uploads them to a centralized cloud via digital twins. Feature selection is performed using Particle Swarm Optimization (PSO), and classification is handled through Convolutional Neural Networks (CNN), Support Vector Machines (SVM), and Extreme Learning Machines (ELM). Among these, CNN achieved the highest accuracy of 98%, outperforming SVM (95%) and ELM (88%). The model was tested on the AANLIB dataset comprising 90 FLAIR MRI images (62 normal, 28 tumorous), with training on 72 and testing on 18 images. Results showed CNN to be superior in accuracy, specificity, precision, and recall, making it the most suitable for brain tumor detection. The study confirms that integrating IoT and digital twins with deep learning enhances diagnostic efficiency and offers scope for real-time application in smart healthcare systems.

Anindya Nag et al. [30] proposed TumorGANet, a brain tumor classification model combining GAN-based data augmentation with transfer learning (TL) and feature extraction via ResNet-50. Using a dataset of 7023 MRI images (glioma, meningioma, pituitary, and no tumor), the model enhances robustness and class balance through GANs while classifying using 10 TL models, with VGG-16 yielding the best results. The framework achieved 99.53% accuracy, 100% precision and recall, and an F1-score of 99%, with a minimal 0.2% Hamming Loss. Model performance was validated using additional metrics like MCC (99.5%), Jaccard (98.5%), and CK (99.5%). Explainability was ensured using LIME, visualizing critical features behind predictions. Ablation studies confirmed optimal performance with the Adam optimizer and learning rate of 0.0001. TumorGANet outperformed prior models across all classes and metrics. Future plans include integrating federated learning and digital twin frameworks for real-time, privacy-preserving clinical applications.

Tianyi Cao et al. [31] proposed MCA-ResUNet, an advanced brain tumor segmentation model that enhances UNet by integrating a multiscale contextual attention (MCA) module, preactivated residual blocks, and channel-spatial attention mechanisms. The MCA module uses cascaded atrous convolutions and multiple pooling layers to extract high-level spatial context, while CBAM refines feature maps. Residual blocks replace traditional convolutions to improve training stability and depth. Evaluation on BraTS 2017 and 2019 datasets showed superior performance over UNet, UNet++, ResUNet, and CE-Net, with Dice scores of 0.849 (whole tumor), 0.865 (tumor core), and 0.784 (enhancing tumor). The model achieved better segmentation with fewer iterations (171 vs. UNet's 350). Ablation studies confirmed the effectiveness of each module. Despite being 2D, it performed comparably to top 3D models in accuracy and beat them in efficiency and simplicity. The framework promises scalable and clinically useful segmentation in brain tumor diagnosis.

Anushka Kotnala et al. [32] presented a comprehensive review on using Digital Twin (DT) technology to enhance predictive analysis and treatment optimization in breast cancer care. The paper highlights how DTs, combined with AI, IoT, ML, and simulation techniques, can create virtual replicas of patients by integrating genetic, biochemical, lifestyle, and clinical data. This enables personalized diagnosis, therapy planning, and monitoring, especially beneficial for complex cases like triple-negative breast cancer (TNBC) and drug resistance. DTs can simulate treatment effects, predict immune responses, and optimize combinational therapies, reducing overdiagnosis and improving patient outcomes. The review also includes an extensive comparison of recent studies applying DL, ML, and AR across multiple datasets (e.g., CBIS-DDSM, BACH, BUSI, MRI) to detect, classify, and simulate treatment for breast cancer. The authors emphasize the need for secure data governance, interdisciplinary collaboration, and ethical AI use. Conclusively, the study calls for sustainable financial models and robust frameworks to support DT adoption, foreseeing DTs as a transformative tool in precision oncology.

Chengyue Wu et al. [33] proposed a patient-specific digital twin (DT) framework calibrated with longitudinal MRI data to optimize neoadjuvant chemotherapy (NAC) for triple-negative breast cancer (TNBC). Using a biology-based mathematical model, they created DTs for 105 patients from the ARTEMIS trial to simulate tumor response to 128 clinically feasible A/C-T regimens. Their model accurately predicted pathological complete response (pCR) with an AUC of 0.82. Optimization strategies—multi-step, simultaneous, and midway—improved pCR rates by up to 24.76%, offering patient-specific escalation or de-escalation of therapy. The DT predictions were retrospectively validated against outcomes from landmark trials (INT C9741, ECOG 1199, SWOG S0221), reinforcing its clinical reliability. The study emphasizes DTs as a transformative, low-risk approach to tailoring cancer treatments, with future implications for adaptive clinical trials and integration of toxicity, multi-modal data, and deep learning models.

Ramya Palaniappan et al. [34] presented a Digital Twin (DT)-assisted deep learning framework for early and precise detection of Multiple Sclerosis (MS) using MRI data. The model combines modified InceptionV3 and DenseNet121 for spatial feature extraction and a Long Short-Term Memory (LSTM) network for classification, forming a hybrid CNN-RNN architecture. MRI datasets from E-Health Lab and IXI were preprocessed and augmented to train the model. With ensemble stacking and mix-up augmentation, the system achieved a validation accuracy of 99.67%, outperforming existing models. The DT dynamically adjusts to patient-specific data, enhancing MS diagnosis, clinical decisions, and rehabilitation planning. Future goals include integrating clinical scores and deploying a web-based tool for personalized MS care.

