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Stereotactic ablative radiotherapy for primary kidney cancer – An international patterns of practice survey

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ABSTRACT

Purpose: To conduct an international survey of radiation oncologists treating primary renal cell carcinoma (RCC) with SABR to ascertain the general patterns of SABR use, common dose/treatment/follow-up details, and expected outcomes.

Materials and methods: A 51-question survey was created containing the following themes: prevalence and clinical scenarios in which RCC SABR is used, dose-fractionation schedules, treatment delivery details, follow-up/outcome assessments, and implementation barriers. The survey was distributed widely across multiple influential radiation oncology societies and social media, and ran from January to April 2023.

Results: A total of 255 respondents participated, mostly from academic centers within Europe/North America. Of these, 40 % (n = 102) currently offer SABR (50 % having begun within the last 3 years). Common barriers in non-users included lack of referrals by urologists and lack of supportive practice guidelines. Of respondents who do offer SABR, 77 % treat both small (4 cm or less) and large (>4 cm) renal masses. Dose-fractionation strategies varied from 27-52 Gy (3–5 fractions) for multifraction regimens, and 15–34 Gy for single fractions. Apart from treatment for medically inoperable disease, scenarios in which SABR was likely to be offered were for recurrence post surgery/thermal ablation and for oligometastatic kidney lesions. Uncommon scenarios included RCC with renal vein/inferior vena cava thrombosis, and as cytoreductive therapy in metastatic RCC. Expected local control outcomes were generally above 70 %, higher for small versus large renal masses.

Conclusions: SABR is a relatively newer indication for primary RCC, offered by less than 50% of respondents, with both consistent and variable practice patterns observed.

Introduction

Kidney cancer, or renal cell carcinoma (RCC) is among the 10 most common cancers, accounting for an estimated 2 % of all global cancer diagnoses and deaths [1]. The incidence of RCC has been steadily increasing by 0.5–1 % per year since the 1980′s, likely due to an increase in incidental detection of renal masses and an aging population, with the greatest increase in incidence for those 70 years of age or older [2].

The standard treatment for RCC is surgical resection via total or partial nephrectomy. However, a growing number of patients are deemed inoperable due to factors such as advanced age and medical comorbidities including chronic renal failure and heart disease, with a higher likelihood of requiring post-operative hemodialysis.

Alternative management options for RCC include active surveillance for small, slow growing RCC [3]. Inoperable patients may also be considered for thermal ablative therapies such as radiofrequency ablation, microwave ablation, and cryoablation. However, these ablative options have notable limitations including tumor size, location, and anesthetic risk [4].

More recently, stereotactic ablative radiotherapy (SABR) has

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emerged as a potential non-surgical alternative for RCC. SABR has been shown both in preclinical and early clinical studies to be an effective treatment and has dispelled the notion of RCC being a radio-resistant malignancy [5,6].

In more recent years, an emerging body of literature has shown SABR for RCC to result in a high rate of local control, with low severe toxicity and a low rate of metastatic spread. In particular, the International Radiosurgery Oncology Consortium for Kidney (IROCK) pooled analysis from 190 patients across 12 institutions demonstrated a local control rate 5-years post SABR of 94.5 % and grade 3 or higher toxicity of 1 % [7]. Other prospective single arm Phase I and II trials have shown similar high rates of local control and cancer-specific survival, with limited impact on overall renal function [8–12]. As a result, SABR has begun to be recognized as a guideline-concordant treatment option for medically inoperable localized RCC [13].

Overall, there is an increasing body of work evaluating the use of SABR for RCC, yet the literature to date reflects the experiences of selected academic centres. As the use of SABR matures, it is important to understand the general patterns of practice, and in which scenarios clinicians feel more or less comfortable offering SABR. Therefore, the objective of our research was to conduct an international patterns of practice survey to determine the overall use of SABR for RCC, and for which indications SABR was more or less likely to be utilized.

