Thieme

Treatment Failure After Image-Guided Percutaneous Radiofrequency Ablation (RFA) of Renal Tumors – A Systematic Review with Description of Type, Frequency, Risk Factors and Management

Therapieversagen nach bildgeführter perkutaner Radiofrequenzablation (RFA) von Nierentumoren – eine systematische Übersicht mit Beschreibung von Typ, Häufigkeit, Risikofaktoren und Management

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Key words

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ZUSAMMENFASSUNG

Hintergrund Die Radiofrequenzablation (RFA) ist ein etabliertes Verfahren zur Behandlung von kleinen Nierentumoren. Das Ziel dieser Übersicht ist die systematische Erfassung von Häufigkeit, Typ, Risikofaktoren und Management von Therapieversagen nach bildgeführter perkutaner RFA von Nierentumoren.

Methode Zehn Studien (967 Patienten, 1033 Tumoren) mit einem mittleren/medianen Beobachtungszeitraum von ≥ 30 Monaten wurden systematisch identifiziert und ausgewertet.

Ergebnisse und Schlussfolgerung Die bildgeführte perkutane RFA ist eine sehr effektive Technik zur Behandlung von umschriebenen Nierentumoren. Der residuelle nicht-abladierte Tumor ist der häufigste Typ des Therapieversagens (5,9 %), gefolgt von lokalem Tumorprogress (4,7 %). De-novo-Nierentumoren treten in 1,3 % und extrarenale Metastasen in 2,0 % der Fälle auf. Lokaler Tumorprogress, de-novo-Nierentumoren und extrarenale Metastasen treten vorwiegend später als 12 Monate nach initialer RFA auf. Eine Tumorgröße > 3 cm und eine zentrale Tumorlokalisation sind die Hauptrisikofaktoren für das Therapieversagen. Im Falle eines Therapieversagens zeigt die erneute RFA eine hohe Erfolgsrate (86,3 % für residuelle nicht-abladierte Tumoren und 87,5 % für lokalen Tumorprogress).

Kernaussagen:

- Therapieversagen kann in residuelle nicht-abladierte Tumoren und lokalen Tumorprogress unterteilt werden.
- Residuelle nicht-abladierte Tumoren treten in 5,9 % der Fälle auf.
- Lokaler Tumorprogress tritt in 4,7 % der Fälle auf.
- Tumorgröße und Tumorlokalisation sind Hauptrisikofaktoren für das Therapieversagen.
- Die erneute RFA ist effektiv und wird regelmäßig durchgeführt.

ABSTRACT

Background Radiofrequency ablation (RFA) is an established treatment for small renal tumors. The objective of this review is to systematically assess the type, frequency, risk factors and management of treatment failure after image-guided percutaneous RFA of renal tumors.

Method 10 studies (967 patients, 1033 tumors) with a mean/median follow-up of ≥ 30 months were systematically identified and analyzed.

Results and Conclusion Image-guided percutaneous RFA of localized renal tumors is very effective. The most common type of treatment failure is residual unablated tumor (5.9 %), followed by local tumor progression (4.7 %). De novo tumors in the kidneys occur in 1.3 % of cases and extra-renal metastases in 2.0 %. Local tumor progression, de novo tumors in the kidneys and extra-renal metastases occur predominantly later than 12 months after initial RFA. Tumor size > 3 cm and central tumor location are the major risk factors for treatment failure. In the case of treatment failure, repeated RFA shows high success rates (86.3 % for residual unablated tumors and 87.5 % for local tumor progression).

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Key Points:

- Treatment failure can be subdivided into residual unablated tumor and local tumor progression.
- Residual unablated tumor occurs in 5.9 % of cases.
- Local tumor progression occurs in 4.7 % of cases.
- Tumor size and location are the major risk factors for treatment failure.
- Repeated RFA is effective and commonly used for management.

