Review Article

Renal Tumor Biopsy Technique

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Abstract

Objective: To review hot issues and future direction of renal tumor biopsy (RTB) technique.
Data Sources: The literature concerning or including RTB technique in English was collected from PubMed published from 1990 to 2015.
Study Selection: We included all the relevant articles on RTB technique in English, with no limitation of study design.
Results: Computed tomography and ultrasound were usually used for guiding RTB with respective advantages. Core biopsy is more preferred over fine needle aspiration because of superior accuracy. A minimum of two good-quality cores for a single renal tumor is generally accepted. The use of coaxial guide is recommended. For biopsy location, sampling different regions including central and peripheral biopsies are recommended.
Conclusion: In spite of some limitations, RTB technique is relatively mature to help optimize the treatment of renal tumors.

Key words: Biopsy; Renal Tumor; Technique

Introduction

The incidence of renal tumor has been rising in the past few decades, with the greatest increase in small renal masses (<4 cm, SRMs).[1] Not all SRMs are renal cell carcinoma (RCC), with approximate 20–30%[2,3] confirmed with benign pathology. Although imaging tests, such as computed tomography (CT) or magnetic resonance imaging (MRI) with contrast, have a pretty high diagnostic yield of renal cancer, the heterogeneity of RCC makes the imaging test incapable to predict the tumor behavior. Previous studies demonstrated that only 20–30% of renal cancers present aggressive malignant potential.[4,5] The problem of RCC overtreatment has caused general attention. Renal tumor biopsy (RTB) could provide tumor issue that might be useful to find some predictors of the natural history of RCC. In the era of individual treatment, RTB has been attracting clinician's attention. In this review, we will discuss the hot issue and future direction of RTB technique.

Why Renal Tumor Biopsy Should be Performed?

Although modern imaging technique has been well developed in the differentiation of benign and malignant tumors, only relying on images without pretreatment histology is not reliable to decide treatment. Up to 30% of SRMs removed by surgery are benign when pretreatment histology is not obtained.[6-8] The accuracy of biopsy in identifying a lesion as benign or malignant is more than 90%,[2,9-18] which is higher than traditional imaging examination.[19] In addition, pretreatment biopsy can obviously decrease unnecessary surgeries for benign disease. Neuzillet *et al*. demonstrated that 15 out of 88 patients (17%) were avoided to undergo unnecessary surgeries after biopsies, 14 were benign disease, and another was lymphoma.[10] Wood *et al*. also avoided surgeries for benign disease in 32 out of 73 patients (44%) after biopsies.[20] Recent studies about active surveillance (AS) of SRMs especially in patients who were unfit for surgery showed that only a small portion of SRMs have the potential of fast growing or metastasis.[21-28] However, not all the SRMs are suitable for AS. It is generally believed that low-grade clear-cell RCC, papillary type 1, and

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chromophobe tumors carry more favorable prognoses.[29] High-grade RCC presented fast growth rate during AS and implied a worse prognosis.[30] Hence, for patients with renal tumors treated by conservative therapy, obtaining histological information before making treatment decision may be more appropriate.

Safety and Complication

Traditionally, safety is one of the concerns that limited the widespread use of renal tumors biopsy. The possible complications of RTB include bleeding, tumor seeding along the needle tract, infection, pneumothorax, and arteriovenous fistula. Of all the complications, tumor seeding along the needle tract is the most feared potential complication. However, the risk of this complication with urologic malignancy is below 0.01%.[13] In the recent studies, a few cases of tumor seeding along the needle tract for RTB were reported.[2,10-12,14,20,31-35] Another concern about safety is the risk of intratumoral and perinephric bleeding. Previous studies showed that significant bleeding was unusual; most of the bleeding was limited without compromise of hemodynamic stability.[2,9-12,14,20,31,32,34,35] Other complications of RTB were rare and treatable. On the whole, with the technique improved, RTB has been relatively safe now. Recent studies on the renal needle core biopsies and fine needle aspiration (FNA) revealed very few or no major complications, which were defined as the need of transfusion, more than 24-h admission, embolization, or surgical intervention.[2,10-12,20,31-35]

Indication

Traditionally, RTB was used to rule out lymphoma, renal abscess or metastatic nature of renal mass with a known nonrenal malignancy and to confirm the histological diagnosis for system therapies. Based on the recent data of RTB,[2,9-12,14,20,31,32,34,35] the indication of RTB has been expanding at present. However, there was still no overall consensus about when to perform RTB. For now, the indications of RTB are mainly based on local practice patterns and investigative interest.

