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Scintigraphic evaluation of the kidney

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Abstract: *There are more than one technique used to evaluate the kidney, besides the standard ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), there is also renal scintigraphy. The renal nuclear medicine procedures are grouped as in vitro (urine counting wells, basic probe detectors for clearance studies) and in vivo procedures (static and/or dynamic examinations done with planar gamma cameras, and single-photon emission computed tomography (SPECT) to determine kidney parameters or for cortical imaging). Renal scintigraphy has been a useful tool, since the early 1950s, in the diagnosis and management of many pathological changes in the kidney, especially in measuring renal function (e.g. obstructive/nonobstructive uropathies, renal inflammatory diseases, tumours, renal hypertension, and renal transplant viability). [1]*

INTRODUCTION

The radionuclide investigation of the kidney includes detection of renal afflictions and measurements of quantitative indices that estimate the renal perfusion and function. Ultrasound and computed tomography are commonly used for the evaluation of renal structural anatomy, and the role of nuclear renal imaging is more for functional analysis, less in anatomical imaging (e.g. cortical imaging).[1,2]

Renal scintigraphy, also known as a "renal scan" or "renal radionuclide imaging" or “renography” includes various investigations that use different radioisotopes to evaluate renal blood flow, renal split function, and the renal excretion performance of both. It yields specific and often unachievable information by using other imaging procedures. [2]

Clinical indications for renal scintigraphy (adapted from *Nuclear Medicine: The Requisites*, 4th ed)**:** [3-5]

1. Blood flow abnormalities
2. Function quantification (reduced performance of one or both kidneys)
   a. Differential function
   b. Glomerular filtration rate (GFR), effective renal plasma flow (EPRF)
3. Cirrhosis of the kidney(s)
4. Differentiation between a mass lesion and a column of Bertin
5. In infants with abnormalities of the urinary tract to study the urinary flow
6. Obstruction: ureteropelvic junction, ureteral
7. Pyelonephritis: both acute and chronic tubule-interstitial nephritis and parenchymal scarring
8. Renal failure: acute and chronic
9. Renal artery stenosis with/without renovascular hypertension
10. Renal vein thrombosis
11. Surgical:

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a. performance assessment before operations in the case of chronic diseases (e.g. diabetes)
b. Renal allographs: for clinical monitoring of renal function, transplant rejection or other complications, transplant anastomosis assessment
12. Trauma

PURPOSE

The purpose of this paper is to provide a better understanding about dynamic renal imaging in several kidney pathologies, with an emphasis on obstructive renal pathology and to clarify the meaning of some quantitative parameters used in renal scintigraphy.

MATERIAL AND METHODS

Nuclear renal scans are various, complex and also a subject to institutional preferences, that is why a standardization of the techniques is hard to achieve. All nuclear renal procedures have some basic common conditions that must be taken into account before, during and after patient examination. First of them involves the intravenous bolus injection of a renotrophic radiopharmaceutical (a medicine marked with a radioisotope) that emits a small amount of radioactivity into the patient. Usually, the radiotracer administered to the patient is well tolerated, with no systemic toxic effects. Some mild-moderate allergies or adverse reactions (such as dizziness, headache, metal taste, flushing) are extremely rare reported. The radiation dose is relatively low, less than the standard chest x-ray. The examination is performed with the patient either lying on the examination table, in the supine position, or standing. [3-7]

The pre-scan preparatory measures that are common are hydration, about 30 minutes prior to the actual examination, the patient should drink about 1 litre of fluid, and an empty bladder, the patient should void before examination. [3-7]

It is of great importance that in the last 3-6 months prior to the renal scintigraphy, no high doses of iodine substances to be taken, like x-ray and CT contrast agents, or certain medicines (e.g. Amiodarone) because the results could otherwise be distorted. [3-7]

In general, chronic therapy medications should not be discontinued prior to the exam. For specific problems, specific blood pressure lowering drugs (ACE inhibitors, diuretics) must be mentioned to the nuclear medicine physician as there is a period of drug abstinence in some cases. [3-7]

Different scanning protocols with various radiopharmaceuticals are available for scanning the kidneys. Choosing the right technique and optimal radiopharmaceutical depends on the patients' medical history, clinical setting and indication. [3-5, 8]

Plenty and divers radiopharmaceuticals have been produced in the last 60 years to assess renal function; some are used in laboratory assays by measuring blood samples and determining the renal clearance of the radiopharmaceutical and others for dynamic or static studies with a gamma camera or a SPECT system. The gamma cameras and SPECT systems monitor the passage of radiopharmaceuticals through the kidney and urinary tract by registering and processing of the emitted gamma radiation. [9, 10]

The radionuclide agents usually used for determining renal function and anatomy can be grouped into three main categories [5,8]: those filtered by glomerular filtration, those excreted by tubular secretion via proximal tubule receptor-mediated endocytosis from the glomerular filtrate, and those retained in the renal tubules for long periods, useful for cortical imaging. [8]

The most frequently used radiopharmaceuticals in renal scintigraphy are illustrated in Table 1.

