

## An integrated approach to dental implantation in patients who underwent Covid-19

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**Abstract:** The feasibility and effectiveness of complex treatment in patients with secondary adentia and past Covid-19 was assessed. The planning of dental implantation in patients who have undergone Covid-19 should be carried out with the most complete use of diagnostic procedures, including clinical, laboratory and functional examination of the patient. A systematic analysis of the studies conducted at all stages of dental treatment allows us to conclude that there are relative contraindications to dental implantation in patients with underlying pathology and who have undergone Covid-19.

**Keywords:** coronavirus pathology Covid-19, dental implantation, hemostasis.

### Relevance of the problem.

Currently, scientists around the world are paying increased attention to the problem of the Covid-19 pandemic, the entire population living on planet Earth was exposed to a mild and moderate coronavirus infection, 58% of the earth's population suffered this infection in a severe form, 27% with a fatal outcome.

On March 11, 2020, the World Health Organization declared COVID-19 a pandemic.

As of 08/03/2021, there were 199,622,425 cases of confirmed morbidity worldwide (including 131,978 in Uzbekistan), 4,250,338 deaths (including 886 in Uzbekistan) [1].

The infectious disease COVID-19 is caused by the SARS-CoV-2 virus, which belongs to the large family of coronaviruses. The virus consists of a single-stranded RNA, an envelope and a lipid layer. The novel SARS-CoV-2 coronavirus, severe acute respiratory syndrome coronavirus (SARS-CoV), belongs to the same genus of betacoronaviruses [10,11].

Ways of transmission of Covid-19 from person to person: airborne - when sneezing or coughing, contact - directly from an infected person, through infected surfaces. The entrance gates for the virus to enter the body are the mucous membranes of the nose, mouth and eyes.

The results of the research, consisting in the fact that the ACE2 enzyme is expressed in the mucous membrane of the oral cavity, and to be more precise, in the epithelium of the tongue. In this regard, the main mechanism has been elucidated, according to which the oral cavity represents a potentially high risk of infectious susceptibility to 2019-nCoV [8].

Excessive activation of systemic immunity after infection with SARS-CoV-2 causes the so-called "cytokine storm", in which released cytokines - tumor necrosis factors (TNF), interleukin-6

(IL-6) and interleukin-1 $\beta$  (IL-1 $\beta$ ) - damage body cells. This can lead to increased vascular permeability, and subsequent damage to organs such as the kidneys and heart, leading to multiple organ failure and death [10,12,13].

In case of circulatory disorders caused by the development of an infectious and inflammatory process, the most vulnerable elements of the microvascular system are primarily affected: arterioles, precapillary arterioles, blood capillaries, postcapillary venules and venules.

In the pathogenesis, clinical manifestations and course of many diseases of the oral cavity, disorders at the microhemocirculatory level are the leading link.

To date, dental implantology is a fundamentally sound approach to the treatment of adentia, which contributes to an increase in the clinical effectiveness of this complex of minimally invasive methods and their widespread introduction into the practice of modern dentistry [Losev F.F., 2010; Mirgazizov M.Z., 1999; Nikitin A.A., 2010; Olesova V.N., 2009, 2010; Robustova T.G., 2003].

However, to date, in domestic dentistry, there are practically no reports on the results of complex clinical and experimental studies in patients with a history of coronavirus infection and devoted to a comparative assessment of the clinical and economic efficiency of using microsurgical methods during dental implantation in patients with partial and complete secondary adentia.

The implantation procedure in patients with somatic pathology, especially infectious-viral etiology, can itself provoke an exacerbation of those diseases that the patient suffers from.

From the point of view of an implantologist, it is important that with prolonged arterial hypertension, reduced immunity due to Covid-19, and regular use of antihypertensive, anticoagulant drugs, the phenomenon of "rarefaction" or "discharge" occurs, which is expressed in a reduction in the total surface of the exchange vessels [Jablonski D, 2004].