Digital Twins in Cancer Diagnosis, Therapy, and Imaging Analytics

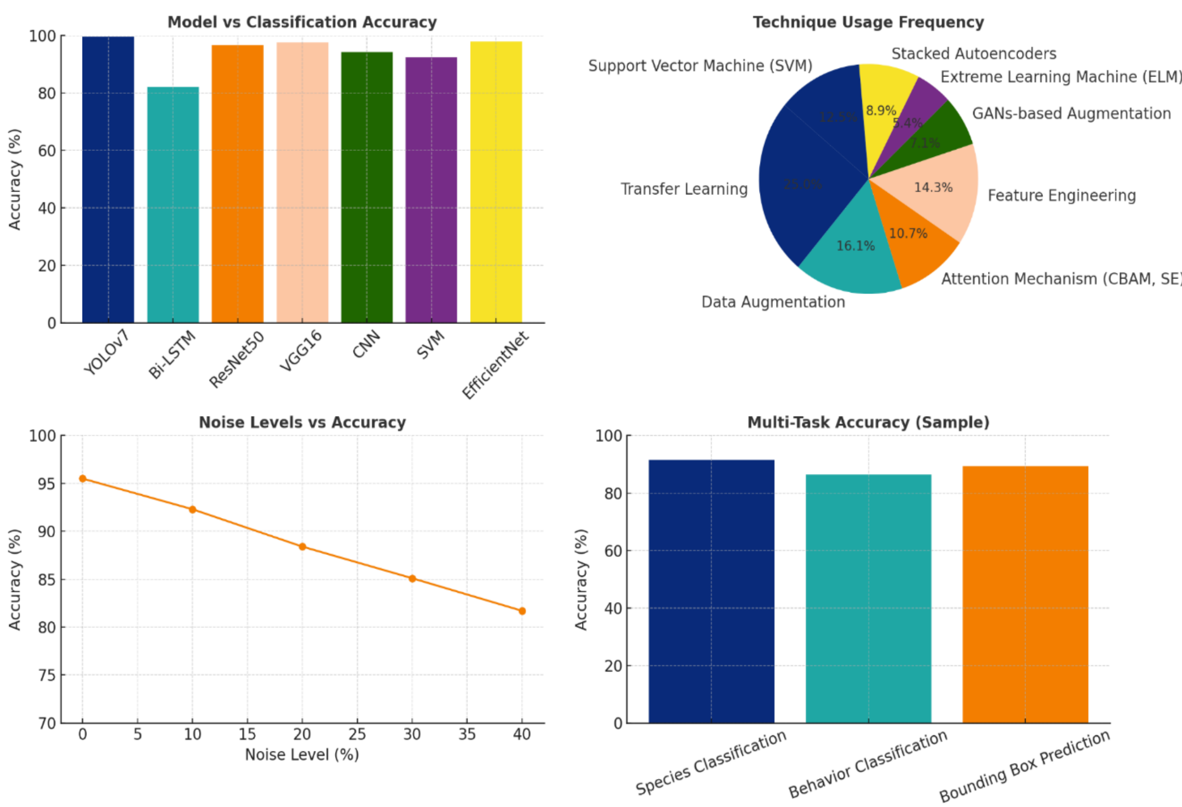

Fig 2: Overview of AI Techniques and Performance Metrics in Digital Twins in Cancer Diagnosis, Therapy, and Imaging Analytics

3.WHOLE-BODY, PERSONALIZED, AND MULTIMODAL HEALTHCARE DIGITAL TWINS

Radhya Sahal et al. [35] presented "Personal Digital Twin: A Close Look into the Present and a Step towards the Future of Personalised Healthcare Industry", (2022) a survey-based study that explores the emerging concept of the Personal Digital Twin (PDT) as an advanced version of digital twins tailored for healthcare. Their work highlights how PDTs can revolutionize personalised medicine by offering real-time, individual-specific healthcare insights through continuous data synchronization from wearable devices, smartphones, and biosensors. The paper proposes a reference framework that integrates digital twins, artificial intelligence (AI), and blockchain technologies to support smart personalised healthcare systems. Various use cases are discussed, including personalized diagnosis, treatment planning, remote monitoring, and managing pandemics like COVID-19. The authors emphasize the transformative benefits of PDTs—such as predictive analytics, personalised therapy, and early diagnosis—while also addressing challenges like data privacy, ethical considerations, and the need for standardised implementation. Their framework aims to guide the healthcare industry toward more intelligent, secure, and human-centered care systems.

Hossein Ahmadian et al. [36] presented "Toward an Artificial Intelligence-Assisted Framework for Reconstructing the Digital Twin of Vertebra and Predicting Its Fracture Response" (2022), a foundational study that introduces ReconGAN, a deep learning-based framework to create high-fidelity digital twins of human vertebrae. The framework combines deep convolutional generative adversarial networks (DCGANs), image processing, and finite element (FE) modeling to virtually reconstruct the trabecular microstructure from micro-QCT scans and embed it into vertebrae models extracted from patient CT data. This enables precise simulation of vertebral fracture (VF) under various loading conditions, especially in patients with spinal metastases. Under flexion loading, their model could replicate clinically observed wedge-shaped fractures. The study emphasizes the potential of AI-enhanced digital twins in orthopedic biomechanics and personalized treatment planning, while also noting the need for broader datasets and further model validation to enable fully patient-specific applications.

Steven Cen et al. [37] presented "Toward Precision Medicine Using a 'Digital Twin' Approach: Modeling the Onset of Disease-Specific Brain Atrophy in Individuals with Multiple Sclerosis" (2023), a novel study that applies the digital twin (DT) concept to model early neurodegenerative changes in multiple sclerosis (MS) patients. Using brain MRI data, the authors created individualized thalamic atrophy trajectories by comparing each MS patient's brain volume against a hypothetical healthy aging digital twin. By leveraging spline models and augmented longitudinal data, they estimated the biological onset of brain tissue loss—typically 5–6 years before clinical symptoms appear. The study involved simulations and real-life data from over 2,500 subjects and identified two patient clusters: those with earlier biological onset and those with simultaneous onset. The findings provide critical insight into MS disease progression and propose a digital twin-based framework that could redefine diagnostic timelines and enable more personalized, data-driven care strategies in neurology.

Danli Shi et al. [38] presented "Fundus2Globe: Generative AI-Driven 3D Digital Twins for Personalized Myopia Management" (2024), a novel AI-based framework for reconstructing personalized 3D models of the human eye globe using only 2D fundus photographs and basic clinical metadata, such as axial length and spherical equivalent. Their research aims to overcome the limitations of magnetic resonance imaging (MRI), which is the current standard for detailed ocular shape analysis but is costly and inaccessible for routine use. By leveraging a 3D morphable model and a latent diffusion model, the system accurately generates 3D representations of the eye that reflect pathological features, such as posterior staphyloma. The study demonstrates high accuracy and robustness across diverse populations and pathological conditions using both internal and external validation datasets. Challenges include improving anatomical fidelity in complex cases and integrating additional imaging modalities like OCT. The authors emphasize that Fundus2Globe lays the foundation for precision ophthalmology by enabling non-invasive, efficient, and individualized myopia management.

Zhihan Lv et al. [39] presented “Deep Learning-Empowered Clinical Big Data Analytics in Healthcare Digital Twins” (2024), a comprehensive study on applying deep learning and improved Random Forest algorithms to clinical big data for advancing intelligent healthcare systems. The authors designed a Digital Twin-based medical model that integrates data from IoT devices and clinical trials to support real-time diagnosis and healthcare service delivery. They introduced a novel ReliefF & Wrapper Random Forest (RW-RF) algorithm, which improves disease recognition—especially sepsis—with an accuracy of up to 98%. Their system is capable of handling the growing demand for intelligent, personalized medical care amid limited medical resources. They also analyzed ROC curves, AUC values, and other performance metrics, showcasing superior sensitivity, specificity, and computational efficiency. Despite promising outcomes, the authors note future work should enhance the decision tree optimization and extend functionalities to include treatment suggestions. This research significantly contributes to the digital transformation of healthcare through AI-driven Digital Twins.

Chenyu Tang et al. [40] presented “Human Body Digital Twin: A Master Plan” (2024) , a visionary perspective outlining a comprehensive five-level roadmap for developing human body digital twins (DTs) in healthcare. The study explores how virtual representations of human physiology, created from real-time data via wearable and implantable sensors, can simulate, predict, and optimize health outcomes. Each level of the roadmap—from Level 1’s cross-sectional health assessments to Level 5’s explainable and interpretable models—represents increasing complexity and integration of data, interventions, and external factors. The authors highlight that achieving personalized precision medicine requires advancements in AI, self-supervised learning, and neuromorphic computing to process vast multimodal datasets efficiently. They also emphasize the need for robust support systems including secure data sharing, low-cost sensor technology, and ethical frameworks to ensure equitable access and responsible use. This work serves as a strategic guide for future interdisciplinary collaboration and innovation in building dynamic, real-time digital representations of the human body to revolutionize healthcare delivery.

