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Image-Guided Adrenal and Renal Biopsy

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Abstract

Image-guided biopsy is a safe and well-established technique that is familiar to most interventional radiologists (IRs). Improvements in image-guidance, biopsy tools and biopsy techniques now routinely allow for safe biopsy of renal and adrenal lesions which traditionally were considered difficult to reach or technically challenging. Image-guided biopsy is used to establish the definitive tissue diagnosis in adrenal mass lesions that can not be fully characterized with imaging or laboratory tests alone. It is also used to establish definitive diagnosis in some cases of renal parenchymal disease and has an expanding role in diagnosis and characterization of renal masses prior to treatment. Although basic principles and techniques for image-guided needle biopsy are similar regardless of organ, this paper will highlight some technical considerations, indications and complications which are unique to the adrenal gland and kidney because of their anatomic location and physiologic features.

Keywords

image-guided biopsy; percutaneous needle biopsy; renal biopsy; adrenal biopsy

Section I: Adrenal Biopsy

Background

As use of Ultrasound (US), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) has increased with ever improving resolution, the number of incidentally discovered adrenal masses has also increased. The vast majority of these adrenal masses are benign adenomas and myelolipomas but differential considerations include pheochromocytoma,

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adrenocortical carcinoma and metastases, especially in patients with known or suspected malignancies such as lung carcinoma and lymphoma. Although the use of adrenal biopsy has declined in recent years due to improvements in and validation of noninvasive CT and MR techniques that can now diagnose benign adrenal lesions with a high degree of confidence (1,2), it remains an accurate and safe means of obtaining definitive tissue diagnosis. Clinical scenarios in which needle biopsy may be indicated include an adrenal lesion in patients with multiple malignancies, the need for staging a known malignancy, defining an unknown primary source or differentiating benign from malignant adrenal masses with equivocal imaging findings.

Pre-biopsy adrenal imaging

The ability to characterize and classify adrenal pathology based on imaging has advanced in step with improvements in CT, MRI, US and nuclear medicine studies. While the sensitivity of US for detecting adrenal tumors is very high (96% for masses <2cm and 100% for masses >2 cm), its ability to further characterize these lesions is limited (3,4). Multidetector row CT is the primary modality for visualizing and characterizing suspected adrenal adenomas, based on the high lipid content of these benign lesions. An adrenal CT protocol uses 3-5 mm slice thickness and consists of an unenhanced CT followed by early and delayed contrast-enhanced studies which are typically obtained 60 seconds and 15 minutes after administration of IV contrast and can be used to calculate percentage of absolute and relative contrast washout. The combination of CT density on noncontrast images (< 10 Hounsfield units (HU) is a lipid-rich adenoma) and degree of contrast washout can diagnose adrenal adenomas with a high degree of accuracy. For example, adrenal masses with absolute contrast washout of >60% and relative contrast washout of >40% can be diagnosed as adrenal adenomas with a reported sensitivity of 98% and a specificity of 92% (5,6). If further imaging characterization is needed, MRI can supplement CT findings. MRI evaluation of adrenal adenomas also takes advantage of their lipid content. T1- and T2- weighted images plus chemical shift imaging (CSI) which consists of in-phase and out-of-phase imaging are required. On MRI, adrenal adenomas appear homogeneous on all sequences with signal intensity equal to or slightly lower than that of normal liver. On CSI, adenomas lose at least 30% of their intensity on out-of-phase images when compared to in-phase images. This is quantified using the signal intensity index (SII) and depending on the set threshold, adrenal adenoma can be diagnosed with a very high accuracy with MRI (3).

Adrenal masses other than adenoma can also be characterized by noninvasive imaging. For example, Pheochromocytoma is characteristically a hypervascular mass that is markedly intense on T2 weighted MRI. Nuclear medicine [¹²³I] MIBG scans are also used to diagnose this lesion with 83-100% sensitivity and 95-100% specificity (7). Furthermore, urine and plasma metanephrines are routinely used to screen patients with suspected pheochromocytoma. The noninvasive characterization diagnosis of pheochromocytoma is especially important because this lesion can be problematic to biopsy due to the potential of precipitating hypertensive crises secondary to catecholamine secretion during the procedure, a risk which can be mitigated by pharmacologic blockade (alpha, beta, and conversion blockade) whenever possible. (8) Metastases are the most common malignancy involving the adrenal glands, and lung carcinoma is the most common adrenal metastasis. [¹⁸F] FDG can differentiate metastatic lesions from adrenal adenomas with a sensitivity >95% of an even higher specificity (3) but, biopsy is still needed for specific diagnosis, especially when adrenal involvement or histology alters staging of disease or therapy. Lymphoma may also be indistinguishable from other adrenal metastases with noninvasive imaging. While primary adrenal lymphoma is rare with fewer than 100 cases reported in the literature, secondary adrenal involvement is common and may occur in up to 25% of patients with lymphoma. In these patients, an adrenal biopsy is often necessary to establish the tissue diagnosis (3,5,7).

