Cancer Imaging (2009) **9,** 44–55
DOI: 10.1102/1470-7330.2009.0005

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REVIEW ARTICLE

Biopsy of renal masses: when and why

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Date accepted for publication 23 March 2009

Abstract

Percutaneous image-guided biopsy of renal masses is a safe and accurate procedure. Although once reserved for the diagnosis of unresectable renal cell carcinoma, metastases, lymphoma, and infection, today percutaneous image-guided biopsy has an expanded role. There is increasing awareness that a substantial proportion of small, solid renal masses are benign neoplasms. Although imaging can be used to diagnose most of them, some are incorrectly believed to represent renal cell carcinoma and unnecessary surgery may be performed. Based largely on advances in cytological techniques, percutaneous biopsy can be now be used to diagnose benign neoplasms and thus prevent them from being treated unnecessarily. Concurrent advances in percutaneous ablation have also promoted its use. As a result, there are 8 established indications for percutaneous biopsy, and reason to believe that the number of indications will expand further in the future.

Keywords: *Percutaneous image-guided biopsy; renal mass.*

The current diagnostic paradigm for evaluating renal masses is primarily dependent on cross-sectional imaging modalities: ultrasonography (US), computed tomography (CT) and magnetic resonance (MR) imaging. These techniques allow most renal masses to be evaluated and characterized accurately using specific imaging criteria[1,2]. As a result, when a renal mass is diagnosed with confidence, appropriate management can be instituted without further investigation. For example, when a mass demonstrates characteristic features of malignancy, surgical resection, if warranted, can be performed without a preoperative biopsy because the prior probability of disease is sufficiently high; a negative biopsy result would not likely alter management[3]. Similarly, published imaging criteria exist for some benign masses, such as simple cysts[1], hyperdense cysts[2] and fat-containing angiomyolipomas[4,5], which can be diagnosed with a high degree of confidence. Historically, therefore, renal mass biopsy has been reserved for a limited number of indications. These have included the diagnosis of metastatic disease, infection, and lymphoma. Biopsy has also been used to diagnose unresectable renal cell carcinoma and diagnose masses in patients who are poor surgical candidates[6]. Percutaneous biopsy of renal masses is now being increasingly used to differentiate between benign and malignant entities safely and accurately[7,8]. Biopsy has been shown to alter clinical management in 60.5% of patients in whom a biopsy is performed[7]. As a result, the approach to the diagnosis and management of renal masses has changed.

The growing need to perform a biopsy on renal masses can be ascribed to several factors. More renal masses are being detected than ever before[9–11] largely due to the increased utilization of US, CT and MR imaging[12]. Just as important, advances in imaging technology allow more small renal masses to be characterized as solid and therefore potentially malignant. Many small masses are being identified in patients with no symptoms attributable to the urinary tract. This has led not only to an increase in the incidence of renal cell carcinoma[13–15] but also a corresponding increase in the incidence of benign renal neoplasms[16]. Concomitantly there has been an increasing awareness in the literature that solid, enhancing, renal masses cannot be presumptively diagnosed as renal cell

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carcinoma and proceed to surgery. In fact, multiple studies demonstrated that between 8% and 27% of surgically resected solid renal masses were benign[16–22]. Furthermore, based on a review of 2770 solid renal masses treated by radical nephrectomy or nephron-sparing surgery, the percentage of benign lesions increased as the size of the lesions decreased; 25% of masses less than 3 cm, 30% of masses less than 2 cm and 46% of masses less than 1 cm are benign[20]. Technological advances in the acquisition and interpretation of renal biopsy specimens has had a major impact on the diagnosis of renal neoplasms. Biopsy using fine needles (20 gauge or thinner) has been shown to be accurate in the diagnosis of renal masses[23,24], in large part due to enhancements in cytologic techniques (immunocytochemistry and cytogenetics) that have allowed for the accurate diagnosis of benign and malignant neoplasms[25–27] and in some cases, determination of renal cell carcinoma subtype and Fuhrman nuclear grade[28,29].

Biopsy performance

Technical details and complications

When performing a renal mass biopsy, consideration should be given to several technical factors that may affect the diagnostic and complication rates. The guidance modality that best depicts the lesion, adjacent structures and the needle-tip should be used to guide the biopsy. Each modality has its advantages and disadvantages[30–33]. US provides real-time imaging without ionizing radiation but may not visualize the lesion. CT is more expensive, however, usually allows better depiction of the mass and surrounding structures. MR imaging is seldom used but may be helpful to biopsy a mass that is not seen by US or CT[34]. Operator preference, and equipment availability will also play a part in deciding which imaging modality is chosen.

Typically fine (20-gauge or thinner) needle specimens are examined cytologically and large (19-gauge or larger) needle specimens histologically. Comparison of diagnostic effectiveness between fine and large needles is difficult. No direct comparative studies exist; many of the studies in which large and fine needles have been used do not assess the performance of each needle independently[8,35]. Fine needles have been shown to obtain a diagnosis in up to 93% of renal masses[24]. High rates of success have also been reported in studies in which only large needles were used[36,37]. Using 18-gauge needles alone, Caoili *et al.*[36] obtained a diagnosis in 92% of lesions and Neuzillet *et al.*[37] in 91%. Large needles may be more effective but probably carry a higher risk of bleeding and pseudoaneurysm formation compared with fine needles[36,38]. Overall, however, renal mass biopsy is a safe procedure; most hemorrhages are subclinical (detected as stranding or small hematoma at CT) and self-limited.

