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THE INFLUENCE OF THE CONSTITUTIONAL FEATURES OF PATIENTS ON THE DIFFERENCE BETWEEN THE PLANNED AND ACTUAL DOSE RECEIVED ON THE MUCOUS OF THE RECTUM

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ВЛИЯНИЕ КОНСТИТУЦИОНАЛЬНЫХ ОСОБЕННОСТЕЙ ПАЦИЕНТОК НА РАЗНИЦУ МЕЖДУ ЗАПЛАНИРОВАННОЙ И ФАКТИЧЕСКИ ПОЛУЧЕННОЙ ДОЗОЙ НА СЛИЗИСТУЮ ПРЯМОЙ КИШКИ

Abstarct. The purpose of this study was to assess the influence of the constitutional features of uterine cancer patients on the difference between the planned and actual dose received on the rectal mucosa. The intention also was to identify how the planning of radiation therapy in this group of patients is complicated by anatomical features of the pelvic organs. Particularly, when dense tissues and hollow organs combine in a limited range, this can affect device displacements and errors in dose calculations for healthy organs. This study examined 110 patients, and in vivo dosimetry was performed for them to determine the dose load on the rectal mucosa. This allowed determining a pattern of deviation between the planned dose and the results of in vivo dosimetry depending on constitutional data. Among all the factors considered, only body weight and body mass index at the tenth irradiation session demonstrate a probable effect in patients who underwent irradiation on the Clinac 600 C linear accelerator. The study ascertained no probable dependence of the influence of constitutional features in patients irradiated on the ROCUS-AM apparatus. The data obtained during the study indicate the need to develop innovative approaches to topometric preparation of overweight genital cancer patients, and for further dosimetric control in this category of patients.

Реферат. Целью исследования было оценить влияние конституциональных особенностей пациенток раком тела матки на разницу между запланированной и фактически полученной дозой на слизистую прямой кишки. Так как планирование лучевой терапии у данной группы пациенток осложняется из-за анатомических особенностей органов малого таза, в частности, сочетании в ограниченном объеме плотных тканей и полых органов, что может влиять на ошибки в расчетах дозовой нагрузки на здоровые органы. Было обследовано 110 больных, которым на этапах лечения проведена дозиметрия in vivo с определением дозовой нагрузки на слизистую прямой кишки, вследствие чего выявлена закономерность отклонения между запланированной дозой и результатами дозиметрии in vivo в зависимости от конституциональных данных. При облучении на аппарате Clinac 600 C среди всех рассмотренных факторов влияние оказывают только масса тела и индекс массы тела на десятом сеансе лучевой терапии. При облучении на аппарате РОКУС-АМ нами не выявлено достоверного влияния конституциональных особенностей. Полученные в ходе исследования данные свидетельствуют как о необходимости разработки новых подходов к топометрической подготовки больных раком гениталий с избыточным весом, так и дальнейшего проведения дозиметрического контроля в этой категории пациенток.

Keywords: constitutional features, obesity, radiation therapy, topometric preparation, in vivo dosimetry, uterine cancer

Ключевые слова: конституциональные особенности, ожирение, лучевая терапия, топометрической подготовка, дозиметрия in vivo, рак тела матки

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Introduction. Endometrial cancer (EC) retains a leading position in the structure of malignant diseases of women over the past decade [1]. For most uterine cancer (UC) patients, the standard of adjuvant treatment is radiation therapy (RT) [2]. It was noted that the increase in the EC prevalence is due to an increase in the incidence of endometrial cancer Type I. Obesity is the leading risk factor for this type of cancer, and not only reduces the patients' quality of life, but also

complicates the planning and implementation of radiation therapy [3, 4].

Planning of RT in UC patients in the postoperative period is complicated by anatomical particularities of the pelvic organs, that is, by a combination of dense tissues (muscles, bones, ligaments) and hollow organs (rectum, bladder) in a limited range.

This heterogeneity is significantly enhanced by soft tissue edema as a result of postoperative trauma, especially in overweight women. In obese patients, artifacts may appear during imaging due to the presence of excess adipose tissue [5]. During radiation therapy in UC patients, especially obese ones, positioning errors are more likely to exceed the limits that were taken into account upon planning [6, 7].