Citation Format

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Introduction

Radiofrequency ablation (RFA) is an established treatment option for small renal tumors [1]. Due to the increasing number of diagnostic procedures, nowadays most renal tumors are detected incidentally at an early stage [1]. The currently available intermediate- and long-term data demonstrate a high rate of oncologic success of image-guided percutaneous RFA with 5-year cancer-specific survival rates of up to 100 % [2, 3]. In the latest controlled trials, percutaneous RFA and nephrectomy show comparable survival rates. Takaki et al. compared percutaneous RFA with partial and radical nephrectomy, and reported 5-year cancer-specific survival rates of 100 % [4]. Turna et al. also reported not significantly different cancer-specific survival rates between percutaneous RFA and partial nephrectomy (83.9 % vs. 100.0 %, respectively) but more cardiovascular complications in patients with long-term follow-up after nephrectomy [5]. The occasionally published superior overall survival in favor of patients undergoing nephrectomy may be explained by selection biases between the study groups (e. g. patient age and comorbidity) [6 – 8]. An alarming sign, however, is high local treatment failure rates of up to 35 % in single-center RFA studies [9]. Beside residual unablated tumor and local tumor progression, recurrence outside the ablation zone in the kidneys and also extra-renal metastases have to be noted. Multiple single-center studies and meta-analyses investigated the outcome after image-guided percutaneous RFA of renal tumors but specific standardized data on mid- and long-term outcome is rare. Especially the data referring to treatment failure after percutaneous RFA of renal tumors is quite heterogeneous. This heterogeneity can be explained particularly by variable follow-up, different techniques and technologies as well as inhomogeneous reporting and non-standardized terminology. The objective of this review is to systematically assess the type, frequency, risk factors and management of treatment failure after image-guided percutaneous RFA of renal tumors in studies with a mean/median follow-up of ≥ 30 months.

Materials and Methods

Selection criteria and search strategy

The systematic literature search and the selection and analysis of articles were conducted in accordance with the PRISMA statement [10]. Studies reporting on the oncologic outcome of image-guided percutaneous RFA of renal tumors with a mean or median follow-up of ≥ 30 months were eligible for inclusion. Studies with insufficient data, a follow-up period of less than 30 months or studies with patient collectives published in more recent studies were excluded. Only studies written in English were analyzed. The search algorithm for MEDLINE (PubMed) was constructed using the following medical subject heading terms (MeSH) and text words: “radiofrequency ablation”, “RF ablation”, “RFA”, “kidney cancer”, “kidney tumor”, “renal cancer”, “renal mass”, “renal neoplasm”, “renal tumor”, “renal cell carcinoma”, “RCC”, “outcome” and “recurrence”. The search was not restricted to years of publication or types of studies. After the systematic literature search, titles and abstracts were screened (primary selection) in order to find potentially appropriate articles. The next step was to perform a detailed evaluation of the main body of these studies (secondary selection) including cross-checking of the reference lists of the retrieved articles. The methodological quality of the studies potentially appropriate for inclusion was checked using the Downs and Black checklist for systematic reviews of non-randomized studies [11]. The search was completed during October 2015.

Definitions

According to Ahmed et al., residual disease in the ablation zone detected in the first follow-up imaging should be defined as “residual unablated tumor”, and viable tumor in the ablation zone detected after an unremarkable first follow-up imaging should be defined as “local tumor progression” [12]. Accordingly, treatment failure was subdivided into (1) residual unablated tumor and (2) local tumor progression. Additionally, patients with de novo tumors in the kidneys and patients with extra-renal metastases were described.