Apart from the above indication, some new concepts about the indication of RTB were proposed. An international panel recommended pretreatment biopsies for every patients intending to receive ablative therapies[36] as histological information was needed for making treatment decision and adequate surveillance strategy. For synchronous or metachronous renal tumors, these lesions have shown the potential for different histology in the sporadic setting.[37,38] Hence, for patients with synchronous renal tumors, it is appropriate to perform RTB for all lesions rather than depending on the histology of one renal mass. AS for renal mass has been gradually accepted with encouraging results.[39] Because RTB could help identify the suitability of AS and make risk-stratified surveillance schedule, the panel recommended RTB before performing AS.[36]

Image Guidance Systems

RTB is usually performed using ultrasound (US)- or CT-guidance. To our knowledge, there are few data supporting which of these methods yield the best results.

US is a useful technique for visualizing the tumor lesion and has the advantages of real-time needle placement, multi-planar imaging, low cost, visualization of vascular structures, and no harmful side effects of radiation.[40] Furthermore, proper experience biopsy with US-guidance is a very quick technique which takes less time than CT- or MRI-guided biopsies. To further improve the reflectivity and visualization of the needle, the surface of needle can be coated or scored by screw and Teflon.[41] Another major benefit of US is that the machines are portable and examinations can be performed at the bedside when necessary. The main disadvantage of US is that not all renal masses can be visualized with this technique, particularly in patients with small and/or endophytic renal lesions and in very obese patients. Some of these problems can be overcome by using intravenous contrast-enhancement with micro-bubbles.[42] However, as the micro-bubbles wash out in just a few minutes, this only gives the operator a short time-window to perform the biopsy. In addition, US is a very operator-dependent technique and there is a significant learning curve, which may affect the final imaging results.[43] In many centers with extensive experience in the US, biopsies are primarily performed with US-guidance and CT is reserved for patients in whom US is not feasible.

CT is also frequently used for RTB and many centers use CT-guidance as the primary technique for RTB.[44] CT has a higher sensitivity for SRMs than US, particularly when lesions are endophytic. The technique of CT-guided biopsy is less operator-dependent than US-guided biopsy although considerable skill is required for adequately biopsy.[43] The detection of renal lesions is improved by using intravenous contrast medium when performing CT.[45] Similar to contrast-enhanced US, CT contrast medium can only provide images during a limited time-window. However, as renal lesions often show a hypodense appearance as compared to normal renal parenchyma on delayed phase CT-imaging, the time-window for needle placement is often sufficient. Moreover, when the renal lesion shows a contour change on CT, the use of contrast medium is not always required for visualization of the lesion. Many of the newer generation CT-scanners are equipped with CT-fluoroscopy technology which enables real-time or almost real-time imaging during needle placement. Otherwise, the patient has to be moved in and out of the bore. With fluoroscopy, the procedure time is decreased and may increase the yield of CT-guided biopsies by more accurate needle placement as well as better use of the relatively short time-window after intravenous contrast injection in which the tumor shows optimal visibility. Laser guidance may also be of benefit in decreasing procedure time and increasing the accuracy of needle placement.[31,46] There are also some disadvantages associated with the use of CT, such as impaired accuracy of needle placement due to the patients'

respiratory motion or difficulties for patients maintaining a fixed position while in prone position during the procedure.

Needle Core Versus Fine Needle Aspiration Biopsy

Core biopsy and FNA are the two most common methods of obtaining renal tumor issue. Core biopsy systems are available with needle diameters ranging from 14- to 20-gauge. Most commonly biopsies are performed using 16- or 18-gauge needles, and these are preferred over FNA because of superior accuracy.[5,12,47] The tissue obtained from core biopsy allows for the assessment of tissue architecture and histologic subtype. A recent meta-analysis on the percutaneous biopsy for renal masses shows that the accuracy of core biopsy distinguishing benign from malignant tumors was 88.9% on the basis of series published before 2001 and vastly improved to 96% between 2001 and 2009.[19] A recent published paper with a large series demonstrated the accuracy rate of core biopsy is up to 94%.[48]