Methods

Survey development

We created a 51-item survey containing a combination of multiple-choice, multi-select, 5-point Likert scale, and short-answer questions. The initial draft survey was completed by two authors (KT, AS), and an initial trial run-through was performed by a third author (SS), Following this initial draft, the survey was circulated to all remaining authors. The final survey was approved by expert consensus amongst all authors, all of whom have expertise in SABR for kidney cancer. The first section of the survey asked for demographic information such as geographical region and scope of practice (e.g. academic vs community), years of experience, and whether participants currently treat RCC using SABR. Respondents who did not currently offer SABR were directed to a separate section of the survey indicating the current barriers they faced with RCC SABR implementation. Subsequent sections targeted respondents currently using SABR and focused on a series of clinical scenarios to assess likelihood of SABR utilization, with more unique and complex scenarios presented in later sections. They were then asked regarding preferred dose schedules, contour simulation datasets, radiation planning techniques, and treatment verification methods for RCC SABR. Finally, questions pertaining to follow-up, outcome assessment approaches, and outcome expectations following SABR were solicited. The full survey was completed in Google Forms and was approved by a research ethics review board from the host institution. The survey is available for review in Appendix A.

Survey dissemination

The survey was disseminated electronically through several radiation oncology societies: the European Society for Radiotherapy and Oncology, the Genitourinary Radiation Oncologists of Canada, the Canadian Association of Radiation Oncology, the Royal Australian and New Zealand College of Radiologists and Faculty of Radiation Oncology Genito-urinary Group, the UK SABR Consortium, the Hong Kong College of Radiologists, and the Radiosurgery Society. Surveys were primarily distributed via e-mail link, with facilitation from contributing authors. The survey link was subsequently picked up over social media platforms such as X©, and via email to collegial contacts.

Survey analysis

Results of the survey were presented using descriptive statistics, including frequencies, percentages, and counting tallies. No formal a priori statistical analysis was performed, and all data was collected and analyzed anonymously.

Results

Demographics

From January to April 2023, 255 radiation oncologists in total completed the survey. The overall response rate could not be determined due to the nature of the survey dissemination, especially through means of social media. Responses were primarily from Europe and North America, with the majority (71 %) practicing in academic institutions (Table 1). In total, 103 (40 %) of respondents currently offer SABR for RCC. Of these, approximately one half (50 %, n = 51) had introduced SABR in the past 3 years, and 77 % (n = 79) within the past 5 years.

For respondents who were not currently offering SABR (n = 152), 62 % (n = 94) were planning on starting an RCC SABR program within the next 3 years. Commonly cited implementation barriers included lack of referrals by urologists (n = 74), lack of or minimal practice guidelines (n = 59), lack of training/experience in planning RCC SABR (n = 58), absent or minimal available technology to accurately deliver SABR (n = 50), and lack of endorsement by major radiation oncology societies (n = 48).

Patterns of practice for RCC SABR

In general, most respondents indicated that referrals for renal SABR are initiated via a urologist/uro-oncologist (Fig. 1), and more than 80 % of respondents would routinely review cases in a multidisciplinary setting (case conference or tumor board) prior to offering SABR. When asked regarding offering SABR for either large (4 cm or greater) or small (<4 cm) renal masses, most respondents (77 %) would treat any size, with a smaller percentage (20 %) offering SABR to small renal masses only. For medically inoperable patients, Fig. 2 depicts the likelihood that SABR would be considered alongside other alternative treatments including active surveillance or thermal ablation. For inoperable

Table 1
Survey demographics.

Characteristic		Total (n)	% using SABR for RCC	% NOT using SABR for RCC
Geographic Location	Total	255	40.4	59.6
	Europe	84	38.6	61.4
	North America	68	47.1	52.9
	Asia	56	17.8	72.2
	Oceania	41	61.0	39.0
	South America	4	50.0	50.0
	Middle East	2	50.0	50.0
Practice Setting	Total	255	40.4	59.6
	HospitalAcademic	177	42.4	57.6
	Hospital/Non-Academic	58	27.6	72.4
	Community/ Academic	5	60.0	40.0
	Community/Non-Academic	9	55.6	44.4
	Other	6	66.7	33.3
Years of Experience	Total	255	40.4	59.6
	0–10 years	100	35.0	65.0
	11–20 years	90	46.7	53.3
	21–30 years	47	42.6	57.4
	>30 years	18	33.3	66.7

