ELSEVIER

Seminars in
ULTRASOUND
CT and MRI

Percutaneous Renal Ablation

Amit Gupta, FRCR, MRCS, MBBS, BSc,* Besma Musaddaq, MA (Cantab), MBBS, MRCP,†
Conrad von Stempel, MBBS, FRCR,†,‡ and Shahzad Ilyas, FRCR*

Incidental small renal cell cancers are increasingly being diagnosed on cross-sectional imaging. This review article describes the indications for percutaneous ablation of small renal cell cancers, choice of ablation technologies and imaging follow-up.
Semin Ultrasound CT MRI 41:351-356

Introduction

Partial nephrectomy is historically the reference standard treatment for patients with small renal lesions ≤4 cm in axial diameter (stage cT1a).[1] Local lymphadenectomy may also be required.

Percutaneous image-guided ablation of renal tumours with thermal (radiofrequency or microwave) ablation, cryoablation and irreversible electroporation have become increasingly important nephron-sparing treatments, particularly in older patients who may have relative contraindications for surgery. Ablation is advantageous to traditional surgical techniques for small renal tumours, because there is reduced morbidity, better preservation of renal parenchyma and overall renal function.[2] It can be considered a curative option in those who are not surgical candidates. In addition, a shorter average length of hospital stay has been found with the percutaneous cryoablation technique[3,4] compared to laparoscopic cryoablation.

This review article describes the indications for percutaneous ablation of small renal cell cancers (RCCs), pre-ablation workup, choice of ablation technologies and imaging follow-up.

Indications for Ablation

Evidence behind the use of thermal ablation (TA) for treatment of localised renal masses has recently progressed with follow-up of 3-5 years in some studies, hence allowing a more valid comparison of TA with surgical resection. TA results are encouraging for smaller renal masses (<3 cm) making it a reasonable alternative to surgical excision. The recent Agency for Healthcare Research and Quality meta-analysis[5] demonstrated comparable metastasis-free survival for partial nephrectomy (PN) and TA, and analysis of population-based and institutional studies demonstrated median 5-year cancer-specific survival rates of 100% (range 97%-100%) and 94% (range 92%-97%) for PN and TA, respectively. However, local recurrence-free survival is generally reported as favouring surgical resection with a risk ratio for local recurrence of 0.37 (95% CI: 0.15-0.89) in favour of PN. Median local recurrence-free survival across the studies included in the meta-analysis was 99.4% for PN and 89.3% for TA.[5] However, since the morbidity of repeat (particularly percutaneous) ablation is generally low, local recurrences may often be salvaged with repeat TA. When considering such salvage attempts in addition to the initial ablation, the Agency for Healthcare Research and Quality meta-analysis reported no statistical difference in the risk ratio for local recurrence comparing PN and TA (RR 1.21; 95% CI: 0.58-2.5).[5]

Currently, however, the European Association of Urology only support the use of radiofrequency or cryoablation for small renal masses in the elderly or co-morbid patients, as an alternative to active surveillance (defined as the initial monitoring of tumour size by serial abdominal imaging with US, CT or MRI, with delayed intervention reserved for tumours showing clinical progression during follow-up).[6]

The American Urological Association go further and state physicians should consider TA for the management of T1a solid renal masses <3 cm in size, and not only in frail patients. The AUA state a percutaneous ablation is preferred over laparoscopic ablation whenever feasible to minimise morbidity.[7]

Relative contraindications to percutaneous ablation include: life expectancy <1 year, multiple metastases, and

*Department of Radiology, Guy's and St Thomas' NHS Foundation Trust, London, UK.
†Department of Radiology, Royal Free Hospital, London, UK.
‡Department of Radiology, University College London Hospitals NHS Foundation Trust, London, UK.
Address reprint requests to Shahzad Ilyas, FRCR, Department of Radiology, Guy's and St Thomas' NHS Foundation Trust, London, UK. E-mail: shahzad.ilyas@gstt.nhs.uk

https://doi.org/10.1053/j.sult.2020.05.004
0887-2171/

low possibility of successful treatment due to size or location of tumour (generally tumours >3 cm, and proximity to the renal hilum, central collecting system or ureter).

