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THE ROLE OF COMPUTED TOMOGRAPHY IMAGING IN THE TRAINING PROGRAM AND MONITORING THE EFFECTIVENESS OF RADIATION THERAPY FOR CERVICAL NEOPLASMS

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Abstract

Relevance: cervical cancer occupies a leading position among the most common types of cancer pathology in the female population worldwide. According to the results of clinical studies, the use of 3D-visualized brachytherapy sessions in the program of complex treatment of cervical cancer at the stage of planning and conducting brachytherapy creates clinically favorable conditions for effective therapy: the risk of displacement of applicators is reduced, the load for the patient and medical staff is reduced, and the stage of brachytherapy is accelerated. The use of computed tomography imaging in a comprehensive approach to diagnosis and treatment provides good indicators of local control in patients with cervical cancer, regardless of tumor size and clinical stage, without increasing the frequency of severe late toxic effects, which is important and remains relevant today.

The purpose of this study is to determine the role of computed tomography in the planning and control of radiation therapy for cervical cancer.

Materials and methods: the present study included 18 patients with a verified diagnosis of squamous cell carcinoma of the cervix, who underwent radiation therapy for the pelvic region, the area of regional metastasis up to 50 Gy, preventive irradiation of paraaortic lymph nodes up to 36-40 Gy TFD (total focal dose), followed by brachytherapy under the control of computer tomography imaging.

Results: an analysis of the effectiveness of brachytherapy under the control of computed tomographic imaging was performed. After comparing computed tomography images before and after radiation treatment, positive changes were detected in the patients included in the study – a decrease in the volume of the tumor, a decrease in the number and size of regional lymph nodes

Conclusions: the use of computed tomography for cervical cancer provides the radiologist with objective information about the state of the primary tumor, the zones of parametral and lymphogenic metastasis.

Thus, the use of computed tomographic imaging for planning and dynamic monitoring during radiation therapy in cervical cancer allows individualizing the radiation conditions, reducing the radiation load on the risk organs, and provides a guarantee of the quality of radiation therapy.

Keywords: *cervical cancer, radiation therapy, brachytherapy.*

Резюме

РОЛЬ КОМПЬЮТЕРНО-ТОМОГРАФИЧЕСКОЙ ВИЗУАЛИЗАЦИИ В ПРОГРАММЕ ПОДГОТОВКИ И КОНТРОЛЕ ЭФФЕКТИВНОСТИ ЛУЧЕВОЙ ТЕРАПИИ ПРИ НОВООБРАЗОВАНИЯХ ШЕЙКИ МАТКИ

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Актуальность: Рак шейки матки (РШМ) занимает лидирующие позиции среди наиболее распространенных видов онкопатологии женского населения во всем мире. По результатам клинических исследований применение 3D-визуализируемых сеансов брахитерапии в программе комплексного лечения рака шейки матки на этапе планирования и проведения брахитерапии создает клинически выгодные условия для эффективной терапии: уменьшен риск смещения аппликаторов, снижена нагрузка для пациента и медицинского персонала, а также ускорен этап проведения брахитерапии. Применение компьютерно-томографической визуализации в комплексном подходе к проблемам диагностики и лечения обеспечивает хорошие показатели локального контроля у пациентов с РШМ независимо от размера опухоли и клинической стадии без увеличения частоты тяжелых поздних токсических эффектов, что имеет важное значение, и остается актуальным на сегодняшний день.

Целью настоящего исследования является определение роли компьютерной томографии в планировании и контроле лучевой терапии рака шейки.

Материалы и методы: В настоящее исследование было включено 18 пациенток с верифицированным диагнозом плоскоклеточной карциномы шейки матки, которым проведена лучевая терапия на область малого таза, зоны регионарного метастазирования до СД 50 Гр, профилактическое облучение парааортальных лимфатических узлов до СОД 36-40 Гр с последующей брахитерапией под контролем визуализации компьютерной томографии.

Результаты: Был проведен анализ эффективности проведения брахитерапии под контролем компьютерной томографической визуализации. После сравнения компьютерных томографических изображений до и после проведенного лучевого лечения у пациентов, включенных в исследование были выявлены положительные изменения – уменьшение объема опухоли, уменьшение количества и размеров региональных лимфатических узлов

Выводы: Применение компьютерной томографии при раке шейки матки, обеспечивает врача-радиолога объективной информацией о состоянии первичной опухоли, зон параметрального и лимфогенного метастазирования.