Thus, while the improvements in diagnostic imaging have made adrenal biopsies less common, there are still situations in which biopsy is necessary and prudent. In summary, if an adrenal lesion can not be characterized as an adenoma by CT, further characterization with MRI using CSI is usually the next step. Most masses which are not typical for adenoma based on CT and MRI and not characteristic for pheochromocytoma based on imaging and laboratory tests, may require biopsy, especially in the setting of known or suspected malignancy (3).

Indications and Contraindications

As previously discussed, staging of known malignancy, identifying an unknown primary malignancy, differentiating benign from malignant adrenal mass in equivocal cases are three accepted indications for adrenal biopsy. Making definitive tissue diagnosis when imaging is equivocal can drastically alter management, in almost a third of patients in one report (9). Relative contraindications to image-guided adrenal biopsy include uncorrectable coagulopathy, inability to reach the tumor via a safe path, or an unsafe target (10), but a skilled interventional radiologist should be able to place a needle in almost any image-able adrenal lesion. In practice, the question of whether to biopsy an adrenal mass is determined by the relative risk-to-benefit ratio of obtaining tissue diagnosis. With thorough pre-procedural planning including review of imaging and laboratory data, careful intra-procedural monitoring and availability of adrenergic blockade or anesthesia assistance, if necessary, these procedures can be performed safely. Because of the proximity of the adrenal gland to the diaphragm, a unique challenge for adrenal biopsy is the patient's inability to cooperate with breathing instruction or suspend respiration (1,10). In these cases, respiratory gating tools may facilitate the procedure, as can performing the biopsy in one swift needle insertion during expiration. In cases where the lesion is visible with both US and CT, use of real time ultrasound to watch the pleural reflection and lung edge during the procedure can also help to avoid diaphragmatic penetration.

Choice of Image-Guidance Modality

Multiple imaging modalities, including fluoroscopy, US, CT, CT fluoroscopy (CTF), MRI, PET-CT, rotational fluoroscopy, and multimodality or single modality electromagnetic (EM) guidance (Medical GPS or Fusion Navigation) may all guide percutaneous adrenal biopsies (11). In addition, adrenal biopsy using endoscopic ultrasound-guided (EUS) through a transgastric approach may also guide biopsy of some large left adrenal masses, but the right adrenal is poorly visualized (9,12). Each modality has its advantages and disadvantages but, in routine clinical practice, the choice of imaging modality is based on equipment availability, cost, lesion conspicuity, and physician preference. US and MRI readily allow for complex oblique angles of approach but US may be limited in large patients and MRI is expensive, often unavailable, and requires MR compatible equipment and needles. By far, the most commonly used image guidance modalities for adrenal biopsy are CT, US, or CT and US (1,11,13).

Benefits of US guidance include real time multi-planar imaging, absence of radiation, low cost, portability, and the ability to rapidly confirm complications such as bleeding. Drawbacks of US guidance include inadequate visualization of the target or needle due to operator experience, lesion depth, or intervening bowel gas or bony structures. Benefits of CT guidance include spatial resolution, ability to identify deep intervening structures along an ideal pathway, and the option for contrast enhancement if needed. However, CT uses radiation, takes more time, is more costly, and real-time oblique imaging either requires gantry tilting, or delayed multiplanar reconstructions (1,10,11). Modality selection may also depend on patient-specific issues. US views from multiple windows may better localize mobile or hard to see lesions, and is often faster than CT (1,11). Both CT and US are used with high success to biopsy adrenal lesions and many operators make use of both CT and ultrasound (with or without fusion

imaging) to get the spatial resolution of CT and the temporal resolution of US (“CT is the eye, US is the hand”).

