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Imaging of infection in Nephro-urology: A practical nuclear medicine–focused review

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Infection of the nephro-urological system remains a common and clinically challenging problem, particularly in patients with atypical presentations, prior instrumentation, or underlying immunosuppression. Conventional anatomical imaging plays a central role in identifying obstruction, collections, and complications but is often limited in distinguishing active infection from sterile inflammation or post-interventional change. Nuclear medicine techniques provide complementary functional and molecular information that can clarify disease activity, define extent, and influence patient management. This review presents a practical, nuclear medicine–focused overview of imaging approaches for nephro-urological infection. Established techniques, including ^{99m}Tc-DMSA imaging, radiolabelled white blood cell scintigraphy, and ^{18}F-FDG PET/CT, are discussed with emphasis on tracer biology, physiological renal handling, and common interpretive pitfalls. Clinical scenarios such as acute and chronic pyelonephritis, renal abscess, transplant infection, and device-related infection are used to illustrate appropriate tracer selection and integration with anatomical imaging. Special populations, including paediatric patients, immunocompromised individuals, and renal transplant recipients, are considered, alongside practical algorithms and teaching points aimed at improving clinical applicability. Emerging developments in bacteria-specific tracers, quantitative imaging, and hybrid modalities are also reviewed. By adopting a biologically informed and question-driven approach, nuclear medicine can play an increasingly important role in the diagnosis and management of nephro-urological infection.

Introduction

Infections of the nephro-urological system are common and may range from uncomplicated lower urinary tract infections to severe, life-threatening renal parenchymal disease. While many cases follow a predictable clinical course, others present with atypical features, recurrent symptoms, or an incomplete response to therapy, creating diagnostic and management uncertainty. Accurate differentiation between lower urinary tract infection and true renal involvement is clinically important, as renal parenchymal infection is associated with a higher risk of complications, including abscess formation, renal scarring, chronic kidney disease, and hypertension.

Pyelonephritis represents a severe form of urinary tract infection, involving the renal pelvis, calyces, and renal parenchyma. In its acute bacterial form, diagnosis based solely on clinical and laboratory findings is frequently unreliable. Systemic features such as fever, leukocytosis, and bacteriuria are common to both lower and upper urinary tract infections and do not consistently indicate renal parenchymal involvement. As a result, imaging plays a central role in confirming the diagnosis, defining disease extent, and identifying complications.

Conventional anatomical imaging modalities, including ultrasound and computed tomography, are indispensable for evaluating obstruction, calculi, and perinephric collections. However, these techniques may be limited in their ability to distinguish active infection from chronic change,

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post-interventional inflammation, or non-infectious pathology. Nuclear medicine offers complementary functional and molecular information by exploiting pathophysiological processes such as altered renal function, inflammatory cell recruitment, and increased metabolic activity.

This review provides a practical, nuclear medicine–focused overview of imaging approaches to nephro-urological infection. Emphasis is placed on understanding tracer biology, physiological renal handling, and common interpretive pitfalls, with the aim of guiding appropriate modality selection and enhancing clinical impact. By integrating nuclear medicine findings with anatomical imaging and clinical context, imaging can move beyond detection to meaningfully inform patient management.

Biological basis of infection imaging in the urinary tract

Imaging of infection in the nephro-urological system presents unique biological and technical challenges that distinguish it from infection imaging in most other organ systems. These challenges arise from the complex interplay between host inflammatory responses, pathogen-related processes, and the physiological handling of radiotracers by the kidneys and urinary tract.[1] A clear understanding of these mechanisms is essential for appropriate tracer selection, image acquisition, and interpretation.

Host response to infection and implications for imaging

Most clinically available nuclear medicine techniques for infection imaging are based on visualising the host inflammatory response rather than the pathogen itself.[1] Acute infection is characterized by increased regional perfusion, enhanced capillary permeability, and recruitment of activated inflammatory cells, particularly neutrophils and macrophages.[2] These processes form the biological basis for uptake of radiolabelled white blood cells and metabolically active tracers such as ^{18}F-fluorodeoxyglucose (^{18}F-FDG).

In the urinary tract, this response may be diffuse or focal, depending on the extent of parenchymal involvement, the presence of obstruction, and host immune status.[3] Acute infections tend to demonstrate intense inflammatory activity, whereas chronic or indolent infections may show lower-grade, heterogeneous uptake patterns . Importantly, nuclear imaging reflects biological activity, not simply structural abnormality, allowing detection of infection before overt anatomical changes are evident on conventional imaging.

Pathogen localization versus inflammation

A fundamental limitation of most current nuclear medicine tracers is their lack of specificity for infection. ^{18}F-FDG and radiolabelled leukocytes accumulate at sites of inflammation regardless of whether the underlying cause is infectious, sterile inflammatory, or malignant. This is particularly relevant in nephro-urological imaging, where prior surgery, instrumentation, radiation therapy, and malignancy are common confounders.

Despite this limitation, the pattern, intensity, and distribution of tracer uptake, when interpreted in the appropriate clinical context, often allow meaningful differentiation between infection and non-infectious processes. For example, focal cortical uptake in acute pyelonephritis, linear uptake along an infected ureteric stent, or intense perinephric uptake associated with systemic inflammatory markers may strongly suggest infection, even in the absence of pathogen-specific imaging.

Acute versus chronic infection

The biological distinction between acute and chronic infection has important imaging implications. Acute infections typically demonstrate robust inflammatory cell recruitment and increased glucose metabolism, resulting in conspicuous tracer uptake on ^{18}F-FDG PET/CT and white blood cell scintigraphy. In contrast, chronic infections may exhibit lower-grade uptake, reflecting granulomatous inflammation, fibrosis, or intermittent inflammatory activity.

This distinction is particularly relevant in patients with recurrent urinary tract infections, renal scarring, or post-transplant complications, where differentiating active infection from residual structural change is critical for guiding management. Nuclear medicine techniques, by reflecting ongoing biological activity, offer a functional perspective that complements anatomical imaging.

Renal physiology and tracer handling

The kidneys play a central role in the excretion of many radiotracers, creating inherent challenges for infection imaging in this region. Physiological tracer activity within the renal parenchyma, collecting system, ureters, and urinary bladder may obscure or mimic pathological uptake. This is most pronounced with ^{18}F-FDG, which is filtered by the glomeruli and excreted into the urine, resulting in high background activity.

