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Features of organotopic remodeling of bone tissue and implanted osteoplastic material in Charcot neuro/osteoarthropathy

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Abstract

Introduction Despite the recognition of MRI as the gold diagnostic standard for Charcot arthropathy, there is evidence in the literature that MSCT is more informative for objective qualitative and quantitative diagnosis of the condition, primarily of the bone skeleton of the Charcot foot, in comparison with standard radiography. The sensitivity and specificity of these methods are different. **Purpose** To reveal the features of organotopic remodeling of bone tissue and implanted osteoplastic material in the course of midfoot and hindfoot subtotal defects management in Charcot neuro-osteoarthropathy. **Materials and methods** The analysis of bone tissue and implanted osteoplastic material density was carried out in a case series that included 11 patients with Charcot neuro-osteoarthropathy who underwent a two-stage procedure for bone defects in the hindfoot and midfoot with the Ilizarov apparatus. We studied CT and MRI scans and measured bone regenerate density before treatment, at the stages of transosseous osteosynthesis, and 3, 6, and 12 months after surgery. **Results** In all patients, varying increase in the amount and volume of bone tissue was visualized due to intensive periosteal bone formation along with the formation of bone ankylosis in the joints along combined with a consistent increase in the optical density of bone regenerates. The formation of the new bone tissue ran without the signs of lysis or sequestration. The conducted studies indicate that the sizes and architectonics of bone fragments are more differentiated in CT than in MRI scans. **Discussion** It is known that the bone, despite its high mineralization, continuously rebuilds, restores and adapts itself to certain functional conditions. This constant dynamic process of adaptive remodeling depends mostly on optimal blood supply, metabolic activity and the coordinated work of bone cell elements. The data obtained show angiogenesis in the compromised tissues in patients with Charcot foot and consistent remodeling of the graft into the new bone tissue. **Conclusion** The allobone in the composition of the combined bone graft does not reduce the likelihood of complete remodeling of the newly formed bone tissue. Higher bone density by filling in a bone defect with a graft differs from distraction regenerate that initially has low bone density. CT and MRI are highly effective and informative diagnostic methods for surgical treatment. In reconstructive interventions in the patients with Charcot foot under the conditions of transosseous osteosynthesis, preference among radiological study methods should be given to CT.

Keywords: Charcot foot, bone grafting, regenerate remodeling, radiological studies

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INTRODUCTION

One of the challenging complications of diabetes mellitus is diabetic foot syndrome, which includes a multicomponent pathological symptom complex: peripheral changes in innervation, arterial and microcirculatory flow, destruction of the osteoarticular apparatus of the foot with the risk of purulent and necrotic processes. According to the literature, neuropathic Charcot foot develops in type 1 diabetes mellitus in 17.9 %, and in type 2 diabetes in 7.4 % of clinical cases [1]. Low incidence of Charcot foot due to diabetes mellitus, despite the severity of the pathology, may be explained by a few publications based on a rather small number of cases and studies. There are publications in the literature about the importance of preoperative histological studies of destructive changes in the cartilage and bone structures in diabetic foot syndrome (DFS) for planning reconstructive interventions on the foot, based on a few morphological studies, which is probably based on the organizational limitations of in vivo studies and their invasiveness [2, 3]. Currently, in the diagnosis of bone pathology in diabetic foot syndrome (DFS) and diabetic osteoarthropathy, mainly at the stages of preoperative planning, computed tomography (CT) and magnetic resonance imaging (MRI) are used in addition to traditional radiography (RG). In the International

IWGDF Guidelines on the Prevention and Management of diabetic foot disease (2019) and domestic clinical guidelines, MRI is recognized as the diagnostic "gold standard" [4]. There are classifications of the diabetic foot syndrome based on MRI data with an assessment of bone marrow edema in the fat suppression mode [5], which has certain advantages as a method that can visualize the bone and soft tissue structures of the foot in the absence of ionizing radiation [6].

However, there is evidence in the literature that MSCT is more informative for objective qualitative and quantitative diagnostics of the condition, and, first of all, of the bone skeleton of the Charcot foot in comparison with standard radiography [7].

