Saudi Journal of Medicine and Public Health

https://saudijmph.com/index.php/pub

https://doi.org/10.64483/202522379

Nuclear Medicine Cerebral Perfusion Imaging: Clinical Protocols, Quantitative Interpretation, and Pharmacologic Considerations for Radiologists and Pharmacists

Al Anoud Abdullah Raheel Al Anzi [(1)] , Mahasen Fawaza Alharbi [(1)] , Watin Hutayl H. Al-Shammari [(1)] , Sheam Saeed Hussain [(2)] , Budur Mohammed Alanazi [(2)] , Samarah Adel Basakran [(2)] , Nouf Derea Alkahtani [(2)] , Manal Awad Alahmari [(2)] , Eman Abdullah Alturki [(2)] , Sara Aman Farj Alsediri [(3)] , Dalal Munays Al-Qahtani [(2)] , Raghad Yasir Abuzaid[(2)] , Faisal Alqahtani[(2)]

(1) King Khalid General Hospital, Hafar Al-Batin,Ministry of Health, Saudi Arabia,
(2) Ad Diriyah Hospital,Ministry of Health, Saudi Arabia,
(3) Ad Diriyah Hospital, Riyadh,Ministry of Health, Saudi Arabia

Abstract

Background: Cerebral perfusion imaging is a cornerstone of neurodiagnostic practice, offering physiologic insights into cerebral blood flow that structural imaging cannot provide. Nuclear medicine techniques—primarily SPECT and PET—enable functional mapping of perfusion and metabolism, aiding diagnosis in stroke, epilepsy, dementia, and other neurologic disorders.

Aim: To review clinical protocols, quantitative interpretation, and pharmacologic considerations in nuclear medicine cerebral perfusion imaging, emphasizing interprofessional collaboration between radiologists and pharmacists.

Methods: This narrative review synthesizes consensus guidelines, physiologic principles, and tracer pharmacokinetics relevant to SPECT and PET imaging. It examines radiopharmaceutical properties, acquisition protocols, quantitative strategies, and pharmacologic challenge testing, particularly acetazolamide-based cerebrovascular reserve assessment.

Results: Lipophilic SPECT tracers (Tc99m-ECD, Tc99m-HMPAO) provide stable perfusion "snapshots," enabling ictal epilepsy localization and cerebrovascular reserve evaluation. PET offers absolute quantification of cerebral blood flow and metabolism using O-15 and F-18 tracers, though logistical constraints limit routine use. Pharmacologic challenges reveal exhausted autoregulatory capacity in chronic occlusive disease, guiding revascularization decisions. Nuclear perfusion imaging demonstrates clinical utility in brain death confirmation, stroke risk stratification, dementia differentiation, and functional assessment after trauma.

Conclusion: Nuclear medicine cerebral perfusion imaging delivers unique physiologic data that complement structural imaging, influencing diagnosis, risk assessment, and therapeutic planning. Optimal outcomes depend on standardized protocols, careful patient preparation, and coordinated teamwork to ensure safety and interpretive validity.

Keywords: Cerebral perfusion, SPECT, PET, radiopharmaceuticals, acetazolamide challenge, cerebrovascular reserve,

epilepsy, dementia, stroke

Introduction

Cerebral perfusion imaging constitutes a central component of contemporary neurodiagnostic practice because it provides physiologic information regarding regional blood flow that cannot be inferred reliably from structural imaging alone. Assessment of cerebral hemodynamics may be achieved through multiple modalities, including magnetic resonance imaging (MRI) techniques such as dynamic susceptibility contrast and arterial spin labeling, computed tomography (CT) perfusion, transcranial Doppler ultrasound, and nuclear medicine approaches. Each modality offers distinct strengths with respect to temporal resolution, quantification, availability, patient tolerability, and susceptibility to artifacts. In clinical practice, modality selection is typically driven by the diagnostic question, the acuity of presentation, patient-specific contraindications, and the need to integrate functional perfusion data with anatomic findings. This discussion focuses on nuclear medicine cerebral perfusion imaging, with emphasis on single-photon emission computed tomography (SPECT) and positron emission tomography (PET). These techniques uniquely interrogate brain perfusion and metabolism through radiopharmaceutical distribution that reflects cerebral blood flow, tissue viability, and, in some PET applications, specific biochemical pathways. By translating radiotracer kinetics into physiologically meaningful maps, SPECT and PET offer both qualitative pattern recognition and quantitative or semi-quantitative metrics that support clinical

*Corresponding author e-mail: anabalanazi@moh.gov.sa (Al Anoud Abdullah Raheel Al Anzi).
Receive Date: 29 November 2025, Revise Date: 24 December 2025, Accept Date: 26 December 2025

decision-making. Importantly, nuclear perfusion imaging provides functional insights that may remain occult on conventional CT or MRI, particularly in disorders where structural changes lag behind physiologic disturbance or where the clinical syndrome arises from dynamic alterations in cerebrovascular reserve [1][2].

In the evaluation of acute and subacute ischemic stroke, perfusion imaging helps characterize regional hypoperfusion, assess tissue at risk, and support differentiation between infarcted and potentially salvageable brain, particularly when interpreted alongside structural imaging. In chronic cerebrovascular disease, nuclear perfusion studies can assess baseline perfusion deficits and evaluate cerebrovascular reserve using pharmacologic or physiologic challenges, thereby informing risk stratification and, in selected settings, revascularization planning. In epilepsy, perfusion SPECT—often performed as ictal and interictal studies—can localize seizure foci by demonstrating regional hyperperfusion during seizures and relative hypoperfusion interictally, complementing electroencephalography and MRI findings. Beyond these indications, PET and SPECT contribute to the assessment of dementia syndromes, inflammatory or infectious processes, and certain movement disorders, depending on the tracer and protocol used. Because nuclear perfusion imaging depends on radiopharmaceutical selection, preparation, administration, and patient factors that influence tracer biodistribution, collaboration between radiologists and pharmacists is integral to high-quality practice. Radiologists provide protocol oversight and interpretive expertise, while pharmacists support safe radiotracer handling, medication reconciliation, and optimization of pharmacologic adjuncts used in stress or challenge paradigms. Together, these disciplines ensure that cerebral perfusion imaging is performed safely, reproducibly, and in a manner that yields clinically actionable information [1][2].

Anatomy and Physiology

Cerebral perfusion imaging in nuclear medicine is grounded in the fundamental anatomy of the neurovascular unit and the physiologic principles that govern cerebral blood flow (CBF) distribution, blood–brain barrier (BBB) transport, and regional coupling between perfusion and neuronal activity. The brain's perfusion is highly heterogeneous: gray matter typically receives greater flow than white matter, and flow is dynamically modulated by metabolic demand through neurovascular coupling. Nuclear medicine techniques leverage this physiology by using radiopharmaceuticals whose delivery and retention within brain tissue reflect perfusion and, in selected PET applications, oxygen utilization and glucose metabolism. Accordingly, understanding how specific tracers traverse the BBB, become trapped or equilibrate, and distribute between gray and white matter is central to protocol selection and to accurate interpretation of SPECT and PET perfusion studies. Multiple radiopharmaceuticals have been developed to evaluate cerebral hemodynamics, particularly for SPECT imaging, where comparative assessments of regional perfusion are most commonly performed. Lipophilic SPECT tracers such as technetium-99m ethyl cysteinate dimer (Tc99m-ECD), technetium-99m hexamethylpropylene amine oxime (Tc99m-HMPAO), and N-isopropyl-p-I-123 iodoamphetamine (I-123 IMP) are widely used to obtain comparative measurements of regional CBF.[1] Their lipophilicity facilitates efficient BBB passage by passive diffusion. After crossing into the brain, these compounds undergo biochemical transformation or intracellular binding that effectively renders them more hydrophilic, thereby limiting back-diffusion and promoting retention within brain tissue for a prolonged interval. This trapping phenomenon is particularly advantageous in routine clinical practice because the tracer distribution becomes a relatively stable "snapshot" of perfusion at—or near—the time of injection, allowing imaging to occur later without losing the physiologic information captured during radiotracer uptake [1].