The presence of concomitant somatic pathology in patients with a coronavirus infection of viral etiology who need dental implantation indicates the relevance of this problem, on the one hand, and its practical significance, on the other hand.

#### **Purpose of research:**

Improve treatment through an integrated approach in the use of dental implantation in patients who have had a coronavirus infection in preparation for prosthetics.

#### **Materials and methods of research.**

49 patients were under observation when applying for treatment for the purpose of implantation and further prosthetics were diagnosed in the anamnesis of a coronavirus infection. Treatment of patients with this pathology was carried out in the period from 2020 to December 2021 at the clinic of the Department of Surgical Dentistry and Dental Implantation of the Tashkent State Dental Institute. Among the patients, men predominated - 26 (53%). Of the examined patients, 20 people received the complex treatment developed by us. A comparison was made with patients receiving traditional treatment - 11 people, with patients without pathology of periodontal tissues - 20 people. Patients in the groups were comparable in age, gender, type of bone tissue and the depth of periodontal tissue damage. The control group included 17 practically healthy people.

The distribution according to the severity of the inflammatory process in periodontal tissues was as follows: patients with gingivitis - 16 people, mild periodontitis - 23 people, moderate - 5 people and severe - 5 people. The age of the examined patients ranged from 21 to 54 years (mean age 31.4 $\pm$ 8.2 years).

#### **Clinical Research Methods**

The program for examining patients was standardized and included the identification of complaints, the collection of anamneses, the assessment and analysis of the dynamics of clinical manifestations aimed at objectifying the disease, the course of the wound process, and determining the effectiveness of treatment. Additionally, a laboratory blood test, urine test was performed.

When assessing the local status, attention was paid to the degree of immune defense of the body, the structure of bone tissue in the area of the planned operation, and the degree of periodontal damage.

Carried out laser Doppler flowmetry using a laser analyzer of capillary blood flow - LAKK-01, coupled with a personal computer. This is a method for the non-invasive determination of tissue perfusion with blood by measuring the Doppler frequency shift that occurs when laser radiation is probed by red blood cells moving in the microvasculature. A light guide probe made of three monofilaments was used as the analyzer sensor.

To clarify the state of the bone structure of the area of the upcoming implantation, 3D Computed radiography of the jaws was performed.

#### **Assessment of the hemostasis system and rheological properties of blood**

As special research methods, indicators of the antithrombogenic activity of the vascular wall and the rheological properties of blood were used.

To determine the antithrombogenic properties of the endothelium of the vascular wall (antiaggregation, anticoagulant and fibrinolytic activity), a method is used based on the creation of a short-term (5 min.) Local ischemia caused by applying a sphygmomanometer cuff to the subject's shoulder and creating a pressure in it that exceeds the systolic pressure by 10 mm Hg. Art., which leads to the release of prostacyclin, nitric oxide, endothelins, antithrombin III, tissue plasminogen activators from the vascular endothelium of healthy people into the blood. Determination of the content or activity of hemocoagulation factors in the blood taken before and after a short-term occlusion of the vessels, makes it possible to judge the state of the antithrombogenic activity of the vessel wall (Baluda V.P. et al., 1992).

Studies in patients who were at rest were carried out in the morning, on an empty stomach. A tourniquet was applied to the shoulder of one arm, the cubital vein was punctured with a siliconized needle, and blood was taken by gravity into a non-wetted plastic tube up to the 10 ml mark. A 3.8% solution of sodium citrate in a ratio of 9: 1 was used as a stabilizer.

A sphygmomanometer cuff was applied to the second arm, systolic pressure was determined, and the pressure in the cuff was increased by 10 mmHg. and after 5 minutes, 9 ml of blood was taken into a test tube containing 1 ml of 3.8% sodium citrate solution.

Both tubes were centrifuged for 10 minutes at 1000 rpm to obtain PRP.

