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Challenges and Future Directions in AI and Medical Imaging Informatics

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Abstract:

This paper gives an outline of the most recent exploration arrangements in clinical imaging informatics, talks about clinical interpretation, and layouts future bearings for progressing clinical practice. It sums up the advances in clinical imaging obtaining advances for various modalities and features the requirement for proficient clinical information the board methodologies with regards to man-made intelligence in huge medical care information examination. The paper also provides an overview of current and emerging algorithmic approaches for disease classification and organ/tissue segmentation. It specifically focuses on artificial intelligence and deep learning frameworks, which have become the predominant methodologies in this field. The clinical advantages of in-silico displaying propels connected with advancing 3D recreation and perception applications are additionally archived.

Finally, the paper concludes that integrative analytics approaches driven by associate research branches highlighted in this study promise to revolutionize imaging informatics as known today across the healthcare continuum for both radiology and digital pathology applications. The latter is projected to enable informed, more accurate diagnosis, timely prognosis, and effective treatment planning, underpinning precision medicine.

Keywords — **Medical Imaging, Image Analysis, Image Classification, Image Processing, Image Segmentation, Image Visualization, Integrative Analytics, Machine Learning, Deep Learning, Big Data.**

I. INTRODUCTION

Medical Imaging Informatics encompasses the application of information and communication technologies (ICT) to the field of medical imaging, playing a pivotal role in the delivery of healthcare services. Over the last three decades, a diverse spectrum of multidisciplinary medical imaging services has emerged, ranging from basic medical procedures to more in-depth research into human physiology and pathophysiology. Medical imaging informatics encompasses the entire imaging chain. It reaches out from picture creation and securing, through conveyance and the executives, stockpiling and recovery, to handling, examination, and cognizance. Moreover, it incorporates representation, information route, understanding, revealing, and correspondence, filling in as an integrative impetus that shapes a significant scaffold among imaging and other clinical disciplines. As per SIIM, the overall goal of clinical imaging informatics is to upgrade the productivity, exactness, and dependability of administrations inside the clinical endeavor, cultivating consistent improvement in understanding consideration and symptomatic cycles.

This paper offers a comprehensive overview of existing concepts, sheds light on prevalent challenges and opportunities, and explores forthcoming trends. Aligned with the key areas outlined in the definition of medical imaging informatics, the subsequent sections of this paper are structured as follows:

- explores advancements in medical image acquisition, highlighting key imaging modalities commonly used in clinical settings.
- investigates evolving patterns concerning data management and sharing within the realm of the medical imaging big data era.
- presents evolving data processing paradigms in radiology, offering a historical context that has driven the widespread acceptance of AI and deep learning analytical methods.
- offers an in-depth review of the state-of-the-art in digital pathology.
- outlines challenges associated with 3D reconstruction and visualization across various application scenarios. It further addresses digital pathology visualization challenges, followed by an exploration of advancements in in-silico modeling and the debate surrounding the necessity of introducing new integrative, multicompartment modeling approaches.
- explores the essential requirement for integrated analytics and examines the emerging radiogenomics paradigm relevant to both radiology and digital pathology methodologies.
- presents concluding remarks, summarizing key insights, and outlining future directions for the evolving landscape of medical imaging informatics.

II. IMAGE FORMATION AND ACQUISITION

By offering an unmatched ability to detect illnesses through imaging of the human body and the high-resolution visualization of cells and Histological samples, biomedical imaging is at the forefront of a medical revolution. The development of pictures is accomplished through the connection of electromagnetic waves at different frequencies (energies) with natural tissues, barring Ultrasound, which uses mechanical sound waves. Operating at shorter wavelengths and higher energies, are ionizing, while optical, MRI, and Ultrasound, operating at longer wavelengths, fall into the nonionizing category. This section covers a range of imaging modalities, including X-ray, ultrasound, magnetic resonance (MR), X-ray computed tomography (CT), nuclear medicine, and high-resolution microscopy [8], [9] (refer to Table 1 for details). Figure 1 visually illustrates examples of images produced by these diverse modalities, showcasing the versatility and depth of biomedical imaging capabilities.

X-beam imaging has become quite possibly of the most broadly utilized strategy in clinical imaging, owing to its low cost and rapid acquisition time. This method involves passing X-rays generated by an X-ray source through the body and detecting the attenuated X-rays on the other side using a detector array. The following two-dimensional projection image, with resolutions as fine as 100 microns, depicts forces characteristic of the level of X-beam weakening [9].For enhanced visibility, iodinated contrast agents are frequently injected into specific regions, such as during fluoroscopy to image arterial disease. Additionally, phase-contrast X-ray imaging leverages the phase-shifts of X-rays as they traverse through tissues, improving soft-tissue image contrast [10]. X-ray projection imaging has found extensive application in cardiovascular, mammography, musculoskeletal, and abdominal imaging, among other medical fields [11].

Ultrasound imaging (US) operates by employing pulses in the range of 1 to 10 MHz to noninvasively image tissue in a cost-effective manner. The backscattering impact of acoustic heartbeats interfacing with inner designs is used to gauge repeats and produce pictures. Ultrasound imaging offers fast, constant representation, for example, imaging blood stream in corridors through the Doppler effect. A significant advantage of ultrasound is the absence of ionizing radiation, making it less unsafe to patients. Bone and air, on the other hand, can impede sound wave propagation, resulting in artifacts. Regardless, ultrasound remains broadly utilized for continuous cardiovascular and fetal imaging [11]. Contrast-upgraded ultrasound, using infused microbubbles to upgrade appearance in unambiguous regions, has further developed difference and imaging exactness in specific applications [12]. Ultrasound versatility imaging estimates tissue solidness for virtual palpation, and the method isn't restricted to 2D imaging, with the reception of 3D and 4D imaging

extending, though with decreased fleeting goal [13] [14].

The ability of magnetic resonance (MR) imaging to produce volumetric images with a high spatial resolution and primarily capture signals from hydrogen nuclei stands out [15]. This is accomplished through the use of a remotely created attractive field related to non-ionizing radio-recurrence (RF) beats [1]. Broadly utilized in different clinical applications, for example, outer muscle, cardiovascular, and neurological imaging, X-ray offers extraordinary delicate tissue contrast [16], [17]. Functional MRI, a significant subfield used to map brain functional connectivity, is now included in the field [18].

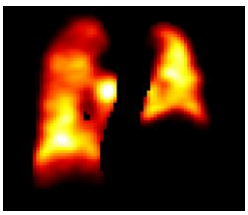
The approach of 4D stream techniques considers wonderful representation of stream in 3D space over the long run [17], [21]. MR imaging has grown and been used more frequently as a result of the incorporation of faster scan acquisition methods like compressed sensing, parallel imaging, and non-Cartesian acquisitions [22, 23]. Mirroring its broad application, in the US alone, 36 million X-ray examines were acted in 2017 [24]. The painlessness, absence of ionizing radiation, and the capacity to give itemized physical and useful data add to the getting through notoriety of MR imaging in the clinical field.

X-ray Computed Tomography (CT) imaging also offers volumetric scans, similar to MRI. However, it generates a 3D image by assembling a sequence of 2D axial slices through the body. Like MRI, it can perform 4D scans by synchronizing with the ECG and respiratory cycles. Modern CT scanners, featuring advanced solid-state detectors, have improved spatial resolutions, achieving details as fine as 0.25 mm. Multiple detector rows enable broader spatial coverage, and slice thicknesses can be reduced to 0.625 mm.