Although Tc99m-HMPAO and Tc99m-ECD share the core property of BBB penetration followed by intracerebral trapping, they differ in practical imaging characteristics that influence tissue contrast and interpretability. Tc99m-ECD is typically described as exhibiting relatively higher uptake in gray matter compared with Tc99m-HMPAO, which translates into improved gray-to-white matter differentiation and, consequently, images that may be easier to interpret for regional cortical perfusion abnormalities.[2] This distinction is clinically meaningful because many perfusion pathologies of interest—such as seizure-related hyperperfusion, cortical hypoperfusion patterns in dementia syndromes, and cortical watershed perfusion deficits—are primarily cortical or gray matter phenomena. Enhanced gray–white contrast can therefore improve reader confidence and may facilitate detection of subtle cortical asymmetries, especially when interpretation is supported by quantitative comparison tools and standardized normal databases. The intracerebral retention of these lipophilic SPECT radiotracers is particularly valuable in epilepsy imaging, where physiologic timing is critical but logistical constraints are unavoidable. In ictal SPECT protocols, the radiotracer is ideally injected as early as possible during a seizure, capturing the characteristic transient pattern of regional hyperperfusion at the epileptogenic focus. Because Tc99m-ECD and Tc99m-HMPAO remain trapped after BBB passage, the distribution fixed at injection is preserved long enough to permit clinical stabilization of the patient in the acute ictal setting

before transportation to the scanner and image acquisition.[3] This temporal decoupling between injection and scanning underpins the clinical feasibility of perfusion SPECT in epilepsy and explains why tracer pharmacokinetics, rather than scanner proximity alone, are central determinants of diagnostic yield. While most SPECT perfusion tracers provide relative or comparative measurements of CBF, xenon-133 (Xe-133) has historically enabled absolute quantification of CBF, representing a conceptual departure from "snapshot" tracers. Absolute measurements are possible with Xe-133 because its kinetics can be modeled more directly through time–activity analysis and by correlating brain uptake with arterial concentrations. The most common approach involves measuring Xe-133 levels in arterial blood gas samples to derive an arterial input function, an equation describing tracer delivery and clearance that can be used to calculate absolute flow values.[2] This concept—relating tissue activity to an arterial input function—highlights a core physiologic principle in nuclear perfusion quantification: absolute flow estimation requires not only tissue counts but also knowledge of how much tracer was delivered to the tissue over time [2].

In contemporary practice, absolute quantitative hemodynamic information is more commonly obtained with PET rather than SPECT, largely because PET technology can interrogate additional metabolic domains—oxygen extraction and utilization, glucose metabolism, and blood volume—alongside perfusion. Nevertheless, the practical clinical benefit of absolute CBF values is often modest for many routine questions. Comparative quantitative approaches (such as side-to-side asymmetry analysis or regional normalization) and pattern-based qualitative interpretation frequently provide the majority of clinically relevant information, especially when the clinical objective is localization (as in epilepsy), characterization of perfusion deficits (as in cerebrovascular disease), or identification of syndrome-specific patterns (as in neurodegenerative disorders). Absolute quantification becomes most impactful when precise physiologic thresholds matter, when research protocols require numeric endpoints, or when sophisticated modeling is needed to differentiate impaired autoregulation from reduced metabolic demand. PET offers a robust platform for quantitative cerebral hemodynamic assessment through a suite of oxygen-15 and carbon monoxide tracers. Intravenous H2^15O (oxygen-15–labeled water) can be used to measure absolute CBF, while inhaled ^15O2 permits calculation of regional oxygen extraction fraction (rOEF) and regional cerebral oxygen metabolism (cMRO2).[4] In addition, C^15O can be used to estimate cerebral blood volume (CBV), completing a physiologic triad that links perfusion, oxygen utilization, and vascular compartment size.[4] These measures are particularly relevant in advanced cerebrovascular assessment, where understanding whether hypoperfused tissue is compensating by extracting more oxygen—the so-called "misery perfusion" concept—can have prognostic and therapeutic implications. Beyond oxygen-based tracers, F-18 fluorodeoxyglucose (F-18 FDG) provides an established method for assessing regional metabolic activity by mapping glucose uptake, enabling identification of hypometabolic or hypermetabolic areas that may correspond to seizure foci, neurodegenerative patterns, or inflammatory processes.[2]

As with Xe-133 SPECT quantification, PET-based absolute CBF measurement with H2^15O classically relies on arterial blood sampling to define an arterial input function.[5] The physiologic logic is the same: accurate absolute flow estimation depends on relating tissue signal to delivered tracer concentration over time. However, because arterial catheterization increases procedural complexity and limits scalability, less invasive quantification methods have been developed that attempt to infer tracer kinetics from imaging data alone, thereby reducing or eliminating the need for arterial access.[6] Such approaches reflect an ongoing evolution in PET methodology, seeking to preserve quantitative rigor while improving feasibility and patient comfort in clinical environments. An important operational dimension of PET physiology is dictated by radionuclide characteristics. Low-molecular-weight isotopes commonly used in PET radiopharmaceuticals, such as F-18 and O-15, require cyclotron production and have relatively short physical half-lives. O-15–labeled compounds are particularly short-lived, with half-lives typically in the range of approximately 2 to 20 minutes, whereas F-18–labeled compounds have longer half-lives, often up to about 110 minutes.[7] These half-life constraints have direct physiologic and logistical consequences: O-15 protocols demand on-site or near-site cyclotron access and tightly coordinated workflows to deliver tracer, perform serial acquisitions, and execute kinetic modeling before substantial radioactive decay occurs. Even with F-18, coordination between radiopharmaceutical production facilities and imaging sites remains crucial to ensure dose integrity, scheduling reliability, and protocol fidelity. The operational realities of tracer decay thus become an integral part of implementing physiologically meaningful cerebral perfusion and metabolism studies in routine practice [5][6][7].

Pharmacologic cerebrovascular challenge testing further illustrates the intersection between physiology and nuclear imaging. Acetazolamide is used in both SPECT and PET perfusion protocols to assess cerebrovascular reserve in patients with chronic cerebrovascular occlusive disease. In normal

brain tissue, acetazolamide inhibits carbonic anhydrase, increasing CO2 levels and inducing reflex cerebral vasodilation. This vasodilation reduces cerebrovascular resistance and leads to an increase in CBF, with normal regions typically demonstrating an approximately 20% to 30% rise in flow following acetazolamide administration. The physiologic premise is that healthy vessels retain vasodilatory capacity and can augment perfusion when challenged. In contrast, brain regions with chronically reduced cerebral perfusion pressure often exhibit compensatory baseline vasodilation as part of autoregulatory mechanisms aimed at maintaining adequate CBF. When arterioles are already maximally dilated, their capacity to respond to acetazolamide is limited. As a result, under-perfused tissue may demonstrate a blunted increase—or even a paradoxical relative decrease when compared with normal regions—following acetazolamide challenge, reflecting exhausted vascular reserve.[8] This differential responsiveness allows nuclear perfusion imaging to function as a physiologic "stress test" for the cerebral circulation, helping distinguish territories with preserved compensatory capacity from those at higher risk for ischemia because autoregulatory reserve is depleted.[8] In clinical interpretation, these findings must be contextualized within the patient's vascular anatomy, symptom profile, and structural imaging, but the underlying physiologic logic remains consistent: acetazolamide challenge reveals the functional elasticity of cerebrovascular regulation, and nuclear imaging provides a spatially resolved map of that reserve across the brain [8].

Indications

Nuclear medicine cerebral perfusion imaging—most commonly performed with SPECT and, in selected settings, PET—provides physiologic information about regional cerebral blood flow that complements structural neuroimaging. Its clinical value is greatest when the diagnostic question hinges on perfusion patterns, cerebrovascular reserve, or functional integrity of the intracranial circulation rather than on anatomy alone. One of the most established indications is the localization of epileptogenic foci for pre-surgical planning.[9][10] In epilepsy, perfusion SPECT is often employed using interictal and ictal acquisitions, leveraging the characteristic shift from relative hypoperfusion interictally to hyperperfusion during seizures within the epileptogenic zone. This functional localization can be particularly helpful when MRI is nonlesional, when electroencephalography is discordant, or when the seizure network is complex, thereby improving the multidisciplinary assessment used to select surgical candidates and to define resection targets.[9][10] Perfusion imaging also plays an important role in cerebrovascular disease, particularly for estimating stroke risk in patients with chronic cerebrovascular occlusive pathology.[8][11] In these patients, baseline perfusion deficits and impaired cerebrovascular reserve—often assessed using vasodilatory challenge—can identify territories at higher ischemic risk and inform decisions regarding medical optimization or revascularization strategies. A related, highly specialized indication is the evaluation of stroke risk in patients who may be candidates for carotid artery sacrifice procedures.[12][13] When carotid occlusion is being considered to treat complex aneurysms, skull base tumors, or other lesions, perfusion imaging can help determine whether collateral circulation is sufficient to maintain cerebral perfusion under conditions of reduced ipsilateral flow, thereby supporting procedural planning and risk counseling.[12][13]

In acute ischemic stroke, nuclear perfusion techniques can support identification of ischemic penumbra versus established infarct core, contributing physiologic context regarding tissue viability and potentially salvageable regions.[14] Although CT and MR perfusion are more commonly used in contemporary acute stroke workflows because of speed and availability, nuclear medicine approaches remain relevant in selected scenarios where other modalities are limited or where physiologic corroboration is needed.[14] Beyond vascular indications, characteristic perfusion patterns can assist in differentiating dementia subtypes, supporting diagnostic refinement when clinical presentation is atypical or when overlapping syndromes are considered.[15] Additionally, nuclear perfusion imaging may be used to confirm brain death by demonstrating absence of intracranial perfusion, providing an objective physiologic assessment that can support institutional protocols when clinical testing is equivocal or confounded.[16] In neurotrauma and complex neurologic presentations, perfusion scans can identify lesions or functional abnormalities that may be occult on MRI or CT, particularly when symptoms are disproportionate to structural findings or when diffuse functional impairment is suspected.[17] Across these indications, the clinical rationale is consistent: nuclear medicine perfusion imaging offers spatially resolved physiologic data that can localize pathology, stratify risk, or provide confirmatory evidence when anatomy alone is insufficient.[8][9][10][11][12][13][14][15][16][17]