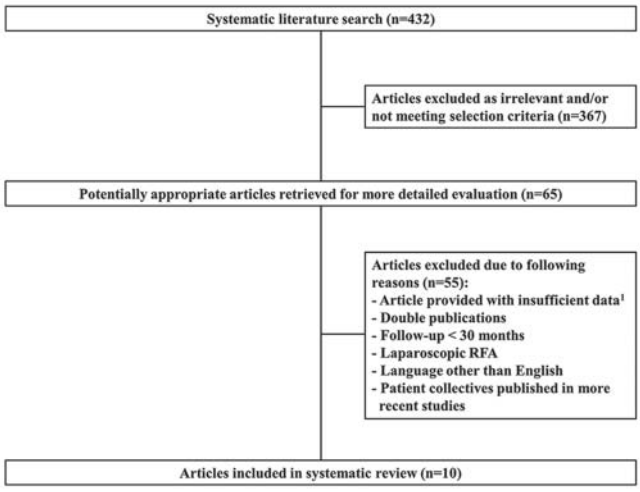
Results

Search results and baseline characteristics of the included studies

After primary and secondary selection, 432 studies were identified. 10 studies published between 2010 and 2015 fulfilled the inclusion criteria and were analyzed in this systematic review. In total, data of 967 patients and 1033 treated tumors could be evaluated. The literature search flow and reasons for exclusion are presented in ▶ **Fig. 1**. An overview of the included studies is presented in ▶ **Table 1**, and a summary of the results is presented in ▶ **Table 2**.

Residual unablated tumor

Across all included studies, 61 out of 1033 treated renal tumors showed residual unablated tumor after initial RFA, resulting in a



▶ **Fig. 1** Literature search flow. Note: [1]rate of residual unablated tumor or local tumor progression not indicated, incomplete description of the follow-up periods, type of image guidance not specified.

▶ **Abb. 1** Flussdiagramm zur Erläuterung der Literaturrecherche. Legende: [1]Häufigkeit von residuellen, nicht-abladierten Tumoren oder lokaler Tumorprogress nicht beschrieben, unvollständige Angabe der Beobachtungszeiträume, keine Spezifizierung der Methode zur Bildführung.

mean frequency of 5.9 %. The following risk factors were described: (1) tumor size [2, 3, 13 – 15], (2) central tumor location [3, 13 – 15], (3) a maximum treatment temperature of ≤ 70 °C [15], and (4) clear cell subtype of renal cell carcinoma [15]. The cutoff for tumor size defined as a risk factor was between 3 and 4 cm [3, 13 – 15]. The results for the management of residual unablated tumor with repeated RFA are presented in ▶ **Table 3**. In 54.1 % of the cases (n = 33), residual unablated tumor was managed with repeated RFA. In 59.1 %, one additional session and in 40.9 % two additional treatment sessions were performed. The treatment success rate, defined as no residual unablated tumor and no local tumor progression in the follow-up imaging, was 86.3 %.

Local tumor progression

The results for local tumor progression after image-guided percutaneous RFA are presented in ▶ **Table 4**. Across all included studies, 48 out of 1033 treated renal tumors showed local tumor progression, resulting in a mean frequency of 4.7 %. In all but one case, imaging was the rationale for diagnosing local tumor progression. In this single case, viable tumor was found in a pretransplant nephrectomy specimen [16]. Local tumor progression occurred most frequently > 24 months after initial RFA (62.5 %; n = 10). The mean time interval between initial RFA and diagnosis of local tumor progression was 28.0 months (range: 4 to 89 months). Risk factors described for local tumor progression were the same as for residual unablated tumor, with tumor size and tumor location as the most relevant risk factors [2, 3, 13 – 15]. Local tumor progression was most frequently managed with repeated RFA (47.8 %; n = 48), followed by active surveillance (12.5 %; n = 6) and surgery (10.4 %; n = 5). For the remaining patients (29.2 %; n = 14), management of local tumor progression was not described. The results for the management of local tumor progression with repeated RFA are presented in ▶ **Table 5**. In the included studies, the outcome of the repeated RFA was given for 8 out of the 48 patients. The treatment success rate, defined as no residual unablated tumor and no local tumor progression in the following follow-up imaging, was 87.5 %.

De novo tumors in the kidneys

Across all included studies, 13 out of 967 treated patients showed de novo tumors in the kidneys, resulting in a mean frequency of 1.3 %. In all patients the de novo tumors were detected via radiological imaging. De novo tumors in the kidneys occurred most frequently between 13 and 24 months (42.9 %; n = 3) or later than 24 months (42.9 %; n = 3) after initial RFA. The mean time interval between initial RFA and diagnosis was 27.9 months (range: 11 to 48 months). Risk factors for de novo tumors in the kidneys were not specified in the included studies. The management of three de novo tumors was described [13, 14, 17]. Two of them were treated with repeated image-guided percutaneous RFA with a treatment success rate, defined as no residual unablated tumor and no local tumor progression in the following follow-up imaging, of 100 %.

