EVALUATION OF THE PERI-IMPLANT BONE DURING THE HEALING PROCESS BY USING SPECT WITH 99\textsuperscript{m}TC MDP

Summary. Osseointegration is an important, essential process that determines successful implant treatment. Clinical evaluation of peri-implant tissue is based mainly on X-ray examination. SPECT has proven to be a useful and reliable method, providing accurate quantitative assessment and study of metabolic activity. It identifies physiological events as osteoblast activity by using a bone-seeking radiopharmaceutical agent.

Introduction: Osseointegration is a condition in which is achieved clinically asymptomatic rigid fixation of alloplastic material in the bone and preserved during functional load. The process involves implant anchorage in the bone through direct implant-tissue contact. This process starts during the surgery [1]. Osseointegration is determined by a number of factors, including the type of implant and its surface, the quantity and quality of the bone in which it is placed, systemic diseases, trauma during the preparation of the osteotomy cavity.

Dozens of implant systems are known today, but there are still restrictions in evaluation of peri-implant environment and bone healing. The most commonly used methods are: histological, histomorphometric, radiological, computed tomography, scintigraphic and SPECT examination [6, 9, 12, 14].

Conventional radiography provides a two-dimensional image in one plane, computed tomography provides quantification of the morphologic changes in the three planes (coronal, transverse, sagittal), but fail to detect functional changes in the newly formed bone/physiologic activity. [2, 5]

Bone Scintigraphy is a well-established imaging technique that can accurately assess osteoblast activity in one plane, but accurate quantitative analysis is limited by the superimposition of anatomical structures [8].

The histomorphometric method gives excellent results, but is associated with trauma, removing the already placed implant together with the surrounding bone. [7]

The SPECT (single photon emission computerized tomography) has found successful clinical application for the study of many organs, including the bone tissue. The method uses a specific radiopharmaceutical (labeled tracer), which accumulates in the bones, in areas with increased bone metabolism. The most common used radioisotope is 99\textsuperscript{m}etastable Tc labeled with methylene diphosphonate. This radiopharmaceutical has been used since 1971. [15]

SPECT provides accurate quantitative and qualitative analysis by assessing osteoblast activity in the area of interest in the three planes, eliminating areas of non-clinical interest [10].
**Aim:** The aim is to study the process of osseointegration around placed intraosseous osseointegrable implants by using the SPECT method.

**Material and methodology:** The study included 4 patients in good general health, aged (32-48 years). Total of 9 implants were placed in edentulous areas of the upper and lower jaw.

Endoosseous 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 were used.

Lengths - 8-10 mm and used diameters - 3.5 mm, 4.3 mm and 5.0 mm.

Thirty days after implant placement, a hybrid scintigraphic examination was performed - single-photon emission computed tomography with low-dose computed tomography (SPECT / CT), aimed at assessing reparative osteoblast activity and bone mineralization as an osteointegrative response around the placed alloplant. The nuclear medical research was conducted in the Department of Nuclear Medicine and Metabolic Therapy at the University Hospital "St. Marina" EAD, Varna.

30 days after implant placement bone scintigraphy immediately 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 received from a 99Mo / 99mTc generator in a specially designed radiochemical laboratory at the same clinic.

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.

Gamma emission (isomeric transition):

60 части

60

99Mo 99mTc 99mTc

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. Patients were carefully positioned and metal objects from the scanned area were removed. Static targeted scintigraphies in the head area in front, rear and lateral projections were performed sequentially, serving as a guide for increased osteoblast activity. Immediately afterwards, SPECT/ CT was performed by rotating the detectors 360° around the patient with 64 consecutively recorded projections for 15 seconds with an angle interval 5°-6° in step and shoot scanning mode. The images were registered on a 128x128 matrix. The obtained information was processed by specialized software, tomographic images were reconstructed by reverse projection in the three orthogonal planes of space - transverse, coronal and sagittal. A Butterworth filter with a cutoff frequency of 0.6 Hz was used. This filter helps to preserve the fine details of the image as much as possible and eliminates background noise. In our study, The technique allows to obtain a three-dimensional representation of the distribution of radioactivity in the area / 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.

Different regions / areas of interest (ROIs) have been identified and drewed by hand. Calvary bones were used as reference area for comparison of physiological fixation on healthy bone and designated as “baseline ROI". The "Baseline" area of each patient was compared with the different ROIs of interest (test) outlined around the implants. The activity (pixel count) in the area of interest was compared with the activity in the skull (control). The Osteoblastic Activity Index (OAI)1 was calculated by dividing average pixel count in the area of interest by average pixel count in the skull (control).

**Results:** In all patients the healing process proceeds normally, without complications. Perimplant bone changes and osseointegration were assessed based on the count / pixel ratio obtained from the SPECT study 30 days after intraosseous implant placement. Osteoblast activity in the area around the implants was compared to the baseline area for each patient. Ratios of count densities (counts/pixel) obtained from each ROI were used for a quantitative-relATIVE evaluation.