Contraindications

SPECT and PET cerebral perfusion studies have relatively few absolute contraindications, reflecting the generally favorable safety profile of commonly used radiopharmaceuticals and the noninvasive nature of image acquisition. In most circumstances, the primary limiting factors are practical and safety-related rather than pharmacologic. The most important constraints are inability to cooperate with the examination, inability to maintain the required positioning, or inability to be positioned in the scanner safely due to agitation, severe pain, unstable vital signs, or the need for

continuous interventions that cannot be accommodated within the scanning environment. These limitations are clinically significant because motion degrades image quality and may invalidate quantitative comparisons, while unsafe positioning can compromise airway protection, hemodynamic stability, or neurologic monitoring. Therefore, patient stability and procedural feasibility are central considerations when determining whether perfusion imaging can be performed at a given time. True hypersensitivity reactions to SPECT or PET radiotracers are exceptionally uncommon, and anaphylaxis is considered extremely rare.[18] Nevertheless, when a patient has a documented prior severe reaction temporally linked to a specific radiotracer or formulation component, it is prudent to avoid re-exposure and to consider alternative radiopharmaceuticals or alternative imaging strategies. In such cases, risk–benefit assessment should be individualized, and documentation should clarify whether the reaction was attributable to the radiotracer itself, an excipient, or an unrelated coincident exposure. When an alternative tracer is available that provides clinically equivalent information, substituting the agent is generally the safest approach.[18] Contraindications become more clinically prominent when pharmacologic challenge testing is incorporated, most notably with acetazolamide for cerebrovascular reserve assessment. Acetazolamide is contraindicated in patients with sulfonamide ("sulfa") allergy because of the risk of hypersensitivity reactions, and it should be avoided in individuals with severe electrolyte disturbances given its potential to exacerbate metabolic derangements. Similarly, severe hepatic or renal dysfunction is a contraindication because acetazolamide can worsen acid–base balance and may accumulate when clearance is impaired, increasing the risk of adverse effects. These contraindications necessitate careful pre-procedure screening by the imaging team, often with pharmacist involvement for medication reconciliation and safety review, to ensure that the benefits of challenge testing outweigh risks and that alternative protocols are considered when acetazolamide cannot be used safely [18].

Equipment

Both single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are tomographic nuclear medicine technologies designed to acquire three-dimensional datasets by detecting radiation emitted from administered radiopharmaceuticals. Although both systems ultimately reconstruct volumetric representations of tracer distribution within the brain, the physics of signal generation and detection differ in ways that directly influence image resolution, noise characteristics, count statistics, and the technical design of the cameras. A clear understanding of these equipment-level distinctions is essential for radiologists interpreting cerebral perfusion studies and for pharmacists and nuclear medicine teams coordinating tracer selection, administered activity, and imaging workflow. In SPECT, the radiopharmaceutical emits gamma photons directly, and those photons are detected by one or more gamma camera heads. Because emitted photons travel in all directions, SPECT systems require mechanical collimation to determine the direction of origin. Collimators—typically parallel-hole designs for cerebral perfusion—physically block most photons and permit only those traveling along specific trajectories to reach the detector. This directional filtering is necessary for spatial localization but comes at a cost: collimation discards a large fraction of emitted photons, reducing overall detection efficiency and limiting the count statistics available for reconstruction. As a result, SPECT images are intrinsically more susceptible to noise, and the achievable spatial resolution is constrained by collimator geometry, detector performance, patient motion, and depth-dependent blurring. These technical constraints are particularly relevant in brain perfusion imaging, where subtle regional asymmetries may be clinically meaningful and where accurate gray–white differentiation can influence interpretive confidence [18][19].

PET systems operate through a fundamentally different detection mechanism. PET radiotracers emit positrons, which travel a short distance in tissue before annihilating with electrons. This annihilation event produces two photons emitted in nearly opposite directions. The PET scanner detects these paired photons simultaneously, using electronic "coincidence detection" to identify events that likely originated from a true annihilation along a line between two detectors. Because PET uses coincidence timing to localize events, it does not require a physical collimator to reject scatter in the same way that SPECT does.[19] This design advantage improves sensitivity because a substantially greater proportion of emitted events contribute to the reconstructed dataset. Higher sensitivity generally yields higher count density, improved signal-to-noise performance, and, in many practical settings, superior spatial resolution compared with SPECT. Additionally, because PET detection is less dependent on restrictive mechanical collimation, PET images often demonstrate reduced image degradation from photon rejection and can achieve more robust quantitative performance under standardized protocols. The energy characteristics of the detected photons also influence image quality and equipment capabilities. In PET, annihilation photons have a characteristic energy of approximately 0.511 MeV, which is consistent across all PET radionuclides because the photon energy is determined by the annihilation process rather than by

the parent isotope.[20] This uniformity has important implications for instrumentation: PET systems are optimized around a single photon energy, facilitating standardized detector design and reconstruction physics. However, it also means that PET cannot readily distinguish between different positron-emitting radiotracers administered simultaneously based on photon energy alone, because the detected photons are of the same energy regardless of tracer identity.[20] By contrast, SPECT systems can, in principle, differentiate multiple radiotracers in the same imaging session when the tracers emit photons at sufficiently distinct energies. Gamma cameras can be configured with energy windows that selectively accept photons within defined energy ranges, enabling multi-isotope acquisition under appropriate conditions. This capability represents a practical advantage in certain specialized nuclear medicine applications, although it is used less commonly in routine cerebral perfusion workflows [18][19][20].

SPECT radiotracers often emit photons of lower energy than PET annihilation photons, and this contributes to differences in signal characteristics and susceptibility to attenuation and scatter. Lower-energy photons are more readily attenuated by overlying tissues and may undergo scatter interactions that degrade effective spatial resolution. Combined with the inherent sensitivity loss from collimation, these physics factors contribute to the general observation that SPECT images tend to have lower intrinsic resolution than PET images under comparable clinical conditions. While modern reconstruction algorithms, iterative techniques, and resolution recovery can partially mitigate these differences, the fundamental equipment physics remain a major determinant of performance, especially when high-resolution regional assessment is required. Hybrid imaging systems further enhance the capabilities of both SPECT and PET by pairing functional imaging with anatomic localization. PET systems in current clinical practice are most commonly deployed as PET/CT scanners, reflecting widespread integration of CT for attenuation correction, localization, and assessment of structural correlates. Hybrid SPECT/CT systems also exist, though they are comparatively less prevalent in some institutions, and dedicated brain SPECT cameras are available commercially for optimized cerebral imaging. Many facilities nonetheless rely on general-purpose SPECT systems designed to image a wide range of organ systems, and these systems can be adapted for brain perfusion protocols with appropriate collimation, acquisition parameters, and reconstruction methods. Hybrid PET/CT and SPECT/CT platforms offer two major advantages beyond simple anatomic correlation. First, CT provides precise structural reference that improves localization of perfusion abnormalities and helps distinguish true perfusion deficits from artifacts related to attenuation, motion, or extracranial activity. Second, CT enables attenuation correction, a process that standardizes measured radiotracer activity by modeling how photons are absorbed by intervening tissue before reaching the detectors. CT attenuation correction improves quantitative accuracy and reduces regional bias introduced by variable tissue density, particularly in deep brain structures and at interfaces where photon attenuation differs substantially. Although attenuation correction can sometimes be performed using a prior CT dataset, accuracy is reduced when patient positioning differs between studies, because even small geometric discrepancies can lead to imperfect alignment and residual correction errors. For cerebral perfusion imaging—where subtle asymmetries may drive clinical interpretation—consistent positioning and contemporaneous CT acquisition generally yield more reliable correction and improved interpretive confidence [18][19][20].

