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# The Experience in the Use of Morphometric Signs In the Differential Diagnosis of Renal Cell Carcinoma with Magnetic Resonance Imaging

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## Abstract

The article provides an experience in the use of morphometric signs in the differential diagnosis of renal cell carcinoma with magnetic resonance imaging. A significant restriction of diffusion in renal cell carcinoma and the presence of a relatively large extra renal component can be used as additional criteria in the differential diagnosis of kidney cancer.

**Keywords:** Magnetic resonance spectroscopy; Renal cell carcinoma; Kidney cancer

## Introduction

The kidney cancer remains in focus of continuous attention of researchers and clinicians on the problem of magnetic resonance imaging in oncourology. This is due to an increase in morbidity with an annual growth rate of 6-10% and suboptimal relapse-free survival of patients after treatment [1]. Renal cell carcinoma is a heterogeneous group of tumours. Renal cell carcinoma is most often diagnosed as an accidental finding on MRI. Currently, among urological tumors, kidney cancer ranks third after neoplasms of the prostate and bladder, and in terms of mortality is in the first place. In the world, approximately 250 thousand and 100 thousand people, respectively, get sick and die from kidney cell cancer every year [4-8]. In 2014, 22,234 new cases of kidney cancer were detected in Russia, of which 45.3% were women and 54.7 % were men. In the structure of cancer incidence in women, this was 3.3 %, which corresponds to the 12th place in the frequency of occurrence, in men-4.7 % and 9th place, respectively [1]. The "rough" indicator of the incidence of RP per 100 thousand male population in 2014 was 17.96. For the period 2004-2014, this indicator increased by 38.3 %. The standardized indicator of the incidence of RP per 100 thousand male population of Russia was 13.13.This indicator increased by 24.3% over a 10-year period [1]. The traditional position of oncologists is based on the fact that for a differentiated diagnosis of kidney cancer with a systemic process, solid tumor metastases and abscesses, a histological examination of the tumour is required, even in cases where the diagnosis seems clear [2]. At the same time, accurate non-invasive diagnosis of large kidney tumors at an early stage is still an urgent task, including for optimizing the biopsy point. The most frequently detected asymptomatic, randomly visualized with radiation methods of investigation, small tissue formations with an unidentified histology structure are grouped into the cohort of kidney incidents or "radiologists tumor". The diagnostic limitations associated with percutaneous biopsy, possible complications of the biopsy (bleeding, urinary fistulas, exacerbation of chronic pyelonephritis), the risk of dissemination of tumor cells along the biopsy channel and the development of implantation metastases, the probability of receiving a false-negative response, once again emphasize the value of accurate characterization of kidney formations by MR imaging. MRI is a decisive argument for examination in the case of local tumor spread, determining its invasion into neighboring anatomical structures, the presence of suspected tumor thrombus in the renal vein or inferior vena cava. It also is extremely useful in cases where the use of X-ray computed tomography (CT) is impossible due to an allergic reaction to a contrast agent, kidney failure [3] or ambiguous results of an already performed CT.

In this regard, the role of imaging, and first of all, magnetic resonance imaging (MRI), as an alternative to X-ray methods of investigation, increases in the algorithm of research in cases of suspected malignant kidney tumors.

