Medical University -Varna
„Prof. Dr. Paraskev Stoyanov”

Faculty „Dental Medicine”
Department “Periodontology and dental implantology”

Single-photon emission computed tomography with 99mTcMDP (methylene diphosphonate) of periimplant bone during the healing period after placement of intraosseous osteointegratable implants

ABSTRACT

of dissertation for the award of educational and scientific degree "Phd"

Dr. Ivaylo Georgiev Hristov

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Supervisors:
Prof. Dr. Stefan Vasilev Peev, PhD, Dsc
Assoc. Prof. Dr. Borislav Georgiev Chaushev, Ph.D.

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The dissertation contains 151 standard pages and is illustrated with 11 tables, 26 figures, 30 photos and 7 appendices. The literature reference includes 402 literary sources, of which 9 in Cyrillic and 393 in Latin.

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External members:

1. Prof. Dr. Irena Dimitrova Kostadinova, PhD, Dsc
2. Prof. Dr. Angelina Pecheva Vlahova-Petrova, Ph.D.
3. Assoc. Prof. Dr. Blagovesta Konstantinova Yaneva, PhD

Spare external member:

1. Prof. Dr. Bozhidar Ivanov Yordanov, Ph.D.

Internal members:

1. Prof. Dr. Anelia Dimitrova Klisarova, PhD, Dsc
2. Assoc. Prof. Dr. Miglena Ilieva Balcheva-Eneva, Ph.D.

Spare internal member:

1. Assoc. Prof. Dr. Georgi Yordanov Papanchev, Ph.D.

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The materials on the defense are available in the Scientific Department of MU - Varna and are published on the website of the Medical University - Varna.

Note: In the abstract the numbers of the tables and figures correspond to the numbers in the dissertation.

CONTENTS

ABBREVIATIONS USED

AOI	Osteoblastic Activity Index
DICOM	Digital Imaging and Communication in Medicine
DRDO	DRDO dental implant system
FEA	Finite element analysis
SRP	Scaling and root planing
MIT	Maximum Insertion Torque
ISQ	Implant Stability Quotient

1. Introduction

Treatment with intraosseous osteointegrable dental implants is a modern therapeutic method that achieves complete rehabilitation by fully restoring the patient's masticatory function and aesthetics. The success of implant application is associated with the process of osseointegration.

Osteointegration is the process of bone formation between the alloplastic material and the surrounding biological environment. Achieving primary stability during implant placement is of paramount importance for this complex multi-stage recovery period.

Successful treatment is determined by the presence of adequate bone structure (quantity and quality), the deficiency of which is a major obstacle to the placement of intraosseous dental implants, especially in the distal parts of the upper jaw. The bone in this area is loose, contains mostly spongy and a small amount of compact bone.

Tooth loss means loss of functional load in a certain bone volume, which leads to functional atrophy of the edentulous area.

Bone resorption begins at 15 weeks after tooth extraction and reaches approximately 60% over a period of 3 years. Jaw resorption of the maxilla is in the centripetal direction, while the mandibular resorption has a centrifugal pattern. jaw.Changes in bone structure are followed by changes in the structure of soft tissues, leading to extraoral facial changes .. These changes become an aesthetic problem for patients.

The resorption of the lower jaw is four times faster than in the maxilla. Mandibular resorption is about 1.2 mm in the first year after extraction, increasing by about 0.2 mm per year [67].

Lack of enough bone for implant placement may also be due to anatomical features: widely exposed maxillary sinus-pneumatic type, anatomical variations in the course and position of the mandibular canal and the vascular nerve bundle passing through it.

What has been said so far requires additional surgical procedures or the use of reduced-length implants.

The implant design, the characteristics of the implant surface, the quantity and quality of the bone in which it is placed, the surgical technique used, the loading conditions and last but not least the patient's health condition are directly related to the process of osseointegration.

Monitoring the healing period after implant placement is an important component of the healing process, the analysis of which allows us to continue with the next stage of treatment or to postpone the load of the implant placed in the bone with the prosthetic structure. Of interest are the methods for studying this process. Assessment of the time and degree of osseointegration, the influence of age and gender.

Bone morphology in the peri-implant area can be assessed radiologically and histologically. The use of computed tomography (based on the Hounsfield scale) determines bone density, but cannot measure the vitality and functional state of bone structure. This can be achieved through nuclear medical research. Nuclear medical research provides data on ongoing physiological processes and activities in various organs based on the accumulation of various markers. The use of radiographic research methods to assess the healing process is considered inaccurate.

Today in the literature there is no sufficiently detailed and systematic analysis of the study of osteoblast activity in the periimplant bone during the healing period, with the placement of intraosseous osteointegrable dental implants..

2. Purpose, tasks

2.1. Purpose

The aim of this dissertation is to evaluate the application of single-photon emission computed tomography (SPECT]) with 99mTc-MDP (methylene diphosphonate) of periimplant bone in the healing period after placement of intraosseous, osteointegratable implants.

2.2. Tasks

2.1 Examination of the peri-implant bone tissue in the recovery period after the placement of intraosseous osseointegrable dental implants using single-photon emission computed tomography [SPECT] with 99mTc-MDP.

2.2 Examination of bone density in the implantation areas using CBST. Comparison of results obtained from single-photon emission computed tomography [SPECT] with 99mTc-MDP with bone density before implantation.

2.3 Evaluation of osseointegration in the third month after placement of intraosseous osseointegrable dental implants with the help of resonance-frequency analysis.

Comparison of the results obtained from the SPECT study with those of resonance-frequency analysis period after placement of intraosseous, osteointegrable implants.

3. Material and methods

3.1. Material task № 1

3.1.1. Material base for realization of task № 1

The study was conducted on the territory of:

- UMDC at the Medical University - Varna:
    - Imaging Diagnostics Department
    - Surgical unit

Department of "Nuclear Medicine and Metabolic Therapy" at the University Hospital "St. Marina ”, Varna

3.1.2. Object of the study

The subject of the study were 10 patients (5 men and 5 women) with a total of 23 implants, with an average age of 40.3 years (28-64 years). They underwent implant treatment at UMDC at the Medical University - Varna.

3.1.3. Selection of patients

The study involved male and female patients over 18 years of age, in good general health: no concomitant diseases, no systematic medication, which may affect the surgical manipulation of implant placement and disrupt the process of osseointegration. The examined patients have extracted teeth in the upper and / or lower jaw and the presence of sufficient bone volume to ensure the placement of implants without the need for bone augmentation.

Each patient was informed of the purpose of the study and signed a declaration of informed consent for the imaging examination for available bone (CBCT) [application 1], a declaration of informed consent for surgical manipulation of implant placement. Annex and declaration of informed consent for the subsequent nuclear test [application 2].

Age, gender and social status do not play a leading role in the distribution of patients in different groups.

Exclusion criteria from the study:

- Insufficient bone volume in the edentulous areas
- conditions of general and local nature that lead to delay or hinder the healing process
- malignant diseases
- intravenous bisphosphonates
- previous radiotherapy in the oral cavity
- uncontrolled systemic diseases
- immunosuppressive therapy in transplant patients
- systemic intake of anticoagulants and antiplatelet agents for other diseases
- mental illness
- sensitivity to titanium
- acute and chronic inflammatory processes involving hard and soft tissues in the oral cavity
- contraindications for nuclear medical research
- pregnancy
- incomplete development of the maxillofacial area

3.1.3.1. Evaluation of the characteristics of patients undergoing treatment with dental implants

During the study, a clinical and paraclinical assessment was performed on 51 patients with a mean age of 46.1 years (20-84 years), of whom 62.7% (32 patients) were men and 37.3% were women (19 patients). Of the examined and evaluated patients 40 (78.4% - 27 men and 14 women) dropped out due to the following reasons [Fig. 3].

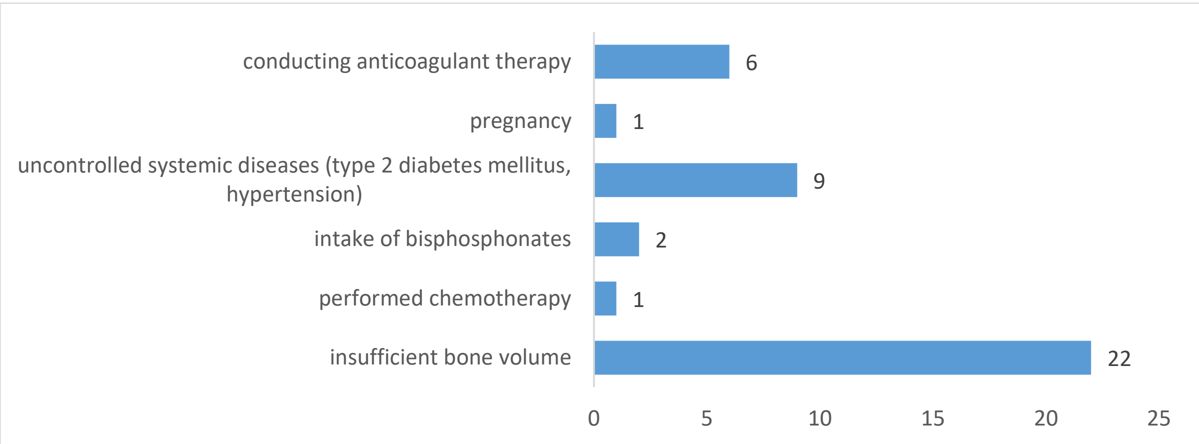

FIG. 3. Number of patients dropped out of the study due to the described exclusion criteria

The study included 10 patients (5 men and 5 women) with a mean age of 40.6 years (28 - 64 years) who underwent implant treatment. The total number of implants is 23, and the distribution is presented in table. 3. The number of implants placed per patient varies from 1 to 5, with the most frequently implanted area being in the range of 36 and 46. About 2/3 of the implant treatment is in the lower jaw (65.2%).

Table 3. Description of the patients participating in the study

Sequence of the patient	Age	Gender	Number of implants	Implant position
1	28	M	1	26
2	48	M	5	15, 24, 25, 46, 47
3	32	M	4	14, 15, 36, 46
4	40	M	3	36, 37, 46
5	37	M	1	24
6	31	F	2	35, 45
7	42	F	2	34, 44
8	28	F	2	16, 45
9	64	F	2	35, 36
10	48	F	1	44

There was a statistically significant difference in the number of implants placed between men and women (respectively 14: 9; $p < 0.05$).

It is impressive that the greater number of implants placed in the upper jaw are in men (7 for men and 1 for women). On the other hand, it was found that patients with implants in the upper jaw were younger (37.6 years for the upper jaw and 42.0 years for the lower jaw, respectively), with no significant difference.

According to the area of the implanted tooth, regardless of the jaw, it was found that the most common implant treatment was performed in the area of the 5th and 6th teeth [Fig. 4].

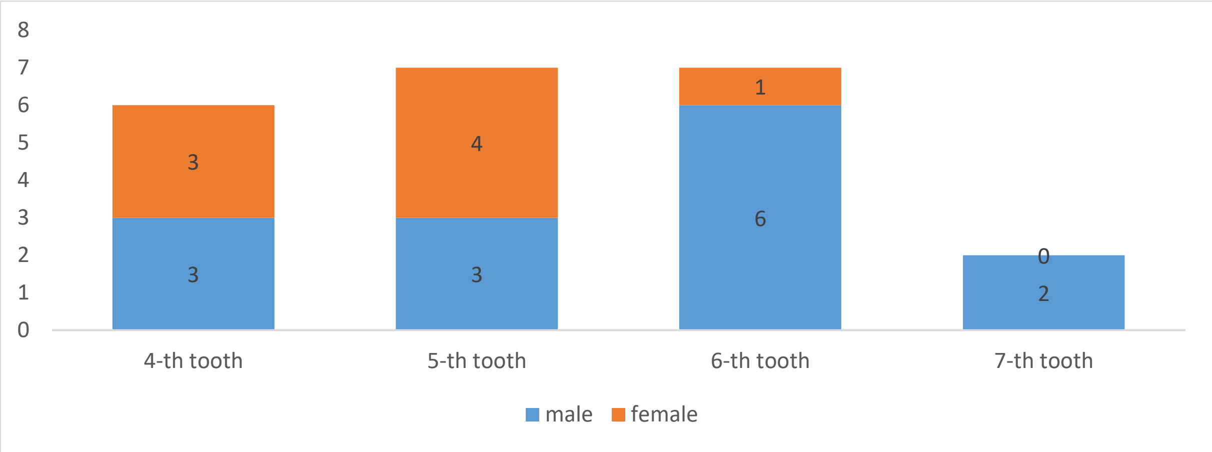

FIG. 4. Distribution of the number of implants according to the area of teeth and gender

Despite the variation in the number of implants placed in different areas, no significant difference was found between men and women. There is no difference in the age of the patients and the implant area.

The high success rate of intraosseous implants is well documented. The five-year survival of dental implants has been reported in the literature to be 95-99% [88, 264]. Despite the high success rate, treatment with dental implants requires a precise assessment of the clinical situation. When choosing the place of implantation, not only the quantity and quality of the bone is taken into account, but also the configuration and type of the future prosthetic structure. The optimal length, diameter and stroke of the implants, the future retention of the prosthesis are determined [213]. Achieving good primary stability during implant placement, rapid and high-quality osseointegration, and asymptomatic functional loading of implants are the three main indicators of the success of dental implant treatment [301].

In terms of demographics, Brager et al reported a higher incidence in 2005 of female patients (55 women to 34 men) who required implant treatment [56]. On the other hand, Ko et al, in a 2006 study in two dental centers in South Korea, reported a higher proportion of male patients who underwent implant treatment [197]. In the present study, the initial assessment of patients in need of implant treatment also showed a higher incidence of men (62.7% versus 37.3% of women).

Systemic diseases influence the decision to treat with dental implants. Uncontrolled systemic diseases are part of the exclusion criteria in the present study and therefore 9 patients (17.6%) dropped out of the further procedure. In his study, Rasouli Ghahroudiet al. [293] in 2015 reported that 7.2% of patients with upper jaw implants and 9.5% of those with lower jaw implants had systemic diseases. Another team, Ko et al., Found that 9% of patients in their sample suffered from systemic diseases [197]. The presence of systemic diseases is among the main risk factors for failure of implant treatment and contraindications when the condition is uncontrolled. Therefore, systemic diseases should be carefully assessed, treated and controlled prior to implant treatment, which reduces the risk of failure.

3.2. Task methods № 1

3.2.1. Patient preparation, clinical trials and research indicators

A thorough clinical examination was performed before conducting and analyzing the imaging study to assess the available bone volume and to determine the site of implantation in the dentate areas. Each patient fills in a questionnaire with questions related to general health, hereditary predisposition, past and concomitant diseases, bad habits, medication, allergies, pregnancy. [application 3]

Extra and intraoral examination was performed, assessment of the edentulous areas was performed - number of missing teeth, location, age and cause of tooth loss, assessment of residual dentition [presence of carious lesions, obturations, prosthetic structures], occlusion assessment, intermaxillary relations, freedom of movement of the lower jaw, blockages and preliminary contacts, search for signs of parafunction (bruxism and bruxomania), the presence of local contraindications, assess the position of adjacent teeth to the jagged areas, and their antagonists from the respective half of the The purpose of this study is to determine the effect of Popov-Godon and to predict the possibilities for positioning the implant and future prosthetic restoration. Examine the mucosa and tongue of patients - color, texture, presence of lesions.

All patients who will be included in the study underwent preliminary preparation and rehabilitation of the oral cavity. A periodontal map was prepared according to Prof. St. Peev, PhD, used in the Department of Periodontology and Dental Implantology, FDM, MU-Varna [Appendix 4] Measured: plaque index [PI], gingival index (BoP), depth of probing (PD) and level of margo gingivalis, furcation damage, width of the attached gingiva, mobility and prognosis of each tooth. Lang and Tonetti periodontal risk assessment was performed on each patient based on information from the periodontal chart. Hexagon with six coordinate axes is used to calculate it (bleeding during drilling, number of surfaces with DS ≥ 5 mm, number of missing teeth, percentage of bone loss and age, smoking and systemic diseases). [Appendix 5]

Probing depth (PD) is the distance from the margo gingivalis to the bottom of the sulcus or pocket, measured in mm with a periodontal probe. The probe is inserted into the pocket parallel to the longitudinal axis of the tooth without losing contact with the tooth surface until a feeling of resistance is felt from the bottom of the sulcus / periodontal pocket. After inserting it into the pocket, the probe advances with a step of 1 mm and an amplitude up and down 1-2 mm, to identify the depth of the pocket for each area, and when lifting the probe for the next step, it does not come out of the pocket. The highest recorded value for each area is recorded.

The measurements are performed with a manual periodontal probe of the University of North Carolina (UNC 15), which is color-coded every millimeter to 15 mm and has colored rings between 4-5 mm, 9-10 mm, 14-15 mm. The pressure is 0.25-0.30 N.

The level of margo gingivalis is the distance in millimeters from the gingival margin to the enamel-cement boundary (ECB). The periodontal map records 6 values for each tooth in the areas described for drilling depth. When the gingival margin is located coronally by the ECB, the values are positive, and if it is located apically, they are negative. In the case of margin gingivalis at the ECB level, a value of "0" is recorded. In the presence of a non-removable prosthetic structure (bridge or crown), the edge of the structure is taken as a reference limit when measuring the level of margo gingivalis.

The clinical level of attachment (CAL) is the distance from the ECB to the bottom of the pocket. It can be measured with a periodontal probe or calculated in the presence of the other two parameters - depth of probing and level of margo gingivalis.

Drilling of furcation areas in multi-rooted teeth is also performed. The study is performed with Nabers - 1 and 2 furcation probes. The probes can be color coded with 3-6-9-12 mm delineation with colored rings between 3-6, 6-9 and 9-12. Nabers 1 is used for probing the upper premolars and molars, and Nabers 2 for the lower molars. The Ramfjord & Ash classification (1979) is used to classify the degree of furcation involvement.

Class 1 - with horizontal drilling the probe enters up to 3 mm

Class 2 - when drilling horizontally the probe enters over 3 mm, but without completely passing the furcation

Class 3 - in horizontal drilling the probe passes completely through the furcation

And Tarnow & Fletcher (1984) divide each class into three subclasses according to the degree of vertical impact:

subclass A - vertical bone loss up to 3 mm

subclass B - vertical bone loss from 3 mm to 6 mm

subclass C - vertical bone loss over 6 mm

Tooth mobility is determined according to the Miller classification, 1985:

1 - horizontal mobility up to 1 mm

2 - horizontal mobility over 1 mm

3 - horizontal and vertical mobility

Plaque control index (PI) according to O'Leary et al., 1972. This index reflects the presence or absence of plaque on all teeth and tooth surfaces. The presence is recorded with a "+" sign in the relevant fields of the periodontal card and the "-" sign reflects the absence. The obtained data are numerically expressed by the percentage of the number of places occupied by plaque in relation to all examined tooth surfaces - 6 for each examined tooth, three vestibular and three lingual / palatal (MV, CV, DV, ML, LC, DL).

The study of gingival status is performed with gingival index (bleeding index BI) according to Animo & Bay, 1975. Bleeding at probing (BP) is registered by gradual introduction of the periodontal probe, similar to the study of DS and respectively in the periodontal map reflects the presence or absence of bleeding with a "+" or "-" sign. The index is recorded as a percentage of the number of bleeding sites relative to all examined sites. The width of the attached site is measured - the difference between the distance from the gingival margin to the mucogingival line and the depth of probing.