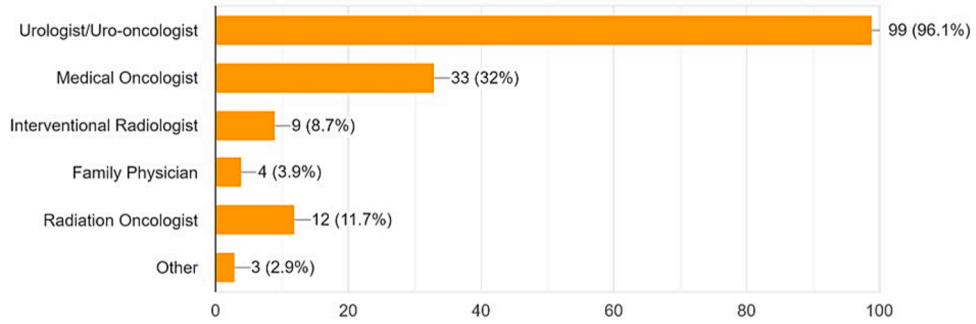

Fig. 1. Patterns of Referral for RCC SABR.

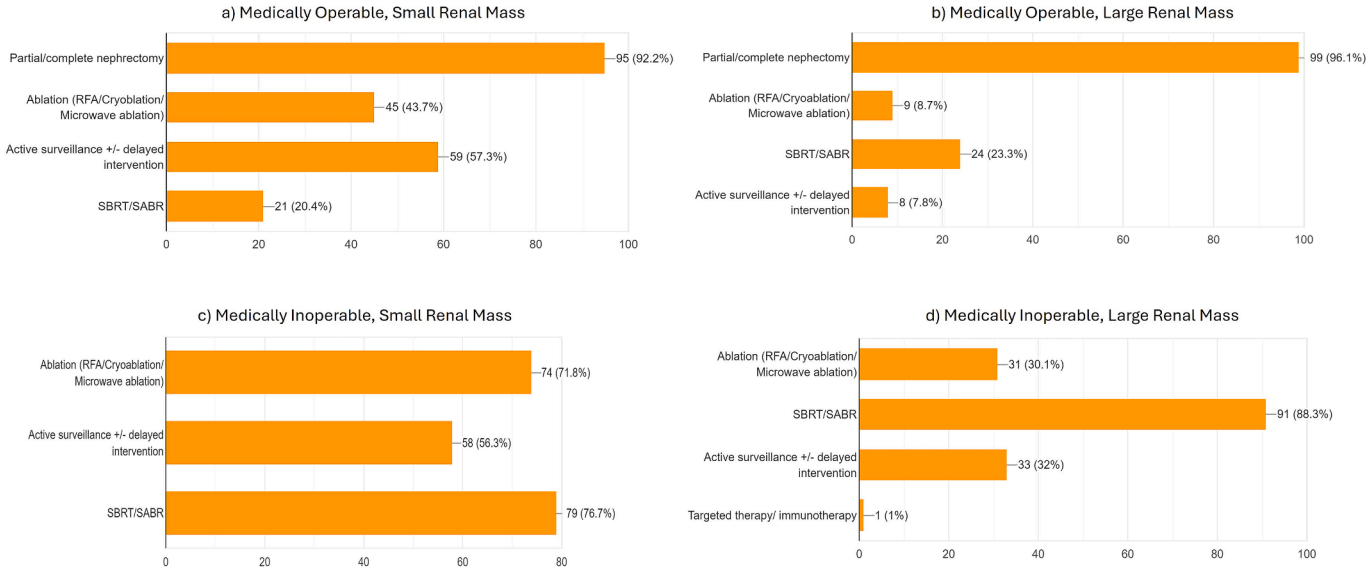

Fig. 2. SABR Utilization vs Alternative Therapies for Small (4 cm or less) Compared to Large (> 4 cm) Renal Masses in Medically Operable and Inoperable Patients (a-d).