In sum, the equipment used for nuclear medicine cerebral perfusion imaging reflects a balance between the physics of emission and detection, clinical workflow, and the need for robust anatomic correlation. Understanding how SPECT and PET differ in collimation requirements, coincidence detection, energy characteristics, and integration with CT or MRI is essential for optimizing protocol design, ensuring reliable quantitative comparisons, and generating diagnostically meaningful studies that guide patient care.[19][20]

Preparation

Preparation for a nuclear medicine cerebral perfusion examination is designed to minimize physiologic and environmental factors that can alter cerebral hemodynamics or introduce variability in radiotracer uptake, thereby improving interpretive reliability. Because cerebral blood flow is sensitive to autonomic tone, vasoactive substances, sensory stimulation, and anxiety, standardized pre-scan instructions are essential to reduce confounding influences and to ensure that the measured tracer distribution reflects the patient's baseline or intended physiologic state rather than transient, avoidable perturbations. Patients should be counseled to avoid caffeine, alcohol, and nicotine for at least 10 hours prior to the study. These substances can meaningfully influence cerebral perfusion through several mechanisms. Caffeine antagonizes adenosine receptors and can produce cerebral vasoconstriction, potentially lowering regional perfusion and altering the apparent distribution of radiotracer. Nicotine exerts complex autonomic effects, including sympathetic activation and vasoactive responses that may change perfusion patterns. Alcohol can also affect vascular tone and neural activity in ways that modify cerebral hemodynamics. Collectively, these exposures may create perfusion alterations that are unrelated to the underlying clinical condition and can therefore confound qualitative interpretation or quantitative comparisons, particularly when the study

aims to detect subtle asymmetries or evaluate cerebrovascular reserve. The environment and timing of radiotracer administration are equally important. Radiotracer injection should be performed in a dimly lit, quiet room to reduce sensory stimulation and to limit activation of visual and association cortices that can occur with bright light, conversation, or environmental stress. The patient should be allowed sufficient time to relax before injection, as anxiety-related sympathetic activation can change cerebral blood flow and potentially introduce nonpathologic regional variability. This is especially relevant for epilepsy protocols and dementia evaluations, where cortical activation patterns may influence interpretation and where standardized resting conditions support comparison with normative databases. Intravenous access should be established at least 10 minutes before radiotracer injection. This practice reduces procedural stress at the critical time of tracer administration and helps ensure a smooth, uninterrupted injection, which is important for consistent tracer delivery and for capturing the intended physiologic snapshot. In addition, patients should be instructed not to speak or interact with the technologist for approximately 5 to 10 minutes around the time of injection. Speech, auditory engagement, and active attention can increase regional perfusion in language and association networks and may therefore alter tracer uptake patterns in a way that complicates interpretation. Maintaining a calm, stimulus-minimized interval surrounding injection supports a more standardized resting-state acquisition and helps reduce artifactual perfusion asymmetries, thereby improving the diagnostic quality of the study.[19]

Technique or Treatment

Professional societies have published consensus-based technical recommendations intended to promote standardization, quality assurance, and interpretive reliability across nuclear medicine procedures. In this context, the Society of Nuclear Medicine & Molecular Imaging (SNMMI) and the European Association of Nuclear Medicine (EANM) have endorsed protocol elements for several study types, including specific guidance relevant to cerebral perfusion applications. The most clearly defined and widely cited recommendations pertain to SPECT examinations performed for the determination of brain death, where the clinical question is binary—demonstration of intracranial perfusion versus absence of perfusion—and where technical rigor is essential because results may carry profound ethical, legal, and management implications. In brain death imaging performed with brain-binding agents such as technetium-99m hexamethylpropylene amine oxime (Tc99m-HMPAO) or technetium-99m ethyl cysteinate dimer (Tc99m-ECD), SNMMI-endorsed methodology emphasizes capturing the early tracer delivery phase and then acquiring delayed planar views to document intracranial distribution. Specifically, dynamic imaging during radiotracer injection is recommended to assess flow-related activity contemporaneous with administration, followed by anterior and lateral planar images of the brain obtained approximately 20 minutes after injection, when tracer localization is expected to be stable and interpretable within the brain parenchyma. When a non–brain-binding radiopharmaceutical is used—such as technetium-99m diethylenetriamine pentaacetate (Tc99m-DTPA)—the imaging strategy necessarily shifts because parenchymal trapping is not expected. Under these circumstances, SNMMI guidance supports a planar imaging set that includes anterior, right lateral, left lateral, and posterior projections, acquired to a prespecified count threshold to ensure adequate statistical quality. Recommended count targets typically range from 500,000 to 1,000,000 counts per image, a strategy that seeks to balance acquisition time against the need for sufficient signal-to-noise performance to evaluate intracranial flow patterns and distinguish true absence of perfusion from technical inadequacy. Dynamic images obtained during tracer injection remain valuable with non–brain-binding agents as well, because the initial angiographic phase can provide critical confirmation of tracer delivery and vascular transit patterns, particularly when delayed planar activity is limited or ambiguous [20][21].

In addition to planar acquisitions, three-dimensional SPECT reconstruction may be employed when brain-binding tracers such as Tc99m-HMPAO or Tc99m-ECD are used, particularly to improve spatial discrimination between intracranial activity and extracranial soft-tissue or scalp uptake. This distinction can be clinically important in brain death determinations, where extracranial activity may mimic or obscure faint intracranial signal on planar views. SPECT can therefore serve as an adjunct to enhance anatomic localization of tracer distribution and strengthen interpretive confidence in differentiating parenchymal activity from background or scalp contamination.[21] Beyond these study-specific recommendations, both SNMMI and EANM have also endorsed broader guidance regarding the use of technetium-99m radiopharmaceuticals in cerebral perfusion imaging, encompassing domains such as patient preparation, acquisition considerations, and post-processing practices that support reproducibility and interpretive quality.[22] Outside the specific setting of brain death assessment, cerebral perfusion imaging protocols are more heterogeneous, reflecting variation in clinical indications, institutional resources, and preferred tracers. Notably, neither SNMMI nor EANM has endorsed a single uniform protocol for routine cerebral perfusion SPECT or PET examinations performed for indications such as epilepsy localization, chronic cerebrovascular disease

evaluation, or dementia characterization. In routine practice, however, protocols commonly share foundational elements: dynamic images are frequently acquired during radiotracer administration to document tracer delivery and early kinetics, followed by tomographic acquisition—SPECT or PET—timed to coincide with anticipated peak or stable radiotracer activity within the brain. This general structure aims to capture a physiologic "snapshot" of cerebral hemodynamics while ensuring adequate count statistics and image quality for qualitative interpretation and, when applicable, quantitative or semi-quantitative analysis [21].

Complications

Complications associated with nuclear medicine cerebral perfusion imaging are generally uncommon, but they can arise from two distinct sources: the radiopharmaceutical used for perfusion imaging and any adjunctive pharmacologic agent administered to provoke or augment hemodynamic responses, most notably acetazolamide in cerebrovascular reserve protocols. Although cerebral perfusion studies are widely performed, the published evidence base specifically addressing adverse effects of commonly used cerebral perfusion radiopharmaceuticals remains limited, and much of clinical safety practice is informed by broader radiopharmaceutical pharmacovigilance data rather than large, indication-specific trials. Within this context, the overall safety profile of standard perfusion tracers is considered favorable, particularly when standard dosing, aseptic technique, and monitoring practices are followed. Adverse reactions directly attributable to perfusion radiopharmaceuticals are generally mild and transient. Reported symptoms are nonspecific and resemble those seen with other injectable diagnostic agents, including transient flushing, nausea, and discomfort or pain at the injection site.[23] Injection-site complications may also reflect extravasation, venous irritation, or local inflammatory response rather than a systemic pharmacologic effect, and they are typically mitigated by ensuring reliable intravenous access and careful administration technique. Although hypersensitivity reactions are biologically plausible with any injected compound, clinically significant allergic reactions to nuclear medicine radiotracers appear to be rare, and reports of true anaphylaxis following radiopharmaceutical administration are exceedingly uncommon.[23] Nonetheless, the low incidence does not eliminate the need for readiness. Imaging departments should maintain standard precautions, including immediate access to emergency medications and trained personnel capable of responding to acute allergic or vasovagal events, particularly because patients undergoing perfusion imaging may have comorbidities that increase vulnerability to transient hemodynamic shifts.

In contrast to the relatively low frequency of radiotracer-related adverse events, complications related to augmenting or challenge agents—especially acetazolamide—are more frequently encountered and are a practical focus of pre-procedure screening and counseling. Acetazolamide is used to assess cerebrovascular reserve by inducing vasodilation through carbonic anhydrase inhibition, but this physiologic effect can produce predictable side effects. The most commonly reported reactions following intravenous acetazolamide include flushing, paresthesias, perioral numbness, and headache. These symptoms are generally self-limited and reflect systemic vascular and neurologic effects rather than structural harm. However, they can be uncomfortable and may provoke anxiety, which in turn can complicate patient cooperation during imaging. Clinicians and technologists should therefore warn patients in advance about these expected sensations, monitor vital signs when clinically appropriate, and provide reassurance to reduce the likelihood that benign symptoms are misinterpreted as dangerous complications. Although uncommon, more severe reactions are possible. Rarely, acetazolamide may precipitate hypersensitivity reactions, including anaphylaxis, particularly in susceptible individuals.[23] This risk is one reason why careful screening for sulfonamide allergy and relevant contraindications is essential before administering acetazolamide. Overall, while complications of nuclear medicine cerebral perfusion imaging are infrequent, safe practice depends on distinguishing the relatively rare adverse effects of radiotracers from the more common and predictable side effects of pharmacologic challenge agents, coupled with appropriate preparation, monitoring, and emergency readiness.[23]

Clinical Significance

Nuclear medicine cerebral perfusion imaging has clinical significance precisely because it interrogates physiology rather than anatomy, allowing clinicians to determine whether cerebral blood flow is present, regionally reduced, regionally increased, or redistributed in patterns that correspond to specific disease states. In practice, SPECT and PET perfusion examinations function as "functional maps" that can confirm catastrophic loss of intracranial flow, identify tissue at risk during ischemia, quantify cerebrovascular reserve, localize epileptogenic networks, and characterize neurodegenerative syndromes. While structural imaging remains indispensable for defining hemorrhage, infarct volume, mass lesions, and anatomic disruption, perfusion imaging contributes a complementary dimension: it captures hemodynamic and metabolic consequences that may precede or exceed visible structural change. This physiologic lens is particularly valuable in conditions where clinical decisions are time sensitive, where symptoms are discordant with anatomic imaging, or where

management hinges on differentiating viable from nonviable tissue [22][23].