Таким образом, использование компьютерной томографической визуализации для планирования и динамического контроля в ходе лучевой терапии при РШМ позволяет индивидуализировать условия облучения, снизить лучевую нагрузку на органы риска и обеспечивает гарантию качества лучевой терапии.

Ключевые слова: *рак шейки матки, лучевая терапия, брахитерпия*

Түйіндеме

ЖАТЫР МОЙЫНЫ ОБЫРЫ СӘУЛЕЛІК ТЕРАПИЯСЫНЫҢ ТИІМДІЛІГІН БАҚЫЛАУ ЖӘНЕ ДАЯРЛАУДАҒЫ КОМПЬЮТЕРЛІК ТОМОГРАФИЯНЫҢ РӨЛІ

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Өзектіліг: жатыр мойны қатерлі ісігі (жатыр мойны обыры) бүкіл әлемде әйелдер популяциясының онкопатологиясының кең таралған түрлерінің арасында жетекші орын алады. Клиникалық зерттеулердің нәтижелері бойынша жоспарлы-брахитерапиялық сатысында жатыр мойны обырын кешенді емдеу бағдарламасында 3D-визуальды брахитерапия сеанстарын қолдану тиімді терапия үшін клиникалық қолайлы жағдай туғызады: аппликатордың орнын ауыстыру қаупі азаяды, науқас пен медициналық персоналға жүктеме азаяды, брахитерапия сатысы жеделдетіледі. Диагностика және емдеу проблемаларына интегралды көзқараста компьютерлік томографиялық бейнені қолдану ісік мөлшері мен клиникалық кезеңіне қарамастан, жатыр мойны обыры бар пациенттерде жергілікті токсикалық әсердің жиілігін арттырмай-ақ маңызды болып табылады, бұл маңызды және маңызды болып қала береді.

Зерттеудің мақсаты - жатыр мойны обырына арналған сәулелік терапияны жоспарлау мен бақылаудағы компьютерлік томографияның рөлін анықтау.

Материалдар мен әдістер: Бұл зерттеуге жатыр мойнының сквамустық жасушалық карциномасының анықталған диагнозы бар 18 науқас кірді, олар жамбас аймағында, SD 50 Gy дейін аймақтық метастаз аймағында, SOD 36-40 Gy дейін параорталық лимфа түйіндеріне профилактикалық сәулелену, содан кейін брахитерапия жүргізілді. компьютерлік томографияның көмегімен бақылау.

Нәтижелері: компьютерлік томографиялық бейнелеуді бақылаудағы брахитерапияның тиімділігіне талдау жасалды. Есептелген томографиялық суреттерді радиациялық емдеуден бұрын және одан кейін салыстырғаннан кейін зерттеуге енгізілген пациенттер оң өзгерістерді анықтады - ісік көлемінің азаюы, аймақтық лимфа түйіндерінің саны мен мөлшерінің төмендеуі

Қорытынды: жатыр мойны обырына арналған компьютерлік томографияны қолдану рентгенологқа бастапқы ісіктің жағдайы, параметрлік және лимфогендік метастаздың аймақтары туралы объективті ақпарат береді.

Осылайша, жатыр мойны обырына арналған радиациялық терапия кезінде жоспарлы және динамикалық бақылау үшін компьютерлік томографиялық бейнені қолдану сәулелену жағдайларын жекелендіруге, қауіпті органдарға радиациялық жүктемені азайтуға мүмкіндік береді және радиациялық терапия сапасының кепілі болып табылады.

Негізгі сөздер: *жатыр мойны обыры, сәулелік терапия, брахитерпия.*

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Introduction

Malignant neoplasms are important problem of our time, not only in medicine and biology, but also in the public life of each state. This problem affects the interests of all mankind living on the Globe. According to the International Agency for research on cancer (IARC), more than 12 million new cases of cancer and about 6.2 million deaths from it are registered annually in the world. The annual growth rate of malignant neoplasms is approximately 2%, which exceeds the growth of the world population by 0.3-0.5% [8].