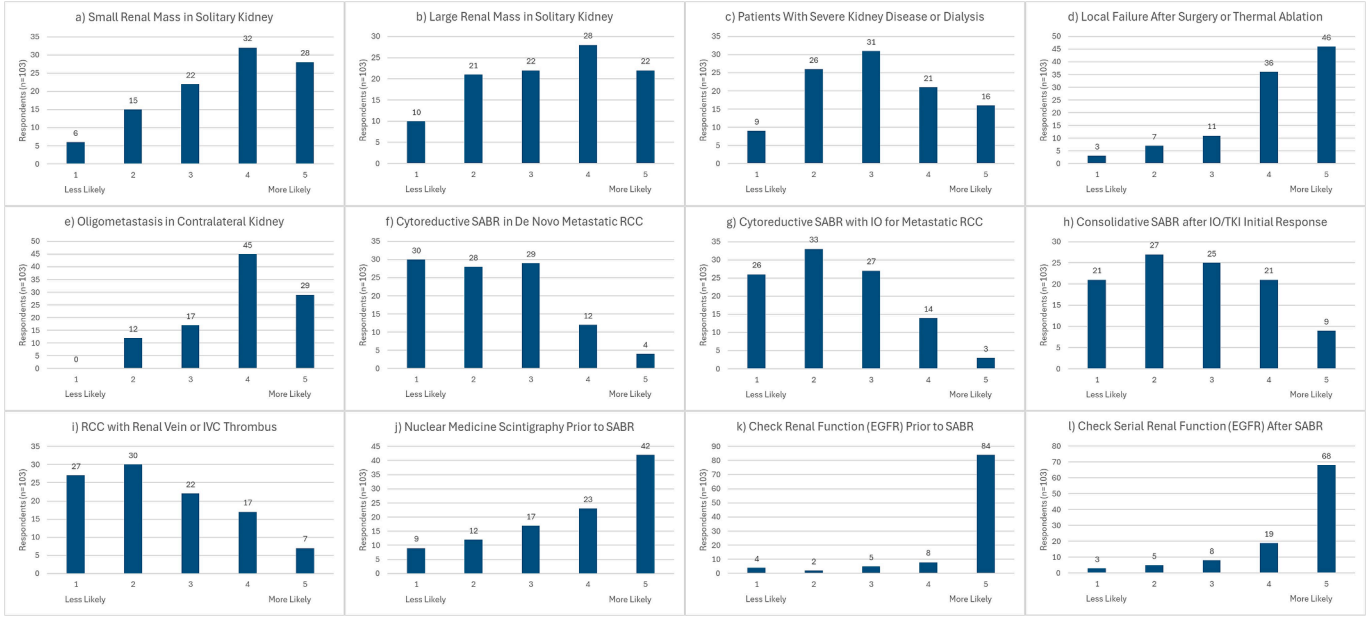

Fig. 3. Clinical Scenarios (a-l) Assessing SABR Utilization in RCC.

patients, SABR would be strongly considered for larger renal masses, whereas with smaller renal masses, responses were similar for SABR and thermal ablation. In medically operable patients, SABR would mainly be offered if patients refused surgery or if multidisciplinary consensus was achieved (62 %, n = 64), as compared to always (2 %, n = 2), sometimes (27 %, n = 28) or never (9 %, n = 9).

Clinical scenarios of SABR Utilization

A number of scenarios were presented in which participants were asked to gauge their likelihood scores regarding RCC SABR using a 5-point Likert scale. Results are provided in Fig. 3, and are summarized below:

Scenario 1: SABR in a Solitary Kidney.

Respondents were more likely (≥4 on the Likert scale) to offer SABR for a small renal mass < 4 cm (60/103, 58 %) than a large renal mass (50/103, 49 %) in a patient with a solitary kidney.

Scenario 2: SABR in Severe Chronic Kidney Disease.

Respondents were less likely (≤3 on the Likert scale) to offer SABR in a patient either on dialysis or with chronic kidney failure with an estimated glomerular filtration rate (EGFR) of less than 30 (66/103, 66 %).

Scenario 3: SABR as Salvage Therapy After Previous Failed Local Therapy.

Most respondents would offer SABR (Likert ≥ 4) after failed thermal ablation, or for local recurrence after surgery (82/103, 80 %).

Scenario 4: SABR to the Primary Kidney in the Metastatic/Advanced Setting.

Responses were mixed in this category. While most respondents would likely offer SABR to an oligometastasis in the contralateral kidney (74/103 with Likert ≥ 4, 72 %), they would be much less likely to offer cytoreductive SABR in the de novo metastatic setting (87/103 with Likert ≤ 3, 84 %), or as consolidative therapy following response to systemic therapy (73/103 with Likert ≤ 3, 71 %). In the setting of advanced RCC with renal vein or inferior vena cava thrombus, respondents were less likely to offer SABR as well (79/103 with Likert ≤ 3, 77 %).