Absolute contraindications include irreversible coagulopathies and severe medical instability such as sepsis.

Pre-Ablation Work Up

Many renal masses are asymptomatic until the late stages of disease. RCC suitable for ablation thus tend to be incidental findings on cross-sectional imaging performed for other indications.

Physical examination should be directed at assessing fitness for ablation which will require conscious sedation or a general anaesthetic.

Imaging has high diagnostic accuracy for renal masses and so biopsy is not always necessary in patients with an enhancing renal mass for whom surgery is planned. Biopsy is indicated to select appropriate therapy in the setting of metastatic disease[8-13] and in radiologically indeterminate renal masses. One study found 37% of solid masses referred for ablation were benign[14] and so ablating based on imaging appearance alone may lead to overtreatment and an over estimation of the clinical efficacy of ablation. Histologic diagnosis prior to ablation allows benign masses to be identified (eg, oncocytoma and fat poor AML[14,15]) and also allows appropriate follow-up based on tumour subtype and grade.[16]

Controversy exists regarding whether histologic analysis should be completed prior to ablation, or if a biopsy should be done at the time of the ablation procedure. The former would prevent benign tumours from being over treated, whereas the latter approach is acceptable if the probability of malignant RCC is extremely high, for example, a suspicious mass in a patient with hereditary renal cancer.[17]

Percutaneous biopsy can be performed under local anaesthesia with US or CT guidance having similar diagnostic yields.[11,18] 18G core biopsy needles are ideal because they provide sufficient tissue for histologic diagnosis and have low morbidity.[8-12,19] A meta-analysis of 57 articles including over 5000 patients showed that spontaneously resolving subcapsular/perinephric haematomas are reported in 4.3% of cases, but clinically significant bleeding is unusual (0%-1.4%, 0.7% in the pooled analysis) and generally self-limiting.[20]

Core biopsy has better accuracy for diagnosis of malignant lesions compared with fine needle aspiration, with a sensitivity and specificity of 99.1% and 99.7%.[20] At least 2 good quality cores should be obtained, and necrotic areas avoided.[8,11,21,22] A co-axial technique (facilitating multiple core biopsies through a co-axial cannula) should be used to avoid the potential risk of tumour seeding along the biopsy tract.[8-12]

Ablation Procedural Considerations

Haemostasis

International normalised ratio (INR) should be less than 1.5, partial thromboplastin time (PTT) within normal limits and a platelet count greater than 50,000/μL.

Renal Function

Baseline renal function should be established because a small rim of peri-lesion disease-free parenchyma is ablated in order to obtain negative ablation margins. The extent of this margin and how aggressive the ablation can be is partially dictated by the renal profile. In addition, intravenous contrast may be used during the procedure to precisely define tumour margins in order to aid the accurate placement of the probe and hence knowledge of the renal function to counter the risk of contrast induced nephropathy is essential. Post-procedure follow-up also requires contrast-enhanced CT or MRI.

Lesion Characteristics

The lesion characteristics on cross-sectional imaging should be carefully evaluated in order to plan the procedure and minimise complications, while maximising efficacy of the ablation.

ABLATE is an example of a planning algorithm that takes into account important tumour characteristics.[23]

A—Axial tumour diameter: maximal tumour diameter is important for risk of future recurrence (4 cm diameter ensures 90% chance of complete necrosis whereas 5.8 cm lowers complete necrosis chance to 63%.[24] The risk of haemorrhage also increases with tumours greater than 3 cm.[24,25]

B—Bowel proximity: bowel within 1 cm of the mass is at risk of injury.

L—Location within kidney: location of tumour relative to the polar line is important, for example, masses near the adrenal gland will require intra-procedural blood pressure monitoring and pre-procedure alpha-receptor blocker therapy.

A—Adjacency to ureter: ureters within 1.5 cm of the ablation zone are at risk of injury and identification provides the opportunity to use retrograde pyeloperfusion to cool the ureter and reduced the risk of damage. A retrograde ureteric catheter is inserted with the tip positioned in the renal pelvis, along with a Foley urethral catheter in the bladder. The renal pelvis is then perfused with cold dextrose (a non-ionic non-conducting fluid) by running this through the ureteric catheter at approximately 80 cmH_20 perfusion pressure.[26] Alternatively, percutaneous hydrodissection may be used to displace the ureter.

