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Percutaneous radiofrequency ablation of renal tumours: 29-month mean follow-up results of 118 patients

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Background. Percutaneous radiofrequency ablation (RFA) is a minimally invasive method of treatment based on thermal effects. This retrospective study aimed to clarify percutaneous RFA of kidney tumors – performance, extremeness and 5-year survival in patients with small renal tumors in a single center.

Materials and methods. Between September 2003 and December 2012, a total of 118 patients underwent percutaneous RFA of renal tumors. During more than 9 years period 144 RFA procedures were performed. Tumors were verified by biopsy. We used 3 RFA techniques: RFA under ultrasound control only (US), ultrasound guided RFA with CT navigation (US/CT) and ultrasound guided RFA with CT navigation, fiducial markers placed around the kidney tumor before the treatment (US/CT/FM). RFA electrodes were one and three. Patients were followed up regularly by CT with contrast enhancement.

Results. The mean patient age was 68.72 years (range 28 to 86). The mean tumor size was 2.8 cm (range 1 to 5.4). The mean follow-up time was 29 months (1–111 months). Radical dependence on technical procedures: only US 39 (66.1%), US/CT 18 (94.7%), US/CT/FM 37 (92.5%), $p = 0.001$. Radical differences between using one and three electrodes: 39 (66.1%) and 55 (93.2%), $p < 0.05$. 17 patients (14%) presented with complications: haematomas 12 (10%), severe bleeding 2 (1.7%), ureteral stricture 1 (0.8%), urinoma 1 (0.8%) and dysuria 1 (0.8%). 27 patients of the cohort have died till January 2013. Survival analysis showed that the 2-year survival probability was 84%, 5-year survival was 57%.

Conclusions. In this study the most radical renal tumor RFAs were done with US/CT and with US/CT/FM. RFA is more radical when performed using three electrodes. Serious RFA complications are rare.

Key words: radiofrequency ablation, survival, observation, fiducial markers

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INTRODUCTION

The kidney tumor altered renal cell growth and multiplication, which is not specific to the kidney structure (1). Kidney tumors are benign and malignant. Kidney cancer accounts for about 2–3% of all diagnosed malign tumors (2). Due to this disease, more than 100,000 people die in the world every year (3), and men are affected more often than women (4). An average kidney tumor growth rate is from 0.27 to 0.66 mm per year, so in the early stages they are rarely seen, although in a few years they can become large (1). The most common kidney tumor clinical symptoms are back pain, abdominal side of palpable tumor, hematuria (5), but these symptoms only occur when the kidney cancer is already advanced.

The most effective kidney cancer treatment is surgery. Chemotherapy and radiation treatments are of low efficiency so are not often used as a kidney cancer treatment (6). Increasing the number of patients with small kidney tumors, scientists started to develop a method of surgery, called minimally invasive therapy, like radiofrequency ablation (RFA), cryotherapy and high-frequency focused ultrasound (HIFU) (7). However, open or laparoscopic surgery remains one of the most popular ways to remove kidney tumors. Unfortunately, some patients are not eligible for this type of operation for some reason – the older, underlying pathology, expressed in renal failure. Open or laparoscopic resection of the kidney, or nephrectomy, in this patient population is dangerous due to the high morbidity and mortality risk, so as an alternative to surgical treatment is applicable to other treatment – Percutaneous Radiofrequency ablation (8).

Percutaneous Radiofrequency ablation is a minimally invasive method of treatment based on thermal effects, the tissues caused by the high-frequency electrical current. The needle-shaped electrode is inserted through the skin into the kidney tumor with bayonet ultrasound (control can be performed with computed tomography, magnetic resonance imaging aid). Shift to high-frequency electrical current, which is a few centimeters around the electrode, causes tissue molecular vibrations. As a result, tissues are heated to 80–100° degrees and die. Later, the scar tissue is formed (9). This method can be used only for small kidney tumors and metastases in the kidney with a diameter of less than 3 cm (8).

