RESEARCH PAPER

Quantitative Bioanalytical Evaluation of Imaging Biomarkers for Drug Delivery and Targeting Assessment in Diagnostic Radiology

[1]Dr. Mohammad Fakruddin , [2] Dr. Sugeet Sethi , [3]Monali D Jadhav , [4*]Dr. Tamanna Bhuyan, [5]Dr. Shruthi S Hegde ,[6] Dr. Ashish Kumar Shukla

[1]Assistant Professor, Department Of Medicine, Specialization in Medicine, Al Ameen Medical College, Vijayapura Karnataka, Pin 586108, Orcid Id: 0000-0002-4508-2906, Email Id: mdfakrubm@gmail.com
[2]Post Doctoral Research Fellow, Chemical Sciences Department, Eudoxia Research University India Centre, Mumbai, Near Lodha Xperia Mall, Palava City, Dombivli, Thane - 421204, Maharashtra. Email Id: sugeetsethi2019@Gmail.com Orcid Id: 0009-0006-4255-1988
[3]Assistant Professor, Department of Pharmaceutical Chemistry, Krishna Institute Of Pharmacy, Krishna Vishwa Vidyapeeth Deemed To Be University, Karad, Email Id: Mshewale949@Gmail.Com, Orcid Id: Https://Orcid.Org/0009-0003-9496-9487
[4]Assistant Professor, Department of Applied Biology, Specialization in Nanobiotechnology, University Of Science And Technology Meghalaya, Meghalaya, India, Email Id: tamanna.bhuyan4@gmail.com, Orcid Id: Https://Orcid.Org/0000-0002-7373-8650?Lang=En
[5]Reader/Associate Professor, Department of Oral Medicine And Radiology, Specialization in MDS, Rajeev Gandhi University / Srinivas Institute Of Dental Sciences, Email Id: Shruthidhama.Dent@Gmail.Com
[6]Professor ,Department Of Radiodiagnosis, Santosh Medical College, Ghaziabad (NCR), Santosh Deemed To Be University ,Ghaziabad (NCR) India, Email Id: Drashish07@Rediffmail.Com

Abstract
In modern pharmaceutics, quantitative imaging biomarkers have been solid bioanalytical approaches of drug delivery and targeting. Widely used bioanalytical methods, e.g., plasma pharmacokinetics and ex vivo tissue assays have limitative invasiveness, and lack of spatial information. On the contrary, imaging biomarkers offer a longitudinal, non-invasive and spatially resolved biodistribution, target-interaction and therapeutic reaction of drugs in intact biological systems. This paper critically evaluates the ways in which imaging biomarkers through diagnostic radiology can be applied as enabling technologies in drug delivery studies with a special emphasis on quantitative positron emission tomography (PET), single-photon emission computed tomography (SPECT), magnetic resonance imaging, and hybrid imaging modalities. We report how imaging-derived parameters are complementary to the conventional pharmacodynamic and pharmacokinetic studies, allowing the nanocarrier-based and targeted delivery platforms to be analysed and allow the formulation design to be optimised at a much earlier stage. The integration of the standardized imaging systems alongside the advanced quantitative measurements and clinical translational imaging strategies are pointed out to be the solution to the reproducibility and clinical relevance. Other new trends, such as theranostics, multimodal imaging and personalized drug delivery, are also discussed.

Keywords: Imaging Biomarkers, Drug Delivery Systems, Targeted Delivery, Quantitative Imaging, Pharmaceutics
How to cite this article: Dr. Mohammad Fakruddin , Dr. Sugeet Sethi , 3Monali D Jadhav , Dr. Tamanna Bhuyan, Dr. Shruthi S Hegde ,Dr. Ashish Kumar Shukla, Quantitative Bioanalytical Evaluation of Imaging Biomarkers for Drug Delivery and Targeting Assessment in Diagnostic Radiology...Int J Drug Deliv Technol. 2026; 16(27s): 34-45; DOI: 10.25258/ijddt.16.27s.5

1. Introduction

This aspect of efficiency in delivering and targeting drugs is among the major issues that should be investigated in the current pharmaceutics and especially in the context of drugs that are getting more intricate and mechanism-driven. Traditional bioanalytical methods like plasma pharmacokinetics and invasive tissue sampling can be of low spatial quality and unable to detect dynamic and heterogeneity in tissue distribution of drugs. The imaging biomarkers have come into sight in this case, and these are powerful tools that have the capability of analyzing biological and physicochemical processes to measurable and spatially resolved effects and provide new possibilities to objectively analyze the delivery of therapeutic and performance[1].

One of the imaging technologies (imaging technology) that can play a significant enabling role is diagnostic radiology as it provides non-invasive platforms on which longitudinal monitoring of the biological processes can be affected. Imaging of radiological modality biomarkers can be a quantitative surrogate endpoint of drug exposure, efficacy of delivery, and efficacy of therapy particularly in cases where standard acquisition and analysis systems are used. This has been achieved through the evolution of consensus-based profiles such as those proposed by the Quantitative Imaging Biomarkers Alliance (QIBA) which has contributed to rebranding the imaging biomarkers as the tools of analysis rather than the descriptive tools[2].

Further relevance of diagnostic radiology to the drug delivery literature is given by perfusion-based imaging biomarkers which offer an indirect measure of vascular transport tissue permeability and microenvironmental determinants of drug access to target sites. Contrast-

*Author for Correspondence: mdfakrubm@gmail.com

enhanced imaging methods can provide data on factors that limit delivery and transport kinetics which are dependent on the formulation when rigorously measured. Such imaging strategies are therefore to be subjected to strong analytical analysis in order to render such methods to become reliable bioanalytical endpoints in drug development pipelines and pharmaceutical development processes[3].

The most remarkable popularity of MRI as a quantitative imaging platform is due to its flexibility and non-ionizing level of radiations. Besides anatomical visualization, advanced compositional and functional biomarkers, which can be established using MRI, can be applied to establish tissue properties of interest in drug and retention penetration. The growing application of radiological measures as valid means that can be used to facilitate quantitative determination of therapeutic delivery and tissue level response has been highlighted by standardized QIBA profiles of MRI based biomarkers, and highlights their relevance to formulation and targeting studies[4].

Response based measures such as Response Evaluation Criteria in Solid Tumors (RECIST) have traditionally been used in the oncologic and other techniques mostly based on measures of anatropy. These criteria though clinically useful do not present a lot of information regarding the effectiveness of early delivery or engagement of the target. With regards to pharmaceutics, this presents the need of imaging biomarkers beyond the macromorphological shift to quantitative measures that can be applied in order to quantify the underlying drug distribution and biomodulation[5].

The response evaluation strategies development has also brought to the fore the fact that only size-based measurements are considered to be limited and that functional and molecular imaging endpoints must take the center stage in response evaluation strategies. Historical analysis of the evolution of RECIST indicates that a shift in the model to more biologically informative criteria has taken place, although the overall recognition of therapeutic efficacy as being dependent on delivery, target, and pharmacodynamic interactions and not necessarily late-stage anatomic events[6].