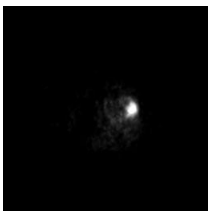
An advanced approach within CT imaging is Spectral Computed Tomography (SCT), which utilizes multiple X-ray energy bands to generate distinct attenuation data sets for the same organs. This data enables material composition analysis, contributing to a more precise diagnosis of diseases [27]. Despite concerns about radiation dosage, due to its excellent resolution and quick scan time, CT is still widely used . In the United States alone, approximately 74 million CT studies were conducted in 2017. The continual refinement of CT technology underscores its pivotal role in medical imaging, offering detailed anatomical information crucial for diagnosis and treatment planning [24], this number will undoubtedly develop because of CT's expanded applications in separating crisis care.

	Technology	Anatomies	Dimensionality	Cost per Scan*	Storage Requirements
X-ray	Produces images by measuring the attenuation of X-rays through the body, via a detector array [9].	Most organs	2D, 2D+t	$15-385	Up to ~1GB
CT	Creates 2D cross-sectional images of the body by using a rotating X-ray source and detector [25].	Most organs	2D, 3D, 4D	$57-385	Up to 10s of GBs
Ultrasound	A transducer array emits acoustic pulses and measures the echoes from tissue scatters [9].	Most Organs	2D, 2D+t, 3D, 4D	$57-230, $633-1483 (with endoscope)	Up to GBs
MRI	Uses a magnetic field to align atoms; RF pulses are then used to excite the molecules to measure their locations within the body [15].	Most organs	3D, 4D	$32-691	Up to 10s of GBs
Nuclear	Measures the emission of gamma rays through decay of radioisotopes introduced into the body via an external detectors/Gamma cameras [9]	All organs with radioactive tracer uptake	2D, 3D, 4D	$182-1375	Up to GBs
Microscopy	Typically uses an illumination source and lenses to magnify specimens before capturing an image [9]	Primarily biopsies and surgical specimens	2D, 3D, 4D	$248-482, $642-1483 (with endoscope)	Can be >1TB

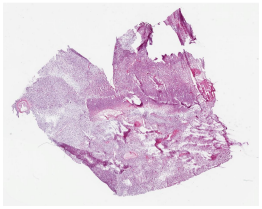
Table I: A Summary of the Characteristics of Imaging Modalities



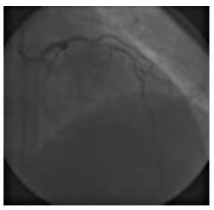
(a) Cine-angiography X-ray



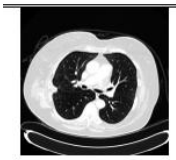
(b) 4D gated planning CT



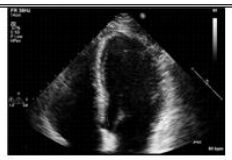
(c) Echocardiogram



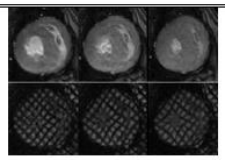
(d) Axial MRI slices



(e) Q SPECT lung Perfusion



(f) 2D slice from a 3D FDG-PET



(g) Magnified, digitized tissue

Two common techniques in nuclear medicine are Single Photon Emission Computed Tomography

(SPECT) and Positron Emission Tomography (PET). Both modalities generate 2D image slices, providing valuable information about the distribution and activity of the radioisotopes within the body .The diagnosis of cancer, the study of physiological processes at the molecular level, and functional imaging are just a few of the medical applications for which these methods are crucial. Not at all like X-beam based modalities that use transmission energy, atomic medication depends on the imaging of gamma beams produced through the radioactive rot of radioisotopes brought into the body. The emitted radiation is detected by an external camera and then reconstructed into an image. Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) are common techniques in nuclear medicine. Both produce 2D image slices that can be combined into a 3D volume. However, PET imaging utilizes positron-emitting radiopharmaceuticals that generate two gamma rays when a released positron interacts with a free electron. This characteristic enables PET to generate images with a higher signal-to-noise ratio and spatial resolution compared to SPECT.

Ultimately, the utilization of microscopy in imagining cells and tissue areas holds critical significance in illness determination, for example, for biopsy or potentially careful examples. Traditional tissue slides typically feature a single case per slide. In this process, a patient's tissue specimen is affixed to a glass slide and subjected to staining. Staining plays a crucial role in enhancing the visual representation of tissue morphology, facilitating more accurate interpretation by pathologists.

Normal staining techniques incorporate Hematoxylin and Eosin (H&E), the most predominant framework that stains cores, and immunohistochemical staining frameworks. Light magnifying lens use an illuminator and different focal points to amplify tests up to 1,000x, However, lower magnifications are often employed in tissue pathology. This magnification capability enables the examination of specimens at resolutions around 0.2 µm, serving as the primary tool in tissue pathology diagnostics.

Where customary microscopy depends on the transmission guideline to notice objects, fluorescence microscopy presents a differentiating approach by using the discharge of light at an unmistakable frequency.

Two-photon fluorescence imaging takes this idea further by utilizing two photons of comparative frequencies to energize atoms. This creative methodology empowers further tissue entrance and lessens phototoxicity.

An alternative to conventional tissue slide techniques is the Tissue Microarray (TMA) mechanism. TMA technology empowers researchers to extract minute cylinders of tissue from histological sections and arrange them in a matrix configuration on a recipient paraffin block, enabling simultaneous analysis of hundreds of samples [36]. TMA has gained recognition as a potent tool, providing insights into the underlying mechanisms of disease progression and patient response to therapy.

In the realm of immune-oncology, TMA technology is rapidly becoming indispensable, complementing traditional single-case slide approaches. TMAs can be visualized using the In identical whole-slide scanning technologies utilized for individual case slides.

In the field of biomedical imaging, challenges and opportunities abound. There is a continual push for faster acquisitions and lower radiation doses in anatomical imaging methods. Factors in imaging boundaries, like in-plane goal and cut thickness, not examined here, can firmly affect picture examination and ought to be viewed as in calculation improvement. The substantial volume of imaging data generated underscores the necessity for informatics in storage, transmission, analysis, and automated interpretation. This emphasizes the role of big data science in enhancing data utilization and diagnosis

III. INTEROPERABLE AND FAIR DATA REPOSITORIES FOR REPRODUCIBLE, EXTENSIBLE AND EXPLAINABLE RESEARCH

Outfitting the maximum capacity of accessible huge information for medical care development requires a change the executive system across both

exploration establishments and clinical locales. In its present form, diverse healthcare data spans from imaging to genomic information, to clinical information.

A key approach to address the limitations mentioned earlier is the creation of effective Clinical Data Repositories (CDRs) that span the entire enterprise. CDRs play a crucial role in systematically aggregating information derived from various sources, including (i) Electronic Health and Medical Records (EHR/EMR, used interchangeably); (ii) Archives in Radiology and Pathology, relying on Picture Archive and Communication Systems (PACS); (iii) a diverse array of genomic sequencing devices, Cancer Registries, and Biospecimen Repositories; and (iv) Clinical Trial Management Systems (CTMS).

The use of the term EHR/EMR is gaining prominence as a comprehensive umbrella term, supplanting CDRs to incorporate the vast array of accessible medical data. Our current study adopts this approach, and as these systems become more widespread.

In this pursuit, numerous clinical and research sites have created tools for data management and exploration with the specific goal of monitoring patient outcomes [46].However, many of these tools face limited adoption within the clinical and research communities due to their reliance on manual data entry and a lack of essential tools for performing advanced queries. A recent shift has emphasized the development of automated Load (ETL) interfaces, Extraction, and Transformation marking a significant improvement.

