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The Road to Precision Medicine: Emergence of Molecular Imaging, Advances, and Artificial Intelligence Applicability

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Abstract: Precision medicine represents a paradigm shift from empirical medicine in healthcare, moving away from the traditional "one-size-fits-all" model toward a more individualized approach tailored to each patient's unique genetic, molecular, and environmental profile. Technological evolution in medical imaging en route to molecular imaging marks the dawn of a new era, from just seeing anatomy to visualizing the underlying cellular and molecular processes in living organisms, driven by advances in molecular biology, probe development, and imaging technology (positron emission tomography, single photon emission computed tomography, magnetic resonance imaging, computed tomography, ultrasound, optical, magnetic particle imaging, hybrid, microwave). Yet, this is only the beginning. Latest empirical evidence shows that artificial intelligence (AI) use promises even greater breakthroughs: faster discovery of next-generation radiopharmaceuticals, real-time treatment adaptation, and seamless integration of imaging with predictive analytics as well as wearable sensors, although with visible challenges that need to be addressed. The future looks positive, where AI-driven innovations will unlock deeper insights into disease, elevate individualized care, and redefine diagnostic-therapeutic frontiers.

Keywords: precision medicine, medical imaging, molecular imaging, artificial intelligence

1. Introduction

Precision medicine is revolutionizing the current healthcare landscape globally by transitioning from the traditional "one-size-fits-all" approach to a more individualized strategy [1]. This evolution has been driven by key breakthroughs in genetics, technology, and clinical practice [2]. Advancements in the field of genomics were the building blocks in the development of precision medicine: from the discovery of the double Helix model of DNA in 1953 to the development of Sanger sequencing in 1977 and finally to the launching of the Human Genome Project in 1990, which took 13 years to complete [3]. The first successful application of precision medicine was the use of "Imatinib" to treat chronic myelogenous leukemia in 2001, which demonstrated the power of targeting specific genetic mutations to treat cancer [4].

Precision medicine can be defined as the use of advanced technologies and rigorous data analysis to optimize patient care and outcomes [5]. According to the recent research of Lip (2025), two key components of precision medicine are omics profiling and imaging techniques [6]. Omics profiling refers to a comprehensive analysis of all biological molecules (genes, RNA, proteins, metabolites) within a cell or organism (Figure 1), often integrated across multiple "omics" layers (genomics, transcriptomics, proteomics, metabolomics) to get a holistic view of health, disease, or response to treatments [7].

The integration of multi-omics data, primarily genomics, transcriptomics, proteomics, and metabolomics, provides a deep understanding of individual health by capturing genetic, molecular, and biochemical information [8]. On the other hand, imaging techniques, rooted in the principle of "molecular imaging," involve the use of imaging devices (otherwise known as modalities) to visualize biological processes and molecular pathways, thus facilitating accurate diagnosis, targeted treatment planning, and monitoring of therapeutic responses. These imaging devices include positron emission tomography (PET), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), computed tomography (CT), contrast-enhanced ultrasound (CEUS), optical imaging, magnetic particle imaging (MPI), and hybrid imaging [9].

Molecular imaging (MI) is a technique that visualizes, characterizes, and quantifies normal/pathological biological processes at the cellular and molecular level for biochemical, biologic, diagnostic, or therapeutic applications. Nonetheless, it operates with certain limitations regarding data standardization, resolution, and quantification [10]. The use of artificial intelligence (AI) in MI depicts a transformative development, fundamentally improving capabilities across the entire workflow from image acquisition to diagnosis and personalized treatment planning. The advent of deep learning (DL) in particular has ushered in a new era of

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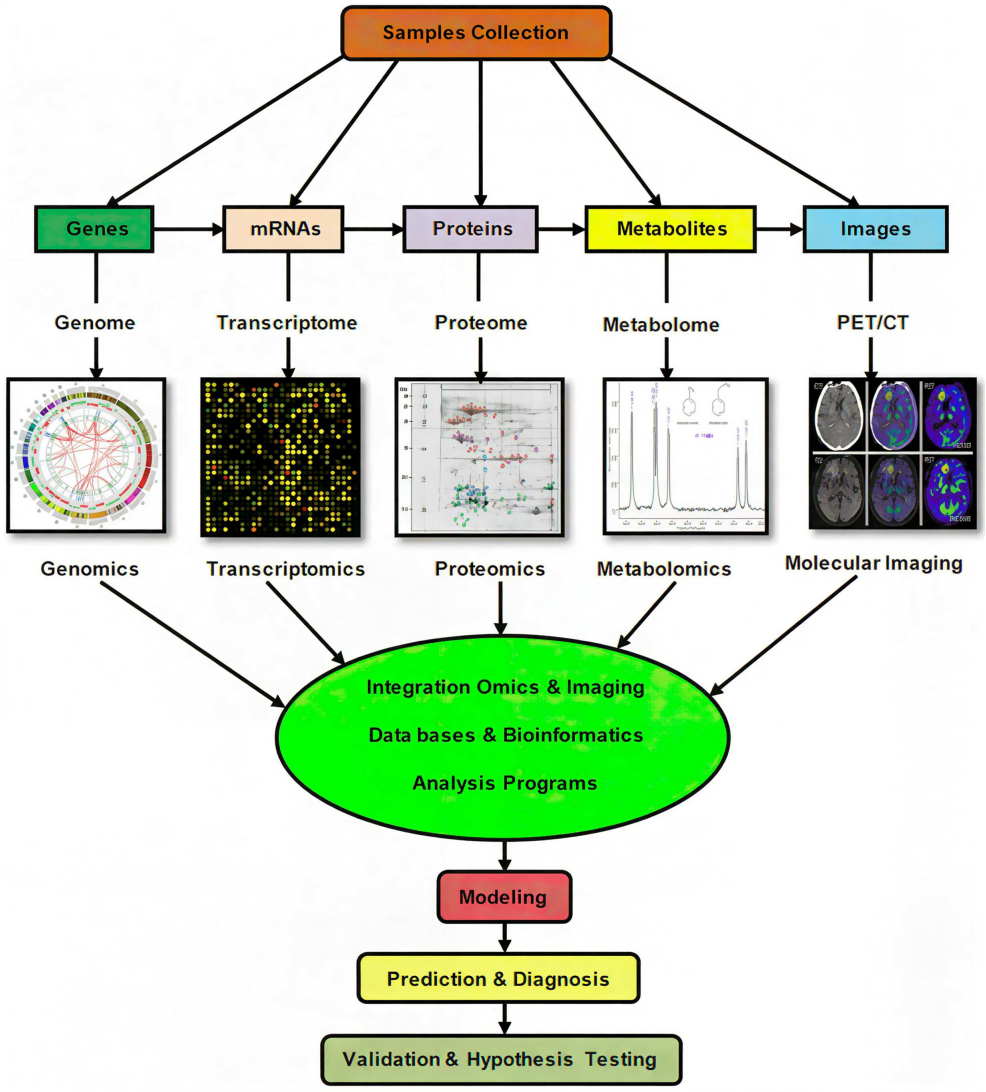
Figure 1
Hierarchy of systems biology approaches integrated with molecular imaging techniques



precision and efficiency, allowing for advancements that were previously unimaginable with traditional methods [11]. This article will look to examine advancements in medical imaging practice and explore the unifying role of MI/advances and AI techniques in achieving more personalized diagnostics and precise-targeted therapies via breakthroughs in imaging modalities/approaches, molecular probes, theranostics, radiomics, AI-driven analytics, and multi-omics integration. Challenges and future directions will be considered.