Pic.1 Periodontal probe UNC 15

Pic.2. Left - Nabers 1 without color marking. Right - Nabers 2 color code

Pic. 3. Combined device - ultrasound with polishing system.

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3.2.2. Imaging research

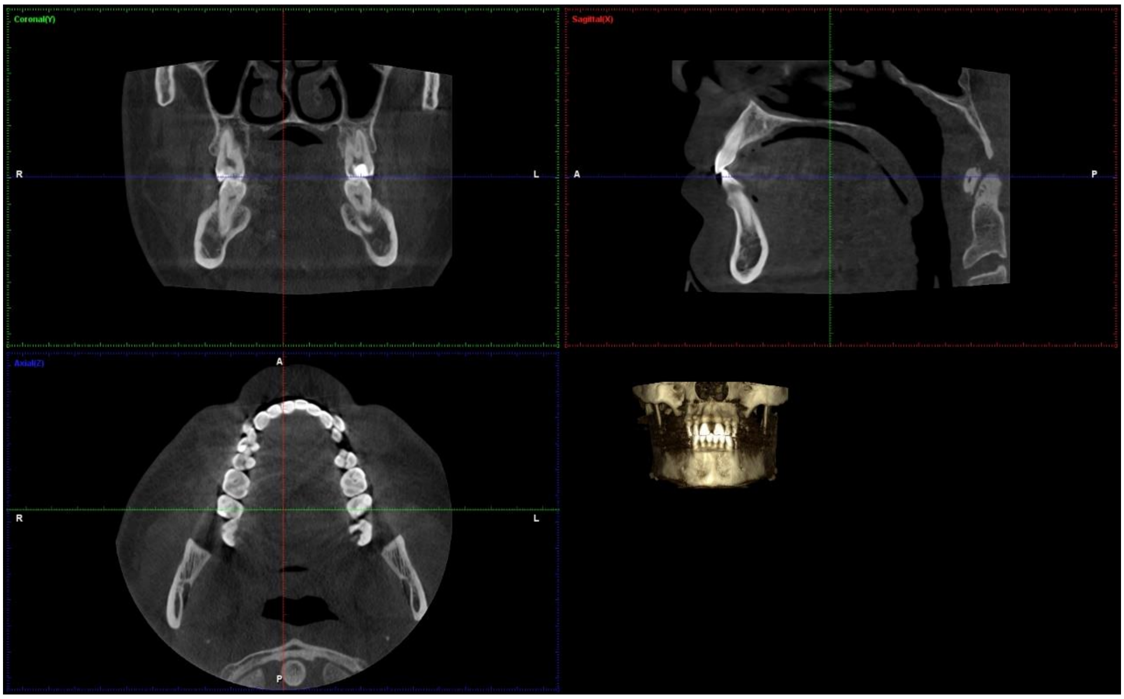
Prior to implantation, each patient underwent 3D imaging - Cone Beam Computed Tomography (CBCT) of the upper and lower jaw with Planmeca Pro Max 3D Max Helsinki, Finland, with the following parameters: pipe voltage of 96kV, current 5.6mA, rotation time of 12.8s,, [Pic. 4] and CCD-detector - flat panel of amorphous silicon transforming the energy from X-rays into a digital signal

Pic. 4. Conical beam computed tomography apparatus

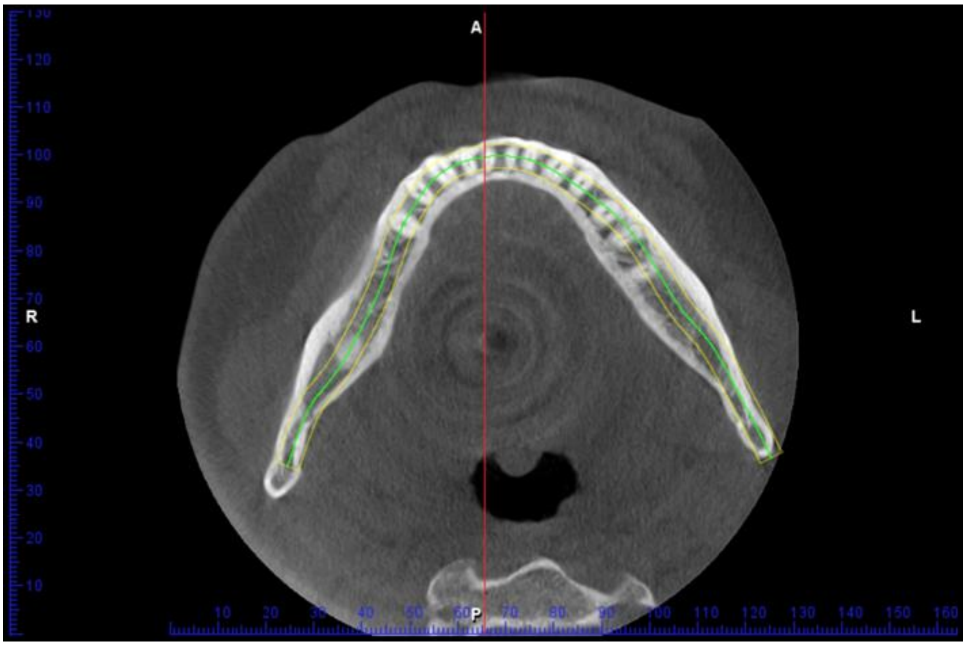
Field of View (FOV) in jaw and maxillary sinus images varies between 90 * 130mm 130 * 160mm

Voxels [volume pixels] are isotropic - with the same size on the three axes of the coordinate system. In the present study, the size of the voxel is 0.2 mm.

Pic. 5. Setting the settings and volume of the study area



Pic. 6. Positioning the image relative to the three main planes



Pic. 7. Draw a panoramic curve

The study was performed in the Department of Imaging Diagnostics at the University Medical and Dental Center (UMHC), FDM, Varna by a specialist in Dental Imaging and X-ray technician.

Prior to the examination, each patient signed an informed consent for the imaging examination. All metal objects falling into the study area are removed. A protective lead apron with 0.50 mm lead equivalent is placed. The patient is in an upright position during the examination, and the head is stabilized in a stationary position with the help of the fixing system of the device, the mouth is slightly open during the scan. The tongue is positioned as distally as possible, touching the palate with its tip so as not to fall into the field of view. planes, the occlusal plane being parallel to the floor. The volume of the studied area is set in advance from the software of the device. The X-ray tube together with the detector rotates from 180 to 360 degrees around the patient's head for a time between 10-40 seconds. software Planmeca Romexis-the obtained image is reconstructed in MPR (-multi-plannar reconstruction) mode in the three planes-

sagittal-separating the object on the left and right part

coronary-separating object at the anterior and posterior

axial-dividing the object into upper and lower part

This study aims at a comprehensive analysis of the condition of the dental apparatus.

The panoramic curve is set on the axial section of the upper or lower jaw.

On the cross-section [cross-section of the upper or lower jaw] with an incision interval of 1.5 mm we move to the implantation area, make measurements of the available bone volume in the edentulous area. of future implants. We assessed the position of natural anatomical structures, such as the level of the sinus floor, the floor of the nasal cavity, the position of the mandibular canal, the location of the mental foramen, anatomical variations are sought and evaluated. We also estimated bone density using Hounsfield units [HU]

3.2.3. Implants used

The study used intraosseous osteointegratable implants Neodent A Straumann Group Brand - Alvin CM Implant Line - conical design of the implant body, double conical trapezoidal thread, apical active tip, optimizing secondary stability, conical morse bond, SLA surface. Used lengths - 8-10 mm and used diameters - 3.5 mm, 4.3 mm and 5.0 mm [Pic. 8].

Pic. 8. Implants used

3.2.4. Implantation protocol

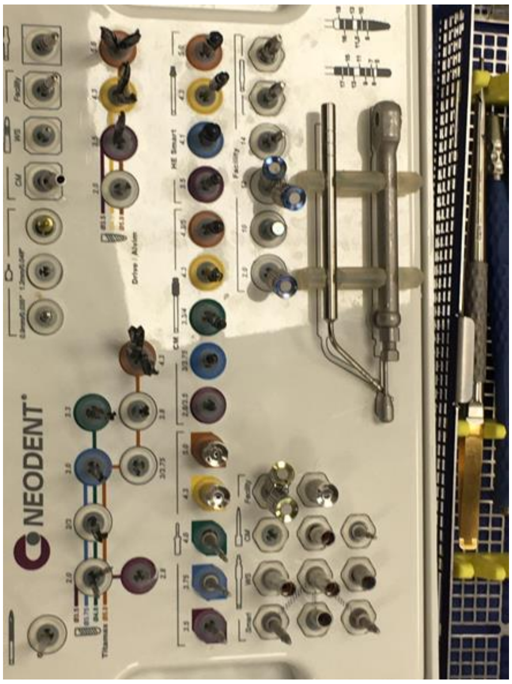
The implants were placed by a specialist in Dental Implantology in the Surgical Unit at the University Medical and Dental Center (UMDC), FDM, Varna, after signing an informed consent (application 6) and in compliance with all rules for asepsis and antiseptics [Pic.9].

Pic. 9. The surgical room where the implantation is performed

We used the following protocol when implanting patients:

Each patient rinses the oral cavity twice within 30-40 seconds before the procedure. with 0.1% nachlorhexidine solution to reduce bacterial count. Clean the skin of the face with a gauze swab soaked in 1% chlorhexidine solution and cover it with a sterile sheet with a pre-cut hole around the mouth. We administered local infiltrative anesthesia 4% articaine solution 40 mg / ml s, 1: 100000 (Septanest-Septodont). Using a blade № 15, a horizontal incision is made along the ridge of the alveolar ridge, followed by sulcular incisions in the presence of adjacent teeth limiting the defect. Using a Buser dissector, the vestibular and oral muco-periosteal flap is dissected. The formation of the osteotomy cavity was performed using an implant set for implant system Neodent Straumann Group Brand and with the help of implant unit NSK-Surgic Pro and implant tip under continuous cooling with 0.9% sterile saline (NaCl).

Pic. 10. Surgical cassette



Pic. 11. Implant set

Pic. 12. Implant unit

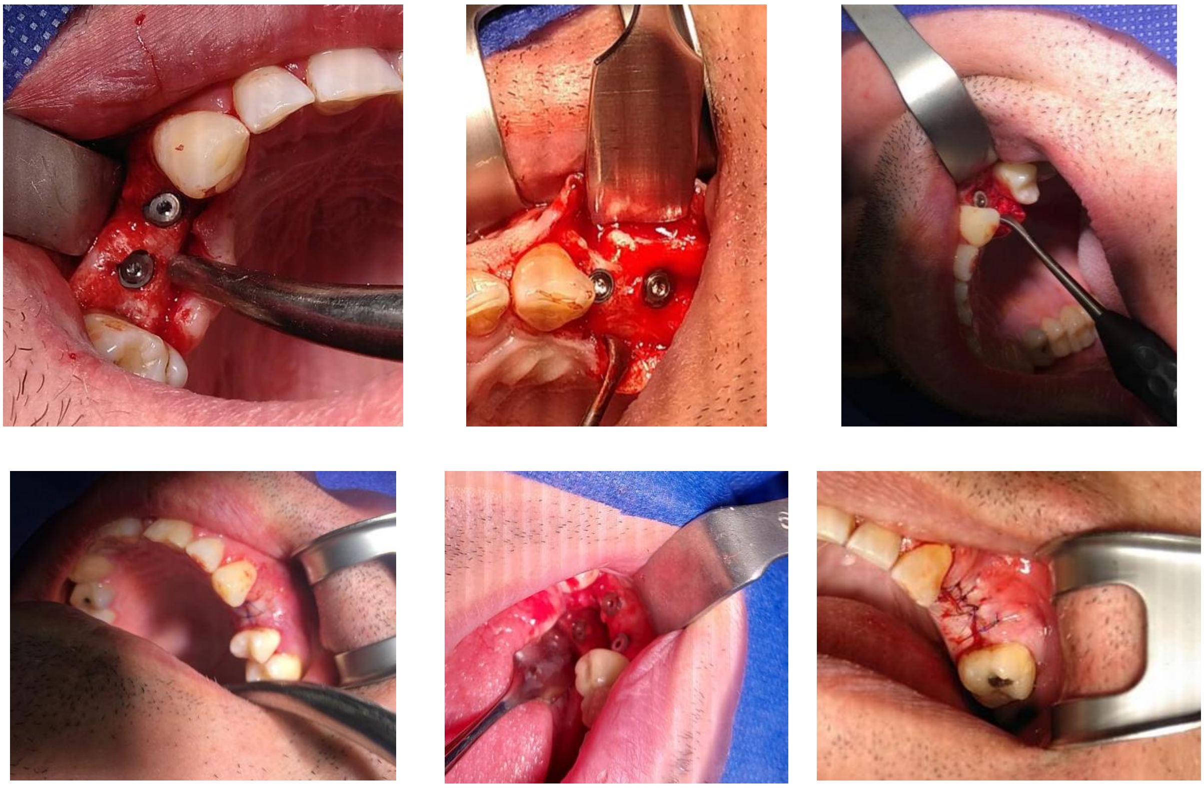
1. We mark the place of the osteotomy cavity with the help of a round drill with a diameter of 1.4 mm - 800 ppm and subsequent embroidery with a drill with a diameter of 2.3 mm. The marking is guided by the prosthetically correct position of the implant;
2. We enter with a pilot cutter to a predetermined depth, consistent with the length of the implant in the specified area, at a speed of 800 rpm. Check the pilot hole with a depth gauge. Measure the depth of the box and the course of osteotomy.
3. We expand the osteotomic cavity with cutters with increasing diameter until reaching the final osteotomic cutter, which is consistent with the diameter of the implant, predetermined for the respective zone-speed of rotation from 600 to 400 rpm

4. Shape the profile of the bone cavity with a profile drill at 300 rpm;

5. We place the implant. The implant is removed from a sterile container using a carrier and carefully inserted into the osteotomy cavity

It is tightened in the bone bed with a torque ratchet with a torque of 25 N / sm; the cover screw is inserted with a screwdriver;

6. We repair and sew the lambda (if necessary, the periosteum is cut at the base of the lambda, which provides greater mobility and allows it to be sewn without tension); sew the flap with single broken stitches with Olsen-Hegar needle holder and sewing material (Dafilon-B.Braun) 5/0 Polyamide monofilament, non-absorbable, 75 cm, articulated with 3/8 atraumatic needle. The number of sutures varies according to the length of the incision and the number of implants placed [Pic. 13].



Pic. 13. Surgical procedure for implant placement

After the manipulation, all patients are given instructions on the care of the surgical wound, the maintenance of oral hygiene during the healing period and is prescribed a broad-spectrum antibiotic of the penicillin group - Ospamox 1000 mg, 3x1 table. for a period of 5 days, as well as non-steroidal anti-inflammatory drug Flamexin 20 mg powder for oral solution at 12 hours for the first three days.

On the day after the surgical procedure and on the seventh day, a control examination was scheduled in order to control the healing process. The sutures were removed on the 12th day after implantation.

In all patients the healing process proceeded without complications in a period adequate for the performed manipulation.

3.2.5. Single-photon emission computed tomography SPECT examination

Patients underwent single-photon emission computed tomography on the 30th and 90th day after implantation.

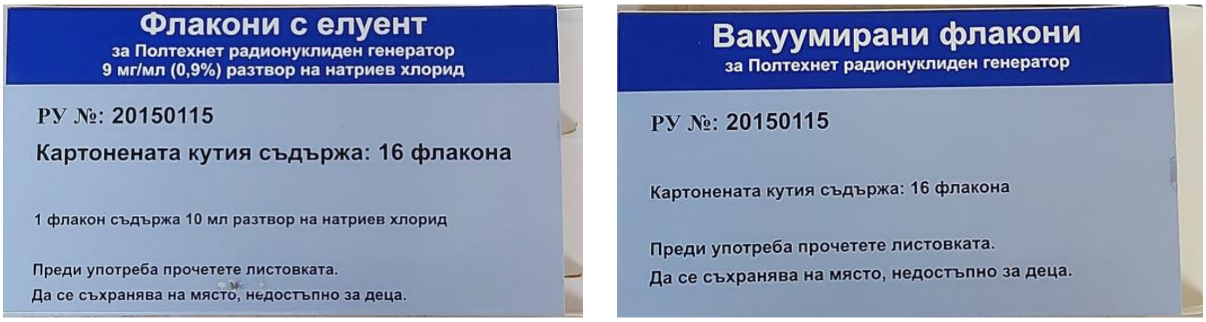
Thirty days after implant placement, a hybrid scintigraphic single-photon emission computed tomography with low-dose computed tomography [SPECT / CT] was performed to assess reparative osteoblast activity as an osteointegrative response around the alloplant. The nuclear medical research was conducted in the Department of Nuclear Medicine and Metabolic Therapy at the University Hospital "St. Marina ”EAD, Varna, specialist in nuclear medicine and laboratory assistant [Photo. 14].

On the day of the study, patients were subject to preliminary preparation, including venous administration and good hydration provided by oral administration of at least 1 liter of water. Bone scintigraphy followed by SPECT / CT was performed 3 hours after intravenous administration of 20mCi [740 MBq] 99mTc-MDP [99mTc-Methylene diphosphonate]. Metastable technetium-labeled methylene diphosphonate was obtained by labeling an MDP kit with eluted sodium pertechnetate Na [99mTcO4] salt of pertechneic acid from a 99Mo / 99mTc generator in a specially adapted radiochemical laboratory at the same clinic.

Pic. 14. Apparatus for SPECT examination and positioning of the patient

The generator consists of a long-lived maternal isotope 99Mo T½ = 65.9 h, which decays to a short-lived daughter isotope - 99mTc T½ = 6 h. Eluent - sterile saline is used. [Pic. 15 and 16]

Сн. 15. Generator for the production of radiopharmaceutical



Pic. 16. Consumables for the production of radiopharmaceuticals

Gamma emission [isomeric transition]:

$$^{99}Mo \xrightarrow{\text{66 hours}} {}^{99m}Tc \xrightarrow{\text{6 hours}} {}^{99}Tc$$

Pic. 17. Apparatus for measuring the activity of producing a radiopharmaceutical

Patients wait in a specially adapted room that meets the requirements for radiation protection. This period of 3 hours is necessary for the fixation of radiopharmaceuticals in the areas under study.

The nuclear medical study was performed using a two-headed SPECT / CTgama camera (Mediso - Medical Imaging Systems Any Scan 2019) low-energy general purpose LEGP (low-energy general purpose) after proper positioning of the patient in a supine position and removal of metal objects from the scanned area. static targeted scintigraphy of the head was performed in anterior, posterior and lateral projections, serving as a guide for increased osteoblast activity. Immediately afterwards, SPECT / CT was performed by rotating the detectors 360º around the patient with 64 consecutively recorded projections for 15 seconds with an angle interval 5º-6º in step and shoot scanning mode. The images were registered on a 128x128 matrix. The obtained information was processed by specialized software, reconstructed by reverse projection tomographic images in the three orthogonal planes of space - transverse, coronal and sagittal. This filter helps to preserve the fine details of the image as much as possible and eliminates background noise. In our study, a Butterworth filter with a cutoff frequency of 0.6 Hz was used.

The technique allows to obtain a three-dimensional representation of the distribution of radioactivity in the field / organ of interest, corresponding to greater diagnostic accuracy, morphological details and details of physiological activity through accurate volumetric measurements, ie. by quantifying the distribution of radioactivity per unit volume of tissue, which helps to ensure accurate measurement of quantitative physiological events such as osteoblast activity and repair process.