CT is able to assess not only structural changes in bone tissue and the cortical layer, but also to identify free bone fragments and sequesters, visualize the position of the fragments [8, 9], and perform 3D reconstruction for a three-dimensional imaging of the anatomical features of the pathological process [10].

Single-photon positron emission computed tomography (PET-CT) significantly improves the image quality during bone scanning and the accuracy of diagnosing Charcot arthropathy even at the roentgen negative stage (stage 1 according to the Eichenholtz classification [11]), enables to determine the severity of damage to bone structures [12], and anatomical location. The high reliability of PET-CT allows more accurate differential diagnosis between the acute stage of arthropathy and osteomyelitis [13].

Any diagnostic search begins with radiography (RG) of the foot in standard views. CT has a number of advantages over RG and is accompanied by a higher radiation exposure. MRI is devoid of this shortcoming, more informative in the early stages of osteoarthropathy; however, data interpretation and differential diagnosis can be difficult. A number of authors point to a high frequency of false positive results in the diagnosis of infectious and aseptic inflammatory processes in diabetic foot [14-20].

The sensitivity and specificity of these methods is different. The highest sensitivity is recorded in computed tomography with 3D reconstruction and contrast enhancement (> 90 %) and magnetic resonance imaging (89-100 %). The highest specificity is also revealed with these research methods (> 90 % and 81-100 %, respectively) [20].

In osteoplastic reconstruction of the Charcot foot, radiological checks should not only assess the geometry of bone structures and the presence of destructive processes, but also the maturity of the bone regenerate.

In order to assess the state of bone regenerate, various methods were proposed over the years with varying reliability of the data obtained: a number of laboratory tests (marker of bone matrix formation – N-terminal propeptide of type 1 procollagen (P1NP), bone remodeling marker (N-osteocalcin), markers of bone resorption (Beta-CrossLaps and Pyrilinks-D), parathyroid hormone and somatotropic hormones, serum calcium and phosphorus, vitamin D (calciferol), alkaline phosphatase, etc.), clinical radionuclide, high-frequency Doppler ultrasound, optical density analysis regenerate, computer simulation [21-24]. However, not all of these methods are available in everyday practice, especially at a municipal hospital. Therefore, the most popular are all the same more replicated methods of radiological diagnosis: RG, CT and MRI.

Purpose To reveal the features of organotopic remodeling of bone tissue and of implanted osseoplastic material in the management of mid- and hindfoot subtotal defects due to Charcot neuro-osteoarthropathy.

MATERIAL AND METHODS

The results of CT and MRI studies in a series of cases of patients with Charcot osteoarthropathy were analyzed, who were treated at the Center for Foot and Diabetic Foot Surgery of the Yudin City Clinical Hospital and the Department of Purulent Surgery of City Clinical Hospital No. 13 of the City Healthcare Department of Moscow in 2020-2022. Two-stage management of bone defects in the hind and midfoot was performed. To standardize the observation, we used the SEDW classification [24, 25]. To clarify the location of the pathological process in the midfoot, the Sanders and Freikberg classification was supplemented with marks M (medial column), L (lateral column) or T (total lesion).

The study included 11 patients: 8 patients with type 2 diabetes and 3 patients with type 1 diabetes. The average age of patients was 49.1 years (range: 24-61 years); there were 6 women (55 %) and 5 men (45 %).

Two-stage management of bone defects in the middle and hindfoot with a combined auto-allograft was performed in 9 patients [256], one patient with type 2 diabetes with a bone defect of the medial column was managed with Biosit hydroxyapatite chips, one patient with type 1 diabetes was treated for a defect in the medial column with a combined autograft with Biosit chips. The period of fixation in the apparatus was 6-8 months. Variation of the fixation time depended on the size of the graft and the volume of bone loss. Filling of a defect of more than 30 cm^3 and the intervention zone 4-5 according to the Sanders & Frykberg classification, fixation was carried out for 8 months, and in other cases for 6 months.

At the stages of treatment and follow-ups at 3, 6, 9, and 12 months after surgery, a CT study of the area of the implanted bone graft was performed. The maximum follow-up period was 13 months. Bone density of regeneration was determined in Hounsfield units along with the changes in the architectonics of the newly formed bone tissue and osteoplastic material. RadiAnt Dicom software was used to process CT data.

