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# EMERGING MRI TECHNIQUES IN KIDNEY CANCER: DIFFUSION-WEIGHTED IMAGING, SPECTROSCOPY, AND BEYOND.

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**Abstract:**

Kidney cancer, especially renal cell carcinoma, is highlighted as a significant contributor to cancer incidence. Advanced volumetric visualization techniques enable the detection of small renal tumors, facilitate prognostic assessments of tumor progression, and support organ-preserving surgical interventions.

**Keywords:** renal cell carcinoma, radiology.

Kidney cancer (RC) ranks 10th in the structure of cancer incidence, accounting for 2% of all malignant tumors. In most countries of the world, the incidence of RP is growing, increasing annually by 2–4.5% [1, 2]. In terms of the absolute increase in newly diagnosed oncological urological diseases, kidney cancer ranks second [3]. From 1992 to 1998, the incidence of RP in our country increased from 6.6 to 9.0 per 100 thousand population, and from 1998 to 2008 - from 9.0 to 12.2, respectively [2].

A huge problem is the aggressiveness of renal cell carcinoma. At the initial visit to the doctor, every third patient has metastases [4, 5]. According to other sources, the number of such patients reaches 50% [6], while the 5-year survival rate does not exceed 5% [7]. In more than 60% of cases, kidney cancer is discovered by chance during clinical observation, preventive examinations, or during a routine examination for any other diseases not related to urology. In this regard, such tumors are called "radiologists tumor". Thanks to modern volumetric imaging methods, the number of accidentally diagnosed small (up to 4 cm) kidney tumors is increasing, which gives hope for a favorable prognosis for the course of the tumor process [8] and the possibility of organ-preserving surgical procedures [9]. The most important task in diagnosing kidney cancer is the choice of an algorithm of diagnostic methods, the distinctive features of which should be non-invasiveness or minimal invasiveness and high information content [10]. With timely diagnosis of early stages of kidney cancer, the 5-year survival rate after radical nephrectomy reaches 80% or more. In patients with a history of clinical symptoms at the time of diagnosis, the 5-year survival rate averages 60% [11].

The literature presents the advantages and disadvantages of X-ray, ultrasound and tomographic imaging methods and algorithms for their use in practical medicine. Plain radiography of the urinary tract and excretory urography are traditional methods for detecting malignant kidney tumors. Excretory urography allows you to assess the functional state of not only the affected, but also the contralateral kidney. Functional failure of the contralateral kidney is a reason for performing organ-preserving surgery on the kidney affected by a malignant tumor. The cheapness and availability of the method are the advantages of x-ray methods for studying the kidneys and urinary tract. Low information content in identifying tumors on the anterior and posterior surfaces of the kidney [12] and low sensitivity in detecting tumors up to 4 cm are the disadvantages of classical radiological techniques. Using excretory urography, only 10% of tumors with a diameter of less than 1 cm are diagnosed, 21% - from 1 to 2 cm, 5% - from 2 to 3 cm in size and 85% - more than 3 cm. In 16% of patients with RP, urography does not detect signs of renal carcinoma, which has predominantly extrarenal growth or is localized on the posterior surface of the kidney parenchyma. X-ray signs are characteristic of all volumetric formations of the kidneys. In view of this, it is impossible to differentiate between benign and malignant formations, kidney cysts after excretory urography and a survey X-ray examination. They are ineffective in determining the stage of the tumor process. There is no possibility of assessing the involvement of the perinephric space, which is of enormous clinical importance [10]. According to Yu.A. Pytelya et al [13], with excretory urography, only 67% of cases revealed a volumetric process in the kidney, which turned out to be a tumor upon additional examination. With excretory urography, there is a possibility of an allergic or toxic reaction to an intravenously administered iodine-containing contrast agent. Don't forget about radiation exposure.

Chest X-ray is performed to evaluate possible distant metastasis and is recommended for all patients with RP. SOUTH. Alyaev et al. [14] believe that excretory urography can be abandoned if ultrasound is performed and then multislice computed tomography (MSCT). There is an opinion that for the initial detection of a kidney tumor, in most cases, it is enough to perform an ultrasound. Echography is considered a method of primary diagnosis of RP, thanks to which it is possible to identify up to 80% of asymptomatic kidney tumors [6], while the number of patients with small (up to 4 cm) tumors increases annually to 6%. The first report on the use of ultrasound in the diagnosis of kidney

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tumors was published in 1963 by J. Donald. Since then, the accuracy of ultrasound diagnostics in identifying this pathology has increased from 85–90 to 96–97.3% [15]. The information content of ultrasound and excretory urography in the diagnosis of malignant kidney tumors up to 3 cm in size is 79 and 67%, respectively [16]. The effectiveness of ultrasonography in detecting renal tumors smaller than 1.5 cm is extremely low. Tumors with an intraparenchymal location without deformation of the kidney contour also pose a problem for imaging. Detection of tumors larger than 3 cm in clinical practice for echographic diagnosis is not difficult. It is believed that it is impossible to distinguish a malignant tumor from an angiomyolipoma with tumors less than 3 cm in size in every third case [6]. For this purpose, color Doppler mapping (CDC) is used, which informs about the type of vascularization of the renal mass [17].