T—Touching renal sinus fat: a tumour touching renal sinus fat corresponds with proximity to central vessels and the collecting system and so the ablation may be less efficacious due to the heat sink effect, with the additional risk of complications such as injury to the collecting system. Cryoablation can be considered here because the growing ice-ball can be visualised intra-procedurally, with a lower risk of damaging the calyceal system.

E—Endo- or exophytic mass: endophytic masses have an increased recurrence rate[27,28] possibly due to the heat sink effect experienced as a result of proximity to large central vessels and potentially less aggressive ablations being performed in masses closer to renal sinus fat, ureter

or hilar vessels. Another reason for the relative increased efficacy of ablating exophytic masses is that the surrounding fat insulates the ablation resulting in less heat or cold loss.[17] However, these masses are more likely to be in proximity to extra-renal structures and so techniques such as hydrodissection may be required.

Another anatomical consideration is the proximity of the mass to nerves such as intercostal nerves, the genitofemoral and ilioinguinal nerves from the lumbar plexus and the lateral femoral cutaneous nerve. In most cases any injury to these nerves is self-limiting.[28]

Choice of Ablation Technologies

The goal of ablation is to achieve a predictable and continuous ablation volume with a negative (tumour free) margin of at least 5-10 mm.[29] Achieving this requires utilising the most appropriate technology for the patient and their renal mass on a case by case basis. Each technology has its own advantages and none is clearly superior to any other. In current clinical practice radiofrequency ablation (RFA), microwave ablation (MWA) and cryoablation are the most commonly used. Irreversible electroporation and high-intensity focussed ultrasound are not widely used and hence are not discussed in this article.

Radiofrequency Ablation

RFA (Fig. 1A-D) employs high-frequency (375-400 kHz) alternating electric current to cause heating of tissue in a relatively short time, typically 8-16 minutes. Current passes between the ablation electrode tip and the grounding pad placed remotely on the patient's skin. Within a few millimetres of the electrode tip there is generation of a high current density, where tissue ions rapidly oscillate causing frictional heating. Heat spreads radially away from the electrode tip by thermal diffusion. At 55°C, there is near instantaneous coagulation necrosis of tissue. Tissue impedance inversely determines ability to achieve this lethal temperature, for example, aerated lung tissue has higher impedance than renal parenchyma and so RFA is not as effective for lung tumour ablation. RFA heating is a self-limiting process in which increased heating results in increased tissue impedance (secondary to water vapour production, tissue desiccation and tissue charring). Subsequent device improvement has included internal electrode cooling to limit tissue charring at the electrode tip. Regardless of the target tissue impedance, thermal diffusion can lead to an inhomogeneous ablation zone, especially in areas of increased perfusion due to the heat sink effect.

For potentially larger lesions RFA may require multiple overlapping ablation with a 10 mm margin in order to achieve the desired results. It is best to place the first electrode to ablate one margin, and then serially place adjacent electrodes until the opposite margin is ablated.[28]

Microwave Ablation

An oscillating microwave electromagnetic field causes water molecule to realign creating kinetic energy and temperature to rise. This mechanism is distinct to RFA in that heating is not related to tissue impedance and allows continuous heat generation in larger volumes. Therefore, MWA produces faster, hotter and larger ablation volumes in multiple tissue types, and relative to RFA does not suffer as much from heat sink. It requires fewer electrodes to create a predictable ablation volume.[30,31]

