Article

Dental implantation and radioprotectors after surgical treatment of head and neck oncology

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Abstract: Worldwide, head and neck cancer (HNC–Head Neck Cancer) is one of the most common types of neoplasms with an ever-increasing prevalence and mortality rate. The aim of the work is to improve the methods of restoring masticatory function in patients who previously received radiation and chemotherapy, dental implantation techniques with immediate loading and the use of radio detectors based on sodium deoxyribonucleate ("Coletex-Gel-DNA-L"). Materials and methods. The main group included 61 patients. For local radiation treatment, the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L" were used. The control group included 77 patients who, for the prevention and treatment of radiation reactions of the mucous membranes of the oral cavity, used the classical method — applications of stone oils (olive, sunflower). Results. Of the 79 dental implants installed in patients of the second group, 17 implants were removed due to perimplantitis. The implant survival rate is 78.5% in the control group. Based on a follow-up period of 12 ± 2 months, the survival rate of implants was calculated in patients of the main and control groups. when using the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L", there was a decrease in the frequency of radiation reactions of the III degree from 66.8 to 24.6% compared with the classical method of prevention, I and II degrees of radioepithelitis prevail, the results are reliable ($p < 0.01$). IV degree was not observed in any patient of both groups. Conclusion. The results obtained indicate the effectiveness of the use of the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L" for the prevention and treatment of radiation reactions of the oral mucosa and pharynx in patients with malignant neoplasms of the oropharyngeal zone. In this regard, this drug may be recommended for use as a therapy to accompany radiation, chemoradiotherapy and combined treatment. The introduction into the practice of dentists, the algorithm of complex restoration of masticatory function in patients with a history of oncology is justified. It is possible to reduce side effects, improve the recovery process.

Keywords: one-stage implantation, radioprotector, bone tissue, tissue transplantation, intraoperative prosthetics, intraoperative implant positioning, beam system.

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1. Introduction

Worldwide, head and neck cancer (HNC–Head Neck Cancer) is one of the most common types of neoplasms with an ever-increasing prevalence and mortality rate. The survival rate of patients suffering from head and neck cancer depends on the type, stage and location of the cancer. More than 2/3 of patients are admitted to specialized hospitals with locally advanced forms of the disease. The sensitivity of tumors to radiation and drug effects, as well as the initial neglect of the process, led to the search for sufficiently effective methods of prevention and treatment of neoplasms and their consequences. Currently, promising areas for solving problems related to the treatment of patients with neoplasms are the use of unconventional dose fractionation regimes,

the use of various radiomodifiers, primarily hypoxic cell radiosensitizers, as well as radioprotectors, the search for effective combinations of radiation therapy and chemotherapy [1]. In radiotherapy, requirements are imposed on radioprotectors, namely: the need for differentiated protective action. It is necessary to ensure a high level of protection of healthy tissues and a minimum level of protection of tumor tissues. Such a distinction makes it possible to enhance the effect of a locally applied therapeutic dose of radiation on a tumor focus without serious damage to the healthy tissues surrounding it. The disadvantages of currently existing chemical radioprotectors include toxic side effects and a limited duration of action. All this served as the basis for the study of the radioprotective properties of low-toxic substances of biological origin, which would increase the overall stability of the body and resistance to infections, as well as stimulate the activity of the hematopoietic system [2].

As a result of antitumor treatment, patients experience a serious decrease in chewing function, which negatively affects their quality of life, since oral sanitation before radiation therapy consists in treating all teeth and removing teeth that may be sources of infection [3]. Partially toothless or completely toothless, they turn to the dentist with extensive anatomical deformities, which are often impossible to restore with conventional prosthetics, as it causes them serious inconvenience [4]. In addition, mucositis, tissue fibrosis and xerostomia are often observed in the oral cavity as side effects caused by radiation [5]. When planning post-oncological maxillofacial reconstructive treatment, such indicators as: time, localization, dose and technique of radiation therapy should be studied and taken into account [6]. In patients cured of HNC, dental implants are a good opportunity to restore masticatory function [7]. Modern requirements for the quality of life of patients motivate specialists to optimize protocols, primarily in time, and, of course, in the quality of life of the patient. There is a large group of patients who have previously undergone radiation and chemotherapy for malignancies in the maxillofacial region, to whom dental implantation is not recommended due to the low regenerative abilities of the tissues exposed to radiation. The tissues of the oral cavity are very susceptible to the effects of radiation and chemotherapy, which have a direct damaging effect on the tissues of the oral mucosa, salivary glands, bone tissue [8]. The main manifestations of dystrophic processes in the dental system are: suppression of vascularization, progressive hypoxia, bone resorption and atrophy, violation of its physiological restructuring, phenomena of osteoporosis, suppression of proliferation in healthy tissues.