Given the lack of conclusive evidence that large needles confer a greater diagnostic effectiveness, the authors obtain fine-needle specimens initially and obtain a preliminary impression by a cytology technologist during the biopsy procedure. If the specimens are not adequate, large needle biopsies are obtained.

Needle track seeding is a potential complication of renal mass biopsy. The true incidence is difficult to ascertain. The scarcity of published reports[39–42] implies that it is a rare event, and probably not more common than other percutaneous biopsy sites. To the best of our knowledge, there is no evidence to suggest that use of large needles increases the risk of needle track seeding relative to fine needles.

Diagnostic effectiveness

The purpose of percutaneous biopsy is to obtain a tissue diagnosis safely. The biopsy result should have implications on patient management. Therefore obtaining a benign diagnosis is as important as a malignant one. The absence of malignant cells from a biopsy, however, does not necessarily confirm benignity and should be viewed with caution. Sensitivities and specificities for renal mass biopsy range from 80 to 92% and from 83 to 100% respectively[43]. False negative results are likely due to inaccurate needle placement or obtaining necrotic tissue[44]. False positive results are rare and are likely much less frequent today due to advances in cytology.

In some cases, renal cell carcinoma subtype and Fuhrman nuclear grade can be determined with a percutaneous biopsy. Current evidence suggests that successful subtyping can be performed with a high degree of success[28,37]. Determination of nuclear grade is more difficult; as biopsy specimens do not correlate as well with surgical specimens[37,45,46]. This information is of particular importance in incidentally detected small renal cell carcinomas. It can help to decide whether minimally invasive nephron-sparing techniques would be appropriate. For example, a confident diagnosis of a small low-grade neoplasm would support using a minimally invasive approach, or perhaps observation.

Most angiomyolipomas can be diagnosed with imaging by identifying intralesional fat attenuation[4,5]. When an angiomyolipoma contains little or no fat, biopsy is the only way to diagnose them without surgery. Using cytologic techniques such as immunocytochemistry, a definitive diagnosis can be made[25,26]. For example, human melanosome-associated protein, HMB-45, and smooth muscle actin, are consistently expressed in angiomyolipomas and not in renal cell carcinoma[47]. Cytokeratin conversely is not seen in angiomyolipomas but is frequently present in renal cell carcinoma[6].

Oncocytoma may be diagnosed percutaneously in some cases. Cellular morphology coupled with immunocytochemical stains allows oncocytomas to be distinguished from oncocytic renal cell carcinoma, the most

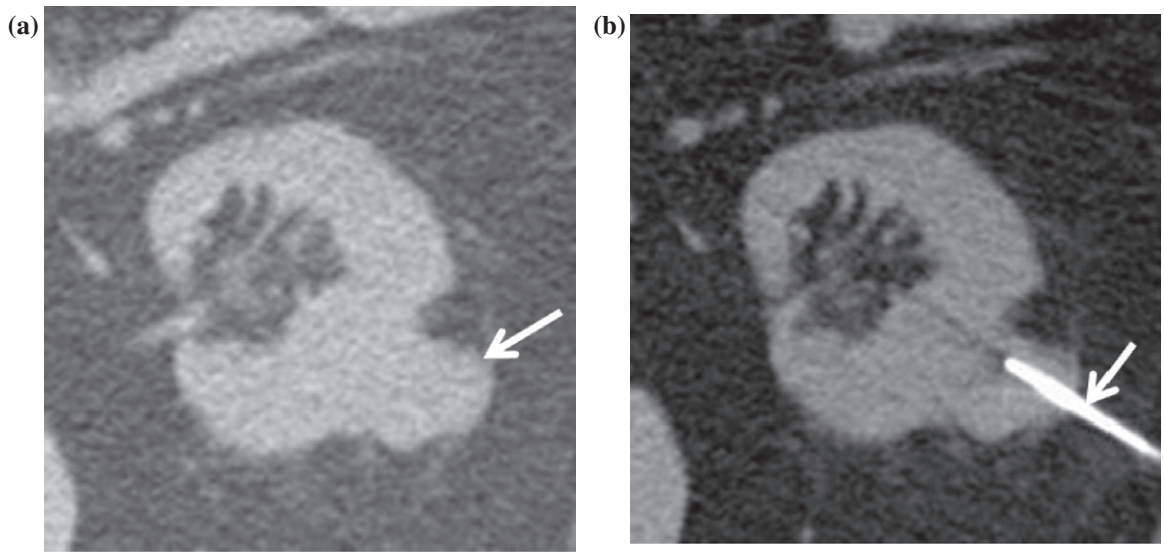

Figure 1 **Incidental 2.1-cm enhancing mass in the interpolar region of the left kidney in a 72-year-old man. (a) Transverse unenhanced CT image shows isoattenuating mass (arrow) with no evidence of fat. (b) CT-guided percutaneous biopsy, shown on transverse CT image, was performed while the patient was prone with 25-gauge needles placed coaxially using a 20-gauge needle (arrow). Diagnosis was chromophobe renal cell carcinoma.**