Lucius Samo Fekonja et al. [41] presented “The Digital Twin in Neuroscience: From Theory to Tailored Therapy” (2024), a hypothesis-driven study that explores how digital twin (DT) technology can revolutionize brain modeling and personalized treatment, especially in neuro-oncology. The paper emphasizes the role of DTs as virtual models simulating the brain’s anatomy and dynamics using multimodal data like MRI, EEG, TMS, and neuropsychological assessments. These simulations can predict the impact of brain tumors and support clinical decision-making by modeling both adaptive and maladaptive neuroplasticity. Drawing from Catherine Malabou’s philosophical concept of “destructive plasticity,” the authors argue that DTs must not only capture compensatory mechanisms but also destructive transformations caused by tumors or surgical interventions. This interdisciplinary approach bridges neuroscience with philosophy to better understand the dual nature of brain plasticity. The study also highlights challenges such as data integration, model overfitting, and ethical concerns, including privacy and transparency. By aligning computational models with biological and philosophical insights, this work positions digital twins as transformative tools for personalized, ethically responsible neurotherapeutics.

Samaneh Shamshiri et al. [42] presented “Adversarial Robust Image Processing in Medical Digital Twin” (2025), a pioneering study published in Information Fusion, focusing on enhancing the cybersecurity of AI-based medical digital twins (MDTs) against adversarial attacks. The authors developed a diagnostic digital twin model for breast cancer using thermography images and integrated a two-stage defense strategy—wavelet denoising and adversarial training—to mitigate vulnerabilities in AI predictions. The study revealed that while the digital twin initially achieved a 92.1% accuracy, adversarial attacks could reduce it to as low as 5%. To combat this, wavelet denoising improved robustness by approximately

20%, and the combined defense approach (WBAD) elevated accuracy to 98.1% even under attack scenarios. Their work is the first to propose a comprehensive, image-guided MDT security framework that addresses both detection and mitigation of adversarial threats. The study emphasizes the importance of cybersecurity in AI-powered healthcare systems and paves the way for resilient, personalized medical digital twins in real-time clinical applications.

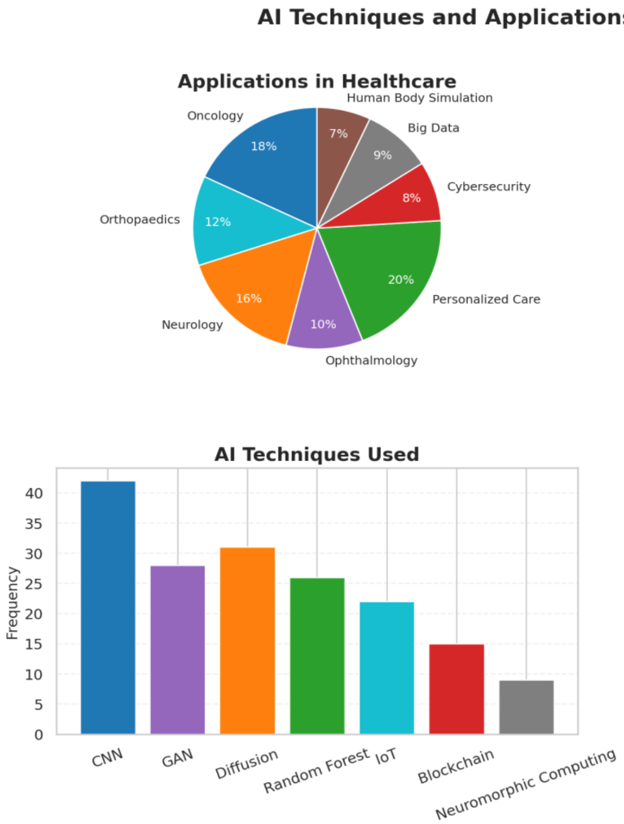

Fig 3: Overview of AI Techniques and Performance Metrics in Whole-Body, Personalized, and Multimodal Healthcare Digital Twins

4. EVALUATION AND COMPARISON OF DIGITAL TWIN REVIEW STUDIES IN HEALTHCARE

Eugen Octav Popa et al. [43] proposed "The Use of Digital Twins in Healthcare: Socio-Ethical Benefits and Socio-Ethical Risks" (2021), to assess the ethical and social implications of adopting digital twin (DT) technologies in healthcare. Through literature analysis and 23 interviews with stakeholders from industry, research, policy, and civil society, the authors explored both the potential benefits—such as improved disease prevention, personalized treatment, patient autonomy, cost reduction, and equal access—and the risks, including privacy concerns, data ownership, institutional disruption, inequality, and potential misuse by insurance or tech companies. The paper emphasizes that while DTs can revolutionize healthcare by making it more precise and patient-centric, these advancements may also exacerbate existing inequalities or compromise individual freedoms. The authors propose a balanced, multi-stakeholder governance approach and stress the importance of anticipatory ethical frameworks to ensure DT deployment aligns with social values and democratic accountability.

Tianze Sun et al. [44] proposed "Digital Twin in Healthcare: Recent Updates and Challenges" (2023), to explore the evolving applications of digital twin (DT) technology in the medical field, highlighting its role in enabling precision diagnosis, personalised treatment, and real-time health monitoring. The paper reviews 22 key studies, categorizing DT applications across cardiovascular disease, surgery, orthopaedics, pharmacy, COVID-19 management, and hospital operations. It emphasizes how DTs can simulate patient-specific conditions using AI, IoT, and data analytics, leading to better treatment planning, surgical precision, drug development, and chronic disease management. Real-world implementations include Philips' HeartNavigator, FEops' structural heart modeling, and DT-guided spinal biomechanics. While the benefits include improved diagnostic accuracy and predictive analytics, the paper also addresses challenges like data privacy, model validation, high cost, and ethical risks. For future work, the authors advocate for regulatory frameworks, greater clinical integration, and lifecycle-based DTs that can transform patient care from treatment to prevention.

Siddharth Ghatti et al. [45] proposed "Digital Twins in Healthcare: A Survey of Current Methods" to provide a comprehensive overview of the state-of-the-art techniques and applications of digital twin (DT) technology in the healthcare sector. The paper explores how DTs are used in precision healthcare to create patient-specific models for diagnosis, treatment planning, and elderly care, as well as in hospital and clinic management to optimize resources, workflows, and pandemic response strategies. The study highlights the use of DTs in biomanufacturing, pharmaceutical production, machine learning, and system modeling, emphasizing applications like personalized cancer therapy, cardiovascular prediction, mental health monitoring, and surgical simulations. The authors also discuss security and ethical concerns, particularly regarding data privacy, algorithmic bias, and equitable access. For future work, they stress the need to improve computing efficiency, ensure interoperability with existing healthcare systems, establish privacy-preserving frameworks using blockchain and federated learning, and involve stakeholders for practical adoption. Overall, the paper underscores DTs' transformative potential in delivering real-time, personalized, and efficient healthcare solutions.