Image-guided biopsy technique

Safe and successful image guided percutaneous adrenal biopsy begins with careful pre-procedural evaluation of imaging and laboratory data and formulation of a thorough procedural plan. Prior imaging studies are used to plan appropriate patient positioning, needle approach and trajectory. Most pre-procedural imaging is obtained with patients in supine position with inhalation and arms up and target lesion location may be significantly altered once the patient is sedated and positioned for the biopsy, and less reliable at following breathing instructions. The need for pre- and intra-procedural anti adrenergic blockade therapy or other protective maneuvers should be considered at initial evaluation or scheduling, especially in the setting of pheochromocytoma. Although this diagnosis can usually be made prior to biopsy based on clinical history, imaging and laboratory data, if biopsy is deemed necessary by a multidisciplinary team (radiology, surgery and endocrinology), the authors advocate careful intra-procedural monitoring and immediate availability of direct acting vasodilators (nitroprusside) and prophylactic adrenergic blockade. A more complete discussion of this topic is provided in a recent study of pheochromocytoma ablation by Venkatasen and colleagues (8) .

Although the value of obtaining routine pre-procedural labs including complete blood count (CBC), metabolic panel (CMP) and coagulation studies (PT, PTT, INR) is somewhat controversial, these screening tests are routinely performed at most institutions. Prior to elective biopsy, anticoagulant use is stopped at the appropriate time. Although there is little sound scientific data, current consensus guidelines and recommendations suggest that aspirin and clopidogrel should be discontinued 5 days prior to the procedure, when safe to do so. Heparin should be discontinued 4-6 hours and low-molecular-weight heparin (LMWH) should be withheld for 8 to 12 hours prior to the procedure, depending upon the biologic half life. Warfarin should be withdrawn 5-7 days before the procedure and the patient can be bridged with LMWH until the biopsy is performed. Warfarin can be reinitiated the day following the biopsy (14, 15). In some special cases, for example patients with mechanical cardiac valves or at-risk coronary stents, abrupt termination of anticoagulation may be dangerous and carry a higher risk than performing the procedure on continued anticoagulation. In these cases, peri-procedural management of anticoagulation may need to be altered and is best done in consultation with the referring physician.

Regarding patient positioning, right-sided adrenal biopsies can be performed though a transhepatic, direct posterior or right-decubitus (target side down) approach. Placing the patient in a slight right-decubitus position restricts diaphragmatic motion. Left-sided adrenal biopsies can be approached with the patient in the left-decubitus position, posteriorly, or anteriorly / transgastrically (16,17). Light sedation may retain the ability to follow breathing instructions and lidocaine is useful from skin to lesion edge. Intervening anatomic structures should be on the operator’s radar. Right adrenal gland masses are generally lower and more accessible by US guidance because the liver provides an acoustic window. Either CT, US, and in many cases, a combination of both modalities is used, with or without electromagnetic tracking of the ultrasound transducer (See Figure 1). Use of enhanced CT or Doppler US allows for visualization of non-target vascular structures. Tracking of the ultrasound transducer enables use of pre-procedural CT, PET-CT, or MR information during the biopsy. Such a strategy may facilitate targeting of tiny or hard to see targets such as a FDG-avid portion of the adrenal mass seen on PET scan.

With US guidance, the first decision is usually whether to use a free hand approach, a needle guide, or fusion guidance technique. For inexperienced ultrasound users, deeper lesions such

as adrenal masses may be more accurately approached through a needle guide than via a free hand approach, although freehand allows for more alterations between imaging window and needle entry point, which may be relevant with intervening ribs. In order to optimize visualization of the needle tip, it is important to optimize the ultrasound image and technique. Therefore, the highest frequency transducer which will penetrate to the target should be chosen. The field of view, focus and gain curves should be optimized, and the focus altered during needle insertion. The use of spatial compounding markedly improves both lesion and needle conspicuity. If the needle becomes difficult to see as it is advanced, slight “jiggling” of the needle will disturb the adjacent tissue and allow its location to be visualized. If an introducer needle is used, the stylet may be moved to improve visualization. A variety of etched needles for enhanced visualization are also available commercially, however manually scratching of the needle shaft tip with a metal clamp accomplishes the same goal. It is important to remember that the needle is best seen from a steep or perpendicular angle (90 degrees for a linear array, and near 45 degrees from a curved array). The most common error with freehand US guidance is letting the US transducer drift away from the needle skin entry point, or letting the needle drift away from the 2D plane of US imaging. Frequently looking back at the needle orientation instead of the monitor, and holding the needle next to the slippery transducer with extended fingers (the hand as a human needle guide) can help prevent this.

A needle path that avoids diaphragm, kidney, aorta and splenic vessels is desirable and in many cases may be best depicted by CT guidance. Often the target-side down decubitus provides the safest paraspinal route. The preferred approach, particularly on the left, is a caudal to cephalad path that avoids the kidney and diaphragm. In order to identify and visualize a clear needle path to the adrenal gland, gantry angulation may be necessary. Many CT scanners allow up to 30 degrees of gantry tilt, which is usually sufficient to provide a clear path. Although rarely required, triangulation technique may be used to calculate a steep craniocaudal angle and path (18). In cases where there is deep uncontrolled breathing or concern for a narrow window for a safe pathway, intermittent narrow beam CT can be used to confirm small increments in needle positioning (“Step and shoot technique”).