Cryoablation

Cell death occurs by rapid freezing to between −20°C and −40°C followed by thawing (Fig. 2A-E). A heat sink is produced near the applicator tip (via the Joule-Thomson theory) that cools the probe to temperatures of −160°C. Adjacent tissue heat then transfers into the cryoprobe by passive thermal diffusion, the limiting factor being the cryoprobe surface area.[32,33] An ice-ball is created which can be visualised intra-procedurally with ultrasound, CT or MRI. This feature facilitates manipulating the ablation zone size and shape in real time by using multiple probes, which can be controlled individually. For example, if a desired ablation margin is achieved on one side of the tumour, or if a critical structure is reached along one edge of the ice-ball, this probe can be stopped whilst the others continue. When monitoring the ice-ball one should be aware that the tissue temperature at the ice-ball edge is non-lethal at approximately 0°C whereas the true ablation zone is approximately 8-10 mm deep to the ice-ball edge.[34] For example, a 40-mm ice-ball is required to ablate a 20-mm lesion. Two freeze-thaw cycles are performed, the time of the freeze-thaw protocol varies according to manufacturer but typically is 10-15 minutes of freezing and 8-10 minutes of thawing, thus total ablation time is generally longer than MWA. An advantage over both the thermal techniques is that the visible ice-ball allows confident treatment of central lesions in contact with renal sinus fat, and an additional advantage over RFA is that cryoablation does not suffer from heat sink.

Post-Ablation Imaging

There is no standard accepted follow-up imaging protocol. RCC with a diameter less than 30mm has a growth rate of approximately 6 mm per year and so imaging follow-up could be contrast-enhanced CT or MRI at 3 months, followed by every 6 months for 1 year and then annually till 5 years post-ablation.[28] On follow-up imaging the ablation zone is correspondingly larger than the tumour. It is seen as a hypoattenuating area on CT whilst on MRI has variable appearances on both T1 and T2 sequences: it can demonstrate diffuse high T1 signal or in a rim surrounding the ablation zone, which can persist