2. Methodology

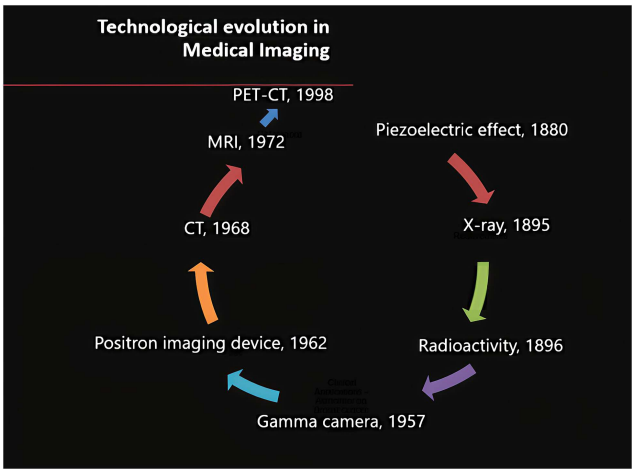
Key concepts ("precision medicine," "medical imaging," "molecular imaging," "artificial intelligence") were identified, and a search for relevant literature on these concepts was conducted in several databases such as PubMed, Web of Science, Google Scholar, ScienceDirect, PLoS, and Scopus. Synonyms and variations were also used in order to explore literature comprehensively, for example, "technological evolution in medical imaging," "molecular imaging techniques," "personalized/individualized medicine," "advances in molecular imaging," and "artificial intelligence use." In addition, a combination of these search terms using symbols and Boolean operators (*, or) was performed to broaden results. Thereafter, inclusion/exclusion criteria were applied to filter only studies in English and conducted in the last 10 years on medical imaging practice and precision medicine. Following review by a team of experienced imaging professionals, only studies with a focus on technological evolution, MI and advances, and AI use were included. Evidence was synthesized in a narrative way, and discussions logically developed that accentuate the evolution in medical imaging practice, leading to MI, the transformative journey of MI toward precision medicine, and AI use in MI. This layout will serve as a roadmap to achieving high-quality individualized medicine in clinical practice, highlighting progress made, current benefits, challenges, and future opportunities.

3. Technological Evolution in Medical Imaging

Medical imaging, a key aspect of radiology, is a branch of medicine that utilizes imaging technology and radiation (ionizing and non-ionizing) to diagnose and treat diseases. This discipline

dates back to the piezoelectric effect in 1880 and has ever since continued to be at the heart of innovations in technology and patient care to meet the demands of the 21st-century healthcare system, with the following milestones (Figure 2) [12]:

Figure 2
Technological evolution in medical imaging



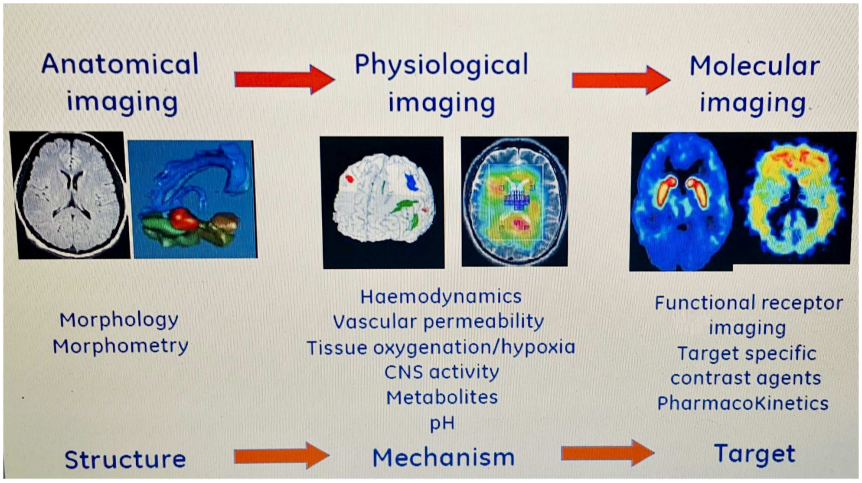
1) Piezo-electric effect discovered (ultrasound predecessor, 1880): French physicist brothers Pierre and Paul-Jacques Curie discovered that when pressure is put on certain crystals, electricity comes out. This effect is used on all modern ultrasound imaging systems [13, 14].
2) X-rays discovered (X-ray Imaging Predecessor, 1895): Rontgen discovered the unknown particles and hence called them X-rays as x typically is an unknown variable [15].
3) Radioactivity discovered (Nuclear Medicine predecessor, 1896): Becquerel, Marie Curie, and Pierre Curie discovered radioactivity, with a Uranium rock being the first demonstration of radioactive decay [16].
4) Noble Prize physics: Rontgen was given the first Nobel prize in physics for the discovery of X-rays in 1901, and Becquerel, Marie Curie, and Pierre Curie granted the Nobel Prize in physics for the discovery of radioactivity in 1903 [13].
5) Positron discovered (PET imaging predecessor, 1932): Carl David Anderson discovered the positron, which is the anti-particle of the electron and produces two photons via an annihilation event when a positron nears an electron. In 1936, he won the Nobel Prize for discovering the positron [17].
6) Gamma camera invented (SPECT predecessor, 1957): Hal Anger developed the gamma camera, also referred to as the Anger camera [18].
7) First positron tomography (PET predecessor, 1962): Sy Rankowitz and James Robertson of Brookhaven National Laboratory invented the first transverse positron imaging device designed for the brain [17].
8) CT invented in 1968: British engineer Godfrey Hounsfield of EMI Laboratories and physicist Allan Cormack of Tufts University generated the first generation of CT scanner that would take hours to acquire an image. In 1979, both received the Nobel Prize for CT [19].
9) MRI invented in 1972: The first MRI images were generated in a laboratory setting by Paul Lauterbur. In 2003, Paul Lauterbur for first to develop a method to make 2D images, and Peter Mansfield demonstrated the first human images, received the MRI Nobel Prize. Mansfield himself was the first human scanned in an MRI machine [20].
10) DICOM, PACS, and teleradiology in the 1980s through the mid-1990s: The paradigm shift from film-based to digital radiography occurred throughout the late 20th century, with key technologies like DICOM, PACS, and teleradiology all introduced during this period [21].
11) First PET/CT scanner in 1998: In a project led by David Townsend and Ronald Nutt, the first PET-CT scanner was built at the University of Pittsburgh Medical Center [22].