Treatment of patients with cancer in the maxillofacial region is carried out using a combination of ablative surgery and radiation therapy. As a result of these methods of treatment, complications may occur, a decrease and change in the anatomical structure, a decrease in the rate of salivation, defects of soft and hard tissues leading to functional disability and aesthetic deformation, as a rule, require tissue transplantation with vascularized or non-vascularized flaps for their reconstruction. Strict selection criteria and soft-tissue autografts for enlargement and stabilization of soft tissues are favorable for the long-term survival of the implant. Accelerated rehabilitation (fast track surgery; enhanced recovery after surgery) is a group of simple measures that reduce morbidity, postoperative complications and accelerate postoperative rehabilitation, reducing hospital stay. [9]. It was first proposed in the 90s of the last century by H. Kehlet. According to the definition of H. Kehlet, it allows to reduce the stress reactions of the body and significantly reduce the time required for full recovery" [10]. Dental implantation occupies a leading position among modern methods of orthopedic treatment of patients with partial or complete absence of teeth. The success of dental implantation is ensured if the indications and generally accepted principles of implantation planning are observed, there are adequate clinical conditions, and a good level of oral hygiene [11]. The beam prosthetic structure was preferable to single structures in terms of retention and chewing ability [12]. Immediate surgical and orthopedic rehabilitation plays an important role in solving such complications [13]. The implantation protocol with intraoperative immediate prosthetics in the area of missing and removed teeth reduces the duration of treatment until the end of the surgical procedure and is most in demand among patients. An undeniable advantage is the ability to start using prostheses immediately after implantation surgery [14].

2. Objective

The improvement of the methods of restoring masticatory function in patients who previously received radiation and chemotherapy, dental implantation techniques with immediate loading and the use of radio detectors based on sodium deoxyribonucleate ("Coletex-Gel-DNA-L").

3. Materials and methods

Two groups of patients were included in the study. The main group included 61 patients. During radiation treatment, the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L" were applied topically. The control group included 77 patients who, for the prevention and treatment of radiation reactions of the mucous membranes of the oral cavity, used the classical method — applications of stone oils (olive, sunflower).The main part was made up of able-bodied men over 50 years

old (70.6%).The majority (85.5%) of patients in both groups had stages III and IV of the disease.In 74.6% of patients, squamous cell carcinoma was detected during histological examination of the tumor, adenocarcinoma, lymphoma, myeloma, mucoepidermoid cancer were detected in 25.4%. The age of patients is from 37 to 60 years. The largest group consisted of patients aged 41 to 60 years, i.e. persons of working age. A standard dental examination was performed. Concomitant diseases, bad habits (smoking, alcohol abuse) were determined. Both groups of patients were evaluated according to the classification of the American Society of Anesthesiologists (ASAIII classification). During the examination of the oral cavity, attention was paid to the type of bite, the number of teeth, carious and non-carious lesions. The presence of dentures and their quality, the condition of existing fillings were recorded. The hygienic condition of the oral cavity was assessed by the Fedorov–Volodkina method. 175 implants were installed in patients, finally supporting 24 beam structures in the 1st group of patients and single and bridge-shaped structures in the 2nd group of patients. At the first stage of the work, an assessment of the stability of dental implants in bone tissue, an assessment of the condition of soft tissues was carried out.

1 group of patients (main group) who had previously received radiation and chemotherapy and were in remission for more than 6 months, in whom the restoration of masticatory function was carried out by means of simultaneous installation of dental implants with immediate loading of orthopedic construction using hydrogel radio detectors based on sodium deoxyribonucleate ("Coletex-Gel-DNA-L")/

2 group of patients (control group), who had previously received chemoradiotherapy and were in remission for more than 6 months, who underwent dental implantation according to a two-stage protocol without the use of radioprotectors.