The study was performed in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association "Ethical principles for medical research involving human subjects" as amended in 2013 and "Rules of Clinical Practice in the Russian Federation", approved by order of the Ministry of Health of the Russian Federation dated June 19, 2003 No. 266. Patients signed an informed consent for the surgical intervention and the publication of the data obtained without identification of the individual.

RESULTS

Primary scanning was performed in the conditions of external fixation and visualization was difficult due to ME artifacts. At the fixation period of 3 months, according to CT data, an increased density of the bone graft (396.5 ± 23.5 HU) was revealed in all patients in comparison with the density of the recipient surrounding bone (123.5 ± 19.6 HU). The authors attribute this to the high density of the implant material and the intraoperative compaction of the graft filling the defect.

As early as 6 months after the operation, bone hardening of the regenerate was observed (447.6 ± 29.9 HU) in all patients in the defect zone, along with an increase in the number and volume of bone fragments due to intensive bone formation.

Twelve months after the operation, the average density of the regenerate was 623.5 ± 153.2 HU, and in the surrounding bones it was 186.3 ± 91.3 HU (Table 1).

In one patient whose defect was filled with Biosit implant material, the average graft density according to CT data after 3 months was 1141 HU and remained without lysis until the end of fixation.

In a patient with combined plasty (autograft RIA + Biosit), 3 months after defect filling, bone density was 380 HU and reached 871 HU by 12 months.

Comparison of CT data of patients at different stages of fixation and MRI after dismantling of the device was carried out. According to CT data, the sizes and architectonics of bone fragments, as well as qualitative and quantitative indicators of changes in the structure and bone density of grafts, could be more optimally differentiated.

The possibility to measure the density of the bone regenerate in Hounsfield units in the RadiAnt Dicom Viewer program enabled to evaluate the dynamic organotypic reorganization of the regenerate and its characteristics in comparison with the surrounding bone structures.

In one of the patients, positive dynamics of the formation of bone regenerate was weakly pronounced 9 months after the operation, probably due to inhibition of the biomaterial through fibrosis; however, bone tissue remodeling was visualized due to periosteal callus and ankylosis of the foot joints. One of the reasons of long bone consolidation of the block was a more extensive defect that needed a higher ratio of allograft to autograft in the implanted osteoplastic material, which required a longer complete organotypic restructuring of the newly formed bone tissue [28].

In two patients, CT showed preservation of marginal residual cavities up to 0.5 cm^3. In our opinion, this was due to the error by filling the defect with a bone graft chips; however, this did not affect the overall dynamics of bone remodeling and the timing of consolidation.

The average density of the regenerate compared to the surrounding bones was 4.5 times higher by 6 months after the operation, and by 12 months it was 3.5 times higher (the authors attribute it to an increase in the density of the surrounding bones due to growing functional load on the foot).

Despite the different genesis of the autograft and distraction regenerate, we observed a gradual restructuring of the biomaterial, an increase in the amount and volume of bone mass without signs of lysis and inflammatory destruction, dynamic compaction of the newly formed bone tissue, as well as the formation of interarticular bone blocks (Fig. 1- 4).

Table 1

Changes in bone density in regard to the defect filling time

Term after the operation	Bone graft density, HU		Surrounding bone density, HU	
	Average value	Min-max	Average value	Min-max
3 months	396.5	313-442	123.5	60-211
6 months	447.6	352-553	114.1	61-154
12 months	623.5	261-884	186.3	24-405