The specific regions / areas of interest (ROIs) of identical size were defined and hand-drawn with special care and precision, with the aim of having the same number of pixels in each zone in order to have comparability of results.1.ROI-control (baseline) Calvary bones were used as a reference area for comparison of physiological fixation on healthy bone.

2. ROI-test, this is the area of interest in which there are implants.

The "Baseline" area in each patient was compared to the different ROI (test) outlined around the implants.

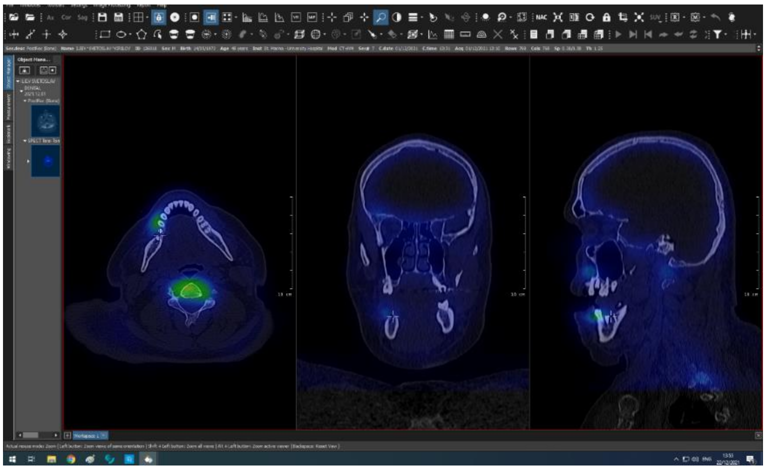
The ROI zones of both the calvary and test zones are the ratio of the number of counts per pixel (caunts / pixel) and reflect the metabolic activity in the respective zone, based on the amount of tracer accumulation in that zone.

We also determined the Osteoblastic Activity Index (OAI). This index is derived from the caunt / pixel ratio reflecting the activity in the test area around the implant divided by the caunt / pixel ratio in the control skull area.

AOI - shows how many times the osteoblast activity in the test area is greater than the osteoblast activity in the control area.

ROI - shows the activity in the individual test areas

The study was performed in the same volume and sequence on the 60th day for group 1 and on the 90th day for group 2, respectively



Pic. 18. SPECT / CT images

After the SPECT study, each patient underwent periapical sector radiography with a Planmeca Pro X apparatus with the following values of 63kV, 8mA, exposure time 1.60 sec. A parallel intraoral technique using a digital sensor holder is used. Before performing the X-ray examination of the patients, a protective collar with 0.25 mm lead equivalent was placed to protect the thyroid gland..

Pic. 19. X-ray machine for sector images

3.3. Material on task № 2

For the realization of the second task the images obtained from the conical beam computed tomography before implantation were used.

3.4. Methods on task № 2

With the assistance of colleagues from the Department of Medical Equipment, Electronic and Information Technologies in Healthcare, at the Faculty of Public Health MU-Varna, a plug-in group of features was developed and added to the software program ImageJ. This software is open source and allows the processing of medical images in several medical formats, including DICOM format (Digital Imaging and Communication in Medicine) [application 7].

The purpose of the created script is to calculate the average values of bone density based on Hunsfield units [HU] in a certain bone volume in the implantation area. The calculated average value of bone density will be related to the results of the SPECT study. correlation between osteoblast activity in the implant area and baseline mean bone density in this region. For this purpose, we decided to measure bone density in a cylinder-shaped volume with dimensions of 4 mm in diameter and 8 mm in height.

The created program allows these values to be changed, depending on the needs of the clinician.

In all our CBCT studies we have a voxel / pixel size constance, namely 0.2 mm, to have a 4 mm cylinder diameter we need a coverage of 20 pixels. In 1 mm there are 5 pixels of 0.2 mm, for 4 mm 20 pixels for diameter and 40 pixels for height are needed [Fig. 5].

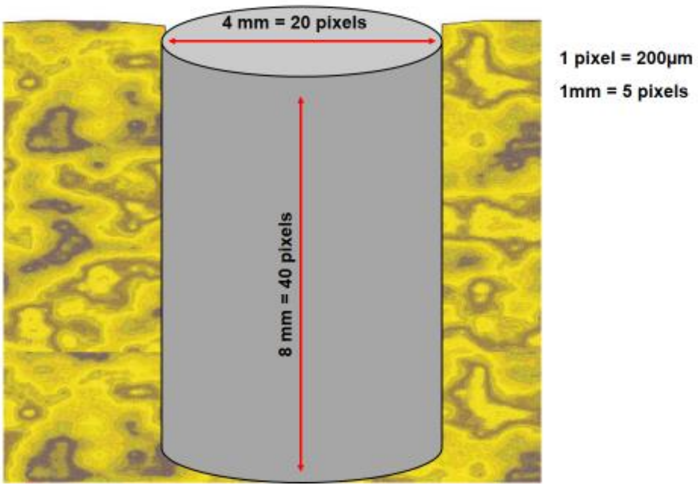
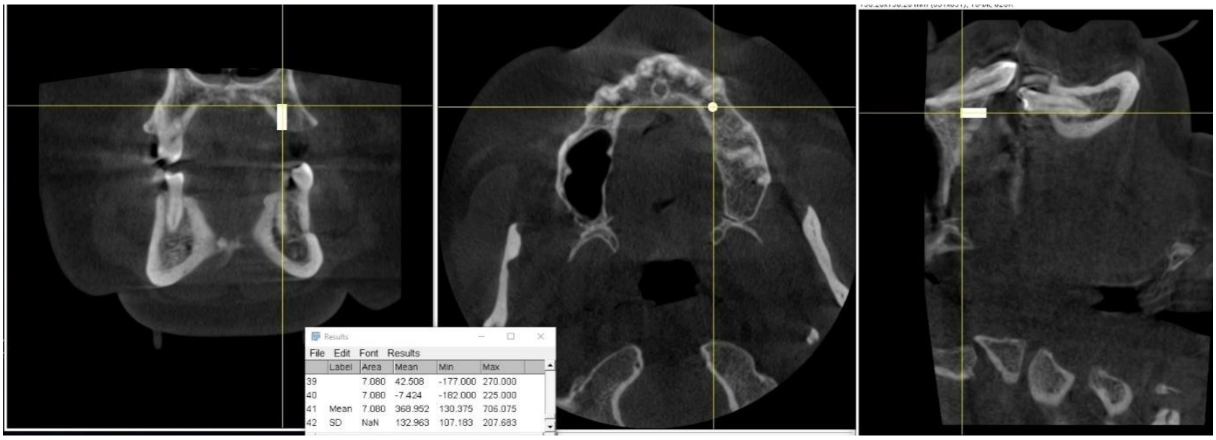


FIG. 5. Image of the volumetric size for estimating bone density

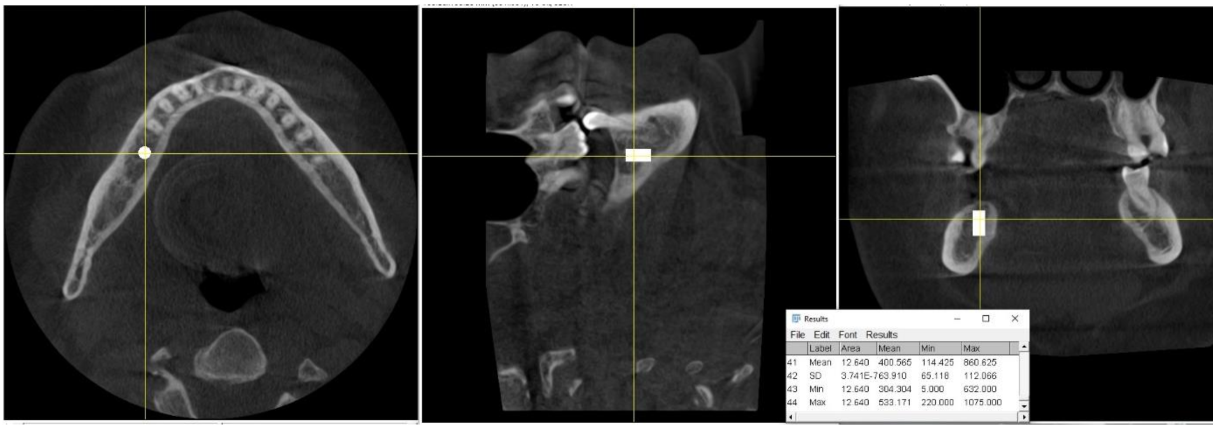
Each patient's DICOM file is imported into the ImageJ program with the plugin added.

A circular ROI area of 20 x 20 pixels is drawn on an axial section when reaching the bone in the edentulous area. The ROI is copied in the next 40 slices, thus generating the ROI of the 3D cylinder, which is used to measure the mean and standard deviation of the volume included in this 3D ROI.

The average value of HU in the entire volume of 3D ROI is calculated by selecting the Measure option from ImageJ [Pic. 20 et Pic. 21].



Pic.20. Application of the algorithm for estimating bone density in a selected area in the upper jaw



Pic. 21. Application of the algorithm for estimating bone density in a selected area in the lower jaw

The whole calculation is facilitated by macros created for this purpose. The macro is executed as soon as the initial ROI is outlined. The macro can be repeated as many times as necessary. The average values of the Hunsfield units in different patients, in different areas are recorded and analyzed.

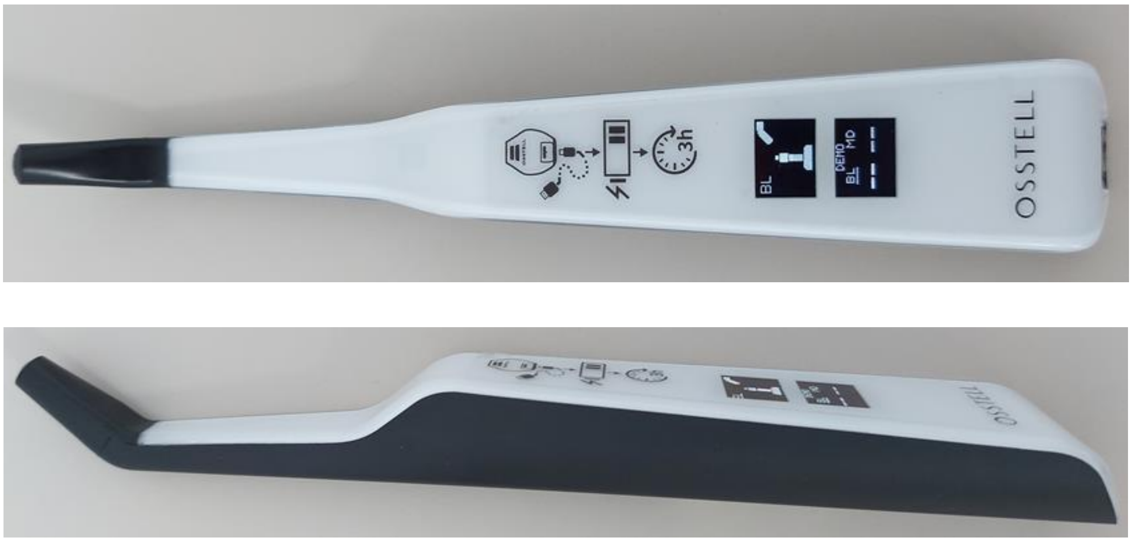
3.5. Material on task № 3

The study under task number 3 was performed on patients from task number 1

3.6. Task methods № 3

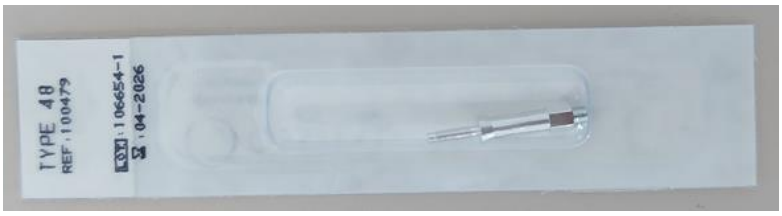
The study is conducted in the surgical sector of the University Medical and Dental Center at the Medical University of Varna.

After the implants were opened, implant stability was measured in all patients by resonant frequency analysis (RFA) using the Osstell® Beacon.



Pic. 22. Osstell Beacon device for measuring implant stability

In 1998 prof. Neil Meredith for the first time introduced resonance frequency analysis for the purposes of dental implantology. This is a non-invasive diagnostic method that can measure the stability of the implant at different time periods using vibration. The RFA uses a small L-shaped transducer that attaches to the implant or abutment with a screw. The transducer connects to the device, which in turn connects to a computer. The transducer consists of two ceramic elements, one of which vibrates from a sinusoidal signal (5–15 kHz), while the other serves as a receptor. The transducer is screwed directly to the implant body and shakes the implant with different amplitude, starting from low frequency and increasing the height while the implant resonates. High-frequency resonance shows stronger bone-implant contact. RFA is widely used for clinical assessment of osseointegration as well as for prognostic assessment.



Pic.23. Smart Peg type 48, packed in sterile packaging

Pic. 24. Smart Peg wrench for implantation

Pic. 25. Test Peg за проверка на апарата

The technique of resonance-frequency analysis makes it possible to objectively determine the stability of the implant and to measure the degree of osseointegration without compromising the healing process. The test method is fast, non-invasive and can be used at different stages in the course of treatment. RFA is a method in which the stability of implants (rigidity of the implant-bone complex) is measured by measuring the resonance frequency - Smart Peg mounted on the implant. The device emits electromagnetic waves to the element attached to the implant. The magnet at the top is caused by oscillation which is transmitted to the implant. of the peri-implant bone and the connection with the implant are determined by the frequency of the resonance obtained as a result of electromagnetic oscillations. The oscillation is recorded by the device and converted into the so-called ISQ Implant Stability Quotient, which is equal to the resonant frequency measured in Hz divided by 100. The higher the resonant frequency, the higher the ISQ value and the higher the implant is stable.

ISQ has values from 1 to 100. ISQ values are shown on a color wheel, which gives information about the degree of osseointegration:

Red low stability -ISQ <60

Yellow-medium stability ISQ от 60 до 70

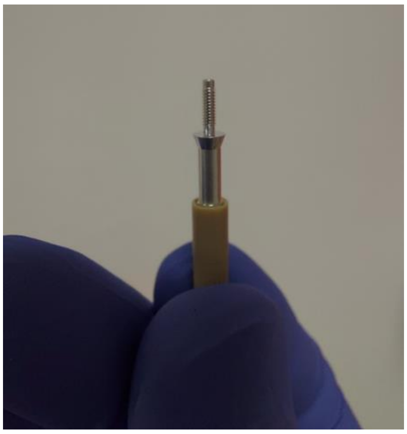
Green-high stability ISQ > 70

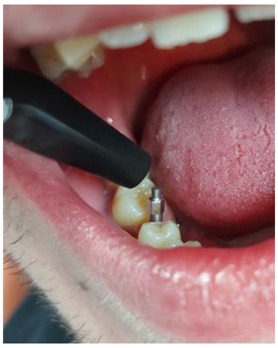
Today, two devices are used: Osstell and Penguin RFA, which work on the same principle, with the difference that in the Osstell system used SmartPegs are disposable, and in Penguin RFA are made of tyrant, can be autoclaved and used up to 20 times.

The device we use is the latest development of Osstell® (Integration Diagnostic AB, Gothenburg, Sweden) - Beacon. This is a compact device that provides wireless Bluetooth connection to a computer, which allows for greater freedom of movement. there is a small display on which the digital expression of the research results is visualized, as well as the direction in which the research will be conducted. The data obtained for each implant can be reliably stored and analyzed in the Osstell Connect platform. Access to the platform can be done from a computer, tablet or smartphone.

A special element, the so-called Smart Peg, is wound on the platform of the implant, a metal pin, which has a screw (thread) at one end, through which it is articulated with the implant, and at the other - a magnet. Smart Pegs have been developed for various implant systems. They are all made of soft metal, which ensures that the SmartPeg can be fixed to the implant without the risk of damaging the titanium prosthetic thread. The Smart Peg thread wears out easily, which in turn reduces the connection with the implant and can become reason for inaccurate measurement. SmartPeg are packaged in sterile packaging and are for single use only, as they are not subject to sterilization and re-use may result in inaccurate readings or damage to the implant. Each SmartPeg is calibrated and customized to fit any system and implant type. This ensures that the readings of the Osstell ISQ will be accurate and completely comparable with each other. For our implant system - NEO DENT, Alvim CM uses Smart Peg type 48.

The measurement is performed in two different, mutually perpendicular directions, bullo-lingual BL and medio-distal MD. When activating the device, the display indicates the direction in which the measurement will be performed.





Pic. 26. Measurement of resonant frequency analysis

The tip of the tool is held at an angle of 45 degrees to the longitudinal axis at a distance of 3 to 5 mm from the magnet without touching it. After the measurement, the device is removed from the patient's mouth. The obtained values are displayed on the display of the device, and they are combined with a color light indication below the tip of the instrument, respectively red / low, yellow / medium, green / high stability. once by changing the direction of measurement. Usually the values in the buco-lingual direction are lower than those in the medio-distal. The average of the two measurements is taken as the result of the measurement.

3.7. Statistical methods

The results were recorded and processed using IBM SPSS Statistics v. 20.0. For the statistical processing of the results of the studied parameters the following statistical methods are applied:

- One-way analysis of variance (ANOVA);
- Variation analysis - of the main characteristics (parameters) of the frequency distributions of the considered quantities (mean±SD);
- Correlation analysis - Pearson coefficient and Spearman coefficient
- Comparative analysis (hypothesis evaluation) – χ^2, F и t-test.
- Graphical and tabular method of displaying the obtained results

An acceptable level of significance $p < 0.05$ is assumed for all analyzes performed.

The clinical trial was conducted after obtaining permission from the Commission for Ethics of Research at MU-Varna - Minutes / Decision № 60, meeting on 23.02.2017. All participants in the study have signed an informed consent.

4. Results

4.1. Results and task analysis №1

Evaluation of the results of single-photon emission computed tomography [SPECT] with 99mTc-MDP of periimplant bone tissue performed using ROI and AOI values.

On the table 4 presents an analysis of the ROI values of individual patients and areas on the 30th day of treatment. In all patients, the delineated area of interest covers 8 pixels.

Table 4. ROI [Counts / Pixel] of the examined patients on the 30th day

Patient	Implant position	ROI - control	ROI - test	Change in ROI [test-control]
1	26	21.42	55.35	33.93
2	46	2.32	6.76	4.44
	47		6.39	4.07
	15		17.22	11.11
	24	6.11	34.10	27.99
	25		41.63	35.52
3	46	12.78	42.16	29.38
	36		49.54	36.76
	14	8.72	30.84	22.12
	15		27.06	18.34
4	36	13.18	51.46	38.28
	37		49.64	36.46
	46		58.41	45.23
5	24	34.84	90.39	55.55
6	45	10.92	40.20	29.58
	35		48.79	37.87
7	44	19.40	45.53	26.13
	34		53.41	34.01
8	16	10.21	41.17	30.96
	45		33.91	23.70
9	36	21.75	34.37	12.62
	35		36.48	14.73
10	44	37.04	47.01	9.97

From the results presented in table. 4 shows that in all patients there is a significant difference between the metabolic activity in the implant area and the control area (skull).

No significant difference in metabolic activity was found on day 30 after treatment [Fig. 6].