common of which is chromophobe renal cell carcinoma (Fig. 1). The Hale's colloidal iron stain is particularly helpful; when positive chromophobe renal cell carcinoma can be diagnosed confidently[27]. When absent, oncocytoma is favored. Cytokeratin 7 expression may help as an adjunct in differentiating the pathologies. It tends to show strong cytoplasmic staining with peripheral accentuation in chromophobe renal cell carcinoma, whereas in oncocytoma the staining is usually weak or absent[48–52]. The usefulness of cytokeratin 20 seems limited given its highly variable expression[51–53]. A new stain, S100A1 seems to be positive in oncocytoma and not chromophobe renal cell carcinoma[54,55]. In other cases, oncocytoma cannot be differentiated from oncocytic renal cell carcinoma.

Indications for percutaneous biopsy of renal masses

In clinical practice, the authors have 8 established indications for renal mass biopsy[6,56]. These have been derived from published literature and a wealth of clinical experience[6,56]. The established indications include patients with masses that are likely malignant, but surgical resection is not indicated and patients with indeterminate masses that may be benign and therefore do not require treatment. A new, emerging indication includes patients with small (less than or equal to 3 cm) solid masses. The rationale for obtaining a biopsy of these masses is based principally on data that show that the smaller the mass the more likely it is benign. Although there may be multiple indications in a given patient, only one indication is needed to proceed with a biopsy.

Established indications

Patients with known extrarenal primary cancer

The identification of an enhancing renal mass in a patient with an extrarenal malignancy poses a diagnostic dilemma regarding whether the mass represents a primary renal cell malignancy or a metastatic lesion (Fig. 2). Metastatic lesions to the kidney are not rare; autopsy studies demonstrate renal metastases in 7–13% of patients with cancer[57,58]. The commonest malignancies to metastasize to the kidney are lung and lymphoma[44,59]. Despite this high propensity for renal metastases, Rybicki *et al.*[44] demonstrated that 31 (57%) of 54 renal masses in patients with extrarenal malignancies represented renal cell carcinoma. Accurate diagnosis is therefore imperative as there are major treatment implications[59]; most metastatic lesions require medical treatment, whereas renal cell carcinomas are resected or ablated. The sensitivity of biopsy in this cohort of patients has been shown to be 90%[44]. Imaging features in most cases cannot be used to differentiate metastases from renal cell carcinoma reliably. Although certain feature such as bilaterality and multiplicity may be suggestive of metastases, these features can also be seen in patients with renal cell carcinoma[60]. Cystic masses, however, are unlikely to represent metastases[44]. Recent evidence suggests that in patients with an extrarenal malignancy and no evidence of disease elsewhere, a renal mass is almost certainly renal cell carcinoma[61]. However, in patients with an extrarenal malignancy and extrarenal metastases, the renal mass cannot be assumed to be a metastasis.

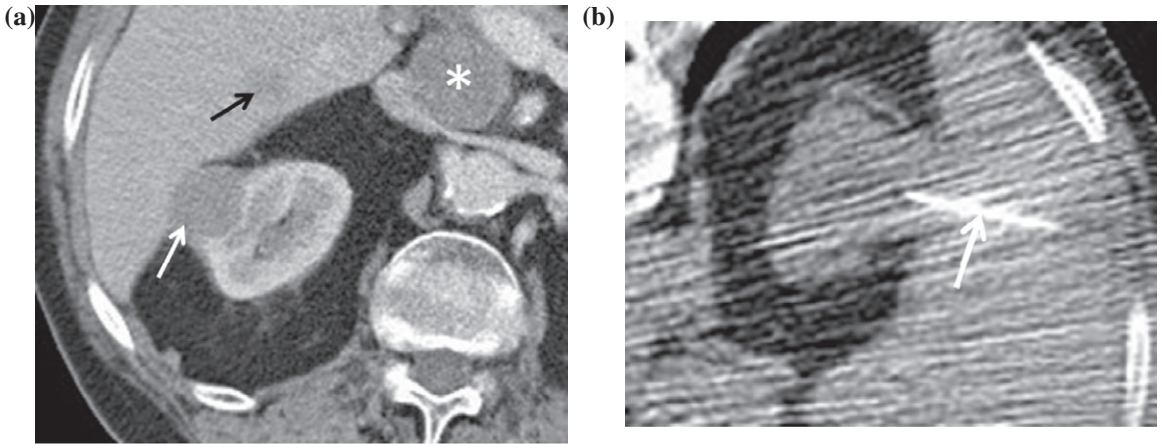

Figure 2 **Small 2.7-cm enhancing mass in the upper pole of the right kidney in an 81-year-old man with metastatic melanoma. (a) Transverse CT image shows enhancement of the mass (white arrow). Portocaval lymphadenopathy (*) and liver metastasis (black arrow) are present. (b) CT-guided percutaneous biopsy, shown on transverse CT image, was performed transhepatically with the patient prone with 25-gauge needles placed coaxially using a 20-gauge needle (arrow). Diagnosis was metastatic melanoma.**

Patients with imaging findings suggestive of unresectable renal cancer

Renal cell carcinoma may be unresectable due to either locally advanced disease or distant metastases. In patients with imaging findings highly suggestive of unresectable renal cell carcinoma, biopsy is important to obtain a diagnosis and institute appropriate management. It can be performed safely with a high sensitivity[44,62].