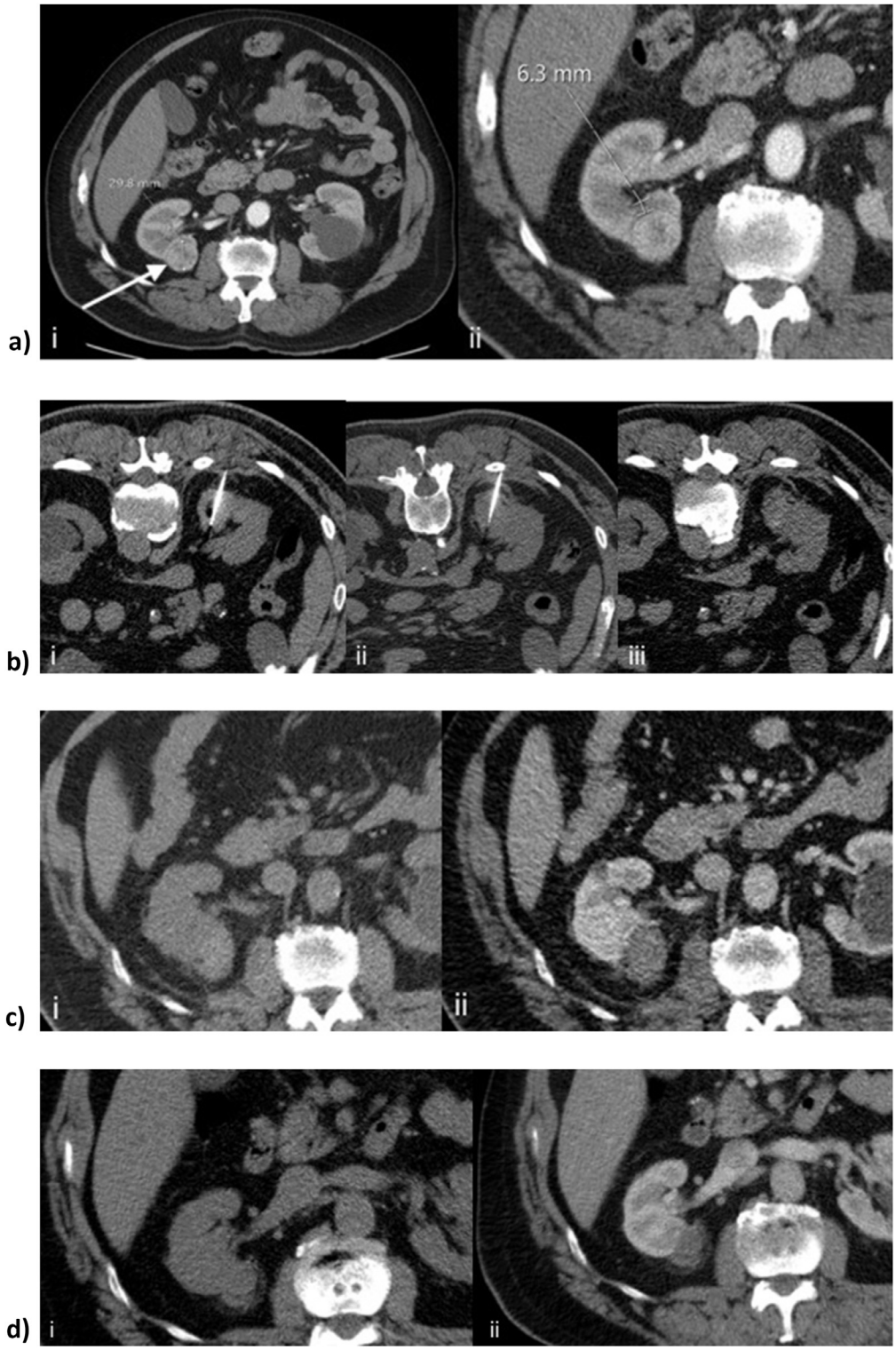

Figure 1 (A) Axial slice of a contrast-enhanced CT demonstrates a right-sided 30 mm partially exophytic inter-polar mass (arrow) located 6 mm away from renal sinus fat, in keeping with RCC. A large simple left renal cyst is also demonstrated. (B) The patient was placed prone and a posterior approach was employed. Two RFA electrodes were utilised to ablate this mass, with overlapping ablation zones, each ablation lasting 12 minutes. Axial slice of an unenhanced CT immediately post ablation following removal of electrodes shows high attenuation material within the ablated zone (haematoma) with no immediate complication (iii). (C) Axial slices of a CT scan (left pre-contrast, right post-contrast) performed at day 1 post RFA shows high attenuation material within the ablated zone which does not increase in HU post-contrast, in keeping with haematoma. (D) Axial slices of a CT scan (left pre-contrast, right post-contrast) performed at 33 months post RFA shows the well-defined ablation zone completely covering the original tumour with increasing prominence of the peri-renal ablated fat resulting in stranding, and no evidence of local recurrence.