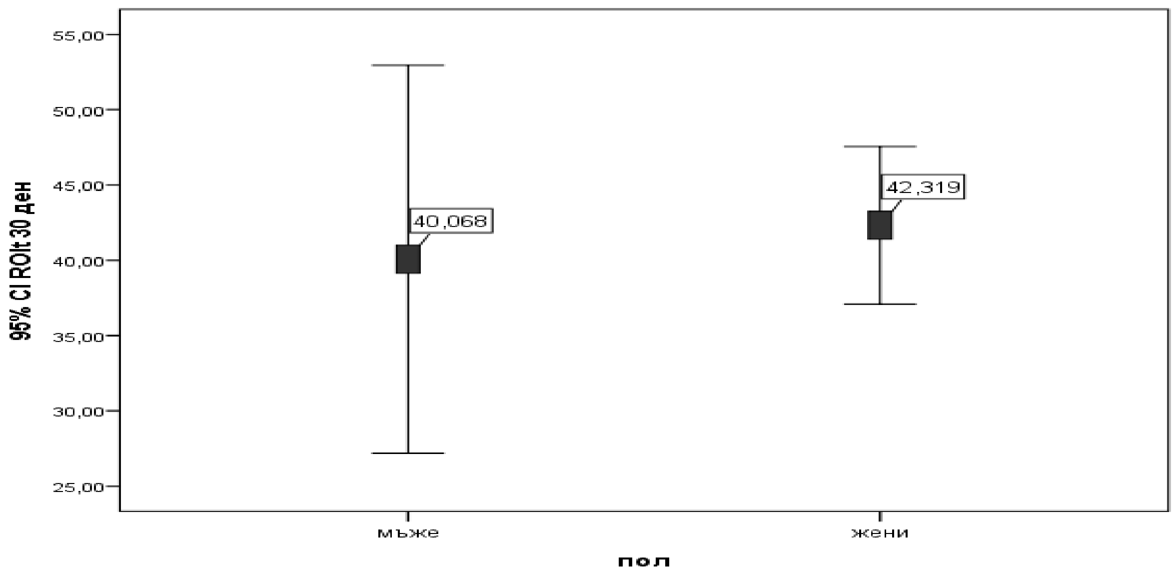


FIG. 6. Mean metabolic activity in the implantation zone by sex

The analysis of the relationship between metabolic activity in the implantation sites and the age of the patients showed a negative dependence (r = -0.286; p = 0.038), which is more pronounced in men (r = -0.463; p = 0.026) than in women. r = -0.243; p = 0.048) [Fig. 7].

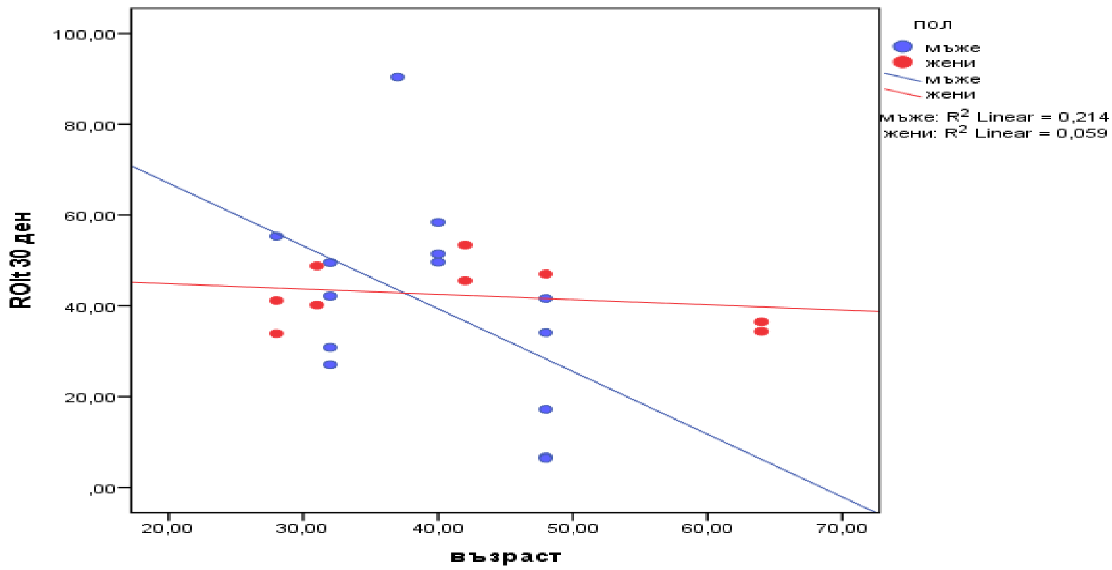


FIG. 7. Correlation analysis between age and metabolic activity in the implanted area according to gender

There was no significant difference in metabolic activity according to the implanted jaw, although the results in the upper jaw are slightly higher [Fig. 8].

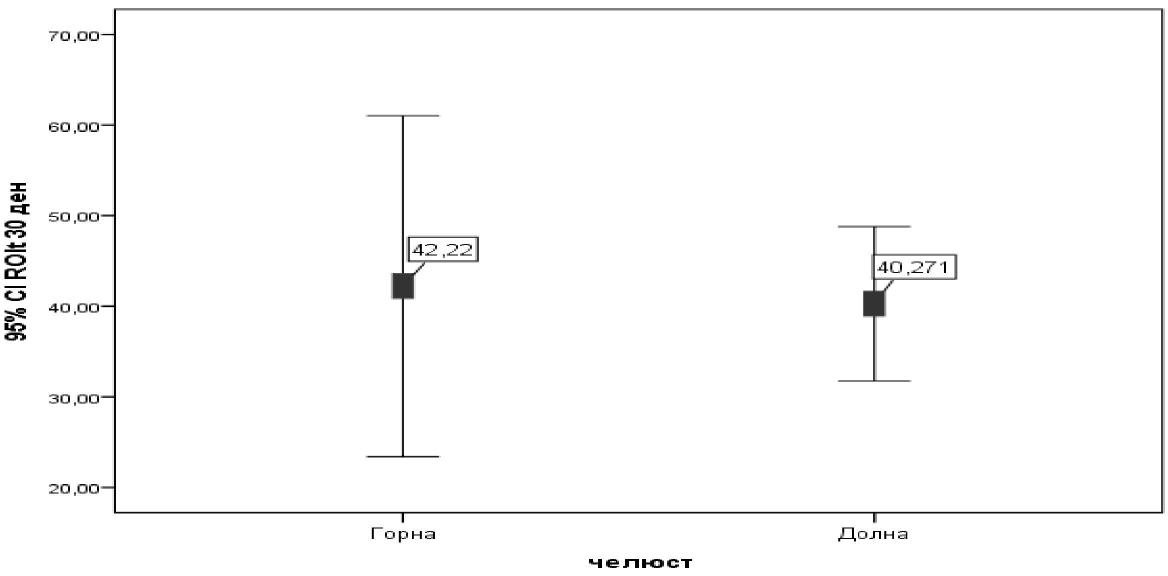


FIG. 8. Mean metabolic activity in the implantation site according to the jaw

Despite the observed variation in the mean ROI values, no significant difference in metabolic activity was demonstrated in the individual implantation sites [Fig. 9]. No such difference was found with regard to the sex of the patients [Fig. 10].

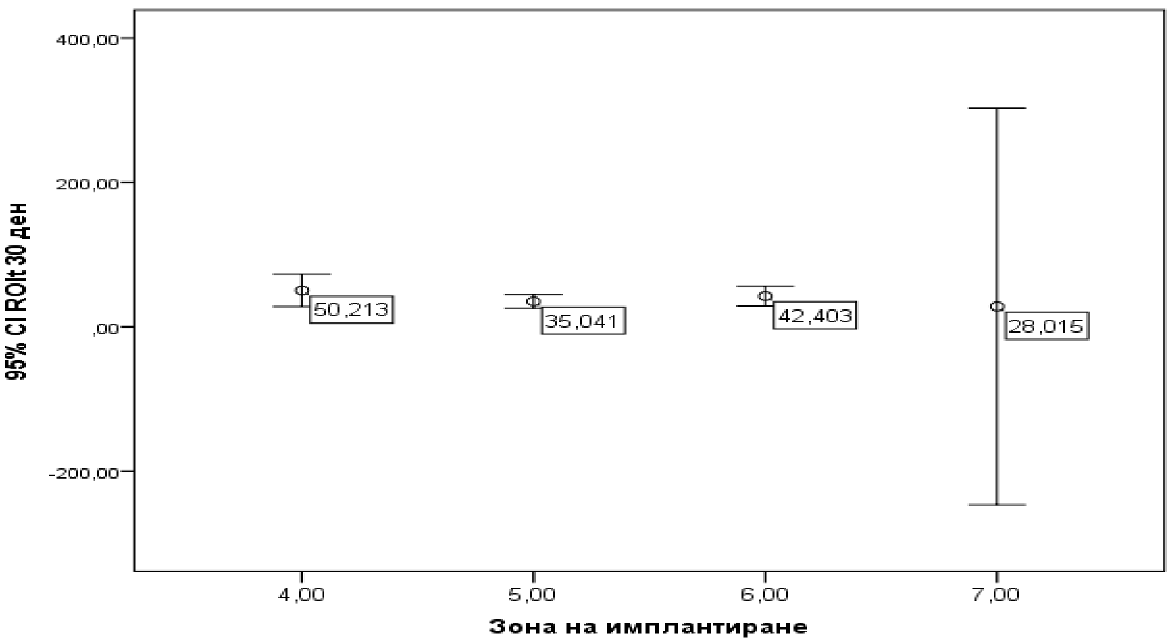


FIG. 9. Mean value of metabolic activity according to the area of implantation

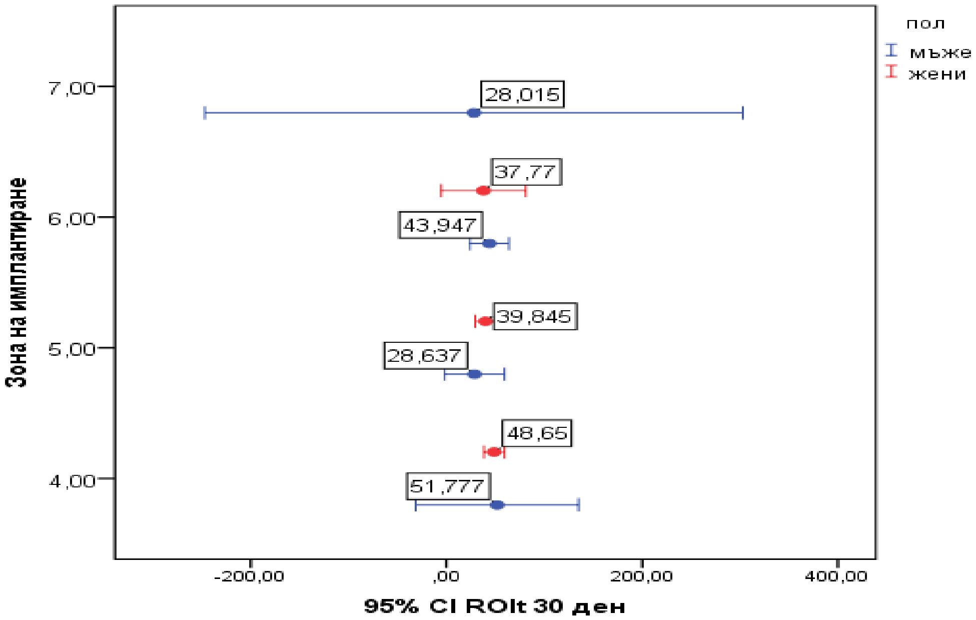


FIG. 10. Mean metabolic activity by implantation site and sex

In 5 patients (3 men and 2 women) the metabolic activity of the same jaw on the left and right was examined [Table. 5].

Table 5. ROI of the examined patients on the same jaw on the left and right

Patient	ROI right	ROI left	ROI change [left / right]
2	17.22	37.86	20.64
3	42.16	49.54	7.38
4	58.41	50.55	-7.86
6	40.02	48.79	8.77
7	45.53	53.41	7.88

The results of table. 5 show that 4 out of 5 patients have higher metabolic activity in the left half of the implanted jaw.

The mean value of AOI was 3.34 ± 1.24 [1.27-6.81], and the detailed results are presented in Table. 6.

Table 6. AOI of the studied patients on the 30th day

Patient	Implant position	AOI
1	26	2.58
2	46	2.90
	47	2.80
	15	2.82
	24	5.58
	25	6.81
3	46	3.29
	36	3.80
	14	3.54
	15	3.10
4	36	3.90
	37	3.70
	46	4.40
5	24	2.60
6	45	3.68
	35	4.46
7	44	2.35
	34	2.75
8	16	4.03
	45	3.32
9	36	1.58
	35	1.68
10	44	1.27

In contrast to the metabolic activity in terms of osteoblast activity, a significant difference was found between men and women (p = 0.047), which shows that women have lower levels of osteoblast acrimony [Fig. 11].

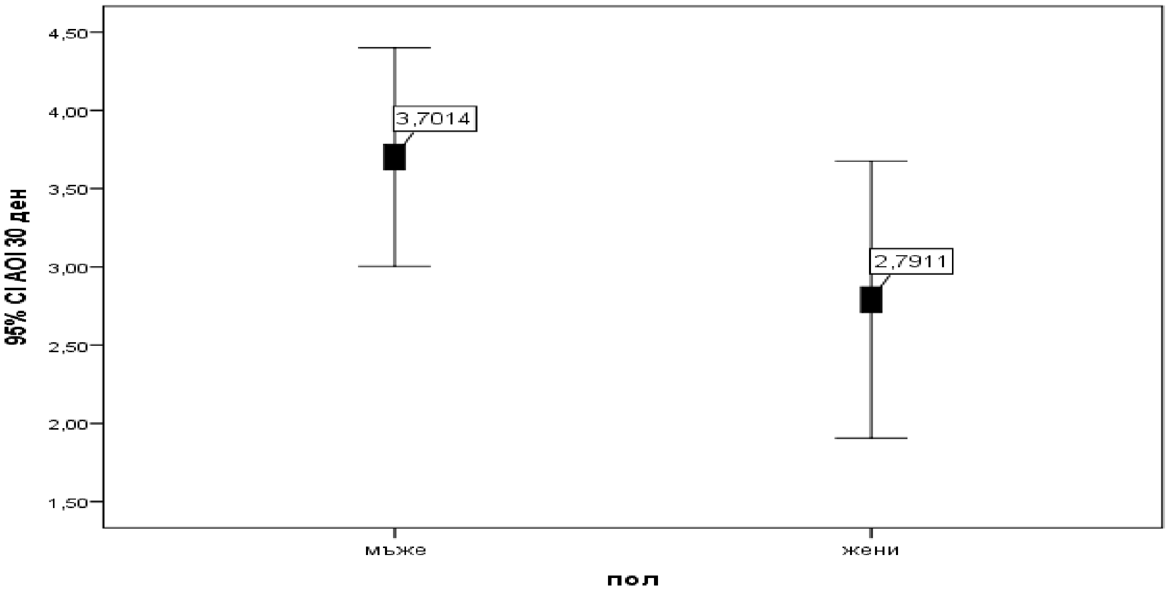


FIG. 11. Mean value of osteoblast activity in the implantation area by sex

Analysis of the relationship between age and AOI showed the same trend as in ROIt, with age correlating negatively with osteoblast activity (r = -0.283; p = 0.036), with women increasing the negative relationship with speed (r = -0.858; p = 0.003) [FIG. 12].

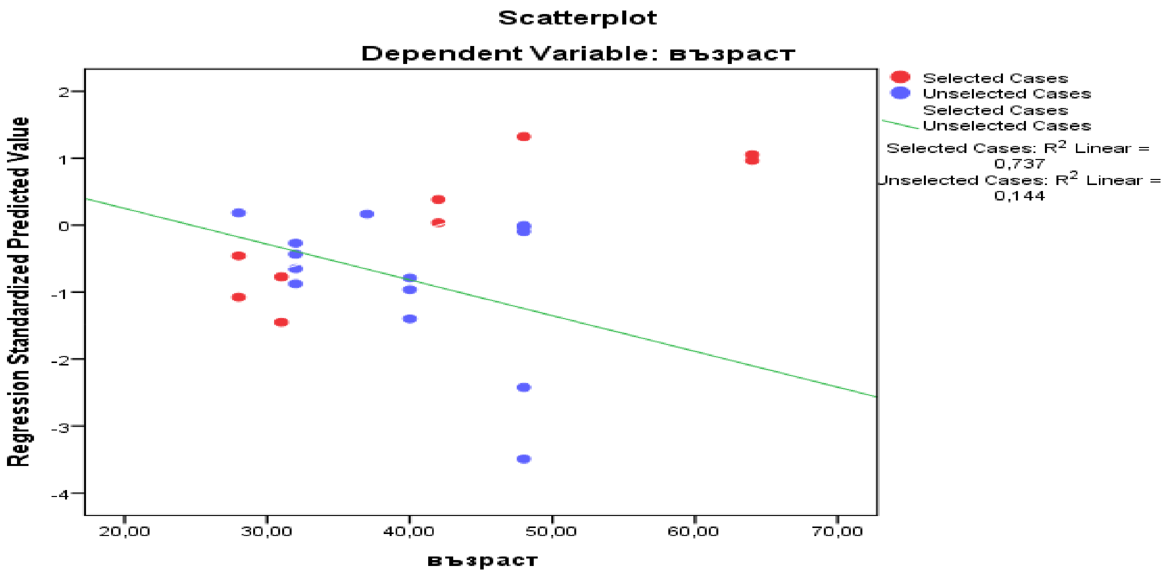


FIG. 12. Correlation analysis between age and osteoblast activity in women

No difference was found in the mean AOI values according to the implanted jaw [Fig. 13].

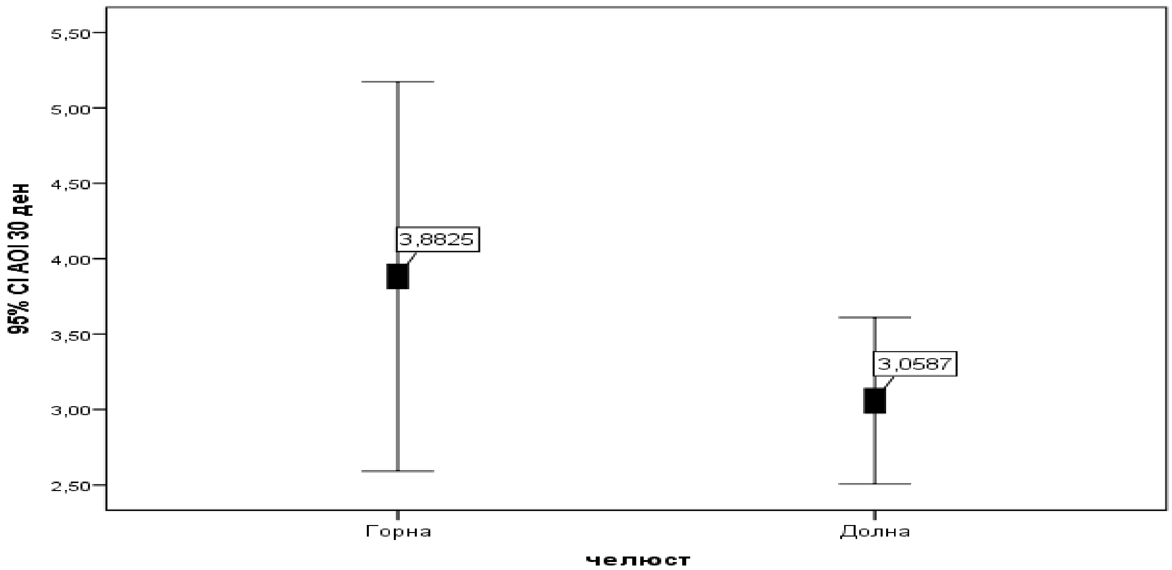


FIG. 13. Mean value of osteoblast activity in the area of implantation according to the jaw

A significant difference was found when a comparative analysis of osteoblast activity was performed according to the implanted jaw and sex, where in women the difference was significant (p = 0.013) [Fig. 14].