This trend is a shift toward precision medicine (Figure 3), from anatomical imaging (showing body structure, e.g., CT, X-ray, MRI, US) to physiological imaging (reveals function, e.g., fMRI, PET, SPECT) and to MI (visualizes biological processes at the cellular/molecular level with tracers, e.g., PET/CT, PET, SPECT).

4. Technological Evolution in Medical Imaging

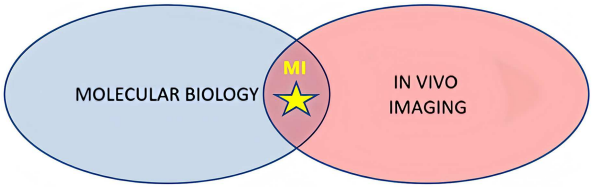
MI is a growing imaging and biomedical research discipline that enables the visualization, characterization, and measurement

Figure 3
Trend toward molecular imaging: from anatomy imaging to molecular imaging



of biological processes occurring at the cellular and molecular level in living subjects, using agents (tracers) that highlight specific molecules like enzymes or receptors to provide functional and biochemical insights, unlike traditional imaging that focuses just on anatomy [23]. It lies at the intersection of molecular biology and medical imaging (Figure 4).

Figure 4
Molecular imaging (MI) domains



Molecular biology deals with the structure and function of molecules and their interactions (Figure 5), while in vivo imaging is concerned with the noninvasive techniques that visualize and study biological processes, cellular activities, and metabolic functions in real time, crucial for understanding disease progression, testing new treatments, and monitoring patient health.

Basic MI requirements are imaging device and imaging probe (Figure 6).

1) Imaging probe: otherwise called "tracers," is an agent used to visualize, characterize, and measure biological processes in living systems, consisting of a signal agent, a linker, and a target (Figure 7).
2) Imaging device: also known as "imaging modalities," detects the imaging probe and creates pictures showing how it is distributed in the body. This distribution tells how well organs and tissues are functioning.

5. Toward Precision Medicine: The Transformative Journey of Molecular Imaging

Precision medicine has many potential applications in healthcare, where MI is crucial by providing noninvasive, real-time insights into a patient's unique molecular and cellular processes, allowing for highly personalized treatment by visualizing disease targets like specific proteins or genes [8] (Figure 8).

MI has sometimes been criticized for a lack of quantitative rigor, low resolution and sensitivity constraints, inefficient workflows, and data heterogeneity, preventing its full, widespread adoption in clinical precision medicine. Ongoing efforts to address this have yielded positive results, with recent quantum leaps witnessed in imaging modalities/approaches, molecular probes, theranostics, radiomics, AI-driven analytics, and multi-omics integration [24, 25]. This headway has hugely contributed to reshaping the landscape of MI and precision medicine.

5.1. Imaging modalities and approaches

1) PET: relies on the detection of two 511 keV gamma photons in opposite directions released following the decay of positron-emitting radioisotopes (annihilation), detected by the PET scanner, useful in monitoring metabolic activity in the brain (neurological function, perfusion, tumor detection), cardiac

