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REVIEW ARTICLE

Is percutaneous image-guided renal tumour ablation ready for prime time?

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ABSTRACT

In the last few decades, thermal ablation (TA) techniques have been increasingly applied to treat small localised renal cell carcinomas. Despite this trend, there is still an underuse of TA compared to surgery and a substantial lack of high-quality evidence derived from large, prospective, randomised controlled trials comparing the long-term oncologic outcomes of TA and surgery. Therefore, in this narrative review, we assess published guidelines and recent literature concerning the diagnosis and management of kidney-confined renal cell carcinoma to understand whether percutaneous image-guided TA is ready to be proposed as a first-line treatment.

INTRODUCTION

In the last few decades, the incidental diagnosis of small renal masses (SRMs), defined as incidentally detected, contrast-enhancing solid or cystic lesions with the largest diameter measuring ≤ 4 cm,¹ has gradually risen,² due to the increased use of abdominal cross-sectional imaging. In up to 80% of cases SRMs are malignant, with T1a (*i.e.* kidney confined tumour measuring ≤ 4 cm) renal cell carcinoma (RCC) being the most common diagnosis.³ However, many of these malignant lesions are often low-grade, early-stage tumours,³ demanding careful case-by-case evaluation by the multi-disciplinary tumour board to establish the best therapeutic pathway, granting the best (and avoidance of over-) treatment.

In this narrative review, we revise non-systematically, the published guidelines and recent literature on the diagnosis and management of kidney-confined malignant tumours, with a particular focus on T1a tumours, in order to understand whether percutaneous image-guided thermal ablation (TA) is ready to be proposed as a first-line treatment.

EPIDEMIOLOGY

RCC is the ninth most common cancer in males and the 14th most common in females worldwide. In terms of

mortality, RCC has been ranked as the 16th most common cause of death from cancer worldwide.⁴ Established risk factors for RCC include smoking (50% increased risk in male and 20% in female smokers)⁵ and obesity (24 and 34% of increased risk in males and females, respectively for 5 kg/m² increments in body mass).⁶ Other reported risk factors include occupational exposure to trichloroethylene,⁷ arterial hypertension⁸ and dialysis.⁹ Moreover, it has been demonstrated that the incidence of RCC increases with age.⁴ On the other hand, regular consumption of fruits and vegetables, especially cruciferous and carotenoids, reduces the risk of developing RCC.^{10,11}

The majority of RCC are sporadic; 2–3% of RCC are developed in the setting of familial syndromes, of which von Hippel-Lindau is the most common.¹² Familial RCC are often multifocal and bilateral, and often diagnosed in patients aged 20–30 years younger than those presenting with sporadic RCC.¹² In addition, nephron-sparing therapies are certainly required in cases of familial syndromes due to the patients' young age at the time of diagnosis, and the multifocal, relapsing/recurrent renal tumoural disease pattern.

DIAGNOSTIC IMAGING AND PERCUTANEOUS BIOPSY

Triple-phase contrast-enhanced CT represents the standard imaging modality to evaluate SRMs in terms of size, location, density, relationships with the urinary collecting and venous systems (*i.e.* renal and inferior vena cava veins). The most specific diagnostic criterion to differentiate malignant SRMs, is their enhancement of 20 or more Hounsfield units.¹³ CT may also be helpful to calculate anatomic scores such as the RENAL one,¹⁴ allowing stratification of SRMs in terms of anatomic complexity in view of surgical or percutaneous treatments. These scores have demonstrated a direct correlation with surgical/interventional outcomes in terms of complications and oncologic efficacy.¹⁵

MRI represents a valid alternative to CT. In fact, even unenhanced MRI is largely informative about the tissular composition of the studied SRMs thanks to T2-, chemical shift and diffusion-weighted imaging. Moreover, MRI theoretically allows use of contrast agents even in patients with renal insufficiency (glomerular filtration rate <30 mL/min), since some gadolinium-based contrast agents may be injected in this cohort¹⁶ (although the final decision is left to the radiologist performing the exam, who should evaluate case by case, the balance between the risks and benefits according to the particular clinical conditions of each single patient). Other categories of patients benefiting from diagnostic MRI are pregnant females, young patients (including those with familial syndromes); and those with complex cystic masses. In the latter cohort, the diagnostic performance of MRI is superior to that granted by CT (71% sensitivity and 91% specificity *vs* 36% and 76%, respectively)¹⁷; and the same occurs also with contrast-enhanced ultrasonography reporting sensitivity, specificity, and negative predictive values of 100, 97 and 100%, respectively.¹⁷