Malignant kidney tumors are in most cases hypervascular. Renal cell carcinomas, depleted of blood vessels, have a more favorable prognosis than conventional hypervascular forms of renal cell carcinoma [18]. Currently, power Doppler mapping (EDC) is widely used, the data of which are comparable to the results of X-ray angiography [10]. Ultrasonography allows differentiation between simple and complex cysts, "questionable" cystic formations, of which 40 to 47% are malignant [19], and solid tumors [20]. Renal cell carcinoma can have a cystic appearance due to the content of cystic, fatty, necrotic areas [18]. Its distinctive features are an unevenly thickened wall and the presence of septa of varying thickness within the cystic formation. Second-tissue harmonic ultrasound allows clear visualization of the pseudocapsule of renal carcinoma. Information about its intermittency is of exceptional importance for resolving the issue of implementing organ-preserving benefits [21]. Echography for RP on an outpatient basis should include a mandatory examination of the renal vessels and inferior vena cava [22]. Scanning of the renal veins, inferior vena cava and right atrium is necessary to determine the extent of invasion of renal cancer [12]. The detection rate of venous invasion by renal cell carcinoma ranges from 50 to 95% [10]. Information about tumor lesions of the inferior vena cava is supplemented by angiography, X-ray computed tomography and magnetic resonance imaging. Among the advantages of ultrasound, it is important to note the detection of metastatic liver disease [2] and assessment of the involvement of lymph nodes in the pathological process. The sensitivity of echography in detecting enlarged lymph nodes ranges from 50–60 to 90% [10]. Under the control of the ultrasound method, an intraoperative assessment of the localization and size of tumors is performed during kidney resection, a fine-needle aspiration biopsy is performed, and subsequent monitoring of patients undergoing surgery is performed [2, 23].

Despite the high value and information content of the ultrasound method, it is necessary to perform computed tomography or magnetic resonance imaging [24]. The accuracy of computed tomography (CT) in diagnosing RP reaches 95% [25], and the specificity is 93%. With the widespread use of CT, the detection rate of renal tumors smaller than 1.5 cm has increased [26]. PL Choyke [27] states that the capabilities of CT in diagnosing renal tumors are limited to 0.5 - 1.0 cm. CT has a high ability to assess the structure of the tumor. Thus, the presence of calcifications in the capsule and a solid soft tissue component in the cystic formation speaks in favor of a malignant process [2]. CT helps in differentiating a malignant kidney tumor from angiomyolipoma. The presence of fat islands within the tumor is a pathognomonic sign of angiomyolipoma [9, 28]. In 12% of cases, a tumor node in renal cell carcinoma can masquerade as an angiomyolipoma, especially when the tumor is small [29]. Sometimes the fatty component is part of renal cell carcinoma, and then it is extremely difficult to distinguish it from angiomyolipoma. Areas of calcification are characteristic of RP.

The sensitivity of native CT in detecting kidney tumors is 85.2%, specificity is 94.8% [20]. Computed tomography performed with contrast enhancement is more informative than a native study, especially in the verification of tumors up to 4 cm with partial deformation of the contours of the kidney or located intraparenchymal. Using contrast CT, it is possible to determine whether a kidney tumor belongs to the parenchyma or the pyelocaliceal system, measure its exact dimensions and study the topographic relationship to the renal vessels, as well as to the perinephric tissues and adjacent organs [21]. A method for determining the histological type of renal cell carcinoma at the preoperative stage is proposed. This requires a dynamic contrast-enhanced CT scan using a standardized technique for measuring contrast uptake. Tumors, the density of which increases immediately after the introduction of an iodine contrast agent into the arterial phase and sharply decreases in the parenchymal phase, are considered hypervascular and, in their histological structure, most often correspond to clear cell RP.

In "non-clear cell" types of kidney carcinoma, gradual accumulation of the contrast agent is observed. The density indicators of such tumors in the parenchymal phase of dynamic contrast enhancement become higher than those in the arterial phase [11].