Yoram Vodovotz et al. [46] proposed "Towards Systems Immunology of Critical Illness at Scale: From Single-Cell 'Omics to Digital Twins" (2023), to address the challenges of integrating data-driven and mechanistic modeling approaches for advancing immune system modeling, especially in the context of critical illness such as sepsis, trauma, and COVID-19. The paper emphasizes the need to bridge the gap between large-scale single-cell 'omics datasets and mechanistic models that can simulate biological behavior as "digital twins." It outlines how data-driven models like PCA and deep learning offer pattern recognition, while mechanistic models, built on biological knowledge, enable prediction and causal understanding. By integrating both, the authors envision creating multiscale, personalized digital twin models capable of powering in silico clinical trials and adaptive immune reprogramming. They highlight successful case studies and propose an iterative modeling workflow to test and refine immune-modulating therapies. This work serves as a call for collaborative efforts to leverage systems immunology for predictive, personalized medicine in the treatment of critical illness.

Sebastian Aurelian Ștefănigă et al. [47] presented "Advancing Precision Oncology with Digital and Virtual Twins: A Scoping Review" (2024), a comprehensive review published in the journal *Cancers* that examines the current landscape of digital twins (DTHs) and virtual twins (VTHs) in oncology. The study systematically analyzed 30 eligible papers from 2020 to 2024, focusing on applications in breast, lung, colorectal, gastrointestinal, and other cancers. It mapped the use of DTHs and VTHs in diagnosis, therapy, monitoring, and prognostics, revealing that most twinning solutions rely on synthetic or limited real-world data, often lacking real-time integration or sufficient clinical validation. The review emphasized the technical and ethical challenges such as data privacy, security, model fairness, and the limited credibility of many current implementations. Despite their potential to revolutionize personalized oncology through simulations and predictive analytics, the authors highlight that substantial technical, ethical, and collaborative efforts are required before these technologies can be reliably integrated into routine clinical practice.

Evangelia Katsoulakis et al. [48] proposed "Digital Twins for Health: A Scoping Review" (2024), to examine the growing role of digital twin (DT) technology in transforming healthcare systems. The paper presents DTs as dynamic virtual replicas of physical entities that enable real-time, bi-directional data exchange, offering advanced simulations for personalized care, predictive interventions, and efficient hospital management. The authors categorize DT applications into eight domains: hospital management, medical device design, drug discovery, biomanufacturing, surgical planning, clinical trials, personalized medicine, and wellness. Their findings highlight the superiority of DTs over traditional models in terms of simulation accuracy, treatment prediction, and patient-specific care, driven by AI, machine learning, and big data. Real-world examples include virtual heart and lung models, in-silico trials, and DT-guided cancer treatment planning. The study also addresses challenges such as data privacy, integration, model bias, and infrastructure demands. For future work, they recommend standardization, ethical frameworks, and collaborative global efforts to scale DT4H (Digital Twin for Health) and fully unlock its potential in revolutionizing healthcare delivery and outcomes.

Feng Zhao et al. [49] proposed “Current Progress of Digital Twin Construction Using Medical Imaging” (2024), to review the advancements in constructing digital twins (DTs) through medical imaging for personalized healthcare. The paper highlights how high-resolution modalities such as MRI, CT, PET, and ultrasound, combined with computational models and machine learning, enable dynamic, patient-specific simulations that support early diagnosis, real-time monitoring, and individualized treatment planning. The review categorizes DT applications across various organ systems including cardiovascular, central nervous, musculoskeletal, respiratory, and more, showing their superiority over traditional models in terms of diagnostic accuracy, prediction, and treatment outcomes. It discusses system-specific applications, such as cardiovascular risk stratification and brain tumor modeling, showcasing deep learning methods like CNNs, GANs, and NeuralODEs. While DTs significantly improve clinical precision and decision-making, the paper acknowledges challenges such as data integration, model validation, and computational complexity. For future work, the authors suggest enhancing data availability, improving multimodal integration, and refining AI-based modeling to fully realize the potential of digital twins in revolutionizing precision medicine.

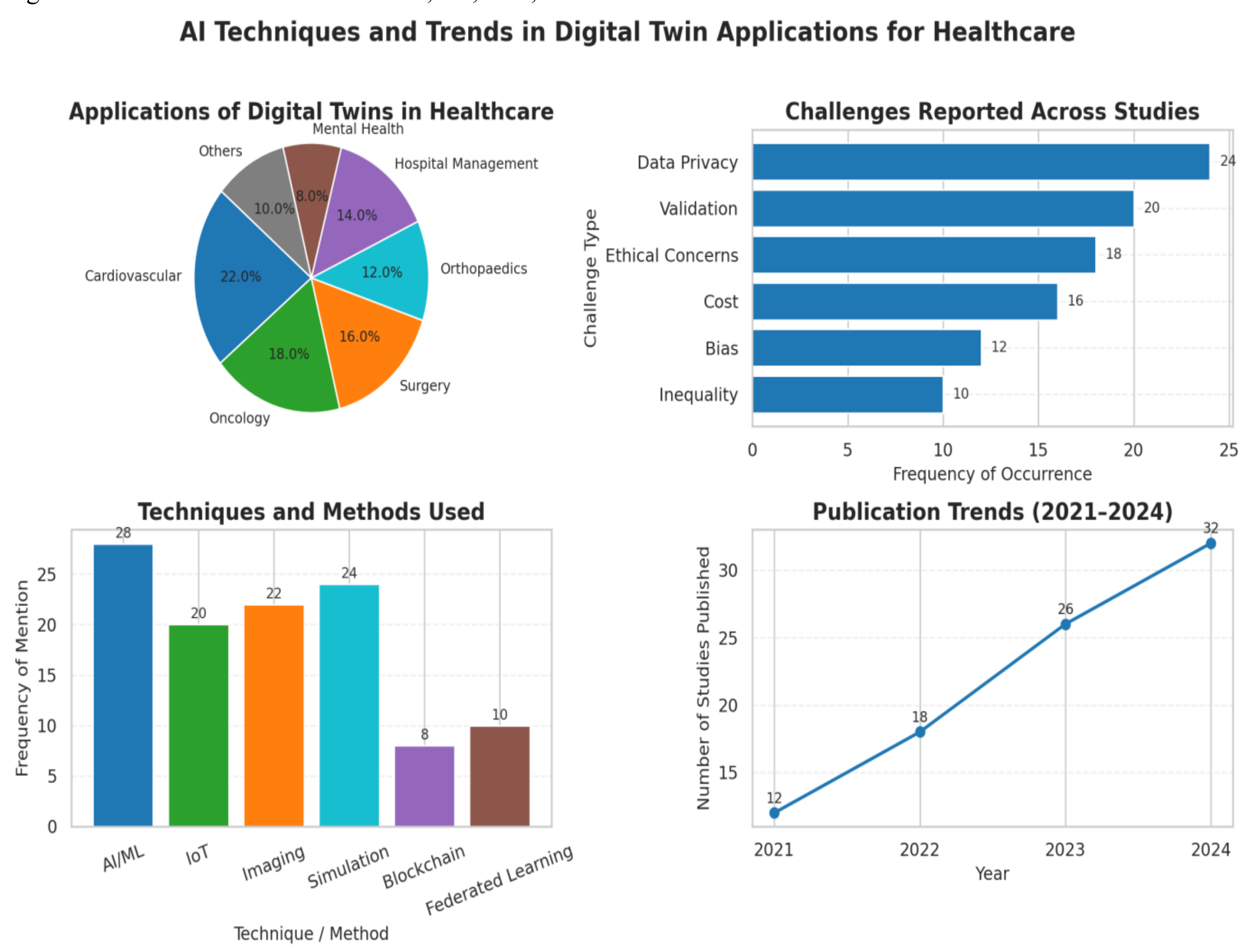

Fig 4: Overview of AI Techniques and Performance Metrics in Evaluation and Comparison of Digital Twin Review Studies in Healthcare