Some authors claim that very small kidney tumors in elderly patients are not so dangerous and it is recommended only to watch as they grow and progress slowly (growth rate – an average of 3 mm per year or less). Metastasis risk while using tactics "wait and watch" is only about 1% (10).

MATERIALS AND METHODS

A retrospective study was conducted at the Institute of Oncology, Urology Department. The study included 118 patients from September 17, 2003 until December 6, 2012. There were performed 144 kidney tumor radiofrequency ablation (RFA) procedures. All renal tumor RFAs were done percutaneously in the projection of the skin, under local or general anesthesia. By one or several small (up to 1 cm) incisions the electrodes were introduced. All the process was observed in the US control.

We analyzed patients' case history cards to collect patient demographics, co-morbidities diseases, radiological investigations and operations protocol data, tumor histology. Patients' general condition prior to the RFA was rated by the American Association of Anesthesiologists developed Risk Score Classification (ASA). The end date of monitoring was January 8, 2013 or the day of patient's death. Dates of deaths were taken from the hospital database, while checking the social insurance status. RFA procedure was performed on patients who could not have an open surgery due to certain clinical situations (solitary kidney, bilateral renal disease, severe comorbidities).

Since September 17, 2003 renal tumor RFAs have been performed only in US control with one electrode (Fig. 1). For this procedure we used ELECTROTOM® 106 hitters BERCHTOLD equipment. Through the electrode the energy was allowed up to 30, 40, 50 watts, respectively, each for 5 minutes.

Since May 11, 2010 we started to use computer tomography (CT) navigation and multifactory electrodes, bringing them parallel to each other in the tumor (Fig. 2). In the control of ultrasound RFA was launched in real time and without tissue ablation conditioned US image distortion (called Real-time Virtual sonographers). This program

Fig. 1. US controled RFA with CT navigation (Real-time Virtual Sonography)

Fig. 2. Fiducial markers placement around the kidney tumor and US controled RFA with CT navigation

allows you to view a live ultrasound machine image compatible with the next screen identical to a moving magnetic resonance or computer tomography images (Fig. 1).

Since May 30, 2011 RFA is also carried out with three electrodes and US control with CT navigation, just a day prior to surgery with additionally added titanium markers around the kidney tumor (Fig. 2).

In case of RFA technical progress, efficiency and observation possibilities improved. If after the first RFA session (from September 2003 to 2007), patients' radicalism was assessed every 3, 6, 9, 12, 18, 24, 30, 36 months in kidney ultrasound imaging (CT with contrast material performed only in exceptional cases), from the year 2007 only the renal CT with contrast material was used to observe patients, and from 2011 control CT was performed immediately after RFA (3–6 min.) and on the 2nd–3rd days. Later kidney CT was routinely performed normally at 3, 6, 9, 12 months and thereafter every 6–12 months. They evaluate the ablation zone contrast material accumulation and ablation margin. Non-radical RFA was discussed when the RFA procedure following kidney CT demonstrated contrast material accumulation in the ablation zone or inadequate ablation margin. In such cases RFA was repeated. If repeated RFA was insufficient and in CT control we observed negative dynamics, it was decided on nephrectomy or resection possibility. If this is not possible, patients require additional treatment with angiogenesis inhibitors or immunotherapy.

Statistical data analysis was carried out using the SPSS 20.0 software. To assess the difference between the RFA technologies and the reliability of statistical methods the χ^2 test was used. Survival was calculated using the Kaplan-Meier survival method. Death risk factors were evaluated using the Cox regression method. Data were considered statistically significant at $p < 0.05$.

RESULTS

From September 17, 2003 until December 6, 2012 there were performed 144 RFA procedures for 118 patients. Patients' demographic data is shown in Table 1.