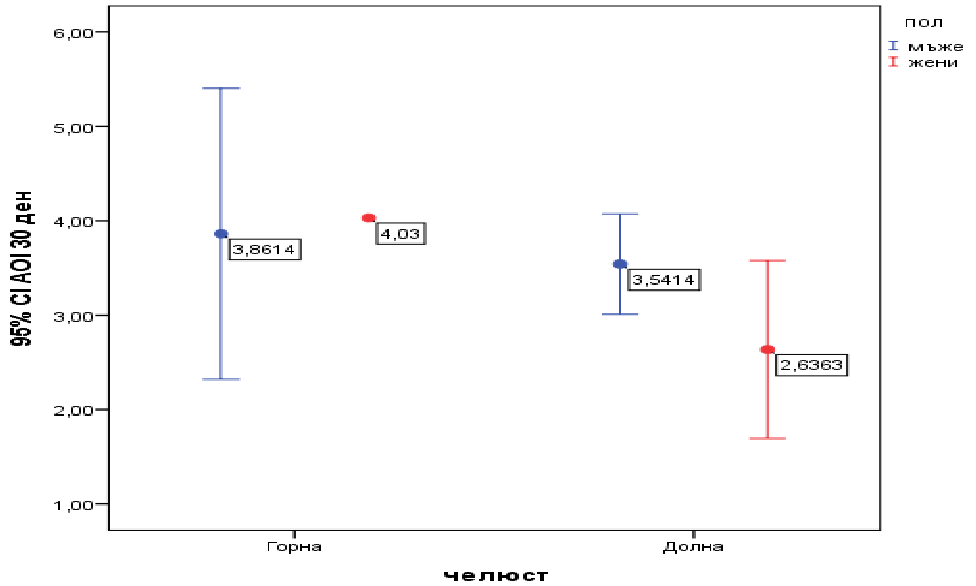


FIG. 14. Mean value of osteoblast activity in the implantation area according to jaw and sex

No significant difference in osteoblast activity was found according to the implantation site (p> 0.05) [Fig. 15].

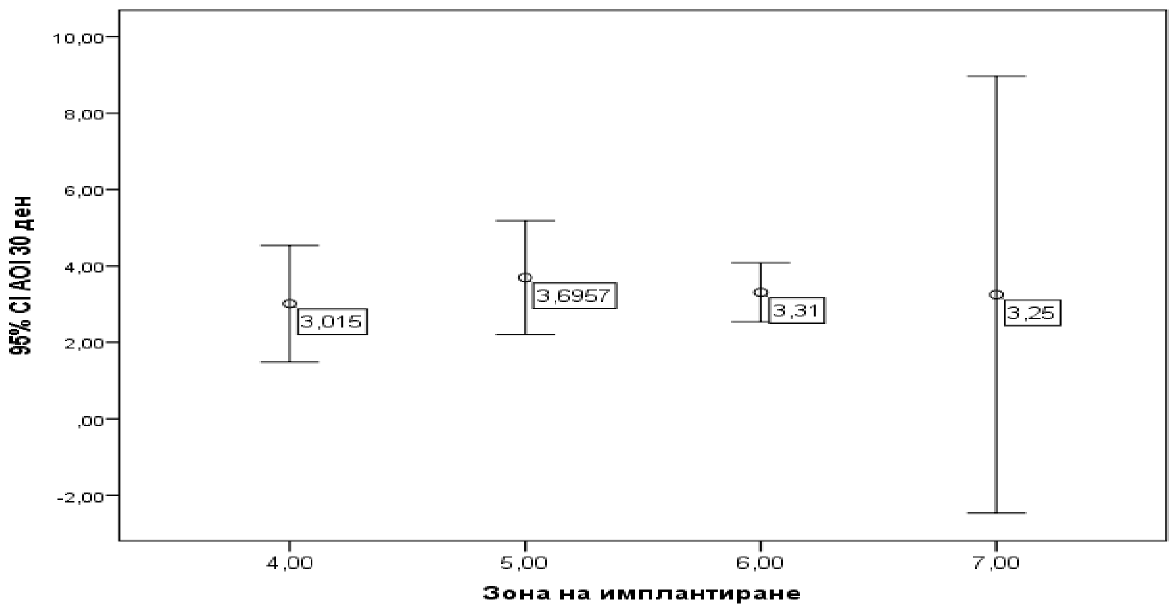


FIG. 15. Mean value of osteoblast activity according to the implantation area

Variation in the mean values of osteoblast activity is also observed with regard to gender and the area of implantation, as in women the results are lower than in men (p = 0.033) [Fig. 16].

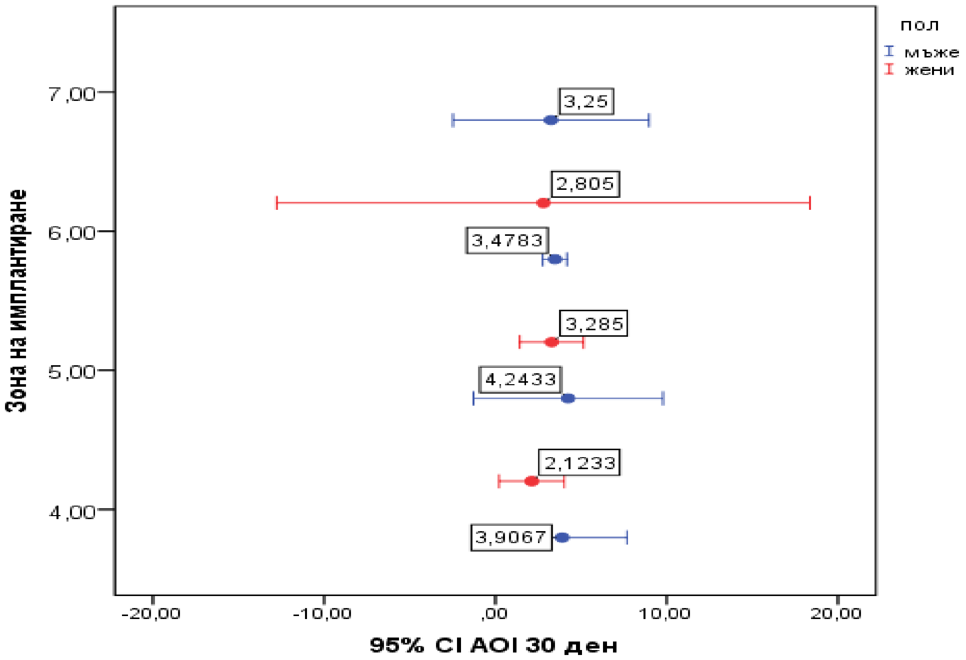


FIG. 16. Mean value of osteoblast activity according to implantation site and sex

In two patients with a total of 4 mandibular implants (46, 47 and 46, 36), SPECT was performed on day 30, which was repeated on day 60 in connection with the follow-up of the one-month period of newly placed mandibular implants. Implants in the upper jaw in both were placed 30 days after those in the lower, due to waiting for a healing process in connection with the extraction of teeth with a poor prognosis. This gave us the opportunity to obtain and compare the SPECT results on the 30th and 60th day for the lower jaw [Table. 7].

Table 7. ROI and AOI of the monitored patients on the 30th and 60th day of the implant treatment

Day	Indicator	Patient 2		Patient 3	
		46	47	46	36
30	ROI - control	2.32	2.32	12.78	12.78
	ROI - test	6.76	6.39	42.16	49.54
	Change in ROI [test-control]	4.44	4.07	29.38	36.76
	AOI	2.9	2.8	3.29	3.80
60	ROI - control	6.11	6.11	8.72	8.72
	ROI - test	12.93	15.47	25.27	32.55
	Change in ROI [test-control]	6.82	9.36	35.87	34.08
	AOI	2.11	2.53	2.89	3.73

The results of table. 7 show that in both patients the metabolic activity in the implantation area continued, but a decrease in osteoblast activity levels was observed on day 60 compared to those measured on day 30 [Fig. 17].

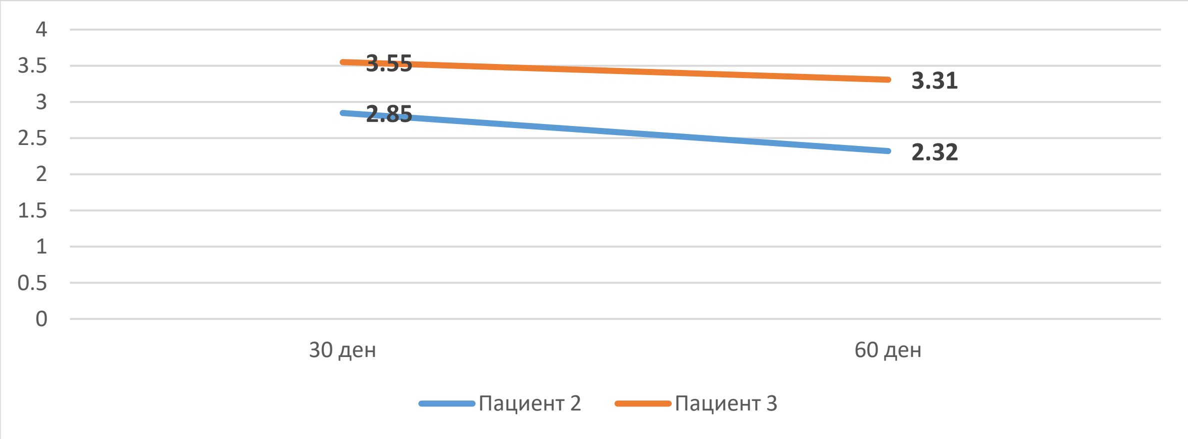


FIG. 17. Mean values of osteoblast activity [AOI] on days 30 and 60

This information shows that during the process of osseointegration, after the first month, osteoblast periimplant activity is very high and then begins to decrease over the next few months. There is also a difference in the indicators of reduction of cellular activity related to the 2 areas [test and control], although these differences are not statistically significant due to the small number of included cases and the lack of absolute reference values.

In 3 patients, the results of the SPECT study revealed osteoblast activity in areas where extraction and endodontic treatment of chronic localized periapical inflammatory process (granuloma) was performed.

In patient 2, metabolic activity was found on the extraction of 25, and the ROI values in this area did not differ significantly from those of the implants (6.75 in the area of extraction to 6.76 and 6.39 in the area of implantation 46 and 47, respectively). of the finding is 2.9 times larger than the control area of the calvary and also does not differ significantly from that of the implants.

In patient 3, two additional extraction-related findings were found on days 18 and 28, which were followed on day 30 and 60. On day 30, the results for osteoblast activity did not show a significant difference compared to those of already placed implants in the upper jaw [Table. 8].

Table 8. ROI and AOI of patient 3 on the 30th and 60th day

Day	Indicator	Extraction		Implants	
		18	28	14	15
30	ROI - control	12.78	12.78	8.72	8.72
	ROI - test	47.57	44.16	30.84	27.06
	Change in ROI [test-control]	34.79	31.38	22.12	18.34
	AOI	3.7	3.5	3.54	3.10
60	ROI - control	8.72	8.72		
	ROI - test	34.08	35.87		
	Change in ROI [test-control]	25.36	27.15		
	AOI	3.91	4.11		

On the 60th there was an increase in the index of osteoblast activity in both extracted areas compared to that found on the 30th day.

In patient 5, metabolic activity was found both in the area of extraction 48 and in the area after root canal treatment of tooth 27. Higher osteoblast activity was observed in zone extraction than in implanted (respectively 3.6 to 2.6). While in endodontic treatment there is more than 9 times more osteoblast activity compared to the implanted area (respectively 25.13 to 2.6).

The results of the analysis of osteoblast activity presented in the present study confirm those of Bhandari et al., Who found a decrease in activity between the 42nd and 56th day (3.70 and 2.99, respectively) [244]. In the present study, the mean AOI values on day 30 were 3.35 ± 1.24 and on day 60 were reduced to 2.82 ± 0.69.

In the study, AOI values were examined on day 30 and day 60 after implant treatment. The decrease in the values of osteoblast activity proves the data given in the literature that the average time for osseointegration and healing is about 3 months, which is also considered to be an appropriate time for loading the implants. The present study shows similar results to other studies on osseointegration and exercise time [Table. 9].

Table 9. Comparison of osteoblast activity of different implant systems

Next number	Implant system	Number of subjects	Increase osteoblast activity per day	Decrease AOI to baseline per day
1	Indian implants [Bhandari SK, Mondal A] [48]	21	14	84
2	Israeli implants [Median et al]	26	14-21	112
3	Italian implants [Cervelli V et al]	25	21	70
4	Astra tech implants [Khan et al]	5	28	112
5	German implants [Jamil et al]	24	21	56
6	Swiss implants [own research]	10	30	60 [there is no information on base levels]

The variations of the results are given in table. 6 can be explained by the fact that the process of osteointegration is influenced not only by the specific metabolic process of bone in individual patients, but also by osteoblast activity against the material, macroscopic design and surface treatment of the implant. Because patient selection protocols were followed in all studies reviewed and unified indices were used to assess metabolic activity.

Table 10. AOI values at 1st and 3rd month.

Patient	Implant position	AOI 30 days	AOI 90 days
1	26	2.58	1.79
2	46	2.90	1.62
	47	2.80	1.52
	15	2.82	1.45
	24	5.58	2.84
	25	6.81	3.25
3	46	3.29	2.36
	36	3.80	2.46
	14	3.54	2.17
	15	3.10	1.95
4	36	3.90	1.88
	37	3.70	1.73
	46	4.40	2.08
5	24	2.60	1.43
6	45	3.68	2.28
	35	4.46	2.67
7	44	2.35	1.81
	34	2.75	1.82
8	16	4.03	2.80
	45	3.32	2.63
9	36	1.58	1.22
	35	1.68	1.32
10	44	1.27	1.02

From the presented results on table. 10, it was found that there was a significant difference in AOI values at 1 and 3 months ($p < 0.01$) after implant treatment. There was a significant reduction in osteoblast activity in all patients.

4.2 Results and analysis by task №2

In the pre-selected areas for implantation of the patients, an assessment of the bone density in HU was made using SVST, with the software algorithm developed by us. The results are presented in table. 11.

Table 11. Mean values of bone density [HU]

Patient	Implant position	Mean
1	26	451.26
2	46	822.66
	47	855.76
	15	523.13
	24	483.81
	25	312.26
3	46	758.27
	36	931.15
	14	368.95
	15	376.19
4	36	922.06
	37	892.37
	46	733.25
5	24	520.67
6	45	638.57
	35	594.69
7	44	743.25
	34	811.19
8	16	378.28
	45	628.59
9	36	400.56
	35	659.31
10	44	787.54

The mean bone density was 634.42 HU ± 197.65 HU, with a minimum value of 312.26 HU and a maximum value of 931.15 HU.

The analysis of the relationship between the age of the patients and the bone density did not show the presence of a correlation, which shows the lack of a systemic relationship between the two indicators [Fig. 18].

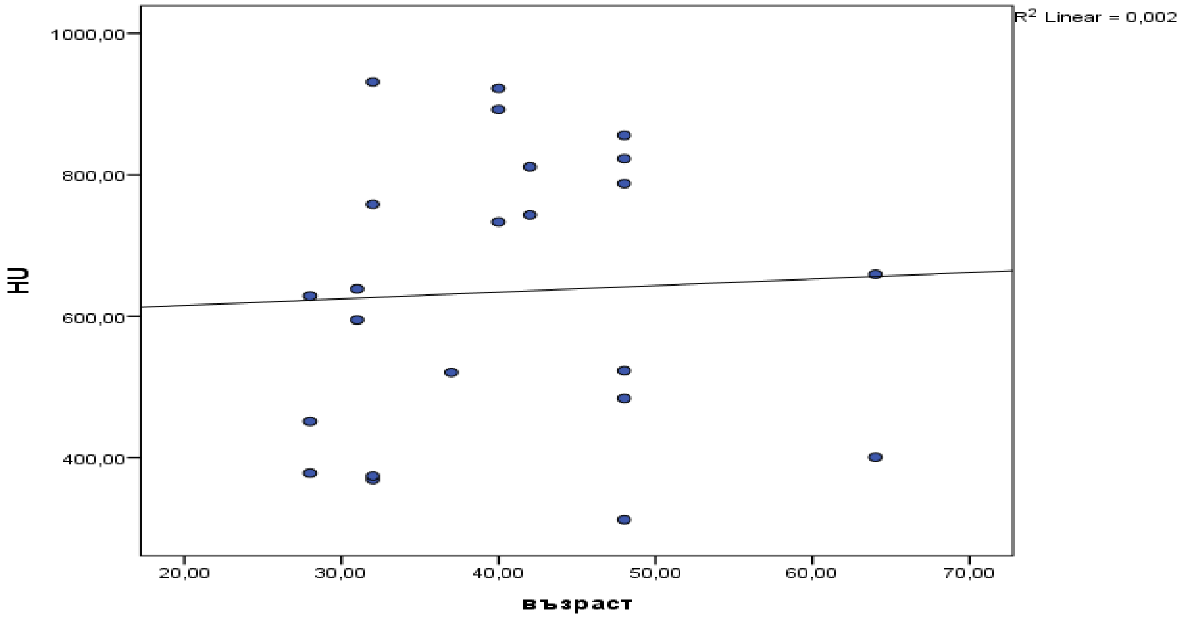


FIG. 18. Correlation analysis of age and bone density

The comparative analysis of the mean values of bone density in men and women did not show a significant difference [p = 0.887] [Fig. 19].