Extra-renal metastases

Across all included studies, 19 out of 967 treated patients showed extra-renal metastases, resulting in a mean frequency of 2.0 %. Most extra-renal metastases occurred later than 24 months after initial RFA (40.0 %, n = 4). The mean time interval between initial RFA and the diagnosis of extra-renal metastases was 22.5 months (range: 4 to 54 months). The most frequent locations of metastases were the lung, liver, bone, abdominal lymph nodes and pancreas. In the cases in which the outcome was reported, the mortality was high. Management or risk factors for patients with extra-renal metastases were not described in the included studies.

Discussion

According to our review, image-guided percutaneous RFA of small renal tumors is very effective. The results of our systematic review do not confirm the alarmingly high treatment failure rates published in very isolated single-center RFA studies. The frequencies of residual unablated tumor, local tumor progression, de novo tumors in the kidneys and extra-renal metastases are 5.9 %, 4.7 %, 1.3 % and 2.0 %, respectively.

Tumor size is a major risk factor for residual unablated tumor and for local tumor progression [2, 3, 13 – 15]. As presented above, treatment failure is more likely for tumors with a diameter of > 3.0 cm compared with smaller ones. The relevance of tumor size regarding the probability of tumor recurrence was published and discussed by Balageas et al. For tumors ≤ 4 cm (T1a), the recurrence-free survival rate was significantly higher than for tumors > 4 cm (T1b) (100 % vs. 57.1 %; p = 0.0001) [14]. With the aid of pre-interventional embolization as an add-on to percutaneous RFA, the technical success, oncologic outcome and safety of RFA of bigger (T1b and T2), central and hardly visible renal

▶ **Table 1** Overview of the included studies: Study, patient and tumor characteristics.

▶ **Tab. 1** Übersicht über die eingeschlossenen Studien: Studien-, Patienten- und Tumoreigenschaften.

authors	year	controlled (C) or non-controlled (NC) study design	patients (n)/ tumors (n)	image guidance	mean or median[1] follow-up (months)	mean tumor size (cm)	tumor location (n, (relative frequency[2])): central/peri-pheral/mixed	tumor histology (relative frequency)[3]
Ferakis et al. [13]	2010	NC	31/39	CT	61.2	3.1 (1.3 – 7.5)	35 (89.7 %)/4 (10.3 %)/0 (0 %)	–
Sung et al. [20]	2012	C[4]	40/45	CT	36.6	2.4 (1.0 – 6.0)	36 (90.0 %)/4 (10.0 %)/0 (0 %)	100 % clear cell RCC
Psutka et al. [2]	2013	NC	185/185	CT	77.2[1]	3.0 (1.0 – 6.5)	139 (75.1 %)/12 (6.5 %)/34 (18.4 %)	54.1 % clear cell, 17.8 % chromophobe, 2.7 % oncocytic RCC
Allen et al. [44]	2013	NC	38/40	CT	33.6	2.3 (1.0 – 4.2)	30 (75.0 %)/10 (25.0 %)/0 (0 %)	61.1 % RCC, 38.9 % inconclusive or non-diagnostic
Balageas et al. [14]	2013	NC	62/71	CT, US[5]	38.8	2.4 (0.8 – 4.6)	57 (80.3 %)/11 (15.5 %)/3 (4.2 %)	48.4 % clear cell, 19.4 % papillary, 11.3 % cystic RCC
Wah et al. [3]	2014	NC	165/200	CT, US[6]	46.1	2.9 (1.0 – 5.6)	84 (42.0 %)/16 (8.0 %)/100 (50.0 %)	80.0 % clear cell, 7.0 % eosinophilic or chromophobe, 4.0 % papillary RCC
Forauer et al. [16]	2014	NC	39/46	CT	35.5	2.6 (1.2 – 4.0)	46 (100 %)/0 (0 %)/0 (0 %)	59.0 % clear cell, 35 % papillary, 2 % mixed type RCC
Thompson et al. [21]	2015	C[4]	166/166	CT	34.8[1]	2.1 (–)	–	52.0 % clear cell, 27.0 % papillary, 4 % chromophobe RCC
Pieper et al. [17]	2015	NC	38/38	CT	54.6	2.1 (–)	–	60.5 % clear cell RCC, 13.2 % oncocytoma, 10.5 % angiomyolipoma
Iannuccilli et al. [15]	2015	NC	203/203	CT	34.1	2.5 (1.0 – 6.0)	135 (66.5 %)/12 (5.9 %)/56 (27.6 %)	47.3 % clear cell, 20.2 % papillary RCC, 10.3 % oncocytoma
Pooled data	2010 – 2015	s. a.	967/1033	s. a.	41.0[1]	2.5	562 (68.2 %)/ 69 (8.4 %)/ 193 (23.4 %)	56.7 % clear cell, 11.8 % papillary, 5.1 % chromophobe RCC