FNA is commonly performed by a 20-gauge needle or smaller. FNA is less accurate than core biopsy.[47,49] Although FNA has some diagnostic value, there is a major limitation in differentiating histological subtype for FNA, and its rate of inadequate sampling is not negligible.[10,47] Hence, there is a controversy on the value of FNA. If biopsy is indicated, 90% of the clinicians choose core biopsy rather than FNA.[50]

Number of Needle Cores for Single and Multiple Tumors

Currently, no consensus has been reached with regard to the optimal number of biopsies that should be performed for renal tumors. Renal tumors are heterogeneous, so multiple biopsy cores should be considered to prevent sampling errors. In an *ex vivo* investigation, investigators showed that adding core numbers improves the diagnostic yield, with a similar rate for two-core (63%) and three-core (67%) RTB.[51] Neuzillet *et al*. reported on 88 RTBs with at least two-core samplings resulting in a total of 90.9% diagnostic yield.[10] Similarly, Wang *et al*. analyzed 110 RTBs and demonstrated that biopsy with at least two cores resulted in 91% diagnostic yield.[52] Although increasing the number of cores is associated with improved diagnostic yield, and biopsy with at least two cores can result in a considerably higher diagnostic yield, ultimately it is the quality of the core that defines the success of RTB. Currently, a minimum of two good-quality cores for a single renal tumor is generally accepted.

Coaxial Technique

Core biopsy is by many operators performed through a coaxial needle or cannula. The use of a coaxial guide has been proven to increase the diagnostic yield of biopsy and improve the standardization of sampling.[53] Appelbaum *et al*. reported a 15% increase of the biopsy success rate without increasing the complication rate.[54] However, the effect of coaxial technique on biopsy success rate is still yet to be confirmed by large studies. Due to the large size and rigidity of the coaxial guiding needle, locating and positioning the needle are facilitated both on US and CT. The coaxial needle allows for multiple needle biopsies with only one access through the skin and underlying tissues, thereby minimizing the risk of need tract seeding.[55] Moreover, with the use of a coaxial needle, there is no need for needle reposition after one pass with the biopsy needle, which may reduce the procedure time and decrease patients' discomfort.

Location of Biopsy

There is no standard pattern of selecting the biopsy location; however, in general, necrotic and cystic areas should be avoided. Hobbs *et al*.[51] investigated the impact of sampling location on the diagnostic accuracy of renal mass biopsy in an *ex vivo* study and found the cancer identification rate could be increased by an additional central or peripheral core, and they recommend at least two peripheral cores for RTB.

It is generally accepted that selecting the location of biopsy should depend on the tumor size. For large tumors (>4 cm), the incidence of central necrosis is higher and proper sampling pattern will be of greater importance when compared with smaller tumors.[56] An international multidisciplinary panel recommended sampling different regions including central and peripheral biopsies for large tumors.[36] Abel *et al*. reported 122 biopsies in 117 renal tumors ≥ cT2 and recommend a multi-quadrant biopsy technique for large renal tumors, which is defined as sampling from at least four separate solid enhancing areas within the tumor.[57] Both US and contrast-enhanced CT may show central areas of hypo-echogenicity or nonenhancement in renal tumors and these findings should be taken into account when planning image-guided biopsy.

For tumors ≤4 cm, also referred as SRMs, the rate of nondiagnostic biopsy seems to be higher than that of larger renal masses. Wunderlich *et al*. reported 250 fine needle RTBs and demonstrated that for tumors smaller than 4 cm, the individual accuracy of a central and peripheral biopsy is 83.3% and 75%, respectively.[56] The accuracy rate could go up to 96.7% when both peripheral and central biopsies are used concurrently.[56] However, it should be noted that peripheral biopsy for SRMs may not obtain enough tissue because of the small lesion size.

Future Directions

Previous studies have confirmed the prognostic value of molecular and genetic markers in RCC such as Ki-67, p53, vascular endothelial growth factor receptor, and loss of 9p.[58,59] Biopsy could help attain tissue samples suitable for molecular or genetic tests. In virtue of these tests, we may better differentiate renal tumors with more metastatic potential and can use the information to optimize individual patient management of RCC. Hence, further studies

investigating the molecular and genetic information from RTB are warranted.