With regards to biopsy technique, needle size and adequacy of sample, either fine-needle aspiration (FNA), core biopsy, or both may be performed depending on local expertise and practice patterns. Both can be performed through either coaxial or tandem technique. The smaller Chiba and Spinal type FNA needles (21-23 gauge) may be preferred when biopsying hypervascular lesions, especially masses surrounded by bowel loops or blood vessels, or masses in the setting of malignancy where the pretest probability of metastasis is high (1,11). If FNA is chosen, many prefer to initially simply move the needle back and forth within the mass to pack cells into the needle (“capillary pass” technique), forgoing syringe aspiration to avoid traumatizing the mass or getting too much confounding blood in the syringe. Subsequent passes are done with syringe aspiration. However, depending on the local availability and expertise of the cytopathologist or cytotechnologist at the time of the procedure, core biopsy may be preferable. Core biopsy specimens may also be a requisite for certain diagnoses including lymphoma, whereas multiple copious FNA samples may be required for flow cytometry. FNA or touch prep of cores (touching and rolling the core on a slide) may be helpful in assessing the adequacy of specimen. Although a non-diagnostic rate of 14% has been reported for adrenal biopsy by Silverman and colleagues, accuracy has been reported to be 90-96%, sensitivity 81-93%, specificity 99%, PPV 99%, and NPV 80-91% (16,17,19).

Potential Complications and Management Strategies

The most frequent complications following adrenal biopsy are hemorrhage and pneumothorax. Less common complications include pain, pancreatitis, and rarely, needle tract seeding. In 666 patients spanning 7 studies, the overall complication rate was 5.3% with a range of 0-12%.

However, most of these were minor, self-limited complications and the rate for major complications necessitating further treatment is likely closer to 0.4-2% (16,17,20). The most frequent reported complication is pneumothorax necessitating further management, but some would argue that pneumothorax requiring chest tube placement is not a complication, but rather, a procedural side effect (like thoracic surgery). Bleeding complications following image-guided adrenal biopsy are not likely to be related to needle size, at least over an 18-23 gauge size range (17). Mody et al found that hematoma and rate of major complications increases with a transhepatic approach and that pneumothorax is associated with prone positioning. Pancreatitis has been reported when the needle transgresses the pancreas during an anterior approach, suggesting that this results from pancreatic duct injury (18).

Post-biopsy patient monitoring is prudent (possibly two to four hours) with frequent check of vital signs. Post-procedure management of pneumothorax is based on size and whether the patient develops symptoms. Vital signs and symptoms are closely monitored with special attention to development of chest pain, cough, tachycardia or decrease in oxygen saturation. In case of a tiny or small pneumothorax which is asymptomatic, observation without chest tube placement may be an option, but requires close clinical and imaging follow up. For a larger pneumothorax, a CXR is obtained and the patient is observed for four hours, at which point a repeat CXR is obtained to assess for interval change. If the pneumothorax has resolved or decreased in size and the patient has remained asymptomatic, they are discharged with short term follow-up. If the size has increased or if the patient develops symptoms, we generally place a 8.5 French pig tail chest tube with or without fluoroscopic guidance and admit the patient for overnight observation. The chest tube is placed to intermittent suction and clamped prior to repeat CXR the following morning. In almost all cases, the pneumothorax resolves and the chest tube is removed the following day. In case of a small pneumothorax, one can also perform a delayed "CT-test" at 10 minutes to assess stability of pneumothorax and need for chest tube placement. Occasionally, suctioning pleural air out of the outer coaxial needle on the way out can help avoid tube placement.

Needle tract seeding is exceedingly rare, but may be more common with primary adrenocortical carcinoma, which is also prone to drop metastases post-surgery (20). Coaxial technique likely reduces risk of needle-tract seeding.