Table 1. Patients' demographic data

Parameter		Result
Amount of patients (abs. No., %)		118 (100)
Males (abs. No., %)		77 (65)
Females (abs. No., %)		41 (35)
Age average, years (±SD)*		68.72 (±10.12)
The only kidney tumor (abs. No., %)		26 (22)
ASA class**(abs. No., %)	1 (%)	7 (6)
	2 (%)	26 (22)
	3 (%)	85 (72)

The average tumor size was 2.8 cm (range 1.0 to 5.4). Slightly more tumors were detected on the left kidney than on the right one (51.7% vs 48.3%). A little more often tumors formed in the middle kidney pole – 40 (40.7%) of all cases, the upper pole – 37 (31.4%) cases, and in the bottom – 33 (28.0%) cases.

Tumor histology was as follows: 92 (78%) malignant, 21 (17.8%) benign and 5 (4.2%) other tumors (Table 2).

Radical dependence on technical procedures was the following: when RFA was performed only with US the effectiveness was 39 (66.1%) at the first time, US/CT 18 (94.7%), US/CT/FM 37 (92.5%), p = 0.001 (Table 3). The tumor recurrence time average was 11.33 (±15.48) months and occurred in 9 (8%) patients. In these patients, RFA was performed only with US control (p < 0.0001).

Of the 24 for the first time unsuccessful procedures, 20 patients have successfully repeated RFA procedure. 3 patients did not have the possibility since they died of other body oncological disease progression, in 1 patient after several unsuccessful renal tumor RFAs nephrectomy was performed.

The success of the RFA significantly correlated with the number of electrodes. Previously used one electrode radicalism was much lower compared to the currently used three electrodes performance: RFA with one electrode 39 (66.1%) and three electrodes 55 (93.2%), p < 0.05 (Table 4).

The RFAs overall complication rate was 16 (14%). The most common complication was paranephric hematoma (asymptomatic) – 12 (10%) cases of all the patients, much rarer complications were active bleeding – 2 (2%), and urinoma – 1 (1%), ureteral stricture occurred in 1 (1%) patient. In the latter case endoscopic ureteral stenting was performed, but the active bleeding underwent a kidney resection. All other cases have not been treated; observing and waiting tactics has been selected, and it all went successfully.

After the RFA procedure patients were further monitored. Abdominal CT with contrast material during the first year was performed every 3 months, after a year it was performed every 6 months, later every 12 months, etc. The mean follow-up time after RFA was 29.4 (1–111) months.

After the RFA procedure 27 (23%) patients died by January 8, 2013. Of these 27 9 (7.6%) patients died due to progressive prostate, breast, pancreas and lung cancer, 9 (7.6%) died due to the contiguous disease and only 9 (7.6%) died because of kidney tumor progression (of which 4 RFA have been applied in patients with a single kidney, and

Table 2. Distribution of tumors by histology

Tumor histology type, abs. No., %		
Malignant 92 (78%)	**Benignant 21 (17.8%)**	**Histologically unconfirmed 5 (4.2%)**
Clear cell renal Ca 80 (67.8%)	Oncocitoma 16 (13.6%)	
Papilliary renal Ca 6 (5.1%)	Angiomiolipoma 1 (0.8%)	
Chromophobic renal Ca 3 (2.5%)	Hemangioma 1 (0.8%)	
Mucin renal cell Ca 1 (0.8%)	Papilliary adenoma 1 (0.8%)	
Colon adenocarcinoma metastases 2 (1.7%)	Metanephric adenoma 1 (0.8%)	
	Leiomioma 1 (0.8%)	

Table 3. Radical dependence on technical procedures

	US	US/CT	US/CT/FM	p
Performed (abs. No., %)	59 (100)	19 (100)	40 (100)	
Radical for the first time (abs. No., %)	39 (66.1)	18 (94.7)	37 (92.5)	0.001
Non-radical (abs. No., %)	20 (33.9)	1 (5.3)	3 (7.5)	