Computed tomography is highly informative in the diagnosis of tumor thrombosis of the renal and inferior vena cava and allows one to assess the extent of the tumor thrombus [10, 12]. The overall accuracy of CT in identifying venous invasion in RP ranges from 68 to 96%. A limitation in visualizing such invasion will be the simultaneous contrast of tumor and blood in the inferior vena cava [2]. X-ray CT makes it possible to determine the interest of perirenal tissue more informatively than the ultrasound method. Some authors claim that CT with 100% accuracy allows one to determine the involvement of nearby structures in the process [10]. Using CT, metastases of RP are detected in the

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lungs, liver, adrenal glands, contralateral kidney, bones, and brain. Currently, CT is considered the "gold standard" in the diagnosis of adrenal lesions in kidney cancer, although it cannot 100% exclude micrometastases [3]. The sensitivity of CT in detecting lymphadenopathy ranges from 83 to 95%, specificity - 88% [26]. CT angiography provides information about the vascular architecture of the kidney affected by a cancerous node, allows you to obtain images of blood vessels with a diameter of 1 - 2 mm in volumetric three-dimensional reconstruction, identify the localization of metastases in the liver parenchyma in accordance with its segmental structure, assess the extent and boundaries of the tumor thrombus of the kidney and lower liver. vena cava The sensitivity of the method is 88%, specificity is 94%. Performing multiplanar and three-dimensional reconstructions makes it possible to study the spatial localization, extent, vascular architecture of a kidney tumor, the condition of the inferior vena cava, regional lymph nodes and assess the condition of the urinary tract, and helps in planning resection of the kidney [14, 24]. Thus, according to some data, comparison of preoperative data obtained by performing CT with 3D reconstruction, such as the position of the kidney, the location and depth of tumor invasion, the condition of the renal artery and vein, the relationship of the tumor to the vessels and the collecting system, with data obtained after surgery revealed a match in 98% of cases [22]. We should not forget that when performing a CT scan of the kidneys, the radiation dose to the patient is on average 3–6 mSv, which is several times higher than the radiation dose during chest radiography. This should be taken into account when examining women of childbearing age and children. When performing an echographic examination or MRI, there is no radiation exposure. When performing X-ray CT, radiopaque iodine-containing drugs are used, which can cause allergic and nephrotoxic reactions. They should not be administered to patients with renal impairment. In such cases, magnetic resonance imaging should replace CT [5].

The ability to perform the study without preparing the patient, obtaining images in three mutually perpendicular planes at different levels without moving the patient, the absence of artifacts from bone structures, changes in pulse sequences, high resolution - all this makes MRI a highly informative method for visualizing kidney tumors and helps in establishing extrarenal spread and invasion of kidney cancer into blood vessels and neighboring organs. Such subtleties make it possible to more accurately determine the stage of the malignant process. The results of an MRI study of the kidneys do not depend on the patient's physique or the presence of gases in the gastrointestinal tract [16]. Today, some sources indicate the high informativeness of the method in identifying small kidney tumors that do not violate the continuity of the renal capsule. The multiphase dynamic contrast technique helps to more accurately differentiate between a small tumor and a renal cyst and assess the type of blood supply to the formation [15]. A disadvantage of MRI is the visualization of calcium deposits. In turn, the presence of calcifications in the wall of a cystic formation may be a sign of a cyst-like form of renal cell carcinoma. The technique is highly informative in the diagnosis of hemorrhagic cysts masquerading as renal cell carcinoma. MRI is recommended in case of questionable CT findings, especially for differentiating complex renal cysts from the cystic form of RP. The use of contrast agents allows MRI to detect renal masses with a diameter of less than 1 cm. In general, MRI is comparable to CT in detecting renal masses: the sensitivity of the method is 93.5% versus 93.8% for CT. But the overall accuracy of MRI in the differential diagnosis of renal masses was superior to that of CT. Fat-suppressed pulse sequences help distinguish fat-containing renal tumors (lipoma, angiomyolipoma, fibrosarcoma) from renal cell carcinoma and detect cysts and tumors smaller than 1 cm [35]. It is believed that data on the extent of a kidney tumor obtained from 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 by MRI in 84% of cases, the N-stage in 81.8 and 79.5%, respectively. MRI, unlike CT, is highly informative in detecting a pseudocapsule of a kidney tumor, which most often has well- or moderately differentiated kidney formations up to 4 cm in size [15]. The presence of a pseudocapsule in the formation is an indication for organ-preserving surgery. Pseudocapsular defects can serve as signs of invasive growth of renal cell carcinoma, allowing more accurate differentiation between stages T1 and T3a [14]. It is believed that MRI is a more informative imaging method in diagnosing extrarenal tumor invasion and infiltration of surrounding organs and tissues [15]. Some authors believe that MRI is inferior to CT in assessing lymph node involvement [17]. A.S. Pereverzev et al. [17] presented the summary indicators of the informativeness of MRI in the diagnosis of retroperitoneal lymphadenopathy in RP, considering metastatically affected lymph nodes larger than 1 cm. According to the authors, the accuracy of the method was 93.5%, sensitivity - 90.6%, specificity - 94.7% . According to other sources, the sensitivity of MRI in detecting lymphadenopathy is more than 95% [18]. Some authors note the advantage of MRI over CT and ultrasonography in more accurate imaging when tumor thrombosis of the renal veins or inferior vena cava is suspected [21, 26]. The accuracy of MRI in detecting tumor thrombosis in the renal vein and inferior vena cava is 98 and 100%, respectively. The sensitivity and specificity of MRI in assessing the condition of the renal pedicle and inferior vena cava are 95 and 100%, respectively [10, 15].