In vivo dosimetry is used as an additional means of controlling the quality of RT [8]; currently, it is the best way to assess the dose delivered to the patient. One of the goals of in vivo dosimetry is to compare the doses obtained from the detector readings with theoretical values calculated using the treatment planning system (TPS) [8, 9].

The purpose of the study – to assess the effect of constitutional characteristics of patients on the difference between the planned and actual dose received on the rectal mucosa.

Materials and methods. We analyzed the results of the treatment of 110 UC patients with stages Ib–II, who were treated from 2016 to 2019 in the radiation therapy department of the SO «Grigoriev Institute for Medical Radiology and Oncology of the NAMS of Ukraine». The patients ranged in age from 41 to 85 years, with an average age of (61.0 ± 8.4) years.

The study involved 110 patients. Of these, 95 (86,4%) patients had stage I of the disease (T1bNxM0), 15 (13,6%) – stage II (T2NxM0). All UC patients underwent combined treatment, which included surgical intervention in the extent of a uterine extirpation with appendixes at the first stage and a postoperative course of radiation therapy at the second stage.

The postoperative course of teletherapy was performed using a Clinac 600 C linear accelerator applying three-dimensional planning based on the computed tomography (CT) data, or a ROCUS-AM cobalt device using two-dimensional planning. In radiotherapy, the method of classical fractionation with a single focal dose (SFD) of 2.0 Gy 5 times a week was used. The total focal dose (TFD) for teletherapy was 42.0–50.0 Gy.

Patients underwent in vivo dosimetry during the first and tenth sessions of radiation therapy operating the UNIDOS-E device manufactured by PTW-Freiburg. To assess the effect of the constitutional features of patients on the difference between the actual and calculated dose, we performed in vivo dosimetry after the first session and in the middle of the postoperative course of teletherapy (after reaching 20.0 Gy).

Results. When analyzing the body mass index (BMI), it was discovered that 32 (29.0%) patients out of 110 maintained normal body weight, 78 (71.0%) patients were obese. The overall median BMI was 31.6 kg/m^2, and the mean value was 32.1 kg/m^2.

Indicators of the degree of obesity, depending on the type of radiation exposure, are presented in Table 1.

Table 1

Indicators of the degree of obesity, depending on the type of radiation exposure

Degrees of obesity	ROCUS-AM Group I n=50	Clinac 600 C Group II n=60	Total n=110
Norm	22 (44,00%)	10 (16,66%)	32 (29,09%)
1	18 (36,00%)	26 (43,33%)	44 (40,00%)
2	10 (20,00%)	12 (20,00%)	22 (20,00%)
3	0 (0,00%)	12 (20,00%)	12 (10,91%)

The median BMI in patients in the first group was 26.6 kg/m^2, and the mean value was 27.2 kg/m^2, while in patients in the second group, these indicators were 34.9 and 34.2 kg/m^2, respectively.

When irradiated on the ROCUS-AM gamma-therapeutic apparatus, there was no probable dependence found on the influence of constitutional features on the studied indicator.

Table 2 shows the effect of constitutional features on the actual dose received on the rectal mucosa measured by in vivo dosimetry in patients of the second group, who underwent treatment on the Clinac 600 C device.

Table 2

The effect of constitutional features on the actual dose on the rectal mucosa received when irradiated on the Clinac 600 C device

Pair of variables	Spearman's rating correlations			
	Available number of patients	Spearman's rating	T (N-2)	P level
Weight & actual dose at session 10	60	0,288534	2,27515	0,026677
Weight & difference at session 10	60	-0,288534	-2,27515	0,026677
BMI & actual dose at session 10	60	0,369646	3,00349	0,003960
BMI & & difference at session 10	60	-0,369646	-3,00349	0,003960

As it can be seen from the data presented in the table, when exposed to the Clinac 600 C device, among all the factors considered, only body weight and BMI at the tenth irradiation session are likely to have an impact (correlation coefficient -0.288534 and -0.369646, respectively).

The results of investigating the effect of BMI on the difference between the calculated and actual dose received are reported in Figure 1.