Understanding normal tracer biodistribution and excretory patterns is therefore essential. Strategies such as hydration, delayed imaging, bladder emptying, and diuretic administration are often employed to improve lesion conspicuity. Importantly, abnormal focal uptake that persists or increases on delayed imaging, or that localizes outside expected excretory pathways, is more likely to represent pathological infection-related activity.

Implications for tracer selection

The biological principles outlined above directly inform tracer selection in clinical practice. Radiolabelled white blood cell imaging remains valuable for detecting active infection, particularly in chronic or device-related infections, due to its relative specificity for inflammatory cell migration. ^{18}F-FDG PET/CT, while less specific, offers high sensitivity, whole-body assessment, and the ability to detect multifocal or unsuspected sites of infection, making it particularly useful in complex or systemic presentations.

Ultimately, no single tracer is ideal for all nephro-urological infections. Optimal imaging requires an understanding of the underlying biology, the clinical question being asked, and the strengths and limitations of each technique. This biologically informed approach underpins the practical application of nuclear medicine in the evaluation of infection in the urinary tract.

Nuclear medicine techniques for imaging nephro-urological infection

Nuclear medicine provides a spectrum of imaging techniques for the evaluation of infection in the nephro-urological system, each grounded in different biological mechanisms and associated with distinct diagnostic strengths and limitations. Unlike anatomical imaging, which primarily depicts structural change, nuclear medicine techniques offer insight into functional and molecular processes, allowing detection of infection-related activity even in the absence of overt morphological abnormalities. The choice of technique should therefore be driven by the clinical question, suspected chronicity of infection, and the need for whole-body versus localized assessment (Table 3).

SPECT–based techniques

^{99m}Tc-dimercaptosuccinic acid (DMSA)

^{99m}Tc-DMSA imaging reflects renal cortical function and integrity through tracer binding to proximal tubular cells with 40% – 65% of the injected dose in the cortex 2 hours post injection.[4] Renal ^{99m}Tc-DMSA scintigraphy is performed 2–3 hours after intravenous administration using a weight-adjusted activity consistent with EANM/SNMMI recommendations (approximately 50 μCi/kg, minimum 300 μCi). Standard acquisition includes posterior planar imaging to assess relative renal size and cortical tracer uptake. High-resolution imaging of each kidney is obtained using magnification or SPECT/CT, which is increasingly preferred in contemporary practice for improved cortical delineation and anatomical correlation. Additional views are acquired selectively when further clarification is required.[5-6] Acute pyelonephritis on DMSA scintigraphy is characterized by focal or multifocal cortical uptake defects without associated loss of renal volume, reflecting active inflammation rather than permanent parenchymal damage.[5] In the setting of infection, areas of reduced or absent tracer uptake correspond to regions of cortical inflammation, oedema, or permanent damage. DMSA scintigraphy remains the reference standard for evaluating renal cortical involvement and scarring, particularly in paediatric patients with acute pyelonephritis or recurrent urinary tract infections.[7] It offers superior sensitivity compared with renal ultrasonography and excretory urography for detecting both acute cortical inflammation and chronic sequelae, making it the preferred imaging modality for diagnosis and follow-up. Ultrasound retains a complementary role, useful for characterizing cortical defects identified on DMSA and for detecting coexisting obstructive uropathies.[8-9]

From an infection-imaging perspective, the principal limitation of ^{99m}Tc-DMSA lies in its lack of specificity for active infection. Reduced cortical uptake may persist long after resolution of acute inflammation, reflecting irreversible scarring rather than ongoing infection. Consequently, ^{99m}Tc-DMSA is best viewed as a tool for assessing the consequences of infection rather than for differentiating active disease from chronic change. In adult practice, its role is therefore more selective, often limited to complex or recurrent infections where long-term functional assessment is required.

Radiolabelled White Blood Cell Scintigraphy

The regulatory approval of indium-111 oxine for autologous leukocyte labelling in the 1980s was a landmark event that advanced nuclear medicine's ability to image infectious processes. This advance provided a specific and reliable method to localize sites of active infection, facilitating accurate diagnosis in a wide range of clinical scenarios, including complicated urinary tract infections, renal abscesses, and device-associated infections.[10] Indium-111–labelled leukocyte imaging established a foundation for modern functional imaging of infection and continues to inform contemporary practice. Despite the proven utility of ^{111}In-oxine–labelled leukocyte scintigraphy in infection and inflammation imaging, clinical practice has gradually shifted toward alternative agents. ^{99m}Tc-HMPAO has largely superseded indium-based labelling because of its advantageous imaging characteristics, greater accessibility, lower cost, and comparatively reduced radiation dose.[11-13] In gamma camera–based leukocyte imaging, standard protocols typically include an initial scan at 30–60 minutes, a delayed acquisition at 3–4 hours, and a final late image at 20–24 hours. This sequential approach permits clearance of circulating tracer from the blood pool, enhancing lesion contrast and improving visualization. For renal infection, imaging with ^{111}In-oxine–labelled leukocytes may be advantageous due to reduced elution of the radiotracer and its metabolites from the labelled cells, leading to lower nonspecific activity within the gastrointestinal and urinary tracts.[14-15] Radiolabelled white blood cell (WBC) scintigraphy using ^{99m}Tc-HMPAO or ^{111}In-oxine directly exploits the migration of activated leukocytes to sites of infection. This characteristic makes WBC scintigraphy particularly useful in chronic, low-grade, or device-related infections, where anatomical imaging and ^{18}F-FDG PET/CT may yield equivocal results. Although both radiolabelled leukocyte scintigraphy and ^{18}F-FDG PET/CT are established tools for infection imaging, the literature presents conflicting evidence regarding their relative specificity and diagnostic superiority across different infectious scenarios.[16-18]

In nephro-urological infection, WBC scintigraphy can aid in identifying renal parenchymal infection, perinephric abscesses, and infection associated with urinary devices or foreign bodies. However, the technique has several practical limitations, including labour-intensive radiolabelling, the need for blood handling, limited spatial resolution, and reduced sensitivity in

acute infections dominated by non-cellular inflammatory mechanisms.[19] Additionally the study may be challenging to perform in children and leukopaenic patients. Interpretation may also be challenging in the presence of physiological renal activity and bowel overlap, underscoring the importance of delayed and, where available, SPECT/CT imaging.