At the same time, malignant neoplasms of the reproductive system organs has the largest share in the structure of women's cancer incidence [12].

Cervical cancer occupies a leading position among the most common types of cancer pathology in the female population worldwide [14], which accounts for 7.9% of all cases of cancer. Malignant neoplasm is the most common cause of death for women in developing countries. In Africa, which has a population of 267.9 million women, approximately 80,372 women are registered with cervical cancer every year and about 60,000 women die from it, according to these indicators, Africa is the country with the highest incidence and mortality rates from cervical cancer. For comparison, in Western Europe, with a total population of 96 million women, there are 9318 cases and 3794 deaths from cervical cancer each year. In 2008, in America, with a total of 175 million women, there were about 12,000 cases of cancer and 4413 deaths [6].

According to the IARC-International Agency for Research on Cancer more than 500,000 new cases of cervical cancer are diagnosed worldwide each year, which is becoming a common cause of death among women: more than 280,000 cases per year [12].

In Kazakhstan, invasive forms of breast cancer are the most common form of malignant neoplasms of the female genital area. Cervical cancer ranks 5th among all neoplasms and 10th in mortality in the General population of the Republic of Kazakhstan. According to the National Cancer registry, the standardized incidence rate of cervical cancer in 2011 was 22.0 per 100,000 population, and the

mortality rate was 9.0 per 100,000 population [4]. The indicator of the ratio of mortality to the incidence of cervical cancer in 2008 for the Republic of Kazakhstan was 0.55, which corresponded to the level of the countries of the Central Asian region [7]. Since 2008, the national program for screening of cervical cancer in the Republic of Kazakhstan has been using a cytological study (PAP test), which is conducted free of charge in women aged 30-60 years with an interval of 5 years. Three times this program has been supplemented and changed in order to improve it, and in order to improve the quality, liquid Cytology has been introduced since 2011 [15].

Since 2011, the country has been systematically implementing a number of measures within the framework of the state program "Salamatty Kazakhstan" and, subsequently, the program "Densaulyk", which could not but affect the improvement of early diagnosis and timely treatment, and inevitably led to a decrease in this indicator. According to Kaidarova D.R. and co-authors, the ratio of mortality to morbidity in 2013 was 37.3, in 2014 – 39.2, in 2015-35.8, and in 2016-already 37.2 [2].

According to 2012 data, a total of 9965 women were registered with cervical cancer, 1625 new cases were registered, and 650 people died. There was a fairly high proportion of the 3-4 stages of the disease, which was 30%, by age composition, the most cases were in the 30-58-year-old cohort, and the annual mortality rate was 21.0% [10].

The main problem is the late remains to treatment of patients for medical care and, accordingly, the increase in the number of cases of cervical cancer in the advanced stage of the process. Locally advanced forms of cervical cancer were and still are a serious social threat and the main cause of death among the female population after breast cancer. For women with locally advanced cervical cancer, the standard of care has evolved from remote radiotherapy alone (RRT) to combined remote radiotherapy and brachytherapy (BT) with parallel chemotherapy [9]. Accordingly, effective treatment of locally common forms of cervical cancer is one of the most important tasks of modern oncogynecology [1, 3].

Thanks to the introduction of new computer technologies, the development of brachytherapy planning also does not stand still. The recommendations of the European Organization for research And Treatment of Cancer (GEC-ESTRO) support the strategy of adaptive brachytherapy, since this treatment method is based on irradiation of the volume, in which the goal changes with each fraction of brachytherapy, based on the response to treatment [5, 11]. According to the results of clinical studies, the use of 3D-visualized brachytherapy sessions in the program of complex treatment of cervical cancer at the stage of planning and conducting brachytherapy creates clinically favorable conditions for effective therapy: the risk of displacement of applicators is reduced, the load for the patient and medical staff is reduced, and the stage of brachytherapy is accelerated.

Thus, the use of computed tomography imaging in a comprehensive approach to diagnosis and treatment provides good indicators of local control in patients with cervical cancer, regardless of tumor size and clinical stage, without increasing the frequency of severe late toxic effects [13], which is important and remains relevant today.

Objective: to determine the role of computed tomography in the planning and control of radiation therapy for cervical cancer.