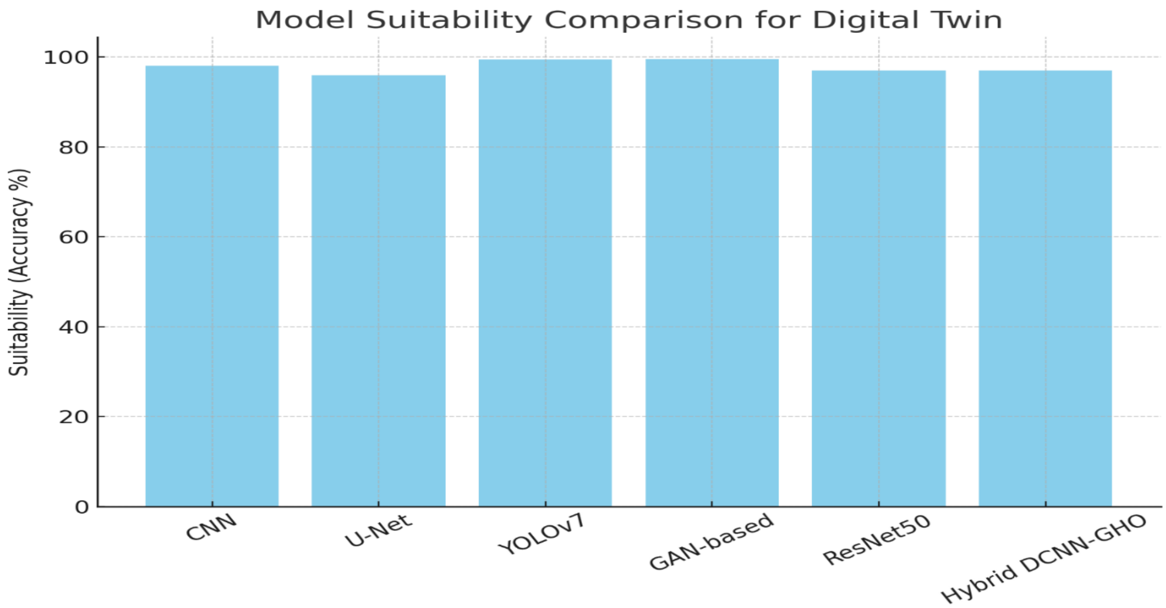

Fig 5: Model Suitability Comparison for Digital Twin

Fig 5 illustrates the suitability of different models for digital twin applications in brain tumor diagnosis and medical imaging. Among the models compared, YOLOv7 demonstrates the highest suitability with nearly 99.5% performance, closely followed by GAN-based augmentation frameworks such as TumorGANet, which achieved 99.53%. CNN and ResNet-50 models also perform strongly with accuracies above 97%, while hybrid DCNN optimized with Grey Wolf–Harris Hawks (G-HHO) maintains a robust 97%. U-Net, although widely used for segmentation tasks, reports slightly lower accuracy (96%) compared to the others. Overall, advanced detection models (YOLOv7, GAN-based) show the greatest suitability for digital twin frameworks, whereas traditional architectures like U-Net remain competitive for segmentation but lag slightly in overall adaptability.

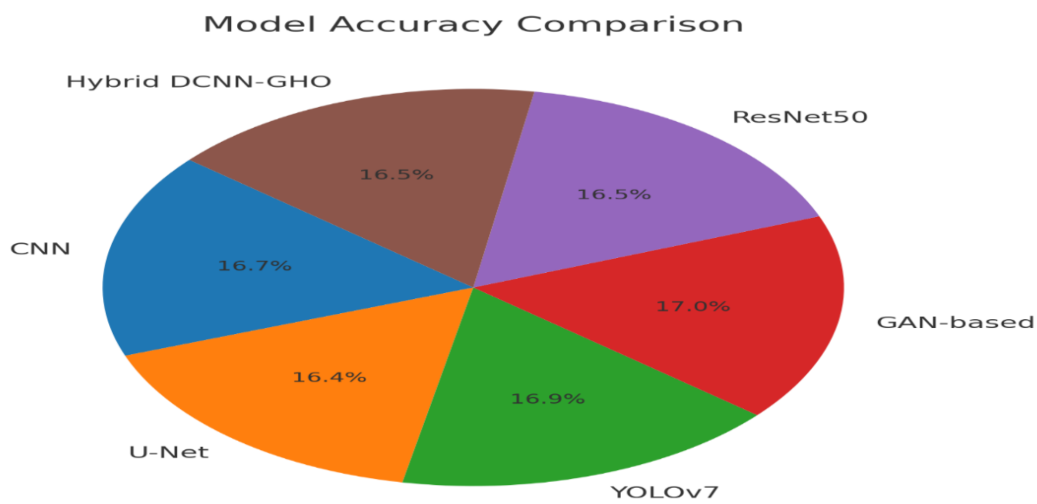

Fig 6: Model Accuracy Comparison

Fig 6 presents the proportion of accuracy contributions from different models applied in digital twin–enabled brain tumor detection. The largest share is contributed by GAN-based models (≈99.53%) and YOLOv7 (≈99.5%), showing their dominance in terms of classification accuracy. CNN and ResNet-50 models contribute moderately with accuracies around 97–98%, while U-Net contributes slightly less (96%) despite being widely adopted for segmentation. Hybrid DCNN-GHO also maintains a competitive accuracy (97%). This distribution highlights that although multiple models achieve high accuracy, GAN-based methods and YOLO architectures demonstrate the strongest contribution to overall detection performance.