Brain Death

Confirmation of brain death through nuclear cerebral perfusion imaging is most commonly performed with SPECT using brain-binding perfusion agents such as technetium-99m hexamethylpropylene amine oxime (Tc99m-HMPAO) or technetium-99m ethyl cysteinate dimer (Tc99m-ECD). The physiologic target in this setting is straightforward: to demonstrate absence of intracranial perfusion consistent with cessation of cerebral blood flow. Most protocols emphasize capturing both the angiographic phase and the delayed parenchymal phase. Dynamic planar imaging acquired during radiopharmaceutical injection evaluates early flow and confirms delivery to the cervical vasculature, while subsequent static planar images document the distribution—or absence—of tracer within the cranial vault. Because scalp perfusion can remain present even when intracranial perfusion is absent, three-dimensional SPECT imaging is commonly obtained in addition to dynamic and planar acquisitions. Tomographic reconstruction enhances spatial discrimination and helps determine whether apparent activity on planar views reflects intracerebral uptake or extracranial scalp signal. On dynamic images, patients meeting imaging criteria for brain death typically demonstrate flow within the internal carotid arteries that terminates at the skull base. This characteristic truncation is understood as a hemodynamic consequence of markedly increased intracranial pressure from cerebral edema, which functionally tamponades the intracerebral arterial system and prevents forward perfusion beyond the skull base. On static planar images, the defining feature is markedly decreased or absent radiotracer activity throughout the brain parenchyma, consistent with absent or profoundly diminished perfusion. A classic supportive sign is redistribution of blood flow into the external carotid circulation, producing increased radiotracer activity in the arteries of the face and nasal region and yielding the “hot nose” sign.[16] While PET could theoretically be used for brain death determinations, it has not achieved widespread adoption in this context, largely because short radiotracer half-lives, the need for rapid coordination, and workflow complexity limit feasibility compared with established SPECT protocols [16].

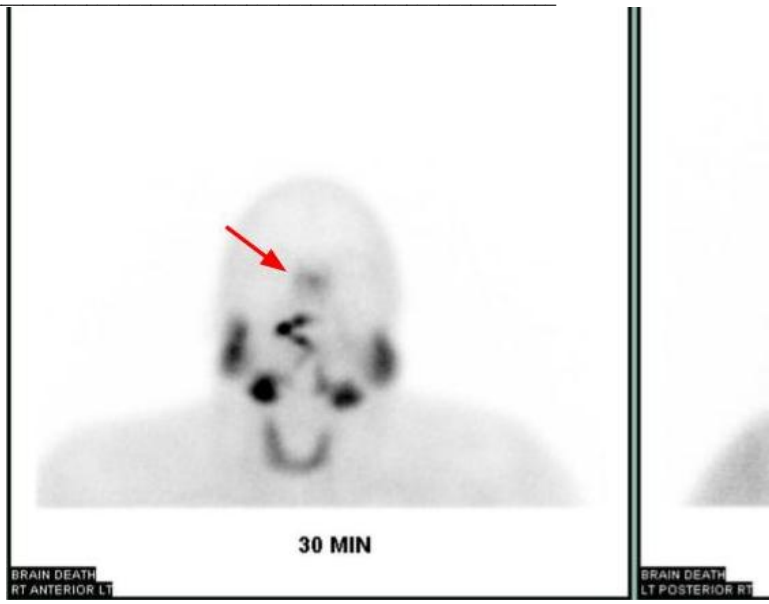

Fig. 1: Brain Death assessment.

Acute Stroke

In acute ischemic stroke, cerebral perfusion imaging is clinically significant because it can characterize regional hypoperfusion, support differentiation between potentially salvageable penumbral tissue and irreversibly infarcted core, and provide physiologic context that can inform reperfusion decisions. In SPECT, brain-binding agents such as Tc99m-HMPAO and Tc99m-ECD are commonly used, with Tc99m-ECD offering improved gray-to-white matter differentiation that may aid detection and delineation of cortical perfusion abnormalities. PET perfusion imaging, when available, can provide a more comprehensive physiologic profile: intravenous oxygen-15 labeled water is used for perfusion assessment, inhaled C^15O can estimate cerebral blood volume (CBV), and inhaled ^15O2 enables measurement of regional oxygen extraction fraction (rOEF) and cerebral oxygen metabolic rate (cMRO2).[24] Because perfusion and glucose metabolism are tightly coupled, F-18 fluorodeoxyglucose (F-18 FDG) PET can also identify metabolically compromised tissue, offering an indirect window into ischemic physiology. SPECT perfusion imaging has been used to stratify patients for intravenous thrombolysis and to anticipate hemorrhagic transformation risk. In this framework, relative perfusion thresholds—often normalized to cerebellar activity—help predict benefit versus risk. Areas demonstrating CBF greater than approximately 55% of cerebellar flow have been described as more likely to benefit from thrombolysis even when treatment occurs beyond a 6-hour window. Regions with CBF in the range of roughly 35% to 55% of cerebellar flow are typically considered more responsive when treated within 6 hours of symptom onset. In contrast, under-perfused tissue with CBF below about 35% of cerebellar flow is associated with a substantially higher risk of

intracerebral hemorrhage following thrombolysis, regardless of onset timing.[25] Although acute stroke PET perfusion imaging is largely restricted to specialized centers, foundational PET research was pivotal in defining ischemic penumbra and core infarct concepts that informed thresholds and compartment models later adapted to SPECT, CT perfusion, and MR perfusion approaches.[24]

A widely referenced framework described by Lee et al proposes a "four-compartment model" of abnormal stroke hemodynamics. Within this model, ischemic penumbra is characterized by relatively mild reductions in cMRO2, an average CBF around 35% of baseline, and a prolonged mean transit time exceeding approximately 6 to 8 seconds. CBV within penumbral tissue may be elevated, normal, or decreased depending on collateral status and autoregulatory response. By contrast, ischemic core infarct is associated with more substantial reductions in cMRO2 and an average CBF below approximately 20% of baseline. Core regions typically demonstrate decreased CBV with similarly prolonged mean transit time, and both penumbra and core exhibit increased rOEF, reflecting compensatory oxygen extraction in response to reduced delivery. The clinical implication is that relative measurements of perfusion, transit time, and blood volume—often compared against the contralateral homologous region—may approximate tissue categorization even when direct cMRO2 measurement is not available, thereby enabling clinically actionable inference using more widely accessible imaging parameters [24].

Chronic Cerebrovascular Disorders

In chronic carotid or intracranial arterial occlusive disease, the central clinical question often shifts from immediate infarct detection to prediction of future stroke risk and identification of patients who may benefit from revascularization or targeted medical intensification. Nuclear perfusion imaging contributes by assessing baseline CBF distribution and, crucially, by evaluating cerebrovascular reserve. Both SPECT and PET protocols can be augmented with intravenous acetazolamide, which induces vasodilation through carbonic anhydrase inhibition, increasing CO2 and provoking reflex dilation of cerebral arterioles. In territories with normal perfusion pressure and intact autoregulation, acetazolamide typically produces an increase in CBF of approximately 30%. In territories with reduced perfusion pressure, compensatory autoregulatory vasodilation may already be maximized at baseline; consequently, these regions demonstrate a blunted response to acetazolamide, with minimal increase in flow.[8] This physiologic behavior underlies the concept of reduced cerebrovascular reserve: the circulation has diminished capacity to augment flow under stress, implying vulnerability to ischemia when systemic pressure falls or when additional vascular compromise occurs. A particularly important pattern is the intracerebral steal phenomenon, which helps identify patients at heightened risk and potentially greater benefit from revascularization. In intracerebral steal, acetazolamide causes vasodilation in healthy brain tissue but cannot further dilate maximally recruited vessels in hypoperfused territories. As a result, blood preferentially flows toward newly dilated normal regions, effectively "stealing" flow from ischemic tissue and leading to a paradoxical further reduction in CBF in the compromised region.[11] Detecting this pattern has practical significance because it indicates exhausted reserve and unfavorable hemodynamic competition, often correlating with higher stroke risk and informing revascularization candidacy in selected clinical contexts [8][9][11].