Table 1. Most frequently used renal radiotracers

Glomerular Filtration (GF)	• Tc-99m diethylenetnamine pentaacetic acid (Tc-99m DTPA) • 99mTc-mercaptoacetyltriglycine (Tc-99m MAG3) • I-131/I-123 orthoiodohippurate (OIH)
Tubular Secretion (TS)	• I-131 OIH • Tc-99m MAG3 • Tc-99m ethylenedicisteine (Tc-99m EC)
Tubular Filtration (TF)	• Tc-99m dimercaptosuccinic acid (Tc-99m DMSA) • Tc-99m glucoheptonate (Tc-99m GHA)

Table 2. Renal radiotracers excretion mechanisms (adapted from *Semin NM Apr.92*)

	GF	TS	TF
Tc-99m DTPA	>95%		
Tc-99m MAG3	<5%	95%	
I-131 OIH	20%	80%	
Tc-99m GHA	40%-60%		20%
Tc-99m DMSA	some		60%

There are four important types of renal imaging methods obtained by using a planar gamma-camera or a SPECT system in order to evaluate whether the kidneys are working normally or abnormally:

- Renal perfusion and renal function imaging are dynamic studies with images taken in series, over a period of 30 minutes immediately after the bolus radiotracer injection and determines the blood flow distributed to the kidneys, recognizes a potential narrowing of the renal arteries, and helps in determining the kidneys functioning. [2, 11]

- Diuretic renal scintigraphy is used to detect kidney obstruction. The procedure is similar to the renal perfusion, and seriated images are taken before and after the introduction of a diuretic (in the 15th minute of acquisition) to help urine elimination from the kidneys. [2, 11]

- ACE-inhibitor renal scintigraphy utility is in detecting renovascular hypertension, not renal artery stenosis, by comparing renographic images before and after taking an ACE-inhibitor. [2, 11] It is also a dynamic study and the image acquisition process begins when the radiotracer is injected intravenously in bolus. [3-5, 8, 10]

- Cortical renal scintigraphy is a static study and detects the amount of normal functioning kidney tissue. [2, 11] After the tracer administration, there is a three hour delay before the imaging acquisition can begin. [3-5, 8, 10]

Generally the dynamic renal functional studies are acquired in two parts. The first part evaluates the renal blood flow, which is calculated in the first pass of the radiopharmaceutical bolus through the abdominal aorta and renal arteries. The second part assess the kidney uptake and clearance function over the next 25 to 30 minutes of acquisition. [3-5, 8, 10]

GFR and EPRF are important kidney function markers evaluated by dynamic renal scintigraphy. Normal GFR varies in accordance with age, sex, weight (nutritional status), diet, race, and kidney size, which is proportional to body surface area. [12, 13, 14] The estimated GFR is calculated using these factors and the serum creatinine value, but it is not helpful when there are unilateral changes or when kidney function is very abnormal. Unilateral renal function changes are difficult to identify with other imaging techniques, but easy to determine with camera-based renal scan split functions. The percent differential function (split function) calculates the contribution of each kidney to the renal function and can be applied to GFR or ERPF data. [3-4, 15]

Nuclear techniques are not 100% "accurate" in measuring kidney function (GFR, ERPF), but are superior to investigations based on the serum creatinine value. [3, 14] Using renal scintigraphy patients can be followed over a long period of time, because this technique is highly reproducible in any one patient. [3, 13, 14]

Table 3. Renal radiotracers used for renal function measures
(adapted from *Requisites of Nuclear Medicine 4th ed*)

Effective Renal Plasma Flow (ERPF)	Tc-99m MAG3 I-123 / I-131 OIH H-3 or C-14 paraamino-hippurate (PAH) I-125 or I-131 iodopyracet
Glomerular Filtration Rate (GFR)	Tc-99m DTPA Cr-51 EDTA I-125 diatrizoate I-125 iothalamate C-14 or H-3 inulin In-111 or Yb-169 DTPA Co-57 vitamin B12