^{67}Ga-Citrate

^{67}Ga-citrate (^{67}Ga) accumulates at sites of infection through a combination of increased vascular permeability, binding to transferrin and lactoferrin, and uptake by inflammatory cells. In efforts to distinguish upper from lower urinary tract infection, Hurwitz and colleagues demonstrated that renal accumulation of ^{67}Ga was associated with pyelonephritis, achieving a diagnostic accuracy of 86%.[20] In renal transplant recipients with polycystic kidney disease, ^{67}Ga scintigraphy proved effective in localizing the origin of recurrent or ongoing urinary tract infection, successfully differentiating native from transplant kidney involvement across the study population.[21-22] Beyond its role in differentiating upper from lower urinary tract infection, ^{67}Ga scintigraphy has demonstrated utility in a range of infective pathologies of the urinary tract.[23] Marked renal tracer accumulation, particularly when observed in patients presenting with fever, enlarging kidneys, and declining renal function, is highly suggestive of renal parenchymal inflammatory involvement, including entities such as renal parenchymal malakoplakia.[24] In patients undergoing prolonged antimicrobial treatment, serial ^{67}Ga imaging may show gradual resolution of abnormal renal uptake, offering an objective means of assessing treatment response and informing therapy duration. Although largely supplanted by PET-based techniques, it retains a limited role in selected clinical scenarios, particularly in centres without PET availability or in the evaluation of chronic infection and renal transplant recipients.[25]

Its disadvantages include prolonged imaging protocols, relatively poor spatial resolution, and higher radiation dose. As such, ^{67}Ga-citrate is now best regarded as a niche or fallback modality, rather than a first-line imaging technique.

Positron Emission Tomography (PET)-Based Imaging

^{18}F-FDG PET/CT

^{18}F-FDG PET/CT has become the dominant PET-based technique for infection imaging, owing to its high sensitivity, superior spatial resolution, and ability to perform whole-body assessment in a single examination.[26-27] ^{18}F-FDG uptake reflects increased glucose metabolism in activated inflammatory cells, particularly neutrophils and macrophages, making it highly responsive to acute and subacute infection.[28]

In the context of nephro-urological infection, ^{18}F-FDG PET/CT is especially valuable in complicated infections, renal transplant recipients, patients with fever of unknown origin, and situations where multifocal or extra-renal infection is suspected [36–38]. In a study primarily evaluating the role of FDG PET/CT in patients with pyrexia of unknown origin, renal infection was identified in 5 of 112 cases.[29] In a systematic review and meta-analysis of patients with suspected renal cystic infection, ^{18}F-FDG PET/CT was shown to be effective in identifying infected cysts in individuals with polycystic kidney disease.[30-31] A 4-point scoring scale has been proposed to build a more systematic and standardized toll for 18F-FDG PET/CT evaluation of suspected cyst infection[32] (Table 1). Demuynck et al. validated the use of a 4-point scale comparing the uptake of ^{18}F-FDG around infected cysts with the uptake in the hepatic parenchyma. A score of ≥3 was associated with a significantly higher risk of cyst infection compared with scores 1 and 2 (OR = 6.03, P = .014).[31] The resulting sensitivity and specificity of the 4-point scale were 64% (Clopper–Pearson 95% CI 30%–89%) and 78% (95% CI 62%–89%), respectively.[31] The technique is also useful for assessing the extent of disease and monitoring response to therapy.

Table 1 Visual scoring system for [^{18}F]-FDG uptake around renal cysts.[32]

Score	FDG uptake intensity	Interpretation
1	cyst ≤ mediastinal bloodpool	Low likelihood of infection
2	>bloodpool, but ≤liver	Low likelihood of infection
3	slightly >liver	High likelihood of infection
4	largely >liver	High likelihood of infection

However, interpretation of ^{18}F-FDG PET/CT in the urinary tract is complicated by physiological tracer excretion, which may obscure lesions or mimic pathological uptake Optimized patient preparation, delayed imaging, and careful correlation with CT findings are therefore essential. While ^{18}F-FDG PET/CT lacks specificity for infection, its sensitivity and broad field of view often make it the most informative modality in complex clinical scenarios.

^{18}F-FDG–labelled White Blood Cells

PET/CT using ^{18}F-FDG–labelled autologous leukocytes has been explored as a method to combine the sensitivity of PET imaging with the specificity of leukocyte-based infection targeting. This approach may improve localization of infectious foci while reducing nonspecific uptake related to sterile inflammation. In a cohort of 21 patients with suspected or confirmed infection, PET/CT demonstrated high sensitivity and specificity for detecting infectious foci. Notably, in this small series, the absence of focal leukocyte uptake on PET/CT was associated with a negative predictive value of 100%.[33] In the context of renal infection, ^{18}F-FDG–labelled autologous leukocyte PET/CT may offer particular value by improving lesion localization and specificity in the setting of high physiological urinary FDG activity, although experience remains limited. Overall, despite the limited number of published studies, ^{18}F-FDG–WBC PET or PET/CT has shown

promising diagnostic accuracy across a range of infectious conditions; however, further large-scale studies are needed to clarify its precise clinical utility.[34-35] Reported applications to date include the detection of infected renal cysts, evaluation of peripancreatic collections in pancreatitis, identification of prosthesis-related infections, and exclusion of osteomyelitis.[34-35]

PET/magnetic resonance imaging

Hybrid PET/MR imaging combines the molecular sensitivity of PET with the superior soft-tissue contrast of MRI, offering potential advantages in the evaluation of nephro-urological infection.[36] Reduced radiation exposure and improved characterization of soft-tissue and pelvic pathology make PET/MR an attractive option, particularly in younger patients and in those requiring repeated imaging.

Although clinical experience remains limited and availability restricted, PET/MR may be particularly useful in renal transplant imaging and in differentiating infection from post-surgical or post-radiation changes. Further studies are needed to define its precise role in routine clinical practice.

Choosing the appropriate technique

No single nuclear medicine technique / tracer is optimal for all nephro-urological infections. Technique selection should be guided by the clinical question, suspected acuity or chronicity of infection, patient characteristics, and local expertise and availability. In many cases, nuclear medicine imaging is most effective when integrated into a multimodality diagnostic pathway, complementing ultrasound, CT, and MRI rather than replacing them.[37]

Clinical applications

The clinical value of nuclear medicine imaging in nephro-urological infection lies in its ability to address diagnostic uncertainty, characterize disease activity, and influence patient management. Rather than serving as a first-line investigation, nuclear techniques are most effective when applied selectively to well-defined clinical questions. The following sections highlight key clinical scenarios where nuclear medicine imaging provides incremental value beyond conventional anatomical imaging.