Overall, contrast-enhanced CT and MRI are highly sensitive for the detection of SRMs (79.7% and 88.1%, respectively); however, their specificity is suboptimal (44.4% and 33.3%, respectively) since they cannot reliably distinguish a typical RCC from an oncocytoma or a fat poor angiomyolipoma.¹⁸

Given the low CT and MRI specificity, percutaneous image-guided biopsy remains the only reliable diagnostic test. Percutaneous core-needle biopsy is commonly performed with coaxial 16–18G needles under ultrasonography/CT guidance. Core-needle biopsy is preferred over fine-needle aspiration.¹⁹ Ultrasonography/CT-guided biopsy yields a high diagnostic performance (sensitivity 91–99.1%, negative predictive value 50–100%, diagnostic accuracy 85.5–97.1%, primary/secondary diagnostic yield 78–92.8%/86.1–94%),^{19–34} and acceptable rates of major and minor complications (0–0.9% and 1.8–20.3%, respectively).^{19–34} More rarely, MRI guidance has been used with reported sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 95.4%, 100%, 100%, 75% and 96%, respectively.³⁵ Compared to standard ultrasonography/CT guidance, MRI-guidance grants some intraoperative technical advantages including the high intrinsic SRMs conspicuity, even in cases of entirely endophytic tumours, and the real-time multiplanar imaging-guidance facilitating tumour targeting.

Table 1. WHO classification of renal tumours³⁸

Clear cell renal cell carcinoma
Multilocular cystic renal neoplasm of low malignant potential
Papillary renal cell carcinoma
Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma
Chromophobe renal cell carcinoma
Collecting duct carcinoma
Renal medullary carcinoma
MiT family translocation renal cell carcinomas
Succinate dehydrogenase-deficient renal cell carcinoma
Mucinous tubular and spindle cell carcinoma
Tubulocystic renal cell carcinoma
Acquired cystic disease-associated renal cell carcinoma
Clear cell papillary renal cell carcinoma
Renal cell carcinoma, unclassified
Papillary adenoma
Oncocytoma

MiT, microphthalmia-associated transcription factor; WHO, World Health Organization.

Adapted from Moch et al (³⁸).

Despite these theoretical MRI advantages, the rate of non-diagnostic samples (*i.e.* those with insufficient material for analysis, sampled non-renal or normal renal tissue) are similar across all imaging modalities (7.2–22% with CT/ultrasonography-guidance^{20–22,24–32,34}; 15% in our unpublished series of 100 consecutive MRI-guided SMRs biopsies).

Percutaneous core needle biopsy is systematically performed whenever it impacts the subsequent (surgical/interventional or medical) management of radiologically indeterminate SRMs.³⁶ In this perspective, it has been shown that performing the biopsy prior to treatment, avoids unnecessarily treating benign tumours in up to 20% of cases.³⁷ Biopsy is also indicated in patients undergoing active surveillance (AS; *i.e.* regular radiological monitoring of tumour size with the intent of performing a delayed intervention if the tumour grows during follow-up); and in patients with synchronous metastatic disease at the moment of diagnosing the primary renal tumour, before undergoing systemic therapies. Conversely, biopsy is not needed for candidates under watchful waiting (*i.e.* patients with comorbidities contraindicating any treatment or requirement for imaging follow-up); suspicion of urothelial carcinoma; uncontrolled haemorrhagic risk; cystic tumour without any solid component; and radiological diagnosis of angiomyolipoma.¹²

Diagnostic biopsy samples are obtained in 78–92.8% of cases^{20–22,24–32,34} thus often allowing a precise histological grading according to the WHO classification (Table 1). Clear cell RCC (ccRCC), papillary RCC (pRCC) and chromophobe RCC (cRCC) are the three most commonly diagnosed malignant SRMs (70%, 15% and 5%, respectively). In case of pRCC, the