When the tumor is locally advanced, the renal mass is the only possible site of biopsy. If there are distant metastases, biopsy offers the opportunity to diagnose and stage the patient. However, a risk-to-benefit analysis needs to be undertaken to determine which site will provide the highest yield and the lowest risk to the patient. For example, obtaining a biopsy from a possible metastatic deposit to the lung carries a risk of pneumothorax, but a diagnosis of metastatic renal cell carcinoma also stages the patient.

Biopsy is also important for determining medical therapy. Chemotherapy for renal cell carcinoma historically has been ineffective. Immunotherapy with cytokines such as interferon alpha and interleukin 2 has demonstrated variable results[63]. Knowledge of tumor subtype, however, is helpful in predicting response. For example, interleukin 2 has produced higher response rates for clear-cell renal cell carcinoma compared with papillary renal cell carcinoma[64]. Tumor subtype is also important for emerging biologic therapies. New agents, such as Sorafenib (Nexavar®; Bayer Pharmaceuticals Corporation, West Haven, CT) and Sunitinib (Sutent®; Pfizer, Inc., New York), target vascular endothelial growth factor (VEGF), which is needed for angiogenesis. Both agents have been approved for use in metastatic renal cell carcinoma and validated in clinical trials[65,66]. VEGF is upregulated by dysfunction of the von Hippel-Lindau (VHL) gene which is characteristically associated with clear-cell renal cell carcinoma[63].

Patients with comorbidity in whom surgery is planned

Patients with a suspected resectable renal cell carcinoma and medical comorbidities are a difficult group for the urologist to manage. Comorbidities often relate to pulmonary or cardiac disease, renal insufficiency or the presence of a solitary functioning kidney. To construct a safe and informed surgical plan, a formal risk-to-benefit analysis needs to be performed. This is dependent on not only assessing the surgical and anesthetic risk for the patient but also determining the likelihood that the mass represents renal cell carcinoma and not a benign neoplasm[9–11]. In these cases, biopsy provides a definitive diagnosis of renal cell carcinoma, and allows the surgery to be planned with more confidence[62].

Patients with a renal mass that may be caused by infection

Although renal infections can have varied radiologic manifestations[67], they may present as a mass-like abnormality and mimic a neoplasm[68]. Imaging features can be used to suggest that the mass is due to an infection. These include ill-defined margins on ultrasound[69] and ill-defined margins, perinephric stranding and patchy enhancement on CT[69,70]. When clinical and laboratory signs of infection are present, an infectious condition can be diagnosed with confidence. However, if signs and symptoms of a urinary infection are absent or occult[71], a renal tumor may be diagnosed inadvertently. Misinterpretation may lead to surgical resection rather than antibiotic therapy. In the small group of patients

in whom a mass-like abnormality may be due to an infection, percutaneous biopsy may help to provide the correct diagnosis.

Patients with a small ($\leq$3 cm) hyperattenuating homogenously enhancing renal mass

Small hyperattenuating renal masses may occur due to a variety of causes[72]. Benign nonenhancing entities include hemorrhagic or proteinaceous cysts and hematomas. Benign lesions that demonstrate enhancement comprise vascular anomalies, angiomyolipomas and oncocytomas. Renal cell carcinoma and lymphoma are among the malignant causes.

Certain benign neoplasms, such as angiomyolipoma with minimal fat, oncocytoma, and metanephric adenoma, may be difficult to differentiate from renal cell carcinoma by imaging alone[73–77]. The identification of regions of fat attenuation on unenhanced CT is diagnostic of an angiomyolipoma[4,5]. Approximately 5% of angiomyolipomas, however, have no imageable fat component[73,78] and typically appear on CT as small hyperattenuating masses that enhance homogenously[73] (Fig. 3). Although this presentation is uncommon for a renal cell carcinoma[73] the two pathologies may be indistinguishable on imaging[73–75,79]. In these cases, MR imaging should be performed. MR imaging allows differentiation between angiomyolipoma with minimal fat and clear-cell carcinoma, which are hypointense[73] and hyperintense[80], respectively, on T2-weighted imaging. The papillary subtype of renal cell carcinoma is more difficult to differentiate from angiomyolipoma with minimal fat because it is also hypointense on T2-weighted imaging[80–82] (Fig. 4). Percutaneous biopsy is therefore required to differentiate angiomyolipoma with minimal fat and papillary renal cell carcinoma when an enhancing, T2 hypointense mass is encountered and does not demonstrate evidence of intratumoral fat.