Section II: Renal Biopsy

Image guided biopsy of renal masses

As with adrenal lesions, the increasing use of CT, MRI and US has also led to increasing detection of incidental solid renal masses, many of which are small (<3 cm) and can not be definitively characterized with imaging alone (21). Traditionally, treatment of such incidentally discovered renal lesions was nephrectomy without pre-operative tissue diagnosis. However, a recent study by Frank and colleagues found that 12.8 % of all masses removed at nephrectomy were actually benign lesions and that this percentage increased to 44% in the subset of smallest lesions (less than 1 cm) (22). Advances in image-guidance methods and biopsy equipment have now made image-guided renal biopsy a safe procedure with excellent diagnostic yield that provides sensitivity and specificity for diagnosis of malignancy in the range 80-92 % and 83–100% respectively (23,24). At the same time, advances in immunocytochemistry and cytogenetics have increased the ability to characterize tumor subtype from biopsy tissue. These factors, combined with an increasing number of small, incidentally detected, indeterminate renal masses have expanded the role of renal mass biopsy prior to treatment. In the past, indications for renal mass biopsy were diagnosis of lymphoma or metastatic disease (for which surgery would typically be unnecessary) or infection. However, these indications are expanding. A thorough discussion regarding currently established and emerging indications for renal mass biopsy is reviewed by Silverman (24).

One emerging indication, especially relevant to IRs, is making a definitive tissue diagnosis prior to treatment of renal masses with percutaneous thermal ablation. As an alternative to surgical resection, percutaneous thermal ablation is gaining wider acceptance in management of renal mass lesions, especially those smaller than 3.5 cm (25). Renal mass biopsy in this setting has tremendous value. Tuncali and colleagues found that 37% of solid renal masses referred for image-guided tumor ablation were actually benign lesions and recommended that renal masses referred for ablation should undergo pre-procedural percutaneous biopsy to establish tissue diagnosis. This allows for a complete discussion of therapeutic options and opportunity for multidisciplinary management (26). In another study, Beland and colleagues found that 26% of patients undergoing renal biopsy in this setting actually had a benign definitive diagnosis when the biopsy results became available after treatment with percutaneous radiofrequency ablation (21). Although the timing of pre-ablation biopsy relative to the ablation (either in a separate procedure before the procedure or just prior to ablation) may be debated, there are several factors which favor obtaining pre-procedural renal mass biopsy. These include avoiding unnecessary treatment of benign lesions, over-estimation of ablation efficacy and guiding appropriate follow-up imaging interval. One exception may be patients presenting with renal masses and Von Hippel Lindau disease or other hereditary renal cancer syndrome in whom the risk of malignancy is very high and therefore, tissue diagnosis prior to ablation may not be necessary.

Image guided random biopsy of renal parenchymal disease

Indications for obtaining a “random” renal biopsy in the setting of diffuse parenchymal disease vary among nephrologists. The decision to biopsy may ultimately be driven by the patients’ presenting signs and symptoms and clinical opinion regarding the value of establishing a definitive diagnosis in determining prognosis, guiding appropriate therapy and deciding when treatment may be futile. In this regard, renal biopsy is used to ascertain the degree of active (potentially reversible) and chronic (potentially irreversible) changes (27-29) which helps to determine likelihood of treatment response. Despite the variability in indications for random renal biopsy, histopathologic examination remains the gold standard for establishing definitive diagnosis of many renal parenchymal diseases (29-32) including certain treatable causes of proteinuria, hematuria and unexplained acute renal failure. Specific examples include determining the cause of nephritic syndrome and determining the cause of nephrotic syndrome in patients with lupus nephritis or without a systemic condition. Results of renal biopsy may impact patient care in up to 40–60% of cases (33-35), but this figure may differ considerably based on the indication for biopsy. Prognostication based on renal histopathology alone is affected by sample size and may not be very accurate in small tissue samples (<5 glomeruli). Therefore biopsy results in this setting should be interpreted in conjunction with laboratory findings and in clinical context (29).

Pre-procedural work up for random renal biopsy is similar to that for renal mass biopsy, with less emphasis on prior imaging. “Random” image-guided percutaneous renal biopsy is generally performed from a posterior-lateral approach and directed to the lower pole of the kidney with guidance under US or CT, depending on which modality best visualizes the target. The posterior lateral approach is usually in the watershed zone of less vascularity in between the terminal branches of the anterior and posterior divisions of the renal arteries. Technical considerations, post procedural complications and management strategies are also similar to renal mass biopsy and discussed below. One important detail regarding random renal biopsy is that routine evaluation of these specimens generally requires examination of the tissue under light, immunofluorescence, and electron microscopy (29). Therefore, it is important to know specific requirements for appropriate specimen preservation and handling prior to delivery to the pathology laboratory. This generally includes specimens submitted in physiological, formalin, and gluteraldehyde solutions, or simply on a wet telfa with close communication

with the pathologist. Some advocate rapid examination of the core specimen to ensure adequacy and inclusion of required glomeruli.