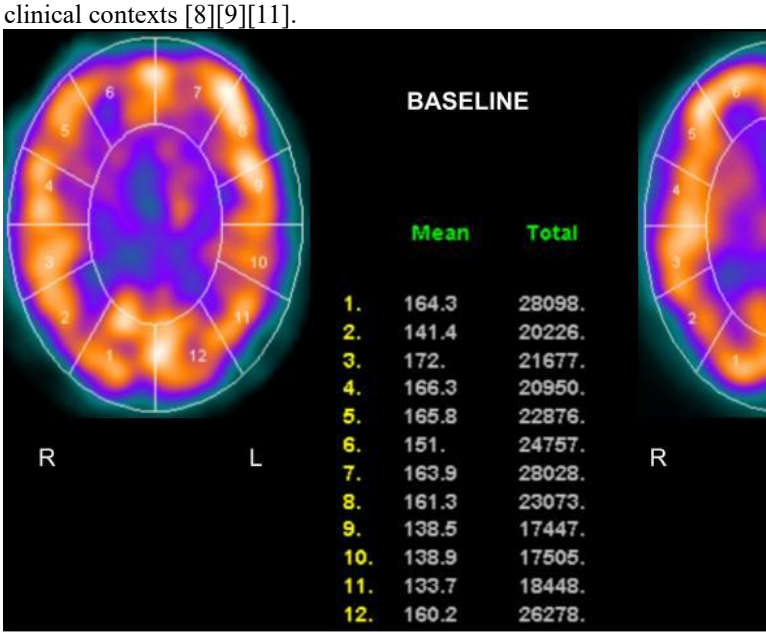

Fig. 2: Normal examination in a patient undergoing evaluation for dementia.

Balloon Occlusion Testing and Assessment of Stroke Risk after Carotid Artery Sacrifice

Carotid artery sacrifice may be necessary in selected patients with massive carotid aneurysms or with neoplasms inseparable from the carotid artery, where excision requires vessel occlusion.[13] Because permanent carotid sacrifice can precipitate catastrophic hemispheric infarction in patients with inadequate collateral circulation, pre-procedural physiologic risk stratification is essential. In this setting, nuclear cerebral perfusion imaging can be integrated with balloon occlusion testing to estimate tolerance to carotid closure. A common approach is to occlude the carotid artery with a balloon catheter for approximately 5 minutes and then administer a perfusion radiotracer—Tc99m-HMPAO for SPECT or oxygen-15 labeled water for PET—during occlusion. Perfusion is then assessed for hemispheric asymmetry. If a decrease in CBF exceeding approximately 10% relative to the contralateral hemisphere is detected, the patient is considered at significantly increased risk of stroke and higher overall mortality if carotid sacrifice is

performed.[12][13] The clinical value of this protocol lies in its ability to move beyond anatomic assumptions and directly test physiologic resilience under simulated occlusion, thereby supporting informed procedural planning, counseling, and selection of alternative strategies when necessary.

Epilepsy

Among functional neuroimaging applications, SPECT cerebral perfusion has become particularly valuable for localizing epileptogenic foci, especially in patients undergoing evaluation for surgical treatment. The clinical advantage of SPECT derives from the pharmacokinetics of brain-binding tracers such as Tc99m-HMPAO and Tc99m-ECD, which become trapped in the brain and thereby preserve the perfusion pattern present at injection. This property is crucial in ictal imaging: clinicians can inject the tracer during or immediately after seizure onset, capturing focal hyperperfusion at the epileptogenic zone, and then stabilize the patient before transport to the scanner. PET plays a more limited role in epilepsy localization largely because many PET perfusion tracers have short half-lives and because practical ictal PET acquisition is difficult; thus PET is most commonly used interictally with F-18 FDG to identify hypometabolic regions that may correspond to seizure networks. The physiologic principle underpinning both SPECT and PET interpretation in epilepsy is state dependence. Epileptogenic regions typically demonstrate increased perfusion and glucose metabolism during the ictal period and reduced perfusion and metabolism interictally. However, interictal abnormalities can be less specific and less reliable for precise localization, particularly in multifocal epilepsy or when network effects produce widespread metabolic alterations. Consequently, ictal SPECT has become the preferred perfusion-based examination for identifying epileptogenic foci in pre-surgical planning, especially when integrated with electroencephalography, MRI, and clinical semiology.[9][10]

Crossed Cerebellar Diaschisis

Crossed cerebellar diaschisis is a noteworthy perfusion-metabolic phenomenon detectable on both PET and SPECT, wherein a supratentorial lesion—most commonly an infarct—produces decreased perfusion and metabolism in the contralateral cerebellar hemisphere. This is attributable to disruption of the corticopontocerebellar pathway, leading to reduced functional input and subsequent downregulation of cerebellar activity. In SPECT, crossed cerebellar diaschisis can be demonstrated with brain-binding perfusion agents such as Tc99m-HMPAO or Tc99m-ECD.[26] In PET, the phenomenon can be visualized either with perfusion agents such as oxygen-15 labeled water or with metabolic agents such as F-18 FDG, reflecting the coupling between flow and metabolism.[27] Although crossed cerebellar diaschisis is benign in itself and does not represent a primary cerebellar lesion, it can provide an important clue to the presence and functional impact of a contralateral supratentorial lesion, particularly when the supratentorial pathology is subtle on structural imaging. The magnitude of diaschisis does not correlate simply with lesion size; rather, lesion location and pathway involvement are more determinative.[26]

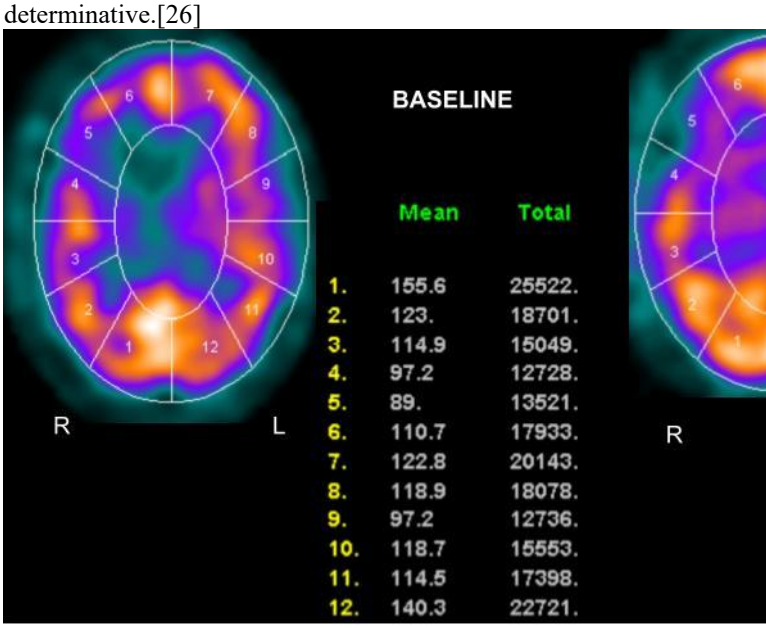

Fig. 3: Unilateral perfusion abnormalities in a patient with Moyamoya disease.

Dementia

Perfusion and metabolic imaging have substantial clinical significance in dementia because characteristic regional patterns can support differentiation among neurodegenerative syndromes, particularly when clinical features overlap or when early disease lacks overt structural atrophy. Because the brain cannot store glucose and because neuronal activity is tightly linked to both glucose utilization and blood flow, cerebral perfusion SPECT with Tc99m-HMPAO or PET metabolic imaging with F-18 FDG can provide complementary pattern information.[28] Distinct syndromes demonstrate reproducible distributions of hypoperfusion or hypometabolism. Frontotemporal dementia, including Pick disease, is often associated with decreased perfusion in the frontal lobes and anterior temporal lobes. Alzheimer dementia more commonly demonstrates reduced perfusion in temporoparietal regions with characteristic sparing of primary sensorimotor cortex, visual cortex, and basal ganglia. Lewy body dementia may share temporoparietal reductions but often differs by involving the sensorimotor strip or occipital lobes, a pattern that can support distinction when clinical features are ambiguous.[15] Huntington disease can show reduced perfusion in the caudate and lentiform nuclei, reflecting preferential involvement of basal ganglia

circuits.[29] In practice, these imaging signatures are interpreted within a clinical framework, but they can refine differential diagnosis, support prognostication, and influence counseling and management planning.