Patients with a renal mass for which percutaneous ablation is considered

Percutaneous ablative techniques are becoming increasingly used to treat renal masses[83–90]. Ablation is nephron-sparing and therefore useful in certain high-risk patients including those with bilateral tumors, solitary kidneys and renal insufficiency. As experience increases and long-term follow-up emerges, the indications for renal mass ablation are becoming more diverse. Its use is now advocated in small unilateral renal cell carcinomas as an alternative to surgical resection[91].

Biopsy of a suspected renal cell carcinoma before ablation is necessary for several reasons. Unlike surgical resection whereby the entire surgical specimen can be examined pathologically, ablation destroys the neoplasm, and thus no tissue is available after the procedure for analysis. Therefore, the only opportunity for a tissue diagnosis is by a percutaneous biopsy. Furthermore, despite dedicated renal CT and MR imaging, a proportion of lesions referred for ablation may be benign[92,93]. Tuncali *et al.*[93] demonstrated that 37% of masses referred for ablation were benign. Benign pathologies included angiomyolipomas with minimal fat, focal bacterial pyelonephritis and benign complicated cysts. Treating a benign lesion with percutaneous ablation inadvertently has important implications. Not only is the treatment inappropriate and exposes the patient to unnecessary risks but the patient is labeled with a diagnosis of cancer, and subjected to lifelong clinical and radiologic follow-up.

Long-term effectiveness of ablation is not yet known. To validate the technique relative to surgery, the pathology of lesions treated must be known prospectively by preprocedural biopsy. Unfortunately several clinical trials of percutaneous ablation[84,85,87,88] included renal masses that were diagnosed solely based on imaging. If many of the lesions treated were in fact benign, the efficacy of ablation was overestimated.

Indeterminate cystic renal mass

The Bosniak classification of cystic renal masses is well established and widely used[1]. Historically it has stratified these masses into two broad groups; types I and II are nonsurgical lesions and types III and IV are typically resected surgically[1]. There is increasing risk of malignancy from type I (virtually 0%) to type IV (near 100%)[94–97]. Resection of type IV lesions is indicated due to the high risk of malignancy[94–97]. Type III lesions are indeterminate and cannot be definitely diagnosed as benign on imaging alone. Although the risk of malignancy is highly variable (31–100%)[94–97], resection is advocated so as not to miss a cancer. Biopsy in this group has been traditionally seen to be of limited use[1] as false negative biopsy results are common. Indeed, examination of the entire lesion at pathology is sometimes needed to render a histopathologic diagnosis. However, some patients are not surgical candidates, and therefore biopsy may be useful.

If malignant cells are not retrieved from the cyst wall or fluid, the cyst is not necessarily benign and a specific diagnosis is often difficult to make[98]. In addition, atypical cells or hemorrhagic aspirates are not necessarily conclusive of malignancy[98]. Studies evaluating the usefulness of percutaneous biopsy have shown a range of accuracies[44,99,100]. Rybicki *et al.*[44] demonstrated a sensitivity of only 33% whereas Harasinghani *et al.*[99] managed to render a diagnosis in 100% of renal cystic lesions. Given this wide spectrum of test performance, biopsy is unlikely to become routine in the diagnosis of Bosniak type III cystic lesions. The authors, however, find it useful in patients with surgical comorbidities. A malignant biopsy result allows surgery to proceed with confidence. A negative result may be definitive when a specific entity such as oncocytoma or metanephric adenoma is diagnosed. Otherwise, a negative result