Table 4. Radical differences between using one and three electrodes

	One electrode	Three electrodes	P
Performed (abs. No., %)	59 (100)	59 (100)	
Radical for the first time (abs. No., %)	39 (66.1)	55 (93.2)	<0.05
Non-radical (abs. No., %)	20 (33.9)	4 (6.8)	

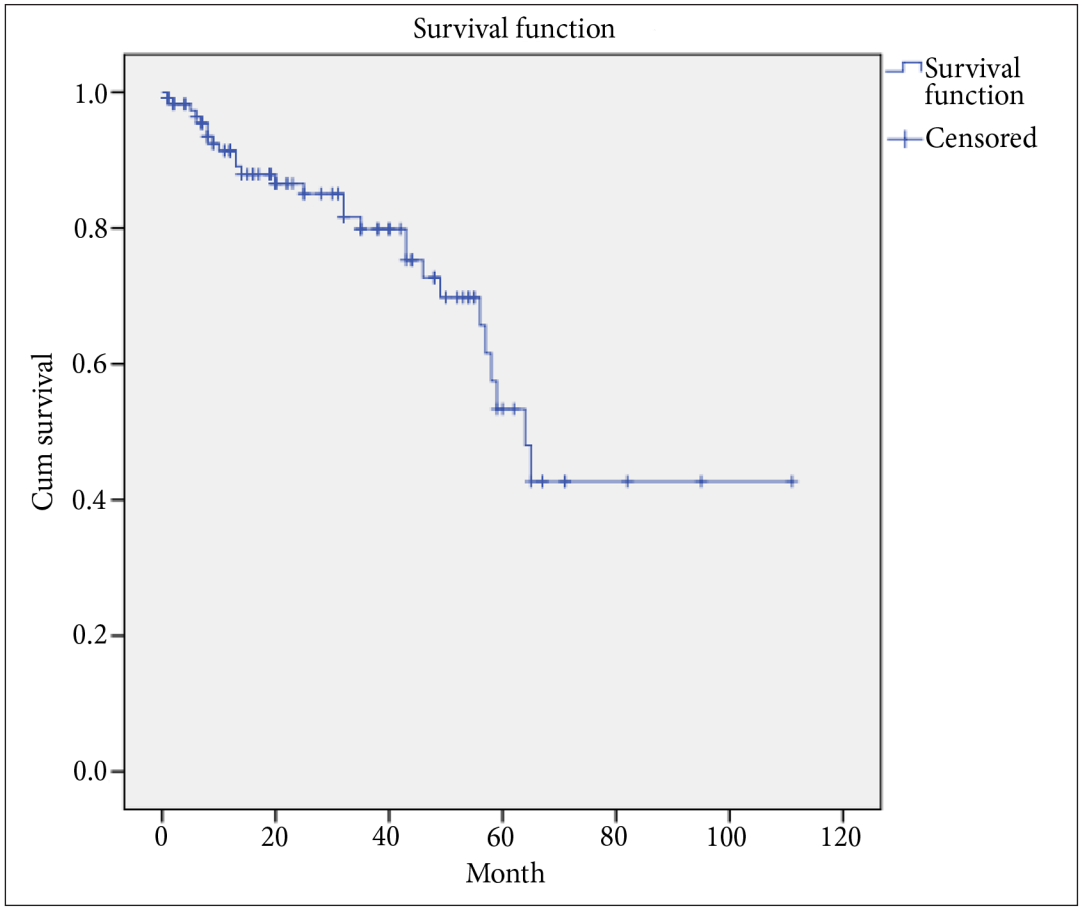

Fig. 3. Survival rate after the RFA procedure (months)

Table 5. The factors influencing survival (Cox regression model)

	Relative risk (95% confidence interval CI)	p
Size of tumor, cm	1.888 (1.181–3.016)	0.008
Non-radical operation	1.899 (1.181–3.054)	0.008
Other oncologic process in body	2.221 (1.042–4.732)	0.039
Metastases in patient's history	4.047 (1.762–9.294)	0.001
ASA class	4.388 (1.368–14.074)	0.013

previous nephrectomy was performed for renal cell carcinoma). The overall survival after the RFA procedure was as follows: 2-year survival rate 84%, 5-year survival rate 57% (Fig. 3).