There are still some limitations of RTB at present. The heterogeneity of renal tumors consistently hinders the accuracy of RTB, and a common biopsy cannot reflect the complex nature of such tumors. Grade heterogeneity in the same renal tumor exists in up to 25% of cases,[13] which contribute to the suboptimal accuracy for grade assessment. For hybrid tumors, such as one that includes the oncocytoma area in a RCC, conventional renal biopsy method could correctly provide diagnostic information only when the biopsy samples the hybrid area by chance. The multi-quadrant method proposed by Abel *et al*. may be a promising way to solve the problem of renal tumor heterogeneity;[57] however, this method still needs to be replicated in further studies. In addition, oncocytoma diagnoses continue to be a challenge in the clinical practice, and the special case of such challenge is the differential diagnosis: oncocytoma, low-grade chromophobe RCC, hybrid oncocytoma-chromophobe RCC lesion, and papillary type 2 (eosinophilic) RCC.[19] More accurate methods that could resolve this diagnostic problem are required.

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Conflicts of interest

There are no conflicts of interest.

References

1. Chow WH, Devesa SS. Contemporary epidemiology of renal cell cancer. Cancer J 2008;14:288-301. doi: 10.1097/PPO.0b013e3181867628.
2. Vasudevan A, Davies RJ, Shannon BA, Cohen RJ. Incidental renal tumours: The frequency of benign lesions and the role of preoperative core biopsy. BJU Int 2006;97:946-9. doi: 10.1111/j.1464-410X.2006.06126.x.
3. Kutikov A, Fossett LK, Ramchandani P, Tomaszewski JE, Siegelman ES, Banner MP, *et al.* Incidence of benign pathologic findings at partial nephrectomy for solitary renal mass presumed to be renal cell carcinoma on preoperative imaging. Urology 2006;68:737-40. doi: 10.1016/j.urology.2006.04.011.
4. Crispen PL, Boorjian SA, Lohse CM, Sebo TS, Cheville JC, Blute ML, *et al.* Outcomes following partial nephrectomy by tumor size. J Urol 2008;180:1912-7. doi: 10.1016/j.juro.2008.07.047.
5. Remzi M, Ozsoy M, Klingler HC, Susani M, Waldert M, Seitz C, *et al.* Are small renal tumors harmless? Analysis of histopathological features according to tumors 4 cm or less in diameter. J Urol 2006;176:896-9. doi: 10.1016/j.juro.2006.04.047.
6. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: An analysis of pathological features related to tumor size. J Urol 2003;170(6 Pt 1):2217-20. doi: 10.1097/01.ju.0000095475.12515.5e.
7. Link RE, Bhayani SB, Allaf ME, Varkarakis I, Inagaki T, Rogers C, *et al.* Exploring the learning curve, pathological outcomes and perioperative morbidity of laparoscopic partial nephrectomy performed for renal mass. J Urol 2005;173:1690-4. doi: 10.1097/01.ju.0000154777.24753.1b.
8. Gill IS, Matin SF, Desai MM, Kaouk JH, Steinberg A, Mascha E, *et al.* Comparative analysis of laparoscopic versus open partial nephrectomy for renal tumors in 200 patients. J Urol 2003;170:64-8. doi: 10.1097/01.ju.0000072272.02322.ff.
9. Rybicki FJ, Shu KM, Cibas ES, Fielding JR, vanSonnenberg E, Silverman SG. Percutaneous biopsy of renal masses: Sensitivity and negative predictive value stratified by clinical setting and size of masses. AJR Am J Roentgenol 2003;180:1281-7. doi: 10.2214/ajr.180.5.1801281.
10. Neuzillet Y, Lechevallier E, Andre M, Daniel L, Coulange C. Accuracy and clinical role of fine needle percutaneous biopsy with computerized tomography guidance of small (less than 4.0 cm) renal masses. J Urol 2004;171:1802-5. doi: 10.1097/01.ju.0000120147.51090.2b.