Materials and methods: This study was carried out within the framework of the" Grant funding for research" of Semey Medical University, agreement No. 26 of 23.05.2018, which is directed by one of the fragments of the gratuitous multicenter project Forum for Nuclear Cooperation of Asia (FNCA). The clinical base of the research is the Center of nuclear medicine and Oncology, Semey city, Republic of Kazakhstan.

The object of the study is patients with squamous cell carcinoma of the cervix of stages IIB and IIIB, who do not have confirmed metastases and without previous chemotherapy (CT), radiation therapy (RT) and surgical interventions for this localization, who underwent complex chemo radiotherapy.

Inclusion criteria:

1. Squamous cell carcinoma of the cervix.
2. Stage IIB (4 cm diameter) and IIIB (according to the international classification FIGO (The International Federation of Gynecology and Obstetrics.
3. Age: from 20 to 70 years.
4. The General condition of the patient (Performance status (PS) on the Karnovsky`s scale and ECOG - who-0-2.
5. Without previous ChT, RT and surgical interventions for this localization.
6. Written informed consent.
7. No metastases to the paraaortic lymph nodes

Exclusion criteria:

1. Concomitant somatic diseases in severe form.
2. A history of other malignancies over the past 5 years, with the exception of basal cell carcinoma or squamous cell carcinoma of the skin.
3. Tumor with infiltration of the lower 1/3 of the vagina.
4. Pregnancy or lactation.

The features of modern radiation therapy of tumors of the female reproductive system are:

1. Irradiation of large volumes of tissue;
2. Simultaneous or sequential use of systemic (often toxic) medications (cytostatics, hormones) with radiation therapy);
3. the use of radiation therapy after surgical treatment (radical, palliative and organ-preserving), which requires an individual approach to planning radiation therapy from the position of individualization of its timing, the volume of radiation, single and total absorbed doses.

Results

This study included 18 patients with a verified diagnosis of squamous cell carcinoma of the cervix, who underwent radiation therapy for the pelvic region, regional metastasis zones up to 50 Gy, and preventive radiation of paraaortic lymph nodes up to 36-40 Gy TFD, followed by brachytherapy under the control of computed tomography imaging.

Radiation plans were calculated using appropriate computer programs (Varian radiotherapy complex, which includes the ECLIPSE planning system, 2015).

The residual tumor volume of the cervix and risk organs (bladder, rectum, and sigmoid colon) were determined using a series of computer tomographic images in relation to the installed applicator system, respectively, in three image projections – axial, sagittal, and coronary.

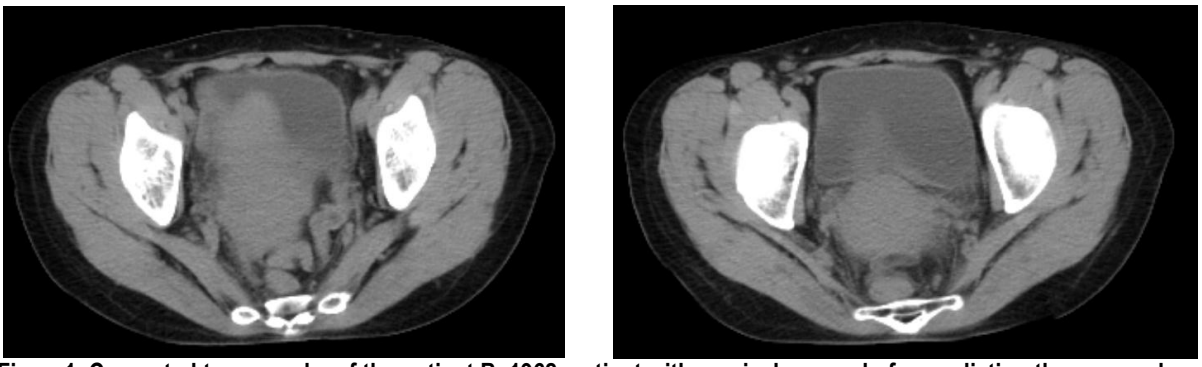

Figure1. Computed tomography of the patient B. 1962, patient with cervical cancer before radiation therapy: a sharp hypertrophy of the supravaginal part of the cervix, deformation of the bladder, which is attached to the cervix throughout; the iliac lymph nodes are visualized.