To find out what increases the risk of dying after the RFA procedure, we considered the factors that significantly influenced survival. We found that the tumor size increase by 1 cm increases the risk of death 1.888 times ($p = 0.008$), non-radical operation of another body oncologic process increases the risk of dying of about 2 times ($p < 0.05$), and metastasis history increases the risk more than 4 times ($p = 0.001$). Increasing ASA class, the risk of death increased as well over 4 times ($p = 0.013$) (Table 5).

DISCUSSION

Our patients' average age was 68 years, a similar average age (60–70 years) was mentioned by other authors in their carried out studies (4, 12–14). Most of the patients were males, and the results of other authors' studies show the same (12, 13, 15). Tumors that had to be treated with the RFA method were selected by size. Global guidelines state that the RDA procedure is only suitable for up to 3 cm tumors, and the average tumor size in patients, undergoing RFA, was 2.8 cm and was not significantly different from the averages of other authors' studies (4, 12, 13). An average size of the tumor in various studies is presented in Table 6.

Table 6. Estimated average size of the tumor (cm) in various studies

Study	Country	Number of patients	Extremeness, %	Observation time, months	Technique	Performed	Tumor size, cm (CI)	Reference
Breen et al. (2007)	England	97	90.5	16.7	CT/UA	P	3.2 (1.1–6.8)	(16)
Sabhawal et al. (2006)	Australia	11	92	11	CT	P	2 (1–4.3)	(17)
Memarsadeghi et al. (2006)	Austria	16	90	11.2	MRI	P	2	(18)
Varkarakis et al. (2005)	U. S.	49	84	27	CT	P	2.2 (1–4)	(19)
Gervais et al. (2005)	U. S.	85	99	28	CT/MRI	P	3.2 (1.1–8.9)	(2)
Weizer et al. (2005)	U. S.	24	78	11.7	CT	P	2.4 (0.5–8.6)	(20)
Ukimora et al. (2004)	Japan	9	78	17	CT/US	P	3.8 (2–5.3)	(21)
Farrell et al. (2003)	U. S.	20	100	9	CT/US	P	1.7 (0.9–3.6)	(11)
Mayo-Smith et al. (2003)	U. S.	32	100	9	CT/US	P	2.6 (1–5)	(22)
Pavlovich et al. (2002)	U. S.	21	79	2	CT	P	2.4 (1.5–3)	(23)
VUOI data (2013)	Lithuania	118	92.5 US/CT/fiducial markkers/three electrodes	29.4	US/CT/fiducial markers/three electrodes	P	2.8 (1.0–5.4)	

We assessed a tumor histology type. Biopsy showed that 78% tumors were malignant and 17.8% were benignant. In other cases malignant kidney tumors were approximately 79% (24).

Although in our study, like in the studies of Balageas et al., we assumed small differences between the kidneys, in which a tumor is located (14), Gupta et al. observed that tumors occurred more often in the left kidney than in the right one (59% vs. 41%) (12).

Renal cell carcinoma was the most common histologic type of tumor and accounted for 76.5% of all tumors. Other articles also state that this histological type is the most widespread and often makes up to 85% of all tumor types (25). In our data angiomiolipoma was not a common histologic type of tumor, the prevalence was less than 1% of all our cases, but in other sources the incidence is markedly higher – up to 10.38%. Meanwhile oncocitoma in our study was quite common and accounted for over 13% of all histological types, but in Ji et al. study the prevalence was less than that of angiomiolipoma and accounted for only 3.78% of all tumors (25).

Although the complication rate after RFA is low, sometimes there may be complications such as hematoma, pain, reaction to the sedatives and other. Many of them do not require intensive treatment (15). Considering our data, complications after RFA procedures were 14%, most of all pararenal hematoma, which is mentioned by other authors as a common phenomenon (4, 12).