Figure 5
Relationship between molecular biology and molecular imaging

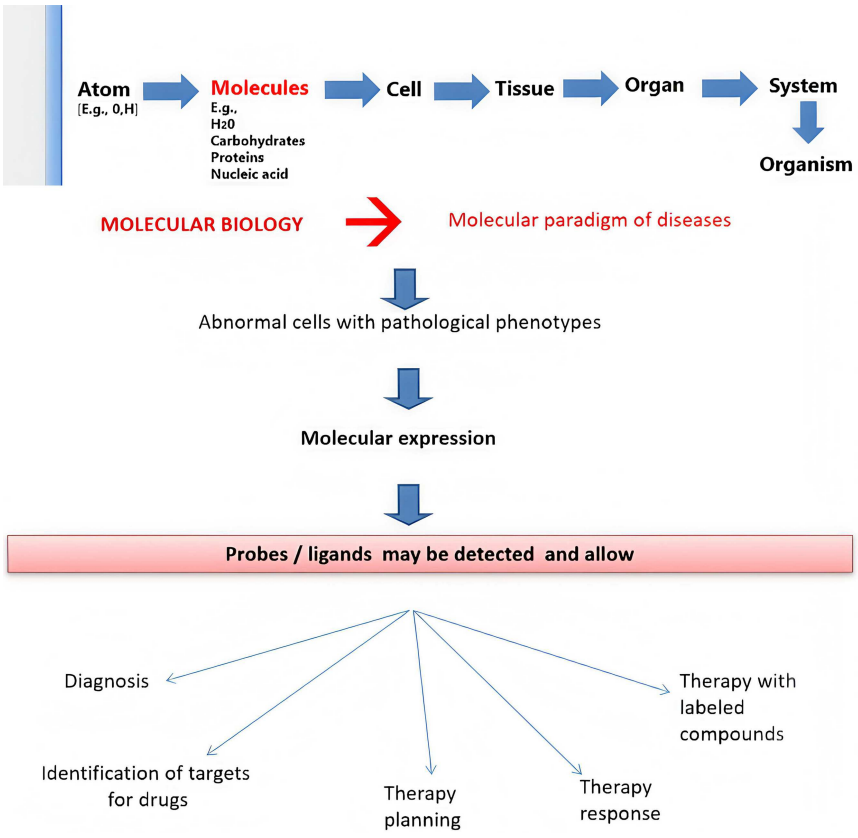


Figure 6
MI requirements: imaging device

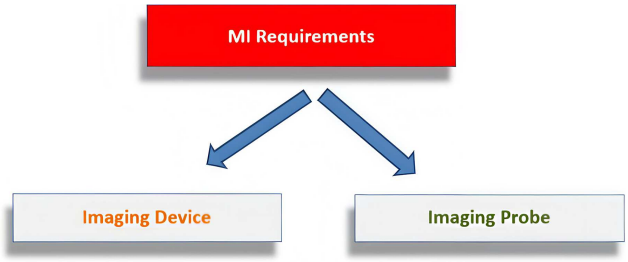


Figure 7
Imaging probe components

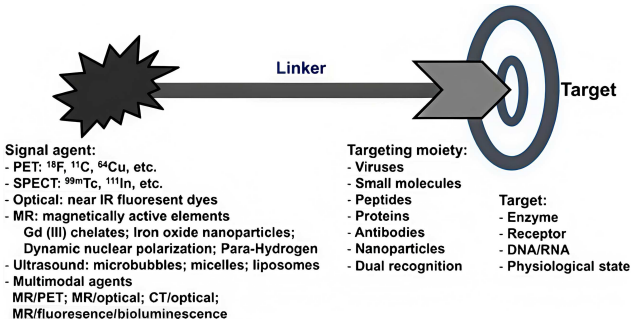
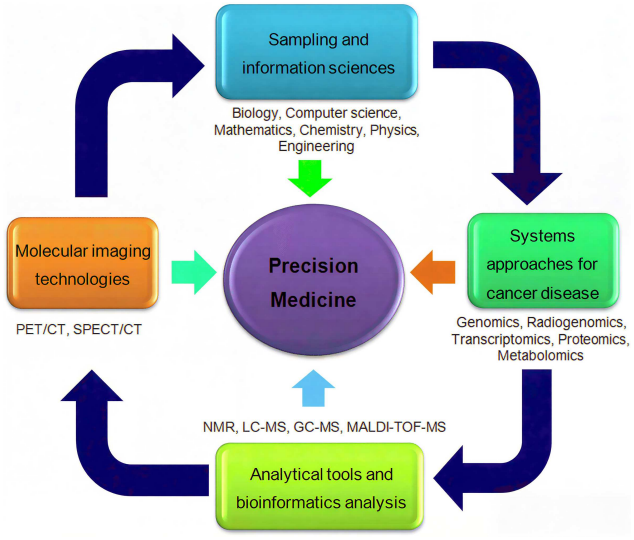


Figure 8
Relationship between precision medicine and molecular imaging



(metabolism, blood flow), and cancer (tumor detection, staging, assessing treatment) [9]. PET supports precision medicine by using specific radiotracers to visualize biochemical process, receptor status, and metabolism at the molecular level, as well as identify phenotypic heterogeneity in individual patients for accurate characterization of diseases. Its ability to map molecular targets and quantify diseases enables clinicians to deliver the right therapy to the right patient. Again, it identifies treatment resistance early in the process, thus preventing unnecessary side effects and cost from ineffective therapies [26]. PET imaging has a significantly better spatial resolution compared to SPECT and higher sensitivity.

2) SPECT: utilizes a gamma camera that detects emitted gamma rays directly following the decay process of the intravenously injected radiotracer [mostly Technetium-99m (99mTc), with a half-life of 6.03 h]. Its role in tailoring medical care to individual patients focuses on enabling early and accurate diagnosis, guiding treatment selection, and monitoring therapeutic treatment in real time. It is commonly used in brain perfusion (to select a specific treatment regimen in complex psychiatric cases), heart disorders (coronary artery disease and myocardial infarcts, by tailoring cardiac care, e.g., deciding between invasive procedures, stents, and medical management), and qualitative tumor assessment [27]. SPECT imaging has gained widespread popularity due to its reliable generation from 99Mo, lower cost compared to PET, and longer-lived tracers.
3) CT: Dual-energy CT (DECT), an advanced CT scanning technique leverages the ability to differentiate materials based on their unique X-ray attenuation at two different energy levels, revealing different attenuation curves for materials like iodine (from contrast) versus bone or water, creating "material-selective density maps." DECT creates material-specific images (e.g., iodine maps, fat maps) to specifically label and quantify tissue composition, aiding differentiation of benign from malignant lesions. This is useful in oncology (tumor characterization, detecting metastasis, adaptive treatment response), cardiology (plaque characterization in coronary arteries), and tissue characterization (bone or fat from edema, contrast from hemorrhage). It makes small lesions more visible as the contrast-to-noise ratio can be increased despite a reduced given contrast dose. Modern DECT allows automatic adjustment for scan settings based on patient size, age, and clinical needs, while ensuring optimal image quality with the lowest necessary dose [28]. Borges et al. [29] noted that despite providing dose reduction techniques and excellent temporal/spatial resolution, it suffers drawbacks such as unsharp distinction between lower- and higher-energy photons by the detector resulting in spectral overlap, susceptibility to cross-scattering between the two detectors, increased technical challenges, and cost.
4) MRI: deploys strong magnetic fields, radiofrequency pulses, and their gradients to noninvasively image tissues. MR spectroscopy (MRS) measures the concentration of specific metabolites (chemical building blocks) in tissues, revealing metabolic pathways in cancer, brain, and heart disorders [30]. On the other hand, diffusion-weighted imaging (DWI) techniques track/measure water molecule movement (Brownian motion) to detect early molecular changes in cases of cancer, ischemia, or stroke [31]. MRS and DWI techniques support precision medicine by providing noninvasive, patient-specific, and molecular-level insights into tissue characteristics, enabling tailored diagnosis, treatment planning, and monitoring. While traditional MRI provides anatomical information, DWI and MRS offer functional and metabolic data (often termed "virtual biopsies") that help distinguish tumor grades, identify molecular subtypes, and assess tumor cellularity [32]. These enhanced MRI techniques face challenges with sensitivity, despite enabling visualization of biological processes at the cellular/molecular level. But as seen in the work by Jørgensen et al. [33], contemporary hyperpolarization techniques have proven to boost MRI signal sensitivity, allowing real-time visualization of metabolic pathways (e.g., cancer's energy use, neuroimaging, heart, liver, and kidney function), cellular activity, and monitoring treatment response.
5) US: CEUS uses microbubble contrast agents that enhance contrast between blood vessels and surrounding tissue. This approach enhances diagnostic precision by allowing for improved visualization of tissue perfusion and blood flow

dynamics in cancer, urology, focal lesions, and tumors cysts [34]. In addition, it aids personalized system planning and guidance central to image-guided biopsies and tumor ablation therapies. Encapsulated microbubbles can be doped with ligands or antibodies to target specific cells or tissues, making them valuable tools for targeted imaging, while offering real-time treatment monitoring (early response assessment and repeatable monitoring). The manipulative ability of these microbubble properties (size, shell composition) opens exciting opportunities for research and development [35]. CEUS is cost effective and widely available and offers real-time imaging, but regulatory approval and commercial sale of new microbubble probes remain barriers [9].