MRI makes it possible to differentiate between tumor and blood thrombus, clearly determine the upper border of the tumor thrombus and its extent, saving the patient from invasive lower venocavography [12]. However, obtaining high-quality MRI scans is limited by artifacts from respiratory movements and cardiac activity. MRI has an advantage

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over CT and echography in the diagnosis of RP metastases in the liver and brain. CT may miss small foci of metastatic lesions localized in the posterior cranial fossa. All patients with RP with spinal and radicular symptoms should undergo MRI of the entire spine and spinal cord [18]. MRI has proven its merit in identifying metastatic bone lesions in RP when other radiological methods are ineffective or their data are equivocal [2, 15]. CT and MRI make it possible to detail secondary changes in bone tissue, clarify the boundaries of intra- and extraosseous spread of the tumor process, thereby helping to plan the expected level of bone resection and the volume of soft tissue removed [19]. Despite its high information content, MRI, according to many authors, cannot compete with ultrasonography and X-ray CT in the primary detection of kidney tumors. MRI is one of the most expensive diagnostic methods in the world [2]. The combination of ultrasonography followed by MRI is considered to be a sufficient set of imaging methods for determining space-occupying lesions in the kidneys and assessing the local and regional extent of the tumor process [6]. If we compare CT and MRI with each other, then both methods can detect kidney tumors and help in assessing the stage of the process [15], as well as provide subsequent monitoring of patients in the postoperative period. A contraindication to MRI examination is the patient's fear of closed spaces (claustrophobia), metal implants and prostheses, and heart rate drivers. Nowadays, selective angiography is performed to obtain more complete information about the renal arteries, their number, the vascular architecture of the kidney, and if the involvement of the great vessels is suspected. Some authors call angiographic examination the "gold standard" in the diagnosis of RP, the information content of which is 95–97%. Accurate knowledge of the topography of the renal vessels allows one to resort to economical organ-saving measures, which is decisive during surgery on a solitary kidney, bilateral RP, when planning complex resection or embolization of the renal artery [2]. X-ray angiography, unfortunately, does not make it possible to differentiate avascular renal carcinoma from a cyst. In the recent past, inferior cavography was performed on all patients with RP with venous invasion. Superior cavography was used in cases of complete block of the inferior vena cava and in case of poor visualization of the upper border of the tumor thrombus [2]. Selective renal venography determines compression, germination, thrombosis and deformation of the branches of the renal vein. If there is a block on the lower cavogram, atrioventricular cavography is considered mandatory [10]. Currently, cavography is performed in patients with RP if there is insufficient information content or there are contraindications to performing other methods of volumetric imaging [2]. When planning kidney resection, it is necessary to add selective venography to the algorithm of contrast vascular diagnostic methods, which includes abdominal aortography and selective arteriography. It is believed that for small tumors without signs of invasion, we can limit ourselves to general abdominal aortography. In other cases, it is necessary to perform aortography, selective renal angiography and inferior cavography. The high value of angiography is noted in determining the spread of renal cell carcinoma to neighboring organs and tissues and metastases in the opposite kidney. On angiograms and cavograms, indirect signs of damage to the lymph nodes can be identified [10]. In advanced cases, only angiography can determine the organ affiliation of the tumor in the retroperitoneal space. Angiography for bone metastases serves to determine the degree of involvement of the great vessels in the process and shows the nature of the vascularization of metastases. Using angiography, it is possible to carry out selective embolization of pathological vessels, which are usually rich in RP bone metastases. This achieves a reduction in the risk and volume of intraoperative blood loss [29]. According to I.G. Figarova et al. [20], when using X-ray angiography, the error rate reaches 12%. Difficulty arises in the angiographic differential diagnosis of volumetric processes in the kidneys and in the perinephric tissue. When using an angiographic method, its invasiveness must be taken into account, as a result of which the study can be accompanied by a number of severe complications, and the patient is exposed to radiation. Recently, angiography has been used less and less due to the widespread use of Doppler ultrasound, which, without prior preparation of the patient and without invasion, informs about the characteristics of renal blood flow [21]. Radionuclide testing for RP is an additional technique. The high value of angiography is noted in determining the spread of renal cell carcinoma to neighboring organs and tissues and metastases in the opposite kidney. On angiograms and cavograms, indirect signs of damage to the lymph nodes can be identified [10]. In advanced cases, only angiography can determine the organ affiliation of the tumor in the retroperitoneal space. Angiography for bone metastases serves to determine the degree of involvement of the great vessels in the process and shows the nature of the vascularization of metastases. Using angiography, it is possible to carry out selective embolization of pathological vessels, which are usually rich in RP bone metastases. 