Table 2. Renal tumour staging

T		N		M	
TX	Primary tumour cannot be assessed	NX	Regional lymph nodes cannot be assessed	M0	No distant metastasis
T0	No evidence of primary tumour				
T1	T1a: Tumour ≤ 4 cm				
	T1b Tumour >4 cm but ≤ 7 cm				
T2	T2a: Tumour > 7 cm but ≤ 10 cm	N0	No regional lymph node metastasis	M1	Distant metastasis
	T2b > 10 cm, limited to the kidney				
T3	T3a: Tumour extends into the renal vein or its segmental branches, or tumour invades the pelvi-calyceal system or tumour invades perirenal and/or renal sinus fat (peri-pelvic) fat but not beyond Gerota's fascia				
	T3b: Tumour extends into vena cava below diaphragm				
	T3c: Tumour extends into vena cava above the diaphragm or invades the wall of the vena cava				
T4	Tumour invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)	N1	Metastasis in regional lymph node(s)		
Stage					
I	1	0		0	
II	2	0		0	
III	3	0		0	
	1, 2, 3	1		0	
IV	4	Any		0	
	Any	Any		1	

histology report should also mention the specific subtype since Type 1 and Type 2 pRCC represent two different oncological diseases (*i.e.* Type 1 presents with multiple/bilateral tumours, and has a better prognosis compared to Type 2 pRCC³⁹). Moreover, in cases of ccRCC and pRCC, it is essential to know the International Society of Urological Pathology (ISUP) score, since low-grade (1 and 2) tumours have a significantly better prognosis compared to high-grade (3 and 4) ones.⁴⁰ Concordance between biopsy and surgery is excellent for determining the histological subtype and moderate for determining the ISUP score.⁴¹ Nevertheless, percutaneous biopsy may be under representative of the entire tumour composition, thus potentially impairing adjuvant therapies in case of metastatic disease evolution with subsequent need for a second biopsy.

In the end, all cases with biopsy-proven malignant SRMs should undergo chest CT to complete tumour staging (Table 2).

Current EUA, AUA and ESMO recommendations for the treatment of localised RCC

The European Urologic Association (EUA), the American Urological Association (AUA) and the European Society of Medical Oncology (ESMO) recognise four different treatment strategies for patients with localised RCC (T1-2N0M0) including

AS, radical nephrectomy (RN), partial nephrectomy (PN), and TA.^{36,42,43}

AS is supported by the fact most RCC's increase their size very slowly and rarely progress to manifesting metastatic disease. A multicentre prospective Phase 2 clinical trial⁴⁴ conducted in 178 elderly/frail patients (209 SRMs) undergoing AS, reported local tumour progression in 25 patients (12%), and metastatic evolution in 2 patients (1.1%). Among 127 patients (out of 178, accounting for 151 SRMs) with follow-up longer than 12 months (mean 28 months), tumour diameters increased by an average of 0.13 cm/year.

Specifically regarding guidelines, EUA recommends³⁶ to:

- offer surgery for curative intent in localised RCC (Strong Recommendation);
- offer PN to patients with T1 tumours (Strong Recommendation);
- not perform minimally invasive RN in patients with T1 tumours for whom a PN is feasible by any approach, including open (Strong Recommendation);
- avoid minimally invasive surgery if this approach may compromise oncological, functional and perioperative outcomes (Strong Recommendation);

- offer AS, radiofrequency ablation (RFA) and cryoablation (CA) for elderly and/or comorbid patients with SRMs (Weak Recommendation).

AUA recommends⁴² to:

- prioritise PN for the management of T1a tumours due to the reduced risk of chronic kidney disease (CKD) and the favourable oncologic outcomes (Moderate Recommendation);
- prioritise nephron-sparing approaches for patients with solid or Bosniak III–V complex cystic tumours and anatomic or functionally solitary kidney, bilateral tumours, known familial RCC, pre-existing CKD, or proteinuria (Moderate Recommendation);
- consider nephron-sparing approaches for patients with solid or Bosniak III–IV complex cystic renal masses who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future (*e.g.* hypertension, diabetes mellitus, recurrent urolithiasis, or morbid obesity) (Conditional Recommendation);
- consider RN for patients with a solid or Bosniak III–IV complex cystic renal mass where increased oncologic potential is suggested by tumour size, core-needle biopsy, and/or imaging characteristics and in whom active treatment is planned (Conditional Recommendation); in this setting, RN is preferred if all the following criteria are met: (1) high tumour complexity and challenging PN even in experienced hands; (2) no pre-existing CKD or proteinuria; and (3) normal contralateral kidney and new baseline estimated glomerular filtration rate >45 ml/min/1.73 m² (Expert Opinion);
- consider TA (RFA and CA, ideally performed percutaneously), as an alternative to surgery for the management of T1a renal masses < 3 cm (Conditional Recommendation) provided an established pathologic diagnosis achieved through previously performed biopsy (Expert Opinion) and clinical counselling to inform patients about the increased likelihood of local tumour persistence/recurrence after primary TA compared to surgery; although repeat TA is feasible for locally persistent/recurrent tumours (Strong Recommendation);
- propose AS as initial management for: (a) patients with a small solid or Bosniak III–IV complex cystic renal mass, especially if < 2 cm (Conditional Recommendation); (b) patients with a solid or Bosniak III–IV complex cystic renal mass when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment (Clinical Principle); (c) patients with a solid or Bosniak III–IV complex cystic renal mass in whom the risk/benefit analysis for treatment is equivocal and who prefer AS (in such cases imaging follow-up is proposed every 3–6 months to assess for interval growth and biopsy may be considered for additional risk stratification, Expert Opinion);
- consider active treatment over AS for patients with a solid or Bosniak III–IV complex cystic renal mass in whom the anticipated oncologic benefits of intervention outweigh the risks of treatment and competing risks of death; in such clinical condition, AS with potential for delayed intervention may be considered if the patient understands and is willing to accept the associated oncologic risk (Moderate Recommendation).

In the end, ESMO recommends⁴³:

- PN in organ-confined tumours measuring up to 7 cm;
- RFA, microwave ablation (MWA) or CA as treatment options in patients with small cortical tumours (≤ 3 cm), especially if they are frail, with high surgical risks, solitary kidney, compromised renal function, hereditary RCC or multiple bilateral tumours;
- to consider renal biopsy before TA;
- to consider AS in elderly patients with significant comorbidities, short life expectancy and solid renal tumours measuring < 40 mm (biopsy is recommended also to select patients for AS, especially due to the significant incidence of non-malignant tumours).

To summarise, TA is recommended to:

- elderly and/or comorbid patients with small renal masses, who may also receive AS (weak recommendation; EUA);
- patients with cT1a renal masses < 3 cm (Conditional Recommendation; AUA);
- frail/comorbid patients with small (≤ 3 cm) cortical tumours (ESMO).

Current CIRSE and SIR recommendations for the treatment of localised RCC

In 2017, the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) guidelines on the treatment of small RCC⁴⁵ concluded that percutaneous TA represents a valid treatment for T1aRCC since excellent long-term (5 years) technical, functional and oncologic outcomes along with very low complication rates are expected. Moreover, according to CIRSE recommendations, given the minimally invasive profile of percutaneous TA, AS has to be reserved only for patients unsuitable for TA due to comorbidities or advanced age.

In 2019, the American Society of Interventional Radiology (SIR) published an official position statement on the same topic.⁴⁶ In this document, the following conclusions were proposed:

- percutaneous TA is safe and effective for the treatment of small T1a renal tumours with fewer complications than nephrectomy and acceptable long-term oncological and survival outcomes (Moderate Recommendation);
- in selected patients with suspected T1a RCC, percutaneous TA should be offered over AS (Moderate Recommendation);
- in high-risk patients with T1b RCC who are not surgical candidates, percutaneous TA may be an appropriate treatment option, although further research in this area is required (Weak Recommendation);
- RFA, CA, and MWA are all appropriate modalities for TA, and the method of ablation should be left to the discretion of the operating physician (Weak Recommendation).

Literature data supporting TA

Although TA has been increasingly used in the last two decades (5.2% in 2004–2007 vs 9.1% in 2008–2011 for T1a RCC),⁴⁷ it is still only used in a 1:10 ratio compared with surgery.^{48,49} Interestingly, it has been reported that Caucasian ethnicity, higher income, living in metropolitan areas, and having health insurance

are independent factors for determining the choice of TA.⁴⁷ Literature reveals also that high-quality evidence supporting percutaneous TA is substantially lacking due to absence of prospective randomised controlled trials directly comparing TA with surgery. Nevertheless, there is growing evidence supporting TA arising from several large-population registries and retrospective studies as well as systematic reviews and meta-analyses that have been recently published.