ETLs can seamlessly handle a comprehensive range of genomic data, clinical information, and imaging studies. This capability allows for the systematic interrogation of multi-modal data, offering objective, refining best practices, and guiding personalized treatment approaches.

One of the main difficulties in the adoption of Electronic Health Records (EHRs) across an entire enterprise arises from the substantial amount of clinical data available in unstructured or semi-structured formats, notably within various reports generated by third-party laboratories. To address this challenge, some institutions opt to convert these documents into images or PDFs for integration into the patient's EHR. Alternatively, certain reports are received in Health Level 7 (HL7) format, where the clinical content is consolidated into a continuous ASCII (American Standard Code for Information Interchange) string.

A primary challenges in implementing Electronic Health Records (EHRs) across an entire organization stems from the significant volume of clinical data present in unstructured or semi-structured formats, particularly within reports generated by third-party laboratories. To tackle this issue, some institutions choose to convert these documents into images or PDFs for incorporation into the patient's EHR. Alternatively, certain reports are received in Health Level 7 (HL7) format, where the clinical content is consolidated into a continuous ASCII string.

Successfully integrating this information into Electronic Health Records and achieving semantic interoperability demands the creation and enhancement of software that conforms to interoperability profiles and standards.

Furthermore, the adoption of clinical terminology coding, such as Systemized Nomenclature of Medicine-Clinical Terms (SNOMED CT) and the International Statistical Classification of Diseases is essential. Importantly, leading to increased statistical power in research studies relying on larger cohorts.

The availability of metadata information is central in unambiguously describing processes throughout the data handling cycle. Metadata underpin medical dataset sharing by providing descriptive information that characterize the underlying data. The latter, can be further capitalized towards joint processing of medical datasets constructed under different context, such as clinical practice, research and clinical trials data [50]. A key medical imaging example concept relevant to metadata usage comes from image retrieval. Traditionally, image retrieval relied on image metadata, such as keywords, tags or descriptions. However, with the advent of machine and deep learning AI solutions (see Section IV), content-based image retrieval (CBIR) systems evolved to exploiting rich contents extracted from

images (e.g., imaging, statistical, object features, etc.) stored in a structured manner. Today, querying for other images with similar contents typically relies on a content-metadata similarity metric. Supervised, semi supervised and unsupervised methods can be applied for CBIR extending across imaging modalities [51].

The FAIR guiding principles initiative aims to address (meta)data availability by providing recommendations for making (meta)data Findable, Reusable (FAIR) [52], Interoperable, and Accessible. Simultaneously , Privacy-preserving data publishing is an evolving research field dedicated to facilitating open data sharing while ensuring the privacy of patients., with the goal of minimizing information loss [53]. Sharing such data enhances the potential for discovering novel findings and replicating existing research results [54]. In the context of anonymizing medical imaging data, approaches like k-anonymity [55], [56], l-diversity [57], and t-closeness [58] are commonly employed.

The convergence of a wide spectrum of interconnected data elements, spanning diverse clinical information, imaging studies, and genomic data, coupled with the application of appropriate data mining tools, plays a pivotal role in integrative analytics strategies. This amalgamation creates distinctive prospects for the progression of precision medicine [67], [68].

IV. RADIOLOGY PROCESSING, ANALYSIS, AND UNDERSTANDING

The integration of a wide range of interconnected data elements, spanning diverse clinical information, imaging studies, and genomic data, coupled with the utilization of appropriate data mining tools, is vital for integrative analytics approaches. This integration creates distinctive opportunities for the advancement of precision medicine.

Medical image analysis usually encompasses two main objectives: outlining objects of interest (segmentation) and characterizing labels (classification). Examples range from delineating the heart for cardiology to detecting cancer in pathology images. However, progress in medical image analysis has often been impeded by a dearth of theoretical comprehension on the optimal selection and handling of visual features. Ad hoc (or hand-crafted) feature analysis approaches have achieved partial success in certain domains by explicitly outlining a predefined set of features and processing steps. Nonetheless, no single method has yielded durable, universally applicable solutions across different domains.

The recent surge in ML approaches has demonstrated encouraging results across various applications. These techniques aim to comprehend and refine parameters based on training examples. Nevertheless, engineering these approaches can pose challenges, as they may encounter unforeseeable failures and are susceptible to biases or erroneous feature identification, frequently originating from constraints in the training dataset.

A crucial means of propelling the field forward involves open-access challenges where participants can assess their me thods using standardized datasets. Prominent instances of such challenges span diverse domains.While these challenges have driven progress in medical image analysis, recent analyses of challenge designs have revealed biases that raise questions about the ease of translating methods to clinical practice [84].

A. Feature Analysis

Numerous studies in clinical image analysis have explored statistical modeling, signal analysis, and other techniques [71]. Among the most successful approaches are:

1.Multi-atlas Segmentation [85]:

This approach employs a collection of labeled cases (atlases) chosen to capture variations within the population. The image intended for segmentation is aligned with each atlas, often using techniques like voxel-based morphometry [89]. The labels from each atlas are then combined to create a consensus label for the target image. This method improves robustness by averaging errors specific to a given atlas, forming a consensus based on maximum likelihood. A similarity metric is subsequently employed to assess and assign weights to candidate segmentations.

2.Active Shape Models [87]-[90]:

In this alternative approach, the object is represented as a deformable structure, and the

optimization of boundary positions is performed using a similarity metric .

3.Graph Cut Algorithms [86]:

Graph cut algorithms provide a global optimal solution, although the initial graph construction is computationally expensive. The advantage lies in real-time computation of updates to the weights (interaction).

Each of these approaches contributes to the field of medical image analysis, offering different strengths and trade-offs in terms of computational efficiency, robustness, and global optimization.

B. Machine Learning:

Before the emergence of deep learning, machine learning involved framing a learning problem to tackle a task using input data [92]. In the early stages of machine learning, the emphasis was on reducing data dimensionality and integrating crucial invariances and covariances. This was accomplished by employing handcrafted features to represent data. In the realm of imaging data, various transforms such as Fourier, Cosine, or Wavelet transforms, and more recently, Gabor filters, were employed. These transforms aimed to capture local correlations, separate frequency components, and offer directionality along with detailed texture information.

In order to acquire features through a data-driven approach, methods such as Principal Component Analysis and Independent Component Analysis are commonly employed, and the K-means algorithm [94] have been utilized [93].

In the subsequent decision-making stage, a range of algorithms was introduced. Support Vector Machines [95] were often chosen for their simple implementation and established nonlinear kernel options. Alternatively, random forest methods [96] utilized an ensemble of decision trees, enhancing the classifier's robustness. Probabilistic boosting trees [97] constructed a binary tree of strong classifiers through a boosting approach.

C. Deep Learning for Segmentation:

One of the earliest applications of Convolutional Neural Network (CNN), which is currently the most common form of deep learning, dates back to 1995. At that time, a CNN was utilized for the detection of lung nodules in chest X-rays [100]. Subsequently, driven by breakthrough outcome like those of Alex Net [101], along with variations that include patch-based adaptations of Deep Boltzmann Machines and stacked autoencoders, the segmentation of anatomy and pathology through deep learning has undergone a revolutionary transformation (refer to Table II for details).

This section aims to analyze key works and trends in the area of deep learning for medical image segmentation. For a more in-depth exploration, readers are directed to relevant, comprehensive reviews in [69] and [70].