The distribution of patients by groups is shown in table 1

1st group	61 pers.	44,2 %
2nd group	77 pers.	55.8 %
Total	138 pers.	100 %

Table 1. Distribution of patients into groups

All patients underwent RT on Clinac C2100 linear electron accelerators in the bremsstrahlung mode with a photon energy of 6 MV. The classical mode of dose fractionation was used (GENUS 2 Gy, 5 fractions per week). The scope of irradiation included a primary tumor detected before the start of treatment, or a clinically determined tumor, and regional lymph nodes. The primary tumor and lymph nodes of levels I and II were irradiated through oncoming lateral fields to a total focal dose (TFD) of 44-46 Gy with brain screening. The middle and lower groups of lymph nodes (level III, IV, V, VI) were irradiated through the anterior direct field to TFD 44-46 Gy. With radical radiation treatment, after reaching TFD 44-46 Gy, the size of the fields was reduced, limited by the volume of the primary tumor and affected lymph nodes detected before treatment. With radical RT, local irradiation (boost) continued up to TFD 68-70 Gy, with postoperative — up to 50-64 Gy, with preoperative RT, TFD was 44-46 Gy.

At the V. N. Orekhovich State Research Institute of Biomedical Chemistry of the Russian Academy of Medical Sciences, studies which were conducted showed that the hydrogel used is characterized by the presence of particles of the nanometer range with a diameter of 20 to 250 nm (up to 90%), large particles of more than 1000 nm were no more than 3% (the analysis was carried out by photon-correlation spectroscopy on device N5 BeckmanCoulter; X = 648 nm) The gel has a yellow-green color characteristic of natural algae, has no specific taste and smell and is available in sterile packages after gamma sterilization of 100 ml.

The use of radio detectors based on sodium deoxyribonucleate ("Coletex-Gel-DNA-L"). Sodium alginate, which is the basis of the gel, is a natural biopolymer obtained from brown algae rich in trace elements, helps to reduce bleeding, cleanses the wound, accelerates tissue repair. It contains more than 90% of nano-meter range particles. In addition to the therapeutic effect, sodium alginate performs the functions of a carrier of a finely dispersed form of a medicinal substance and a protective colloid to prevent aggregation of drug particles. The gel envelops the mucous membrane, lubricates it and stays on this surface. Gradually, a drug is released from the gel, which has its inherent therapeutic effect. The rate of release of the drug is due to the rate of swelling of the gel. This process takes a long time, which makes it possible to attribute the "kolegel" to the therapeutic materials of prolonged action. Both the biopolymer base of the gel (sodium alginate) and the drug injected into it (derinat) have a positive effect. The gel base releases the medicine faster than the fat base, and the feeling of moisture in the mouth and pharynx persists longer.

In the preparation "Coletex-gel-DNA", the preparation "derinate sodium salt" (sodium deoxyribonucleate (Na-DNA)), approved by the Ministry of Health and Social Development of Russia

for widespread use, is impregnated into sodium alginate, which is an immunomodulator and antioxidant. The composition of the drug "Coletex-gel-DNA-L", in addition to sodium alginate and derinate, includes lidocaine for pain relief. Derinat is a universal metabolic modulator that has a non—specific general biological stimulating effect on all organs and tissues, normalizes the immune status, enhances tissue regeneration, stabilizes hematopoiesis.

Patients of the main group from the first day of RT independently applied the preparations "Coletex-gel-DNA" and "Coletex-gel-DNA-L" to the mucous membrane of the oral cavity 3 times a day for 5 ml for 40 minutes after preliminary sanitation of the oral cavity, periodically redistributing it with the tongue along the oral mucosa.

In the control group, patients from the first day of RT applied olive or sunflower oil 3 times a day after preliminary sanitation of the oral cavity.

All patients before the start of RT were informed about the occurrence of local side effects from the oral mucosa during RT and received recommendations on oral care and nutrition. Patients from the first day of treatment began rinsing the oral cavity with solutions of chamomile, furacilin. Antibacterial therapy was not used. Spicy, salty, hot, cold food, carbonated drinks were excluded from the diet.