We determined platelet aggregation before and after the creation of short-term ischemia of the upper limb by the method proposed in 1989 by Z.A. Gabbasov et al., using a laser aggregation analyzer "BIOLA" 230 Ltd (Russia), interfaced with an IBM-compatible computer and a specialized MS Windows - compatible program "Aggr" (SPF "Biola").

Based on the determination of the maximum degree of platelet aggregation in plasma obtained before the cuff test, the aggregation ability of the patient's platelets was judged. Based on the results of determining the maximum degree of platelet aggregation in plasma obtained before and after the cuff test, and calculating the index of antiaggregation activity, the antiaggregation activity of the endothelium of the vascular wall was judged. The total antiaggregatory activity of the vessel wall was expressed by an index equal to the quotient of dividing the indicator of the maximum degree of platelet aggregation before cuffing by the indicator of the maximum degree of platelet aggregation after cuffing.

An open method of dental implants was used (with simultaneous installation of gingival edge shapers)

When examining patients at the preoperative stage, we used general clinical (taking an anamnesis, examining the site of the proposed implantation, measuring blood pressure and pulse), radiological (aimed radiography, panoramic sonography (orthopantomography) and computed tomography), functional and laboratory methods of examination (laser Doppler flowmetry, ECG, periotestometry, biochemical blood test)

To assess the quality of the bone, we used the classification of bone density Misch and Judy, 1987, in comparison with the data of the X-ray scale for assessing tissue density, expressed in Hounsfield units

To confirm the diagnosis of Covid-19 in history, PCR studies and testing for the presence of antibodies to SARS-CoV-2 coronavirus infection IgM Screen (Covid-19) were carried out

Statistical processing of the obtained data was carried out using variational statistics, the arithmetic mean value was calculated, the degrees of freedom of the arithmetic mean value. The significance of differences between the mean values of the study groups and control groups was determined by Student's t-test.

### Research results and discussion.

All patients had partial absence of teeth, where the last extraction was carried out at least 6 months ago. After the completion of the procedure for installing dental implants, clinical observation of patients was carried out, which included the following steps: clinical assessment of the effectiveness of the functioning of the orthopedic crown and the condition of the periodontal tissues near the implants; measurement of their stability by resonance frequency analysis (RFA) using the Osstell ISQ apparatus (Osstell AB, Sweden).

In the immediate postoperative period, when examining the patient, his general condition after intraosseous implantation was also assessed according to the following criteria: the presence of complaints, including pain in the area of the operation; Body temperature; the presence of hematoma and swelling of the face;

The condition of the submandibular and cervical lymph nodes; the degree and nature of changes in the mucous membrane of the alveolar process in the area of operation; discomfort and pain during the act of chewing in cases of immediate loading of the implant.

Photographing of the patient and the implantation site was carried out immediately at the time of implantation, 7–10 days, 1,2,3,4,5, 6 months after implantation in the upper jaw and 7–10 days, 1,2,3 months after implantation on the lower jaw (Fig. 1 and Fig. 2).