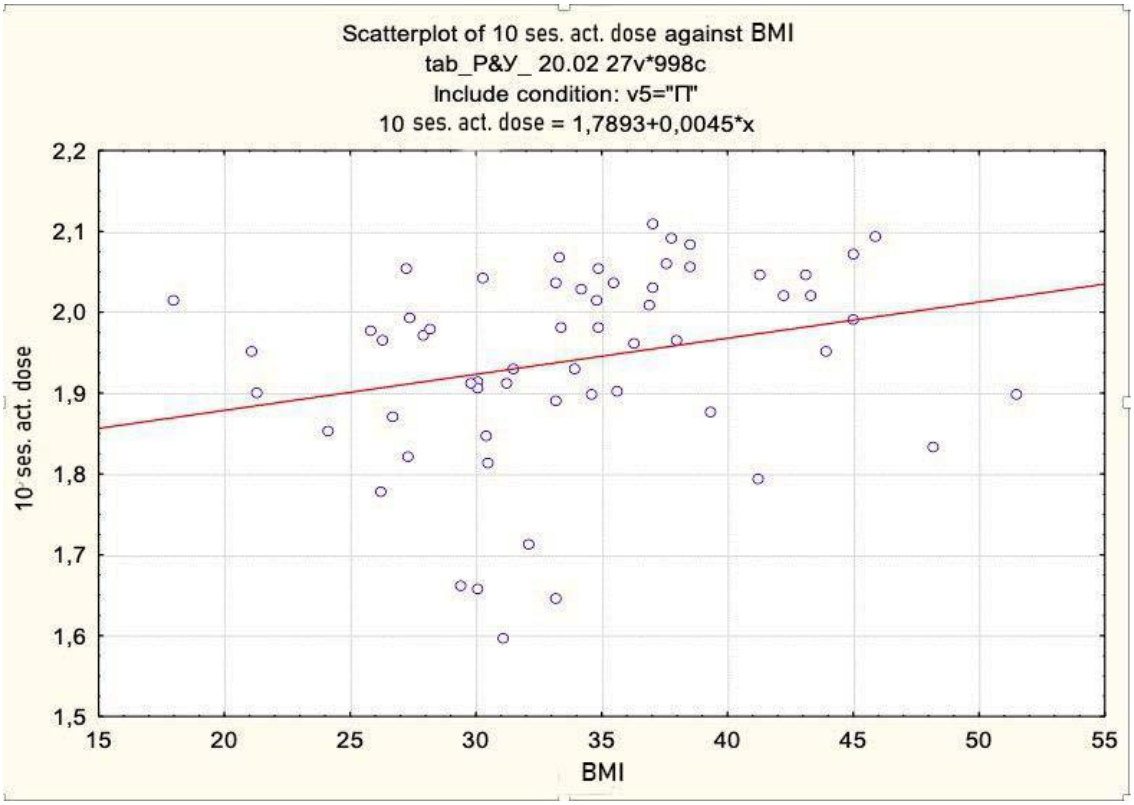

Figure 1 – Interrelation between the BMI and the difference between the calculated and actual dose received at session 10

In the presented figure, it can be observed that with an increase in BMI, the actual dose received on the mucous of the rectum, measured by in vivo dosimetry, at the 10th irradiation session approaches the calculated one. With a BMI of 43.0–50.0 kg/m^2, the actual dose received on the mucous of the rectum corresponds to the planned dose and is 2.0 Gy.

This is confirmed by the data in Figure 2.