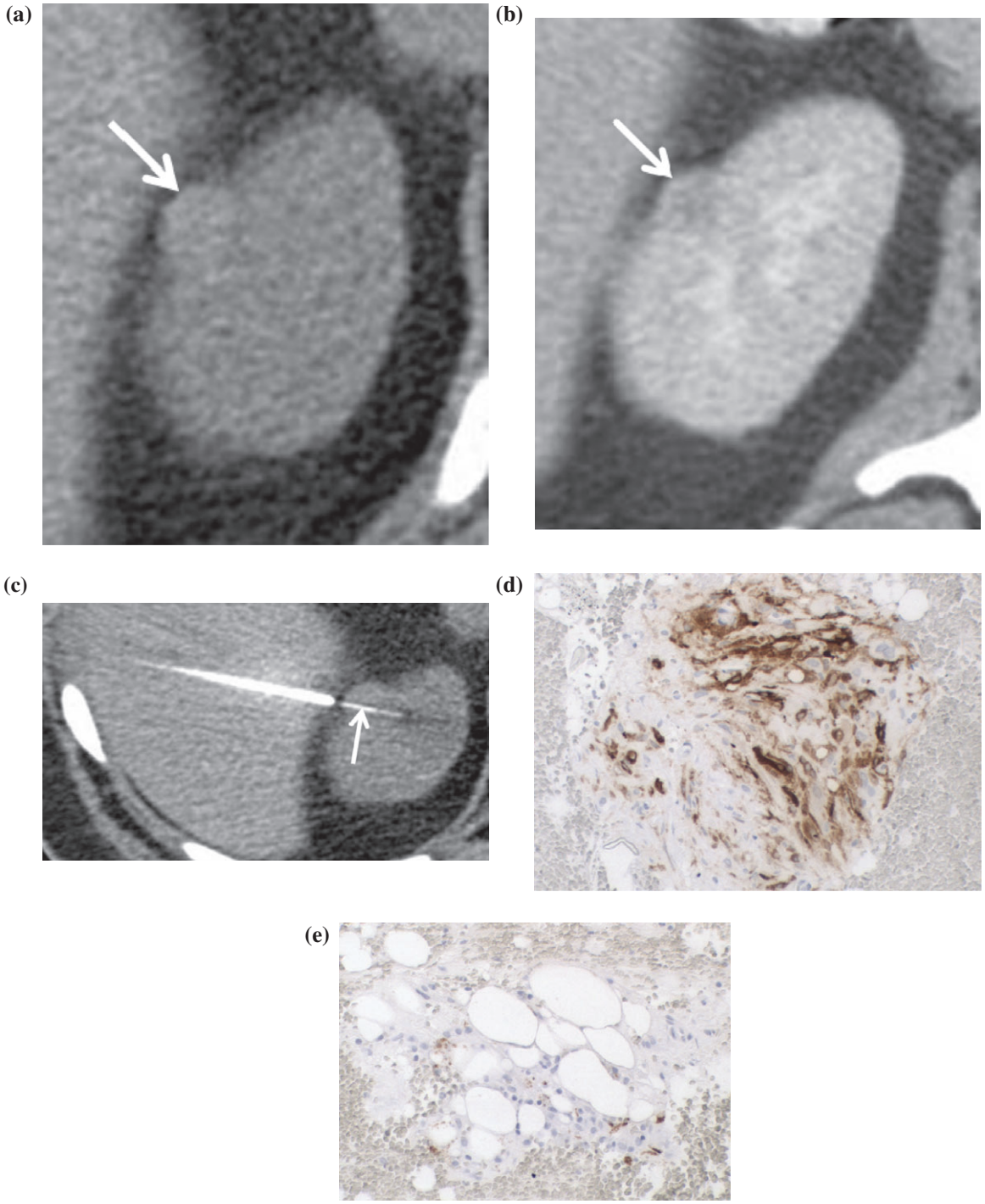

Figure 3 **Small 1-cm hyperattenuating enhancing mass in the upper pole of the right kidney in a 46-year-old woman incidentally noted on chest CT. (a) Transverse unenhanced CT image shows hyperattenuating mass (arrow) with no evidence of fat. (b) Transverse CT image shows enhancement of the mass from 50 HU to 112 HU (arrow). (c) CT-guided percutaneous biopsy, shown on transverse CT image, was performed transhepatically with the patient prone using 25-gauge needles (arrow) placed coaxially using a 20-gauge needle. (d,e) Photomicrographs of immunocytochemical-stained specimens are positive for (d) smooth muscle actin and weakly positive for (e) HMB-45, which are both shown as brown areas. Diagnosis was angiomyolipoma with minimal fat.**

may provide more confidence in following patients. Biopsy results that simply report no malignant cells should be viewed with caution and do not necessarily represent a benign lesion.

Multiple solid renal masses

Multiple solid renal masses can be due to several diagnoses including metastases and primary lymphoma. In both