Dental treatment of patients was carried out according to a certain algorithm (figure 1)

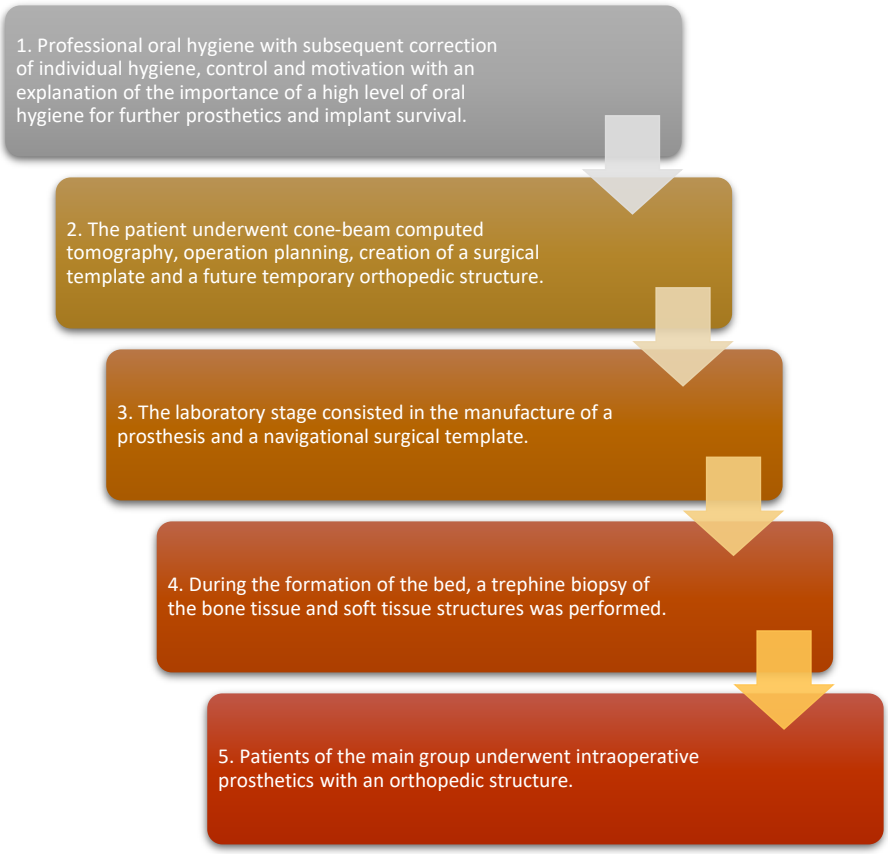


Diagram 1. Algorithm of dental treatment of patients after radiation therapy.

4. Results and discussion

Of the 79 dental implants installed in patients of the second group, 17 implants were removed due to perimplantitis. The implant survival rate is 78.5% in the control group. The evaluation of implant survival in group I and group II patients during 12 ± 2 months of follow - up is presented in diagram 2.