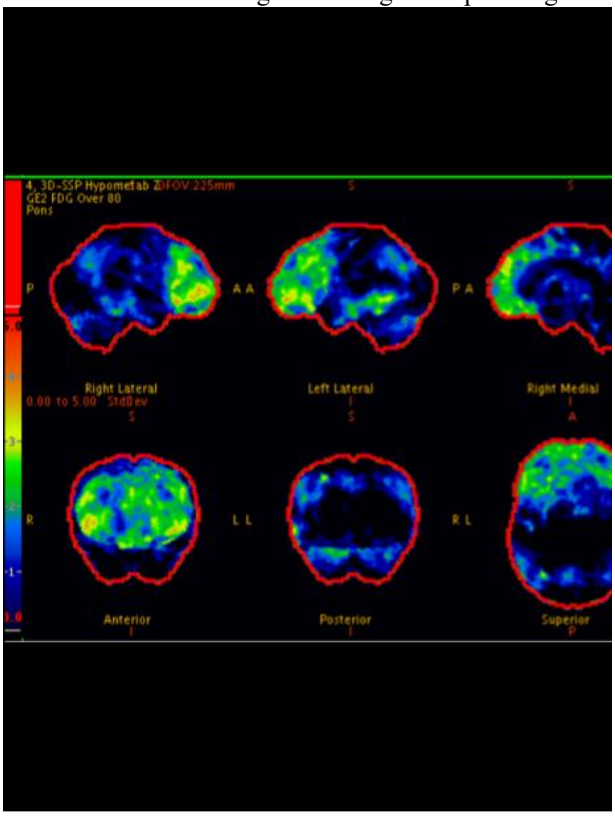

Fig. 4: Frontotemporal Dementia. PET/CT images were obtained following intravenous injection of F18 FDG.

Trauma

In traumatic brain injury (TBI), nuclear medicine perfusion imaging can be clinically significant when neurobehavioral symptoms are disproportionate to structural findings or when CT and MRI fail to reveal lesions that plausibly explain persistent cognitive, affective, or executive dysfunction. SPECT perfusion imaging may identify regions of decreased perfusion that are occult on conventional imaging and that correlate with specific neuropsychiatric symptom clusters, thereby supporting targeted rehabilitation strategies and treatment decisions.[17] This application is not intended to replace structural imaging for acute hemorrhage or fracture detection; rather, it addresses the chronic, functional dimension of TBI, where diffuse axonal injury, network disruption, and microstructural changes may manifest physiologically without clear anatomic correlates. PET imaging in TBI is most commonly performed with F-18 FDG to identify areas of decreased metabolism, leveraging the same physiologic coupling between perfusion and glucose utilization that supports dementia evaluation.[30] By revealing functional deficits that align with clinical symptoms, nuclear imaging can contribute to a more comprehensive understanding of injury burden and guide multidisciplinary care plans, especially in complex, persistent post-traumatic syndromes.[17] Across these clinical domains, nuclear medicine cerebral perfusion imaging derives its significance from a consistent principle: by measuring flow and metabolism rather than structure, it provides a physiologic map that can confirm absence of perfusion in brain death, delineate tissue at risk in stroke, quantify reserve in chronic occlusion, test tolerance to carotid sacrifice, localize seizure foci, reveal network-level diaschisis, characterize dementia patterns, and uncover functional deficits after trauma. The ultimate clinical value lies not merely in generating images, but in translating these physiologic patterns into decision-relevant information that meaningfully alters diagnosis, risk stratification, and therapeutic planning [17].

Enhancing Healthcare Team Outcomes

Optimizing outcomes in nuclear medicine cerebral perfusion imaging requires an intentionally coordinated, interprofessional workflow in which each discipline contributes to patient safety, protocol fidelity, and interpretive validity. Because perfusion and metabolic patterns are sensitive to physiologic state, medication effects, and environmental stimulation, performance quality is not determined solely by scanner technology; rather, it reflects the consistency with which the healthcare team can standardize pre-imaging conditions, maintain patient stability, and document factors that could confound tracer biodistribution. Within this framework, clear communication between radiologists, nuclear medicine physicians, pharmacists, technologists, nurses, and—when needed—anesthesia services is essential to ensure that imaging results remain clinically actionable and reproducible. A core, team-wide responsibility is verifying adherence to pre-procedure restrictions that influence cerebral hemodynamics. Providers should confirm that the patient has abstained from alcohol, caffeine, and nicotine for at least 10 hours prior to the examination, as these substances can meaningfully alter vascular tone, autonomic balance, and neuronal activation patterns, thereby confounding qualitative interpretation and quantitative comparisons.[22][31] This verification should not be treated as a perfunctory checklist item; rather, it should be documented and communicated explicitly, because failure to meet abstinence requirements can reduce specificity, introduce artifactual asymmetries, and in some clinical contexts lead to inappropriate conclusions regarding ischemia, seizure localization, or dementia-related perfusion patterns. Pharmacists and nurses can provide particular value by reviewing medication and substance-use histories, clarifying potential vasoactive exposures, and advising on whether a study should proceed as scheduled or be deferred to preserve diagnostic integrity.

Patient monitoring and physiologic support represent an additional domain where team-based practice directly improves outcomes. In vitally unstable patients who require imaging for urgent decision-making, continuous monitoring of vital signs and pulse oximetry by nursing staff may reduce procedural risk, enabling early recognition of deterioration and timely intervention. Even in stable patients, nursing presence can be important when there is risk of aspiration, altered mental status, or cardiorespiratory comorbidity. The imaging team must ensure that monitoring equipment is compatible with scanner constraints and that clear thresholds exist for terminating the study if instability develops. When clinical instability is anticipated, pre-imaging coordination with the referring service and radiology leadership helps align expectations regarding feasibility, safety, and the potential need for alternative diagnostic approaches. A distinct challenge arises when patients cannot cooperate with the examination due to agitation, cognitive impairment, pain, or neurologic deficits. Because motion can compromise image quality and because patient behavior around the time of injection can alter perfusion patterns, a thoughtful plan is required. In such cases, consultation with anesthesia may benefit the case, particularly when controlled sedation is necessary to permit safe positioning and acquisition. However, the team must recognize that sedating medications may reduce the specificity of imaging findings by altering neuronal activity, cerebral metabolic demand, and vascular tone. This risk reinforces the importance of multidisciplinary decision-making: radiologists and nuclear medicine physicians should communicate the potential interpretive consequences of sedation, pharmacists can advise on sedative selection and interaction risk, and anesthesiologists can tailor dosing to achieve the minimum necessary sedation while preserving physiologic stability. When sedation is required, coordination around timing is critical. Administering sedation after radiotracer delivery reduces the likelihood that drug-induced changes in cerebral activity will confound the tracer distribution intended to represent the baseline or clinical state of interest. Accordingly, it is recommended that sedation be given at least 5 minutes after radiotracer administration, allowing tracer uptake to capture the desired physiologic snapshot before sedation-related hemodynamic or metabolic effects become dominant. This timing strategy depends on precise communication between technologists, nursing staff, and anesthesia providers to ensure that injection, observation, and sedation occur in the correct sequence without delay or confusion. Finally, resuscitative equipment should always be immediately available within the imaging suite, reflecting standard safety preparedness in nuclear medicine environments. The presence of emergency medications, airway equipment, and trained personnel ensures prompt treatment of allergic reactions, vasovagal episodes, respiratory compromise, or unforeseen clinical deterioration, thereby reinforcing a culture of safety that supports both high-quality imaging and patient-centered care [31].

Conclusion:

Nuclear medicine cerebral perfusion imaging occupies a critical role in modern neurodiagnostics by providing physiologic insights that structural modalities cannot capture. Through SPECT and PET, clinicians can visualize cerebral blood flow and metabolism, enabling differentiation between viable and nonviable tissue, localization of epileptogenic zones, and characterization of neurodegenerative patterns. These capabilities are particularly impactful in conditions where management hinges on functional integrity rather than anatomy alone—such as acute stroke, chronic cerebrovascular disease, and complex epilepsy. Pharmacologic challenge testing, notably with acetazolamide, further enhances diagnostic precision by revealing cerebrovascular reserve and identifying territories at heightened ischemic risk. Despite its strengths, successful implementation requires meticulous attention to protocol standardization, patient preparation, and interprofessional collaboration. Radiologists, pharmacists, technologists, and nursing staff must coordinate to minimize confounding variables, ensure safe tracer handling, and maintain procedural integrity. While PET offers superior quantitative performance, logistical constraints often favor SPECT in routine practice. Ultimately, the clinical significance of nuclear perfusion imaging lies in its ability to transform physiologic data into actionable insights that guide treatment decisions, improve prognostication, and support patient-centered care. Continued refinement of protocols and integration with multimodal imaging will further enhance its role in precision neurodiagnostics.