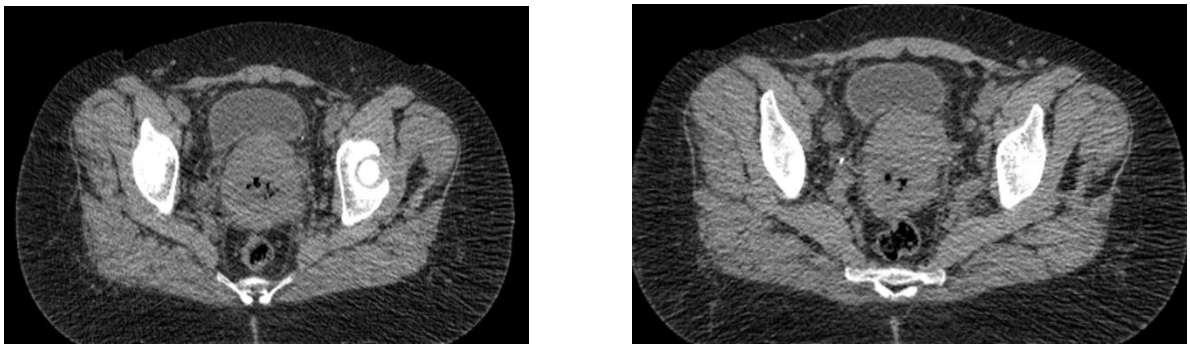

Figure 2. Computed tomography of the patient L. 1960: enlarged supravaginal part of the cervix, not pronounced deformation of the posterior wall of the bladder; external and internal inguinal lymph nodes are visualized.

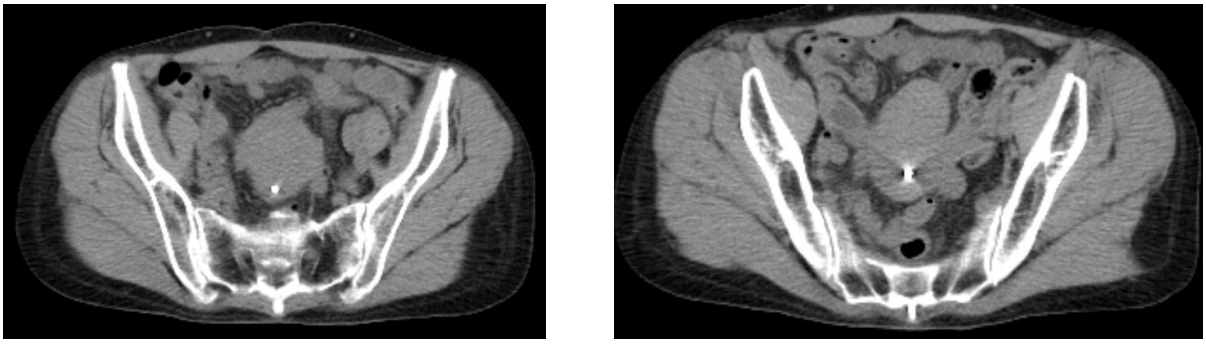

Figure 3. Computed tomography of patient B. 1962, a patient with cervical cancer after radiation therapy: reduction of the volume of the supravaginal part of the uterus, reduction of the deformation of the bladder; lymph nodes are not visualized.