Imaging biomarkers have also undergone changes, an example of which is the positron emission tomography (PET)-based imaging biomarkers, which may be utilized to quantitatively assess metabolic activity and tracer uptake and therapeutic response in the early stage. Adaptations are made by the use of standardized quantitative thresholds such as PERCIST to be applied in preclinical and co-clinical settings to determine the impacts of treatment. The techniques are particularly useful in the field of drug delivery research whereby the uptake values derived by imaging could be adopted as a surrogate of formulation effectiveness and targeting precision[7].

The higher the use of radiomics in imaging biomarker research, the higher the mode of analysis that can be employed to assess drug delivery. Radiomics refers to the act of extracting high-dimensional quantitative data of medical images which could be helpful data regarding heterogeneity of tissues and variability of delivery. However, the validity of such characteristics is rather a matter subject to a valid methodology, standardization, and validation, which is an important ad-hoc factor where biomarkers are proposed as bioanalytical tools in pharmaceutical space[8].

Global initiatives, such as the Image Biomarker Standardization Initiative (IBSI), have attempted to solve the problem of reproducibility and comparability by developing standard definitions of quantitative imaging features and their computational standards. The initiatives are critical in ensuring that the imaging-based measures can undergo satisfactory analyses across research and platforms, therefore justifying its use in drug delivery studies and regulatory-relevant evaluation processes[9].

The recent guidance documents of QIBA that do not focus on the oncology area (use in infectious disease) can also be viewed as an indicator of the versatility of quantitative imaging biomarkers in therapeutic fields. Such a direction is introduced with the purpose to emphasize the more generalizability of the diagnostic radiology as a technology-intensive, quantitative discipline capable of contributing to research in pharmaceutics. In this regard, imaging biomarkers are increasingly insisting on bioanalytical tools to determine drug delivery, targeting performance, and translational performance[10]. The major aims of this review are:

1. To critically assess the significance of quantitative imaging biomarkers as bioanalytical techniques of assessing drug delivery performance, targeting and pharmacokinetics in vivo in the paradigm of contemporary pharmaceutics.
2. To comprehend the ways that imaging-based tools can be deployed to support optimization, standardization, and clinical translation of developed drug delivery systems, e.g. nanocarriers and theranostics platforms.

2. Imaging Biomarkers as Bioanalytical Tools in Drug Delivery Research

2.1 Definition and Classification of Imaging Biomarkers

The imaging biomarkers are objectively measurable medical imaging data features that reflect biological, physiological or molecular processes to relate to disease and other therapeutic intervention. The imaging biomarkers in the scenario of the drug delivery research might be utilized to describe the response of the pharmaceutical agents to the biological systems in space and time on a non-invasive level. Those biomarkers are typically separated into structural, functional and molecular. Anatomical (volume of tissue or size of lesion) biomarkers are called structural biomarkers and physiological (perfusion, permeability and metabolic activity) biomarkers are called functional biomarkers. The biomarkers in molecular imaging are the literal imaging of any interaction or biochemical reaction, i.e.

receptor interaction, enzyme action or uptake of a tracer, which is linked to therapeutic agents[11].

The inherent difference in the imaging biomarker in research is the difference between qualitative and quantitative biomarkers. The qualitative biomarkers would be a graphical representation of the details and the quantitative biomarkers would be numbers which can be analyzed comparatively over both time, subjects and branches of treatment. The quantitative imaging biomarkers find their application especially in drug development since they may be used to supplement kinetic modelling, dose/response as well as measurement of target engagement. The further development of radiochemistry and optimization of tracers, augmented the possibilities of positron emission tomography (PET) and single photon emission computed tomography (SPECT) as a quantitative biomarker platform that has the potential to be able to match molecular kinetics to therapy, a step that formalizes their use as bioanalytical tools in pharmaceutics[12].

2.2 Imaging Biomarkers vs Conventional Bioanalytical Assays

Plasma pharmacokinetics and ex vivo tissue analysis have formed the basis of the conventional bioanalytical analysis of drug delivery to infer the systemic exposure and tissue concentration. Though they are found to be good analytic sensitivity methods, they possess a number of weaknesses which include invasive sampling, lack spatial resolution, and do not detect intratumoral or regional heterogeneity. Imaging biomarkers address such issues by enabling visualisation and measurement of the drug movement, accumulation and retention in living systems that are not disturbed. Imaging derivable pharmacokinetic parameters can therefore be employed to complement (in some cases) or even surpass plasma-based measurements, providing spatially resolved information on delivery efficiency[13].

Unlike bulk tissue concentration measurements, imaging biomarkers may be applied to measure the regional uptake and heterogeneity which are the most significant predictors of therapeutic efficacy, particularly of targeted and nanomedicine-based delivery systems. Molecular imaging techniques can illustrate the discrepancies between the systemic exposure and target-site delivery, which prove transport barriers either in the formulation or in off-target accretion of the formulations. Systematic reviews of the literature on clinical drug development prove that imaging biomarkers can be utilized to make an early decision to conclude that the methods of delivery are not optimal or that sufficient target interaction is not reached before the conventional efficacy endpoints, as shown in Figure 1. The power renders imaging biomarkers powerful adjuncts to previously existing bioanalytical assays regarding formulation optimization and validation of targets in drug delivery investigations[14].

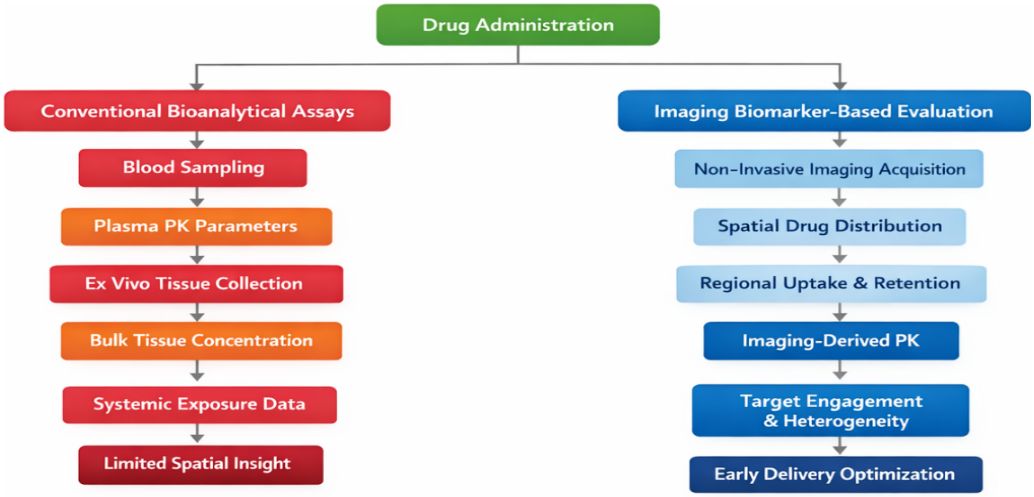

Figure 1. Comparative workflow of conventional bioanalytical assays and imaging biomarkers for drug delivery evaluation