References:

1. Saha GB, MacIntyre WJ, Go RT. Radiopharmaceuticals for brain imaging. Seminars in nuclear medicine. 1994 Oct:24(4):324-49
2. Wintermark M, Sesay M, Barbier E, Borbély K, Dillon WP, Eastwood JD, Glenn TC, Grandin CB, Pedraza S, Soustiel JF, Nariai T, Zaharchuk G, Caillé JM, Dousset V, Yonas H. Comparative overview of brain perfusion imaging techniques. Journal of neuroradiology = Journal de neuroradiologie. 2005 Dec:32(5):294-314
3. Kim S, Mountz JM. SPECT Imaging of Epilepsy: An Overview and Comparison with F-18 FDG PET. International journal of molecular imaging. 2011:2011():813028. doi: 10.1155/2011/813028.

4. Fan AP, An H, Moradi F, Rosenberg J, Ishii Y, Nariai T, Okazawa H, Zaharchuk G. Quantification of brain oxygen extraction and metabolism with [(15)O]-gas PET: A technical review in the era of PET/MRI. NeuroImage. 2020 Oct 15:220():117136. doi: 10.1016/j.neuroimage.2020.117136.
5. Herscovitch P, Markham J, Raichle ME. Brain blood flow measured with intravenous H2(15)O. I. Theory and error analysis. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 1983 Sep:24(9):782-9
6. Islam MM, Tsujikawa T, Mori T, Kiyono Y, Okazawa H. Estimation of arterial input by a noninvasive image derived method in brain H(2)(15)O PET study: confirmation of arterial location using MR angiography. Physics in medicine and biology. 2017 May 8:62(11):4514-4524. doi: 10.1088/1361-6560/aa6a95.
7. Shahhosseini S. PET Radiopharmaceuticals. Iranian journal of pharmaceutical research : IJPR. 2011 Winter:10(1):1-2
8. Vagal AS, Leach JL, Fernandez-Ulloa M, Zuccarello M. The acetazolamide challenge: techniques and applications in the evaluation of chronic cerebral ischemia. AJNR. American journal of neuroradiology. 2009 May:30(5):876-84. doi: 10.3174/ajnr.A1538.
9. la Fougère C, Rominger A, Förster S, Geisler J, Bartenstein P. PET and SPECT in epilepsy: a critical review. Epilepsy & behavior : E&B. 2009 May:15(1):50-5. doi: 10.1016/j.yebeh.2009.02.025.
10. Grünwald F, Menzel C, Pavics L, Bauer J, Hufnagel A, Reichmann K, Sakowski R, Elger CE, Biersack HJ. Ictal and interictal brain SPECT imaging in epilepsy using technetium-99m-ECD. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 1994 Dec:35(12):1896-901
11. Sleight E, Stringer MS, Marshall I, Wardlaw JM, Thrippleton MJ. Cerebrovascular Reactivity Measurement Using Magnetic Resonance Imaging: A Systematic Review. Frontiers in physiology. 2021:12():643468. doi: 10.3389/fphys.2021.643468.
12. Brunberg JA, Frey KA, Horton JA, Deveikis JP, Ross DA, Koeppe RA. [15O]H2O positron emission tomography determination of cerebral blood flow during balloon test occlusion of the internal carotid artery. AJNR. American journal of neuroradiology. 1994 Apr:15(4):725-32
13. Tansavatdi K, Dublin AB, Donald PJ, Dahlin B. Combined Balloon Test Occlusion and SPECT Analysis for Carotid Sacrifice: Angiographic Predictors for Success or Failure? Journal of neurological surgery. Part B, Skull base. 2015 Aug:76(4):249-51. doi: 10.1055/s-0035-1547363.
14. Lee DH, Kang DW, Ahn JS, Choi CG, Kim SJ, Suh DC. Imaging of the ischemic penumbra in acute stroke. Korean journal of radiology. 2005 Apr-Jun:6(2):64-74
15. Yeo JM, Lim X, Khan Z, Pal S. Systematic review of the diagnostic utility of SPECT imaging in dementia. European archives of psychiatry and clinical neuroscience. 2013 Oct:263(7):539-52. doi: 10.1007/s00406-013-0426-z.
16. Sinha P, Conrad GR. Scintigraphic confirmation of brain death. Seminars in nuclear medicine. 2012 Jan:42(1):27-32. doi: 10.1053/j.semnuclmed.2011.07.007.
17. Raji CA, Tarzwell R, Pavel D, Schneider H, Uszler M, Thornton J, van Lierop M, Cohen P, Amen DG, Henderson T. Clinical utility of SPECT neuroimaging in the diagnosis and treatment of traumatic brain injury: a systematic review. PloS one. 2014:9(3):e91088. doi: 10.1371/journal.pone.0091088.
18. Pérez-Iruela JA, Pastor-Fructuoso P, De Gracia-Rodríguez C, Soler-Vigil M, Gómez-Martínez MDV. Adverse reactions to radiopharmaceuticals. Farmacia hospitalaria : organo oficial de expresion cientifica de la Sociedad Espanola de Farmacia Hospitalaria. 2021 Mar 30:45(3):142-149. doi: 10.7399/fh.11669.
19. Davis KM, Ryan JL, Aaron VD, Sims JB. PET and SPECT Imaging of the Brain: History, Technical Considerations, Applications, and Radiotracers. Seminars in ultrasound, CT, and MR. 2020 Dec:41(6):521-529. doi: 10.1053/j.sult.2020.08.006.
20. Lu FM, Yuan Z. PET/SPECT molecular imaging in clinical neuroscience: recent advances in the investigation of CNS diseases. Quantitative imaging in medicine and surgery. 2015 Jun:5(3):433-47. doi: 10.3978/j.issn.2223-4292.2015.03.16.
21. Donohoe KJ, Agrawal G, Frey KA, Gerbaudo VH, Mariani G, Nagel JS, Shulkin BL, Stabin MG, Stokes MK. SNM practice guideline for brain death scintigraphy 2.0. Journal of nuclear medicine technology. 2012 Sep:40(3):198-203. doi: 10.2967/jnmt.112.105130.
22. Juni JE, Waxman AD, Devous MD Sr, Tikofsky RS, Ichise M, Van Heertum RL, Carretta RF, Chen CC, Society for Nuclear Medicine. Procedure guideline for brain perfusion SPECT using (99m)Tc radiopharmaceuticals 3.0. Journal of nuclear medicine technology. 2009 Sep:37(3):191-5. doi: 10.2967/jnmt.109.067850.
23. Meher BR, Agrawal K, Gnanasegaran G. Review of Adverse Reactions Associated with the Use of Common Diagnostic Radiopharmaceuticals. Indian journal of nuclear medicine : IJNM : the official journal of the Society of Nuclear

Medicine, India. 2021 Apr-Jun:36(2):163-167. doi: 10.4103/ijnm.ijnm_219_20.
24. Heiss WD. Radionuclide imaging in ischemic stroke. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2014 Nov:55(11):1831-41. doi: 10.2967/jnumed.114.145003.
25. Ueda T, Sakaki S, Yuh WT, Nochide I, Ohta S. Outcome in acute stroke with successful intra-arterial thrombolysis and predictive value of initial single-photon emission-computed tomography. Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism. 1999 Jan:19(1):99-108
26. Komaba Y, Mishina M, Utsumi K, Katayama Y, Kobayashi S, Mori O. Crossed cerebellar diaschisis in patients with cortical infarction: logistic regression analysis to control for confounding effects. Stroke. 2004 Feb:35(2):472-6
27. Han S, Wang X, Xu K, Hu C. Crossed Cerebellar Diaschisis: Three Case Reports Imaging Using a Tri-Modality PET/CT-MR System. Medicine. 2016 Jan:95(2):e2526. doi: 10.1097/MD.0000000000002526.
28. Bohnen NI, Djang DS, Herholz K, Anzai Y, Minoshima S. Effectiveness and safety of 18F-FDG PET in the evaluation of dementia: a review of the recent literature. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2012 Jan:53(1):59-71. doi: 10.2967/jnumed.111.096578.
29. Hasselbalch SG, Oberg G, Sørensen SA, Andersen AR, Waldemar G, Schmidt JF, Fenger K, Paulson OB. Reduced regional cerebral blood flow in Huntington's disease studied by SPECT. Journal of neurology, neurosurgery, and psychiatry. 1992 Nov:55(11):1018-23
30. Byrnes KR, Wilson CM, Brabazon F, von Leden R, Jurgens JS, Oakes TR, Selwyn RG. FDG-PET imaging in mild traumatic brain injury: a critical review. Frontiers in neuroenergetics. 2014 Jan 9:5():13. doi: 10.3389/fnene.2013.00013.
31. Guedj E, Varrone A, Boellaard R, Albert NL, Barthel H, van Berckel B, Brendel M, Cecchin D, Ekmekcioglu O, Garibotto V, Lammertsma AA, Law I, Peñuelas I, Semah F, Traub-Weidinger T, van de Giessen E, Van Weehaeghe D, Morbelli S. EANM procedure guidelines for brain PET imaging using [(18)F]FDG, version 3. European journal of nuclear medicine and molecular imaging. 2022 Jan:49(2):632-651. doi: 10.1007/s00259-021-05603-w.

.