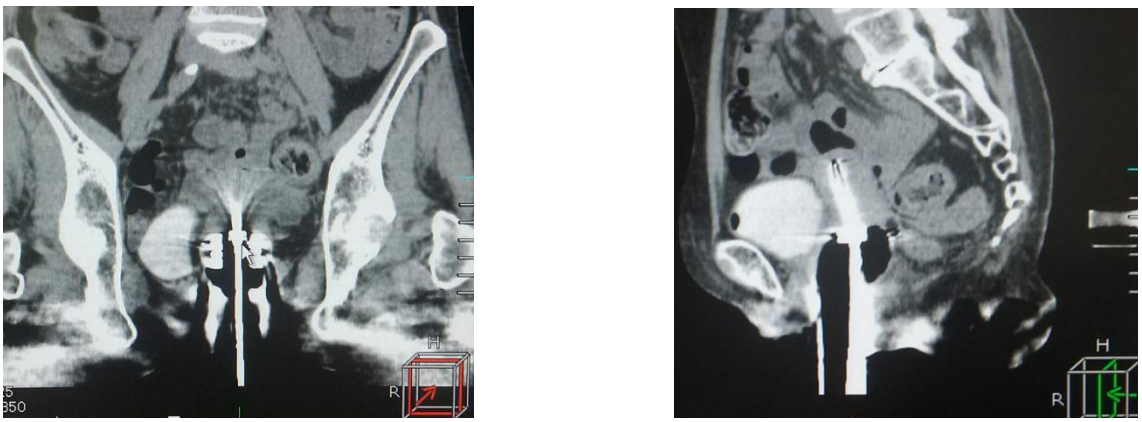

Figure 4. Assessment of the correct location of the tandem and ovoids. On tomograms of a patient born in 1959 with cervical cancer, the installed Central applicator in the uterine cavity and ovoid applicators in the vagina, axial and sagittal sections are visualized. The neck applicator is indicated by a white arrow.

The correct location of the central applicator and two side ovoid applicators was evaluated using a series of tomographic images. The correct and precise location of the applicators is necessary, since this determines the efficiency and uniformity of the distribution of the specified radiation dose. At this stage, it is very important that the radiologist critically assess the location of the tandem and ovoids and determine the optimal placement of sources used in brachytherapy. The cervical limiter should be at the level of the cervix, and the tandem should be in the middle of the distance between the two ovoids, thus separating them, as shown in figure 4. The same picture of the location of the applicators must be obtained on the side tomograms to confirm the correct location of the applicators, which will guarantee the uniformity and correct distribution of the radiation dose.

After that, the cervical tumor and critical organs were delineated using CT images according to GEC-ESTRO recommendations.

CT images were used to distinguish:

* HR-CTV (high risk, high risk zone) - a zone that includes a cervical tumor and possible spread of the tumor beyond the cervix (residual infiltration of parametral / paravesical / pararectal tissue)

* IR-CTV (Intermediate risk, intermediate risk zone)- microscopic spread of the tumor process, covering HR-CTV with a margin.

Critical organs: the bladder, rectum, and sigmoid colon.

An analysis of the effectiveness of brachytherapy under the control of computed tomographic imaging was performed. After comparing computed tomography images before and after the treatment, positive changes were detected in all cases – a decrease in the volume of the tumor, a decrease in the number and size of regional lymph nodes.

Discussion

The tasks that are solved when planning radiation therapy for cervical cancer have significant differences and also depend on many factors.

These factors include:

- treatment method (combined, complex, radical / palliative, combined radiotherapy, etc.);

- morphological structure of the tumor, which indirectly "reflects and affects" the radiosensitivity of the tumor;

- functional state of the body and radiation-risk organs located near the tumor.

The above is dependent on the General clinical concept of special treatment and the actual course of radiation therapy. At the same time, it should be noted that individual planning of radiation therapy largely depends on the location of the tumor itself.

Based on the above, it is necessary to clearly select the irradiation area when planning 3D-visualized BT sessions, which is carried out strictly under the control of computed tomography.

At stage 1, all patients with cervical cancer received conformal radiation therapy for the pelvic area and regional metastasis zones up to a total focal dose (TFD) of 50 Gy against the background of weekly administration of chemotherapy using the Cisplatin 40 mg (Cisplatin Pharmachemie, B.V. (Netherlands) scheme at week 5, remote radiation therapy was performed to assess the residual volume of the cervical tumor, all patients underwent a control CT examination of the pelvic area. At stage 2, prophylactic irradiation of paraaortic lymph nodes was performed by remote radiation therapy, TFD 36-40 Gy.

At 3 stage, BT was performed with three-dimensional dosimetric planning based on computer tomographic images.

Before choosing a specific system type applicator for a particular patient were evaluated by anatomy-pathological situation when the recto vaginal examination: it was determined a residual tumor volume of the cervix at the time of BT planning, the severity of the arches, the length of the uterine cavity during the preliminary sensing. Additional information about the residual volume of the cervical tumor was analyzed using pre-performed computed tomography of the pelvic organs at the end of the course of remote irradiation.