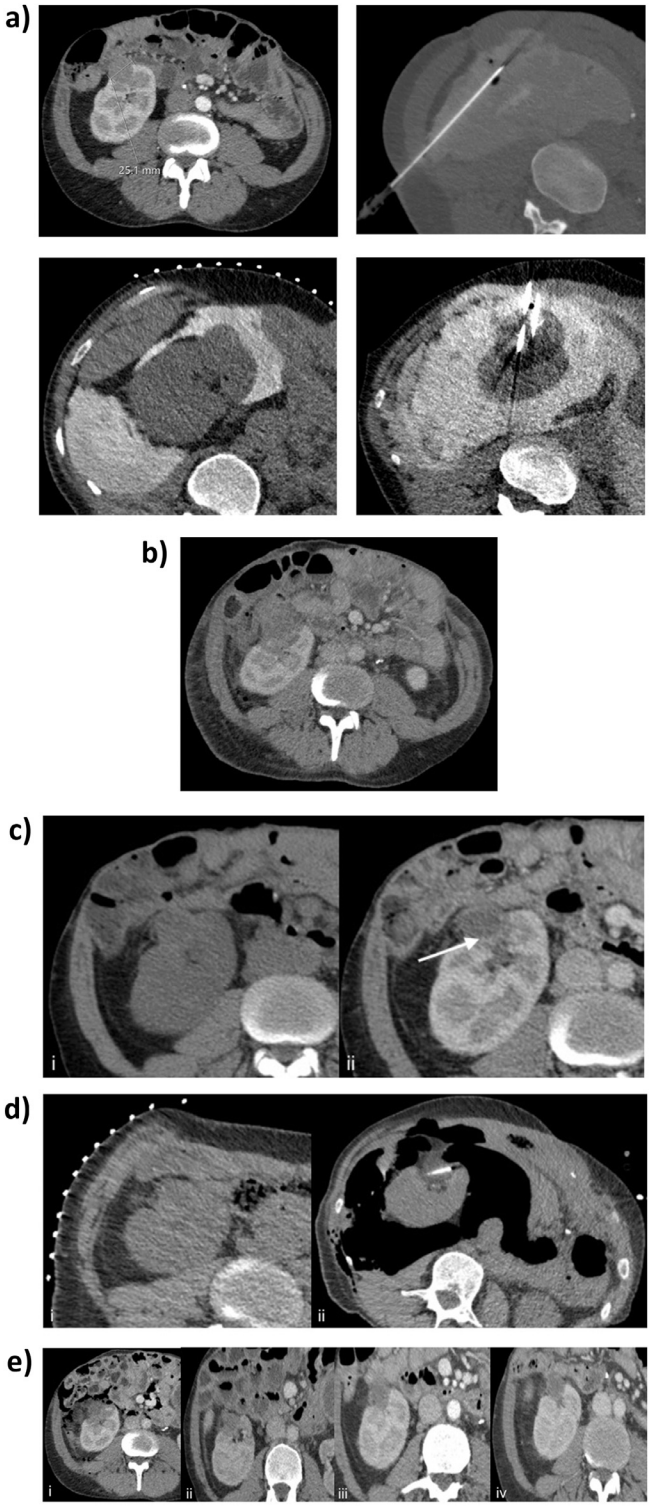

Figure 2 (A) top left image Axial slice of a contrast-enhanced CT demonstrates a right-sided 25 mm partially exophytic lower pole mass in contact with adjacent bowel, in keeping with RCC. (A) top right image The patient was positioned supine-oblique, right side up. The adjacent bowel was hydrodissected away by infusing 2L of 5% dextrose with 10 mL of contrast (as is the authors' preference), via a 21G needle. (A) bottom left image Subsequent planning CT with localisation grid in situ demonstrates satisfactory displacement of adjacent bowel away from the renal mass. (A) bottom right image Four cryoprobes were inserted, the resulting ice ball can be identified intra-procedurally. (B) Axial slice of a contrast-enhanced CT scan performed at day 1 post-cryoablation shows high attenuation material within the ablated zone which did not increase in HU post-contrast, in keeping with haematoma. Note the hydrodissection fluid has largely been absorbed at 24 hours. (C) Axial slices of a CT scan (left pre-contrast, right post-contrast) performed at 3 months post-cryoablation shows tissue enhancement posteriorly with the ablation zone in keeping with local recurrence (arrow). (D) Repeat cryoablation was performed 1 month later. Axial slices of the planning CT with localisation grid in situ (left), ice-ball seen covering the tumour after a combination of hydrodissection and carbon dioxide gaseous dissection to lift the adjacent bowel away (right). (E) (i) Axial slice from a post-contrast CT performed at day 1 post-cryoablation. Some residual intra-abdominal gas is seen which makes identification of any potential bowel injury or perforation challenging, and so oral contrast is advised for the day 1 check CT if intra-procedural gaseous dissection has been utilised. No complication identified. Follow-up post-contrast CT scans taken at (ii) 3 months, (iii) 7 months and (iv) 12 months post-cryoablation, no enhancing tissue is seen in the ablation zone suggesting no local recurrence.

for approximately 9 months; there is often corresponding low T2 hypointense band surrounding the ablation zone in keeping with fibrosis that is usually detected after 1 month post-treatment.[35] On subsequent follow-up scans, the ablation zone should involute (by up to 50% at 12 months). The key imaging feature to detect tumour recurrence is a growth of the ablation zone after initial stability and presence of enhancement, but this can be extremely difficult in equivocal cases.[36] Recurrent tumour is often seen as an asymmetrical focal nodular or crescentic enhancement (Fig. 2C) (on either CT or MRI) and on MR can be seen as nodular high T2 signal that interrupts the circumferential low T2 signal scar surrounding the ablation zone. It is accepted that post-contrast enhancement of greater than 10 HU on CT follow-up is suspicious for local recurrence,[37] whilst on MR persistent enhancement can be seen in up to 9 months in 15% of patients despite successful treatment.[35,38] This can be made further problematic by high T1 signal in the ablation zone pre-contrast administration. Han-Jui describes the nature of benign enhancement on MRI after successful cryoablation is most prominent in the delayed dynamic phase, which clearly differs from RCC that is a strongly arterialised lesion.[35] Additional post-processing techniques such as image subtraction can aid with detecting true enhancement.