In general, MRI is comparable to CT in detecting kidney formations: the sensitivity of the method is 93.5 % compared to 93.8% in CT [5]. The complete accuracy of MRI in the differential diagnosis of renal formations was superior to that of CT. It is known that MRI data on the size and localization of the neoplasm, the type of its growth, the presence and preservation of the pseudo-capsule, the fibrous capsule of the kidney anterenal and retrorenal fascia, the severity and nature of secondary changes in the tumor tissue are comparable with the results of path morphological examination of the removed tumor, which allows the radiologist to make a reasonable assumption about the benign or malignant neoplastic process. Pulse sequences with suppression of the signal from fat help to distinguish fat-containing kidney tumors (lipoma, angiomyolipoma, fibrosarcoma) from renal cell carcinoma, detect cysts and tumors smaller than 1 cm [5]. It is believed that the data on the prevalence of kidney tumors obtained during MRI are more informative than similar CT data and help to more reliably determine the T-and N-stages of the malignant process. It was shown that the T-stage was reliably determined by CT in 78.4 % and MRI in 84 % of cases, and the N-stage in 81.8 and 79.5%, respectively. MRI, in contrast to CT, is highly informative in detecting the pseudocapsule of a kidney tumor, which is most often characterized by highly or moderately differentiated kidney formations up to 4 cm in size [5]. Among kidney cancers in adults, renal cell carcinoma occurs in 90-95 % of cases, and light cell carcinoma accounts for 70-75 % of all cases of renal cell carcinoma, thus being the main object for research.

One of the directions of modern oncourology is the identification of factors that allow non-invasively obtaining information about the malignant nature of the process. For example, a non-invasive diagnosis of renal cell carcinoma is difficult, given the coincidence in appearance with epithelioid angiomyolipoma containing a small amount of fat and oncocytoma. Despite the fact that angiomyolipomas are usually clearly delineated and grow expansively, pushing and squeezing the surrounding tissues, there are cases of invasive growth, both in the direction of the pelvis, and extrarenally with the germination of the renal capsule and infiltration of the perinephral tissue. Blood vessel invasion and metastasis were not observed in typical angiomyolipoma. Observations of renal sarcoma on the background of angiomyolipoma are rare [7]. The examination often reveals a picture of retroperitoneal hematoma caused by spontaneous rupture of the angiomyolipoma Along with the classic angiomyolipoma, consisting of 3 components and designated as a benign tumor, the WHO histological classification provides for the isolation of a potentially malignant mesenchymal tumor, called epithelioid angiomyolipoma. Epithelioid angiomyolipoma is characterized by a predominant proliferation of epithelioid cells and a small amount of adipose tissue [6]. Due to the relatively low fat content, epithelioid angiomyolipomas are often visualized as renal cell carcinoma when using radiation diagnostic methods. The tumor may have foci of necrosis, may spread to extrarenal tissues, renal and inferior vena cava. Epithelioid angiomyolipoma is capable of metastasis to the lymph nodes, liver, and lungs [5-8]. The morphometry of the kidney tumor process is determined by the ratio of the expansive and infiltrative components. The microenvironment of tumor cells is characterized by such factors as interstitial blood flow, oxygen concentration, acidity, osmolarity, and oncotic pressure of interstitial fluid. The metabolic and cellular-molecular aspects of the microenvironment, being closely interrelated, can significantly affect the properties of the neoplasm-heterogeneity, invasiveness, metastatic potential and tumor progression [5-7].

Factors of the stromal microenvironment include: endothelial cells, pericytes, smooth muscle cells, fibroblasts, myofibroblasts, extracellular molecules (adhesion molecules, growth factors, hormones, proteases and other enzymes, metabolites, extracellular matrix, collagen, elastic and argyrophil fibers, as well as nerves. The extracellular matrix determines the structure of the tumor. The presence of an infiltrative component of tumor growth leads to the presence of an irregular shape and violation of the anatomical structure due to its replacement, against the background of compression due to the volumetric effect. The shape of the tumor is determined by the localization of the source of its growth, its relationship with the microenvironment and the presence of anatomical barriers (capsules, fascia, and bone structures). One of the signs of a tumor is a deformation of the border of the parenchyma and sinus structures, which allows us to assume the presence of a focal lesion. Deformity, change in structure, or infiltration of the kidney capsule also allows you to clarify the nature of the process. The combination of deformation and infiltration leads to morphometric changes, and on the basis of empirical data, a hypothesis is formed about an independent sign of malignancy – the value of the cortical-tumoral angle of more than 90◦. The method of differential diagnosis, according to MRI data with tumor morphometry, allows you to get a reliable result in the diagnosis of kidney cancer without lengthening the scan time and description.