11. Lechevallier E, André M, Barriol D, Daniel L, Eghazarian C, De Fromont M, *et al.* Fine-needle percutaneous biopsy of renal masses with helical CT guidance. Radiology 2000;216:506-10. doi: 10.1148/radiology.216.2.r00au01506.
12. Schmidbauer J, Remzi M, Memarsadeghi M, Haitel A, Klingler HC, Katzenbeisser D, *et al.* Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. Eur Urol 2008;53:1003-11. doi: 10.1016/j.eururo.2007.11.041.
13. Herts BR, Baker ME. The current role of percutaneous biopsy in the evaluation of renal masses. Semin Urol Oncol 1995;13:254-61.
14. Caoili EM, Bude RO, Higgins EJ, Hoff DL, Nghiem HV. Evaluation of sonographically guided percutaneous core biopsy of renal masses. AJR Am J Roentgenol 2002;179:373-8. doi: 10.2214/ajr.179.2.1790373.
15. Hara I, Miyake H, Hara S, Arakawa S, Hanioka K, Kamidono S. Role of percutaneous image-guided biopsy in the evaluation of renal masses. Urol Int 2001;67:199-202. doi: 10.1159/000050987.
16. Eshed I, Elias S, Sidi AA. Diagnostic value of CT-guided biopsy of indeterminate renal masses. Clin Radiol 2004;59:262-7. doi: 10.1016/j.crad.2003.09.022.
17. Imaide Y, Saitoh M. Clinical implication of selective renal tumor biopsy. Hinyokika Kiyo 1995;41:745-52.
18. Dechet CB, Zincke H, Sebo TJ, King BF, LeRoy AJ, Farrow GM, *et al.* Prospective analysis of computerized tomography and needle biopsy with permanent sectioning to determine the nature of solid renal masses in adults. J Urol 2003;169:71-4. doi: 10.1097/01.ju.0000042211.18318.ba.
19. Lane BR, Samplaski MK, Herts BR, Zhou M, Novick AC, Campbell SC. Renal mass biopsy – A renaissance? J Urol 2008;179:20-7. doi: 10.1016/j.juro.2007.08.124.
20. Wood BJ, Khan MA, McGovern F, Harisinghani M, Hahn PF, Mueller PR. Imaging guided biopsy of renal masses: Indications, accuracy and impact on clinical management. J Urol 1999;161:1470-4. doi: 10.1016/S0022-5347(05)68929-X.
21. Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MA. The natural history of incidentally detected small renal masses. Cancer 2004;100:738-45. doi: 10.1002/cncr.20025.
22. Kassouf W, Aprikian AG, Laplante M, Tanguay S. Natural history of renal masses followed expectantly. J Urol 2004;171:111-3. doi: 10.1097/01.ju.0000102409.69570.f5.
23. Wehle MJ, Thiel DD, Petrou SP, Young PR, Frank I, Karsteadt N. Conservative management of incidental contrast-enhancing renal masses as safe alternative to invasive therapy. Urology 2004;64:49-52. doi: 10.1016/j.urology.2004.02.026.
24. Kato M, Suzuki T, Suzuki Y, Terasawa Y, Sasano H, Arai Y. Natural history of small renal cell carcinoma: Evaluation of growth rate, histological grade, cell proliferation and apoptosis. J Urol 2004;172:863-6. doi: 10.1097/01.ju.0000136315.80057.99.
25. Chawla SN, Crispen PL, Hanlon AL, Greenberg RE, Chen DY, Uzzo RG. The natural history of observed enhancing renal masses: Meta-analysis and review of the world literature. J Urol 2006;175:425-31. doi: 10.1016/S0022-5347(05)00148-5.
26. Abou Youssif T, Kassouf W, Steinberg J, Aprikian AG, Laplante MP, Tanguay S. Active surveillance for selected patients with renal masses: Updated results with long-term follow-up. Cancer 2007;110:1010-4. doi: 10.1002/cncr.22871.
27. Abouassaly R, Lane BR, Novick AC. Active surveillance of renal masses in elderly patients. J Urol 2008;180:505-8. doi: 10.1016/j.juro.2008.04.033.
28. Zhang L, Li XS, Zhou LQ. Natural history of small renal masses. Chin Med J 2015;128:1232-7. doi: 10.4103/0366-6999.156139.
29. Patard JJ, Leray E, Rioux-Leclercq N, Cindolo L, Ficarra V, Zisman A, *et al.* Prognostic value of histologic subtypes in renal cell carcinoma: A multicenter experience. J Clin Oncol 2005;23:2763-71. doi: 10.1200/JCO.2005.07.055.