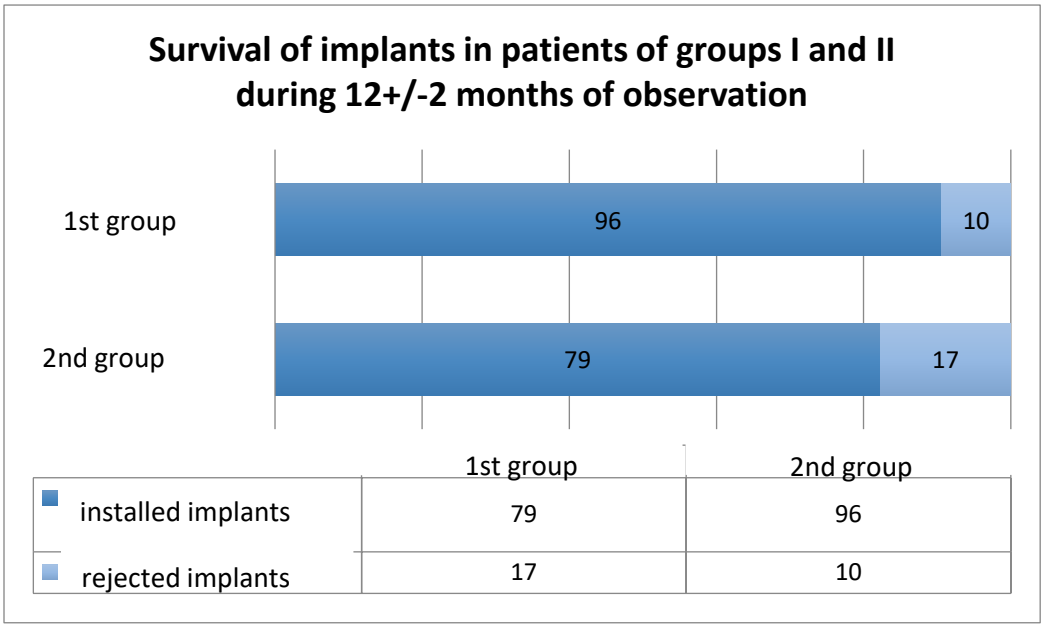
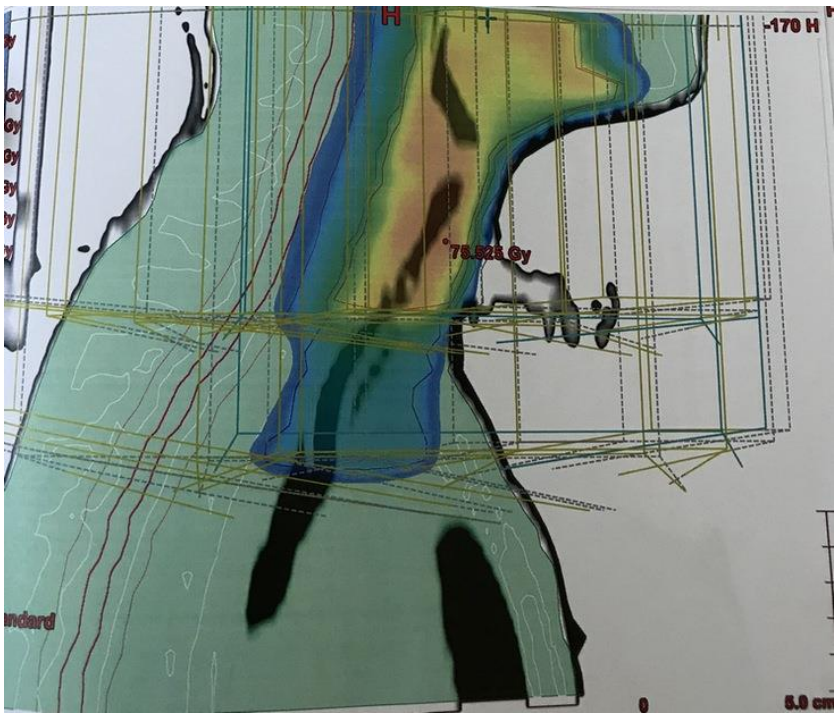


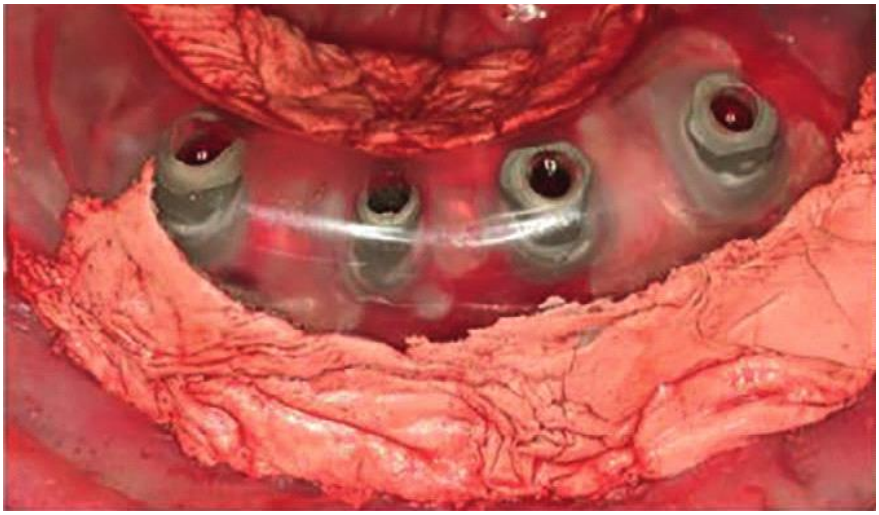
Diagram 2. Implant survival in group I and group II patients during 12 ± 2 months of follow-up.