"–": no data available in the respective study; s. a. = see above (data not pooled); CT: computed tomography, US: ultrasound; RCC.: renal cell carcinoma.

"–" Keine Angabe in der jeweiligen Studie; s. a. = siehe oben (Daten nicht statistisch zusammengefasst); CT: Computertomografie; US: Ultraschall; RCC: Nierenzellkarziom.

[1] pooled data could only be calculated from the studies in which the mean was available.
gepoolte Daten konnten nur aus den Studien bestimmt werden, in denen der Mittelwert angegeben wurde.

[2] on the basis of treated tumors.
auf Basis der behandelten Tumoren.

[3] the three most frequent types of tumor histology are indicated, on the basis of tumors with histological examination.
die drei häufigsten histologischen Tumorarten sind angegeben, auf Basis der Tumoren mit histologischer Sicherung.

[4] control group: partial nephrectomy.
Kontrollgruppe: partielle Nephrektomie.

[5] CT guidance: 60 patients, US guidance: 2 patients.
Bildführung mittels CT: 60 Patienten, Bildführung mittels US: 2 Patienten.

[6] CT guidance: 179 RFA procedures, US guidance: 31 RFA procedures.
Bildführung mittels CT: 179 Interventionen, Bildführung mittels US: 31 Interventionen.

▶ **Table 2** Overview of the results of the included studies.

▶ **Tab. 2** Übersicht über die Ergebnisse der eingeschlossenen Studien.

authors	residual unablated tumor (n (relative frequency[1]))	local tumor progression (n (relative frequency[1]))	de novo tumors in the kidney (n (relative frequency[2]))	extra-renal metastases (n (relative frequency[2]))
Ferakis at al. [13]	4 (10.3 %)	3 (7.7 %)	1 (3.2 %)	0 (0 %)
Sung et al. [20]	8 (17.8 %)	1 (2.2 %)	0 (0 %)	1 (2.5 %)
Psutka et al. [2]	24 (13.0 %)	12 (6.5 %)	5 (2.7 %)	4 (2.2 %)
Allen et al. [44]	0 (0 %)	0 (0 %)	1 (2.6 %)	0 (0 %)
Balageas et al. [14]	4 (4.2 %)	2 (2.8 %)	4 (6.5 %)	4 (6.5 %)
Wah et al. [3]	9 (4.5 %)	5 (2.5 %)	0 (0 %)	4 (2.4 %)
Forauer et al. [16]	0 (0 %)	1 (2.2 %)	0 (0 %)	0 (0 %)
Thompson et al. [21]	0 (0 %)	5 (3.0 %)	0 (0 %)	4 (2.4 %)
Pieper et al. [17]	2 (5.3 %)	4 (10.5 %)	2 (5.3 %)	2 (5.3 %)
Iannuccilli et al. [15]	11 (5.4 %)	15 (7.5 %)	0 (0 %)	0 (0 %)
pooled data	61 (5.9 %)	48 (4.7 %)	13 (1.3 %)	19 (2.0 %)

[1] on the basis of treated tumors.
auf Basis der behandelten Tumoren.
[2] on the basis of treated patients.
auf Basis der behandelten Patienten.