In our study, taking into account the available capabilities, all patients used a uterine endostat with different angles of inclination along the Central axis of 30, 45, 60 degrees with two ovoid applicators.

The introduction of endostats into the uterine cavity was performed under General sedation in order to ensure good relaxation of the pelvic muscles, provide comfort for the patient and facilitate the introduction of the endostat for the doctor. Prior to the introduction of applicators, a Foley catheter was inserted into the bladder with a contrast of the last 1.5-2 ml of 76% urographin for subsequent CT examination. Under general anesthesia, the cervical canal was expanded with Gegar dilators to no. 5-6. A uterine endostat of the selected length was inserted into the uterine cavity, then ovoid applicators were inserted into the vaults of the vagina, which were fixed together with a lock.

The next stage is computed tomography preparation for planning and monitoring radiation therapy in patients diagnosed with cervical cancer.

The study was carried out on a 16-slice computer tomography device by General Electric "Optima" (2014, Germany).

At the first stage, computed tomography was performed as a diagnostic method included in the General research algorithm to clarify the organ and non-organ spread of the tumor, especially in patients with adverse prognosis factors. In the future, computed tomography was performed in the mode of computer tomographic planning and computer tomographic control.

As shown by our research and subsequent data analysis the following methodological principles must be followed for optimal planning of radiation therapy and subsequent computed tomography control:

1. the position of the patient on her back, using an individual vacuum mattress with fixation, and identical conditions were met, both during planning and during therapy;

2. scan parameters: the thickness of the slice and the step of the tomograph is 5mm

3. reducing the size of the image field.

All patients were examined with a full bladder.

The volume of the study was determined depending on the clinical diagnosis and the task of computer tomography - from the level of the Th12 - L1 vertebral bodies to the upper third of the femur bones, which was in accordance with the nature of metastasis of these tumors.

When a clinically determined lesion of the vaginal tube to the lower third (or including it along the vulvar edge) - the beginning of a CT scan-the first scan was oriented to the entrance to the vagina.

Next, several scans were performed at the level of the maximum tumor size with a tomograph step of 5 and a slice thickness of 5 mm to clarify the spread to neighboring organs and to the surrounding tissue. Further, the study was performed according to the usual program for the pelvic area.

After the diagnostic stage of the computed tomography study, the further study was completed according to the topometric study program: two "marking" scans were oriented along the upper, lower borders and the center of the planned radiation field in front and behind with marking on the skin and marking the study levels on the front topogram for computer tomographic control and correction of the radiation program if there are appropriate clinical indications.

Computed tomographic examination of regional metastasis zones with signs of metastatic lymph node lesions performed to clarify the localization of pathological lymph nodes relative to the bone structures of the pelvis and to make their projection on the patient's skin.

Figure 5. Patient placement during planning of radiation therapy.

At the same time, computed tomography allows us to determine the linear dimensions and volumes of the visualized lesions, as well as "areas of medical interest" (organs located near the tumor).

The radiation load during computer tomography was 4.8 mSv-5.6 mSv.

When monitoring the effectiveness of radiation therapy using computed tomography for cervical cancer and drawing up a Protocol for describing the study, the following algorithm for analyzing the data of a computed tomography study must be followed:

- the size of the cervix and the body of the uterus with manifestations that characterize the accompanying non-oncological pathology (fibroids, cysts and other similar formations);
- signs of tumor spread to the lower segment of the uterus;
- signs of infiltration of parametral and / or retrovesical fiber;
- signs of growth of the tumor in the bladder;
- visualized groups of metastatic lymph nodes of the pelvis and paraaortic group.

According to the computer tomographic study, the conclusion was made about the decrease or increase in the pathological formation, which could be caused by the phenomena of edema as a manifestation of the radiation reaction or the progression of the main process.

Conclusions

The use of computed tomography for cervical cancer provides the radiologist objective information about the state of the primary tumor, the zones of parametral and lymphogenic metastasis.

Thus, the use of computed tomographic imaging for planning and dynamic monitoring during radiation therapy in cervical cancer allows individualizing the radiation conditions, reducing the radiation load on the risk organs, and provides a guarantee of the quality of radiation therapy.

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Contribution of authors:

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