## The Purpose of the Study

The aim of this study was to improve the MR-diagnosis of renal cell carcinoma based on MR-morphometric and diffusion parameters, taking into account the microenvironment of tumor cells.

## Objectives of the Study

To determine the differential diagnostic morphometric and diffusion parameters based on the results of MRI in the diagnosis of renal cell carcinoma.

## Research Materials and Methods

The material for the study was tomographic data of 20 patients with renal cell carcinoma, 10 patients with angiomyolipomas and 10 patients with simple intraparenchymal kidney cysts.

### The algorithm we used included

Protocol of retroperitoneal MRI Visualization in T2, T2fs, T1 FS, DWI, embedded axial, sagittal, and coronal planes. Detailed characteristics of MRI semiotics of kidney formations, including MRI signs of individual structural elements and path morphological examination. The cortical-tumoral angle was measured using a T2-weighted sequence in the axial and coronal planes. The series were laid through the cup-pelvic system and the area of the kidney gate to obtain the maximum cross-sectional area of the kidney parenchyma and its pelvis. The top of the cortical-tumoral angle was set at the border of the pelvis and the renal pyramid closest to the tumor, and its sides were laid tangentially to the tumor borders. The ADC in the tumor was measured by DWI (b0-b1000) using the small areas of change method. Diffusion parameters were measured in the solid and cavity components of the tumor, the parenchyma of the cerebral and cortical layers of the kidney. We calculated the value of the measured diffusion coefficient, apparent diffusion coefficient (ADC), which is determined by the formula: ADC = -In (S/S0) /b, where: S0, S is the intensity of the MP signal without and under the action of diffusion gradients, b is the diffusion factor. Statistical data processing was carried out using Microsoft Excel programs. The reliability of differences in the frequency of detection of the trait was evaluated using the Student's criterion. The differences were considered significant at $p < 0.05$. The material for path morphological examination was obtained after biopsy, various types of surgical intervention and autopsy. The reliability of the MRI data was evaluated directly during the operation or familiarized with its protocol.

## The Results of the Study and Their Discussion

According to MRI data, tumor processes in the kidney were visualized and described, the exact size of the formations was determined, and the local spread and invasion of tumors into neighboring anatomical structures were studied. As a result of the study, it was found that the average diameter of the malignant tumor was 3.2 cm (from 2.6 to 11.5 cm). The average volume of the tumor was 19 cm3. Tumors were more often located in the middle segment of the kidney, and more than one segment was involved in 12 (60 %) patients. The tumor tissue involved the kidney capsule in 15 (75%) patients, the spread to the pelvis was detected in 7 (35%) cases, and the vessels of the renal pedicle were involved in 3 (15%) cases.

***Table 1:*** *The value of the cortical-humoral angle depending on the prevalence of education.*

| T-criterion for TNM | T1 | | T2 | T3 | | | T4 | AML | | Simple intraparenchymal cysts | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | a (less than 4 cm) | b (4-7 cm) | | a | b | c | | Less than 4 cm | 4-7 cm | Less than 4 cm | 4-7 cm |
| | 9 | 5 | 4 | - | 1 | - | 1 | 7 | 3 | 6 | 4 |
| The average value of the cortical-tumoral angle in the axial projection | 111 | 117 | 121 | - | 127 | - | 155 | 43 | 73 | 62 | 77 |
| The average value of the cortical-tumoral angle in the coronal projection | 123 | 109 | 132 | - | 135 | - | 147 | 50 | 81 | 59 | 75 |

In the group with angiomyolipomas, the average diameter of the formation was 2.7 cm (from 0.9 to 3.6 cm). The average volume of the tumor was 10 $cm^3$. Tumors were more often located in the lower segment of the kidney, and more than one segment was involved in 3 (30%) patients. Among patients with simple intraparenchymal kidney cysts, the average diameter of the formation was 3.5 cm (from 1.1 to 5.2 cm). The average volume of the tumor was 22 $cm^3$. Tumors were more often located in the lower segment of the kidney, and more than one segment was involved in 3 (30%) patients. The value of the cortical-tumoral angle was different depending on the prevalence of the tumor, the results are presented in Table 1. The prevalence of renal cell