The fundamental appeal of deep learning and convolutional architectures lies in their ability to simultaneously learn relevant features and decision functions. While Alex Net initially established the benchmark for categorization tasks (subsequently extensively adapted for medical applications, as discussed in the next subsection), it was the recognition that classification networks could yield dense predictions through convolutionalization that paved the way for potent partitioning algorithms [103].

Now a days, U-Net remains one of the most successful and widely used architectures for medical image partitioning.

The U-Net is an encoder-decoder network with a bottleneck and skip connections between the encoding and decoding layers. It is straightforward conceptually. These skip associations empower preparing with restricted input information and yield exceptionally precise division limits, in spite of the fact that it might come at the expense of a plainly characterized idle space. Originally designed for 2D segmentation, the 3D U-Net was introduced in 2016, allowing full volumetric processing of imaging data while retaining the principles of the original U-Net [105].

Regarding picture division as a picture to-picture interpretation and combination issue has enlivened a few works. This approach has led to different techniques that help solo and semi-directed learning, frequently combined with ill-disposed preparing [106], to improve preparing information utilizing mark guides or info pictures from different areas.

D. Deep Learning for Classification:

Deep learning algorithms have been widely applied to disease classification or screening, achieving outstanding performance in various tasks (refer to Table II). Applications span a wide range.

Similar to segmentation tasks, convolutional neural networks (CNNs) have significantly improved classification tasks. Many network architectures that have proven effective in the ImageNet image classification challenge [117] have been adapted for medical imaging tasks by fine-tuning previously trained layers. Early studies, such as [118] and [119], investigated the possibility of using CNN-based models trained on large natural image datasets for medical tasks. They demonstrated that pre-training a model on natural images and fine-tuning its parameters for a new medical imaging task yielded excellent results. This finding was further supported in [120], which indicated that fine-tuning a pre-trained model generally outperforms training from scratch. Ensemble methods involving fine-tuning pre-trained models have also shown strong performance, as illustrated in [121].

However, the transfer learning approach faces challenges when the objective involves tissue classification in 3D image data. Transfer learning from natural images becomes impractical without first condensing the 3D data into two dimensions. Various successful strategies have been proposed to tackle this issue, including architectures performing 3D convolutions and training networks from scratch on 3D medical images [122]-[126]. Other techniques involve slicing 3D data into various 2D views before merging them to obtain a final classification score [127]. Some approaches utilize a 2D autoencoder to learn lung nodule features and then utilize a decision tree for distinguishing between benign and malignant nodules [128, 129].

In general, regardless the preparation procedure utilized, order errands in clinical images are overwhelmed by some detailing of a CNN - frequently with completely associated layers toward the finish to play out the last characterization. CNNs frequently have the ability to achieve state-of-the-art performance with abundant training data; in any case, profound learning strategies by and large endure with restricted preparing information. As examined, move learning has been valuable in adapting to sparse information, however the proceeded with accessibility of enormous, open datasets of clinical pictures will have a major impact in fortifying grouping undertakings in the clinical space.

V. RESULTS

E. CNN Interpretability

Albeit Profound CNNs have accomplished incredibly high precision, they are as yet black-box capabilities with numerous layers of nonlinearities. Therefore, it is essential to have faith in these networks' output and to be able to confirm that the predictions are the result of learning appropriate representations rather than overfitting the training data. A new area of machine learning research called "deep CNN interpretability" aims to learn more about how the network learns and makes its classification decisions. One straightforward methodology comprises of picturing the closest neighbors of picture patches in the completely associated highlight space [101]. One more typical methodology that is utilized to reveal insight into the expectations of Profound CNN depends on making saliency maps [132] and directed backpropagation [133], [134]. Another comparable methodology, that isn't intended for an info picture, utilizes inclination rising streamlining to produce an engineered picture that maximally enacts a given neuron [135]

TABLE II. SELECTED DEEP LEARNING METHODS FOR MEDICAL IMAGE SEGMENTATION AND CLASSIFICATION

Year - [REF] Author	Disease	Imaging Data	Patients	DL Method	Segmentation/ Classification	Description
1995 - [100] Lo et *al*	Lung Cancer	X-ray	55	2 layer CNN	Nodules detection in a patch fashion	First ever attempt to use CNN for medical image analysis
2015 - [104] Ronneberger et *al*	Cells	Electron and optical microscopy	30 /35	U-net	Segmentation of EM images and cell tracking	Image to image tasks architecture depicting exceptional segmentation performance even with limited data
2016 - [118] Shin et *al*	Interstitial Lung Disease	CT	120 (905 slices)	Transfer learning (AlexNet, GoogleNet, CifarNet CNNs)	Interstitial lung disease binary classification	Showed that networks pre-trained on natural image data could be succesfully used on medical data
2016 - [122] Dou et *al*	Cerebral Microbleeds	MRI	320	Two-stage: 1) 3D Fully-convolutional network (FCN), 2) 3D CNN	3D FCN for candidate microbleed detection	A two-stage system used a 3D FCN to detect candidate microbleeds before a 3D CNN was applied to reduce false positives
2016 - [127] Setio *et al*	Pulmonary Cancer	CT	888 scans, 1186 nodules	Two-stage: 1 1) Candidate detector with feature engineering 2) Multi-view 2D CNN for false positive reduction	Detection of potential pulmonary nodules.	A notable reduction in false positives was achieved through the fusion of multiple 2D CNNs at different views around a nodule.
2017 - [268] Lekadir et *al*	Cardiovascular (carotid artery)	US	56 cases	Four convolutional and three fully connected layers	Characterization of carotid plaque composition	High correlation (0.90) with plaque composition clinical assessment for the estimation of lipid core, fibrous cap, and calcified tissue areas
2017 – [128] Yu et *al*	Melanoma	Dermoscopic Images	1250 images	Very deep (38/50/101 layers) fully conv. residual network	Binary melanoma classification	Used a very deep residual network (16 residual blocks) to classify melanoma
2017 - [102] Komnitsas et *al*	TBI, LGG/ GBM, Stroke	MRI	61 /110/ ISLESSISS data	11-layers, multi-scale 3D CNN with fully connected CRF	Brain lesion segmentation algorithm	Top-performing segmentation results on TBI, brain tumours, and ischemic stroke at BRATS and ISLES 2015 challenges
2017 - [246] Lao et *al*	GBM	MRI	112	Transfer learning	Necrosis, enhancement, and edema tumour subregions	Overall survival prognostic signature for patients with Glioblastoma Multiforme (GBM)
2017 - [247] Oakden-Rayner et *al*	Overall Survival	CT (chest)	48	ConvNet transfer learning (3 convolutional and 1 fully connected layers)	Tissue (muscle, body fat, aorta, vertebral column, epicardial fat, heart, lungs)	Predict patients' 5-year mortality probability using radiogenomics data (overall survival)
2017 - [241] Zhu et *al*	Breast Cancer	DCE-MRI	270	Transfer learning (GoogleNet, VGGNet, CIFAR)	Breast tumour lesions	Discriminate between Luminal A and other breast cancer subtypes
2018 - [112] Chartsias et *al*	Cardiovascular	MRI	100	Various networks	Segmentation of cardiac anatomy	Limited training data when appropriate autonecoding losses are introduced
2020 – [121] McKinney et *al*	Breast Cancer	X-ray	25,856 & 3,097 cases	Ensemble and transfer learning	Breast cancer classification	Cancer prediction on two large datasets with comparison against human readers
2019 - [170] Hekler et *al*	Melanoma	Whole slide H&E tissue imaging	695	Transfer learning (ResNet50)	Binary melanoma classification	Human level performance in discriminating between nevi and melanoma images

US: Ultrasound; MRI: Magnetic Resonance Imaging; DCE-MRI: Dynamic Contrast Enhancement MRI; CT: Computed Tomography; PET: Positron Emission Tomography; GBM: Glioblastoma; LGG: Lower-Grade Glioma; CNN: Convolutional Neural Networks.