The Tc-99m DMSA cortical scan is used to evaluate renal cortical lesions in patients with suspected pyelonephritis, to detect renal scarring in a patient with reflux, and, in some occasions, to differentiate a prominent column of Bertin from a tumorous formation. Renal cortical scintigraphy provides additional information by showing changes and improvements over time, that are impossible to evaluate with conventional structural and anatomical imaging modalities, like ultrasound, CT, and MRI. [3,

13, 14]

RESULTS

The images obtained with the gamma camera should be inspected after acquisition in order to evaluate if the examination was done in proper conditions. After visual inspection the image data is processed and regions of interest (ROIs) are defined over the kidney and surrounding background so that the renogram curves can be generated. [5, 7]

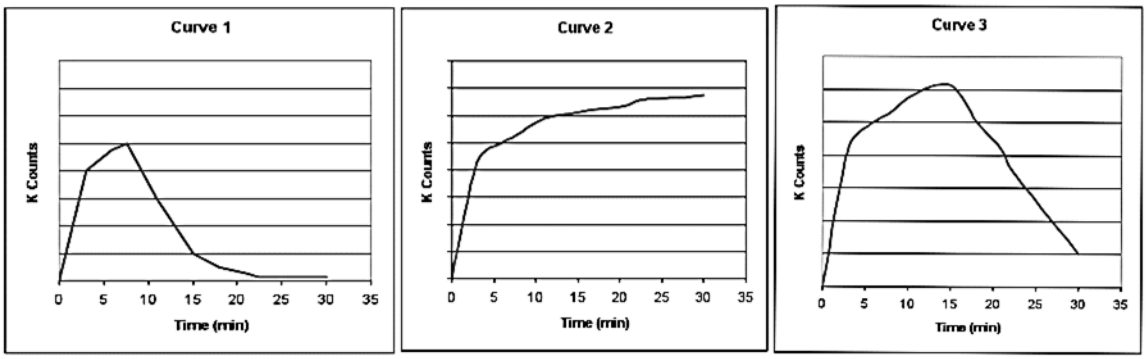
The time-activity curve (TAC) represents a graphic illustration of the renal function and is composed of 3 parts: initial rise, upslope and downslope. The first part reflects the radioactivity that arrives via the renal artery to the kidney. The upslope (ascending limb) reflects kidney uptake before the radiopharmaceutical begins to be excreted by the kidney (the descending limb). The peak time accurately indicates the point at which the extraction and accumulation trend is reversed to the evacuation process. [5, 7]

This curve is important in diuretic renal scintigraphy. Diuresis renography helps to discern between obstructive (calculus) and nonobstructed dilated urinary tract, and in the postsurgical evaluation of the renal system function and urodynamic. Acute obstructive uropathy is a commonly encountered condition. When unilateral obstruction occurs the changes in the measured renal function are a little decrease or imperceptible, but the bilateral form can result in significant kidney function losses. [5, 16]

The radionuclide renogram TAC provides an accurate graphic illustration of the dynamics of urinary excretion. In obstructive uropathy a calculus can give various degrees of hydronephrosis, depending on the site in which it is lodged. In the case of acute obstruction due to a renal calculus, pressures increase fast in the pyelocaliceal system and in the ureters above the point of obstruction. The affected kidney has a characteristic aspect: a dilated urinary tract with a thin cortex, and it shows on the TAC a slow continuous accumulation of tracer in the collecting system, a slow increasing ascending curve with no downslope. In contrast, the opposite kidney, which has a normal function and no obstruction, will show a good uptake and excretion, and the three part TAC. [7, 17]

In some cases the calculus produces a partial obstruction of the urinary excretion pathways. In order to demonstrate this a diuretic like Furosemide is administrated at various times during the course of the renal scan. The decreasing aspect of the curve after the administration of the diuretic indicates an incomplete obstructive pattern (as in Curve 3), and as for the rising curve a complete obstruction (as in Curve 2). [7]

Figure 1. Time activity curves
(adapted from *EANM: Dynamic renal imaging in obstructive renal pathology. A Technologist's Guide*)
Curve 1- normal kidney function; Curve 2- complete obstruction; Curve 3 - incomplete obstructive pattern after the administration of Furosemide at minute 15.