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carcinoma was estimated taking into account the TNM classification (2002) and the R. E. N. A. L. classification. The nephrometric score system R. E. N. A. L. (R. E. N. A. L. scale) is used to predict the complexity of performing kidney resection and predict possible complications after performing kidney resection (Table 1).

From the results of the measurements shown in Table 1, it follows that the average value of the cortical-tumoral angle (including all measurements in axial and coronal projections) for renal cell carcinoma is 120◦. The average value of the cortical-tumoral angle for angiomyolipomas is 56◦, for cysts it is 67◦. According to the Student's criterion, the difference between the obtained values of the cortical-tumoral angle for renal cell carcinoma and benign processes is significant at p=0.001(TEM = 18.9) for angiomyolipomas and p=0.001 (TEM = 19.1) for cysts (Table 2).

***Table 2:*** *ADC values depending on the staging criteria for T.*

| T-criterion for TNM | T1 | | T2 | T3 | | | T4 | Other conditions | |
|---|---|---|---|---|---|---|---|---|---|
| | a (less than 4 cm) | b(4-7 cm) | | a | b | c | | Simple intraparenchymal cysts | AML |
| The value of the ADC from the solid component of the tumor | 0,00073mm²/s | 0,00077 mm²/s | 0,00072 mm²/s | - | 0,00085 mm²/s | - | 0,00083 mm²/s | 0,0033 mm²/s | 0,00173 mm²/s |
| The value of the ADC value from the medullary layer of the kidney along the periphery of the tumor | 0,00165 mm²/s | 0,00175 mm²/s | 0,00167 mm²/s | | 0,0012 mm²/s | | 0,00133 mm²/s | 0,00173 mm²/s | 0,00165 mm²/s |

According to analysis of the measurement data in table 2, it shows that the mean ADC value for renal cell cancer in its solid component is 0,00075мм²/s/ It is significantly below the calculated values of the diffusion coefficient for the renal parenchyma 0,0016мм²/s, the contents of the cyst 0,0033мм²/s (p=0.001 t = 45.7), and angiomyolipoma 0,00165мм²/s (p=0.001 t = 32.8). Appraisal values for R. E. N. A. L. and cortico-tumoural the angle of the operated patients are presented (Table 3).

***Table 3:*** *RENAL score values and cortical-tumoral angle.*

| R.E.N.A.L. | The average value of the cortical-tumoral angle | | Number of observations |
|---|---|---|---|
| | Axial projection | Coronal projection | |
| 4-6 | 113 | 118 | 14 |
| 7-9 | 122 | 133 | 5 |
| 10-12 | 155 | 147 | 1 |

***Table 4:*** *Ratio of extrarenal and intraparenchymal components.*

| T-criterion for TNM | T1 | | T2 n=4 | T3 | | | T4 n=1 | Other conditions | |
|---|---|---|---|---|---|---|---|---|---|
| | a (less than 4 cm) n=9 | b (4-7 cm) n=5 | | a | B n=1 | c | | Simple intraparenchymal cysts n=10 | AML n=10 |
| Ratio of extrarenal and intraparenchymal components | 0,23 | 0,35 | 0,42 | - | 0,62 | - | 0,76 | 0,11 | 0,14 |

From the obtained data (Table 3), it is assumed that a more obtuse cortical-tumoral angle corresponds to higher values on the R. E. N. A. L scale, but the small size of examined group does not allow us to consider the observational data statistically reliable.

The results of the measurement of the extra renal and intraparenchymal components, measured by the formula h (height of the formation component above the parenchymal boundary)/H (height of the formation component below the parenchymal boundary) are presented (Table 4).