Acute and complicated pyelonephritis

Pyelonephritis refers to a serious infectious process affecting the renal collecting system and extending into the renal parenchyma. In its acute bacterial form, the condition poses significant diagnostic challenges across multiple disciplines.[38] Its clinical importance is underscored by the risk of long-term sequelae, including chronic kidney disease, and the potential association between acute renal infection and the subsequent development of hypertension.[39] Reliance on clinical and laboratory findings alone is frequently inadequate. Common indicators such as fever, leukocytosis, and bacteriuria fail to reliably discriminate between lower urinary tract infection and true renal parenchymal involvement, emphasizing the need for imaging approaches that can accurately localize and characterize infection.

Most cases of uncomplicated acute pyelonephritis are diagnosed clinically and managed without advanced imaging. Serial contrast-enhanced CT performed to assess treatment response was unable to reliably identify persistent or residual infection. In a prospective study of patients with upper urinary tract infection, Soulen and colleagues demonstrated that abnormalities in renal size and enhancement frequently persist for weeks to months after clinical resolution, highlighting that renal scarring in adults with urinary tract infection is likely under-recognized.[39-41] Nuclear medicine imaging becomes relevant in complicated presentations, including severe sepsis, atypical clinical courses, immunocompromised patients, or failure to respond to appropriate antimicrobial therapy.

In this setting, ^{18}F-FDG PET/CT may demonstrate focal or multifocal cortical uptake corresponding to areas of active infection, even when CT findings are subtle or nonspecific.[39] Whole-body imaging allows detection of extra-renal infectious foci, which may alter management in patients with systemic symptoms. Nuclear imaging may also assist in identifying complications such as abscess formation or perinephric extension, particularly when conventional imaging is inconclusive.

Chronic and recurrent urinary tract infection

Patients with recurrent or chronic urinary tract infection present a diagnostic challenge, particularly when structural abnormalities persist despite clinical improvement. Differentiating active infection from residual post-inflammatory change or scarring is critical to avoid unnecessary prolonged antimicrobial therapy.

Radiolabelled white blood cell scintigraphy is particularly valuable in this context due to its relative specificity for active infection. Persistent or increasing tracer accumulation on delayed imaging supports ongoing inflammatory activity, whereas absent or decreasing uptake favours inactive disease. ^{18}F-FDG PET/CT may also be useful, particularly when disease extent is uncertain or multifocal involvement is suspected, although interpretation must be cautious in the presence of chronic inflammatory or malignant conditions.

Renal and perinephric abscess

Renal and perinephric abscesses are typically identified on contrast-enhanced CT; however, nuclear medicine imaging may play a complementary role in selected cases.[42] Early abscess formation typically appears as poorly defined, non-enhancing regions of reduced attenuation. With maturation, abscesses evolve into well-circumscribed, complex cystic lesions containing necrotic or fluid components and surrounded by a characteristic peripheral enhancing rim.[43] MRI serves as a valuable adjunct in the evaluation of renal

abscesses, particularly when iodinated contrast is contraindicated. Abscesses typically demonstrate low signal intensity on T1-weighted images, high signal on T2-weighted sequences, restricted diffusion on diffusion-weighted imaging, and peripheral enhancement following gadolinium administration, aiding differentiation from phlegmon or non-infectious cystic lesions.[44-45] ^{18}F-FDG PET/CT can assist in delineating the extent of inflammatory activity, identifying satellite lesions, and assessing response to therapy, particularly in patients managed conservatively or those with persistent symptoms despite drainage. Functional imaging may be especially helpful when anatomical findings lag behind clinical improvement or when residual collections raise uncertainty regarding ongoing infection.

Renal transplant infection

Transplantation has become a cornerstone therapy for end-stage organ disease, with kidney transplantation demonstrating consistently high success since the landmark operation by Joseph Murray in the mid-20th century. Nevertheless, lifelong immunosuppression, while essential for graft survival, substantially increases susceptibility to infection and malignancy, which remain among the principal causes of death in renal transplant recipients.[46] Over one-fifth of kidney transplant recipients develop at least one infectious complication within the first year following transplantation.[47] Infection remains a major cause of morbidity in renal transplant recipients, where clinical presentation may be atypical and conventional imaging findings subtle.[48-50] Nuclear medicine imaging plays a particularly important role in this population.

^{18}F-FDG PET/CT is valuable in evaluating suspected transplant pyelonephritis, peri transplant infection, and fever of unknown origin. Its whole-body capability allows identification of extra-renal infectious sites, which is critical in immunosuppressed patients. Interpretation requires careful correlation with clinical data, as rejection, drug toxicity, and malignancy may produce overlapping imaging features.

Radiolabelled white blood cell imaging may be considered in selected cases to improve specificity, particularly when ^{18}F-FDG PET/CT findings are equivocal.

Infection associated with urinary devices and obstruction

Urinary devices, including ureteric stents, nephrostomy tubes, and long-term catheters, are common sources of persistent or recurrent infection. With the rise in utilization of ureteral stents and other devices, the incidence of complicated urinary tract infection, which is one of the complications of ureteral stent, also increased.[51-52] Differentiating colonization from clinically significant infection is often challenging.

Linear or focal tracer uptake along the course of a device on ^{18}F-FDG PET/CT or WBC imaging may support active infection, particularly when associated with systemic inflammatory markers.

Fever of unknown origin with suspected urinary tract source

^{18}F-FDG PET/CT is increasingly used in the evaluation of fever of unknown origin, where a urinary source is suspected but not confirmed by conventional imaging.[53] Detection of occult renal or perinephric infection, as well as extra-renal foci, may substantially alter diagnostic and therapeutic pathways. In this context, the strength of PET lies in its global assessment of inflammatory activity, rather than detailed characterization of a single lesion.

Impact on clinical management

Across these clinical scenarios, nuclear medicine imaging contributes most when it answers a specific management-relevant question: Is the infection active? How extensive is the disease? Is there an alternative or additional source of infection? When used judiciously, nuclear imaging can reduce diagnostic uncertainty, guide targeted intervention, and support rational antimicrobial stewardship.

Practical aspects of imaging and interpretation

Successful nuclear medicine imaging of nephro-urological infection requires careful attention to patient preparation, acquisition protocols, and image interpretation. Physiological tracer handling by the kidneys and urinary tract introduces unique challenges that can significantly affect diagnostic accuracy. A structured and standardized approach is therefore essential to maximize the clinical value of these studies.