Source: Author's own contribution

2.3 Regulatory and Translational Relevance

Regulatory: The applicability of imaging biomarkers by the regulatory agencies has increased considerably because the agencies have now realized the potential of the biomarkers to aid in the development of drugs, companion diagnostics and personalized therapy. The regulatory systems are appreciating the application of quantitative imaging biomarkers with the increasing number of regulatory authorities accepting quantitative imaging biomarkers as an exploratory or secondary endpoint in order to comprehend dose selection, patient stratification and monitoring of treatment. At the same time, the creation of theranostic platforms, where diagnostic imaging and therapy are co-located has contributed further to the translational relevance of imaging biomarkers to the evaluation of delivery and therapeutic outcome in one platform. As one form of this convergence, hydrogel-based multifunctional delivery systems able to locally release drugs and visualise at the

same time the dynamics of treatments in the form of imaging-enabled hydrogels can have an impact[15].

Imaging biomarkers can also serve to close the gap between preclinical and clinical research also by enabling the possibility of performing consistent and non-invasive measurements across the species and developmental stages. This continuity assists in the enhanced translation of the delivery performance and targeting efficacy to the clinical context. Biodistribution analysis by imaging technology has also become significant in the case of sophisticated systems of delivery such as the extracellular vesicles where the conventional tools of bioanalysis cannot determine such complex in vivo behavior (Table 1). The rising focus of regulators on such platforms underscores the significance of the rising role of imaging biomarkers as enabling technologies that can aid the process of pharmaceutical innovation to fulfill the clinical and regulatory expectations[16].

Table 1. Imaging-based platforms and quantitative biomarkers used for evaluation of drug delivery and targeting

Platform / Context	Imaging Modality	Quant Metric	Primary Use in Delivery/Targeting	References
Nanoradiopharmaceuticals	PET/SPECT	SUV, kinetic rates	Target engagement, biodistribution	17
Targeted inorganic NPs	MRI + CT	T2 signal, HU	Tumor targeting verification	18
Oral nanoformulation	Imaging-enabled PK (preclinical)	Uptake / exposure proxy	Absorption improvement assessment	19
Delivery modeling	Multimodal (general)	Delivery efficiency model	Predict/compare NP delivery	20
Image-guided targeting	Image-guided radiology	Target localization	Non-invasive targeted delivery	21

3. Quantitative Imaging Modalities for Drug Delivery Assessment

3.1 PET and SPECT Imaging

The outstanding technologies of quantitative evaluation of drug delivery and targeting are positron emission tomography (PET) and single-photon emission computed tomography (SPECT) due to their very high sensitivity and molecular specificity. Direct visualization of in vivo biodistribution, target engagement and clearance kinetics can be directly visualized using these modalities with the use of radiolabeled drugs, probes or carrier systems. The quantitative PET/SPECT measures provide the insight of the efficiency of delivery which cannot be studied in the traditional bioanalytical sampling. Nuclear imaging of theranostic systems helps in designing formulation optimization through both signal of therapeutic delivery and diagnostic signal that can be measured simultaneously, which enables therapeutic formulation design optimization in an iterative structure. Longitudinal measurements also can be done using radiotracer methods and this allows the accumulation, retention and washout of target sites to be measured dynamically. The applications are particularly helpful in terms of the assessment of focused nanomedicines and image-directed delivery platforms, where the spatial heterogeneity can have a powerful impact on a therapeutic response, as presented in Figure 2. As the existing trend of drug delivery systems, precision and personalization, PET and SPECT imaging are inescapable bioanalytical tools in determining the interactions between molecular dynamics and therapeutic achievement[22].

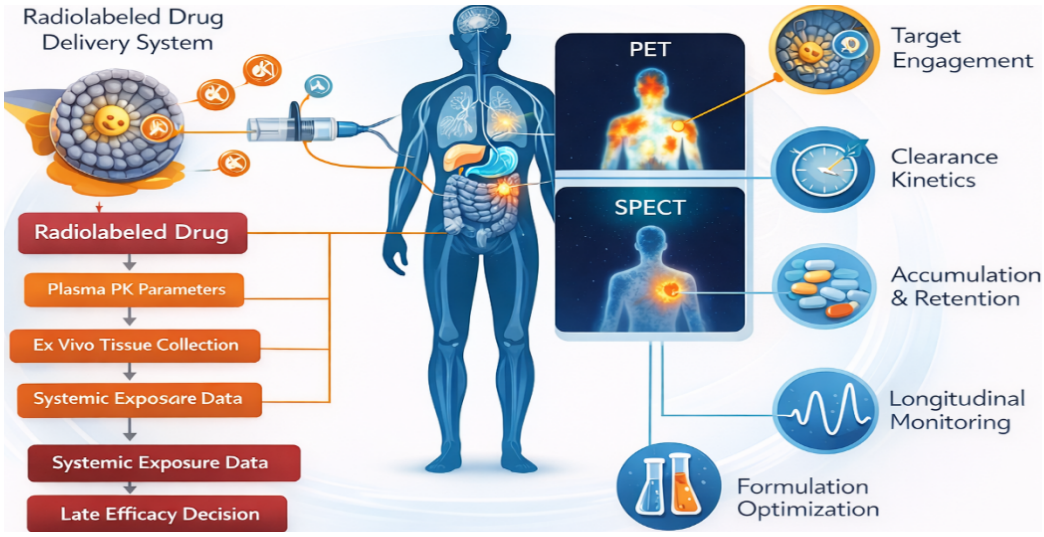

Figure 2. PET and SPECT imaging–based quantitative evaluation of drug delivery, targeting, and in vivo pharmacokinetics

Source: Author's own contribution

3.2 MRI-Based Quantitative Biomarkers

The magnetic resonance imaging (MRI) has provided a radiation-free and multidimensional system of quantitative analysis of drug delivery, especially with intricate contrasting mechanisms and functional imaging parameters. Bio-markers based on MRI can be used to determine the level of vascular permeability, tissue microstructure and transport properties which are directly proportional to drug penetration and retention. The theranostics can be implemented using an MRI-traceable system of delivery which can be used to provide real time localization of the carriers and can also be used to provide therapeutic intervention. Image-guided drug delivery plans take advantage of the MRI application in the ideal spatial localization and temporal mediating of drug release to enhance a translation application. Diffusion-weighted imaging is another step further to expand the applications of MRI to offer quantitative data of the apparent diffusion coefficient that demonstrates cellularity and microenvironmental movements of the tissue in respect of drug uptake. This increases the reproducibility and makes MRI-based measures as plausible conclusion of the pharmaceutics research due to the development of standardized quantitative profiles of diffusion biomarkers. Taken together, these capabilities lead to the point that MRI is becoming increasingly important as a quantitative bioanalytical modality of inquiry to establish the efficiency and fidelity of delivery[23].