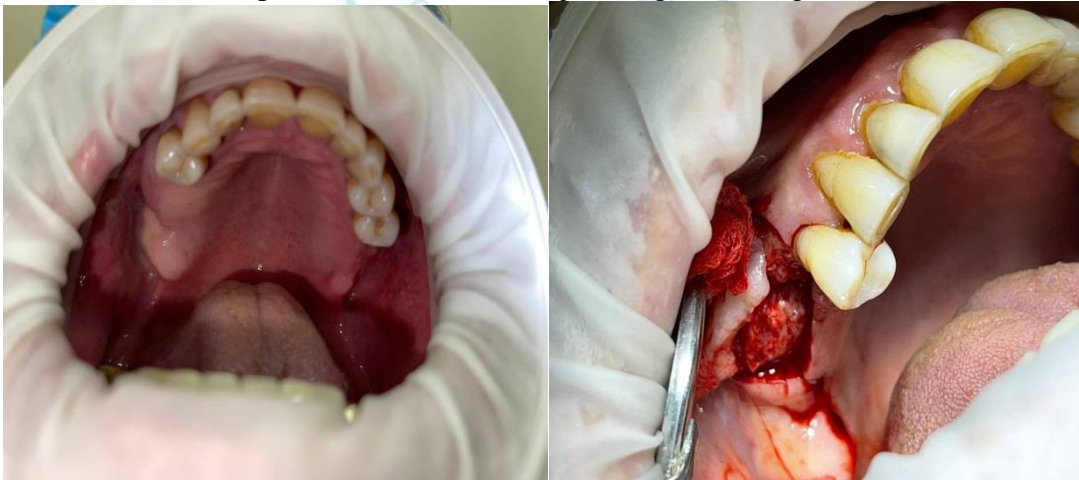


Fig.1 a - upper jaw before treatment; b-moment of implant installation

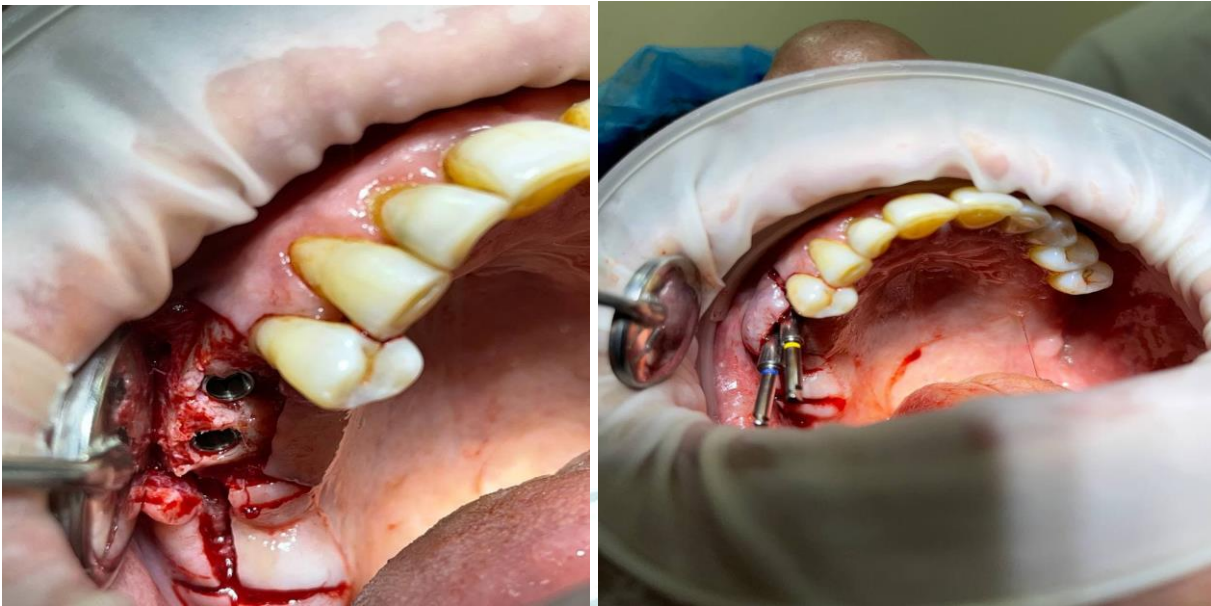


Fig. 2 a - the implants are immersed in the implantation bed; b-checking the parallelism of the installed implants.

LDF-metry of patients was performed in a dental chair, in a sitting position before the start of treatment and 1 month after the proposed drug treatment.