6) MPI: is a cutting-edge technique that excels in providing a direct quantitative map of superparamagnetic iron oxide nanoparticles (a tracer that generates a signal only where they are present, unlike MRI, which images tissues) distribution in vivo. This is useful in achieving precision medicine by directly quantifying cells (like stem cells or immune cells) at a target site with high sensitivity, real-time high-resolution (spatial/temporal) imaging, monitoring cancer (diagnosis, individual therapy, and drug delivery), and image-guided surgeries/interventions. It offers high sensitivity, with no ionization radiation and background noise benefits [36].
7) Optical imaging: offers noninvasive ways to visualize cellular processes with high resolution, sensitivity, and cost-effectiveness using fluorescent or bioluminescent probes that bind to specific molecules or track biological activities (like enzyme activity or protein interactions) within the body. It is mostly combined with CT or MRI (PET/CT, PET/MRI) to overcome anatomical depth limitation, giving both molecular details and precise anatomical locations, and plays a crucial role in detecting tumors, drug development, surgical guidance, and postoperative monitoring [37].
8) Hybrid technologies: denotes an integrated system that combines complementary imaging modalities (PET/CT, PET/MRI, SPECT/CT, PET/DECT). Recent literatures by El Yaman et al. [38] and de Cecco et al. [39] have shown this to be associated with deeper molecular insights in oncology, cardiology, neurology, theranostics, and precision medicine than traditional molecular techniques. PET/CT hybrid technology, first introduced in 2001, marks a monumental feat in medicine and fundamentally shaped modern MI, effectively addressing the primary limitations of standalone PET or SPECT imaging. The ongoing rapid advancement in hardware (total-body PET, PET/MRI), software (AI, advanced reconstruction algorithms, radiomics), and radiopharmaceuticals (theranostics, immune-PET) demonstrates that the field is continuously evolving, perpetually building upon past breakthroughs to offer ever-greater precision in patient care. The pursuit of a more holistic understanding of disease at a molecular level continues to drive exciting innovations [23].
9) Microwave imaging system (MWI): uses low-power, non-ionizing electromagnetic waves (300 MHz–300 GHz) to detect, locate, and image tissues (healthy and malignant tissues) based on variations in dielectric properties (permittivity and conductivity). It is a novel technique, particularly valuable for personalized screening, allowing for more frequent treatment monitoring and tracking therapeutic responses during chemotherapy or after breast-conserving surgery without radiation risks; this makes it safer for high-risk, younger populations [40]. When combined with nanoparticle contrast agents, it offers targeted therapy and molecular diagnostics. In neurology, MWI-based wearable devices and mobile stroke units are useful in differentiating between ischemic and hemorrhagic stroke, enabling rapid, tailored treatment during the "golden hour" [41]. Despite its potential, it faces challenges in achieving high spatial resolution comparable to MRI or X-ray, with current research focusing on overcoming these limitations through AI, better antenna design, and developing hybrid systems (e.g., MWI with MRI or ultrasound) to improve accuracy and clinical adoption [42].

5.2. Multi-omics integration

The unification of MI with multi-omics data (genomics, transcriptomics, proteomics, and metabolomics) is accelerating the transition from reactive to precision medicine (P4 medicine: predictive, preventive, personalized, and participatory). The current frontier involves integrating imaging with omics data layers to create a holistic patient profile. This synergy allows for the detection of molecular alterations such as DNA mutations, RNA expression levels, and protein abundancies, correlated with tumor morphology and metabolism [43, 44]. This involves the following steps:

1) Imaging-Omics (Radio-omics): linking MRI/PET image characteristics to molecular profiles.
2) Spatial Omics: imaging technologies map the spatial distribution of diverse cell types and molecular processes directly within tissue, providing context that bulk omics approaches miss.
3) Liquid Biopsy and Imaging: a combination of circulating tumor DNA or proteomic signatures from liquid biopsies and PET-based tumor tracking allows real-time, minimally invasive monitoring of treatment response and disease evolution.

This merger is starting to see widespread applications. First is in oncology, where specific genetic mutations or biomarkers in cancer cells can be identified and targeted with drugs for more effective and personalized treatments [45]. MI guides cancer therapy, playing vital roles in detection, staging, and monitoring. This also includes identification of specific targets (receptors, enzymes) for targeted therapies and selecting the most effective drug for an individual [46]. Thus, it is able to modify treatments, connoting a move from broad treatments to customized therapies for maximum effectiveness.

Precision medicine can help identify the genetic variations that cause neurological disorders (such as Alzheimer's and Parkinson's diseases), cardiovascular diseases (inflammation, plaque stability, and blood vessel function), and Gastrointestinal tract (GIT) anomalies (e.g., detecting and grading inflammatory processes) [4]. Again, as seen in several studies, MI is crucial for early diagnosis and more targeted treatments for each of these abnormalities [47–49].

Precision medicine assists in identifying genetic variations that make individuals more susceptible to certain diseases, leading to more targeted prevention and treatment. Recent studies have proven that MI supports treatment monitoring and prognosis, which involves assessment of the patient's response to therapy in real time (allowing for early adjustments), predicting disease progression and patient outcomes [46, 50, 51].

Precision medicine tailors treatments to individual patients using their unique genetic/molecular profiles; cell and gene therapies are powerful tools within this approach, directly modifying cells or genes to correct disease (such as CAR-T cells for cancer or gene editing for inherited disorders), representing a shift

from one-size-fits-all to highly personalized, fundamental biological interventions [52]. Empirical evidence shows that MI is useful for cell and gene therapy by noninvasively tracking therapeutic cells and gene expression, guiding treatment, assessing efficacy, and optimizing delivery in real time using technologies like PET, SPECT, CT, MRI, and hybrid that provide spatial and temporal insights to ensure treatments reach targets and work as intended [53, 54].

5.3. Theranostics

Theranostics, a powerful application of precision medicine, entails merging diagnostics and therapy (therapeutics + diagnostics) using matched pairs (often radioactive), to pinpoint and treat disease, especially cancer, offering personalized, "see-what-you-treat" approaches for better outcomes. It uses imaging to guide and assess targeted therapies, improving effectiveness and reducing side effects [55]. As seen in studies by Velikyan [56] as well as Salgueiro and Zubillaga [57], MI is a core component of theranostics, providing crucial data at every stage of the theranostic journey, transforming it from a reactive process to a predictive one. It requires using the same targeting molecule (e.g., a ligand) for both diagnosis (imaging) and therapy (drug delivery). As demonstrated in the "bad berka experience" research of Baum and Kulkarni, this works by attaching a diagnostic agent/radioactive tracer (e.g., Gallium-68) to a molecule that binds to specific disease markers, imaging using PET/SPECT to reveal exactly where the disease is and its extent, and administering a therapeutic radioisotope (e.g., Lutetium-177 with a similar molecule, delivering targeted radiation precisely where the diagnostic scan showed the disease) [58]. Therefore, by simply changing the radioactive atom, the same molecule can be used to image a tumor and then treat it. This nascent approach is fundamental to precision medicine, enabling clinicians to identify molecular targets, select suitable patients, and deliver tailored treatments with minimal damage to healthy tissues. This technology has resulted in a significant improvement in outcomes for patients with metastatic castration-resistant prostate cancer, minimal side effects associated with conventional chemotherapy (by using targeting vectors such as ligands, antibodies to deliver radiation to cancer cells), and is expanding beyond oncology to include inflammatory, neurological, and cardiovascular diseases [50, 59].

