Diffusion weighted magnetic resonance imaging (DW-MRI) and multislice CT (MSCT) evaluation of the stereotactic radiosurgical treatment effectiveness of renal cancer carcinoma (RCC).

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Aims and objectives

Currently, kidney cancer is one of the most common urological tumors and up to 3% of all cancer pathology. [1,2]. In Ukraine the annual incidence of renal cell carcinoma were over 5000 cases with more than 2,500 mortalities recorded. The disease is more prevalent in the urban population; mostly men aged 50-70 years [3].

The renal cell carcinoma usually develops from the epithelium of the proximal tubule and its usually unilateral with equal probability of occurring on either side. Clear cell subtype of RCC is the most encountered in clinical practice.

Its risk factors are smoking, genetic predisposition, polycystic kidney disease, chronic renal failure, hemodialysis, von Hippel-Lindau and hazardous industrial chemicals [3].

Five-year survival in stage I RCC (tumor restricted within kidney, the tumor size of about 4 cm) is 56-82% with stage II (tumor size of more than 7 cm, traction bath in the perirenal fat within Gerota's fascia) - from 43 to 75% [4,5].

Previously surgical techniques was considered the most effective treatment for RCC [4] however a new direction in the radical treatment of kidney cancer is the method of stereotactic radiosurgery (SRS) using the CyberKnife system. This allows stereotactic radiotherapy under visual control (Image-guided radiation therapy (IGRT) for precise exposure and targeting on the pathological focus . The accuracy of summing ionizing radiation on this complex led to the use of single focal dose steep gradient that protects the surrounding healthy tissue [6].

CyberKnife, as a progressive, non-invasive technology is currently used to treat malignant tumors including kidney tumors. Best results were achieved especially at early stage of tumor development and small size (less than 6 cm) with clear boundaries. stereotactic radiosurgical treatment represents a valid alternative to open surgical procedures, especially for patients whom radical surgical procedures are absolutely or relatively contraindicated [6,7,8].

In modern technology irradiation, there are various imaging systems that allow for accurate exposures under control images (MSCT, MRI, etc.) [7,8].

For the diagnosis and treatment monitoring RCC used methodology were MSCT, MRI, US [9,10,11,12].

MSCT and MRI are essential intosscopic methods in recognition of renal tumors, but MRI detects focal lesions 2-4 mm in size and has a large differential diagnostic capabilities. MSCT allows differentiation of calcified and soft tissue structures, causing obstruction of the urinary tract. MR-urography is highly informative method detecting obstructive processes of upper urinary tract. Its advantages includes non-invasiveness, lack of
radiation exposure, do not require the use of contrast. Contrast 3D MR-angiography evaluates renal arteries adequately.

Diffusion-weighted MRI is one of the pulse sequences, which allows you to qualitatively and quantitatively evaluate the morphological characteristics of the various components of the tumors (stroma, cysts, necrotic zones, peritumoral edema, additional inclusion) that is necessary for planning and surgical treatment [10,11, 12,13]. Contrast enhanced MRI plus DWI clearly delineates boundaries of cancers and other pathological processes.

Therefore, the aim of the work is to evaluate the effectiveness of radiosurgical treatment of the RCC using DW-MRI and MSCT.
Methods and materials

In the Center of oncology and radiosurgery "Cyber Clinic Spizhenko" in Kiev (fig. 1) in 63 patients with solid RCC 1-2stage examined within 3 and 6 months intervals after radiosurgical treatment using Cybernife G4 (fig. 2). Complex modern radiological studies where used to assess the dynamics of the flow of the tumor.

Utilized DW-MRI with diffusion-weighted echo-planar pulse sequence (DWEPI) in conjunction with a conventional T1 and T2-WI apparatus on Toshiba Exelart Vantage (1.5Ts) (fig. 3). To determine the apparent diffusion coefficient (ADC) using b = 0, 500, and 1000 s / mm² and the same noise threshold. Apparent diffusion coefficient is characterized by the mean square of the distance travelled by a molecule per unit time. DWI at each voxel (three dimensional pixel) image has an intensity that reflects the degree of freedom of diffusion of water corresponding localization.

Standard sequence: T1-W/I, T2-W/I, Short tau inversion recovery (STIR), T1-, T2 weighted fat-suppressed gradient echo, postcontrast T1-W/I. Used intravenous contrast with Omniscan 20ml, 2ml/s.

MSCT with intravenous contrast Visipaque-320 100ml 5ml/s slice thickness of 1 mm on the CT-unit "Toshiba Activion 16".

During preparation for radiosurgical intervention, the patient was positioned, fiducials and radiopaque markers were installed for stereotactic CT guidance toward tumour (fig. 4).

With the planning system «MultiPlan», a plan was designed for radiosurgical treatment of kidney cancer (fig 5).

Evaluated cases of RCC were 38 men and 25 women, aged 41-76 years. Solitary kidney RCC was diagnosed in 21 patients.

During radiosurgical treatment single tumor dose was 10-14Gy, number of fractions 3-4.

Dynamic monitoring of patients ranged from 2 -18 months. Data from long-term results of treatment of kidney cancer in Cyber Clinic Spizhenko show a very high efficiency of radiosurgical treatment. Five-year survival in stage I is 66%, with II - 64%, and III - 42% and IV - 11%.
Fig. 1: Cyber Clinic of Spizhenko is a clinic of radiotherapy full cycle, where effective chemoradiotherapy, radiosurgery of tumors of any localization are conducted.

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Fig. 2: System of Cyberknife G4. Figure shows the biological effects of ionizing radiation.