QUANTITATIVE INDICES

Renal perfusion is evaluated by visual and quantitative analysis (1- to 3-second images) of the initial bolus as it transits the abdominal aorta and enters the renal arteries (used in renal number anomalies, renal transplant). [10, 11]

Relative Function represents the relative uptake of the radiopharmaceutical for the evaluation of uni-/ bilaterally impaired kidneys. [10] The split function is particularly useful because estimated GFR and serum creatinine may not identify unilateral lesions. [3]

Renal Size. Several chronic renal diseases will result in bilaterally small kidneys, whereas the kidneys may be bilaterally enlarged in early diabetic renal disease, acute interstitial nephritis, HIV nephropathy, and amyloidosis. The resolution of structures of the renal parenchyma with nuclear medicine may not be as clear as with other imaging techniques, such as CT or MRI that is why nuclear renal images are not usually used to differentiate between cysts and tumours. [10, 11, 18]

The time to peak, or T max, refers to the time from radiopharmaceutical intravenous administration to the peak height of the renogram curve. 99mTc-MAG3, 99mTc-DTPA and OIH renograms normally peak by 5 min and drop to half-peak value until the 15th minute after injection; however, in some cases, physiologic retention of the radiotracer in the renal calyces or pelvis can alter the aspect of the TAC in normal kidneys and lead to prolonged values for the time to peak, 20-min/ maximum count ratio, and T½. [8, 10, 19, 20]

Figure 2. Normal right kidney renogram. Specific scintigraphic aspect of left kidney obstruction (kidney calculus).