Clinical example: Patient K., 47 years old. Diagnosis: laryngopharyngeal cancer, condition after combined treatment in 2016. Radiation therapy of TFD 38 G was performed (Field 1 – 14.3cmx10.3cm, Field 2 - 15.0 cm x 10.6 cm, setup-0 – 12.9cmx 13.5cm) (Fig. 21), two courses of chemotherapy according to the scheme: Taxotere 150 mg, Cisplatin 150 mg, 5-fluorouracil 8000 mg.

A treatment plan has been drawn up: - consultation with an oncologist; CBCT to determine the volume of bone tissue in the alveolar part of the lower jaw; study of the radiological map (in order to obtain information about the tissues of the oral cavity that have fallen into the direct focus of radiation and cannot be used to place dental implants) (Fig. 21);- surgery to install four dental implants on the lower jaw with intraoperative load; for two weeks of application with a hydrogel radioprotector based on sodium deoxyribonucleate with lidocaine.



Picture 1. Patient K. Radiation map. The irradiated area is the larynx.



Picture 2. Installation of the operational template.

Picture 3. 4 implants are installed in the intermental space of the lower jaw.

Picture 4. A metal milled beam with support on implants is made.

Picture 5. The final view of the prosthesis on the lower jaw, fixed on the beam.

We recorded changes in the mucous membrane of the oral cavity and pharynx. The results obtained were compared with the results of the control group, which used standard prevention of radiation reactions of the oral mucosa and pharynx (olive, sunflower oil) during radiation treatment. When using "Coletex-gel-DNA" and "Coletex-gel-DNA-L", allergic reactions were not detected in any patient.

Based on a follow-up period of 12 ± 2 months, the survival rate of implants in patients of the main and control groups was calculated.

Patients of the first group: out of 96 installed dental implants, 7 implants were removed due to perimplantitis. The survival rate of implants in the first group was 89.6% Table 2. In the main group, the disintegration of implants is associated with non-compliance with the recommendation (smoking, poor oral hygiene). In the control group, the disintegration of implants was manifested at the stage of installing gum shapers and fixing single and bridge-shaped structures based on dental implants.

Data on the condition of the soft tissues around the implant in comparison with the main and control groups: when using hydrogel radioprotectors based on sodium deoxyribonucleate with lidocaine, there was a decrease in the severity of pain and edema, as well as a reduction in tissue regeneration.

Based on the results obtained, it can be noted that when using the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L", there is a decrease in the frequency of radiation reactions of the III degree from 66.8 to 24.6% compared with the classical method of prevention, I and II degrees of radioepithelitis prevail, the results are reliable ($p < 0.01$). Grade IV was not observed in any patient of both groups.

The degree of severity of radiation reactions was assessed depending on the timing of their occurrence. Based on these data, it can be concluded that when using the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L", the period before the occurrence of radiation reactions of the oral mucosa and pharynx increases by an average of 8 days ($p < 0.05$).

The degree of severity of radiation reactions was assessed depending on the dose of RT. As the TFD increases, the advantage of using a gel compared to the classic option of preventing radiation reactions is noted. Thus, when summing up TFD 68-70 Gy, the frequency of grade III radioepitheliitis significantly decreases from 90.4 to 20.0% ($p < 0.05$), which is important, since 65.6% of the patients included in our study received RT according to the radical program. All patients of the main group managed to perform RT without interruption, in the control group 63.6% (49 patients) had a forced break in treatment, the results were reliable ($p < 0.05$).

5. Conclusion

The use of the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L" significantly reduces the severity of radiation reactions of the oral mucosa and pharynx of the III degree from 66.8 to 24.6% compared with the classical method of preventing these reactions. When using the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L", the continuity of the RT course is reliably ensured, which increases locoregional control. The frequency of grade III radioepithelitis significantly decreases from 90.4 to 20.0% when summing up TFD 68-70 Gy in patients who used the drugs "Coletex-gel-DNA" and "Coletex-gel-DNA-L". The period of the patient's stay in the hospital is reduced by an average of 10 bed days.

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Conflicts of Interest*:* The authors declare that there is no conflict of interest.

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