▶ **Table 3** Management of residual unablated tumor with repeated RFA.

▶ **Tab. 3** Management von residuellen nicht-abladierten Tumoren mit erneuter RFA.

authors	residual unablated tumor (n)	tumors re-treated with RFA (n (relative frequency))	number of sessions for repeated RFA		outcome of repeated RFA –available data (n (relative frequency[1]))	outcome of repeated RFA – treatment success[2] (n (relative frequency))
			one session	two sessions		
Ferakis at al. [13]	4	4 (100 %)	3	1	4 (100 %)	3 (75.0 %)
Sung et al. [20]	8	8 (100 %)	3	5	8 (100 %)	8 (100 %)
Psutka et al. [2]	24	–	–	–	–	–
Allen et al. [44]	0	–	–	–	–	–
Balageas et al. [14]	4	2 (50.0 %)	2	0	2 (100 %)	2 (100 %)
Wah et al. [3]	9	8 (88.9 %)	5	3	8 (100 %)	6 (75.0 %)
Forauer et al. [16]	0	–	–	–	–	–
Thompson et al. [21]	0	–	–	–	–	–
Pieper et al. [17]	2	–	–	–	–	–
Iannuccilli et al. [15]	11	11 (100 %)	–	–	0 (0 %)	–
pooled data	61	33 (54.1 %)	13/22[3] (59.1 %)	9/22[3] (40.9 %)	22 (66.7 %)	19 (86.3 %)

"–": no data available in the respective study or no data indicated since no case of residual unablated tumor was reported in the respective study.
"–": Keine Angabe in der jeweiligen Studie oder keine Daten angegeben, da kein residueller nicht-abladierter Tumor in der jeweiligen Studie berichtet wurde.
[1] on the basis of tumors re-treated with RFA.
definiert als kein residueller nicht-abladierter Tumor und keine lokale Tumorprogression in den Verlaufkontrollen nach erneuter Intervention.
[2] defined as no residual unablated tumor and no local tumor progression in the follow-up imaging.
[3] for 11 tumors the number of sessions was not indicated.
für 11 Tumoren wurde die Anzahl der Behandlungssitzungen nicht angegeben.

▶ **Table 4** Local tumor progression.

▶ **Tab. 4** Lokale Tumorprogression.

authors	local tumor progression (n (relative frequency[1]))	rationale for classifying as local tumor progression	time of diagnosis after initial RFA (months; n (relative frequency))					risk factors	management (n (relative frequency))
			<6	6–12	13–24	>24	mean/median (months)[2]		
Ferakis et al. [13]	3 (7.7 %)	imaging	0 (0 %)	1 (33.3 %)	1 (33.3 %)	1 (33.3 %)	28.0	tumor size ≥ 4.0 cm, central tumor location	RFA (2 (66.7 %)), surgery (1 (33.3 %))
Sung et al. [20]	1 (2.2 %)	imaging	–	–	–	–	–	–	–
Psutka et al. [2]	12 (6.5 %)	imaging	–	–	–	–	30.0	tumor size ≥ 4.0 cm	RFA (6 (50 %)), active surveillance (6 (50 %))
Allen et al. [44]	0 (0 %)	–	–	–	–	–	–	–	–
Balageas et al. [14]	2 (2.8 %)	imaging	0	1 (50.0 %)	1 (50.0 %)	0	18.0	tumor size ≥ 4.0 cm, central tumor location	–
Wah et al. [3]	5 (2.5 %)	imaging	0	0	0	5 (100.0 %)	58.3	tumor size ≥ 3.0 cm, central tumor location	no management with RFA (0 (0 %))
Forauer et al. [16]	1 (2.2 %)	surgical specimen	1 (100 %)	0	0	0	4.2	–	surgery (1 (100 %))
Thompson et al. [21]	5 (3.0 %)	–	0	1 (20.0 %)	0	4 (80.0 %)	50.0	–	–
Pieper et al. [17]	4 (10.5 %)	–	–	–	–	–	25.7	–	no management with RFA (0 (0 %)), surgery (3 (75.0 %))
Iannuccilli et al. [15]	15 (7.5 %)	imaging	–	–	–	–	23.3	tumor size ≥ 3.5 cm, clear cell subtype of RCC, maximum treatment temperature ≤ 70 °C, non-exophytic tumors	RFA (15 (100 %))
Pooled data	48 (4.7 %)	s. a.	1 (6.3 %)	3 (18.8 %)	2 (12.5 %)	10 (62.5 %)	28.0	s. a.	RFA (23 (47.9 %)), active surveillance (6 (12.5 %)), surgery (5 (10.4 %)), not indicated (29.2 %)