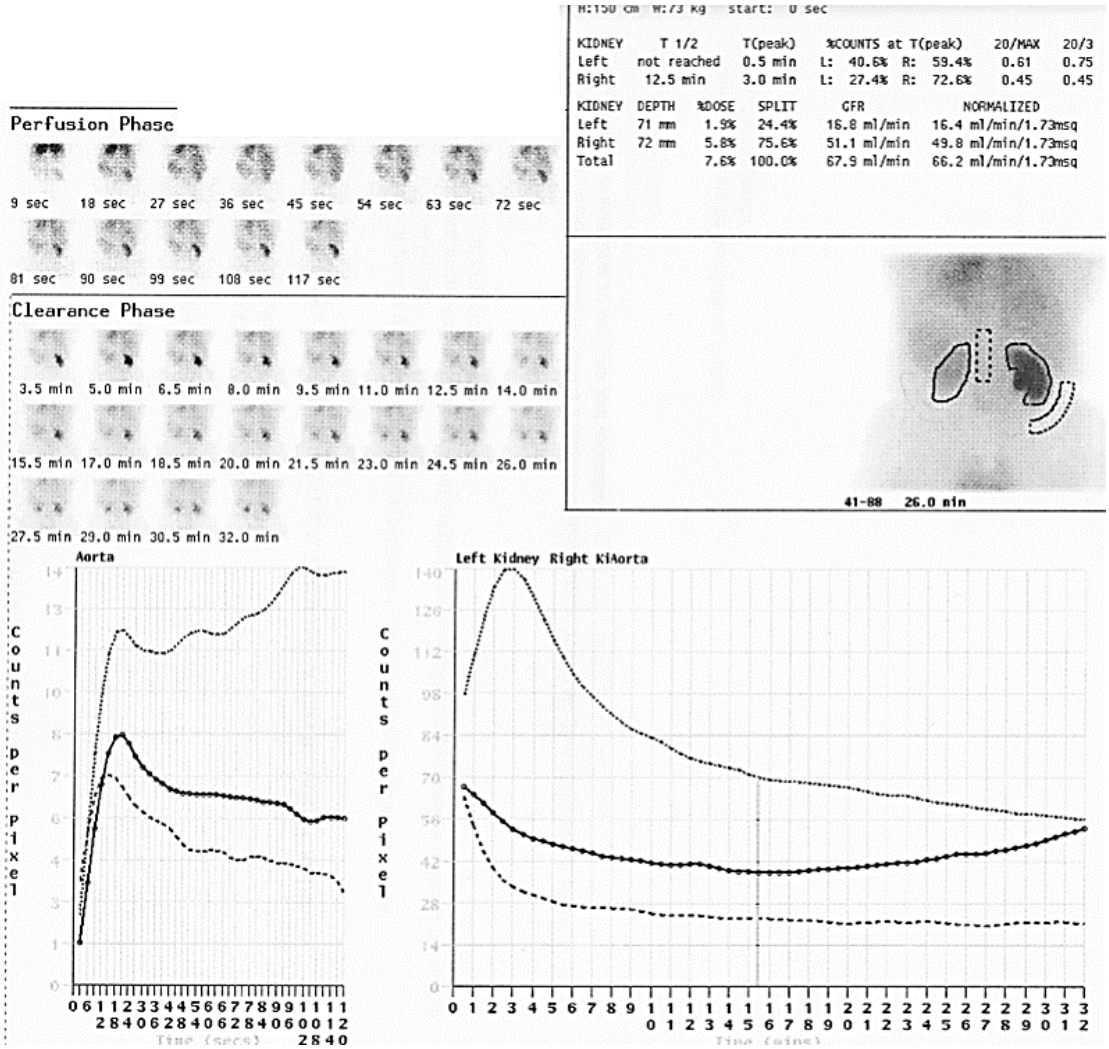
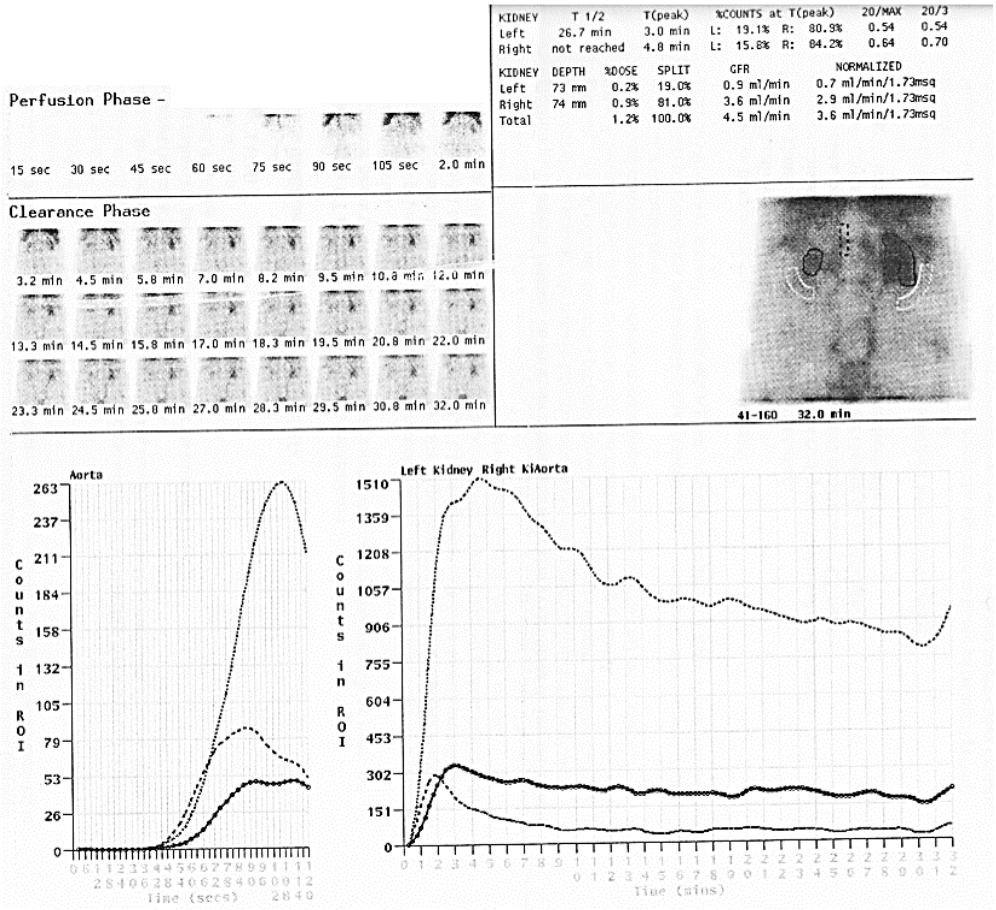


Figure 3. Renal scintigraphic appearance of chronic renal failure; hypoplasic left kidney.



The T½ represents the time is necessary for the radioactivity in the kidney to drop to 50% of the maximum value (time to peak, or T max); this index is important in diuretic renography for patients with suspected urinary tract obstruction. [8, 10, 19]

The 20-min/maximum count ratio is an index of the transit time and a measurement of residual cortical activity, the ratio between the kidney counts at 20 min to the maximum (peak) radioactivity; it is useful in monitoring patients with suspected urinary tract obstruction and for detecting renovascular hypertension. [8, 10, 19]

CONCLUSION

Renal radionuclide studies are versatile procedures and vary depending on institutional preference, clinical setting of the patient and medical indication.

Renal scintigraphy is a complex subject and understanding some basic principles, the use of radiopharmaceuticals available to image the kidney and monitor its function, the quantitative indices that can be generated and protocols can be useful for the physicians specialized in nephrology and urology in evaluating patients with diseases of the urinary tract and renal physiology.