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Renoscintigraphy is a fairly informative method for diagnosing kidney cancer: sensitivity - 98%, specificity - 89%. In case of total damage to the kidney by a cancerous tumor with thrombosis of the renal vessels, the sensitivity of the method reaches 100%, and the specificity is 98% [10]. The sensitivity and specificity of radionuclide studies have increased significantly nowadays thanks to the beginning of the use of modern radiopharmaceuticals, gamma cameras and computer processing of the data obtained. Radionuclide testing allows you to determine the side of the lesion, obtain information about the perfusion of the affected kidney, impaired urine outflow, changes in the renal arteries, for example, renal artery stenosis [22], and provides a quantitative assessment of the damage to the renal parenchyma [23]. The emergence of radionuclide research methods in urology has significantly improved the ability to determine the function of the renal parenchyma, thereby contributing to the emergence of new and informative methods for predicting the course of renal failure after partial nephrectomy or organ-sparing surgery for RP [24]. Currently, there is an absolute need for research methods that make it possible to objectively determine the functional reserve of the renal parenchyma before performing organ-sparing treatment and to monitor the function of the remaining renal parenchyma in the postoperative period. When planning nephrectomy, it is of paramount importance to assess the sufficiency of the function of the remaining kidney, because in the postoperative period it will face an increased load, which poses a risk of developing acute renal failure or exacerbation of chronic renal failure [25]. Skeletal scintigraphy is used to detect skeletal bone metastases from cancer. Bone metastases in renal cell carcinoma occur in every third patient and in the vast majority of cases are osteolytic in nature. Radioisotope skeletal scanning is performed for bone pain and elevated serum alkaline phosphatase levels [2]. Bone scintigraphy has a high resolution in diagnosing the location, extent of the lesion and the degree of dissemination of the tumor process throughout the skeletal system [29]. In the terminal phase of the process, with widespread damage to the skeleton by metastases, due to the depletion of the protective forces of the suffering body, the uptake of the radiopharmaceutical can be completely low [10]. To determine distant metastases in order to clarify the stages of the process, radionuclide studies of the brain and liver are used [23]. When planning the scope of lymphadenectomy and to justify the removal of the adrenal gland, they also resort to the use of isotope diagnostics [14]. Despite the enormous possibilities of radiation research methods, it is often necessary to establish the morphological structure of the kidney tumor before surgery. This can only be done by biopsy [14]. To clarify the histological structure of a kidney tumor, a fine-needle biopsy is used under ultrasound or CT control, thanks to which the safety and accuracy of the method have increased. A biopsy is necessary if an abscess, metastatic lesion, lymphoma is suspected and before starting conservative therapy. The method is sensitive in 80–95% of cases. According to A.S. Pereverzeva et al. [26], the accuracy of biopsy is 77.8%, specificity is 71.4%.

Recently, the clinical importance of biopsy has increased, and the impetus for this comes from the results of some observations, as a result of which it was found that in 20% of cases, kidney tumors up to 7 cm in size can be benign [27]. When differentiating a renal cyst from a cyst-like tumor, the diagnostic role of preoperative puncture of a cystic formation is of limited value. Negative findings during the examination of punctate specimen cannot exclude the presence of a malignant neoplasm due to the localization of tumor cells in another part of the specimen [26]. The importance of ultrasound-guided biopsy in the diagnosis of atypical cysts and cystic tumors of the kidney is highly appreciated. In the literature, echographic, Doppler and radiation (CT, MRI) signs of kidney cancer and their diagnostic value at various stages of the pathological process have not been studied or systematized.

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