"–": no data available in the respective study or no data indicated since no case of local tumor progression was reported in this study; s. a. = see above, data not pooled; RCC: renal cell carcinoma.

"–": Keine Angabe in der jeweiligen Studie oder keine Daten angegeben, da keine lokale Tumorprogression in der jeweiligen berichtet wurde; s. a. = siehe oben (Daten nicht statistisch zusammengefasst); RCC: Nierenzellkarzinom.

[1] on the basis of treated tumors.
auf Basis der behandelten Tumoren.

[2] pooled data could only be calculated from the studies in which the mean was available.
gepoolte Daten konnten nur aus den Studien bestimmt werden, in denen der Mittelwert angegeben wurde.

▶ **Table 5** Management of local tumor progression with repeated RFA.

▶ **Tab. 5** Management von lokaler Tumorprogression mit erneuter RFA.

authors	local tumor progression (n)	tumors re-treated with RFA (n (relative frequency))	outcome of repeated RFA –available data (n (relative frequency[1]))	mean follow-up period (months)	outcome of repeated RFA – treatment success[2] (n (relative frequency))
Ferakis at al. [13]	3	2 (66.6 %)	2 (100 %)	62.0	2 (100 %)
Sung et al. [20]	1	–	–	–	–
Psutka et al. [2]	12	6 (50.0 %)	6 (100 %)	45.1	5 (83.3 %)
Allen et al. [44]	0	–	–	–	–
Balageas et al. [14]	2	–	–	–	–
Wah et al. [3]	5	–	–	–	–
Forauer et al. [16]	1	–	–	–	–
Thompson et al. [21]	5	–	–	–	–
Pieper et al. [17]	4	–	–	–	–
Iannuccilli et al. [15]	15	15 (100 %)	0 (0 %)	–	–
Pooled data	48	23 (48.0 %)	8 (34.8 %)	49.3	7 (87.5 %)

"–": no data available in the respective study or no data indicated since no case of local tumor progression was reported in the respective study.
"–": Keine Angabe in der jeweiligen Studie oder keine Daten angegeben, da keine lokale Tumorprogression in der jeweiligen Studie berichtet wurde.
[1] on the basis of tumors re-treated with RFA.
auf Basis der mittels RFA erneut behandelten Tumoren.
[2] defined as no residual unablated tumor and no local tumor progression during the follow-up period.
definiert als kein residueller nicht-abladierter Tumor und keine lokale Tumorprogression in den Verlaufkontrollen nach erneuter Intervention.

tumors can be optimized [18 – 20]. Another major risk factor for treatment failure is a central tumor location [3, 13 – 15]. In the study of Wah et al., 77.8 % of the residual unablated tumors were centrally located, whereas all exophytic or parenchymal tumors, regardless of size and location, were completely ablated in one RFA session [3].

According to our analysis, de novo tumors in the kidneys after image-guided RFA are rare but can occur up to 48 months after initial RFA. Compared with radical (contralateral kidney) and partial nephrectomy, the frequency of de novo tumors after treatment is comparable [21 – 23]. As synchronous renal cell carcinoma occurs with a frequency of up to 4.7 %, it is likely that some of the analyzed patients of this review had an occult tumor at the time of initial RFA [24]. The relevance of synchronous and metachronous renal tumors should not be underestimated in terms of cardiovascular-specific morbidity and mortality. As previously reported, preservation of renal function is extremely important to avoid cardiovascular events and hospitalization as well as to improve overall survival [25 – 27]. The manner in which image-guided RFA can be used very effectively for both tumor control and preservation of renal function has been demonstrated in multiple trials with high-risk patients (e. g. patients with single functioning kidneys and hereditary renal cell carcinoma [e. g. von Hippel Lindau disease]) [28 – 30].