3.3 CT and Hybrid Imaging (PET/CT, PET/MRI)

The quantitative assessment of drug delivery was strengthened by the multimodal examination of anatomy, functional, and molecular data that became feasible with the help of computed tomography (CT) and hybrid methods of PET/CT and PET/MRI. CT has a high resolution of contextual structure and quantitative outcomes of improvement that allow the evaluation of tissue perfusion and vascular access. Hybrid platforms can be employed when communicating with molecular imaging, which can be applied in spatial correlation of the distribution of drugs with anatomical structures and increase the impression of the effectiveness of the delivery and the target localization. The type of integration is particularly applicable in therapeutic directed application, where imaging biomarkers inform and influence treatment planning, reaction assessment and adaptive control. Being an illustration of quantitative imaging techniques that have evolved in radiotherapy, the standardization of imaging measures means can be useful in the accurate positioning and dose optimization, which is currently being applied to the more image-guided drug delivery systems, as shown in Table 2. The hybrid imaging can therefore be regarded as a powerful prototype of testing delivery output on-scale, which justifies the significance of diagnostic radiology as a technological foundation of the current pharmaceutics[24].

Table 2. Representative applications and integration pathways of quantitative imaging biomarkers for drug delivery and targeting evaluation

Use-case focus	Imaging biomarker/readout	Setting	Key value for drug delivery/targeting	Ref.
Field landscape	Mapping QIB research trends	System-level	Identifies gaps, maturity, and adoption	25
Trial integration	Multicentre QIB guidance	Clinical trials	Standardizes QIB endpoints & workflows	26

Nanocarrier delivery	^{89}Zr–StarPEG uptake heterogeneity	Preclinical/Translational	Quantifies EPR variability, delivery efficiency	27
Target phenotyping	Multiparametric PET/MRI with nanobodies	Translational	Links molecular targeting with tissue phenotype	28
Biomarker biology	MAA adducts + antibody responses	Clinical/Pathobiology	Supports imaging–biology linkage for targeting context	29

4. Imaging Biomarkers for Evaluation of Drug Delivery Systems

4.1 Nanocarriers and Targeted Delivery Platforms

The methods of targeted cancer therapy have been developed based on nanocarrier delivery systems like polymeric nanoparticles, inorganic nanomaterials and hybrid theranostics platform. Imaging biomarkers play a role in measuring the in vivo behavior of these systems because they can quantitatively measure biodistribution, tumor accumulation and retentions. The heterogeneity of the delivery efficiency is an important determinant of therapeutic success that can be determined with the help of the molecular imaging technique because it is possible to observe the nanocarrier delivery across the biological barriers and determine its heterogeneity. The results of working with quantitative imaging also help in comparing the carrier designs and optimization of the physicochemical characteristics to enhance performance regarding targeting. Comprehensive analyses of nanoparticles-based theranostics indicate the importance of the visualization of the body in the delivery system in order to determine the localization and therapeutic effects. At the same time, the realisation of nanomaterials to be employed in bio-imaging has expanded the application of multifunctional platforms of drug delivery and real time tracking, as shown in Figure 3. Together, the advances make the imaging biomarkers the essential tools of analysis to verify the functionality of nanocarriers and make rational decisions about the choice of substrates to be delivered to the target[30].

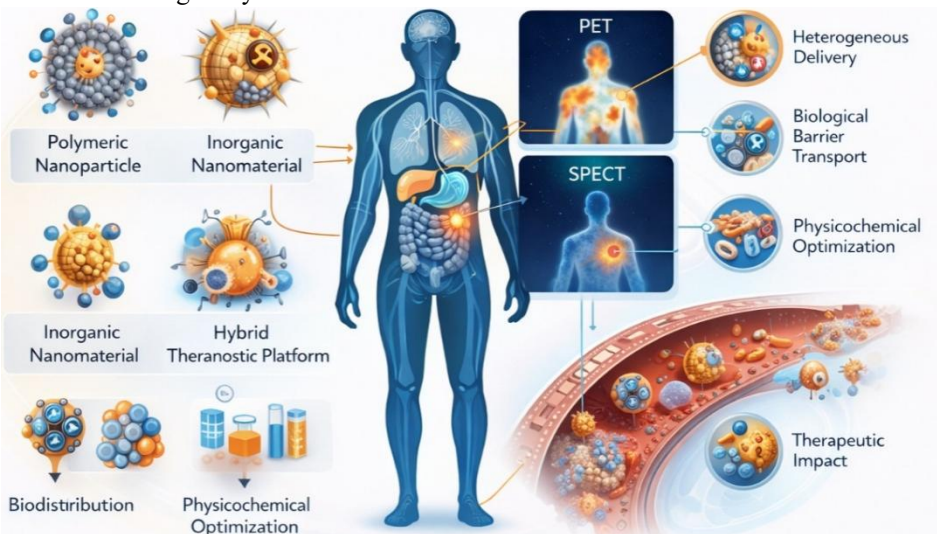

Figure 3. Imaging-guided evaluation of nanocarrier-based targeted drug delivery platforms and in vivo therapeutic performance

Source: Author's own contribution

4.2 Image-Guided Evaluation of Targeting Strategies

The change in the drug delivery systems switching to molecularly specific and personalized methods has made the analysis of targeting strategies based on images even more significant. Specific targeting requires a fine assessment of target engagement beyond anatomical response including ligand-based targeting, specific targeting and immune based. Molecular imaging biomarkers can be used to determine, non-invasively, receptor expression, ligand binding, and downstream biological activity, which can be used in validation of targeting fidelity. The current advancement in PET and SPECT immune checkpoint imaging such as the programmed death-ligand 1 (PD-L1) demonstrates that patient selection and therapeutic stratification can be performed using imaging biomarkers as the input. Quantitative imaging can be used to help in early treatment response prediction by imaging functional changes which can be observed before the tumour has shrunk in size, as demonstrated by Table 3. The oncology imaging world is exposed to systematic alterations that center their attention on the growing importance of quantitative biomarkers in evaluating the treatment effectiveness, accommodating treatment methods to demand. Such imaging methods are applicable as bioanalytical endpoints to drug delivery studies since they provide significant information as to whether target systems can find and engage target biological systems[31].