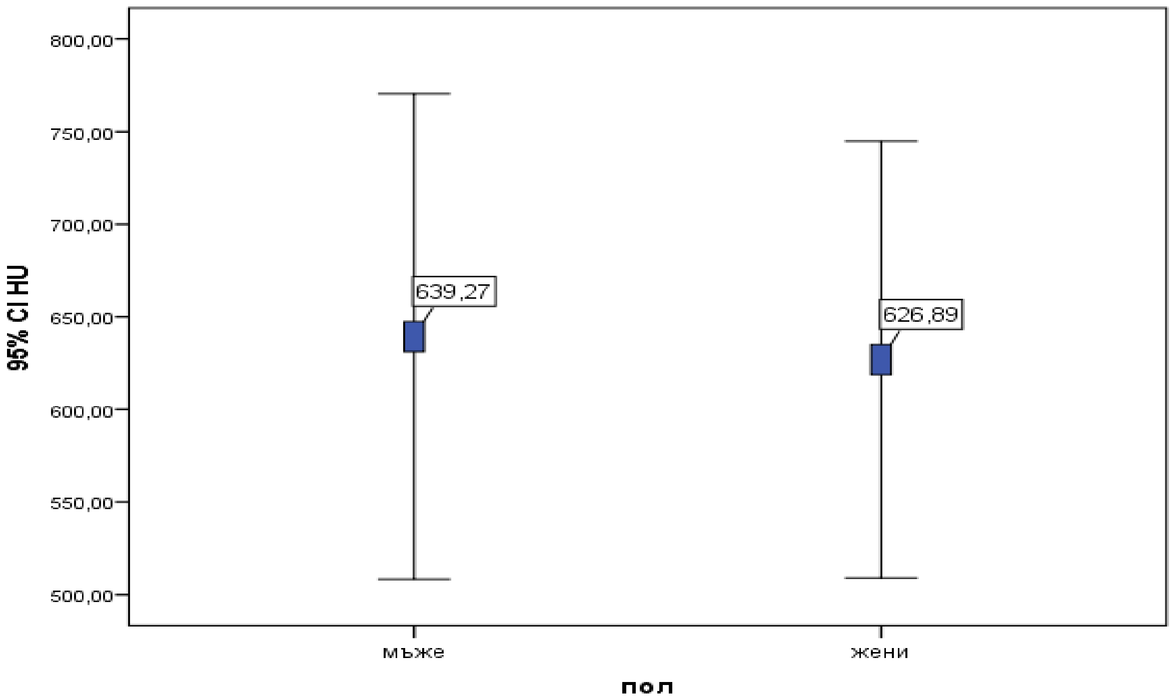


FIG. 19. Mean values of bone density according to the sex of the studied patients

Comparative analysis of bone density in the upper and lower jaw showed a significant difference [p <0.001], with mean values in the upper jaw being significantly lower 426.56 ±

78.85 HU [312.26-523.13 HU] than those in the lower jaw 745.28 ± 142.92 HU [400.56-931.15 HU] [Fig. 20].

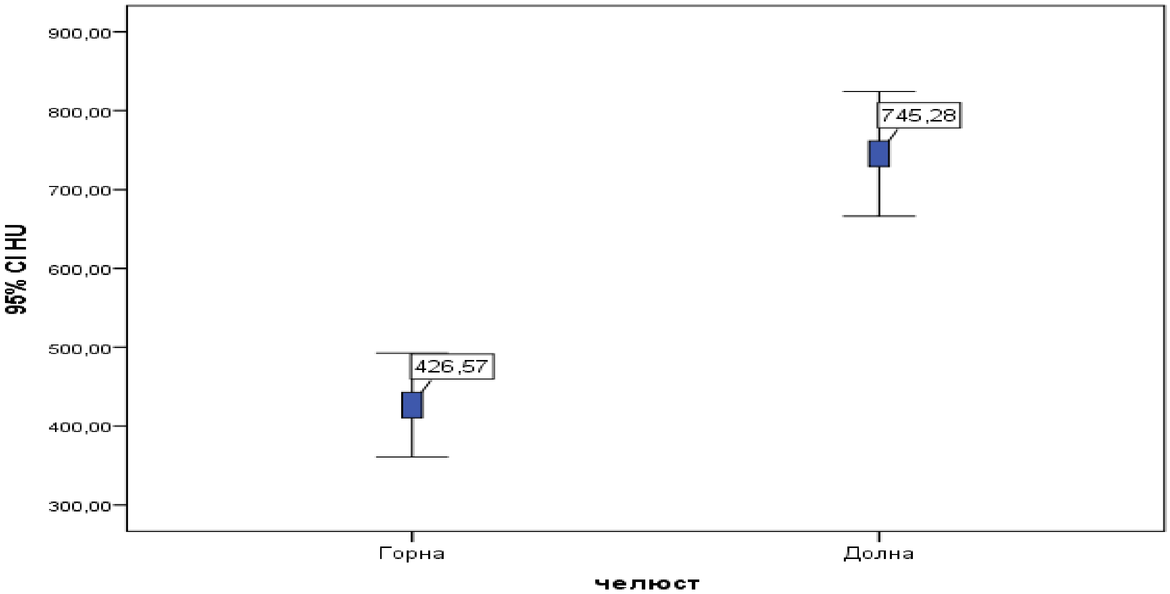


FIG. 20. Mean values of bone density according to the upper and lower jaw of the studied patients

Bone density correlates positively with the lower jaw [r = 0.785; p <0.001], and it can be said that in 61.7% of cases the bone density is determined by whether the jaw is upper or lower.

Comparison of the results obtained from the single-photon emission computed tomography [SPECT] with 99mTc-MDP and in radiography / CBST bone density

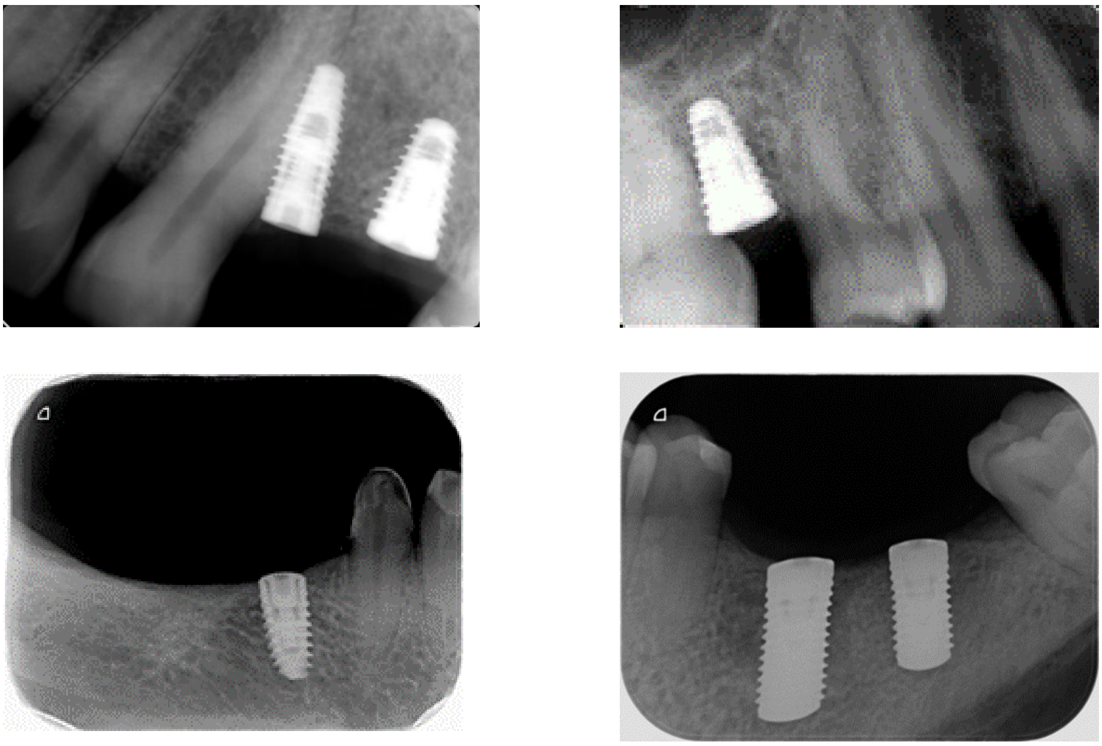
The assessment of osseointegration was also performed by evaluating the results of single-photon emission computed tomography [SPECT] with 99mTc-MDP. The assessment of bone density in the area before implantation performed by CBST.

The role of radiographic images in implant treatment is mainly related to the initial assessment of bone and available volume in the choice of implant size [Fig. 27].

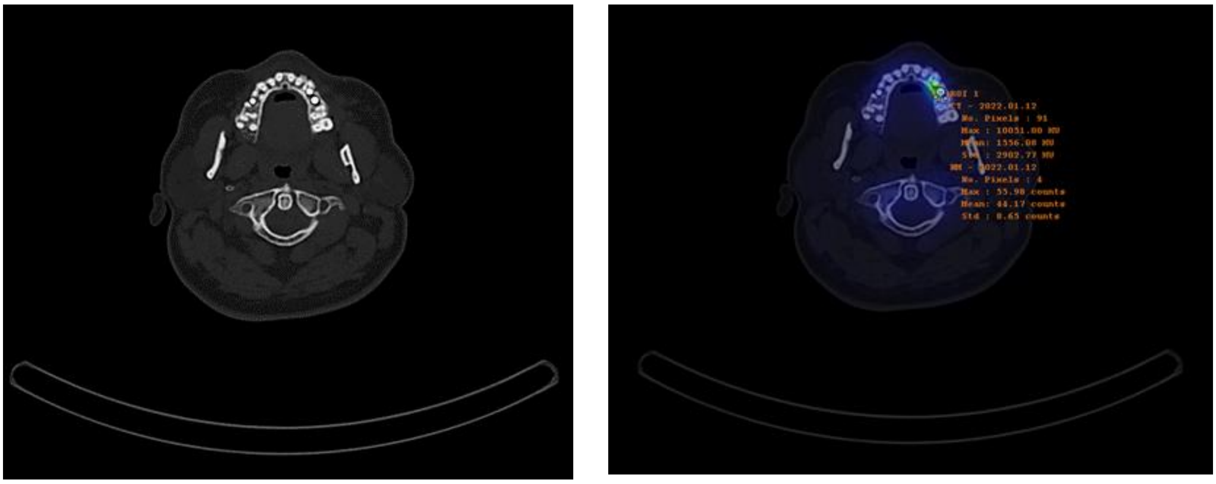
Pic. 27. Panoramic radiography

Before performing the implant treatment by radiography, the position of the implant in relation to the initial stability was determined and the prognosis for the duration of the healing process was determined [Pic. 28]

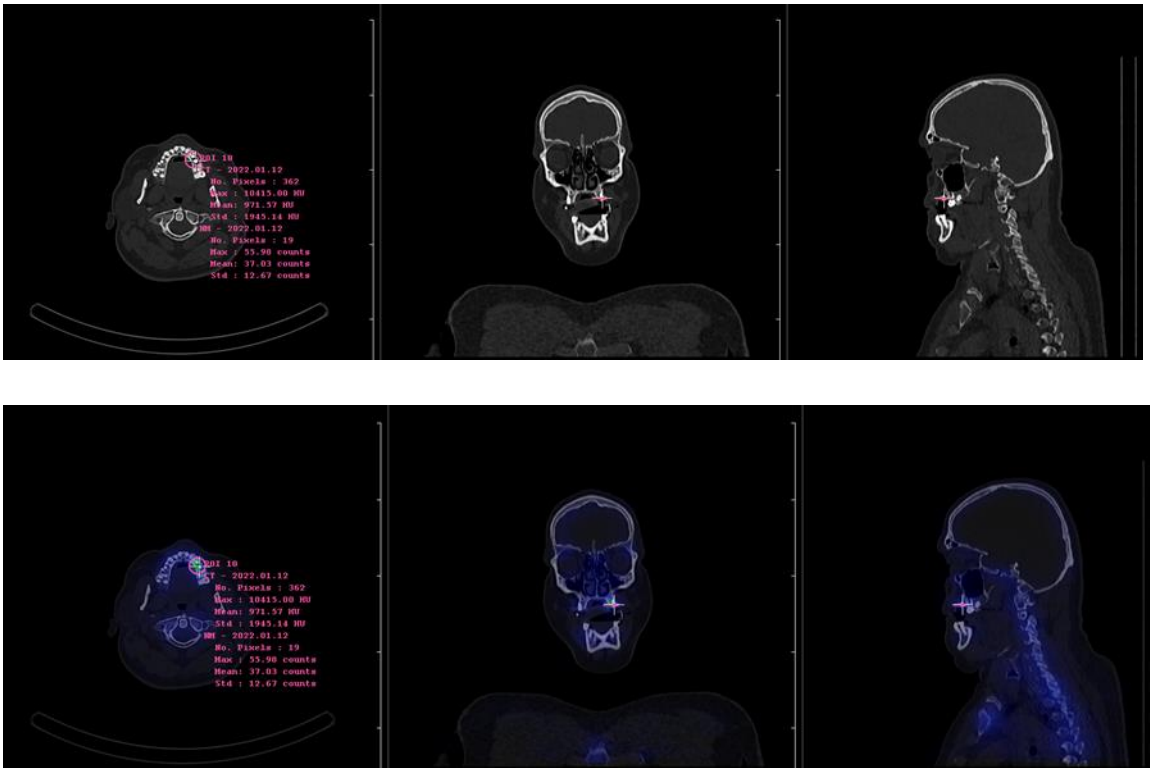
The disadvantage of radiographs is that they do not allow for an objective assessment of bone density and osteoblast activity, which requires additional imaging.



Pic. 28. Radiographs of patients after implant treatment



Pic.29. Image CT and Fusion



Pic. 30. Image CT and Fusion in three planes

The analysis of the relationship between AOI in the implanted area and HU units in the area before implantation did not reveal a direct relationship [Fig. 21], although thicker bone is a prerequisite for better primary stability, which is associated with better healing process and higher success rate of implant treatment.

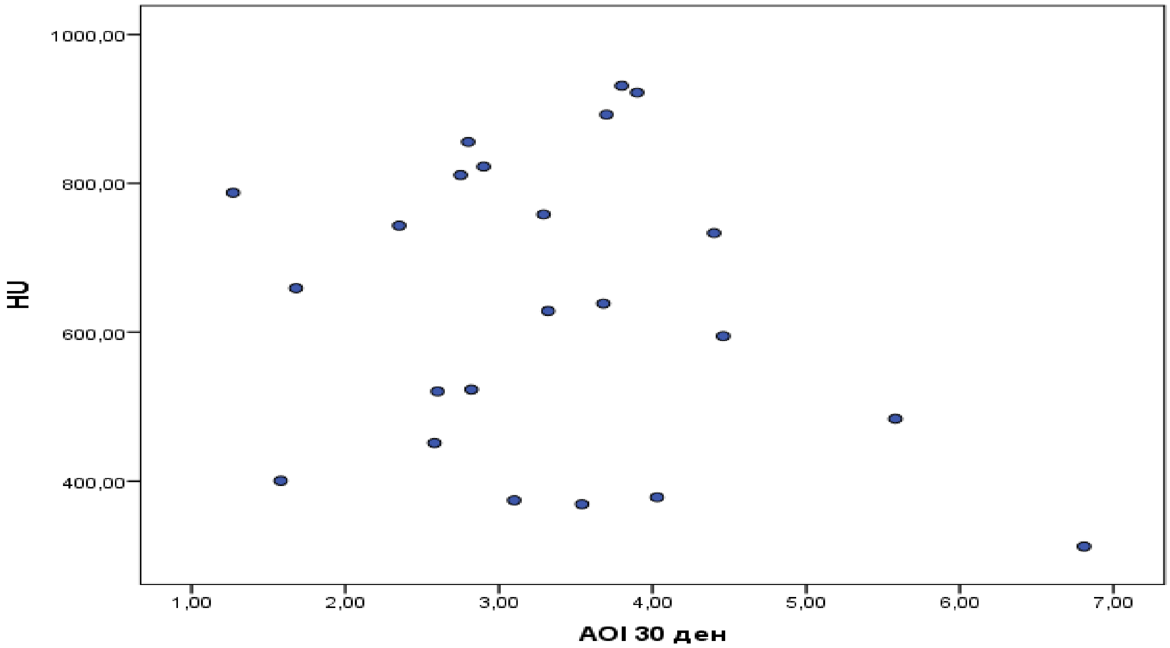


FIG. 21. Correlation analysis between AOI on day 30 and HU

From the results so far, it was found that bone density and osteoblast activity do not correlate with the age of patients. On the other hand, it was found that despite the lack of a significant difference in bone density between men and women, men have higher levels of metabolic activity.

It is impressive that there is a significant difference in bone density between the upper and lower jaw, and in the upper jaw it is smaller. At the same time, higher metabolic activity is found. These results prove once again that there is no direct relationship between the two indicators.

4.3 Results and analysis by task № 3

High ISQ values were observed in all patients in the third month after implant placement, with a mean ISQ of 75.95 ± 3.44 ranging from 70.00 to 82.00. These values indicate that the implants are osseointegrated and have high stability. The values obtained are also an indication that the implants can be loaded with the prosthetic structure. There was no significant difference in ISQ values depending on age and gender, with the average ISQ value for men being 75.78 and for women being 76.22 (Fig. 22).

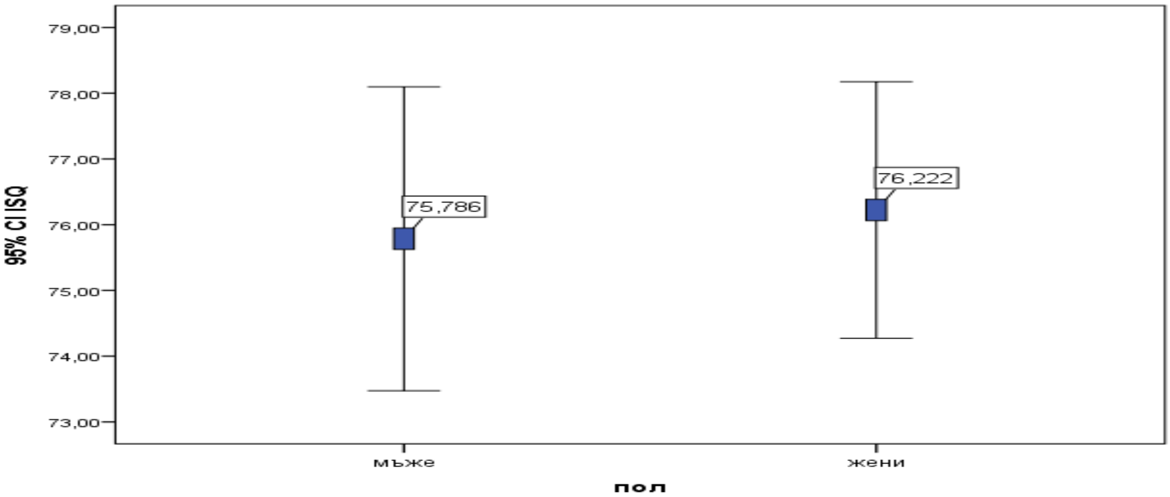


FIG. 22. Mean values of ISQ by gender

Such a difference is found for the two jaws, as the average values for the upper jaw are slightly lower than the average values for the lower jaw (respectively 72.37 and 77.87; p <0.001) (Fig. 23), which can be explained by more -lower bone density in the upper jaw compared to the same in the lower. There is a strong relationship between ISQ values and jaw type (r = 0.777; p <0.001) Lower density is due to lower ISQ values, ie there is a relationship between bone density and ISQ.