The average value of the ratio of extra renal and intraparenchymal components in the group of observations of renal cell carcinoma is 0.34, for simple mainly intraparenchymal cysts 0.11, and for typical angiomyolipids 0.14.

According to the Student's criterion, the difference between the obtained values of the ratio of extra renal and intraparenchymatous components for renal cell carcinoma and benign processes was significant at p=0.001 (TEM = 3.9) compared with angiomyolipomas and p=0.001 (TEM = 4.6) compared with cysts. Typical observations of renal cell carcinoma, angiomyolipoma, and simple kidney cyst with measurement examples (Figure 1).

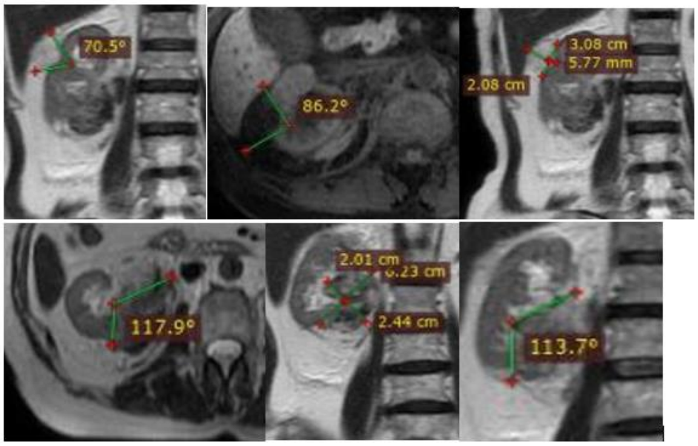


***Figure 1:*** *MR picture of angiomyolipoma of the right kidney typical and epithelioid with hemorrhagic impregnation.*

In the posterior lip of the lower segment of the right kidney, a solid structure of the formation was revealed, measuring 35 x 34 x 38 mm. Along the contours of the formation in the sinus and pararenal tissue, areas of fat structure, with dimensions of at least 56 x 59mm. Pronounced edema of the paranephral fiber, areas of hemorrhagic impregnation in the tumor and posterior to the kidney (the process is limited to the Gerot fascia), epithelioid angiomyolipoma with signs of infiltrative growth, with the presence of restriction of diffusion ADC 0.000925-0.0014 $mm^2/s$.

In the lateral parts of the upper segment of the right kidney, a formation with extrarenal growth and the presence of fat in the structure, measuring 24 x 26 x 37 mm, a typical angiomyolipoma, restricts the diffusion of ADC 0.001052-0.001628$mm^2/s$ (Figure 2).

In the lower segment of the right kidney, a formation, measuring 37 x 40 x 33 mm, with a thickened wall, the presence of partitions and restriction of diffusion in the node. The tumor grows beyond the kidney into the fiber by 18 mm, adheres to the walls of the jejunum, and is inseparable from them. The kidney vessels are intact.

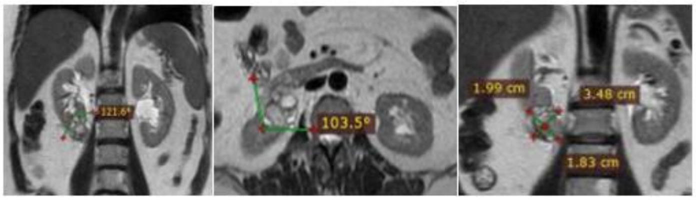


***Figure 2:*** *MR-picture of renal cell carcinoma.*

## Conclusions

Thus, the data obtained indicate that the observed cortical-tumoral angle for renal cell carcinoma is at least 90 degrees and the obtuse angle is characteristic of infiltrative growth in a malignant tumor. A significant restriction of diffusion in renal cell carcinoma and the presence of a relatively large extra renal component can be used as additional criteria in the differential diagnosis of kidney cancer.

## Conflicts of Interest

The authors declare no conflicts of interest.

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