Conclusion

The literature on ablation for small RCCs has matured in recent years, and percutaneous ablation is an acceptable and viable alternative treatment to partial nephrectomy. Careful planning and understanding of the tumour characteristics are important to avoid complications. In addition, one needs a sound knowledge of the ablative technology available to treat these lesions, as well as an awareness of imaging appearances post-ablation.

References

1. Bonkat G, Pickard R, Bartoletti R, et al: EAU guidelines on urological infections. In: Presented at the EAU Annual Congress Copenhagen 2018, European Association of Urology, 2018 ISBN 978-94-92671-01-1
2. Woldu SL, Thoreson GR, Okhunov Z, et al: Comparison of renal parenchymal volume preservation between partial nephrectomy, cryoablation, and radiofrequency ablation using 3D volume measurements. J Endourol 29:948-955, 2015
3. Kim EH, et al: Outcomes of laparoscopic and percutaneous cryoablation for renal masses. J Urol 189:e492, 2013.
4. Goyal J, et al: Single-center comparative oncologic outcomes of surgical and percutaneous cryoablation for treatment of renal tumors. J Endourol 26:1413-1419, 2012
5. Pierorazio PM, Johnson MH, Patel HD, et al: Management of Renal Masses and Localized Renal Cancer. Agency for Healthcare Research and Quality Publication 16-EHC001-EF, 2016 (Comparative Effectiveness Reviews, No. 167.)
6. Bonkat G, Bartoletti RR, Bruyère F, et al: EAU guidelines on urological infections. In: Presented at the EAU Annual Congress Barcelona 2019, European Association of Urology, 2019 ISBN 978-94-92671-04-2
7. Campbell S, Uzzo RG, Allaf ME, et al: Renal mass and localized renal cancer: AUA guideline. J Urol 198:520-529, 2017
8. Richard PO, et al: Renal tumor biopsy for small renal masses: A single-center 13-year experience. Eur Urol 68:1007-1013, 2015
9. Shannon BA, et al: The value of preoperative needle core biopsy for diagnosing benign lesions among small, incidentally detected renal masses. J Urol 180:1257-1261, 2008
10. Maturen KE, et al: Renal mass core biopsy: Accuracy and impact on clinical management. AJR Am J Roentgenol 188:563-570, 2007
11. Volpe A, et al: Contemporary results of percutaneous biopsy of 100 small renal masses: A single center experience. J Urol 180:2333-2337, 2008
12. Veltri A, et al: Diagnostic accuracy and clinical impact of imaging-guided needle biopsy of renal masses. Retrospective analysis on 150 cases. Eur Radiol 21:393-401, 2011
13. Abel EJ, et al: Percutaneous biopsy of primary tumor in metastatic renal cell carcinoma to predict high risk pathological features: comparison with nephrectomy assessment. J Urol 184:1877-1881, 2010
14. Tuncali K, vanSonnenberg E, Shankar S, et al: Evaluation of patients referred for percutaneous ablation of renal tumors: Importance of a pre-procedure diagnosis. AJR 183:575-582, 2004
15. Heilbrun ME, Zagoria RJ, Garvin AJ, et al: CT guided biopsy for the diagnosis of renal tumors before treatment with percutaneous ablation. AJR 188:1500-1505, 2007
16. Wood BJ, Khan MA, McGovern F, et al: Imaging guided biopsy of renal masses: Indications, accuracy and impact on clinical management. J Urol 161:1470-1474, 1999
17. Uppot, et al: Imaging-guided percutaneous ablation of renal cell carcinoma: A primer of how we do it.. AJR 192:1558-1570, 2009