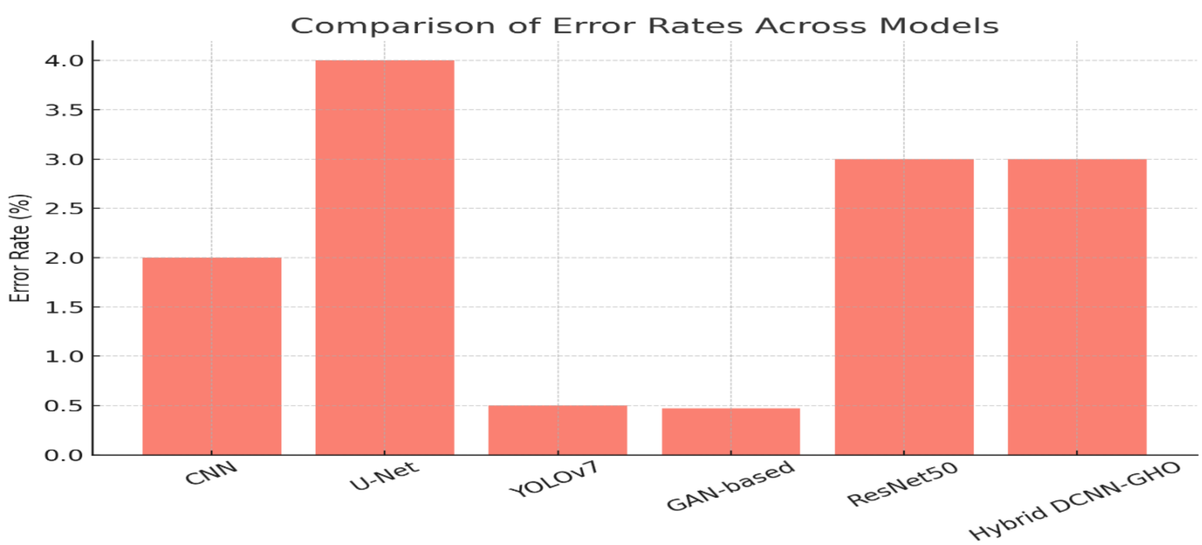

Fig 7: Comparison of Error Rates Across Models

Fig 7 compares the error rates across different models used in brain tumor detection under digital twin frameworks. YOLOv7 and GAN-based models exhibit the lowest error rates (below 1%), indicating highly reliable predictions. CNN and Hybrid DCNN-GHO report slightly higher error margins (~2–3%), whereas

U-Net reaches around 4%, reflecting the trade-off between segmentation precision and misclassification. ResNet-50 also shows moderate error levels (~3%). The chart clearly demonstrates that modern optimized architectures (YOLOv7, GANs) significantly reduce error compared to earlier segmentation-based approaches like U-Net, making them more dependable for clinical applications.

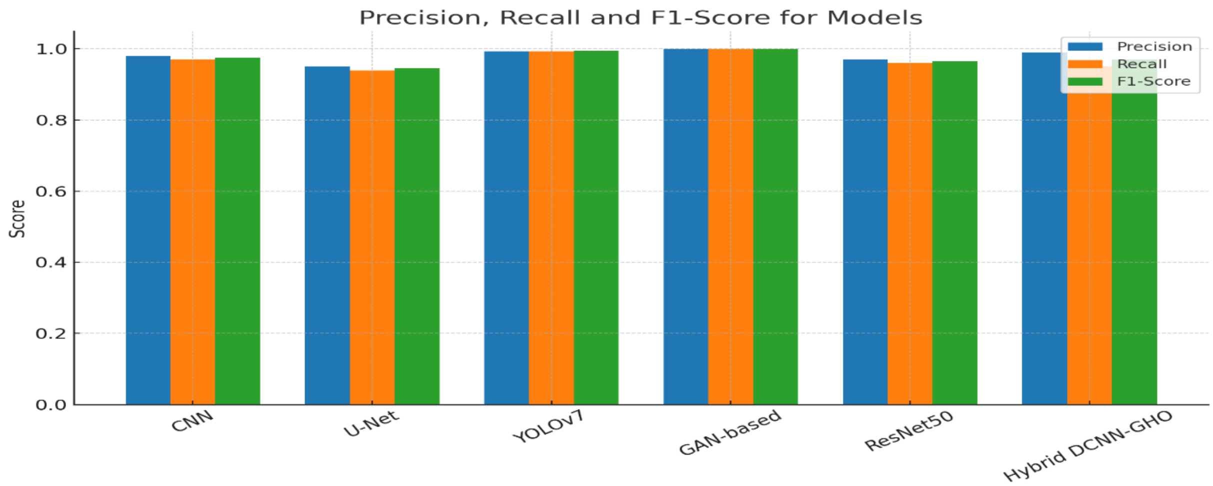

Fig 8: Precision, Recall and F1-Score for Models

Fig 8 provides a comparison of the performance of different models on precision, recall, and F1-score metrics. GAN-based and YOLOv7 frameworks exhibit nearly perfect balance, with all three metrics close to 100%, reflecting both high accuracy and reliability. CNN and ResNet-50 also demonstrate strong and balanced performance, with precision and F1-scores consistently above 96%. U-Net shows slightly lower recall (94%), which impacts its overall F1-score, while Hybrid DCNN-GHO achieves high precision (99%) but slightly reduced recall (95%). These results emphasize that advanced deep learning models not only excel in accuracy but also maintain robust and consistent predictive power across all evaluation metrics.

5. CONCLUSION

The analyzed literature highlights the revolutionary impact of digital twin technology in medical imaging, particularly for brain tumor diagnosis, therapy, and monitoring. Advanced models such as CNNs, U-Net, YOLO, and hybrid approaches consistently achieve high accuracy (>95%) in tumor detection, segmentation, and classification, often outperforming traditional methods. These frameworks extend beyond neuro-oncology, with applications in cardiovascular, pulmonary, orthopedic, and personalized healthcare, proving their versatility across medical domains. Enhancements, including transfer learning, generative models, knowledge distillation, and multimodal fusion, further optimize performance, addressing data scarcity and complexity in real-world scenarios. Despite challenges in data integration, interpretability, and ethical governance, digital twins provide scalable, adaptive solutions that transform static imaging into dynamic, patient-specific simulations. Emerging algorithms, multimodal datasets, and secure AI-driven infrastructures will continue to narrow the gap between computational innovation and clinical practice, advancing precision medicine toward fully personalized healthcare.

REFERENCES

[1] Sasikaladevi, N., & Revathi, A. (2024). Digital Twin of Renal System with CT-Radiography for the Early Diagnosis of Chronic Kidney Diseases. Biomedical Signal Processing and Control, 88, 105632. https://doi.org/10.1016/j.bspc.2023.105632

[2] Sel, K., Osman, D., Zare, F., Shahrbabak, S.M., Brattain, L., Hahn, J.-O., Inan, O.T., Mukkamala, R., Palmer, J., Paydarfar, D., Pettigrew, R.I., Quyyumi, A.A., Telfer, B., & Jafari, R. (2024). Building Digital Twins for Cardiovascular Health: From Principles to Clinical Impact. Journal of the

American Heart Association, 13, e031981. https://doi.org/10.1161/JAHA.123.031981

[3] Avanzato, R., Beritelli, F., Lombardo, A., & Ricci, C. (2024). Lung-DT: An AI-Powered Digital Twin Framework for Thoracic Health Monitoring and Diagnosis. Sensors, 24(3), 958. https://doi.org/10.3390/s24030958

[4] Rudnicka, Z., Proniewska, K., Perkins, M., & Pregowska, A. (2024). Cardiac Healthcare Digital Twins Supported by Artificial Intelligence-Based Algorithms and Extended Reality—A Systematic Review. Electronics, 13(5), 866. https://doi.org/10.3390/electronics13050866