Patient preparation

Appropriate patient preparation is a critical determinant of image quality, particularly for PET-based techniques.

For ^{18}F-FDG PET/CT, adequate hydration before and after tracer administration is essential to promote urinary clearance and reduce tracer retention within the collecting system and bladder.[54] Patients should be encouraged to void frequently prior to imaging. In selected cases, particularly when evaluating the renal pelvis, ureters, or peri vesical regions, the use of forced diuresis with intravenous furosemide may be considered to further reduce urinary activity.[55-56]

Standard fasting protocols should be followed to minimize nonspecific muscular and soft-tissue uptake. In diabetic patients, glucose control should be optimized to ensure reliable ^{18}F-FDG biodistribution. For gamma camera–based studies, preparation requirements are generally less stringent, although hydration remains important to facilitate tracer clearance and improve lesion conspicuity.

Acquisition protocols

SPECT-based imaging

For DMSA imaging, delayed planar and SPECT or SPECT/CT acquisitions are recommended to accurately assess cortical tracer

distribution and identify focal defects.[6] SPECT/CT improves anatomical localization and differentiation of true cortical abnormalities from attenuation or superimposition artifacts.

In radiolabelled white blood cell scintigraphy, acquisition at multiple time points is essential. Early and delayed imaging allows assessment of tracer accumulation over time, helping to distinguish infection from physiological or nonspecific uptake.[14] SPECT/CT is strongly recommended where available, particularly in the retroperitoneum and pelvis, to improve localization and diagnostic confidence.

PET-based imaging

For ^{18}F-FDG PET/CT, whole-body imaging from skull base to mid-thigh is generally appropriate, particularly in patients with systemic symptoms or fever of unknown origin. In nephro-urological infection, inclusion of delayed or dedicated pelvic imaging can be valuable to assess tracer persistence or clearance within the urinary tract (Ref).

Low-dose CT is typically sufficient for attenuation correction and anatomical correlation, although contrast-enhanced CT may be helpful in selected cases to better delineate abscesses or complex anatomy. PET/MR protocols, where available, should be tailored to include sequences optimized for soft-tissue infection and transplant evaluation.

Interpretation principles

Interpretation of nuclear medicine studies in nephro-urological infection requires integration of tracer distribution patterns with clinical, laboratory, and anatomical imaging findings.

Key principles include:

- Differentiating physiological excretory activity from pathological uptake
- Assessing uptake pattern, symmetry, and intensity
- Evaluating changes between early and delayed images

Focal or asymmetric tracer uptake within the renal cortex, perinephric tissues, or along urinary devices is more suggestive of infection than diffuse, symmetric activity. Persistence or increase of uptake on delayed imaging supports pathological involvement, whereas clearance over time favours physiological excretion.

In ^{18}F-FDG PET/CT, correlation with CT findings is essential. Uptake corresponding to structural abnormalities such as collections, stranding, or device interfaces increases diagnostic confidence. Conversely, uptake without anatomical correlation should be interpreted cautiously, particularly in post-operative or post-radiation settings.

Common pitfalls and sources of error

Several pitfalls are specific to nephro-urological infection imaging (Table 2):

- Physiological urinary activity mimicking disease
- Post-surgical and post-instrumentation inflammation, which may persist for weeks to months
- Malignancy-associated ^{18}F-FDG uptake, particularly in urothelial and renal tumours
- Partial-volume effects in small cortical lesions

Awareness of recent interventions, catheterization, stent placement, or biopsies is essential to avoid false-positive interpretations. In equivocal cases, correlation with laboratory markers of infection and follow-up imaging may be necessary.

Reporting considerations

Structured reporting improves clarity and clinical utility. Reports should explicitly address:

- Presence or absence of imaging findings consistent with infection
- Location and extent of disease
- Degree of diagnostic confidence
- Limitations related to tracer excretion or technical factors

Where appropriate, reports should comment on how the findings influence clinical management, such as guiding antimicrobial therapy, prompting drainage, or excluding active infection.

Integrating nuclear medicine findings into clinical decision-making

The value of nuclear medicine imaging lies not only in detection but in its ability to influence patient management. Functional and molecular imaging can clarify equivocal findings, identify unsuspected sites of infection, and help differentiate active infection from chronic or post-treatment change. Close collaboration with referring clinicians is therefore essential to ensure appropriate utilization and interpretation of results (Fig. 1, Fig. 2).

Nuclear medicine in the multimodality imaging pathway

Imaging of nephro-urological infection is inherently multimodal, with ultrasound, CT, and MRI forming the foundation of initial anatomical assessment. Nuclear medicine techniques are most effective when integrated into this diagnostic pathway to address specific unresolved clinical questions, rather than as standalone investigations.

Ultrasound is typically the first-line modality, particularly for the evaluation of hydronephrosis, obstruction, and perinephric collections. Contrast-enhanced CT remains the mainstay for defining anatomy, identifying abscess formation, and detecting complications such as emphysematous infection. MRI provides an alternative in patients with contraindications to iodinated contrast or where superior soft-tissue characterization is required.

Nuclear medicine imaging adds value when conventional imaging is equivocal, discordant with clinical findings, or

Table 2 Nuclear medicine tracers for nephro-urological infection: indications, strengths, and limitations.

Tracer / Technique	Primary indications	Key strengths	Key limitations / pitfalls
^{99m}Tc-DMSA scintigraphy	• Acute pyelonephritis in children • Assessment of renal cortical involvement • Detection of post-infectious renal scarring	• High sensitivity for cortical defects • Established reference standard in paediatrics • Low radiation dose	• Limited role in adults • Reduced sensitivity in early infection • Cannot reliably distinguish acute inflammation from established scarring without follow-up
Radiolabelled white blood cell scintigraphy (^{99m}Tc-HMPAO or ^{111}In-oxine)	• Suspected renal or peri-renal infection • Device-related infection • Differentiation of infection from sterile inflammation	• High specificity for active infection • Useful in chronic or low-grade infection • SPECT/CT improves anatomical localization	• Time-consuming and labour-intensive • Reduced sensitivity in immunocompromised patients • Limited spatial resolution
^{67}Ga-citrate scintigraphy	• Selected cases in resource-limited settings • Chronic infection when other modalities unavailable	• Wide availability in some regions • Historically validated for infection imaging	• Low spatial resolution • Long imaging protocols • Largely supplanted by FDG PET/CT
^{18}F-FDG PET/CT	• Complicated or atypical infection • Fever of unknown origin • Immunocompromised or transplant patients • Assessment of disease extent	• High sensitivity • Whole-body evaluation in a single study • Excellent anatomical correlation with CT	• Limited specificity (uptake in sterile inflammation, malignancy) • Physiological urinary excretion may obscure lesions • Higher cost and radiation dose
Emerging bacteria-specific PET tracers	• Research and early clinical studies • Differentiation of bacterial infection from inflammation	• Potential for improved specificity • May enable precision infection imaging	• Limited clinical availability • Organism-specific uptake variability • Currently investigational

Table 3 Common pitfalls in nuclear imaging of nephro-urological infection and practical solutions.