Transjugular random renal biopsy

A relatively new technique for random renal biopsy is based on the transjugular liver biopsy approach well known to most interventional radiologists. Originally described by Mal and colleagues in 1990 (36), this technique has been suggested as an alternative to percutaneous renal biopsy in some high risk patients including those with uncorrectable high bleeding risk, uncontrolled hypertension, morbid obesity, small, solitary, or horseshoe kidneys, and those who are on mechanical ventilation (32,37,38). The rationale for a transjugular approach is that there is a theoretical benefit because bleeding from the needle pass occurs back along the needle track and into the venous system and there is a lower likelihood of capsular puncture. Proponents of this technique also suggest that if capsular puncture occurs and results in significant contrast extravasation, it may be treated with elective tract embolization during the procedure (32,38).

The image guidance, biopsy tools and procedural steps used for transjugular renal biopsy are similar to those used for transjugular liver biopsy under fluoroscopic guidance. A renal access and biopsy set which includes a blunt tipped, 19 gauge, 70 cm long, side-cutting needle with a 2 cm needle throw length is available (Cook, Inc.). The procedure is generally performed via right internal jugular vein access and through the right renal vein, which is preferred over the left renal vein because it is shorter and allows a more direct access from the superior vena cava. Using US guidance, a 7 Fr vascular sheath is placed in the right internal jugular vein. The right renal vein is catheterized using a guidewire and 5 Fr Cobra or Multipurpose catheter. Under fluoroscopic guidance, the catheter is advanced into the posterior lower branch and the vascular sheath is then advanced over a stiff guidewire. The biopsy needle and its' protective catheter are then inserted and advanced into a peripheral cortical vein of the lower pole. A small amount of contrast is injected through the vascular sheath to confirm appropriate positioning just prior to biopsy, which is defined when a wedge of cortical parenchyma is seen following contrast injection as there is low likelihood of injury to central vascular structures and a high yield of glomeruli from this location (See Figure 5). An average of 4-6 passes are then made under fluoroscopic guidance using the spring loaded biopsy needle. A small amount of contrast is injected through the catheter to evaluate for capsular perforation, which may occur in up to 74 % - 90% of cases (32,39). If significant extravasation is present, the biopsy tract can be embolized using coils or Gelfoam. The total amount of contrast used during the procedure is generally less than 30 mL.

In centers with a large experience, rates of obtaining adequate diagnostic specimen and complication are similar to those reported for percutaneous renal biopsy. However, bleeding due to arterial trauma can occur, and some centers have reported contrast-induced nephropathy (37-39). The greater cost in time, personnel, and equipment make this approach impractical for routine image-guided renal biopsy, but it may be an option in highly selected cases in centers with such experience. Care should be taken to avoid capsular transgression anywhere near bowel or other anatomy, and cone-beam CT / rotational angiography may facilitate assessment of proper sheath location. Contraindications to a transjugular renal biopsy include right internal jugular vein or SVC obstruction, and lack of experienced operators (32).

Biopsy of renal transplants

Another clinical scenario in which image-guided renal biopsy is commonly requested is in the case of renal transplant dysfunction. At many academic medical centers, the number of image-guided biopsies of renal transplants may exceed the number of renal biopsies performed in native kidneys. Percutaneous biopsy of a renal allograft is generally technically easier to

perform than biopsy of native kidneys. It is generally performed with US Doppler guidance because of good visualization of the target organ and adjacent vascular structures which may be relatively superficial in the pelvis (although CT guidance may also rarely be required). The superficial location without intervening ribs also allows for more effective post biopsy manual US compression to control hemorrhage.

The most common indication for biopsy of a transplant kidney is to make the diagnosis of allograft rejection (See Figure 4) (40,41). Essentially all renal transplant patients undergo early allograft evaluation with Doppler ultrasound which can exclude other causes of allograft dysfunction such as renal artery thrombosis or stenosis, renal vein thrombosis or stenosis, large perinephric fluid collection, hydronephrosis or arteriovenous fistula. The needle path should avoid peritransplant fluid collections when possible in order to minimize the risk of infection and also because these collections may increase the risk of hemorrhage. The appearance of new focal mass(es) in the allograft may represent post transplant lymphoproliferative disorder (PTLD) and require biopsy for confirmatory diagnosis. If PTLD is suspected, an extra core specimen or flow cytometry analysis may be suggested. Repeat biopsy may also be needed to assess therapeutic response in this setting.

Indications and Contraindications

Established and emerging indications for renal biopsy have grown in recent years. The very few absolute contraindications to renal biopsy may include uncontrollable bleeding diathesis, uncontrolled severe hypertension and uncooperative patient (10,29). In practice, most contraindications can be overcome by correction of coagulation parameters, good control of hypertension in the peri-procedural period, careful pre-procedural planning of approach and technique, and selection of appropriate image-guidance modality or modalities.