Andrews et al⁵⁰ retrospectively reported their large institutional (Mayo Clinic, Rochester) series including cT1 renal masses receiving TA or PN. They analysed local recurrence, metastases, and death from RCC with propensity-score-adjusted Cox models. Benign tumour/unknown histology rates were 21%/0%, 33%/26%, and 35%/7% for PN, RFA, and CA, respectively; and RCC rates were 79%, 41%, and 58%, respectively. Tumour grade was not available in 1%, 22% and 22% of renal masses getting PN, RFA and CA, respectively. There were 1422 T1a patients who received PN ($n = 1055$), RFA ($n = 180$), and CA ($n = 187$) with a median clinical follow-up of 9.4, 7.5, and 6.3 years, respectively; and 376 T1b patients, who received PN ($n = 324$) or CA ($n = 52$) with a median clinical follow-up of 8.7 and 6.0 years, respectively. In the T1a subpopulation, comparisons of RFA with PN resulted in hazard ratios (HRs) of 1.49 [95% confidence interval (CI) 0.55–4.04, $p = 0.4$], 1.46 (95% CI 0.41–5.19, $p = 0.6$), and 1.99 (95% CI 0.29–13.56, $p = 0.5$) for local recurrence, metastases, and death from RCC, respectively. Comparisons of CA to PN resulted in HR of 1.88 (95% CI 0.76–4.66, $p = 0.18$), 0.23 (95% CI 0.03–1.72, $p = 0.15$), and 0.29 (95% CI 0.01–6.11, $p = 0.4$) for the same outcomes, respectively. 5-year cancer-specific survival (CSS) was 99%, 96%, and 100% for PN, RFA, and CA, respectively. In the T1b subpopulation, comparisons of CA with PN resulted in HR of 1.22 (95% CI 0.33–4.48, $p = 0.8$), 0.95 (95% CI 0.21–4.38, $p > 0.9$), and 1.94 (95% CI 0.42–8.96, $p = 0.4$) for local recurrence, metastases, and death from RCC, respectively. 5-year CSS was 98% and 91% for PN and CA, respectively.

Zhou et al⁵¹ used data from the Surveillance, Epidemiology, and End Results Program (SEER) database to compare TA in 809 patients to PN in 3783 patients with T1a RCC treated between 2004 and 2013. After matching the two populations with the propensity-score method for age, sex, race, tumour grade and size, they found greater 5 year overall survival (OS) with PN compared to TA (91.0% vs 86.3%; HR 1.442; 95% CI, 1.005–2.068; $p = 0.0457$) and no difference in terms of CSS (HR 1.466; 95% CI, 0.599–3.59; $p = 0.4023$).

Xing et al⁵² also used data from the SEER database to compare adverse events and survival outcomes in patients treated with PN (2820 patients), RN (4522 patients), TA (898 patients), or AS (1978 patients) due to a T1a RCC between 2002 and 2011. In their study, populations were matched 1:1 for each pair of treatment groups on the basis of 17 different covariates (age, sex, race, Charlson comorbidity index, cardiovascular disease, hypertension, diabetes, moderate or severe renal disease, socio-economic status, marital status, region, urban or rural location, tumour size, histologic characteristics, Fuhrman grade, year of diagnosis, and length of follow-up); 9 year CSS rates of 96.4% vs 96.3%,

and 96.1% vs 96.0% were reported for PN vs TA ($p = 0.07$), and RN vs TA ($p = 0.14$), respectively; 9 year rates of CSS and OS were significantly lower for AS compared with TA (95.4% vs 96.8%; $p = 0.03$; and 84.1 vs 91.8%; $p < 0.001$, respectively). In the end, compared with TA, surgery resulted in increased renal and cardiovascular morbidity up to 1 year after the procedure ($p < 0.05$ for all comparisons). Another study used data from the SEER database⁵³ to specifically compare TA to AS in populations matched for patients' age at diagnosis, gender, race, marital status, socio-economic status, population density, year of diagnosis, Charlson comorbidity index and tumour size. Once again, socio-economic factors (*i.e.* being Caucasian, married, and with high socio-economic status) favoured TA over AS. After applying a propensity-score matching, 553 TA patients were compared to 553 AS patients and an advantage for TA over AS was noted (3.5% vs 9.1%) at 5 year follow-up in terms of cancer-specific mortality (CSM). Multivariable regression analyses demonstrated that TA had a protective effect on CSM [HR 0.47 (95% CI: 0.25–0.89); $p = 0.02$].