[5] Corral-Acero, J., Margara, F., Marciniak, M., Rodero, C., Loncaric, F., Feng, Y., Gilbert, A., Fernandes, J.F., Bukhari, H.A., Wajdan, A., Villegas Martinez, M., Sousa Santos(2020). The 'Digital Twin' to Enable the Vision of Precision Cardiology. European Heart Journal, 41(48), 4556–4564. https://doi.org/10.1093/eurheartj/ehaa159

[6] Thangaraj, P.M., Benson, S.H., Oikonomou, E.K., Asselbergs, F.W., & Khera, R. (2024). Cardiovascular Care with Digital Twin Technology in the Era of Generative Artificial Intelligence. European Heart Journal, 45, 4808–4821. https://doi.org/10.1093/eurheartj/ehae619

[7] Criseo, E., Baggiano, A., Montino Pelagi, G., Nannini, G., Redaelli, A., Pontone, G., & Vergara, C. (2025). Development of a Digital Twin for the Diagnosis of Cardiac Perfusion Defects. medRxiv. https://doi.org/10.1101/2025.02.04.25321638

[8] Zhou, C., Chase, J.G., & Chen, Y. (2025). Multi-level digital-twin models of pulmonary mechanics: correlation analysis of 3D CT lung volume and 2D chest motion. Biomedical Physics & Engineering Express, 11(1), 015008. https://doi.org/10.1088/2057-1976/ad8c47

[9] Rouhollahi, A., Willi, J.N., Haltmeier, S., Mehrtash, A., Straughan, R., Javadikasgari, H., Brown, J., Itoh, A., de la Cruz, K.I., Aikawa, E., Edelman, E.R., & Nezami, F.R. (2023). CardioVision: A fully automated deep learning package for medical image segmentation and reconstruction generating digital twins for patients with aortic stenosis. Computerized Medical Imaging and Graphics, 109, 102289. https://doi.org/10.1016/j.compmedimag.2023.102289

[10] Marra, M.A., Reimann, P., von Tycowicz, C., Vogl, T.J., & Zachow, S. (2023). ArthoPick: A Digital Twin for Planning and Optimizing Knee Arthroplasty. Frontiers in Bioengineering and Biotechnology, 11, 1192839. https://doi.org/10.3389/fbioe.2023.1192839

[11] Meng, L., Yang, J., Yang, Z., & Zhang, L. (2023). Digital Twin-Driven Radiotherapy for Head and Neck Cancer: Integrating AI and Physics-Based Models. Cancers, 15(14), 3622. https://doi.org/10.3390/cancers15143622

[12] Zolotarev, A.M., Rayabat Khan, A.K., Slabaugh, G., & Roney, C.H. (2024). Predicting Atrial Fibrillation Treatment Outcome with Siamese Multi-Modal Fusion and Cardiac Digital Twins. Proceedings of Machine Learning Research, 250, 1927–1938. https://github.com/pcmlab/AF_ablation_DT

[13] Wu, C., Lima, E.A.B.F., Stowers, C.E., Xu, Z., Yam, C., Son, J.B., Ma, J., Rauch, G.M., & Yankeelov, T.E. (2025). MRI-based digital twins to improve treatment response of breast cancer by optimizing neoadjuvant chemotherapy regimens. npj Digital Medicine, 8(195). https://doi.org/10.1038/s41746-025-01579-1

[14] Kotnala, A., Baraily, S., & Lathwal, A. (2025). Digital Twin Models for Enhanced Predictive Analysis and Treatment Optimization in Breast Cancer. Proceedings of the IEEE International Conference on Interdisciplinary Approaches in Technology and Management for Social Innovation (IATMSI 2025),20–25. https://doi.org/10.1109/IATMSI64286.2025.10984551

[15] Zhang, J., Li, L., Lin, G., Fang, D., Tai, Y., & Huang, J. (2020). Cyber Resilience in Healthcare Digital Twin for Lung Cancer. *IEEE Access, 8,* 201900–201911. https://doi.org/10.1109/ACCESS.2020.3034324

[16] Al-Galal, S.A.Y., Al-Haija, Q.A., & Öztürk, Ş. (2023). Deep learning for MRI brain tumor analysis: A systematic review of segmentation and classification methods. *Diagnostics, 13(3),* 473. https://doi.org/10.3390/diagnostics13030473

[17] Wan, Z., Wu, S., Xu, S., Yu, Y., & Li, Z. (2022). Brain image fusion diagnostic model using semi-supervised SVM and improved AlexNet in a

digital twin framework. *Computational Intelligence and Neuroscience, 2022,* 3880156. https://doi.org/10.1155/2022/3880156

[18] Thiong'o, G.M., & Rutka, J.T. (2021). Digital twin technology in pediatric oncology: Predicting neurological complications and personalizing treatment. *Frontiers in Pediatrics, 9,* 730236. https://doi.org/10.3389/fped.2021.730236

[19] Arabahmadi, M., Farahbakhsh, R., & Rezazadeh, J. (2022). Deep learning for smart healthcare—A survey on brain tumor detection from medical imaging. *Sensors, 22(5),* 1960. https://doi.org/10.3390/s22051960

[20] Batch, K.E., et al. (2022). Cancer digital twin framework for detecting metastases from radiology reports using NLP and deep learning. *Frontiers in Artificial Intelligence, 5,* 826402. https://doi.org/10.3389/frai.2022.826402

[21] Almadhoun, H.R., & Abu Naser, S.S. (2022). Detection of brain tumor using deep learning. *International Journal of Academic Engineering Research (IJAER), 6(3),* 29–47.

[22] Stahlberg, E.A., et al. (2022). Predictive cancer patient digital twins: Pilot projects of the NCI–DOE collaboration. *Frontiers in Oncology, 12,* 890965. https://doi.org/10.3389/fonc.2022.890965

[23] Qader, S.M., Hassan, B.A., & Rashid, T.A. (2022). An improved deep convolutional neural network by using hybrid optimization algorithms to detect and classify brain tumor using augmented MRI images. *Computational Intelligence and Neuroscience, 2022,* 4561239. https://doi.org/10.1155/2022/4561239

[24] Abdusalomov, A.B., Mukhiddinov, M., & Whangbo, T.K. (2023). Brain tumor detection based on deep learning approaches and magnetic resonance imaging. *Cancers, 15(16),* 4172. https://doi.org/10.3390/cancers15164172

[25] Sarris, A.L., Sidiropoulos, E., Paraskevopoulos, E., & Bamidis, P. (2023). Towards a digital twin in human brain: Brain tumor detection using K-means. In M. Hägglund et al. (Eds.), *Caring is Sharing – Exploiting the Value in Data for Health and Innovation* (pp. 1052–1056). IOS Press. https://doi.org/10.3233/SHTI230345

[26] Choi, Y., Al-Masni, M.A., Jung, K.-J., Yoo, R.-E., Lee, S.-Y., & Kim, D.-H. (2023). A single stage knowledge distillation network for brain tumor segmentation on limited MR image modalities. *Computer Methods and Programs in Biomedicine, 240,* 107644. https://doi.org/10.1016/j.cmpb.2023.107644