Table 1. Indicators of LDF signal amplitudes before treatment

Indicators	M, perf. units	$\sigma$ , perf. units	Kv,%
Control group	26,51 ± 1,88	2,60 ± 0,40	12,44 ± 0,80
I group	32,57 ± 1,98	1,85 ± 0,16	6,60 ± 1,05
II group	32,29 ± 0,67*	2,98 ± 0,77*	6,93 ± 1,43



Fig.3 a-patient with atrophied lower jaw; b-separation of the mucous membrane

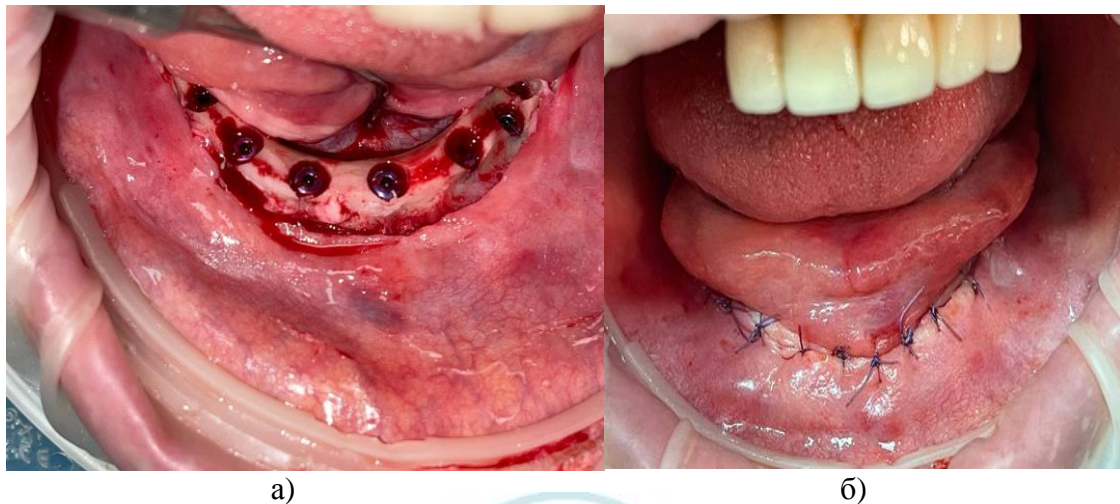


Fig. 4 a-Implants were installed in the alveolar process of the lower jaw;  
b-mucous membrane sutured with polyamide thread

In the group of individuals with complete secondary adentia of the upper jaw, the LDF-gram made it possible to identify the normative parameters of microcirculation in the oral mucosa (Table 1). Thus, in the group of healthy individuals, the value of capillary blood flow in terms of the microcirculation parameter (PM) was  $26.51 \pm 1.88$  perf. units. The mean square deviation of blood flow fluctuations (RMS) was  $2.60 \pm 0.40$  perf. units, and the coefficient of variation (Kv) was  $12.44 \pm 0.80\%$ .

From table 1 it follows that the values of the LDF-gram are increased in the group with the most pronounced inflammatory reaction of the oral mucosa compared to the control group. This is evidenced by an increase in the index of microcirculation in group II by 48-53%, which reflects stagnation in the study area. A pronounced decrease in the level of such indicators as "flux" and the coefficient of variation indicates violations of the rhythmic structure of tissue blood flow oscillations, which is associated with a deterioration in tissue perfusion with blood.

In the second group of patients, with severe periodontitis, before the start of treatment, when studying the capillary blood flow of the mucous membrane, pronounced microcirculatory disorders were noted: the microcirculation index was  $32.57 \pm 1.98$ , SD -  $1.85 \pm 0.16$ ; the coefficient of variation was  $6.60 \pm 1.05\%$ , at which a complex of changes occurs, associated with a sharp difficulty in the outflow of blood, disturbances in the structure of microvessels and the barrier function of their walls. When studying the statistical analysis of the data obtained using LDF-metry, we did not reveal significant differences between groups I and II ( $p > 0.05$ ). In the first group of patients, we obtained the following average values of capillary blood flow: PM —  $32.29 \pm 0.67$ ; SD —  $2.98 \pm 0.77$ ; Kv -  $6.93 \pm 1.43\%$ . The data obtained show that the blood flow intensity of both comparison groups differ significantly from the values of the control group (table).

Table 2. Indicators of LDF signal amplitudes one month after the start of treatment.