Uhlig et al⁵⁴ have recently compared PN, RFA, CA and MWA in a large systematic review and meta-analysis. They included 47 studies accounting for 24,077 patients. Their results showed that patients receiving RFA, CA or MWA were older and with more comorbidities compared to those receiving PN. All-cause mortality was higher for CA and RFA compared with PN [incidence rate ratio (IRR)=2.58 and IRR = 2.58, respectively; $p < 0.001$]. No significant differences in CSS were noted. Local recurrence was higher for CA, RFA and MWA compared with PN (IRR = 4.13, IRR = 1.79, IRR = 2.52, respectively; $p < 0.05$). A decline in renal function was significantly less pronounced after RFA vs PN, CA and MWA. Pierorazio et al⁵⁵ confirmed that local recurrence-free survival is suboptimal for TA with one treatment but demonstrated that equivalence with surgery is reached after multiple treatments.

In the end, Hu et al⁵⁶ pooled data from 20 different articles (5011 patients) to compare oncologic and functional outcomes with PN and TA for clinical T1a renal masses. They reported fewer perioperative complications with TA compared to PN [Odds Ratio (OR) = 0.76; 95% CI, 0.60–0.97; $p = 0.025$], and higher risk of local recurrence for the former compared to the latter (OR = 1.88; 95% CI, 1.29–2.72; $p = 0.001$). Moreover, TA had lower OS (HR = 1.53; 95% CI, 1.16–2.00; $p = 0.002$), although there were no differences in terms of CSS and disease-free survival (DFS). Decline of renal function at 6 months follow-up was lower with TA compared with PN ($p = 0.047$). Besides, TA had a trend towards lower reduction of renal function in the long-term ($p = 0.247$).

Concerning T1b RCC, although some data about 5 year CSS are encouraging,⁵⁰ it should be noted that few retrospective TA series have been published for T1b RCC,^{57–59} and most of them have highlighted a peri-procedural complication rate ranging between 11.2 and 16.2%, thus stressing the objective technical challenge in achieving satisfactory large ablation areas without secondary iatrogenic damage. Moreover, actual 3-year local recurrence rates are 37–39%.^{57,59}

In the end, concerning specific TA safety, in a recently published multicentre retrospective observational study on 713 RCC (mean tumour size 2.8 cm) undergoing a total of 647 CA sessions, Garnon et al⁶⁰ found that the overall and major complication rate was 8.3% and 3.4%, respectively. The most frequent complication was bleeding (3.2%), which rarely required subsequent treatment (nine cases only; 1.4%). Non-T1a tumours (*i.e.* >4 cm) were more likely to result into a major periprocedural complication.

DISCUSSION

According to the aforementioned literature, patients with T1a RCC receiving TA compared to those receiving PN have a higher risk of local recurrence, although such risk does not result in lower CSS and DFS rates. Repeated TA may be considered for locally persistent/recurrent RCC without increased morbidity. Lower OS has been reported for TA, which probably reflects the typical clinical practice of the late '90s and early '00s, when TA was mainly reserved to old/comorbid patients. In the end, TA granted better preservation of the renal function and lower periprocedural complications. Based on such assumptions, it was possible for the radiology community, especially the American one, to significantly push in favour of TA. On the other hand, the oncological community, especially in Europe, is still somehow stricter about recommending TA; and common arguments used to justify such attitude may be summarised as follows.

1. *Absence of systematic biopsy to select patients for TA.* This attitude was particularly evident in the early years of TA and resulted in studies with many benign tumours (20–50% of the TA arms) treated unnecessarily.^{37,61} Accordingly, inclusions of these populations into systematic reviews/metanalyses,⁵⁴ or unreported histologic data in systematic reviews/metanalyses,⁵⁶ may definitively undermine the scientific evidence supporting TA for RCC. Similar considerations are applicable also for the ISUP score data, which were not systematically incorporated in multiple studies included in systematic reviews/metanalyses.^{54,56} Nevertheless, the recently published large series with perfectly matched biopsy-proven RCC populations^{51,52} have definitively contributed to mitigating the impact of this erroneous attitude of the past.