Table 3. Clinical imaging biomarker domains supporting targeting and delivery-relevant decision-making

Clinical domain	Key imaging biomarkers	Primary modality	Delivery/targeting relevance	References
Neuro-oncology	perfusion, diffusion, metabolic markers	MRI / PET	Target localization, response mapping	32
Pan-cancer profiling	quantitative feature sets (radiomics/QIB)	CT / MRI / PET	Stratify targets, monitor heterogeneity	33
Breast cancer	receptor-linked imaging, functional metrics	MRI / PET/mammography	Selection for targeted therapy	34
RNA therapeutics	delivery barriers, tissue access limits	multimodal (context)	Guides platform + targeting strategy	35
Alzheimer's disease	amyloid/tau target positivity criteria	PET	Target confirmation for therapy	36

4.3 Imaging Assessment of Controlled and Triggered Release

The objective of the controlled and triggered drug release systems is to deliver space and time-specific therapeutics to minimize off-target effects but maximize efficacy. One notable advantage of the visual biomarkers is also the ability to analyze these systems as they give a real time analysis of the kinetics of release as well as therapeutic distribution. The changes in functions after the interventional or image-guided delivery procedures can be assessed using the quantitative PET-based methods, in particular, and provide the idea concerning the modulation of the tissue functions following the treatment. Evaluation based on Imaging Aids the verification and evaluation of the therapeutic effects at the target sites during on-demand release mechanisms. PET-generated quantitative measures have been effectively applied in the field of oncology to identify procedural efficacy and treatment response, and the fact that imaging-guided assessment systems are applicable throughout a translational spectrum. They are also being applied to the complex drug delivery systems of the case of locally activated formulations, stimuli-responsive and stimuli-responsive. The capacity to quantify dynamic changes concerning controlled discharge renders the imaging biomarkers more potent instruments of validating operation of delivery, along with optimal product of the system design[37].

5. Quantitative Bioanalytical Metrics and Data Interpretation

5.1 Quantification Methodologies

The imaging biomarkers are bioanalytical systems based on strong quantification tools which are used in studying drug delivery. The other method is ROI-based analysis which is highly applied to obtain quantitative data on a particular anatomical/functional area to be able to compare time or treatment arms. Besides the stationary schemes, kinetic and compartmental modeling schemes can be employed to describe dynamic schemes that include tracer transport, binding and washout that can be simply applied to drug delivery and efficiency of targeting. Diffusion weighted and dynamic contrast enhanced MRI are modern imaging protocols, which are most likely to be subjected to high-order modeling approaches to ensure that the parameters are properly estimated. Multicentre studies indicate that there may be a wide range of variation of the obtained metrics because of the methodological variability that highlights the importance of harmonized practices in the process of acquiring and analyzing. The Quantitative Imaging Biomarkers Alliance have recommended that standardized modeling approaches, quality assurance approaches and protocol optimization be used to improve the reliability and validity of the quantitative imaging biomarkers, particularly in drug development and drug assessment programs in cancer biology[38,39].

5.2 Standardization and Reproducibility

There are also issues of standardization and reproducibility in quantitative biomarkers of imaging translation to stable endpoints of bioanalysis. The disparity in the scanner hardware, the acquisition parameters and post-processing algorithms may introduce a bias thus undermining on inter-study comparability. This is particularly the case in the complex clinical scenario wherein measures based on imaging could be disturbed by treatment-related changes and difference in biology, such as in recurrent glioblastoma. In order to get a reproducible measurement of imaging biomarkers, there is therefore need to have strict standard operating procedures, cross-site calibration of the measurement and having the measurement cross-referenced to standard biological or clinical reference values. The editorial opinion of radiological practice has given an emphasis on the lack of connection between technical and clinical reliability, and emphasized the necessity to be realistic with regard to expectation, and to possess well constituted interpretive schemas. In drug delivery evaluation, reproducibility is required to assist in distinguishing between real variations in delivery quality against noise in measurements, and it also establishes the reality that there should be consensus-based standards and open reporting processes to assist in interpreting high-confidence data[40].

5.3 Correlation with Pharmacokinetics and Pharmacodynamics

The last utility of the imaging biomarkers in medicine drug delivery research is that, it can be applied to correlate with pharmacodynamics (PD) and pharmacokinetics (PK) effects. Parameters derived through imaging are either spatially resolved surrogates of drug exposure which can be employed to complement PK measurements on plasma. In order to reach significant correlations between imaging parameters and treatment results, however, one should carefully combine data and rigorously analyze it. The comparative study of the response assessment criteria has revealed that different imaging-based frameworks may deliver diverse prognostic implications with the importance of appropriate selection of quantitative end points. Response criteria based on PET such as PERCIST, have been shown to have certain advantages in the field of oncology in the ability to respond to changes in response that are biological rather than size-based, also presented in Figure 4. With imaging biomarkers coupled with PK/PD modeling, one can therefore learn about the efficacy of delivery, target occupancy and therapeutic effect and can make improved decisions in the course of drug development and translation to the clinic[41].

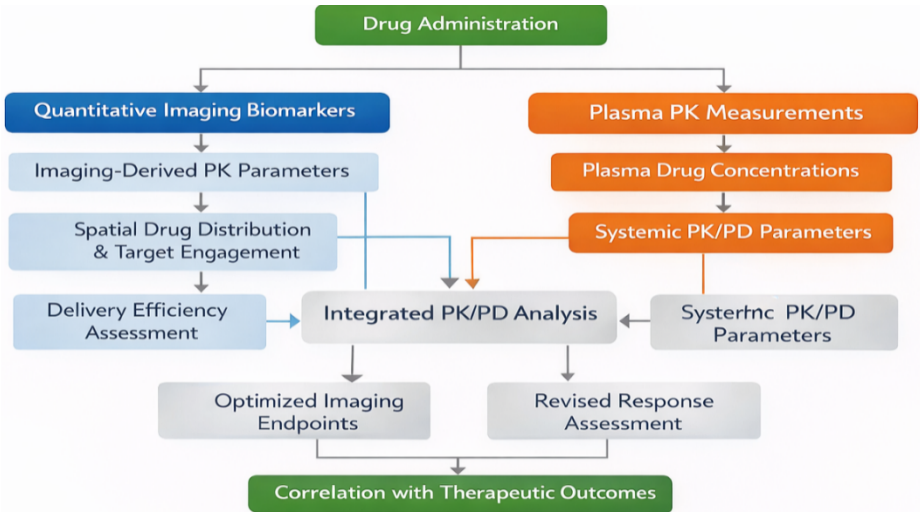

Figure 4. Integration of quantitative imaging biomarkers with pharmacokinetic and pharmacodynamic modelling for prediction of therapeutic outcomes

Source: Author's own contribution

6. Imaging Biomarkers in Translational and Clinical Drug Delivery Research

6.1 Preclinical to Clinical Translation

The application of drug delivery systems in preclinical models to clinical use is facing a great challenge due to the level of complexity of biology and disparities between species. One of the most significant intermediates that could be used to conduct quantitative analysis of delivery performance at any level of the experiment, without invasiveness, is imaging biomarkers. However, standardization and reproducibility play a significant role in the confirmation of similarity of the imaging-derived measures in preclinical and clinical trials. The biomarkers of radiomics are responsive to modification of acquisition protocols, reconstruction patterns, and feature extraction pipeline, especially. Image Biomarker Standardisation Initiative (IBSI) is a solution to these problems by developing agreement terminology, feature definitions and implementation guidelines to help create reproducible biomarkers in imaging. By introducing these structures, the confidence in translational imaging data would increase and reduce the variation in the correlation of the efficiency of deliveries or the targeting of behavior in animals to human experiments. Improved details through the use of standardised imaging biomarkers can be used to improve the research pathway of translational drug delivery by promoting harmonised methods of data analysis and assist in safety in a clinical adoption[42,43].