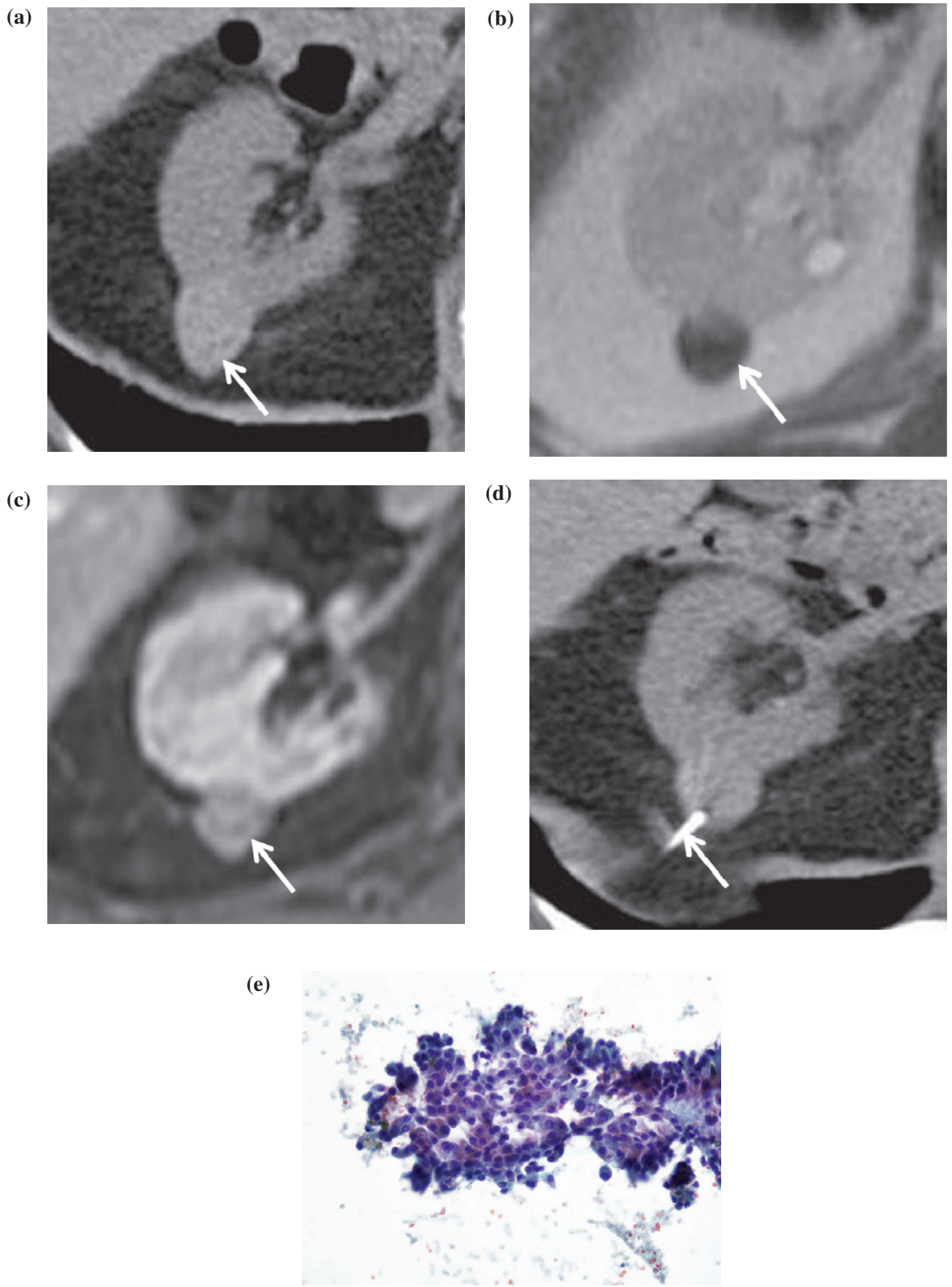

Figure 4 **Small 1.3-cm hyperattenuating enhancing mass in the interpolar region of the right kidney in a 68-year-old man. (a) Transverse unenhanced CT image shows a hyperattenuating mass (arrow) with no evidence of fat. (b) Transverse T2-weighted MR image shows that the mass is hypointense (arrow). (c) Transverse T1-weighted post contrast MR image shows enhancement of the mass (arrow). (d) CT-guided percutaneous biopsy, shown on transverse CT image, was performed with 25-gauge needles placed coaxially using a 20-gauge needle (arrow). (e) Photomicrograph reveals characteristic morphologic features of papillary renal cell carcinoma, which are demonstrated by blue areas.**

conditions, however, clinical history and extrarenal findings are usually supportive. For example, metastases to the kidney are usually accompanied by metastases elsewhere[61]. Likewise, the kidney is usually involved with lymphoma secondarily[101]; primary lymphoma of the kidney is rare[102].

Hereditary conditions can result in multiple solid renal masses. A diverse group of hereditary syndromes exist that may result in renal cell cancer that is typically multiple and bilateral[60]. In addition, hereditary renal cell carcinoma usually occurs at an earlier age than the more common sporadic variant[103]. A fine balance needs to be reached between successfully eradicating these tumors and the need to spare functioning renal tissue to avoid dialysis. Nephron-sparing techniques such as partial nephrectomy and ablation are often used in combination. Not all hereditary syndromes, however, produce malignant masses. Renal oncocytosis results in multiple oncocytomas that are benign and do not require treatment[104]. Percutaneous biopsy is therefore crucial to establish the correct diagnosis before definitive treatment is undertaken[56].

Emerging indication

Small ($\leq$3 cm) solid masses

The principal criterion for determining the role of biopsy in this emerging indication is the size of the solid renal mass. Surgical data have consistently demonstrated that as the size of a solid renal mass decreases, the probability of it representing a benign entity increases[16–22]. Benign masses most commonly resected include angiomyolipomas with minimal fat and oncocytomas[19,20]. Rarer benign neoplasms include metanephric adenoma, papillary adenoma, and leiomyoma (Fig. 5). These masses have historically undergone unnecessary surgical resection because they cannot be distinguished from malignant lesions by imaging alone[73–77]. Radical nephrectomy is associated with quantifiable perioperative complications and risks[105]. These risks have been reduced by using nephron-sparing techniques such as partial nephrectomy and percutaneous ablation. They also preserve renal function[105]. The appropriateness, however, of any treatment of benign lesions is questionable regardless of the technique. By performing biopsy