F. Interpretation and Understanding:

Once the geometry and function of objects are quantified, the study of patient cohorts involves analyzing the statistical variations in shape and motion across a large number of cases. In the Multi-Ethnic Study of Atherosclerosis, variations in heart shape derived from MRI examinations were correlated with established cardiovascular risk factors [143]. Furthermore, the application of imaging informatics methodologies in the cardiovascular system has yielded significant insights, enhancing our understanding of normal function and contributing to advancements in the comprehension of pathophysiology, diagnosis, and treatment of cardiovascular disorders [144]. In the field of neuroscience, atlas-based neuroinformatics enables the extraction of new information about structure to predict neurodegenerative diseases [145].

At the same time, medical imaging data can offer valuable insights into the biophysical parameters of tissues and organs. For instance, in elastography, tissue compliance can be estimated from the motion of waves imaged using ultrasound or MRI [146]. In the case of the heart, myocardial stiffness is associated with disease processes. With knowledge of boundary loading, imaged geometry, and displacements, finite element analysis can be employed to estimate material properties compatible with the observed deformation [147]

V. PROCESSING, ANALYSIS, AND UNDERSTANDING IN DIGITAL PATHOLOGY

Traditionally, pathology classifications and interpretations have relied on pathologists examining tissue prepared on glass slides using microscopes. However, the advent of digital pathology has opened new avenues for in-depth analysis.

These datasets can be correlated with specific disease attributes, enabling the quantitative characterization of tissue at various spatial scales. This process, in turn, facilitates the development of biomarkers capable of predicting outcomes and treatment responses.

Over the past two decades, digital pathology has made significant progress, with some sites now utilizing whole slide imaging for primary anatomic pathology diagnostics Certainly, The FDA approved the utilization of a commercial digital pathology system in clinical settings in 2017 . For a comprehensive overview of challenges and advancements in digital pathology, several publications offer insightful reviews [155]-[157]. The integration of artificial intelligence-based medical imaging systems gaining FDA approval is summarized in Table III.

A. Segmentation and Classification:

The widespread availability of digitized pathology images, Paired with recognized difficulties concerning the variability in pathologists' interpretations among different observers [159], This has generated an increasing interest in systems that offer computer-assisted decision support..

One significant challenge in pathology decision support arises from the intricate and nuanced characteristics inherent in many pathology classification systems. These classifications often revolve around the percentage of the specimen displaying specific patterns of tissue abnormality, and assessing abnormality as well as estimating tissue area entails subjective judgment. During the era when interpretation relied solely on glass slides, minimizing inter-observer variability necessitated multiple pathologists collectively examining the same slides and collaborating on interpretation.

The difficulties associated with pathology image interpretation have prompted considerable endeavors to create image analysis methods with the goal of automating the analysis of entire pathology slides. While only a limited number of these methods have been integrated into clinical practice, the outcomes are promising. It appears highly probable that ongoing initiatives will eventually produce successful methods for consistently providing algorithmic second opinions in anatomic pathology. For a thorough review of these initiatives, please refer to [160]-[162].

In earlier efforts within this field, statistical techniques and machine learning algorithms were applied for the segmentation and classification of tissue images. For example, Bamford and Lovell

utilized active contours to segment nuclei in Pap stained cell images [163]. Malpica et al. employed watershed-based algorithms to separate nuclei in cell clusters [164]. Kong et al. combined grayscale reconstruction, thresholding, and watershed-based methods in their work [165]. Gao et al. adopted a hierarchical approach involving mean-shift and clustering analysis [166]. In the study by Al-Kofahi et al., graph-cuts and multiscale filtering methods were used for the detection of nuclei and the delineation of their boundaries [167].

Identifying malignant growth metastases addresses a basic indicative test, and AI strategies have been applied to resolve this issue. The CAMELYON challenges explicitly center around algorithmic identification and order of bosom disease metastases in H&E entire slide lymph hub segments [171]. The best strategies in these difficulties ordinarily include convolutional brain organizations, differing in network engineering, preparing strategies, and pre-and post-handling procedures. Over the long run, there has been persistent improvement in the presentation of calculations intended for the discovery, division, and arrangement of cells and cores. These calculations frequently assume crucial parts in malignant growth biomarker calculations, creating quantitative rundowns and guides connected with the size, shape, and surface of cores, alongside measurable portrayals of spatial connections between various kinds of cores [172]-[176].

Characterizing nuclei presents a challenge in terms of generalizing the task across various tissue types, mainly due to the labor- intensive and time-consuming process of creating ground truth datasets for training, requiring the expertise of pathologists. Deep learning generative adversarial networks (GANs) have proven valuable in addressing this challenge by assisting in the generalization of training datasets [177].

B. Interpretation and Understanding:

There is a growing emphasis on understanding the role of cancer-immune interactions in influencing outcomes and responses to treatment, particularly with the increasing prominence of immune therapy in cancer treatment. Elevated levels of lymphocyte infiltration have been associated with extended disease-free survival and improved overall survival (OS) in various cancer types, such as early-stage triple-negative and HER2-positive breast cancer [178, 179].

Recent efforts have utilized deep learning algorithms to classify cancer-infiltrating lymphocyte (TIL) regions in H&E (Hematoxylin and Eosin) images. One study focused on characterizing TIL regions in lung cancer, while another, conducted within the context of the TCGA Pan Cancer Immune group, explored various cancer types to correlate deep learning-derived spatial TIL patterns with molecular data and outcomes. A third study utilized a structured crowd-sourcing method to generate maps of cancer-infiltrating lymphocytes [152, 181]. These investigations demonstrated correlations between characterizations of TIL patterns, analyzed by computerized algorithms, and patient survival rates, highlighting the potential for grouping patients based on subclasses of immunotypes. These studies underscore the value of whole-slide tissue imaging in producing quantitative evaluations of sub-cellular data and providing opportunities for more comprehensive correlative studies.

While there have been advancements in automating the assessment of TMA (Tissue Microarray) images, numerous existing systems face limitations. These limitations include being closed and proprietary, not fully leveraging advanced computer vision techniques, and not adhering to emerging data standards. Beyond analytical challenges, the substantial volume of data, text, and images from even modest tissue microarray studies presents significant computational and data management hurdles (see Section VI.B). Understanding the cancer immune status through the expression of immune system-related proteins is crucial for determining suitable immunotherapy options. However, objectively evaluating cancer biomarker expression poses challenges. For instance, assessing the expression of human leukocyte antigen (HLA) class I in the growth epithelium is challenging due to its presence on both cancer epithelial and stromal cells, as well as infiltrating immune cells [182].

Improving the flexibility and convenience of advancing computational imaging instruments requires addressing batch effects. Batch effects arise from variations in the appearance of histopathology tissue slides from different sources due to differences in tissue preparation and staining techniques. Predictive models have been explored to facilitate robust learning from one domain and directly applying it to another domain. Through unsupervised domain adaptation, it becomes possible to transfer discriminative knowledge from the source domain to the target domain without the need to re-label images in the target domain [183].