5.4. Molecular probes

Precision medicine accelerates drug development. MI techniques (e.g., PET, SPECT, MRI, CT, US, Hybrid) noninvasively visualize and quantify biological processes at the cellular and subcellular levels in living subjects, crucial at various stages of the complex and expensive drug development pipeline. Progress made in these technologies is directly linked to the advancement of molecular probes—targeting agents conjugated to signaling components that reveal specific pathological markers. As reported in a range of studies by Luo et al. [60], Vermeulen et al. [61], and Rudin and Weissleder [62], it includes:

1) Target identification and validation: providing insights into disease mechanisms and abnormal cellular pathways.
2) Compound screening and optimization: assessing the effects of candidate drugs on specific biological pathways, allowing for rapid identification and termination of compounds that are unlikely to succeed.
3) Assessing biodistribution and pharmacokinetics: noninvasive tracking of where the drug goes in the body and how it is absorbed, distributed, metabolized, and excreted.
4) Determining optimal dosing and efficacy: proof of concept, demonstrates that a drug is engaging its target and producing the desired biological effect at a safe dose by providing functional or metabolic information.
5) Patient selection and stratification: identifies patients who are most likely to respond to a specific treatment based on their unique molecular profile.
6) Monitoring treatment response: metabolism shown in a real time by the radiotracer in response to a therapy, allowing for timely adjustments to the treatment plan.
7) Developing theranostics: combining a diagnostic imaging agent and a therapeutic agent into a single system.

5.5. Radiomics

MI, empowered by radiomics, has transformed from a purely qualitative diagnostic tool into a quantitative high-throughput assay that captures intratumoral heterogeneity and drives precision medicine. By extracting a large amount of advanced quantitative features from standard medical images (PET, MRI, CT, etc.) and combining them with AI, radiomics provides noninvasive longitudinal and comprehensive insights into tumor biology, enabling personalized treatment planning and prognosis [63, 64]. This represents a major revolution in cancer care, moving the field toward a future where treatment is tailored to the molecular and phenotypic profile of each patient, due to its synergy with genomics (radiogenomics) [65]. It does this by analyzing the entire tumor volume across its entire course, thus addressing the spatial and temporal limitations of traditional tissue biopsies. Furthermore, radiomics-based models can identify patients likely to respond to immunotherapy or targeted therapy, avoiding unnecessary treatment for non-responders. It can predict progression-free survival and overall survival in various cancers, monitor treatment response or changes to therapy over time, and act as an automated decision support tool for personalized oncologic management [66, 67].

6. Artificial Intelligence Use in MI

1) Probe design: AI and machine learning (ML) facilitate molecular-probe design, with studies [11, 68] showing new methods of AI application and simulation software to an increasing number of probes and its probability to have desired features such as bioavailability, safety, and stability. In a critical appraisal, Zhang et al. [69] noted that AI has disrupted the conventional methodologies (target identification, compound screening, pharmacokinetic [ADME: absorption, distribution, metabolism, and excretion] investigations, toxicity evaluation, and clinical trial design), and this was confirmed [70] to significantly enhance efficiency across multiple phases of the drug development process-target identification and validation, drug-target affinity prediction, design for innovative radioactive ligands, and optimization of drug delivery system. However, this is still in the preliminary stages.
2) Plan definition: Research on AI use in plan definition (MI) has been promising, revealing that AI can significantly cut down examination planning in a cost-effective manner, offer precise dosimetry, and eliminate human errors [11]. The automated integration of advanced AI algorithms into complex

medical workflows represents a paradigm shift, moving healthcare toward a more streamlined, precise, efficient, and patient-centered future [71]. The 2026 review on clinical trials [72] affirms this, recording improved enrollment dates by 65%, accelerated timeline by 30–50%, cost reduction by 40%, 85% accuracy in outcomes, and 90% sensitivity for adverse event detection.

3) Image acquisition process: AI particularly DL neural networks has been found to improves timing performance (position of interaction and time of interaction), event positioning, offering higher spatial and energy resolution, noise reduction (by 26%, denoising algorithms that produces high-quality, low-dose scanning in PET and SPECT), image reconstruction, image segmentation, and quantitative imaging [73, 74]. Table 1 further summarizes AI clinical utility in data analysis.
4) Image quality: Results from the use of DL models in recent comprehensive review works by Apostolopoulos et al. [75] and Arabi et al. [76], involving several studies, show increased efficiency and image quality for PET and SPECT reconstruction. In particular, the use of generative adversarial networks (GANs) consists of two networks: a generator that creates a sample of the input data and a discriminator that boosts accuracy in the classification of genuine and replicate samples [21].
5) Outcome interpretation: Prediction of survival and response to therapy are key areas of AI application, which are beginning to show signs of future success [77]. In 2025, Huang and Zhang [78] demonstrated that AI is able to extract imaging features and link to genomic data, enabling predictive modeling and identifying biomarkers for targeted treatments, an emerging field known as "radiomics." Papp et al. [79] explored the potential of ML models trained with PET/MRI data to distinguish low and high-risk prostate lesions and predict biochemical recurrence in prostate cancer patients; findings were impressive. In spite of these largely promising signs, scarcity of evidence exists.
6) Diagnosis and reporting: Certain AI models built on convolutional neural network (CNNs) approaches have recorded superior differential diagnosis, micro-metastatic detection, and complex case identification (cancer, brain, cardiology disorders) in comparison to radiologists, even surpassing the accuracy of experts [11, 80]. In a comparative study, Frood et al. [81] found that AI-assisted PET/CT reading workflow increased reporting efficiency without adversely affecting image quality ($p < 0.001$), thus reducing costs and report turnaround times.
7) Wearable sensors application: this is a rapidly evolving field focusing on creating unobtrusive, flexible, and self-powered devices for continuous, real-time health monitoring and performance tracking. It has evolved from 18th-century mechanically powered timepieces (pocket watches) and early pulse-measuring devices (1700s) to sophisticated, 21st-century internet-connected biocompatible devices. Three key evolutionary phases include an initial mechanical stage