References:

1) *What is Nuclear Medicine?,* http://interactive.snm.org/docs/whatisnucmed.pdf, November 19, 2015

2) *Renal Scintigraphy*, http://www.radiologyinfo.org/en/info.cfm?pg=Renal, November 19, 2015

3) Harvey A. Ziessman, Janis P. O'Malley, James H. Thrall. *Nuclear Medicine: The Requisites*, Saunders, 4th ed., Philadelphia, 2014: 168-203

4) Cook GJR, Maisey MN, Britton KE, Chengazi V, eds.

Clinical Nuclear Medicine, 4th ed. Hodder Arnold: Oxford University Press Inc, 2006: 896.

5) *ACR–SPR Practice parameter for the performance of renal scintigraphy*, http://www.acr.org/~/media/1169D04DFABF4C10938D2E3DFADC4477.pdf, November 19, 2015

6) National Kidney And Transplant Institute: *In-Vitro Glomerular Filtration Rate (GFR),* http://nkti.gov.ph/11-services/597-in-vitro-glomerular-filtration-rate-gfr**,** November 19, 2015

7) François H, Dennan Suzanne, Boubaker Ariane, et all. *EANM: Dynamic renal imaging in obstructive renal pathology.A Technologist's Guide*: European Association of Nuclear Medicine, August 2009

8) Taylor A, Nally J. *Clinical applications of renal scintigraphy.* American Journal of Roentgenology, 31-41, November 19, 2015

9) Russell CD, Taylor AT, Dubovsky EV. *Measurement of renal function with technetium-99mMAG3 in children and adults.* J Nucl Med. 1996; 37:588–593, November 19, 2015

10) Taylor AT*: Radionuclides in Nephrourology, Part 1: Radiopharmaceuticals, Quality Control, and Quantitative Indices*, J Nucl Med. 2014 April; 55(4): 608–615, November 19, 2015

11) Taylor A, Blaufox M, Palma D, Dubovsky E, Erbaş B, Eskild-Jensen A, et all. *Guidance Document for Structured Reporting of Diuresis Renography*. Semin Nucl Med. 2012 Jan;42(1):41-8, November 19, 2015

12) National Kidney Foundation: *Frequently asked questions about GFR estimates* https://www.kidney.org/sites/default/files/docs/12-10-4004_abe_faqs_aboutgfrrev1b_singleb.pdf, November 19, 2015

13) Sirota JC, Klawitter Jelena, Edelstein CL. *Biomarkers of Acute Kidney Injury*, Journal of Toxicology, vol. 2011, Article ID 328120, 10 pages, 2011. http://www.hindawi.com/journals/jt/2011/328120/, November 19, 2015

14) Stevens LA, Levey AS. *Measurement of kidney function*. Med Clin North Am. 2005; 89(3):457–73. doi: 10.1016/j.mcna.2004.11.009.

15) White, C., Huang, D., Akbari, A., Garland, J., & Knoll, G. *Performance of Creatinine-Based Estimates of GFR in Kidney Transplant Recipients: A Systematic Review.* American Journal of Kidney Diseases, 1005-1015, November 19, 2015

16) Hamed MAE. *New advances in assessment of the individual renal function in chronic unilateral renal obstruction using functional CT compared to 99mTc-DTPA renal scan.* Nucl Med Rev Cent East Eur. 2014;17(2):59-64, November 19, 2015

17) Rao S, Lin EC. *Acute Obstructive Uropathy Imaging.* Updated October 27, 2015. http://emedicine.medscape.com/article/382530-overview#a6, Accessed November 19, 2015

18) Taylor, A., Shenvi, N., Folks, R., Garcia, E., Baruch, B., & Manatunga, A. (n.d.). Reference Values for Renal Size Obtained From MAG3 Scintigraphy. Clin Nucl Med. 2013 January; 38(1): 13–17. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3688252/, November 19, 2015

19) Taylor, A., & Schuster, D. (2000). *The Genitourinary System.* In A clinician's guide to nuclear medicine. 45-76. Reston, VA: Society of Nuclear Medicine, November 19, 2015

20) Erbsloh-MOller B, Dumas A, Roth 0, Sfakianakis G, Bourgoignie JJ. Furosemide -131 hipppuran ranography after angiotensin-converting enzyme inhibition for the diagnosis of renovascular hypertension. Am J Med 1991; 90:23-29, November 19, 2015