18. Leveridge MJ, et al: Outcomes of small renal mass needle core biopsy, nondiagnostic percutaneous biopsy, and the role of repeat biopsy. Eur Urol 60:578-584, 2011
19. Breda A, et al: Comparison of accuracy of 14-, 18- and 20-G needles in ex-vivo renal mass biopsy: a prospective, blinded study. BJU Int 105:940-945, 2010
20. Marconi L, et al: Systematic review and meta-analysis of diagnostic accuracy of percutaneous renal tumour biopsy. Eur Urol 69:660-673, 2016
21. Vasudevan A, et al: Incidental renal tumours: The frequency of benign lesions and the role of preoperative core biopsy. BJU Int 97:946-949, 2006
22. Neuzillet Y, et al: Accuracy and clinical role of fine needle percutaneous biopsy with computerized tomography guidance of small (less than 4.0 cm) renal masses. J Urol 171:1802-1805, 2004
23. Schmit GD, Kurup AN, Weisbrod AJ, et al: ABLATE: A renal ablation planning algorithm. AJR 202:894-903, 2014
24. Gervais DA, McGovern FJ, Arellano RS, et al: Radiofrequency ablation of renal cell carcinoma. Part 1. indications, results, and role in patient management over a 6-year period and ablation of 100 tumors. AJR 185:64-71, 2005
25. Hafron J, Kaouk JH: Ablative techniques for the management of kidney cancer. Nat Clin Pract Urol 4:261-269, 2007
26. Cantwell CP, Wah TM, Gervais DA, et al: Protecting the ureter during radiofrequency ablation of renal cell cancer: A pilot study of retrograde pyeloperfusion with cooled dextrose 5% in water. J Vasc Interv Radiol 19:1034-1040, 2008
27. Gupta A, Raman JD, Leveillee RJ, et al: General anesthesia and contrast-enhanced computed tomography to optimize renal percutaneous radiofrequency ablation: Multi-institutional intermediate-term results. J Endourol 23:1099-1105, 2009
28. Higgins LJ, et al: Renal ablation techniques: State of the art. AJR 205:735-741, 2015
29. Clark TWI, Millward SF, Gervais DA, et al: Reporting standards for percutaneous thermal ablation of renal cell carcinoma. J Vasc Interv Radiol 20:S409-S416, 2009
30. Carrafiello G, Laganà D, Mangini M, et al: Microwave tumors ablation: Principles, clinical applications and review of preliminary experiences. Int J Surg 6(suppl 1):S65-S69, 2008
31. Simon CJ, Dupuy DE, Mayo-Smith WW: Microwave ablation: Principles and applications. Radiographics 25:S69-S83, 2005
32. Lagerveld BW: Cryosurgical induced injury of human cancerous tissues: How it works. Br J Med Surg Urol 5(suppl 1):S24-S27, 2012
33. Dominguez-Escrig JL, Sahadevan K, Johnson P: Cryoablation for small renal masses. Adv Urol 2008:1-10, 2008
34. Georgiades C, Rodriguez R, Azene E, et al: Determination of the nonlethal margin inside the visible "ice-ball" during percutaneous cryoablation of renal tissue. Cardiovasc Intervent Radiol 36:783-790, 2013
35. Lee HJ, Chung HJ, Wang HK, et al: Evolutionary magnetic resonance appearance of renal cell carcinoma after percutaneous cryoablation. Br J Radiol 89, 2016
36. Gill IS, Remer EM, Hasan WA, et al: Renal cryoablation: Outcome at 3 years. J Urol 173:1903-1907, 2005
37. Kawamoto S, Solomon SB, Bluemke DA, et al: Computed tomography and magnetic resonance imaging appearance of renal neoplasms after radiofrequency ablation and cryoablation. Semin Ultrasound CT MRI 30:67-77, 2009
38. Stein AJ, Mayes JM, Mouraviev V, et al: Persistent contrast enhancement several months after laparoscopic cryoablation of the small renal mass may not indicate recurrent tumor. J Endourol 22:2433-2439, 2008