Indicators	M, perf. units	$\sigma$ , perf. units	Kv,%
Control group	$29,57 \pm 1,38$	$2,80 \pm 0,46$	$14,41 \pm 0,35$
I group	$31,97 \pm 1,65$	$2,15 \pm 0,11$	$6,58 \pm 1,43$
II group	$34,50 \pm 0,13^*$	$3,01 \pm 0,14^*$	$8,98 \pm 1,62$

Statistical analysis of LDF-metry data after a month in patients showed the following values (Table 2).

When examining a month later in patients of the group without additional treatment, the arithmetic mean values of the PM index in the study area of the tissues of the prosthetic bed were  $31.97 \pm 1.65$  perf. units,  $\sigma$  -  $2.15 \pm 0.11$  perf.un. and Kv -  $6.58 \pm 1.43\%$ . In the group of patients who were prescribed, in addition to the complex treatment, the drug "thyrocalcitonin" (Fig. 3 and

Fig. 4), the average values of the LDF-metry parameters were: PM -  $34.50 \pm 0.13$ ; SD —  $3.01 \pm 0.14$ ; Kv -  $8.98 \pm 1.62\%$

Insignificant changes in LDF-metry parameters were noted in the group of the most pronounced inflammatory changes in the mucous membrane and without additional treatment, compared with the control group. This is evidenced by PM: there is a slight increase in the level of the LDF signal on the mucosa of the prosthetic bed. An increase in the RMS by only 7.4% compared with the previous study indicates a low elasticity of the vascular wall, an increase in the inflow of arterial blood into the microcirculatory bed, reduced microcirculatory pressure, deterioration of blood outflow, and residual manifestations of blood stagnation in the microcirculatory bed.

The constant values of the coefficient of variation indicate a decrease in the elasticity of the vascular wall, impaired outflow in the microcirculatory bed, as a result, an increase in blood volume in the microcirculatory link, which indicates the presence of congestion in the oral cavity. It should be noted that during this period of time there were no exacerbations of the disease, the LDF-gram was performed on the unchanged oral mucosa, and not in the lesion.

A statistically significant difference between the values of the coefficient of variation in group II, in relation to group I, indicates an improvement in the state of microcirculation in patients who, in addition to local treatment, received the drug thyrocalcitonin. In this group, the coefficient of variation increased by 1.3 times compared with the initial values, which indicates a decrease in congestion in the oral cavity, which indicates the launch of compensatory-adaptive mechanisms in group II. Perhaps this is due to the ability of calcitonin, which is involved in the regulation of phosphorus-calcium metabolism in the body, as well as the balance of osteoclast and osteoblast activity. A statistically significant difference in Kv values indicates more pronounced inflammatory manifestations in patients who did not take any additional treatment.

Thus, the use of LDF-metry in patients with secondary edentulous jaws on the background of Covid-19 disease makes it possible to optimize existing pathogenetic therapy regimens based on various combinations of drugs. Laser Doppler flowmetry can be used both to monitor the state of microcirculation and to control drug exposure.

Measurement of stability by resonance frequency analysis (RFA) using the Osstell ISQ apparatus was carried out in groups 1 and 2 - immediately at the time of implantation, 6 months after implantation in the upper jaw and 3 months after implantation in the lower jaw.

X-ray assessment of the degree of osseointegration of the dental implant and the state of the jaw bone tissue near it was performed during the following time intervals: 3 months and 6 months after implantation.



Fig. 5 Computer study of a patient with a history of secondary edentulism with Covid-19. postoperative monitoring.

As a rule, to assess the state of the tissues of the bone-implant interface, targeted radiography in the area of installed implants and a standard orthopantomographic study were used.