6.2 Clinical Trials and Patient Stratification

The use of imaging biomarkers to stratify patients is becoming more widespread in order to monitor treatment and determine the efficiency of drug delivery during clinical drug development. The quantitative imaging outcomes can be used as inclusion / exclusion criteria since it can aid in identifying the patients who have the highest probability of responding to the targeted or delivery-based therapies. Neurodegenerative as well as oncology studies have also utilized molecular imaging biomarkers to confirm the presence of targets, to establish disease burden and to assess therapeutic response. One such example of executing the standardized imaging biomarkers in multicentre clinical trials with performance allegations and validation strategies is the RSNA Quantitative Imaging Biomarkers Alliance (QIBA) profiles. The above profiles permit the consistent validation of the outcomes of the experiments within the locations and scanners. This standardization is particular to studies involving drug delivery in instances where the biomarkers, which are studied by

imaging, are used to study biodistribution, target engagement or response to therapy. In the advancement of precision medicine, patient stratification by imaging guidance will be virtually in every clinical trial and will become more central to the design and analysis of clinical trials[44].

6.3 Theranostics and Personalized Drug Delivery

Theranostics therapies are a type of treatment that is a combination of diagnostic and therapeutic systems that give the individual a personalized treatment plan and real time tracking. This approach is founded on the imaging biomarker to give a quantitative answer on the target expression, the delivery efficiency, and biologic response. The standardized imaging frameworks support companion diagnostics to provide the dosing decisions and adjust treatment courses per the specifics of a certain patient. The molecular imaging biomarkers, such as amyloid or receptor-targeted imaging, can be used as an example of how quantitative thresholds can be applied to informing the eligibility of the therapeutic use or response measurement. Simultaneously, radiomics is reproducible and feature extractors can be standardized to enhance the efficiency of imaging personalization solutions. The applications of theranostics systems can offer the way of personalized drug delivery with the highest effectiveness and the minimum of the undesirable exposure, combining the effective standardization efforts with the established quantitative imaging biomarkers (Table 4). Such an imaging science-pharmaceutics interface is noteworthy in how diagnostic radiology is increasingly becoming significant in the personalized drug delivery paradigm[45].

Table 4. Standards and enabling frameworks supporting personalized, image-guided drug delivery

Enabling area	Standard / key output	Practical use for theranostics	Reference
Radiomics standardization	Standardized convolutional filters	Reproducible feature extraction	46
Tissue biomarker quantification	Digital pathology QA guidance	Imaging–histology validation	47
Image-guided navigation	Emerging navigation techniques	Precise interventional targeting	48,49
Global implementation	Imaging & nuclear medicine commission	Access, quality, scale-up	50

7. Challenges and Limitations

Nevertheless, despite the improvement, there still exist some outstanding issues when it comes to the use of quantitative imaging biomarkers in drug delivery research that restrict its use. Variability of quantification due to variations in hardware of the scanners, protocols used during the acquisition process, reconstruction processes and post-processing pipelines is among the largest limitations. The inconsistency of the measurements might be explained by the inter-scanner and inter-site variation and make it difficult to compare the studies and rely on the imaging-based endpoints. These concerns are especially troublesome in the situation when the measures of minimal differences in the delivery efficiency or targeting performance are represented by the imaging biomarkers.

Imposition is also regulated and economically restricted. Standards Biomarker validation highly entails standardization, multicentre validation and quality assurance which are more time and cost consuming to produce. Even that imaging has often been a discovery stage and not a regulatively credentialed endpoint in any of the drug development programs and consequently, has performed to play a restrained regulatory role. It also does not exist since the regions are not evenly spread in their access to the advanced imaging infrastructures and expertise.

The other problem is the problem of biological heterogeneity. The tumor microenvironment variability may lead to the heterogeneous distribution of drugs that is complicated by the dynamic behaviour of the vascular system and specific factors of a certain patient. The imaging can only identify the inefficiency in delivery and, never necessarily, whether some of the limits can be ascribed to the formulation design, biological or disease-specificity.

8. Emerging Trends and Future Perspectives

The manner in which the imaging biomarkers are likely to evolve in terms of the drug delivery research field is by means of convergence of technologies and focusing on precision medicine. The quantitative image analysis is rapidly approaching the field of artificial intelligence and machine learning as soon as it is possible to draw the automatic characteristics, identify the patterns, and issue the prediction. These instruments can deliver power, reduced dependency of observers and the establishment of complex relationships of imaging attributes and the performance of delivery that cannot be easily observed in routine practice.

The trend that is also interesting is the multimodal imaging. A complete structure, functional and molecular imaging system is featured by a complete narrative about the drug delivery, including a biodistribution and biological response of an anatomical image representation. The hybrid systems will be able to assist in the cross-validation of the imaging biomarkers in addition to giving more interpretability in situations of the complicated cases such as the compound delivery systems as nanomedicines and theranostics.

Optimisation of formulations through imaging is also gaining popularity. The quantitative imaging is capable of assists in the carrier design, analysis of targets strategy and optimization of release profile at a lower drug formulation development step. This trick changes the position of imaging that takes a more active part in the decision making in pharmaceuticals than an evaluative effort.

Further effect is further amplified when it is combined with digital medicine and precision drug. Computer modelling, patient-specific and pharmacokinetic modelling can be supplemented with the use of imaging biomarkers, which allows the development of adaptive dosing and individual delivery plans. The data-driven innovation of drug delivery and clinical translation will be replaced by the imaging biomarkers since the standardization efforts will stand a greater probability to be met.

9. Conclusions

Quantitative bio-markers of imaging have been identified today as being vital bioanalytical techniques in drug delivery and targeting in the pharmaceutical industry. Imaging biomarkers successfully address the critical flaws of conventional bioanalytical methods, which comprise non-invasive, spatially resolved, and longitudinal assessment of therapeutic distribution and response. Its application helps in the rational form design, justifying targeting policies as well as understanding the efficiency of delivery systems in biological systems much better Imaging-derived measures may be applicable in early development decision-making, scale-up uncertainty, and patient stratification in clinical trials. These biomarkers are even better in terms of increasing reproducibility and the evidentiary framework required in order to be accepted by the regulating authority in case of their proper standardization. Diagnostic radiology will be more impactful in pharmaceutical innovation in the future. Imaging biomarkers have reached the limits of their analytical capabilities because of the growth of quantitative imaging, artificial intelligence, and multimodal integration. As the increasingly advanced yet more personalized delivery mechanisms continue to advance, imaging biomarkers will be required to bridge the gap that exists between formulation science, biological complexity and clinical practice. Their future growth and application will be a determining factor in the accuracy improvement in the delivery of drugs and improved treatment outcomes.