Examining the technical effect of extremeness, the most radical ablation of kidney cancer was by the US and CT control, and in case of introduction of the titanium fiducial markers around the tumor site. This procedure extremeness was over 90%. Significantly worse extremeness was observed during the procedure made only by US control, so lately RFAs are no longer performed only by using the US control. To compare the most advanced and only in the Vilnius University Institute of Oncology approved method (US/CT/FM) with the technique used in the rest of the world (usually CT/

US, only CT, only MRI or CT/MRI), radicalism of the RFA in the CT control after the introduction of fiducial markers is one of the best. We note that the extremeness depended not only on the technology and methods used, but also on the size of the tumor – larger tumors by RFA procedure were removed worse. For comparison Table 6 presents the RFA data of radical procedures provided by other authors.

Considering more radical dependence on the number of electrodes, we see a clear trend that the introduction of three electrodes instead of one is much more effective, as the extremeness significantly increased – from 66.1% to 93.2%. This discovery explains the fact that the introducing of three electrodes can be much better to remove the entire tumor mass than introducing one electrode, which does not cover a large area. In general, our study using three electrodes imposed by ultrasound and CT control after the introduction of titanium fiducial markers around the location of the tumor was in a relatively high position in comparison with other studies and reached 92.5% in extremeness case. The largest percentage of the most radical procedures (100% and 99%) reached the United States, however, depending on the studies that were carried out, extremeness ranged from 78% to 100%. It should be noted that in all of the studies that were made most patients (118) were monitored in our study and the monitor was the longest (29.4 months).

According to the survival rate of new study data compared with our study, 5-year survival rate still is not as good as in the United States or France. According to various studies, 5-year survival rate after RFA in the United States is as high as 91%, although in other studies it is limited to lower survival possibilities – Leveilee et al. indicate 74.2%, Zagoria et al. indicate 66% 5-year survival rate. In France, this figure is 61.9%. According to the Japanese RFA studies, patients' 2-year survival rate is up to 79%. Our study shows that percentage of patients with 2-year survival rate is 84%, with 5-year survival rate it is 57%, which is slightly less than in other mentioned studies, but in the 2-year survival rate Lithuania's data is greater than Japan's. It should be borne in mind that in these countries life expectancy is significantly longer than in Lithuania. The survival rates of different studies and a comparison with our study are presented in Table 7.

We examined the factors that influence the survival rate and using the Cox regression model we found out that the size of the tumor increased the risk of dying, but Olwen et al. estimated that the size of the tumor did not influence survival negatively (31).

Comparing the radicalism and the effectiveness of the treatment between types of operations, RFA has been compared with nephron-conserving surgery (partial nephrectomy) and cryoablation. Following meta-analysis, kidney tumors re-grew

Table 7. The survival rates of different studies and a comparison with our study

Study	Country	Age in years	Number of patients	Observing time in months	Technique	Performed	Size of tumor, cm	Survival rate, %	Reference
Psutka et al. (2013)	U. S.	73	185	77	CT	P	3 (2.1–3.9)	5 year – 73.3	(26)
Balageas et al. (2013)	France	73.5	62	38.8	US/CT	P	2.4 (0.8–4.6)	3 year – 88.3 5 year – 61.9	(14)
Leveile et al. (2013)	U. S.	67	274	26	CT	P/L	2.5 (0.7–5.3)	3 year – 90.4 5 year – 74.2	(27)
Nitta et al. (2012)	Japan	73.3	22	18	CT	P	2.4 (1–4.5)	2 year – 79	(28)
Best et al. (2012)	U. S.	Unknown	Unknown	54	CT	P	2.4 (0.9–5.4)	5 year – 91	(29)
Zagoria et al. (2011)	U. S.	72	41	56	CT	P	2.6	5 year – 66	(30)
VUOI (2013)	Lithuania	68.72	118	29.4	US/CT/ fiducial markers	P	2.8 (1.0–5.4)	2 year – 84 5 year – 57	

back in 2.6% of patients after partial nephrectomy, in 4.6% after cryoablation and in 11.7% after RFA (24), but the RFA, as already mentioned, is not a routine procedure and has clearly defined indications.