This paper primarily focuses on the analysis of Hematoxylin and Eosin (H&E) stained tissue images, as H&E is a primary tissue stain widely used in histopathology for cancer diagnosis. The analysis encompasses a significant body of research dedicated to H&E stained tissue. While fluorescence microscopy and immunohistochemical techniques are employed in both research and clinical settings to enhance the visualization of specific morphological features, such as proteins and macromolecules in cells and tissue samples, a growing number of histopathology imaging projects are now oriented towards methods for analyzing images obtained from fluorescence microscopy and immunostaining techniques (e.g., [186]-[192]).

In medical imaging applications involving human tissues, the registration of slices is crucial, ideally performed in an elastic form [195]. Feature-based registration becomes a more suitable approach in this context, especially when dealing with the contours and centerline of vessels [196]. Conversely, intensity-based registration proves effective for aligning image slices depicting abnormal morphologies, such as cancers [197].

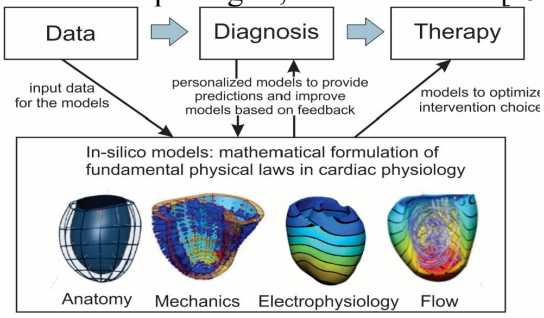


Fig. 2. In silico modelling paradigm of cardiovascular disease with application to heart.

The selection of meshing and rendering techniques is closely linked to the specific imaging modality and the corresponding tissue type. Surface rendering techniques are utilized when reconstructing the 3D boundaries and geometry of arteries and vessels. This process involves creating iso-contours extracted from individual slices of intravascular ultrasound or CT angiography. Additionally, Non-Uniform Rational B-Splines (NURBS) serve as an effective meshing technique for generating and characterizing surfaces of vascular geometric models, including aortic, carotid, cerebral, and coronary arteries. These models play a pivotal role in the reconstruction of aneurysms and atherosclerotic lesions [196], [198].

On the other hand, when depicting solid tissues and masses such as cancers, organs, and body parts, Volume Rendering techniques like ray-casting are commonly used. These methods enable the visualization of the entire medical volume as a cohesive structure, offering transparency even when derived from image data with relatively low contrast.

The reconstruction process, which necessitates expert knowledge and guidance, becomes impractical and time-consuming when analyzing extensive sets of patient-specific cases. In such scenarios, the use of automatic segmentation and reconstruction systems becomes imperative. However, a significant challenge arises from the difficulty in achieving complete automation in the segmentation process, attributed to variations in imaging modalities, diverse vessel geometries, and fluctuating image quality [199]. Efficient algorithms for rapid segmentation and reconstruction are crucial when dealing with a large number of images. Approaches to address this challenge include the utilization of parallel algorithms for segmentation, the application of neural networks (discussed in Sections IV-V), multiscale processing techniques, and the deployment of multiple computer systems, each operating on an image in real-time.

c. Data Management, Visualization, and Processing in Digital Pathology

At its essence, digital pathology is fundamentally an interactive, human-guided process that encompasses a variety of tasks. These tasks include labeling data for algorithm development, visualizing images and features to refine algorithms, interpreting findings, and aligning systems with clinical applications. The effectiveness of digital pathology in imaging informatics applications relies on the ability of interactive systems to query underlying data and manage features within the system, along with supporting interactive visualizations. This interactivity is crucial for the widespread adoption of digital pathology.

A multitude of open-source tools simplify the visualization, organization, and querying of characteristics derived from whole slide images. These systems also facilitate the creation of annotations and markups for whole slide images. One such open-source tool is the QuIP software system [201], which enables interactive viewing of images, image annotations, and segmentation results presented as overlays of heatmaps or polygons using the caMicroscope viewer [202]. FeatureScape, another tool, is a visual analytics tool that supports interactive exploration of features and segmentation maps and is integrated with QuIP. Other open-source programs designed for similar purposes include QuPath [203], the Pathology Image Informatics Platform (PIIP) [204] for administration, analysis, and visualization, the Digital Slide Archive (DSA) [205], and Cytomine [206]. These systems are tailored for whole slide viewing, administration, and analysis and can be used either locally (QuPath, PIIP) or online (QuIP, caMicroscope, DSA).

The ongoing work entails developing new instruments and techniques to facilitate the indexing of photographed specimens using improved feature metrics and knowledge representation. These metrics include similarity-indexed computational biomarkers, which provide quick searches and extractions of comparable regions of interest from large picture datasets. When combined, these technologies enable researchers to analyze tissue microarrays including huge patient cohorts in a high-throughput manner. They make it easier to create and test ideas, as well as to store and mine large datasets [200].

Digital pathology algorithms are made to function well with high-resolution pictures so that tissue data may be used to extract certain traits. Computational limitations may impede local processing on an interactive workstation since digital pathology pictures might be several terabytes in size. Certain algorithms can function on down sampled, lower-resolution photos that the user has identified.

Cloud computing is also gaining traction in the field of digital pathology due to decreasing costs, making it an increasingly cost-effective solution for large-scale computing. Several groups, particularly in the genomics community, have developed solutions for deploying genomic pipelines on the cloud [212]-[214]. QuIP, for instance, incorporates cloud-based pipelines for tasks like cancer-infiltrating lymphocyte analysis and nuclear segmentation. These pipelines are available as APIs and deployed as containers or pipelines in a workflow definition language (WDL), supported by a cross-platform workflow orchestrator compatible with multiple cloud and high-performance computing (HPC) platforms. Handling computerized pathology pictures presents huge difficulties, fundamentally because of the broad size of entire slide pictures, the variety of picture designs, and the intermittent requirement for human direction and mediation during handling. Endeavors have been started to consolidate DICOM (Computerized Imaging and Correspondences in Medication) in advanced pathology, exemplified by apparatuses like the Orthanc DICOMizer [207].

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The rise of containerization innovations like Docker [211] has acquainted a clever methodology with dispersing calculations and pathology pipelines. Cloud computing is gaining prominence in digital pathology due to decreasing costs, rendering it an increasingly cost-effective solution for large-scale computing. Various groups, particularly in the genomics community, have developed solutions for deploying genomic pipelines on the cloud [212]-[214]. QuIP, for example, integrates cloud-based pipelines for tasks like cancer-infiltrating lymphocyte analysis and nuclear segmentation. These pipelines are accessible as APIs and deployed as containers or pipelines in a workflow definition language (WDL), supported by a cross-platform workflow orchestrator compatible with multiple cloud and high-performance computing (HPC) platforms. While this field is still in its early stages, widespread adoption is anticipated in the upcoming years. Potential applications incorporate calculation approval, sending calculations in clinical examinations and preliminaries, and calculation advancement, particularly in frameworks utilizing move learning.