30. Zhang L, Yin W, Yao L, Li X, Fang D, Ren D, *et al.* Growth pattern of clear cell renal cell carcinoma in patients with delayed surgical intervention: Fast growth rate correlates with high grade and may result in poor prognosis. Biomed Res Int 2015;2015:598134. doi: 10.1155/2015/598134.
31. Lebret T, Poulain JE, Molinie V, Herve JM, Denoux Y, Guth A, *et al.* Percutaneous core biopsy for renal masses: Indications, accuracy and results. J Urol 2007;178(4 Pt 1):1184-8. doi: 10.1016/j.juro.2007.05.155.
32. Brierly RD, Thomas PJ, Harrison NW, Fletcher MS, Nawrocki JD, Ashton-Key M. Evaluation of fine-needle aspiration cytology for renal masses. BJU Int 2000;85:14-8. doi: 10.1046/j.1464-410x.2000.00417.x.
33. Maturen KE, Nghiem HV, Caoili EM, Higgins EG, Wolf JS Jr., Wood DP Jr. Renal mass core biopsy: Accuracy and impact on clinical management. AJR Am J Roentgenol 2007;188:563-70. doi: 10.2214/AJR.06.0220.
34. Beland MD, Mayo-Smith WW, Dupuy DE, Cronan JJ, DeLellis RA. Diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses: Should we biopsy all that are indeterminate? AJR Am J Roentgenol 2007;188:792-7. doi: 10.2214/ajr.06.0356.
35. Somani BK, Nabi G, Thorpe P, N'Dow J, Swami S, McClinton S; Aberdeen Academic and Clinical Urological Surgeons (ABACUS) Group. Image-guided biopsy-diagnosed renal cell carcinoma: Critical appraisal of technique and long-term follow-up. Eur Urol 2007;51:1289-95. doi: 10.1016/j.eururo.2006.10.022.
36. Tsivian M, Rampersaud EN Jr., del Pilar Laguna Pes M, Joniau S, Leveillee RJ, Shingleton WB, *et al.* Small renal mass biopsy – How, what and when: Report from an international consensus panel. BJU Int 2014;113:854-63. doi: 10.1111/bju.12470.
37. Capaccio E, Varca V, Simonato A, Toncini C, Carmignani G, Derchi LE. Synchronous parenchymal renal tumors of different histology in the same kidney. Acta Radiol 2009;50:1187-92. doi: 10.3109/02841850903236120.
38. Patel AR, Lee BH, Campbell SC, Zhou M, Fergany AF. Bilateral synchronous sporadic renal tumors: Pathologic concordance and clinical implications. Urology 2011;78:1095-9. doi: 10.1016/j.urology.2011.06.051.
39. Kunkle DA, Egleston BL, Uzzo RG. Excise, ablate or observe: The small renal mass dilemma – A meta-analysis and review. J Urol 2008;179:1227-33. doi: 10.1016/j.juro.2007.11.047.
40. Uppot RN, Harisinghani MG, Gervais DA. Imaging-guided percutaneous renal biopsy: Rationale and approach. AJR Am J Roentgenol 2010;194:1443-9. doi: 10.2214/AJR.10.4427.
41. Charboneau JW, Reading CC, Welch TJ. CT and sonographically guided needle biopsy: Current techniques and new innovations. AJR Am J Roentgenol 1990;154:1-10. doi: 10.2214/ajr.154.1.2104689.
42. Piscaglia F, Nolsøe C, Dietrich CF, Cosgrove DO, Gilja OH, Bachmann Nielsen M, *et al.* The EFSUMB guidelines and recommendations on the clinical practice of contrast enhanced ultrasound (CEUS): Update 2011 on non-hepatic applications. Ultraschall Med 2012;33:33-59. doi: 10.1055/s-0031-1281676.
43. Volpe A, Kachura JR, Geddie WR, Evans AJ, Gharajeh A, Saravanan A, *et al.* Techniques, safety and accuracy of sampling of renal tumors by fine needle aspiration and core biopsy. J Urol 2007;178:379-86. doi: 10.1016/j.juro.2007.03.131.
44. Lechevallier E. Core biopsy of solid renal masses under CT guidance. Eur Urol Suppl 2007;6:540-3. doi: 10.1016/j.eursup.2007.01.019.