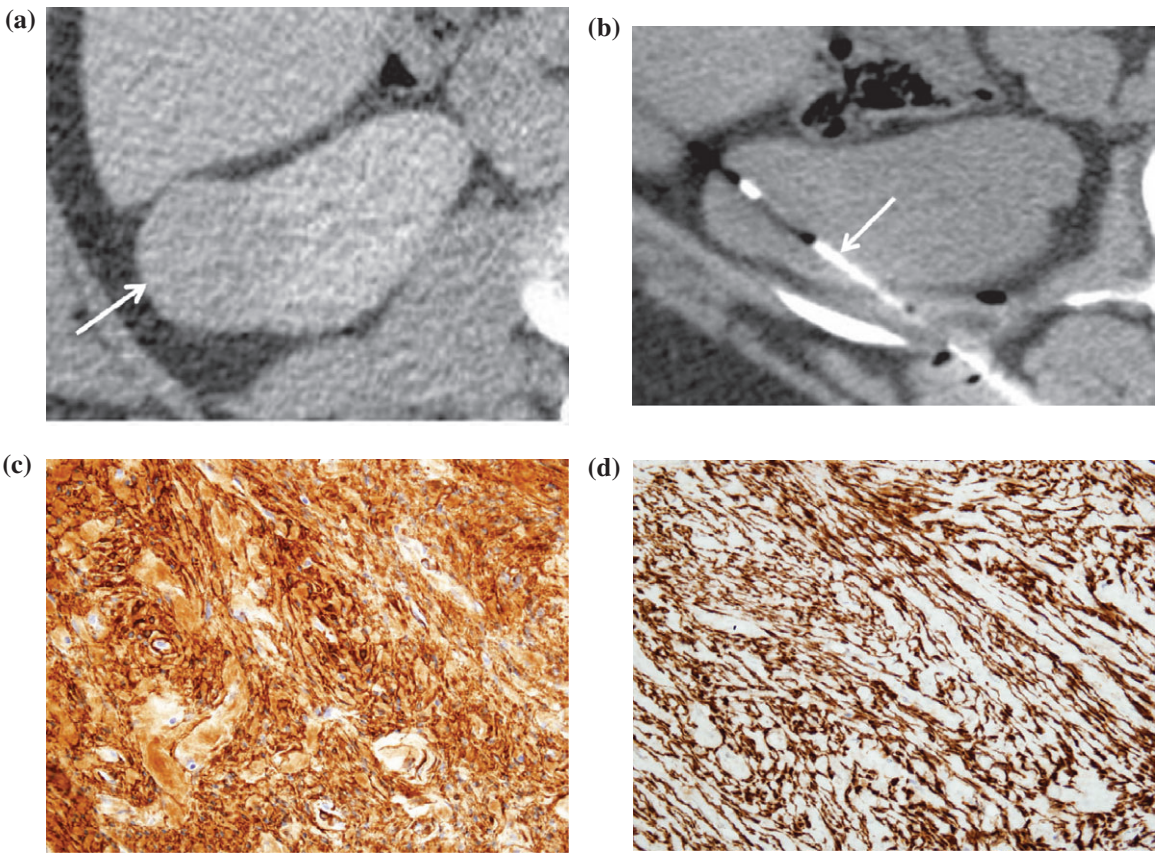

Figure 5 **Incidental 2.5-cm enhancing mass in the upper pole of the right kidney in a 42-year-old woman. (a) Transverse CT image shows enhancement of the mass (arrow). (b) CT-guided percutaneous biopsy, shown on transverse CT image, was performed with 18-gauge needles (arrow) placed coaxially using a 17-gauge introducer. (c,d) Photomicrographs of immunohistochemical-stained specimens are positive for (c) smooth muscle actin (orange staining) and (d) desmin (brown staining). Diagnosis was leiomyoma.**

of small solid renal masses, a significant proportion of benign lesions may be confirmed, obviating the need for treatment. It is unclear whether a biopsy should be taken from all small renal masses and what the size cut off should be. Because the likelihood of a benign etiology increases with decreasing mass size, biopsy would be more appropriate in smaller masses, however, masses less than 1 cm are difficult to target for biopsy.

The increasing treatment of incidentally detected small renal masses is an area of continued controversy[106]. Mixed results regarding the biologic aggressiveness of small renal cell carcinomas with respect to size have been reported[20,107,108], however, consensus suggests that smaller renal cell carcinomas tend to be of lower grade and more indolent. Although limited data exist on their natural history[109,110], many grow slowly if at all, and some may never result in mortality. Surgical comorbidity, patient preference, life expectancy and age are factors that may be used to decide on management. The indolent nature of some small renal cell carcinomas have prompted some to consider observation in lieu of resection or ablation[111,112]. Percutaneous biopsy can help determine the most appropriate management plan by providing information such as cell subtype and Fuhrman nuclear grade, which can be used to judge the tumor's potential for growth and metastases.

Conclusion

Although imaging is the primary diagnostic tool in the evaluation of renal masses, in many specific clinical scenarios, percutaneous renal mass biopsy plays a crucial role in determining clinical management. Unlike years past, biopsy can now be used to diagnose benign neoplasms that previously underwent inadvertent surgical resection. The burgeoning field of tumor ablation has necessitated the use of percutaneous biopsy: the only means to render a tissue diagnosis. Biopsy may be helpful in characterizing some small renal cancers as indolent, thus allowing a watchful waiting approach to be considered in selected patients.

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