VII. INTEGRATIVE ANALYTICS

A. Medical Imaging in the Era of Precision Medicine:

Radiologists and pathologists regularly dissect naturally visible and tiny pictures to make analyze and participate in research. Predictions of the patient's treatment and outcome are influenced by the assessments' decisions. Accuracy medication, an arising medical care approach, means to upgrade the precision of clinical choices, working on customized therapy and treatment making arrangements for patients (portrayed in Fig. 3 [67]). Advanced molecular and genomic tests are becoming increasingly essential tools for physicians, complementing conventional pathology and radiology procedures, to enhance patient stratification and individualized care management. Recent advancements in computational imaging, clinical genomics, and high-performance computing enable the simultaneous consideration of various clinicopathologic data of interest, providing unprecedented insight into disease progression mechanisms. These experiences could prompt the improvement of another age of analytic and prognostic measurements and devices. From a clinical imaging outlook, the radiogenomics worldview incorporates these goals to propel accuracy medication. Radiologists and pathologists regularly dissect naturally visible and tiny pictures to make analyze and participate in research. Predictions of the patient's treatment and outcome are influenced by the assessments' decisions. Accuracy medication, an arising medical care approach, means to upgrade the precision of clinical choices, working on customized therapy and treatment making arrangements for patients (portrayed in Fig. 3 [67]). Advanced molecular and genomic tests are becoming an increasingly important tool for physicians to use in addition to conventional pathology and radiology procedures in order to improve patient stratification and individual care management. Late headways in computational imaging, clinical genomics, and elite execution registering permit the concurrent thought of various clinicopathologic data of interest, offering phenomenal understanding into sickness movement components. These experiences could prompt the improvement of another age of analytic and prognostic measurements and devices. From a clinical imaging outlook, the radiogenomics worldview incorporates these goals to propel accuracy medication. Radiologists and pathologists regularly dissect naturally visible and tiny pictures to make analyze and participate in research. Predictions of the patient's treatment and outcome are influenced by the assessments' decisions. Accuracy medication, an arising medical care approach, means to upgrade the precision of clinical choices, working on customized therapy and treatment making arrangements for patients (portrayed in Fig. 3 [67]. These experiences could prompt the improvement of another age of analytic and prognostic measurements and devices. From a clinical imaging outlook, the radiogenomics worldview incorporates these goals to propel accuracy medication.

B. Radiogenomics for Integrative Analytics:

Radiomics research has turned into an important harmless methodology with huge prognostic worth [224]. By building imaging marks (joining shape, surface, morphology, power, and so on., robust predictive models or quantitative imaging biomarkers are created by taking these characteristics (or features) and linking them to clinical outcomes [225]. The consolidation of longitudinal and multi-methodology radiology and pathology highlights (likewise talked about in Area VII.C) further improves the oppressive force of these models. Broad writing shows the extraordinary capability of radiomics in illness organizing, including malignant growth, neurodegenerative, and cardiovascular sicknesses [224]-[228].

The overall objective is to create proxy imaging biomarkers that interface malignant growth aggregates to genotypes, giving doctors a powerful yet painless prognostic and indicative device.

The integrated mining of imaging and omics features is necessary for concurrently developing radiogenomic signatures. This approach means to build strong prescient models that all the more really correspond and depict clinical results contrasted with utilizing imaging, genomics, or histopathology in disconnection [68].

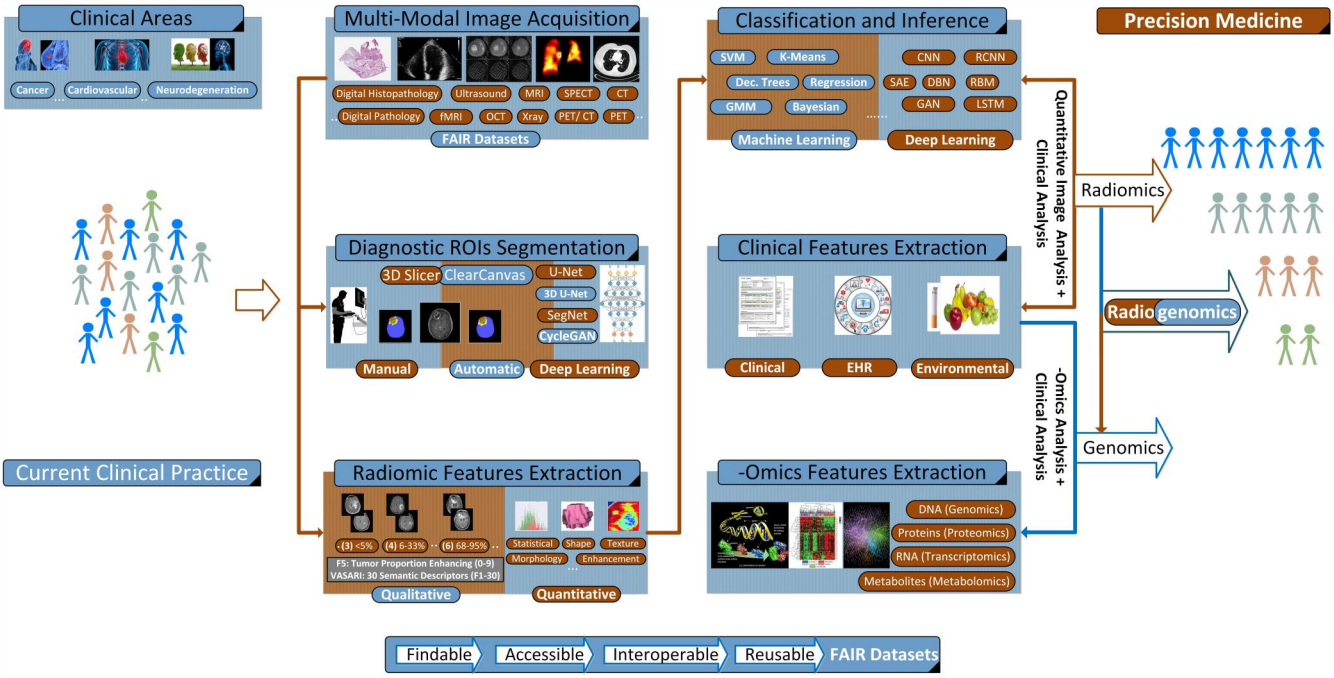

Fig. 3 .Radiogenomics System Diagram

As the disease progresses from a benign to a dangerous state and throughout its course, changes occur in the underlying molecular, histological, and protein expression patterns. Each of these aspects provides a distinct perspective and corresponding significance.

1) The TCIA/TCGA Initiatives Paradigm:

Within TCIA, specific phenotype groups, such as those focused on breast invasive carcinoma (BRCA) and glioblastoma (GBM) and lower-grade glioma (LGG), exemplify initiatives in radiogenomics research. The breast phenotype group, for instance,

identified 38 radiomics features from T1-weighted Dynamic Contrast Enhancement (DCE) MRI, categorized into six groups: (i) size (4), (ii) shape (3), (iii) morphology (3), (iv) enhancement texture (14), (v) kinetic curve (10), and (vi) enhancement variance kinetics (4). Concurrently, the glioma phenotype group utilizes the VASARI feature set for subjective interpretation of MRI visual cues, featuring 30 descriptive elements related to non-enhanced cancer, contrast-enhanced cancer, necrosis, and edema. The TCGA website, along with software like TCGA-Assembler, facilitates the extraction of genetic features for analysis.

Studies from the group characterized by breast phenotype reveal significant associations between breast cancer staging and specific radiomics features . These highlights additionally exhibited prescient capacities for clinical receptor status, multigene examine repeat scores, sub-atomic subtyping, and relationship with miRNA and protein articulations [236]-[239]. In the glioma aggregate gathering, speculation testing affirmed huge relationship between certain radiomic and genomic elements and in general and movement free endurance. Model predictive power was improved by combining radiogenomic signatures, and imaging characteristics were linked to the classification of molecular GBM subtypes, providing non-invasive prognostic insights [68, 240].

2) Deep Learning-Based Radio genomics:

Deep learning methods are poised to revolutionize radiomics and radiogenomics research, despite the fact that they are still in their infancy and primarily rely on transfer learning strategies. Eminent examinations in malignant growth research include recognizing Luminal An and other sub-atomic subtypes in bosom malignant growth [241], foreseeing bladder disease treatment reaction [242], deciding IDH1 transformation status for LGG [243], [244], foreseeing MGMT methylation status for GBM [245], and determining generally endurance for both GBM patients [246] and non-sickness explicit subjects [247].