References

1. Waterhouse DJ, Fitzpatrick CR, Pogue BW, O'Connor JP, Bohndiek SE. A roadmap for the clinical implementation of optical-imaging biomarkers. Nature biomedical engineering. 2019 May;3(5):339-53.
2. Kinahan PE, Perlman ES, Sunderland JJ, Subramaniam R, Wollenweber SD, Turkington TG, Lodge MA, Boellaard R, Obuchowski NA, Wahl RL. The QIBA profile for FDG PET/CT as an imaging biomarker measuring response to cancer therapy. Radiology. 2020 Mar;294(3):647-57.
3. Mittermeier A. *Robust evaluation of contrast-enhanced imaging for perfusion quantification* (Doctoral dissertation, lmu).
4. Chalian M, Li X, Guermazi A, Obuchowski NA, Carrino JA, Oei EH, Link TM, RSNA QIBA MSK Biomarker Committee. The QIBA profile for MRI-based compositional imaging of knee cartilage. Radiology. 2021 Nov;301(2):423-32.
5. Lathrop K, Kaklamani V. The response evaluation criteria in solid tumors (RECIST). InPredictive biomarkers in oncology: applications in precision medicine 2018 Dec 7 (pp. 501-511). Cham: Springer International Publishing.
6. Smesseim I, Groot Lipman KB, Lalezari F, Burgers JA, Trebeschi S. The legend of the response evaluation criteria in solid tumors: A historical overview. Cancer. 2025 Sep 1;131(17):e70064.
7. Savaikar MA, Whitehead T, Roy S, Strong L, Fettig N, Prmeau T, Luo J, Li S, Wahl RL, Shoghi KI. Preclinical PERCIST and 25% of SUVmax Threshold: Precision Imaging of Response to Therapy in Co-clinical 18F-FDG PET Imaging of Triple-Negative Breast Cancer Patient–Derived Tumour Xenografts. Journal of Nuclear Medicine. 2020 Jun 1;61(6):842-9.
8. Avanzo M, Soda P, Bertolini M, Bettinelli A, Rancati T, Stancanello J, Rampado O, Pirrone G, Drigo A. Robust radiomics: a review of guidelines for radiomics in medical imaging. Frontiers in Radiology. 2025;5:1701110.
9. Zwanenburg A, Vallières M, Abdalah MA, Aerts HJ, Andrearczyk V, Apte A, Ashrafinia S, Bakas S, Beukinga RJ, Boellaard R, Bogowicz M. The image biomarker standardization initiative: standardized quantitative radiomics for high-throughput image-based phenotyping. Radiology. 2020 May;295(2):328-38.
10. Avila RS, Fain SB, Hatt C, Armato III SG, Mulshine JL, Gierada D, Silva M, Lynch DA, Hoffman EA, Ranallo FN, Mayo JR. QIBA guidance: Computed tomography imaging for COVID-19 quantitative imaging applications. Clinical imaging. 2021 Sep 1;77:151-7.
11. Park SM, Park JY, Lee TS, Kim JY, Yoon HJ, Kim BS, Moon BS. Unlocking drug development: the distinctive roles of PET and SPECT imaging from molecular kinetics to therapeutic response. Archives of Pharmacal Research. 2025 Dec 20:1-24.
12. Nerella SG, Singh P, Sanam T, Digwal CS. PET molecular imaging in drug development: the imaging and chemistry perspective. Frontiers in medicine. 2022 Feb 28;9:812270.
13. Zeng Q, Cao X, Feng J, Shan H, Chen X. Imaging Technology in Oncology Pharmacological Research. Frontiers in Pharmacology. 2021 Jul 23;12:711387.

14. Son H, Jang K, Lee H, Kim SE, Kang KW, Lee H. Use of molecular imaging in clinical drug development: a systematic review. Nuclear medicine and molecular imaging. 2019 Jun 1;53(3):208-15.
15. Lee KK, Go K, Lee E, Kim H, Kim S, Kim JH, Chae MS, Jeong JO. Multifunctional hydrogels for advanced cancer treatment: Diagnostic imaging and therapeutic modalities. Gels. 2025 Jun 1;11(6):426.
16. Su X, Wang H, Li Q, Chen Z. Extracellular vesicles: A review of their therapeutic potentials, sources, biodistribution, and administration routes. International Journal of Nanomedicine. 2025 Dec 31:3175-99.
17. Roy I, Krishnan S, Kabashin AV, Zavestovskaya IN, Prasad PN. Transforming nuclear medicine with nanoradiopharmaceuticals. ACS nano. 2022 Mar 16;16(4):5036-61.
18. Yan Y, Yang C, Dai G, Zhang Y, Tu G, Li Y, Yang L, Shu J. Folic acid-conjugated CuFeSe2 nanoparticles for targeted T2-weighted magnetic resonance imaging and computed tomography of tumors in vivo. International Journal of Nanomedicine. 2021 Sep 17:6429-40.
19. Biswas M. *Developing a Bioengineered Nanoparticle for Improving Oral Absorption of Iron Supplements* (Master's thesis, The University of Texas at El Paso).
20. Wu JL, Stordy BP, Nguyen LN, Deutschman CP, Chan WC. A proposed mathematical description of in vivo nanoparticle delivery. Advanced Drug Delivery Reviews. 2022 Oct 1;189:114520.
21. Haemmerich D. Non-invasive image-guided targeted drug delivery. The Lancet Oncology. 2018 Aug 1;19(8):1000-1.
22. Anani T, Rahmati S, Sultana N, David AE. MRI-traceable theranostic nanoparticles for targeted cancer treatment. Theranostics. 2021 Jan 1;11(2):579.
23. Thanou M, editor. Theranostics and image guided drug delivery. Royal Society of Chemistry; 2018 Jan 2.
24. Gurney-Champion OJ, Mahmood F, van Schie M, Julian R, George B, Philippens ME, van der Heide UA, Thorwarth D, Redalen KR. Quantitative imaging for radiotherapy purposes. Radiotherapy and Oncology. 2020 May 1;146:66-75.
25. Boss MA, Malyarenko D, Partridge S, Obuchowski N, Shukla-Dave A, Winfield JM, Fuller CD, Miller K, Mishra V, Ohliger M, Wilmes LJ. The QIBA profile for diffusion-weighted MRI: apparent diffusion coefficient as a quantitative imaging biomarker. Radiology. 2024 Oct 8;313(1):e233055.
26. Meseguer E, Barberá-Tomás D, Benito-Amat C, Díaz-Faes AA, Martí-Bonmatí L. What do biomarkers add: Mapping quantitative imaging biomarkers research. European Journal of Radiology. 2022 Jan 1;146:110052.
27. van Houdt PJ, Saeed H, Thorwarth D, Fuller CD, Hall WA, McDonald BA, Shukla-Dave A, Kooreman ES, Philippens ME, van Lier AL, Keesman R. Integration of quantitative imaging biomarkers in clinical trials for MR-guided radiotherapy: Conceptual guidance for multicentre studies from the MR-Linac Consortium Imaging Biomarker Working Group. European Journal of Cancer. 2021 Aug 1;153:64-71.
28. Meher N, Bidkar AP, Wadhwa A, Bobba KN, Dhrona S, Dasari C, Mu C, Fong CO, Cámara JA, Ali U, Basak M. PET imaging using 89Zr-labeled StarPEG nanocarriers reveals heterogeneous enhanced permeability and retention in prostate cancer. Molecular Cancer Therapeutics. 2025 Jan 2;24(1):141-51.
29. Senders ML, Hernot S, Carlucci G, van de Voort JC, Fay F, Calcagno C, Tang J, Alaarg A, Zhao Y, Ishino S, Palmisano A. Nanobody-facilitated multiparametric PET/MRI phenotyping of atherosclerosis. JACC: Cardiovascular Imaging. 2019 Oct;12(10):2015-26.
30. England BR, Duryee MJ, Roul P, Mahajan TD, Singh N, Poole JA, Ascherman DP, Caplan L, Demoruelle MK, Deane KD, Klassen LW. Malondialdehyde–acetaldehyde adducts and antibody responses in rheumatoid arthritis–associated interstitial lung disease. Arthritis & Rheumatology. 2019 Sep;71(9):1483-93.
31. Dev ID, Puranik AD, Singh B, Prasad V. Current and future perspectives of PDL1 PET and SPECT imaging. InSeminars in Nuclear Medicine 2024 Nov 1 (Vol. 54, No. 6, pp. 966-975). WB Saunders.
32. Gillman JA, Pantel AR, Mankoff DA, Edmonds CE. Update on quantitative imaging for predicting and assessing response in oncology. In Seminars in Nuclear Medicine 2020 Nov 1 (Vol. 50, No. 6, pp. 505-517). WB Saunders.
33. Adnan A, Basu S. PET-based Quantitative Techniques in Assessing Efficacy of Interventional Radiology Procedures in Oncology. PET clinics. 2025 Jul 1;20(3):265-79.
34. Al-Thani AN, Jan AG, Abbas M, Geetha M, Sadasivuni KK. Nanoparticles in cancer theragnostic and drug delivery: A comprehensive review. Life sciences. 2024 Sep 1;352:122899.
35. Priyanka P, Hemalatha S. Nanomaterials for Bio-Imaging and Cancer Theranostics. Current Pharmacology Reports. 2025 Sep 8;11(1):48.
36. Chiu FY, Yen Y. Imaging biomarkers for clinical applications in neuro-oncology: current status and future perspectives. Biomarker Research. 2023 Mar 29;11(1):35.
37. Tharmaseelan H, Hertel A, Rennebaum S, Noerenberg D, Haselmann V, Schoenberg SO, Froelich MF. The potential and emerging role of quantitative imaging biomarkers for cancer characterization. Cancers. 2022 Jul 9;14(14):3349.