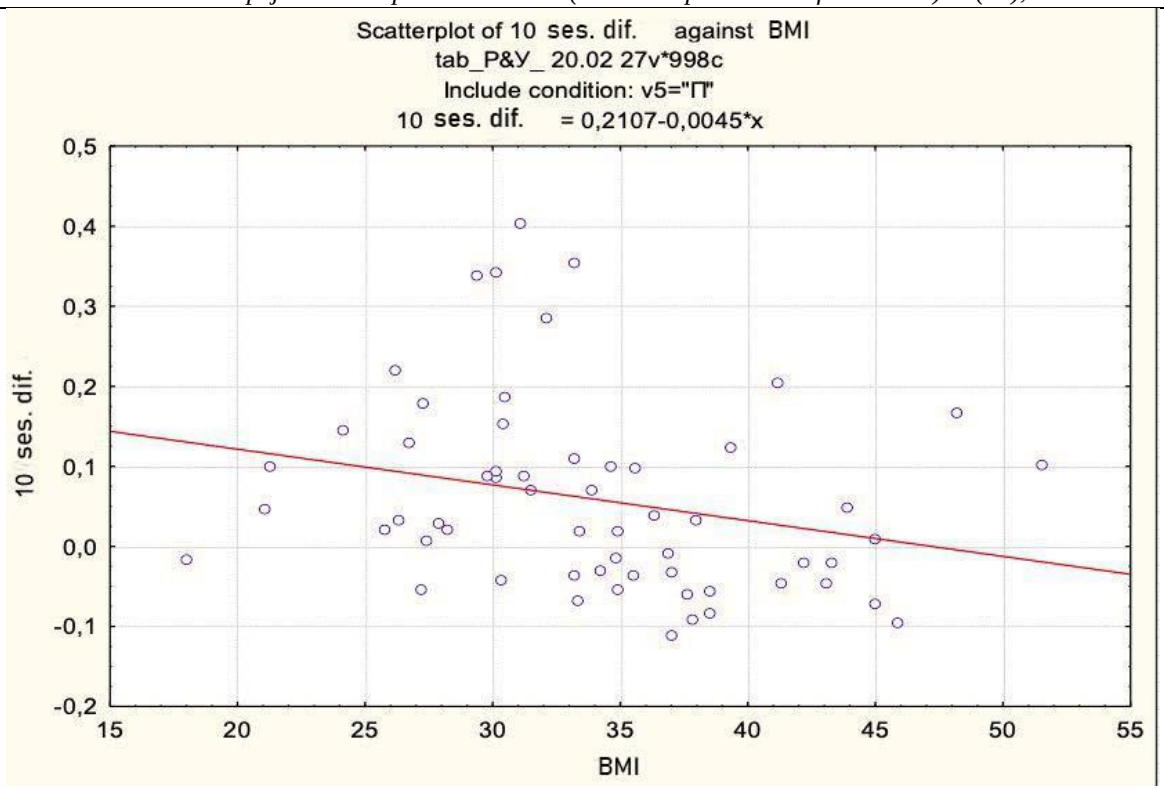

Figure 2 – Dependence of the difference between the calculated and actual dose received on the BMI at session 10

From the presented data, it could be noted that the difference between 2.0 Gy and the actual dose, received by the patient with an increase in the BMI, aspires to 0.

Discussion. It is well-known that severe obesity and comorbidity in patients cause an increase in anesthetic and surgical risks, and certain difficulties in conducting radiation therapy. Moorcraft et al. describe that obesity in patients with EC leads to significant intraoperative blood loss, an increase in the duration of surgery, and a decrease in the radical nature of surgical treatment [10].

Wong et al. investigated the correlation between BMI and daily systemic error in 117 prostate cancer patients treated with image-guided radiation therapy (IGRT). They reported that the displacement of the device by more than 10.0 mm in the medial-lateral direction augments significantly with the increasing BMI: from 1.3% for people with normal body weight to 21.2% for the obese. Potent correlations were found between factors such as subcutaneous adipose tissue thickness, BMI, body weight, and random errors in daily shifts in the medial-lateral direction [11].

Lin et al. demonstrated that mean absolute deviation in three translational directions positively correlates with BMI in 30 patients with EC who received adjuvant pelvic radiation therapy [12].

Kim et al. showed that mean changes in the medial-lateral direction were 0.9 mm and were observed in patients with a BMI of ≥ 30, and 0.1 mm in patients with a BMI of < 30 (P = 0.02). Besides, Bray et al. showed that obese patients had large to medium shifts and random errors in the medial-lateral direction. Undoubtedly, some bodyweight factors have a big impact on equipment errors. However, a scoring system is required to identify high-risk patients for daily IGRT or to apply a larger PVT-CTV margin [13, 14].