Irrespective of the type and time of diagnosis of treatment failure, repeated RFA is an effective option for tumor control with a treatment success rate of 86.3 % for residual unablated tumor and 87.5 % for local tumor progression. The data supports the concept of multi-step RFA that is performed successfully for the treatment of T1a and T1b renal tumors with a very low major complication rate, preservation of renal function, high tumor control and a high rate of patient satisfaction. [1 – 3, 22, 30].

According to our review, extra-renal metastases after image-guided RFA of renal tumors are very rare but slightly more frequent than de novo renal tumors, and occur up to 4.5 years after initial RFA [3]. In a controlled study, the metastasis-free survival after treatment of T1a renal tumors was significantly better for surgery when compared with RFA ($p = 0.005$). However, the age at treatment and Charlson score – but not the treatment itself (partial nephrectomy vs. RFA) – were the independent predictors for overall survival [23]. In general, the outcome of patients developing metastatic disease after successful RFA of the primary renal tumor is often fatal, as it is the case after nephrectomy and during active surveillance [2, 3, 31 – 33].

Regarding the imaging follow-up after RFA of renal tumors, no generally accepted protocol has been identified. Different centers propose CT or MR imaging 1, 3, 6 and 12 months after RFA, and then annually for the following years [34 – 36]. The results of our review may specify the protocol: contrast-enhanced MRI of the kidneys 1, 3 and 6 months after RFA due to the rates of residual unablated tumors and local tumor progression, and afterwards annual imaging of the abdomen (contrast-enhanced MRI) and lung (non-enhanced CT) for 5 years due to the rates of local tumor progression, de novo tumors in the kidneys and extra-renal me-

tastases. Also since image-guided percutaneous RFA is very effective and safe as a multi-step approach, the role of active surveillance in patients with localized renal tumors seems to be increasingly irrelevant [33, 37 – 39].

Besides RFA, percutaneous cryoablation is also commonly used. RFA and cryoablation are regarded as essentially equivalent for the treatment of small renal tumors [40, 41]. The currently available mid- and long-term data indicate that the oncological outcome of both techniques is comparable, and depends more on patient selection and operator experience than on the ablation technique itself [40 – 44]. The advantages of RFA are shorter ablation time, higher availability and excellent cost-effectiveness, whereas the advantages of cryoablation are direct visualization of the ablation zone ("ice ball") and lower rate of injury to the collecting system for larger central tumors [40, 41, 45].

This study has limitations. First, patients and tumors from different studies and institutions were analyzed, reducing the homogeneity of the included patients. Second, the included studies were conducted at some point during the last 6 years, a time in which the technical advantages and clinical experience of the relatively modern technology RFA have continuously improved. Third, the analyzed studies included not only patients with biopsy-proven renal cell carcinomas.

In conclusion, image-guided percutaneous RFA of localized renal tumors is very effective. Treatment failure can be subdivided into residual unablated tumor (occurring in 5.9 % of cases) and local tumor progression (occurring in 4.7 % of cases). Patients developing de novo tumors in the kidneys or extra-renal metastases after RFA are rare. Major risk factors for treatment failure are tumor size and location. For the management of both residual unablated tumor and local tumor progression, repeated RFA is commonly used and very effective.

Erratum (10.10.2016): Vollherbst D, Bertheau R, Kauczor U et al. Treatment Failure After Image-Guided Percutaneous Radiofrequency Ablation (RFA) of Renal Tumors – A Systematic Review with Description of Type, Frequency, Risk Factors and Management. Fortschr Röntgenstr 2016; DOI: 10.1055/s-0042-115817

The number of treated patients was corrected in the abstract and in the results section (incorrect number: 1033 patients, correct number; 967 patients). Moreover, the number of treated renal tumors was corrected in the abstract (incorrect number: 967 renal tumors, correct number: 1033 renal tumors).

Conflict of Interest

No conflict of interest has been declared by the author(s).

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