Pitfall	Underlying Cause	Practical Solution
Physiological urinary 18F-FDG activity mimicking infection	Renal filtration and urinary excretion	Hydration, frequent voiding, delayed imaging, diuretic administration
Difficulty localizing uptake on planar imaging	Superimposition of renal, bowel, and pelvic structures	Use SPECT/CT or PET/CT whenever available
False-positive 18F-FDG uptake post-surgery or instrumentation	Sterile inflammation	Correlate with timing of intervention; consider WBC scintigraphy or follow-up
Inability to differentiate acute infection from chronic scarring	Persistent cortical defects	Use 18F-FDG PET/CT or WBC imaging to assess biological activity
Underestimation of low-grade or chronic infection	Reduced inflammatory cell recruitment	Prefer WBC scintigraphy over 18F-FDG PET/CT
Missed multifocal or extra-renal infection	Limited field of view on conventional imaging	Whole-body 18F-FDG PET/CT
18F-FDG uptake related to malignancy	Overlapping metabolic pathways	Correlate with CT/MRI morphology and clinical history
Low sensitivity in acute infections with WBC imaging	Predominantly humoral inflammatory response	Prefer 18F-FDG PET/CT in early or acute disease
Overinterpretation of symmetric renal uptake	Normal physiological variation	Assess asymmetry, focality, and delayed persistence
Technical variability in image quality	Suboptimal preparation or acquisition	Standardized protocols and structured reporting

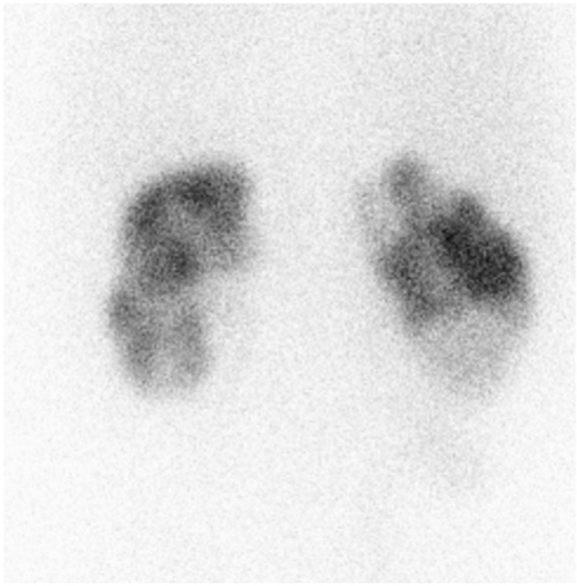

Fig. 1 A 47 year old female with pyelonephritis on day 2 of antibiotics. Ultrasound examination demonstrated severe bilateral hydronephrosis (right > left), vesicoureteric junction stenosis and calcified bladder. Following 4mCi of ^{99m}Tc-DMSA static images were acquired 3 hours post injection. Both kidneys demonstrate inhomogeneous tracer accumulation with wedge-shaped defects in keeping with acute pyelonephritis. The split renal function was calculated as 49% and 51% for the right and left kidneys, respectively.

unable to distinguish active infection from chronic or post-interventional change. By depicting biological activity, functional and molecular imaging can clarify disease status, determine extent, and identify unsuspected sites of infection.

^{18}F-FDG PET/CT is particularly valuable in complex clinical scenarios requiring whole-body assessment, such as fever of unknown origin, immunocompromised patients, and renal transplant recipients. Radiolabelled white blood cell scintigraphy may be preferred when specificity for infection is paramount, particularly in chronic or device-related infections. ^{99m}Tc-DMSA remains useful for assessing renal cortical integrity and long-term sequelae, especially in paediatric practice.

Effective integration requires close collaboration between nuclear medicine physicians, radiologists, and referring clinicians, with shared understanding of the strengths and limitations of each modality. A question-driven approach to imaging selection optimizes diagnostic yield, avoids unnecessary investigations, and enhances clinical impact.

Special considerations

Imaging of nephro-urological infection requires adaptation of nuclear medicine techniques to specific patient populations and clinical environments. Differences in physiology, immune status, prior intervention, and resource availability all influence tracer selection, acquisition protocols, and interpretation. Awareness of these factors is essential to ensure accurate diagnosis and meaningful clinical impact.

Paediatric patients

Paediatric nephro-urological infection presents distinct diagnostic challenges, with a particular emphasis on identifying renal parenchymal involvement and preventing long-term sequelae such as cortical scarring. ^{99m}Tc-DMSA imaging remains central to this evaluation and is widely regarded as the reference standard for assessing renal cortical integrity following acute pyelonephritis.

In the acute setting, DMSA may demonstrate focal or diffuse cortical defects corresponding to inflammatory involvement, while delayed imaging can help identify permanent scarring. Interpretation must take into account the timing of imaging relative to infection, as transient defects may resolve with appropriate therapy. In selected cases of recurrent or atypical infection, nuclear medicine imaging may complement ultrasound and voiding cystourethrography by providing functional information that influences long-term management.

Radiation dose optimization is a critical consideration in children. Imaging protocols should adhere to the "as low as reasonably achievable" principle, and PET-based techniques should be reserved for highly selected cases where the expected diagnostic benefit outweighs radiation exposure.

Immunocompromised patients

Immunocompromised patients, including solid organ transplant recipients, patients with malignancy, and those receiving immunosuppressive therapies, often present with atypical or attenuated clinical features of infection. Laboratory markers may be unreliable, and conventional imaging findings may be subtle or nonspecific.