Pre biopsy evaluation

Prior to an image-guided renal biopsy, the patient's clinical history and physical exam should be reviewed with attention to recent vital signs and findings which might limit patient cooperation or optimal positioning for the procedure (i.e. the ability to lie flat due to respiratory distress). Available laboratory tests including complete blood count (CBC), basic metabolic panel (BMP) and coagulation studies should be reviewed along with imaging studies to help determine relative risk and biopsy approach. In general, some centers prefer the INR to be less than 1.6, PT less than 17 seconds and PTT less than 40 although there is little published evidence to support this approach. However, patient specific needs and individual risk to benefit ratio may dictate exceptions or redefining these guidelines.

General Technical Considerations

Regardless of the image-guidance modality, technique or type of needle chosen for renal biopsy, it is important to ensure that the patient is in a comfortable and in a stable position that can be maintained during the procedure and also allows good visualization of the target. Bean bags or axillary rolls for decubitus positions are requisite to avoid nerve injury. Intravenous sedation and analgesia can help ensure a safe and successful procedure, but too much sedation may also preclude the patient from following breathing instructions, which may be very important for biopsy of mobile small lesions. The use of US + CT can help in this scenario, where US is used for fine-tuning or puncturing a moving target. Next, a brief US or CT survey is performed to estimate the location of the target and a spot for needle entry and the skin is prepared in a sterile fashion. After administration of local anesthesia with 1% lidocaine, subsequent steps are determined by the image-guidance modality selected.

For US guidance, a more detailed evaluation is performed to optimize the image, identify vessels at risk, and select the site and angle of needle entry. A needle guide may be helpful to

those less experienced with US, but the freehand technique has fewer constraints for the needle and allows for visualization of needle tip from multiple US windows if needed (See Figure 2). For CT guidance, a radiopaque marking grid is placed on the skin to aid in selection of a spot for needle entry and angle. For cases in which the renal lesion is not well visualized on unenhanced CT, IV contrast can be administered to aid visualization and targeting of the lesion (See Figure 3). A spinal needle is used to administer lidocaine to the level of the renal capsule. Subsequently, we usually use coaxial technique with a 17 gauge introducer and an 18 gauge, side cutting, spring loaded biopsy needle to obtain the core specimens. In regard to obtaining fine needle aspiration (FNA) in the kidney, some studies have shown that lower diagnostic yield with FNA alone can lead to a high rate of false-negatives and its usefulness is highly dependent on the expertise and availability of the cytopathologist. In one study FNA and core biopsy had similar diagnostic yield, such that combining both may be better than doing either one alone. Adequate numbers of glomeruli are more consistently obtained using core biopsies and 18 gauge biopsy guns have been shown to be safer and equally efficacious to 14 gauge needles (42). As the needle is withdrawn, color Doppler may be used to evaluate for bleeding along the biopsy site. Bleeding is commonly seen with ultrasound or CT and is usually well controlled with 5 -10 minutes of sonographic guided probe compression. There are also other options which can be used to obtain hemostasis when continued brisk back-bleeding is noticed via the outer cannula following highly vascularized biopsies or in the presence of coagulopathy or bleeding diathesis. These options include thermal ablation of the tract, injection of a drop of collagen thrombin gel (D-stat), or the more conventional plugging with a gelfoam collagen pledget advanced with a stylet or small injection into the tract. Care must be taken not to over inject the parenchyma and into vessels.

Complications and Management Strategies

Image guided renal biopsy in current practice is a very safe procedure with mortality rates reported between .02 - 0.1 percent (43,44). Following renal biopsy, patients are placed on bed rest for four to six hours and vital signs are closely monitored to detect bleeding or other complications. Minor, subclinical bleeding is the most frequent perceived complication (or treatment effect) and is generally self-limited. With US guidance, this is often detected in real-time and controlled by simple ultrasound guided compression. Major bleeding complications can be minimized by correcting coagulation parameters prior to the procedure, using good technique, and controlling hypertension in the peri-procedural period with a goal of <140/90 mmHG (29,45). Some have advocated routine closure of the biopsy tract with Gelfoam collagen, collagen thrombin gel, or coil embolization (especially in transjugular approach or if large (>18 Gauge) needles are used for percutaneous approach) in order to prevent symptomatic bleeding. Bleeding requiring blood-transfusion or other intervention is rare and was reported in up to 1.5 % of procedures (24), but with modern image guidance and biopsy needles, this is likely to be more rare. Regarding optimal period of observation following renal biopsy, one study found that clinical recognition of major complication occurred within 4, 8, 12, and 24 hours among 38, 67, 89, and 91 percent of patients respectively. Based on these findings, the authors concluded that a 24 hour period of observation was optimal. However, this may not be practical at all centers and others have suggested shorter observation times for low risk patients (29,44). High risk patients can be monitored overnight.