45. Israel GM, Bosniak MA. Pitfalls in renal mass evaluation and how to avoid them. Radiographics 2008;28:1325-38. doi: 10.1148/rg.285075744.
46. Herts BR. Imaging guided biopsies of renal masses. Curr Opin Urol 2000;10:105-9. doi: 10.1097/00042307-200003000-00010.
47. García-Solano J, Acosta-Ortega J, Pérez-Guillermo M, Benedicto-Orovitg JM, Jiménez-Penick FJ. Solid renal masses in adults: Image-guided fine-needle aspiration cytology and imaging techniques-"two heads better than one?". Diagn Cytopathol 2008;36:8-12. doi: 10.1002/dc.20733.
48. Richard PO, Jewett MA, Bhatt JR, Kachura JR, Evans AJ, Zlotta AR, *et al.* Renal tumor biopsy for small renal masses: A single-center 13-year experience. Eur Urol 2015;68:1007-13. doi: 10.1016/j.eururo.2015.04.004.
49. Truong LD, Todd TD, Dhurandhar B, Ramzy I. Fine-needle aspiration of renal masses in adults: Analysis of results and diagnostic problems in 108 cases. Diagn Cytopathol 1999;20:339-49. doi: 10.1002/(SICI)1097-0339(199906)20:6<339:AID-DC4>3.0.CO;2-7.
50. Kümmerlin IP, Borrego J, Wink MH, Van Dijk MM, Wijkstra H, de la Rosette JJ, *et al.* Nephron-sparing surgery and percutaneous biopsies in renal-cell carcinoma: A global impression among endourologists. J Endourol 2007;21:709-13. doi: 10.1089/end.2006.0409.
51. Hobbs DJ, Zhou M, Campbell SC, Aydin H, Weight CJ, Lane BR. The impact of location and number of cores on the diagnostic accuracy of renal mass biopsy: An *ex vivo* study. World J Urol 2013;31:1159-64. doi: 10.1007/s00345-012-0868-3.
52. Wang R, Wolf JS Jr., Wood DP Jr., Higgins EJ, Hafez KS. Accuracy of percutaneous core biopsy in management of small renal masses. Urology 2009;73:586-90. doi: 10.1016/j.urology.2008.08.519.
53. Rapp DE, Orvieto M, Sokoloff MH, Shalhav AL. Use of biopsy sheath to improve standardization of renal mass biopsy in tissue-ablative procedures. J Endourol 2004;18:453-4. doi: 10.1089/0892779041271616.
54. Appelbaum AH, Kamba TT, Cohen AS, Qaisi WG, Amirkhan RH. Effectiveness and safety of image-directed biopsies: Coaxial technique versus conventional fine-needle aspiration. South Med J 2002;95:212-7.
55. Silverman SG, Gan YU, Mortele KJ, Tuncali K, Cibas ES. Renal masses in the adult patient: The role of percutaneous biopsy. Radiology 2006;240:6-22. doi: 10.1148/radiol.2401050061.
56. Wunderlich H, Hindermann W, Al Mustafa AM, Reichelt O, Junker K, Schubert J. The accuracy of 250 fine needle biopsies of renal tumors. J Urol 2005;174:44-6. doi: 10.1097/01.ju.0000162063.86400.de.
57. Abel EJ, Heckman JE, Hinshaw L, Best S, Lubner M, Jarrard DF, *et al.* Multi-quadrant biopsy technique improves diagnostic ability in large heterogeneous renal masses. J Urol 2015;194:886-91. doi: 10.1016/j.juro.2015.03.106.
58. Klatte T, Seligson DB, LaRochelle J, Shuch B, Said JW, Riggs SB, *et al.* Molecular signatures of localized clear cell renal cell carcinoma to predict disease-free survival after nephrectomy. Cancer Epidemiol Biomarkers Prev 2009;18:894-900. doi: 10.1158/1055-9965.EPI-08-0786.
59. Brunelli M, Eccher A, Gobbo S, Ficarra V, Novara G, Cossu-Rocca P, *et al.* Loss of chromosome 9p is an independent prognostic factor in patients with clear cell renal cell carcinoma. Mod Pathol 2008;21:1-6. doi: 10.1038/modpathol.3800967.