In this population, ^{18}F-FDG PET/CT offers significant advantages due to its high sensitivity and ability to detect multifocal or unexpected sites of infection in a single examination. Whole-body assessment is particularly valuable in patients with fever of unknown origin or suspected disseminated infection. However, interpretation requires careful consideration of confounding factors, including malignancy, drug-related inflammation, and graft rejection in transplant recipients.

Radiolabelled white blood cell scintigraphy may be useful in selected cases to improve specificity, particularly when ^{18}F-FDG PET/CT findings are equivocal or when distinguishing infection from sterile inflammatory processes is critical for management decisions.

Resource-limited settings

In many regions, access to advanced hybrid imaging modalities such as PET/CT or PET/MR may be limited. In such settings, gamma camera–based techniques continue to play an important role in the evaluation of complex or unresolved infections.

Radiolabelled white blood cell scintigraphy and, in selected cases, ^{67}Ga-citrate imaging may provide valuable functional information that complements ultrasound and CT. A pragmatic, context-sensitive approach to tracer selection and protocol optimization is required to maximize diagnostic yield while minimizing cost and resource utilization. Importantly, the principles of biologically informed interpretation remain applicable regardless of imaging platform.

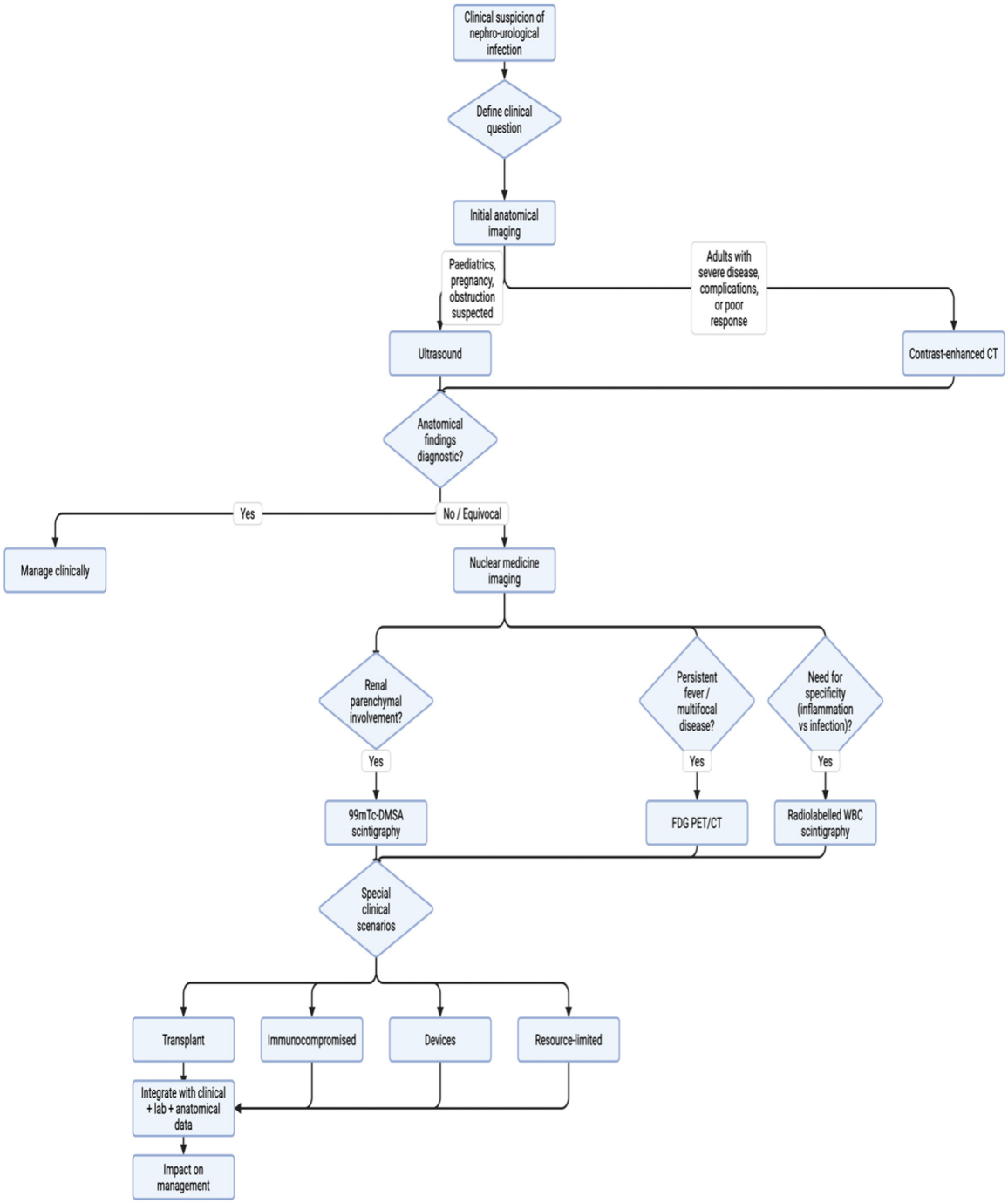

Fig. 2 Practical Imaging Algorithm for Suspected Nephro-Urological Infection. Stepwise diagnostic algorithm integrating clinical presentation, conventional anatomical imaging, and nuclear medicine techniques. Selection of imaging modality is guided by disease acuity, suspected chronicity, presence of devices or transplantation, and availability of imaging resources. Nuclear medicine imaging is positioned as a problem-solving and management-directing tool in equivocal or complex clinical scenarios.

Implications for training and practice

The expanding role of nuclear medicine in infection imaging underscores the need for focused training in tracer biology, multimodality image interpretation, and interdisciplinary collaboration. Familiarity with common pitfalls and an understanding of clinical decision-making pathways are essential for nuclear medicine physicians to provide meaningful and actionable reports.

Emerging concepts and future directions

Advances in molecular imaging are expanding the potential role of nuclear medicine in the evaluation of infection, including within the nephro-urological system. While current clinical practice relies largely on non-specific inflammatory tracers, ongoing research is focused on

improving specificity for infection, refining quantitative assessment, and integrating imaging more directly into therapeutic decision-making.

Bacteria-specific or novel radiotracers

One of the most promising developments in infection imaging is the emergence of bacteria-specific radiotracers designed to target microbial metabolism or cell-wall components. These agents aim to differentiate true infection from sterile inflammation, a limitation of existing tracers such as ^{18}F-FDG. Early clinical and preclinical studies suggest potential utility in distinguishing bacterial infection from post-surgical or inflammatory change, although validation in nephro-urological infection remains limited.