Scenario 5: Assessment of Renal Function Prior to and Following SABR.

Almost all respondents (92/103, 89 %) would check estimated glomerular filtration rate (eGFR) (Likert ≥ 4) prior to treatment, with a similar percentage (87/103, 84 %) checking eGFR serially post SABR. Fewer respondents but still a majority (65/103, 63 %) would check renal function prior to SABR using nuclear medicine split renal function scintigraphy.

SABR dose selection

In general, the range of doses offered for single fraction SABR was between 15–34 Gy and for multifraction regimens between 27–52 Gy. Fig. 4 attempts to summarize the most commonly cited regimens. In general, single and multifraction regimens were more likely to be utilized for small renal masses, whereas fractionated SABR was more commonly cited for large renal masses.

SABR planning

Participants were asked to select which planning datasets would be commonly used for RCC SABR planning. While individual responses varied somewhat in terms of the number of datasets to acquire, almost all respondents did ensure some form of motion-mediated imaging – most commonly 4DCT. Additionally, 4DMRI and/or fiducial insertion with tumor tracking were also cited. In patients with normal/mild/moderate renal function, some form of contrast (on primary or secondary datasets) was recommended by all respondents. In the case of severe renal dysfunction (or dialysis), there were varied approaches – some would offer contrast but ensure that patients had *peri*-simulation hydration and/or dialysis, others with MRI availability would attempt to simulate with non-contrast MRI and assess tumor visibility, some would attempt to plan without contrast, and others would not continue with planning if contrast was not possible.

For organs at risk (OARs), >90 % of participants would include both kidneys, luminal GI organs (stomach/duodenum and small/large bowel) and spinal cord/cauda equina at a minimum. Less agreement occurred on whether to include the renal hilum and cortex (ipsilateral) as kidney substructures (44 % and 39 % respectively), as well as great vessels (55 %). For target metrics, coverage of 95–99 % of the planning target volume (PTV) by the prescription dose was most often selected (90/103, 87 %). Others selected 90 % PTV coverage, and a minority emphasized compromising PTV coverage at expense of proximity to OARs.

SABR treatment delivery

All respondents (100 %) selected daily image guidance for treatment verification, with imaging varied based on treatment unit, with the majority using linear-accelerator based SABR with daily cone-beam CT matching and no additional fiducial marker tracking (70/103, 68 %).

Expected outcomes following SABR

Fig. 5 summarizes the opinions as to expected outcomes post SABR for both large and small renal masses. Expected local control at 3-years was estimated to be at least 70 % for both small and large renal masses. However, it was generally felt that smaller renal masses had a higher chance of local control than large renal masses. In terms of follow-up practices, 85 % of replies (n = 87) indicated a first scan (most likely contrast enhanced CT) should be performed at 3 months, with the most commonly cited follow-up scan schedule at a minimum of every 6 months thereafter. 59/103 (57 %) of individuals would perform Response Evaluation Criteria in Solid Tumor (RECIST) measurements to determine response to therapy, whereas a few participants (4/103, 3 %) would request a renal mass biopsy at 1–2 years post SABR.

Discussion

The results presented herein represent the first attempt to understand international patterns of practice for renal SABR. It is not surprising to report that 40 % of initial respondents would currently offer SABR for RCC, as most of the high-level evidence to date has been generated within the past 5 years. It is also not surprising that most renal SABR is being performed in academic institutions, as current evidence has largely stemmed from these centers. However, there is a strong desire for increasing the scope of renal SABR worldwide, with almost 2/3 of those not currently offering SABR having interest in starting/

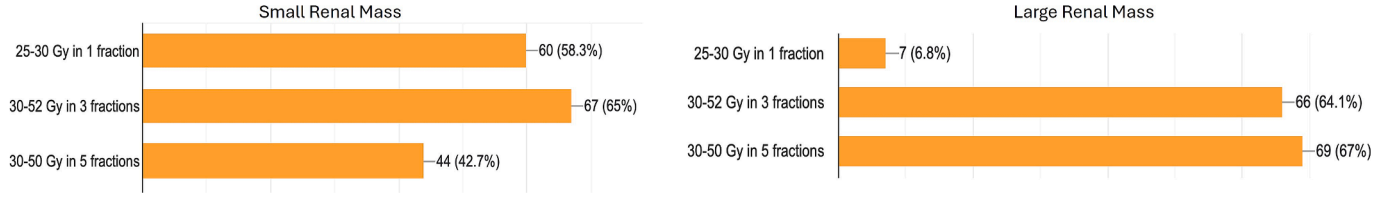

Fig. 4. Commonly Utilized Dose Fractionations for RCC SABR.