From planar images acquired after 30 days, we obtained the following values For patient A, 2 ROIs of 18 pixels each were placed. This provided 832.73 counts from the test area (A/1) with a ratio of 46.26 counts/pixel and 89.49 counts/pixel from the control area (A/2) with a ratio of 12.78 counts/pixel (Fig. 1; Table 1).
Fig. 1. SPECT images of patient A performed at 30 days

For patient B, 2 ROIs of 47 pixels each wereplaced. This provided 309.36 counts from the test area (B/1) with a ratio of 6.58 counts/pixel and 118.25 counts/51 pixels from the control area (B/2) with a ratio of 6.58 counts/pixel (Fig. 2, Table 1).

Fig. 2. SPECT images of patient B performed at 30 days

For patient C, 1 ROI of 4 pixels each were placed. This provided 361.55 counts from the test area (C/1) with a ratio of 90.39 counts/pixel and 139.34 counts/4 pixels from the control area (C/2) with a ratio of 34.84 counts/pixel (Fig. 3, Table 1).

Fig. 3. SPECT images of patient C performed at 30 days

For patient D, 3 ROIs of 19 pixels each were placed. This provided 1008.56 counts from the test area (D/1) with a ratio of 53.08 counts/pixel and 171.38 counts/13 pixels from the control area (D/2) with a ratio of 13.18 counts/pixel (Fig. 4, Table 1).
Discussion: Nuclear medicine offers the clinician great diagnostic potential in bone pathology. SPECT examines bone metabolism, providing both anatomical images and data on the physiological and dynamic changes that occur during osseointegration in the three orthogonal planes. In dentistry, this method can be used to quantify the healing process around placed intraosseous implants, bone grafts and single-implant grafts. [13]

In the present study, we demonstrated the efficiency of SPECT in assessing osteoblast activity in the peri-implant area during the healing process of intraosseous implants. We used bone tracer - methylene diphosphonate, which accumulates in areas with bone metabolism, to assess osteoblast activity and receive information for the process of osseointegration. That was done by measuring the number of counts per pixel and comparing it to the reference area of the calvary, where a bone structure has been already built.

The results show that in all patients, in all areas except one area, was found increased osteoblast activity. There are no data on clinical complaints in this area, no bone resorption (radiolucency around the implant) is observed radiographically. Information on whether the implant is osseointegrated will be available after flap preparation.

Increased osteoblast activity was also found in areas of bone where no implants were placed. These are areas where bone healing is result from- root canal treatment of periapical inflammatory process, extraction of severely damaged third molars. This confirms the effectiveness of SPECT examination in the bone repair process. We did not find a difference in osteoblast activity in implants of different length and diameter. Such a difference was not found in patients of different age groups. In the future, it would be good to conduct a SPECT study in patients who have used implant systems with different surface treatments.

A number of authors use SPECT in the evaluation of the osteointegrative process in dental implants. Khan et al. in 2000 they conducted a similar study. They examined 5 patients who were placed with titanium implants in a edentulous jaw. They found an increase in cellular activity immediately after the postoperative period. On the 30th day they report a peak in activity and a gradual decrease to normal physiological levels after 4 months [11].

In 2004, other authors used SPECT to assess the osteointegrative response in immediately loaded intraosseous implants. Two types of implant systems have been used. On the 30th day, the authors report a peak in osteoblast activity, which gradually decreases in the coming months. They also found that the activity also depends on the surface of the implant, as it is higher in implants with a rough surface [3].

Bhandari received similar results in 2012. He published a study using SPECT to assess osseointegration in a local implant system [4].

The results obtained by us were processed according to the methodology used by them. The values for a certain period of time were compared with theirs. We found similarity in the obtained results obtained - increased osteoblast activity on the 30th day. These results give us reason to believe that the implant system use creates conditions for rapid and high-quality osseointegration. It should be noted that the authors report a gradual decline in osteoblast activity, which returned to pre-implant about 3rd /4th month after implantation. These results indicate that the implants are osseointegrated and can be functionally loaded. We are waiting for the 3-month period for the next SPECT study. We have no doubt about the success of our treatment. The additional results will allow us to make additional analyzes and compare them with similar studies already conducted.

Conclusion: The nuclear medical SPECT study provides images and measurements of the distribution

<table>
<thead>
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<th>Patients</th>
<th>Test</th>
<th>Control</th>
<th>Test - Control</th>
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<td>Patient A</td>
<td>46.26</td>
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<td>Patient C</td>
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<tr>
<td>Patient D</td>
<td>53.08</td>
<td>13.18</td>
<td>39.9</td>
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Table 1.

Count Density Ratios (Counts/Pixel) in Test and Control Areas of Both Patients at 30 Days

Fig. 4. SPECT images of patient D performed at 30 days
of radiopharmaceuticals, which provides information on activity in these areas of interest. Osteoblast activity can be used to assess the healing process at an early stage of implant treatment and can assess any variable in the process of osseointegration.

References:

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APPLICATION OF SPECT EXAMINATION WITH 99MTC MDP IN DENTAL IMPLANTOLOGY

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ПРИМЕНЕНИЕ ОФЭКТ ИССЛЕДОВАНИЯ С 99MTC MDP В СТОМАТОЛОГИЧЕСКОЙ ИМПЛАНТОЛОГИИ