Challenges to widespread adoption include variability in bacterial species, differences in tracer uptake across organisms, and regulatory and logistical hurdles. Nevertheless, bacteria-targeted imaging represents an important future direction with potential to significantly enhance diagnostic confidence.

Derlin and colleagues investigated whether CXCR4-targeted PET imaging using ^{68}Ga-Pentixafor, in conjunction with diffusion-weighted MRI, could enable in vivo detection of leukocyte-driven inflammation in renal allografts. Using this multimodality approach, acute allograft infection and urinary tract infection were reliably identified, with PET findings closely matching MRI diffusion abnormalities and confirmed by histopathology.[57] To date, this remains an isolated report, and further studies are required to validate these findings, define diagnostic accuracy, and explore the applicability of CXCR4-directed imaging in other renal and nephro-urological infectious processes.

FAP-targeted PET imaging has been applied to the evaluation of renal fibrosis, demonstrating a stepwise increase in tracer uptake with advancing disease severity.[58] This observation is clinically important, as fibrosis represents a final common pathway of many chronic kidney disorders.[59] By distinguishing active reparative processes from established fibrotic change, FAPI-based PET imaging may help define the most appropriate therapeutic window and potentially avert progression from acute injury to irreversible chronic or end-stage renal disease.

Quantitative imaging and therapy response assessment

Quantitative PET parameters, including standardized uptake values and volumetric metrics, offer opportunities to move beyond qualitative interpretation. In nephro-urological infection, quantitative assessment may aid in evaluating disease burden, monitoring response to antimicrobial therapy, and guiding treatment duration.

Standardization of acquisition protocols and interpretation thresholds is essential before quantitative metrics can be reliably incorporated into routine practice. Future studies focusing on outcome-based validation will be critical to define the role of quantitative imaging in infection management.

Hybrid and multimodality imaging

Hybrid imaging platforms, particularly PET/MR, offer potential advantages by combining molecular sensitivity with superior soft-tissue characterization and reduced radiation exposure. In nephro-urological infection, PET/MR may be particularly useful in transplant recipients, paediatric patients, and those requiring repeated imaging.

Beyond hardware integration, closer conceptual integration of nuclear medicine findings with radiological and clinical data will further enhance diagnostic accuracy and clinical relevance.

Toward infection theranostics

Although still largely conceptual, the application of theranostic principles to infection imaging is an emerging area of interest. Molecular imaging may eventually play a role in selecting patients for targeted antimicrobial strategies, monitoring biofilm-associated infection, or guiding interventional procedures.

While true theranostic approaches in infection remain in early stages, the increasing sophistication of molecular imaging supports a future role for nuclear medicine in precision infection management.

Summary and key teaching points

Imaging of infection in the nephro-urological system is complex and frequently requires a multimodal approach. Nuclear medicine techniques offer unique advantages by visualizing functional and molecular aspects of infection that are not accessible through anatomical imaging alone.

Understanding tracer biology, physiological renal handling, and disease-specific uptake patterns is essential for accurate interpretation. When applied selectively and integrated into clinical decision-making pathways, nuclear medicine imaging can clarify disease activity, define extent of infection, and directly influence patient management.

Ongoing advances in molecular imaging, quantitative assessment, and hybrid technologies are likely to further expand the role of nuclear medicine in infection imaging. A practical, biologically informed, and question-driven approach will remain central to maximizing clinical impact.

Box 1 Key Teaching Points

- Nuclear medicine imaging of nephro-urological infection reflects biological activity and inflammatory response, providing information beyond structural imaging.
- Physiological renal tracer handling and urinary excretion are major challenges; optimized preparation, delayed imaging, and hybrid techniques are essential for accurate interpretation.
- ^{18}F-FDG PET/CT offers high sensitivity and whole-body assessment and is particularly valuable in complicated infection, renal transplant recipients, and fever of unknown origin.
- Radiolabelled white blood cell scintigraphy provides greater specificity for active infection and is especially useful in chronic, recurrent, or device-related infection.
- ^{99m}Tc-DMSA is best suited for evaluating renal cortical involvement and long-term sequelae rather than distinguishing active infection.
- Selection of imaging technique should be question-driven, tailored to disease acuity, chronicity, and clinical context.
- Nuclear medicine imaging is most effective when integrated into a multimodality diagnostic pathway alongside ultrasound, CT, and MRI.
- Awareness of common pitfalls, including post-procedural inflammation and malignancy-related uptake, is essential to avoid false-positive interpretations.
- When appropriately applied, nuclear medicine imaging can directly influence management, supporting targeted intervention and rational antimicrobial stewardship.

Conclusion

Imaging of infection in the nephro-urological system remains diagnostically challenging due to the complex interplay between physiological tracer excretion, overlapping inflammatory processes, and frequent structural abnormalities related to prior disease or intervention. Nuclear medicine techniques, by providing functional and molecular information, offer unique advantages in this setting when applied in a biologically informed and clinically targeted manner.

Rather than serving as first-line investigations, nuclear medicine studies are most valuable as problem-solving tools in complicated, recurrent, or equivocal cases. An understanding of tracer biology, optimized acquisition protocols, and awareness of common interpretive pitfalls are essential to maximize diagnostic accuracy and clinical impact. When appropriately selected, techniques such as radiolabelled white blood cell scintigraphy and ^{18}F-FDG PET/CT can clarify disease activity, define extent of infection, and meaningfully influence patient management.

Integration of nuclear medicine imaging into a multimodality diagnostic pathway, supported by close collaboration between nuclear medicine physicians, radiologists, and referring clinicians, is central to effective patient care. Emerging PET tracers and hybrid imaging techniques hold promise for improving specificity and expanding the role of molecular imaging in infection, although further clinical validation is required.

In summary, nuclear medicine provides a powerful and complementary approach to the imaging of nephro-urological infection. A practical, question-driven application of these techniques can reduce diagnostic uncertainty, guide targeted intervention, and support rational antimicrobial stewardship in complex clinical scenarios.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Kgomotso M.G. Mokoala: Conceptualization, Writing – original draft, Writing – review & editing. **Chimbabantu Kaoma:** Validation, Writing – review & editing. **Farida Jibril:** Validation, Writing – review & editing. **Joseph Kabunda:** Validation, Writing – review & editing. **Mike Sathekge:** Conceptualization, Writing – original draft, Writing – review & editing.

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