C. Integrative Analytics in Digital Pathology:

In recent time , the extent of picture based examinations has extended to incorporate outcomes from pathology pictures, genome data, and related clinical information. For example, tests using 86 bosom malignant growth cases from the Genomics Information Lodge (GDC) storehouse exhibited that joining picture based and genomic includes altogether further develops arrangement precision [248]. Integrating genomic and computational imaging signatures to characterize prostate cancer was demonstrated in another study. Convolutional neural network image biomarkers, genomic pathway scores, and a recurrence network model (Long Short-Term Memory, LSTM) were found to have a stronger correlation with disease recurrence than image-based texture features and standard clinical markers [249].

Really incorporating omics information with digitized pathology pictures for biomedical examination is a computational test. Different factual and AI strategies, including agreement grouping [250], direct classifier [251], Tether relapse demonstrating [252], and profound learning [253], have been applied. These techniques were utilized in examinations on malignant growths, for example, bosom [250], lung [252], and colorectal [253]. The combination of morphological elements from digitized pathology pictures and - omics information further developed visualization exactness as well as given experiences into the atomic premise of malignant growth cell and tissue associations. Yuan et al., for instance [251] showed that consolidating morphological data on Growth Penetrating Lymphocytes (TILs) with quality articulation information fundamentally upgrades anticipation expectation for trama center negative bosom cancers. Circulation designs for TILs and related genomics data were portrayed for numerous malignant growths [152], prompting new bearings in integrative genomics for accuracy medication and natural theory age.

Building on current research, there is a growing interest in utilizing multimodal combinations of image and genomic signatures to enhance the classification of pathology specimens. By integrating information from both imaging and genomic data, researchers aim to develop more

accurate and comprehensive diagnostic and prognostic models. This approach allows for a deeper understanding of the underlying molecular mechanisms and histopathological features associated with various diseases, leading to improved patient stratification and personalized treatment strategies. efforts are being revitalized to create dependable Content-Based Retrieval strategies . These techniques consequently search through enormous reference libraries of pathology tests to distinguish sores with qualities like a given question case, working with deliberate examinations of cancers inside and across understanding populaces. One benefit of CBR frameworks over customary classifier-based frameworks is their capacity to permit specialists to cross examine information while imagining the most applicable profiles [254].

TABLE III. AI-BASED MEDICAL IMAGING SYSTEMS WITH FDA-APPROVAL

Software	Company	Imaging Data	Description
SubtlePET/ SubtleMR	Subtle subtlemedical.com	PET/ MRI	Enhancement of PET/MR images
LungAI LiverAI	Arterys www.arterys.com	Lung CT Liver CT, MRI	Segmentation of lesions and nodules
AmCAD-UT	AmCad BioMed www.amcad.com.tw	Thyroid ultrasound	Characterisation and assessment of thyroid tissue
IDx-DR	IDx www.eyediagnosis.co	Retinal	Feedback on image quality, and instructions for patient follow-up or referral
icobrain	Icometrix icometrix.com	Brain MRI, CT	Interpretation of CT and MRI brain images
OsteoDetect	Imagen www.lify.io	Wrist X-ray	Detection of distal radius fracture
AI1	Zebra Medical Vision www.zebra-med.com	CT, X-ray of various diseases	Detection and quantification of abnormalities
Aidoc Head/Chest/Spine/Abdomen	Aidoc www.aidoc.com	Radiology images	Detection of acute abnormalities across the body
ProFound AI	iCAD www.icadmed.com	2D mammograms	Detection of malignancies and calcifications
Transpara	ScreenPoint Medical screenpoint-medical.com	2D and 3D mammograms	Detection and likelihood of cancer
Accipio	MaxIQ AI http://www.maxq.ai/	Head CT	Triaging of intracranial haemorrhage
Paige AI	Paige https://paige.ai/	Digital slides	Diagnosis for digital pathology

US: Ultrasound; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; PET: Positron Emission Tomography.

VIII. CONCLUDING REMARKS & FUTURE DIRECTIONS

Medical imaging informatics has been a driving force in clinical research, translation, and practice for over three decades. The advances in associated research branches discussed in this study hold the promise to revolutionize imaging informatics across the healthcare continuum. This transformation enables informed, more accurate diagnosis, timely prognosis, and effective treatment planning.

A significant percentage of FDA-approved AI-based solutions, particularly those utilizing machine- or deep-learning methodologies, Information related to medical imaging. The FDA serves as the official regulator for both medical devices and software classified as medical devices (SAMD)., has granted approval to solutions performing various image analysis tasks. These tasks include image enhancement (e.g., SubtlePET/MR, IDxDR), segmentation, and detection of abnormalities (e.g., Lung/Liver AI, Osteo Detect, Profound AI), as well as the estimation of the likelihood of malignancy (e.g., Transpara). While radiology images are predominantly addressed in these FDA-approved applications, digital pathology images are also starting to be addressed .

Table III offers a concise overview of currently approved AI-based solutions by the FDA. The future directions in this field anticipate significant growth in the number of systems obtaining FDA approval, further expanding the capabilities of medical imaging informatics.

Hardware Breakthroughs and Big Medical Data:

Advancements in medical imaging hardware for acquisition have enabled the generation of high-throughput and high-resolution images across various modalities, exhibiting unprecedented performance while minimizing radiation exposure. The ongoing era of extensive medical data is anticipated to witness additional expansion in imaging data, supplemented by information-rich Electronic Medical Records (EMR/EHR), The key challenge involves unlocking the complete potential of this abundant data wea+lth while concurrently safeguarding privacy and maintaining anonymity.

Efforts to standardize workflows and processes include multi-institutional collaboration, datasets that are freely accessible, featuring extensive cohorts with thorough annotations, and research studies that are both reproducible and explainable.

Deep Learning Dominance and Challenges:

Deep learning methods are dominating new research endeavour's, optimizing issues such as complexity, domain dependence and reproducibility. Unprecedented accuracy along with transfer learning approaches, has catalysed deep learning's adoption.

Obstacles endure, such as the requirement for transparent AI techniques, the utilization of sophisticated logic, and the application of 3D reconstruction. There is a pressing need to investigate the intersection of traditional machine learning and deep learning techniques, particularly to address vulnerabilities in generalization stemming from diverse populations and smaller datasets in the medical domain. By combining the strengths of both approaches, researchers can develop more robust and adaptable models capable of effectively handling variations in data distribution and size. This integrated approach holds promise for improving the performance and reliability of machine learning algorithms in medical applications, ultimately leading to better patient care and outcomes.

Future Directions and Challenges:

While the success of deep learning has been remarkable, challenges remain, requiring breakthroughs in explainable AI, combining traditional and deep learning methods, and overcoming generalization weaknesses. The medical domain's unique challenge lies in the difficulty of matching the enormous datasets used in natural image deep learning tasks.

As medical imaging informatics advances, the adoption of innovative solutions presented in this study is expected to elevate the quality of care, potentially transforming precision medicine. Emerging paradigms, such as radiogenomics, aim to facilitate knowledge extraction from heterogeneous, multi-level data, offering new

insights into disease etiology, progression, and treatment efficacy. Integrative analytics approaches are crucial for constructing advanced models that accurately portray biological processes in diseases.

In conclusion, the transformative potential of medical imaging informatics is poised to enhance the quality of care, paving the way for a new era in precision medicine.

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