38. Weaver O, Leung JW. Biomarkers and imaging of breast cancer. American Journal of Roentgenology. 2018 Feb;210(2):271-8.
39. Rhym LH, Anderson DG. Nanoscale delivery platforms for RNA therapeutics: Challenges and the current state of the art. Med. 2022 Mar 11;3(3):167-87.
40. Rabinovici GD, Knopman DS, Arbizu J, Benzinger TL, Donohoe KJ, Hansson O, Herscovitch P, Kuo PH, Lingler JH, Minoshima S, Murray ME. Updated appropriate use criteria for amyloid and tau PET: a report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. Journal of Nuclear Medicine. 2025 Jun 1;66(Supplement 2):S5-31.
41. Shukla-Dave A, Obuchowski NA, Chenevert TL, Jambawalikar S, Schwartz LH, Malyarenko D, Huang W, Noworolski SM, Young RJ, Shiroishi MS, Kim H. Quantitative imaging biomarkers alliance (QIBA) recommendations for improved precision of DWI and DCE-MRI derived biomarkers in multicenter oncology trials. Journal of Magnetic Resonance Imaging. 2019 Jun;49(7):e101-21.
42. Wolf RL. MRI of recurrent glioblastoma: reliability and reality. Radiology. 2019 Feb;290(2):477-8.
43. Amjad AH, Danish M, Jah B, Gulzar MA. Accessibility Issues in Ad-Driven Web Applications. arXiv preprint arXiv:2409.18590. 2024 Sep 27.
44. Velez EM, Desai B, Ji L, Quinn DI, Colletti PM, Jadvar H. Comparative prognostic implication of treatment response assessments in mCRPC: PERCIST 1.0, RECIST 1.1, and PSA response criteria. Theranostics. 2020 Feb 10;10(7):3254.
45. Aguirre-Meneses H, Stoehr-Muñoz P, Molina-Gonzalez M, Nuñez-Gaona MA, Roldan-Valadez E, Molina-Gonzalez Sr M. Radiomics and the Image Biomarker Standardisation Initiative (IBSI): A Narrative Review Using a Six-Question Map and Implementation Framework for Reproducible Imaging Biomarkers. Cureus. 2025 Oct 24;17(10).
46. Smith AM, Obuchowski NA, Foster NL, Klein G, Mozley PD, Lammertsma AA, Wahl RL, Sunderland JJ, Vanderheyden JL, Benzinger TL, Kinahan PE. The RSNA QIBA profile for amyloid PET as an imaging biomarker for cerebral amyloid quantification. Journal of Nuclear Medicine. 2023 Feb 1;64(2):294-303.
47. Whybra P, Zwanenburg A, Andrearczyk V, Schaer R, Apte AP, Ayotte A, Baheti B, Bakas S, Bettinelli A, Boellaard R, Boldrini L. The image biomarker standardization initiative: standardized convolutional filters for reproducible radiomics and enhanced clinical insights. Radiology. 2024 Feb 6;310(2):e231319.
48. Lara H, Li Z, Abels E, Aeffner F, Bui MM, ElGabry EA, Kozlowski C, Montalto MC, Parwani AV, Zarella MD, Bowman D. Quantitative image analysis for tissue biomarker use: a white paper from the digital pathology association. Applied Immunohistochemistry & Molecular Morphology. 2021 Aug 1;29(7):479-93.
49. Roshanfar M, Salimi M, Jang SJ, Sinusas AJ, Kim J, Mosadegh B. Emerging Image-Guided Navigation Techniques for Cardiovascular Interventions: A Scoping Review. Bioengineering. 2025 May 2;12(5):488.
50. Hricak H, Abdel-Wahab M, Atun R, Lette MM, Paez D, Brink JA, Donoso-Bach L, Frija G, Hierath M, Holmberg O, Khong PL. Lancet Oncology Commission on medical imaging and nuclear medicine. The Lancet. Oncology. 2021 Mar 4;22(4):e136.