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Fig. 3: Magnetic-resonance scanner Toshiba Exelart Vantage.
Fig. 4: MSCT. Radiopaque marker in the tumor of the right kidney.
**Fig. 5:** Plan radiosurgical treatment and isodose distribution during renal cancer.

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Results

MRI data revealed the following: neoplastic process in the kidney, size of RCC, intrarenal invasion and metastasis to adjacent anatomical structures including inferior vena cava causing suspected tumor thrombus, the state of regional lymph nodes. The use of IV contrast significantly improved visualization of tumor areas.

The tumor boundaries and shape were clearly well visualized, often pineal, with loosely diffused infiltrative lymph nodes and inhomogeneous structure diameter of up to 1,8-5,1cm.

According to DWI indicator, the ADC in the tumor ranged from $0,7-1,0 \times 10^{-3}$ mm$^2$/s while ADC in the surrounding normal renal parenchyma was $1,2-1,8 \times 10^{-3}$ mm$^2$/s.

Results of IV-MSCT clearly visualized all patients with renal mass lesion homogeneous or inhomogeneous internal structure, including small calcifications and cysts. MSCT was used to determine the following: tumor diagnosis, tumor staging, evaluation of vascular system and urinary tract anatomy, anatomic and renal function in all phases of contrast (fig. 6). CT elicited renal neoplasms sizes 0,5-6,8 cm. 58 (92%) renal tumors patients were better visualized during corticomedullary phase.

It's a fact, that radiosurgical treatment irradiates tumor cell DNA, induces its fragmentation thus tumor cells loses mitotic ability, necrotize and shrinks over 1,5-2years. Some malignant and metastatic lesions may decrease in size even faster, sometimes within 2-3 months. Also there will be a gradual thickening of the wall of the vessel and the complete closure of its lumen within same time frame [6, 7].

The criteria for effective radiosurgical treatment according to this imaging were as follows: 1- no increase in tumor size, 2- appearance of new necrotic areas, 3- improvement of indicators ADC.

The criteria for the negative dynamics of RCC were: 1- increase in tumour size, 2 - increased restriction ADC based on DWI data.

Full local control attained in 6 cases including one patient with a solitary kidney.

The MRI and MSCT images (fig. 7, 8, 9) show good results of treatment in the form of a gradual reduction of the size of the tumor area in patient with RCC solitary kidney. So, one month posttreatment, the tumor decreased by 14% and over the course of next 3 months it diminished further by 22% compared to the original size. On DWI the loosely diffused areas in the central parts of the tumor were probably due to the tumor necrosis (fig.7). Eight months post radiosurgical treatment tumor size diminished further by 32% and zone of ADC increased by 41%. (fig. 8). MRI studies performed after 2,5 years (fig.
9) show marked deformity and fibrotic changes only on the right kidney, the tumor tissue is invisible thus a full positive response.

After radiosurgical treatment satisfactory partial tumor regression was observed in 40 cases (fig.10,11) while tumor process stabilized in 13 cases. During stereotactic radiosurgical treatment reduction of tumor sizes detected with DWI and inhomogeneous ADC increase. This indicates the effectiveness of the treatment in terms of ultrastructural changes due to decrease in the density of cancer cells and enhanced diffusion.

However in 4 patients, tumour progressed within 7-10 months after treatment. Data from irradiation parameters of RCC after treatment shows significant decrease in tumor size and increase in ADC in the tumor (fig. 12), indicating that the morphological and functional changes in the tissues due to irradiation changes.
Fig. 6: MSCT. Renal cancer carcinoma in the lower segment of right kidney (reconstruction: a-MPR, b-VRT, c-MIP).

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Fig. 7: Complete regression. Patient N., 44 years. Renal cancer carcinoma in middle segment of right kidney. MSCT: before treatment (a) and one month after radiosurgical treatment (b). One month after treatment - tumor size reduced by 14%. MRI, DWI three months after treatment (c, d). Tumor size decreased by 22%, areas of weak diffusion in the central regions of the tumor zone were due to disintegration.

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**Fig. 8:** Complete regression. Patient N., 44 years old. Renal cancer carcinoma in middle segment of right kidney. MRI study (a b c) after 8 months: the size of the tumor reduced by 32%, an increase of 41% on the ADC.

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**Fig. 9:** Complete regression. Patient N., 44 years old. Renal cancer carcinoma in middle segment of right kidney. MRI study after 2.5 years, observed full positive response, visualized deformation and kidney fibrosis, tumor tissue was not detected.

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**Fig. 10:** Partial regression. Patient C., 44 years old. Renal cancer carcinoma in middle and lower segments of right kidney. MRI (a, b, c) and MSCT study (d) before treatment. Soft tissue tumor with inhomogeneous structure is visualized. On DWI there was notable restriction ADC in the tumor zone.

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**Fig. 11:** Partial regression. Patient C., 44 years. Renal cancer carcinoma in middle and lower segments of right kidney. MRI (a, b, c) followed up 3 months after treatment: tumor reduction by 9%, uneven ADC increase by 24%.

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![Bar chart showing size of neoplasms and value of ADC in patients with renal cancer carcinoma before, 3rd and 6th months after radiosurgical treatment.](image-url)

**Fig. 12:** Size of neoplasms and value of ADC in patients with renal cancer carcinoma before, 3rd and 6th months after radiosurgical treatment.

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Conclusion

Complex radiological study using DWI, standard MRI and contrast-enhanced MSCT allows monitoring and evaluation of tumor response with stereotactic external radiation in patients with renal cell carcinoma. DWI is a qualitative and quantitative method for detecting radiation necrosis RCC after radiosurgical treatment.
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