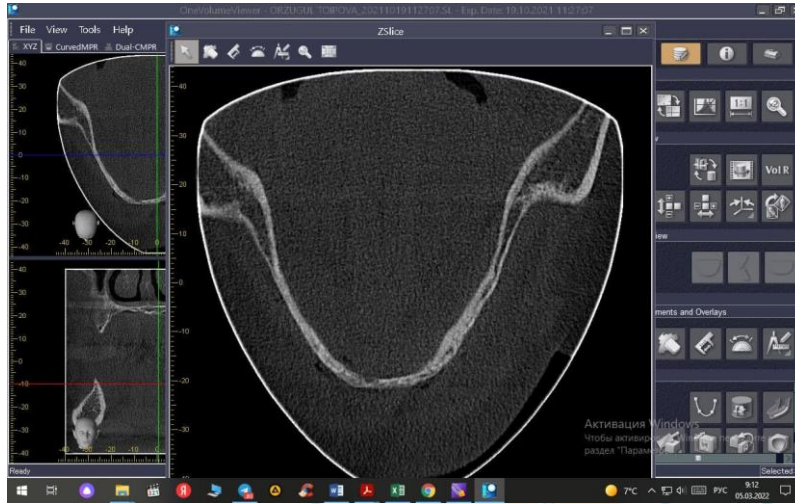


Fig.6 Computed tomography before implant placement

Computed tomography was performed before the installation of implants (Fig. 6) a week after the surgical stage of implantation, after the installation of prostheses, 6 months after prosthetics, then, in the absence of complaints from the patient, with an interval of one year.



Fig.7 One week after the surgical stage of implantation,



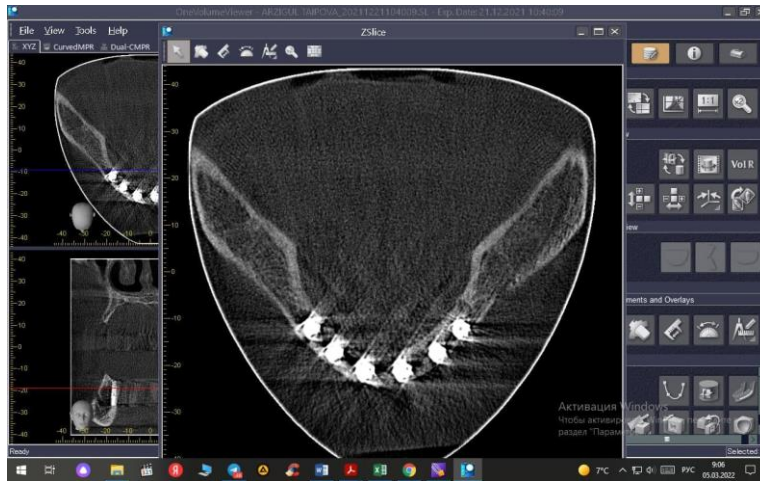


Fig. 8. 3 months after surgery.

Six months after the start of the full functioning of the implants, the X-ray study also did not show any visible bone resorption, both in the control group and in the studied ones.

A week after the manipulation, in patients of the control group, as a rule, there was a slight horizontal resorption in the area of the necks of the installed implants.

Two years later, after the surgical stage of dental implantation, some patients of the control group (40%) have horizontal bone resorption in the area of the bone-implant interface. Its average value is approximately  $0.8 \pm 0.2$  mm.

It should be noted that the presence of horizontal resorption of the bone tissue of the bone-implant interface with a depth of no more than 1.5 mm at a period of 2 years from the moment of implant placement is normal and does not have any negative prognostic impact.

### Conclusions.

1. Based on the results of modern diagnostic methods, a comprehensive approach has been developed for dental implantation in patients with a history of Covid-19, which allows assessing the local status of mucosal tissues in the area of planned intervention.

2. When planning the implantation operation, evidence was obtained of a slowdown in the blood flow of the microvasculature in the tissues of the area of the proposed intervention, which undoubtedly has a negative impact on the process of osseointegration.

3. For patients who received the drug "thyrocalcitonin" during the interventions, the coefficient of variation increased by 1.3 times compared with the initial values, which indicates an improvement in the state of microcirculation, as well as a decrease in congestion in the oral cavity, which indicates the launch compensatory-adaptive mechanisms in group II.

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