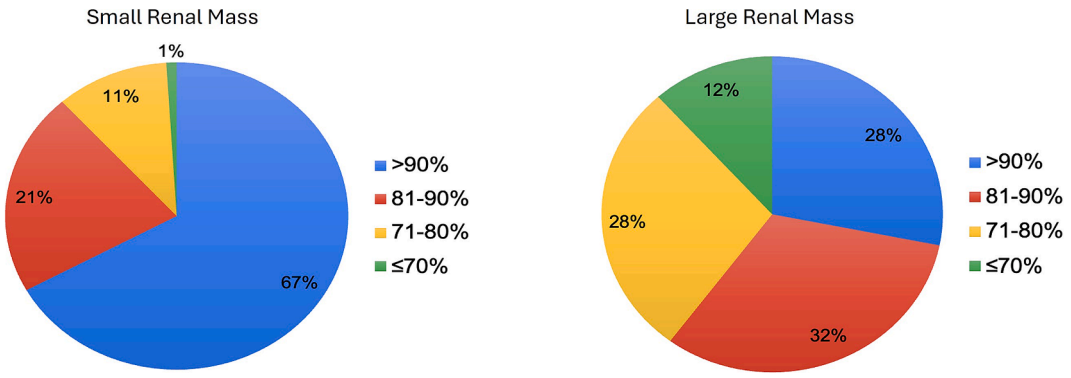

Fig. 5. Response Expectations (Local Control at 3-Years) Following RCC SABR.

developing programs within the short future.

In this survey we noted some interesting findings. For instance, we identified that a significant barrier for implementation seems to be related to referral patterns – in this case mainly from urologists/uro-oncologists. Survey respondents noted that most cases referred resulted from involvement within multidisciplinary case conferences or tumor boards. This is an important point of understanding as engagement and education of referring physicians within such multidisciplinary groups is more likely to stimulate interest and increase referrals to overcome these barriers. Furthermore, results from trials such as the recently reported FASTRACK II [11] study and the pilot randomized RADSTER [14] study will hopefully supply much-needed prospective data to aid in this effort.

We also attempted to understand patterns of practice for renal SABR in various clinical scenarios. In general, most survey respondents were comfortable treating both small and large renal masses, although we did not specify an upper limit on size. However, there was less enthusiasm to offer SABR in patients with poor renal function or on dialysis. We did not specify a lower limit on eGFR as there are no guidelines to suggest such a value, but often these patients have limited options for alternative therapies especially with large or rapidly growing RCCs. In general, studies have reported an eGFR reduction within the range of 10–15 mL/min post-SABR [7,9,12,15], yet it is sometimes difficult to attribute causation especially with competing risks such as diabetes or chronic kidney disease. The purpose of this survey is not to make recommendations, only to inform on patterns of practice – therefore if SABR is to be offered then as per most respondents it would be important to follow eGFR serially post treatment and consider such strategies as pre-treatment nuclear medicine split renal function in order to better assess potential risks with SABR relative to contralateral renal function [16].

Scenarios that were less likely to be considered for SABR were in the domain of more advanced or metastatic RCC. There was overall low eagerness to consider cytoreductive SABR or SABR for renal vein/inferior vena cava thrombus. The current evidence supporting these indications is sparse, with small retrospective cohort and Phase I studies showing mainly proof of concept in these scenarios [17,18]. Fortunately, ongoing trials will hopefully provide supportive evidence in the future; in particular, the CYTOSHRINK [19] and SAMURAI [20] trials which are evaluating cytoreductive SABR and immunotherapy in metastatic RCC.