Table 1
Interpretation of the mean scale for belief, concern, and practice

Study	AI algorithm/tool	Modality	Description	Key finding	Critical assessment of evidence
Xiang et al. [82]	CNN	PET/MRI	Image reconstruction and enhancement	Approximately 2s, compared to about 16 min by the state-of-the-art method	Randomized controlled trials, prospective, and external validations on real human brain PET/MRI data performed. Proposed method uses a deep neural network to map the inputs to the output directly (without any pre/post-processing beyond the optimization in the training stage), which is different from previous sparse-learning-based techniques that contain time-consuming steps such as patch representation, nonlinear mapping, and reconstruction
Gong et al. [83]	DDPM	PET	Image reconstruction and enhancement	DDPM is a flexible framework that offers better performance and further reduction in the uncertainty during image denoising. Providing the prior image as the input or supplying the prior image as the network input was crucial to achieving this	Experimental and prospective. Regional and surface quantification techniques were performed. Meanwhile, solely relying on MR prior while ignoring the PET information resulted in large bias

(*Continued*)

Table 1
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Study	AI algorithm/tool	Modality	Description	Key finding	Critical assessment of evidence
Lu et al. [84]	3D U-net	PET	Image reconstruction and enhancement	Optimal quantitative performance - smaller NMSE, higher Signal-to-noise ratio (SNR), < 15% SUV_{mean} bias, and lower SUV_{max} bias	Experimental and prospective. The fully 3D U-net model used in comparison to 2D and 2.5D U-net effectively reduces control bias even for sub-centimeter small lung nodules when generating standard dose PET using 10% low count down-sampled data
Wang et al. [85]	3D c-GAN	PET	Image reconstruction and enhancement	Radiation exposure reduction while maintaining high-quality PET images	Experimental, prospective and validation on a real human brain dataset. Randomization between normal subjects and mild cognitive impairment patients, but with a small training sample size The estimation error loss considered in the objective function to enhance the robustness of the proposed approach, which adopts concatenated 3D c-GANs and transfer learning. Study restricted to only brain PET image data and lacks multi-modality incorporation information
Ramon et al. [86]	CNN	SPECT	Image reconstruction and enhancement	Significant improvement in image quality in the low-dose studies over conventional noise reduction methods (proposed method at 1/16 achieves similar image quality to that from 1/8 dose with conventional denoising)	Experimental and prospective. Lack of external validation, with only a simulation performed. Limited clinical data
Sun et al. [87]	Pix2Pix GAN	SPECT	Image reconstruction and enhancement	Superior in reducing the noise level of low-dose SPECT compared to the reference across all physical indices (NMSE, SSIM, CV, FWHM, RSD)	Experimental and external validation performed. Only the physical indices measurement was considered, with existing literatures showing that evaluation of denoising methods with physical metrics such as NMSE and SSIM is not reflective of performance on clinical tasks. Possibility of variability due to different types of scanners and acquisition protocols utilized in the simulated and actual datasets (although it was found to be consistent). Limited clinical data

(*Continued*)

Table 1
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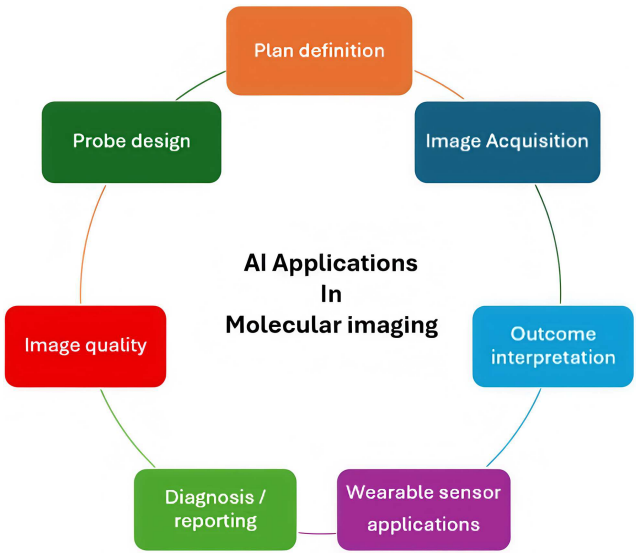
Study	AI algorithm/tool	Modality	Description	Key finding	Critical assessment of evidence
Han et al. [88]	CNN (3D U-net)	PET/CT	Image segmentation and quantitative analysis	Good diagnostic accuracy (AUCs: SUV_{max}, 0.95; MTV, 0.85; TLG, 0.87) and significant prognostic value (HRs: SUV_{max}, 1.31 [95% confidence interval, 1.16–1.48]; MTV, 2.11 [1.09–4.06]; TLG, 1.90 [1.12–3.23]).	Experimental and retrospective. Lack of external validation as well as limited clinical data
Ghezzo et al. [89]	CNN	PET/CT, PET/MRI	Image segmentation and quantitative analysis	Results were robust to the modality used to acquire images (median dice score = 0.74), and to the ground truth labels (no significant difference between the model's performance when compared to reader 1 or reader 2 manual contouring)	Experimental, retrospective, and robust external validation performed. Monocentric nature of study, as PET images were acquired in a single institution, although population represents a large independent and external testing cohort
Matkovic et al. [90]	MSR-CNN	PET/CT	Image segmentation and quantitative analysis	Promising end-to-end segmentation, with mean surface distance and DSC values of 0.666 ± 0.696 mm and 0.932 ± 0.059 for prostate and 0.814 ± 1.002 mm and 0.801 ± 0.178 for DILs	Experimental, retrospective, cross-validation and a hold-out test performed to train and evaluate the method, adopting cascaded and mask regional strategies. Limited datasets, all from a single facility. Too much focus on the geometric accuracy, with the likelihood of errors in the segmented contours, affecting the treatment planning process
Wang et al. [91]	Mask R-CNN	PET/CT	Image segmentation and quantitative analysis	Great improvement in the efficiency of segmentation, with average centroid distance, volume difference and DSC value of 0.83 ± 0.91 mm, 0.01 ± 0.79, and 0.84 ± 0.09, respectively	Experimental, retrospective, cross-validation. Limited datasets and lack of generalizability

Note: Normalized mean square error (NMSE), structural similarity index (SSIM), coefficient of variation (CV), full-width-at-half-maximum (FWHM), relative defect size differences (RSD), standard update value maximum (SUVmax), metabolic tumor volume (MTV), total lesion glycolysis (TLG), area under the curve (AUC), hazard ratios (HRs), Dice similarity coefficient (DSC), and dominant intraprostatic lesions (DILs).