Microscopic and gross hematuria can occur in up to 5-7% of cases and are also generally self-limited. Pseudoaneurysm and arteriovenous fistula may cause persistent symptoms of pain, bleeding and hematuria and their prevalence has been reported to be between 1-18% in older literature, but most of these are clinically silent and resolve spontaneously (46-48). Although rarely required, these complications can be successfully managed with routine transcatheter coil embolization if needed. Pneumothorax can rarely occur and is best avoided using a subcostal approach, and by looking for the mobile pleural reflection or diaphragm. Real-time

ultrasound may be used simply to define the pleural location in real time even when the target lesion cannot be seen by US and is targeted with CT. In rare cases, hydronephrosis caused by bleeding may require temporary ureteral stenting. Needle tract seeding is a very rare complication of renal mass biopsy with six cases reported in the literature but none in the last ten years (24,49).

Conclusions

Renal biopsy has become a much more relevant and routine procedure over the past decade as improvements in diagnostic cross sectional imaging have increased discovery of smaller renal masses and as tumor ablation techniques have been developed and refined. Although adrenal biopsy is performed less frequently, the risks associated with this procedure can be dramatically mitigated by with careful pre-procedural planning, patient positioning, and close attention to detail.

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Figure 1.

(a-c): CT guided left adrenal biopsy in a 62 yo female with history of left thigh melanoma resected 9 yrs ago and an incidentally discovered 3 cm adrenal mass. Biopsy requested to help determine diagnosis and stage disease. (a): CT image after patient positioning and placement of the marker grid. (b): CT image during needle advancement from a left paraspinal approach. Note the restricted movement of the left hemidiaphragm in this position. (c): Coaxial technique with the introducer needle tip at the periphery of the lesion. FNA and core specimens were obtained without complication. Pathology revealed metastatic melanoma - Stage IV disease.

Figure 2.

(a-c): US guided renal mass biopsy in a 75 yo male with diabetes, CRI, and history of melanoma with new incidentally detected bilateral renal masses. (a,b): Gray scale images demonstrate bilateral, solid, exophytic, heterogeneous renal masses. US guided renal mass biopsy of both masses was performed through a subcostal approach using coaxial technique without complication. (c): Image shows the biopsy needle within the left renal mass. Pathology revealed papillary RCC on the right and RCC with mucinous components on the left. The patient was not a surgical candidate and referred for percutaneous ablation.

Figure 3.

(a-c): CT guided renal mass biopsy in a 45 yo female with VHL and history of partial right nephrectomy and RFA of two left and one right renal lesions (RCC). (a,b): CT demonstrated a new 3 cm enhancing mass in the lower pole of the right kidney. (c): Biopsy was performed from a posterior approach with the patient in prone position but a target side down decubitus position could also have been used with an oblique approach. FNA and core specimens were obtained using coaxial technique without complication. Pathology revealed clear cell type RCC, Fuhrman nuclear grade 2. Total right nephrectomy was performed two weeks after biopsy.

Figure 4.

(a-d): US guided random biopsy of a patient with renal transplant and ARF. (a): Gray-scale image after obtained after optimizing visualization of target and needle trajectory. (b): Image shows an 18 gauge needle in the target using coaxial technique. (c): Color Doppler image following biopsy shows flow along the tract and into the perinephric space (d): Color Doppler image of the same area following 10 minutes of US guided compression. The flow along the tract has resolved and a small perinephric hematoma is seen. The patient remained completely asymptomatic and was discharged home following overnight observation. Pathology revealed no evidence for acute rejection.

Figure 5.

(a-d): Sequential steps during transjugular renal biopsy. (a): Opacification of the IVC and renal veins (carbon dioxide) with subsequent placement of the biopsy sheath and catheter (arrow) in the right renal vein over a guidewire (dashed arrow). (b): Venography demonstrates appropriate position of the sheath and catheter in a peripheral lower pole renal vein just prior to needle deployment (arrows). (c): Image obtained after the biopsy needle was deployed demonstrating the extent of needle excursion into the renal cortex (d): Same image with a schematic outline of the kidney showing that the needle tip did not breach the capsule.