CONCLUSIONS

RFA is a safe treatment option in cases where more invasive surgical treatment is not feasible. The correct technique of renal RFA is very important if complete ablation is to be considered. The most radical renal tumor RFAs were completed by US control with CT navigation and before RFA procedure titanium tumor markers were additionally introduced in the US control. Also RFA is most radical when performed using three electrodes. The most common postoperative complication was paranephric hematoma.

After RFA the 2-year survival rate in the Vilnius University Institute of Oncology was 84%, the 5-year survival rate was 57%. Death risk factors are as follows: tumor size, higher ASA class, non-radical surgery, metastases or other body oncologic process.

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INKSTŲ NAVIKŲ PERKUTANINĖ RADIODAŽNUMINĖ ABLIACIJA: 118-os PACIENTŲ VIDUTINIS 29 MĖNESIŲ STEBĖJIMO LAIKOTARPIS

Santrauka

Įvadas. Perkutaninė radiodažnuminė abliacija (RDA) yra minimalios invazijos gydymo metodas, paremtas šiluminiu efektu. Mūsų atliktos retrospektyvinės studijos tikslas buvo išsiaiškinti RDA efektyvumą, radikalumą ir pacientų, turinčių mažus inkstų navikus, 5 metų išgyvenamumą.

Pacientai ir metodai. Nuo 2003 m. rugsėjo mėnesio iki 2012 m. gruodžio mėnesio 118-ai pacientų buvo atliktos 144 perkutaninės RDA procedūros. Navikai buvo verifikuoti atlikus histologinį ištyrimą. Naudotos trys RDA technikos: tik ultragarsu kontroliuojama (UG), ultragarsu kontroliuojama su kompiuterinės tomografijos navigacija (UG, KT) ir ultragarsu kontroliuojama su KT navigacija RDA, prieš kurią įvesti titaniniai žymenys aplink inksto naviką (UG, KT, TŽ). RDA atlikta su vienu ir trimis elektrodais. Atliekant KT su kontrastine medžiaga, pacientai reguliariai buvo stebėti.

Rezultatai. Vidutinis pacientų amžius buvo 68, 72 m. (28–86 metai), vidutinis naviko dydis – 2, 8 cm (1–5,4), vidutinis stebėjimo laikas – 29 mėnesiai (1–111). RDA technikų radikalumas: tik UG – 39 (66, 1%), UG, KT – 18 (94, 7%), UG, KT, TŽ – 37 (92, 5%); p = 0,001. Su vienu ir trimis elektrodais atliktos RDA

radikalumo pasiskirstymas: 39 (66,1 %) ir 55 (93,2 %); $p < 0,05$. 17-ai (14 %) pacientų pasireiškė komplikacijos: hematomos – 12 (10%), aktyvus kraujavimas – 2 (1,7 %), šlapimtakio striktūra – 1 (0,8 %), urinoma – 1 (0,8 %), dizurija – 1 pacientui (0,8 %). Iki 2013 m. sausio mėnesio mirė 27 pacientai. Po RDA procedūros dvejų metų išgyvenamumo tikimybė – 84 %, 5 metų – 57 %.

Išvados. Radikaliausios inkstų navikų RDA buvo atliktos kontroliuojant UG su KT navigacija, taip pat prieš operaciją stebint UG ir dar papildomai aplink naviką įvedus titaninius žymenis. RDA taip pat yra radikalesnė, kai atliekama naudojant tris elektrodus. Dažniausia pooperacinė komplikacija buvo paranefrinė hematoma.

Raktažodžiai: radiodažnuminė abliacija, išgyvenamumas, stebėjimas, titaniniai žymenys