Patterns of dose-fractionation selection were also studied. A previous *meta*-analysis demonstrated that a single fraction regimen of approximately 25 Gy or fractionated treatment using 35–40 Gy in 5 fractions were most commonly utilized – likely influencing the results obtained in this survey (along with 3-fraction regimens as per FASTRACK) [5,11]. The most recent IROCK exploration of single versus multifraction SABR suggested perhaps some benefits of local control and progression-free survival with single fraction, with those patients trending slightly younger, with better performance status. Based on this survey, it appears that choice of single versus multifraction may be more size-dependent, with larger renal masses more likely receiving multifraction SABR, smaller renal masses receiving both single/multifraction SABR, and no obvious dose–response reported to date [21].

Responses outlining SABR planning/delivery were similar to other upper abdominal sites including liver [22], which would include at a minimum some form of contrast imaging at time of planning, as well as tumor motion mitigation, and daily image guidance. Planning goals were also similar to other SABR sites, as well as OAR considerations – however we did query participants if kidney substructures such as renal cortex and/or hilum should be considered as critical OARs, with less than half of respondents responding affirmatively. While there is some data supporting dose/volume to the uninvolved kidney cortex as predictive of eGFR decline post-SABR [12], there is no general consensus on whether this should be included as a critical OAR. This lack of consensus is even more so the case for the renal hilum. There may be several reasons for this. First, there is minimal evidence that RCCs abutting or invading the renal pelvis/hilum are at higher risk for complications post-SABR (such as ureteric strictures or urothelial necrosis). Second, there is no consensus on the extent and scope of the renal hilum contour. Finally, studies utilizing SABR for upper tract urothelial cancers have reported minimal toxicity to the renal pelvis and proximal ureter [23].

The final section of the survey dealt with outcomes, response assessment and follow-up patterns of care. Most respondents indicated a routine follow-up schedule of every 6-month imaging. Only about half would use RECIST measurements to determine response to SABR, which likely reflects the challenges clinicians face in response assessment following RCC SABR. Various reports have suggested that tumors can initially grow prior to response [24], and there is evidence now showing that even stable disease with contrast enhancement at 1- and 2-years post treatment may not be indicative of active RCC [9]. Positive biopsies are also common post-SABR, but the proliferative index on biopsy specimens has been demonstrated to be low based on pathological analysis [25]. Therefore, RECIST in isolation may not be helpful following SABR. Some reports suggesting perhaps growth kinetics [26] or volumetric change [27] may be more indicative of early response rather than overall linear change, and such strategies could help compliment RECIST in the post-SABR setting.

While the intention of this survey was to better understand patterns of practice with respect to renal SABR, we do acknowledge potential limitations. First, we do not have a good sense of our overall response rate, given the nature of our survey dissemination – although we did attempt to engage multiple influential societies, it may not have reached all our intended population. Similarly, we were not able to determine what proportion of respondents were through targeted e-mail versus via social media. Due to the anonymous nature of this survey, we did not specifically ask whether an individual was brought to answer via e-mail vs through social media. Second, it is possible we are underestimating, or (more likely) overestimating the proportion of individuals currently

using SABR for RCC, as those not using SABR may not have opened the survey (even though they were prompted to respond either way) or were not reached. Finally, our questions were meant to capture a broad sense of patterns of practice, and as such we cannot make any firm recommendations on such details as ideal dosing, appropriate EGFR limits, tumor size limits, or appropriate imaging follow-up frequency. Furthermore, specific details regarding certain scenarios were not fully described – for example we asked for general recommendations regarding treatment of a small renal mass; this may change depending on tumor location relative to OARs. However we did allow for multiple responses for such questions understanding that certain decisions may vary depending on the clinical scenario.

In summary, we present the current state of practice for RCC SABR internationally. We hope that the results of this survey will stimulate discussions that will generate consensus and guidelines on best practices for RCC SABR and identify gaps that will enable future research to advance this exciting field forward.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Taplin: none, Hannan: none, Lo: Kuni Foundation – research funding; Radiosurgery Society – Member of Board of Directors; ACR – assistant councillor and chair of CARROS nomination committee, Morgan: none, Ali: none, Sigurdson: none, Guckenberger: none, Swaminath: Bristol-Myers Squibb – honoraria.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2024.100891.

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