In this study, the required CTV-PTV margins for all populations in the upper-lower, anterior-posterior, and medial-lateral directions were 4.5, 4.0, and 8.1 mm, respectively. The most significant deviations were in the medial-lateral direction, similar to previous studies. Although IGRT may reduce deviations in patients receiving pelvic radiation, it is not always available due to limited options in some institutions, as well as due to concerns about increasing the daily dose for patients [15]. Based on the indicators, it is possible to adapt the necessary PTV-CTV fields (5.4 mm for systemic error and 8.2 mm for medial-lateral direction) for patients with a high risk of error. Of course, the clinical validity of the assessment system must be confirmed by an external verification [13, 14].

Laaksomaa et al. [16] investigated the effect of gender error in patients receiving pelvic radiation therapy and found large systemic and random errors in women. As a result, women needed more PTV-CTV margin in three translational directions. The researchers also suggested the difference in the amount of subcutaneous fat between the sexes may contribute to this difference.

In several studies, the margin of error was higher in obese patients, despite the use of immobilization devices [13, 14, 17]. In particular, obesity negatively affects toxicity in prostate cancer patients receiving three-dimensional radiation therapy without IGRT [18]. Therefore, for prostate cancer patients who cannot use IGRT or surgery, a comprehensive PTV-CTV margin guide is required to reduce the error during radiation therapy.

At this time, obesity is typically determined exclusively based on the BMI indicator. However, there are two types of obesity: central and peripheral, depending on the area of fat accumulation. The BMI is unable to distinguish completely between the two adiposities: the central type and the peripheral type [19]. Based on external surface markers on the abdomen, the type of obesity can affect errors because skin folds will be more mobile in central obesity.

To resolve these problems, in this study, the researchers measured abdominal circumference, hip circumference, and diameters in the anterior-posterior and lateral directions using CT simulations, which can include the effects of various types of obesity. As follows, the data suggest that abdominal or hip circumference and diameters are more effective in predicting an error compared to BMI.

This study experienced complications in the form of several limitations. Before all else, patients' circumferences and diameters were taken retrospectively from CT images instead of direct measurements. Although the mean deviation between the two methods was less than 5.0% per the results of the previous comparison test, the consistency of the two approaches should be additionally evaluated. Furthermore, organ movement or tumor regression can affect the accuracy of daily treatment, and the values for various types of cancer can be fundamentally different. This study did not examine the impact of these two factors. Subsequent studies should include patients prospectively and evaluate further dosimetric changes according to the development of body weight factors.

Conclusions. After analyzing the results of the study, it should be noted that a pattern of deviation between the planned dose and the results of in vivo dosimetry was revealed in patients with oncogynecological cancer after the surgical stage of treatment, depending on constitutional data.

The median BMI in patients in the first group was 26.6 kg/m^2, and the mean value was 27.2 kg/m^2. In patients in the second group, this indicator was 34.9 and 34.2 kg/m^2, respectively. In this manner, the BMI index is 1.3 times higher in patients treated on the Clinac 600 C linear accelerator.

Using in vivo dosimetry when irradiated on the ROCUS-AM gamma–therapeutic apparatus, no probable dependence of the influence of the patient's constitutional characteristics was determined on the difference between the calculated and actual dose received on the rectal mucosa. At the same time, when exposed to the Clinac 600 C linear accelerator, among all the factors considered, only body weight and BMI at the tenth irradiation session are likely to have an impact (correlation coefficient -0.288534 and -0.369646, respectively).

It was noted that with an increase in BMI, the actual dose received on the rectal mucosa, measured by in vivo dosimetry, at the 10th irradiation session approaches the calculated one. With a BMI of 43.0–50.0 kg/m^2, the actual dose received on the rectal mucosa corresponds with the planned dose and is 2.0 Gy, and the relative deviation is close to 0.

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ВІДДІЛЕНИЙ ПЕРІОД ЛЕГКОЇ БОЙОВОЇ ЧЕРЕПНО-МОЗКОВОЇ ТРАВМИ: КЛІНКО-НЕВРОЛОГІЧНІ ОСОБЛИВОСТІ.

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ОТДАЛЕННЫЙ ПЕРИОД ЛЕГКОЙ БОЕВОЙ ЧЕРЕПНО-МОЗГОВОЙ ТРАВМЫ:КЛИНИКО-НЕВРОЛОГИЧЕСКИЕ ОСОБЕННОСТИ

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