2. *Absence of careful stratification of the population in literature, reporting more favourable results for TA over surgery in terms of post-operative complications and decline of renal function, along with comparable oncologic results.* In this perspective, although perfect population matching (for many different variables including among others, the ISUP score and the tumour size) was carefully performed in large retrospective American series,^{51,52} the pre-operative evaluation of the RENAL score has almost never been considered in these analyses^{50–52,54}; therefore, preferential allocation of complex, aggressive and large tumours to surgical treatments has been likely to occur, thus potentially justifying the better results for TA.^{50–52,54} Just to give a practical example, a 2 cm peripheral exophytic tumour may have more or less a similar chance of being eradicated without complications and without significant impact on the renal function both with surgery and TA.

3. *Absence of widely shared procedural ablation protocols.*⁵⁴ In this perspective, the sole use of ultrasonography guidance

does not seem the most appropriate method to guide TA due to the absence of a large intra operative field-of-view facilitating objective assessment of tumour destruction (*e.g.* tumour coverage by the iceball if CA is used) and protection of nearby non-target structures. Accordingly, systematic CT or MRI guidance definitively seems more appropriate. Moreover, application of several different TA techniques with different energy sources and different underlying physical principles, may further undermine the scientific power of TA.⁵⁴ This drawback seems particularly pronounced with hot TA techniques and much less with CA since the 10 min double-freezing ablation protocol seems to have become the standard.⁶²

4. *Absence of systematic long-term imaging follow-ups, which is often performed by the same interventional team having performed TA.* Although 9 year results were sporadically reported thus proving long-term follow-ups,⁵² there is no formal agreement on the intervals at which such follow-up should be performed. Moreover, although radiologic semeiology criteria useful to describe the evolution of the ablation area have been reported,⁶³ they are hardly used on a systematic and large-scale basis; and lack of robust prospective validation proving their reproducibility (which may facilitate reporting also by diagnostic radiologists) exists. Moreover, adoption of widely shared protocols to evaluate the results of TA by diagnostic radiologists may definitively contribute to the spread of TA and avoid a potential bias about the oncologic efficacy of TA. In fact, often, imaging follow-up is performed by the same team that had previously performed TA; which is not the case for surgeons whose results are “judged” by pathologists and radiologists.

5. *Caution about TA for T1b RCC.* Although interesting data about TA of T1b RCC have been reported in terms of CSS,⁵⁰ given the periprocedural complication and the actual local recurrence rates, TA should be solely and strictly reserved to non-surgical candidates.

6. *Difficulty in conducting AS.* Although some data may favour TA over AS, it should be noted that probably with systematic biopsies (currently hardly obtained in all patients undergoing AS⁵³) at the moment of the diagnosis and strict imaging follow-up, AS may potentially perform as well as TA in old patients with low-grade tumours. Moreover, it is not irrational to think that in a near future, even young patients with small (<10–15 mm) low-grade RCC may effectively benefit from AS rather than TA or surgery.

FUTURE DIRECTIONS AND CONCLUSIONS

Given the curative role of TA for localised RCC, a rigorous reasoning is needed. In fact, it is no longer possible to neglect the curative value and the advantages of TA for localised RCC which, after a careful evaluation from the tumour board, may be potentially proposed even to young patients with good performance statuses as an alternative to surgery. Nevertheless, there are still some aspects in TA literature, mostly derived from poor previous practices, that may still actively contribute to the undermining of the therapeutic value of TA and its wide acceptance by the oncological community. For this reason, we firmly believe that continuing with these practices cannot be permitted any longer.

A practical solution to this impasse may derive from a new era of fair collaboration between oncurologists and interventional radiologists with corporativisms left behind. In practice, there is an urgent need for shared inclusion criteria, treatment and follow-up protocols useful to select, treat and follow-up patients

homogeneously. Adoption of these practises will pave the way for the much-needed prospective studies that, in the end, will naturally result in unanimous guidelines, endorsed by oncurological and interventional radiology societies.

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