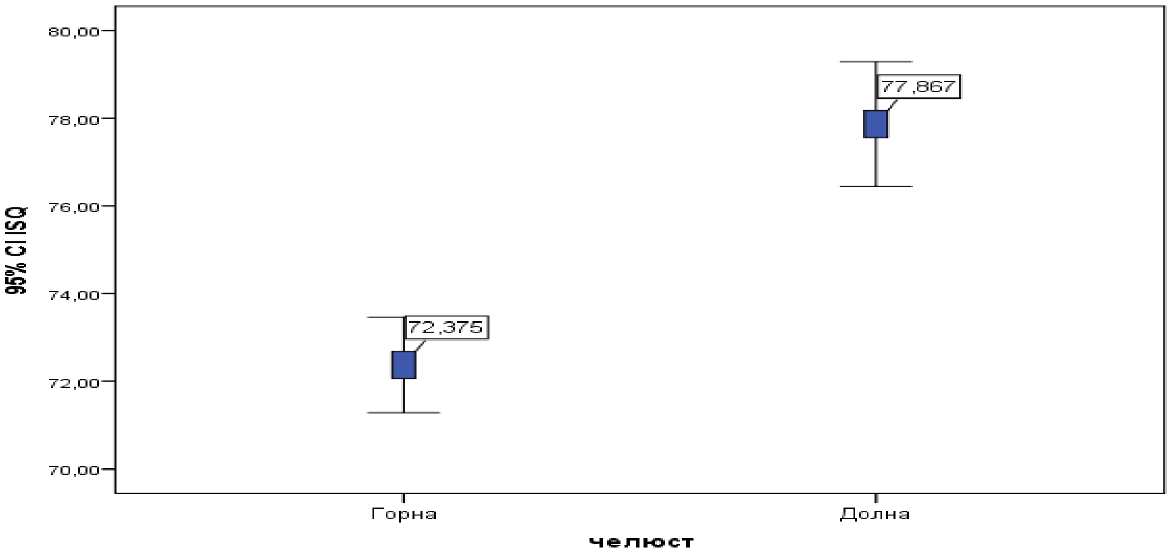


FIG. 23. Mean values of ISQ according to the jaw

The analysis of the results of the resonance-frequency analysis with those obtained from the single-photon emission computed tomography revealed a significant correlation (r = 0.829; p = 0.002). , which shows the lack of scintigraphic data for active reparative bone process (Fig.

24 and Fig. 25). From these data we can conclude that the process of osseointegration is over and the implants can be loaded. From the values obtained in the resonance-frequency analysis (the average value from the measurements in the two mutually perpendicular directions) a high implant stability is established, which is also an indicator of the achieved secondary stability. Both methods examine different characteristics of the healing process and confirm the same thing, namely that implants can be loaded. Also, no significant differences in gender and age were found between the two methods.

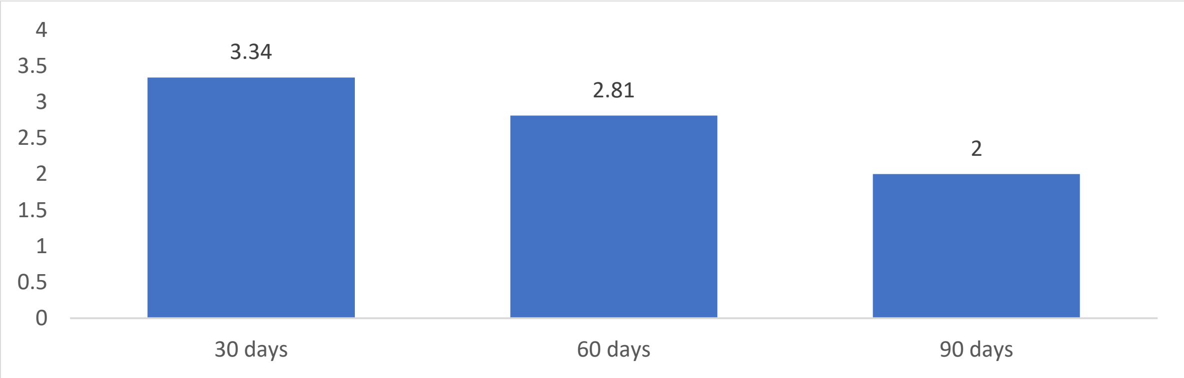


FIG. 24. Mean AOI values in the study period

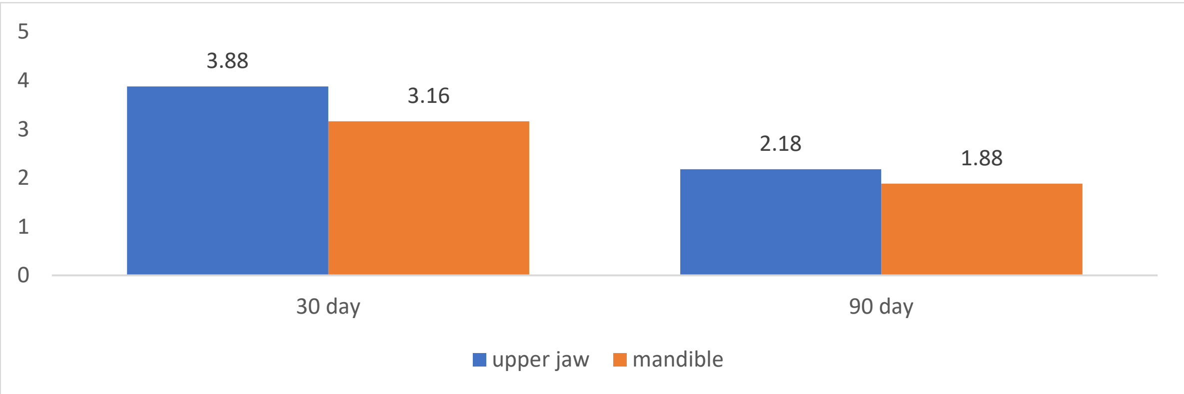


FIG. 25. Mean values of AOI according to the type of jaw in the study period

5. Discussion

5.1 Discussion by task № 1

Bone is vascularized tissue and platelet activation occurs immediately after disruption of its integrity, during the formation of a hematoma. Platelet-released growth factors act locally at the site of injury, mediating early bone regeneration events.99m Tc-MDP accumulates in bone mainly through chemical adsorption into the bone matrix, which in turn is influenced by environment. Bone acidification due to lesions, inflammation or healing increases 99m Tc-MDP deposition in bone and changes are easily visualized by scintigraphy. Osteoblast activity using 99m Tc-MDP bone scintigraphy peaks in the first 4 weeks after dental implant placement, then gradually decreases over a period of time.

This is established in the research of Kahn, Bhandari, Median, Bambini. Our study confirmed that the healing process around intraosseous osteointegrable dental implants is associated with increased accumulation of specific radiopharmaceuticals in periimplant bone. This is observed in the first month after implant placement, the accumulation decreases in the second and third month, which shows a decrease in osteoblast activity. The results obtained by us demonstrate similarity with the research conducted so far. We believe that in order to determine the peak in osteoblast activity in the first month, a bone examination should be performed before the implant placement procedure and regular examinations this month. In the studies conducted so far, the authors report a peak in the second and third week after implantation. Reaching the initial levels is an indicator of the completion of osseointegration and the healing process, which in turn makes it possible to continue with the next stage of treatment - opening and loading the implant. In the literature, this period occurs in 3/4 month. All implants placed by us showed activity in the peri-implant bone, which is an indicator of an active metabolic process. Non-accumulation of radioisotopes in areas of interest is associated with bone alteration and lack of metabolic activity with subsequent implant dropout. This allows the SPECT study to be used for early assessment and predictability of treatment outcome. Bhandari [39] documented that in patients with compromised healing, tracer accumulation is significantly less than in areas with a normal healing process. Also the nuclear medical research technique has the potential to register areas with progressive bone loss at a very early stage. The increase in tracer accumulation levels at the end of the recovery period, when levels should be close to baseline, has correlated with previous studies in which increased levels of accumulation have been reported in regions with peri-implant bone inflammation. In its study, Median Z. [235] performed periodic scans of peri-implant bone tissue, observing a gradual decrease in metabolic activity reaching baseline levels at week 16. At week 23, the author reported a significant increase in activity without clinical manifestation. The examination revealed a torn bridge structure between two implants, which caused trauma. After replacement with a new structure, the levels of metabolic activity returned to baseline. From what has been said so far, it is clear that the method showed high sensitivity and can detect active resorptive changes around the implants before the onset of clinical symptoms or changes in peri-implant bone tissue detectable on radiography.

The increased levels of accumulation of radiopharmaceuticals in areas outside the implantation areas (extraction wounds) are an indicator of reactive metabolic changes in the bone in connection with the healing process after surgical manipulation to remove teeth that are not promising for treatment. This confirms that scintigraphic examination of the peri-implant bone can be used to assess the healing process and gives us a unique opportunity to compare the activity in implanted and non-implanted bone area, of course with some conditionality in terms of how to obtain bone marrow. From an ethical point of view, it is inadmissible to perform an osteotomy procedure without subsequent implant placement. From the obtained results we find similarities in the activity in the two zones.

We did not observe a difference in activity between the left and right side in the same patients with the same implantation area, as in the study of Kalayci A, et al. [182]. Does not distinguish left from right side in the area of canine teeth.

One-photon emission computed tomography is a sensitive, non-invasive method that allows for regular traceability over time and comparability of results in the assessment of different factors and conditions of implantation in individual patients. but we find increased activity in the upper jaw, this is confirmed by the study of Median H, in which baseline levels in the lower jaw are reached at week 12 compared to the upper jaw, which is observed at week 20.Cerveli [69] also confirms that the metabolic activity in the upper jaw lasts longer and is more pronounced. These data prove that the upper jaw is more metabolically active, which can be explained by better vascularization of the jaw. The question needs to be answered as to whether longer osteoblast activity is an indicator of slower but better quality osteointegration and whether faster access to baseline, which marks the end of osseointegration, leads to qualitative osseointegration. These issues are raised in the context of implant loading time.

In 2014, Yamamoto et al [396] conducted a study using bone scintigraphy, the aim of which was to investigate the impact of immediate and early exercise and the impact on dynamic changes in bone metabolism around dental implants. The researchers placed two titanium implants in the right tibia of 21 rats. loading 3 days after implant placement (3-D). Rats were injected intravenously with technetium-99 m-methylene diphosphonate (Tc99 m-MDP) (74 MBq / rat) and scanned by bone scintigraphy at 1, 4, 7, 11, 14, 21, 28 and 35 days after placement. The ratio of Tc99 m-MDP accumulation around implants to that at the reference site was used to calculate and evaluate bone metabolism. In each group, the absorption ratio increased up to 7 days after application of the load and then gradually decreased. It was significantly higher than baseline at 4, 7, 11 and 14 days (P <0.001). The absorption ratio in the 1-D and 3-D groups was significantly higher than in the control group and also in the 0-D group (P <0.001).

Based on the results obtained, the authors conclude that bone metabolism initially increases and then gradually decreases to baseline, despite differences in exercise time. The increase in bone metabolic activity varies depending on the time of application of the load; the later the load is applied, the stronger the bone metabolism.

Suzuki et al. (2007) [359] claim that bone remodeling is different in loaded implants than in unloaded ones. They reported that implants that were loaded immediately had a higher percentage of implant bone contact at month 3 than unloaded implants. Loaded implants showed 10% -12% higher BIC values than unloaded implants [373].

Bambini also observed an increase in metabolic activity during the first 30 days with an implant loaded on the 48th hour and unloaded on the contralateral side, which progressively decreased on the 90th day. notices a faster decline in activity during exercise on the 90th day, which may be a sign of faster osseointegration. In the case of immediate loading, the process of osseointegration ends earlier than in the case of unloaded work [39].

To answer this question, we believe that different studies such as histological, resonant frequency and SPECT should be combined.

Histological examination is the gold standard, a classic method that, based on implant bone contact, provides objective data on the percentage of newly formed bone tissue and the implant surface. data at different stages of the recovery process, ie it cannot be used for dynamic monitoring of osseointegration. Resonant frequency analysis-RFA is a non-invasive diagnostic method that measures implant stability and bone density at different time points [240]. Abdel-Haq et al. [10]. RFA report does not correlate with % BIC.

In 2007 in his study Zhou. [402] analyzed the role of two non-invasive techniques for assessing osseointegration - bone scintigraphy and resonance analysis (RFA) Researchers placed 60 implants in the femurs of 30 rabbits. The placed implants are divided into two groups according to the different treatment of their surface. One is treated by sandblasting and subsequent acid treatment, and the other is by machine treated surface. bone scintigraphy is performed, the authors also perform X-ray, resonance frequency and histological examination. Scintigraphic examination reflects the activity of new bone formation, but does not show a difference between implants with different surface treatment. RFA values increase with increasing bone-implant contact during the healing phase, which collapses with the histomorphometric data. Also, the values of the resonant frequency analysis are different in the two surface treatments of the implants.

In 2012 Sanchez et al. [315] conducted a study to compare the metabolic activity of machine-treated and rough-surface implants using bone scintigraphy during the in vivo process of osseointegration in rabbits, as well as to establish a correlation between the osteoblast index activity (AI) and -percent of implant bone contact (% BIC). 24 implants were placed, two of each species of 12 animals. Before surgery, on the 15th day and at monthly intervals, bone scintigraphy of technetium 99m-methylenediphosphate (Tc-99m-MDP) was performed.% BIC was measured by scanning electron microscopy in 10 samples from each type of implant surface. 15 days after implantation and is higher for machined implants. No significant differences were found in% BIC by implant type.

Bone scintigraphy and resonance analysis allow multiple comparisons within a single subject.

It would be interesting to study how the metabolic activity changes during the placement of the prosthetic structure and the implant load. [317]

In 2008 Sasaki et al. Conducted a SPECT study in rats to determine the metabolic activity around implants during placement and mechanical loading this gradually decreases. In the process of applying the load, the absorption coefficient increases with increasing load - 2.0- and 4.0-N; it was significantly higher for a period of 6 weeks than before the application of the load. The authors conclude that the bone metabolism around the implants increases with the load and depends on the size and period of the load.

Given the progress of technological processes and the large number of implant systems with different surface treatments and modifications, it would be interesting to do a SPECT study to assess osteoblast activity over time in implants with different macrodesign and implant surface characteristics. The last such study was conducted more than 25 years ago, in which knife-shaped and screw-on implants were used, in which, according to the author, the bone healing process is not affected by differences in implant design, with the achieved implant stability in bone.

The choice of method of examination in dental implantology in connection with the healing process and the prediction of the success of the treatment should be applicable under identical conditions for a large number of patients. The method should be highly sensitive and applicable during process.

Observing the healing process around dental implants has always been an interesting topic, which is the reason for conducting a number of histological examinations. Histological examination is the gold standard, a classic method for assessing osseointegration that determines implant bone contact. However, this type of study is not an appropriate method in clinical practice for monitoring the dynamic process of osseointegration. about the same implant in different periods [176; 333].

The method is invasive and involves trauma during sampling, encounters and ethical constraints. Histological analysis does not allow traceability of results over time. [25,249] The use of histological and histomorphometric methods [64, 170] requires sacrificing the area of interest along with the implant.

Resonance-frequency analysis of implants has proven to be a reliable method for assessing implant stability [18,179], but can not assess bone morphology and physiological activity of processes in it.

The value of the torque when placing the implant in the first surgical stage is related to the initial stability, but cannot be used in the time to monitor the healing process [260].

Conventional radiography provides two-dimensional morphological quantification of the area of interest in one plane. [127]

Radiography is a routine tool in clinical practice, the method has low sensitivity in detecting pathological processes and bone remodeling at an early stage [54].

Conical tomography can provide quantification of morphological changes in all three planes, but fails to provide information on physiological activity. [132]

The use of nuclear medical research with the use of a specific radiopharmaceutical that selectively accumulates in the bones with pronounced bone metabolism-osteoblast metabolic activity and vascularization is a method that finds application in clinical practice. [234, 44, 354]

Unlike non-sensitive conventional radiography, bone scintigraphy has a high sensitivity with low specificity [364, 226]

Scintigraphy can reflect physiological changes, in one plane, [78] The method shows a limitation in the accurate quantitative analysis associated with distortion and overlap of unwanted anatomical structures.

SPECT studies provide further improvement over planar scintigraphy, allowing for accurate qualitative and quantitative analysis [105, 106].

SPECT offers the possibility to reconstruct 3-dimensional [3D] images with a distribution of radiopharmaceuticals taken from selected bone structures, providing accurate data on the prognosis of treatment. [32] This study provides an opportunity to study bone metabolism in peri-implant areas, providing not only anatomical images but also information related to the physiology and dynamic changes that occur during osseointegration. [32]

Radioisotope scintigraphy using technetium-99m-methylene bisphosphonate (Tc-99m-MDP) has proven to be a reliable method for measuring increased metabolic activity at specific sites of skeletal tissue [8, 173, 179]

5.2. Discussion on task №2

In the present study, in order to exclude the subjective factor in determining bone density, a study was performed on patients with the same CBST device at identical infusions in order to have maximum comparability of results. A specially developed software algorithm determined the average values of HU in the studied areas [23 in number] in all patients.

Bone quality is a term that is not clearly defined in the literature. The term includes various aspects such as: bone density, degree of mineralization, vascularity and bone metabolism. [46, 257].

Bone quality can be described by factors other than bone density, such as bone size, architecture, 3-dimensional trabecular orientation, [151].

The influence of each of these factors and its relationship to implant treatment is not yet fully understood. Bone density is one of the main factors influencing primary stability, which is crucial for the rapid and quality process of osseointegration and survival of dental implants [228].

Conical beam computed tomography, based on Hunfield units, makes it possible to determine bone density. The determination of preoperative values of bone density in the implantation area shows a significant correlation with the primary stability at implantation [280, 286].

Other authors also confirm the relationship between HU values determined by computed tomography and the stability of the implant during its placement [374, 28,108,228].

There is evidence in the literature for a relationship between bone density and torque values when implants are placed. The relationship is positive: higher density, higher torque [163, 164].

The bone density information obtained from CBST can be taken into account when planning the implant load [312].

Both conventional computed tomography and conical computed tomography can be used to estimate bone density [66,269,367].

Other authors define conical computed tomography as an unreliable method for studying bone density and binding to the primary stability of implants [30, 66].

This is probably due to the fact that the presence of artifacts can make it difficult to measure the bone density around them. Molteni et al state that the presence of artifacts makes it difficult to accurately determine bone density values in Hunsfield units [HUs] of CBCT. [258]

Nackaerts et al. reported obtaining different values of bone density using different scanners for CBCT analysis. [263]

Other difficulties are related to the calculation of the average values of Hansfield units in the bone volume in which it will be implanted, as well as the fact that the value of HU units displayed on the monitor during the movement of the pointer are for a certain section and not for the entire volume.

According to the Mish classification, the results obtained for bone density of the lower and upper jaw, measured in HU, can be said that the studied patients fall into the bone group D3.Identical results are observed in studies by other authorsNorton and Gamble connection with forthcoming implantation, found that the average value was 682 HU [270]

In his study, Turkyilmaz et al. examined bone density during the placement of 158 implants in 85 patients, finding HU values of 278-1227 with an average value of 751.4HU [375]

Shapurian et al. measured the values for Hunsfield units [HU] in relation to the placement of 219 implants, the authors did not find a relationship between the value of bone density measured in Hunsfield units with the age or sex of the patient [338].

The results of our study are confirmed by the conclusions in the literature, which gives us reason to believe that our chosen design of the study of bone density can be used as a reliable tool for assessment in clinical practice, as an additional guide in planning implant treatment. In addition, our design is quick and easy to implement, allows for consistency in measurements, both for individual patients and for individual regions in the same patient. The method can be used for measurements in a large number of patients and to serve for future analysis and research.

Sectoral radiographs are a routine means of examination in clinical practice, which is also used in the field of dental implantology. The method allows to evaluate the implant placed in the bone immediately after implantation, reflects bone morphology, but the method has low sensitivity in detecting early pathological and / or bone remodeling changes. Sectoral periapical radiography (Dick radiography) can be used as a baseline study on the basis of which to conduct comparative graphs over time in order to assess the degree of bone resorption / loss. The presence of enlightenment (weak shadow) between the implant and the bone is an indication of a lack of contact between the two surfaces. The increase in the size of this enlightenment is an indicator of bone resorption. Unfortunately, these changes become visible only with the loss of at least 30% of the mineral content. Metal artifacts are a limiting moment for the measurement and diagnosis of possible periimplantitis in conical beam computed tomography. They are the result of scattered radiation and the absorption of low-energy photons from objects with a high atomic number-metal. The result is image deformation and the presence of hyper-hypodense stripes extending from the object radially in the axial plane. For these reasons, the method of choice for imaging in suspected periimplantitis is intraoral radiography. It has a lower dose, better resolution, lower cost and no metal artifacts.