(16th to early 20th century, non-electronic, for tracking time or movement), multifunctional stage (90s–00s, early digital, Bluetooth, and basic biosensors), and a smart technology phase (2010s–now, AI-integrated, comprehensive physical, biochemical, and biophysical sensors; real-time, wireless data connectivity) [92, 93]. The conceptual link between wearable sensor architectures and imaging lies in the shift from sparse, 1D signal monitoring to spatiotemporal, high-density, and 2D/3D visualization of physiological, anatomical, and mechanical data, facilitated by advanced materials, flexible electronics, and AI-driven data processing. Notwithstanding, AI-integrated wearable molecular-enabled imaging technologies that offers individualized care includes wearable electrochemical sensors (drug monitoring/pharmacokinetics and neurotransmitter detection, aiding personalized therapy), wearable Electroencephalogram (EEG)-based devices for real-time brain activity imaging (e.g., earbud-style sensors enable long-term monitoring), flexible wearable ultrasonic

devices (continuous noninvasive imaging of vascular and cardiac activity), wearable electrical impedance system (identify specific abnormal tissues based on heterogeneous electrical conductivity), and wearable bandage-based and microneedle electrochemical sensors (tracking treatment efficacy/safety, as well as predictive health monitoring in cancer theranostics) [94–96]. Figure 9 provides a schematic summary of AI use in MI.

Figure 9
Applications of artificial intelligence in molecular imaging



7. Challenges and Future Directions

The realization of this grand vision is not without the following considerable challenges.

7.1. Data acquisition and quality

1) Scarcity and Heterogeneity: Developing robust AI models necessitates access to massive, diverse, and high-quality datasets that represent a wide range of patient demographics, disease states (including rare diseases), and imaging equipment. Currently, data are often siloed in different hospital systems, acquired using variable protocols, scanner models, and reconstruction settings, which introduces significant heterogeneity and bias. Data standardization across institutions, interdisciplinary collaboration, and robust clinical validation remain pivotal [97].
2) Data Labeling and Annotation: Training supervised AI models requires accurate, high-quality labels or annotations, often from expert physicians. This process is time-consuming, expensive, and subject to inter-observer variability and subjective interpretation, which can lead to "annotation bias" in the training data [98].
3) Privacy and Sharing Concerns: Medical imaging data are highly sensitive, and strict regulations like HIPAA and GDPR limit easy data sharing across institutions. This significantly restricts the ability to create the large, multicenter datasets needed to train generalized models. Patients should be actively educated on informed consent for data sharing, data rights like access, deletion, and the right to restrict data processing [99]. This will also benefit the future development of AI systems.

7.2. Technical and algorithmic limitations

1) The "Black Box" Problem: Many powerful DL models are opaque, meaning their decision-making processes are not easily understandable or explainable to humans. This lack of transparency, or interpretability, makes it difficult to trust the AI's recommendations, posing a significant barrier to clinical adoption. Ongoing research and model development should focus on interpretable AI frameworks and technologies to aid clinicians in understanding and evaluating models [21].
2) Generalizability and Brittleness: AI models often perform well in the specific environment where they were developed but fail to generalize to new patient populations, different scanners, or variations in clinical practice (known as dataset shift or model brittleness). Training models on large and diverse datasets will improve robustness and real-world applicability among different patient groups [100].

7.3. Clinical integration and human factors

1) Workflow Integration: Seamlessly integrating AI tools into existing, often complex, clinical workflows remains a major logistical and technical hurdle, as poor integration can disrupt clinical practice and lead to clinician resistance. AI literacy, stakeholder engagement, multidisciplinary approaches, and continuous training are required [101].
2) Clinician Trust and Automation Bias: Over-reliance on AI outputs (automation bias) can lead to human error if clinicians stop using their own judgment. Conversely, skepticism and a lack of trust in the technology (algorithmic aversion) can hinder adoption [102].
3) Lack of Clinical Evidence: A scarcity of prospective, randomized controlled trials demonstrating that AI improves actual patient outcomes (beyond just technical accuracy metrics) makes it difficult to justify long-term investment and widespread adoption [103].

7.4. Ethical, legal, and regulatory ambiguities

1) Accountability and Liability: Clear legal frameworks are needed to determine who is accountable in the event of an AI-driven error or misdiagnosis—the physician, the hospital, or the AI developer [104].
2) Regulatory Oversight: Traditional regulatory frameworks are not well-suited for adaptive, continuously learning AI models, requiring modern guidelines that balance innovation with patient safety [101].
3) Algorithmic Bias and Health Inequities: Biases embedded in training data can perpetuate or even amplify existing health disparities, leading to suboptimal care for underrepresented demographic groups. Ensuring fairness and equity in AI performance across all populations is a significant ethical obligation [72].

7.5. Wearable sensor-specific issues

1) Biocompatibility and Skin Interface: Irritation, inflammation, and allergic reactions (contact dermatitis) due to long-term

skin contact with sensor materials, adhesives, and sweat accumulation, including signal degradation and loss of sensitivity in implantable or microneedle-based sensors [105].
2) Energy Efficiency and Autonomy: Current batteries are often too bulky and flexible self-powered alternatives (e.g., biofuel cells, thermoelectric) currently lack the necessary energy for long-term uninterrupted operation [106].
3) Continuous Monitoring Feasibility: Continuous monitoring is hampered by signal drift, where sensor sensitivity changes over time, thus requiring frequent recalibration. Lack of understanding regarding the longitudinal profile of molecular biomarkers, making it difficult to distinguish true disease progression from normal metabolic fluctuations [105].
4) Clinical Workflow Integration: Noisy nature of wearable data due to motion artifacts (body movement) and the need for raw data to be translated into clinically meaningful information exists. Lack of standardized data protocols and the isolated nature of many wearable devices, failing to integrate into existing electronic health records and hospital workflows [107].
5) Sensor Accuracy and Validation: Lack of extensive clinical validation on wearable sensors to compare their performance with traditional gold-standard diagnostic tools, as well as regulatory approval for clinical use, continues to persist [106].

8. Conclusion

The road to precision medicine is a transformative journey, and the convergence of MI, substantial technological advances, and AI is carving a path toward a healthcare paradigm that is highly personalized, predictive, and preventative. Although the seamless and responsible integration of these domains still appears to be in its early stages, findings so far have been hugely promising in making better diagnosis and treatment choices, improving assessment of disease heterogeneity and progression planning, patient stratification, treatment, molecular features, continuous real-time monitoring, and long-term follow-ups. It is anticipated that MI techniques will experience far greater advancements in the next decade, which will ultimately impact precision medicine in a positive way.

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Ethical Statement

This study does not contain any studies with human or animal subjects performed by any of the authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest to this work.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Author Contribution Statement

Victor Chigbundu Nwaiwu: Conceptualization, Methodology, Software, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Visualization. **Sreemoy Kanti Das:** Validation, Writing – review & editing, Supervision, Project administration.

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