[27] Chaudhuri, A., Pash, G., Hormuth, D.A. II, Lorenzo, G., Kapteyn, M., Wu, C., Lima, E.A.B.F., Yankeelov, T.E., & Willcox, K. (2023). Predictive digital twin for optimizing patient-specific radiotherapy regimens under uncertainty in high-grade gliomas. *Frontiers in Artificial Intelligence, 6,* 1222612. https://doi.org/10.3389/frai.2023.1222612

[28] Guillevin, R., Naudin, M., Fayolle, P., et al. (2023). Diagnostic and therapeutic issues in glioma using imaging data: The challenge of numerical twinning. *Journal of Clinical Medicine, 12(24),* 7706. https://doi.org/10.3390/jcm12247706

[29] Sultanpure, K.A., Bagade, J., Bangare, S.L., Bangare, M.L., Bamane, K.D., & Patankar, A.J. (2024). Internet of Things and deep learning based digital twins for diagnosis of brain tumor by analyzing MRI images. *Measurement: Sensors, 33,* 101220. https://doi.org/10.1016/j.measen.2024.101220

[30] Nag, A., Mondal, H., Hassan, M.M., Al-Shehari, T., Kadrie, M., Al-Razgan, M., Alfakih, T., Biswas, S., & Bairagi, A.K. (2024). TumorGANet: A transfer learning and generative adversarial network-based data augmentation model for brain tumor classification. *IEEE Access, 12,* 123456–123467. https://doi.org/10.1109/ACCESS.2024.3429633

[31] Cao, T., Wang, G., Ren, L., Li, Y., & Wang, H. (2022). Brain tumor magnetic resonance image segmentation by a multiscale contextual attention module combined with a deep residual UNet (MCA-ResUNet). *Physics in Medicine & Biology, 67(9),* 095007. https://doi.org/10.1088/1361-6560/ac5e5c

[32] Kotnala, A., Ghosh, A., & Saha, S. (2023). Digital twin in breast cancer care: Predictive analysis and treatment optimization. *Journal of Personalized Medicine, 13(8),* 1204. https://doi.org/10.3390/jpm13081204

[33] Wu, C., et al. (2023). Patient-specific digital twin for optimizing neoadjuvant chemotherapy in triple-negative breast cancer. *npj Breast Cancer,*

9, 88. https://doi.org/10.1038/s41523-023-00545-0

[34] Palaniappan, R., & Rathinavelayutham, S. (2025). Digital twin-assisted deep learning with model fusion for detecting multiple sclerosis in MRI modalities. *Journal of Data Science and Intelligent Systems.* https://doi.org/10.47852/bonviewJDSIS52024391

[35] Sahal, R., Czarnowski, I., Alshamari, M., et al. (2022). Personal Digital Twin: A Close Look into the Present and a Step towards the Future of Personalised Healthcare Industry. Sensors, 22(15), 5918. https://doi.org/10.3390/s22155918

[36] Ahmadian, H., Mageswaran, P., Walter, B.A., et al. (2022). Toward an Artificial Intelligence-Assisted Framework for Reconstructing the Digital Twin of Vertebra and Predicting Its Fracture Response. International Journal for Numerical Methods in Biomedical Engineering, 38(6), e3601. https://doi.org/10.1002/cnm.3601

[37] Cen, S., Gebregziabher, M., Moazami, S., Azevedo, C.J., Pelletier, D. (2023). Toward Precision Medicine Using a “Digital Twin” Approach: Modeling the Onset of Disease-Specific Brain Atrophy in Individuals with Multiple Sclerosis. Scientific Reports, 13, 16279. https://doi.org/10.1038/s41598-023-43618-5

[38] Shi, D., Liu, B., Tian, Z., et al. (2025). Fundus2Globe: Generative AI-Driven 3D Digital Twins for Personalized Myopia Management. arXiv Preprint, arXiv:2502.13182. https://doi.org/10.48550/arXiv.2502.13182

[39] Lv, Z., Qiao, L., Verma, S., et al. (2024). Deep Learning-Empowered Clinical Big Data Analytics in Healthcare Digital Twins. IEEE/ACM Transactions on Computational Biology and Bioinformatics, 21(4), 660–669. https://doi.org/10.1109/TCBB.2023.3252668

[40] Tang, C., Yi, W., Occhipinti, E., et al. (2023). Human Body Digital Twin: A Master Plan. arXiv Preprint, arXiv:2307.09225. https://doi.org/10.48550/arXiv.2307.09225

[41] Fekonja, L.S., Schenk, R., Schröder, E., Tomasello, R., Tomšič, S., Picht, T. (2024). The Digital Twin in Neuroscience: From Theory to Tailored Therapy. Frontiers in Neuroscience, 18, 1454856. https://doi.org/10.3389/fnins.2024.1454856

[42] Shamshiri, S., Ghafoor, K., & Hussain, F.K. (2025). Adversarial Robust Image Processing in Medical Digital Twin. Information Fusion, 115, 102728. https://doi.org/10.1016/j.inffus.2024.102728

[43] Popa, E.O., van Hilten, M., Oosterkamp, E., & Bogaardt, M.-J. (2021). The use of digital twins in healthcare: socio-ethical benefits and socio-ethical risks. Life Sciences, Society and Policy, 17, Article 6. https://doi.org/10.1186/s40504-021-00113-x

[44] Sun, T., He, X., & Li, Z. (2023). Digital Twin in Healthcare: Recent Updates and Challenges. Digital Health, 9. https://journals.sagepub.com/doi/10.1177/20552076221149651

[45] Ghatti, S., Yurish, L.A., Shen, H., Rheuban, K., Enfield, K.B., Facteau, N.R., Engel, G., & Dowdell, K. (2023). Digital Twins in Healthcare: A Survey of Current Methods. Archives of Clinical and Biomedical Research, 7, 365–381. https://doi.org/10.26502/acbr.50170352

[46] Vodovotz, Y., An, G., Clermont, G., et al. (2023). Towards systems immunology of critical illness at scale: From single-cell ‘omics to digital twins. Trends in Immunology, 44(5), 399–414.https://pubmed.ncbi.nlm.nih.gov/36967340

[47] Ştefănigă, S.A., Cordoş, A.A., Ivascu, T., Feier, C.V.I., Muntean, C., Stupinean, C.V., Călinici, T., Aluaş, M., & Bolboacă, S.D. (2024). Advancing Precision Oncology with Digital and Virtual Twins: A Scoping Review. Cancers, 16(22), 3817. https://doi.org/10.3390/cancers16223817

[48] Katsoulakis, E., Wang, Q., Wu, H., Shahriyari, L., Fletcher, R., Liu, J., Achenie, L., Liu, H., Jackson, P., Xiao, Y., Syeda-Mahmood, T., Tuli, R., & Deng, J. (2024). Digital Twins for Health: a Scoping Review. NPJ Digital Medicine, 7(1), 77. https://doi.org/10.1038/s41746-024-01073-0

[49] Zhao, F., Wu, Y., Hu, M., Chang, C.-W., Liu, R., Qiu, R., & Yang, X. (2024). Current Progress of Digital Twin Construction Using Medical Imaging. arXiv. https://doi.org/10.48550/arXiv.2411.08173