Both CBCT and conventional radiography cannot reflect functional changes in bone. This is achieved by single-photon emission computed tomography. For example, a metastatic lesion can reveal areas of increased fixation long before bone loss is positive on X-ray..

The values of radiopharmaceuticals peak in the first month and reach baseline levels with the completion of the osseointegration process, which is observed in the 12th / 14th week. In his study, Median found an increase in the accumulation of radiopharmaceuticals at week 23, and a clinical examination revealed a torn bridge structure between the two implants, causing trauma. Increased activity is an indicator of resorptive changes around implants before the onset of clinical symptoms or changes in periimplant bone tissue detectable by radiography, which confirms that X-ray examination of preimplantable bone tissue reflects morphological changes and can not register functional features. can lead to failure in diagnosis and subsequent erroneous conclusions and actions related to the treatment process. An example of such a discrepancy is a study in experimental animals conducted by Cho et al [74], which aims to evaluate the possibility of using non-invasive scintigraphy to study the effect of platelet-rich plasma to improve osseointegration during implantation. To confirm the result, the author conducts a parallel radiological and histological examination. In the two shins of 4 dogs are placed 2 implants - a total of 16 pieces. Prior to implantation, 0.5

ml of PRP was deposited in the osteotomy cavities on the right side and -0.5 ml of saline in the left half-control. On control radiographs there was no difference in the process of ossification of the periimplant bone between the two groups. However, scintigraphic findings reveal a significant difference in radioisotope accumulation in the two groups. Higher uptake was observed in the PRP-treated group at week 4, which decreased more rapidly at week 8, 12, 16 compared to the contralateral side, a sign of significantly higher bone activity and faster regeneration compared to with the control group. Pearson's correlation coefficient was used. The differences are considered significant when the value of p is <0.05. The percentage of implant-bone contact in the histological examination is higher in the group treated with PRP compared to the control. Quantitative histological analysis correlates well with that of scintigraphic examination.

Unlike conventional radiography, conical beam computed tomography allows for: linear measurements, estimation of objects in the three planes of space and to determine bone density based on Hunsfield units. predetermined bone volume, one can look for the relationship between two indicators at different stages of the healing process in all our patients. In order to have maximum accuracy, the bone volume we set is consistent with the size of the implants used. We did not find a correlation between bone density measured in the implantation area before the procedure and osteoblast activity after implantation. This may be due to the fact that in our patients no semen measured bone densities at both extremes: D1 and D4. The already existing algorithm for determining bone density will be able to serve as a basis for comparison in future scintigraphic studies of pre-implant bone.

5.3 Discussion by task № 3

Resonance frequency analysis is used to assess changes in implant stability over time, ie it can be used to measure primary stability, stability assessment in already osteointegrated implants, can also be used as a prognostic method to determine the course of osseointegration. The method can also be used to determine the loading time of dental implants - immediately or early. In Bulgaria for the first time Prof. Peev introduces resonant frequency analysis as a method of research for immediately loaded implants.

In implants with low primary stability, low ISQ values are observed, with the progress of the osseointegration process and the measurement of ISQ immediately before loading, a significant increase in ISQ is observed. In the case of implants with high primary stability and high ISQ in the course of osseointegration, not only may there be no significant increase in these values, but even a slight decrease may be observed [241, 242, 333, 334]. Lower primary stability determines the greater increase in ISQ over time, and implants with high primary stability show a decrease in ISQ values. Values in the lower jaw are usually higher than in the upper jaw [314]. There is evidence in the literature for a directly proportional relationship between implant diameter and ISQ values and an inverse relationship with implant length [218]. A relationship between resonance frequency analysis and implant-bone contact has also been established.

In our study conducted in the third month after implant placement, high ISQ values were found, showing high stability of the implants and the possibility of their loading. The values obtained do not differ statistically in terms of gender and age, although in his study in 2019.Peter Andersson et al. [27] found that women had lower ISQ values than men, which he and his colleagues attributed to the higher incidence of osteoporosis in women.

Today, RFA is used in research related to design, implant surface, and their impact on primary stability and osseointegration. [293].

5.4. Development of an algorithm for evaluation and monitoring of peri-implant bone tissue in the recovery period after placement of intraosseous, osteointegrable implants

A review of the literature shows that there are already established algorithms for clinical evaluation of implant treatment, the main parameters are:

• Evaluation of soft tissues: color, contour, texture, texture - The mucosa around the implant is evaluated for clinical signs of inflammation such as redness, erythema and edema, which can be determined by probing bleeding. [250]. Several gingival indices have been modified and are used in implants. [251]

• Depth of drilling - Periimplant probing with a force of 0.25 Ncm at regular intervals is important for identifying and assessing the progression of the periimplant inflammatory process. [252, 253] Increasing the drilling depth would require further X-ray evaluation to determine the presence of bone loss around the implant. [255] The depth of drilling can vary depending on the depth of implant placement and the force of pressure during drilling.

• Bleeding from drilling - Bleeding from drilling around implants has a higher diagnostic accuracy and a better indicator of disease than bleeding from drilling around natural teeth. [256]

• Radiographic evaluation - Radiographs taken after implant placement and before loading a prosthetic structure have diagnostic value, they serve as a starting point for comparison with subsequent radiographs for signs of inflammation [257, 258]. If clinical signs indicate the presence of periimplantitis, a new periapical radiograph of the implanted area should be taken and compared with previous graphs to confirm or rule out bone loss. X-rays have limitations in terms of bone loss in the buccal or lingual part of the implant. [259]

• Exudation - The presence of purulent exudate may be due to a change in the bacterial environment in the groove around the implant and is usually associated with peri-implant disease and bone loss. [258, 260, 263].

• Free gingival margin position - [261, 262] Progressive apical migration of the gingival margin means loss of clinical attachment around the implant and need for further evaluation.

• Presence / absence of keratinized mucosa - Keratinized gingiva is measured from the gingival margin around the implant to the muco-gingival line. To maintain health, an adequate area of keratinized mucosa is defined as two or more millimeters. [264] There is no consensus on the importance of keratinized tissue around implants - some studies have shown that implants with more keratinized tissue have better plaque indices and reduced alveolar bone loss, two authors argue that there is no link between the lack of keratinized tissue tissue and peri-implant bone loss, despite greater plaque accumulation [251, 265, 266]

• Mobility - Implant motility should be assessed in conjunction with other clinical parameters. The mobile implant has a poor prognosis due to lack of osseointegration or severe bone loss around the implant. [262]

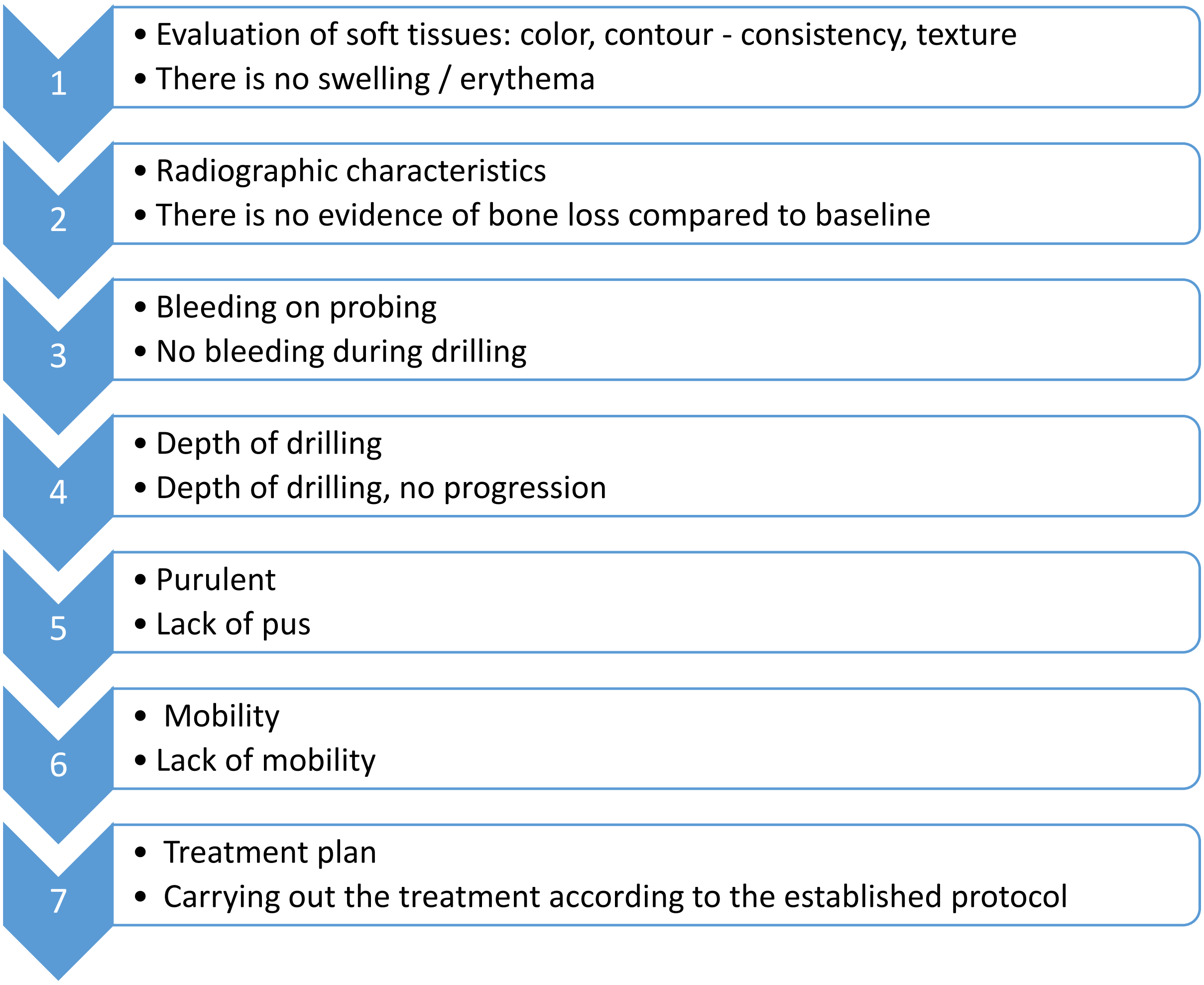


FIG. 26. Stages of clinical evaluation during implant treatment

Despite the established methods for clinical evaluation of the performed implant treatment, the possible complicated and subsequent recovery process, the detailed systematic analysis showed that there is no established algorithm for evaluation and monitoring of periimplant bone tissue in the healing period after intraosseous implantation.

The possibilities for morphological functional assessment of the periimplant bone can be achieved through two main methods - SPECT and histological examination. Of the two methods, we believe that the SPECT method is more widely used because is non-invasive, allows for regular recurrence over time, reflects changes in osteoblast activity, allowing to assess the peak and decline of this activity. conclusions are made about the relationship between cellular activity and the healing process in relation to age, sex, mode of exercise (immediate / delayed), implant system.

In order to be able to assess the above, it is necessary to use unified indices, such as AOI and ROI-areas of interest to be precisely delineated in different areas with similar diameter and number of pixels in them in order to achieve comparability and traceability of results over time.

Regarding osteoblast activity, two periods are important - peak activity and decline to baseline levels, which indicates that the healing process is over and can continue with the next stage of treatment - loading the implant with a prosthetic structure.

For this purpose, it is necessary to conduct regular SPECT studies, which should begin before implant treatment to determine baseline levels of metabolic activity in the area, followed by regular tests on the 14th, 30th, 60th and 90th day after implantation.

The protocol for regular SPECT examination and the calculation of osteoblast activity makes it possible to quantify the progress in the integration of implants. SPECT can provide the study of the process of osseointegration and the influence of various implant characteristics on it such as: the material from which they are made, features in macro design and surface treatment, at different bone densities.

The placement of the implant is preceded by the formation of a bone cavity, a bone box. The injured bone is initially resorbed, followed by the formation of new bone tissue. This healing process can be influenced by systemic and local factors as well as functional load. Physical forces will modulate the type of tissue that will form in the bone interface of the implant; namely bone or fibrous tissue, or both. Radioisotope scintigraphy using 99mTc-MDP provides a reliable method for measuring increased metabolic activity in specific areas, 99mTc-MDP accumulates in the bones and the remainder is excreted through the kidneys. [29, 101, 111, 182]

SPECT uses a targeted image with a radionuclide indicator based on the detection of gamma rays emitted by the radionuclide when incorporated into biologically specific compounds after intravenous administration. The radionuclide emits gamma rays, which can be detected separately by collimation techniques using a gamma camera, so known as a "single photon image". Said imaging technique maps three-dimensional structures into two-dimensional images, the third dimension being included by tomographic technique. These multiple projections are compiled using image reconstruction software to reconstruct the 3D image of the area of interest.

Bone scintigraphy is a study that evaluates the dynamics of peri-implant bone healing, while RFA can be a reliable biomechanical technique. Our combination of these two research techniques may facilitate the assessment of osseointegration. RFA can distinguish differences in stability [159,184] with different surface morphology. Some articles also report the ability of RFA to distinguish between different surfaces [193]. Resonance frequency analysis assesses the stability of the implant. From the results obtained, it can be determined quickly and easily which implants can be loaded and which require additional integration time. It also makes it possible to compare the values when implants are placed and to assess the primary stability with those when opening them and to assess the secondary stability. Assessing the stability of the implant, a motivated decision can be made for its loading.

Conclusion

The growth of the medical device industry provides many new devices, biomaterials and technologies that find different applications in medical practice. Central to the management of biological evaluation of these materials is testing safety and efficacy before widespread clinical use. Preclinical evaluation is mandatory and facilitates the interpretation of complex interface responses, catheter factors, and tissue responses that modulate the success or failure of medical devices. Thus, histological evaluation is an indispensable property for assessing the safety and efficacy of bone implants [223]. Histological tests on humans are limited, so alternative and more gentle methods of examination should be sought and applied.

One-photon emission computed tomography is a non-invasive, highly sensitive method that provides not only anatomical imaging of the study area, but also quantitative information related to physiological and dynamic changes that occur during the process of osseointegration.

One of the main challenges for modern dental implantology is the development of treatment protocols allowing shorter time and faster rehabilitation of edentulous areas. This necessitates the development of new implant systems, research of new materials and testing of new implant surfaces. The growing number of patients with risk factors raises the need to assess the process of osseointegration and its follow-up over time. All this requires research, analysis and comparison of the results of different methods. Just as there is no "ideal" material for the production of dental implants, which fully meets all requirements, and there is no "ideal" study that evaluates all variables in the course of osseointegration: quantity and quality of bone, material for implant production, features of macro design of the implant, treatment of the implant surface, loading conditions, concomitant diseases, etc. Therefore, we have different research methods, the combination of which can cover a larger percentage of these variables and can give us answers to questions that all those working in the field of dental implantology ask. The more methods the clinician knows and applies, the more critical he will be to his work, which benefits not only science but also the patient in whose name new work protocols and research algorithms are developed. Conventional methods such as torque testing when placed and percussion are insufficient. Resonance-frequency analysis and single-photon emission computed tomography, due to their non-invasiveness and specificity can be used to assess all variables in the course of treatment with dental implants..

Inferences

1. The most commonly implanted area is in the area of the 6 teeth, with no difference in sex, age and jaw.
2. Bone density is strongly colored with the lower jaw, but is not associated with gender and age.
3. Metabolic activity in the implantation area shows a stronger dependence on age in men.
4. On the 30th day, increased osteoblast activity is found in all implanted areas, which decreases in the second month after implant treatment.
5. On the 90th day there is no increased fixation of the osteotropic radiopharmaceutical in the area of dental implants.
6. The lack of accumulation of radiopharmaceutical in the implanted areas is a sign of lack of metabolic activity in the area and completed integration process.
7. There is no difference in osteoblast activity with respect to the implantation site.
8. The healing process after tooth extraction and root canal treatment can also lead to the accumulation of radiopharmaceuticals in the course of healing.
9. Panoramic radiography can be used for initial assessment of the dental and maxillofacial system before implantation can be used to predict the outcome of treatment.
10. No direct relationship has been established between osteoblast activity in the implantation site and bone density in the same area prior to implantation.
11. The results of the SPECT study with 99mTc-MDP (99mTc-Methylene diphosphonate) are characterized by high sensitivity and can be used as part of an algorithm for assessing and monitoring the outcome of implant treatment.
12. Resonance frequency analysis is a method that can be used to assess implant stability before loading.
13. There is no difference in the values of the resonant frequency analysis in terms of sex and age, but they differ in the type of jaw.
14. Resonance frequency analysis and SPECT research are used to assess the process of osseointegration, but evaluate it on various indicators.
15. There is a correlation between the values of the resonant frequency analysis and the nuclear medical examination in terms of the time for loading the implants.

Contribution

Contributions of a confirmatory nature:

1. It is confirmed that different paraclinical methods (sector radiography, resonance-frequency analysis, single-photon emission computed tomography) are used to assess osseointegration, which complement each other.
2. Confirmation that the application of SPECT with 99mTc-MDP (99mTc-Methylene diphosphonate) is a reliable method for assessing osteoblast activity in periimplant bone during the healing period after placement of intraosseous osteointegrable dental implants.
3. Confirm that SPECT is a non-invasive test method that can predict and evaluate at an early stage the outcome of implant treatment.
4. Confirm that bone density in the implantation area can be determined on the CBCT.
5. It was confirmed that the resonant frequency analysis and the SPECT study are used to assess the process of osseointegration.

Contributions of an original character to the world

1. For the first time, a software algorithm for determining the mean values of Hunsfield units in a predetermined bone volume has been developed to determine the bone density of CBCT.

Contributions with an original character for the country

1. For the first time in Bulgaria one-photon emission computed tomography with radiopharmaceutical 99mTc-MDP is applied to assess the osteoblast activity in the peri-implant bone tissue in the healing period after placement of intraosseous osteointegrable dental implants.
2. For the first time in Bulgaria the osteoblast activity was compared with one-photon emission computed tomography with 99mTc-MDP radiopharmaceutical according to sex and age
3. For the first time in Bulgaria the relationship between bone density in edentulous areas of the jaw and osteoblast activity in these areas after implantation is studied.

4. For the first time in Bulgaria a comparative assessment was made between the values of the resonant frequency analysis and the single-photon emission computed tomography on the 3rd month after the placement of intraosseous osteointegrable dental implants.

Publications related to the dissertation

1. Hristov I.G., Peev St.V. Chaushev B.G. EVALUATION OF THE PERI-IMPLANT BONE DURING THE HEALING PROCESS BY USING SPECT WITH 99MTC MDP. East European Scientific Journal #12(76), 2021, 32-36
2. Hristov I.G., Peev St.V. Chaushev B.G. APPLICATION OF SPECT EXAMINATION WITH 99MTC MDP IN DENTAL IMPLANTOLOGY. East European Scientific Journal #12(76), 2021, 36-42
3. Hristov I.G. IMPLANT DESIGN FACTORS THAT AFFECT PRIMARY STABILITY AND OSSEOINTEGRATION. East European Scientific Journal #1(77), 2022, 60-65