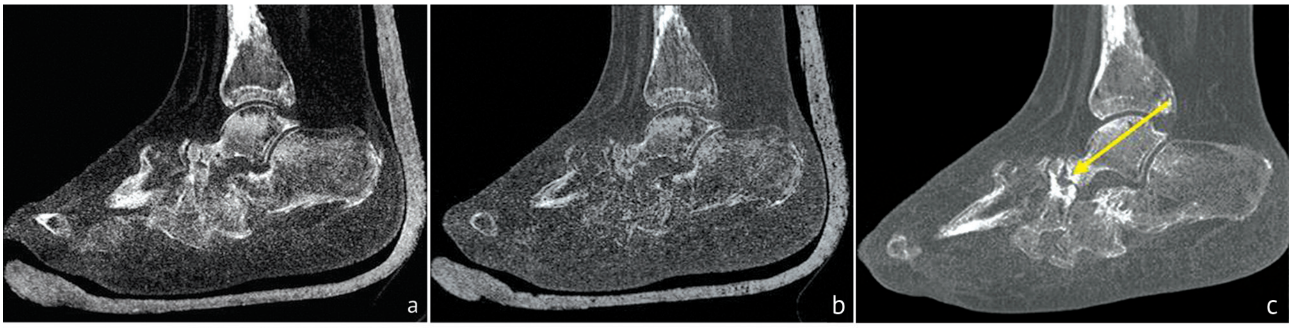
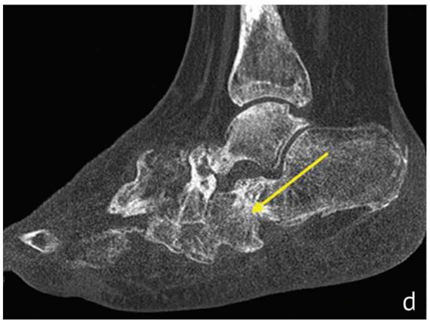
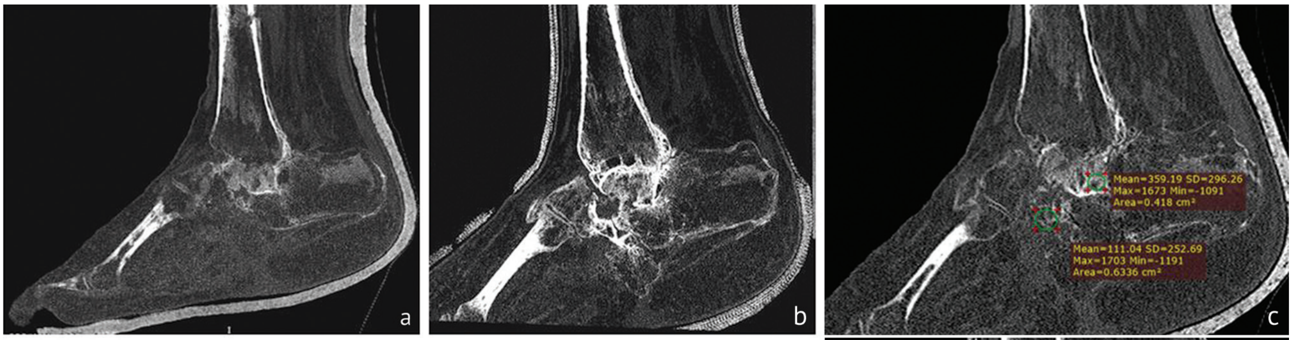



Fig. 1 Patient Sh., 50 years old. MSCT, sagittal plane, 6 months after surgery (a, b): remodeling in the talonavicular and calcaneocuboid joints, formation of bone regenerate in the midfoot. MSCT, sagittal plane, 12 months after surgery (c, d): formation of dense bone regenerate in the midfoot with ankylosis in the calcaneocuboid joint; remodeling of the bone regenerate



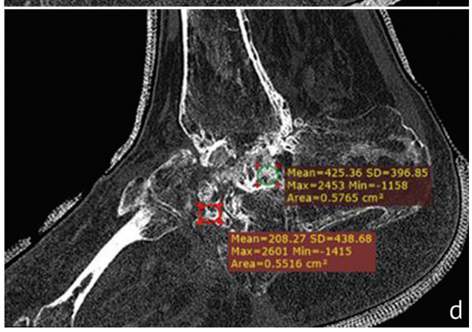


Fig. 2 Patient P., 42 years old. MSCT 9 months (a, c) and 12 months (b, d) after surgery. There is a tendency to form a dense bone regenerate in the midfoot, the formation of bone ankylosis in the tibio-talar and talocalcaneal joints (a, b), an increase in the volume and density (c, d) of the bone regenerate in the defect zone: 111.04 HU -– 208 .27HU; 359.19 HU – 425.36 HU

Fig. 3 Patient Ya., aged 24. MSCT of the foot, sagittal plane (a, b). Six months after the operation, we observed the formation of a compact bone regenerate (706.65 and 671.54 HU) in the middle part of the foot; foci of decreased density are noted due to transient regional osteoporosis

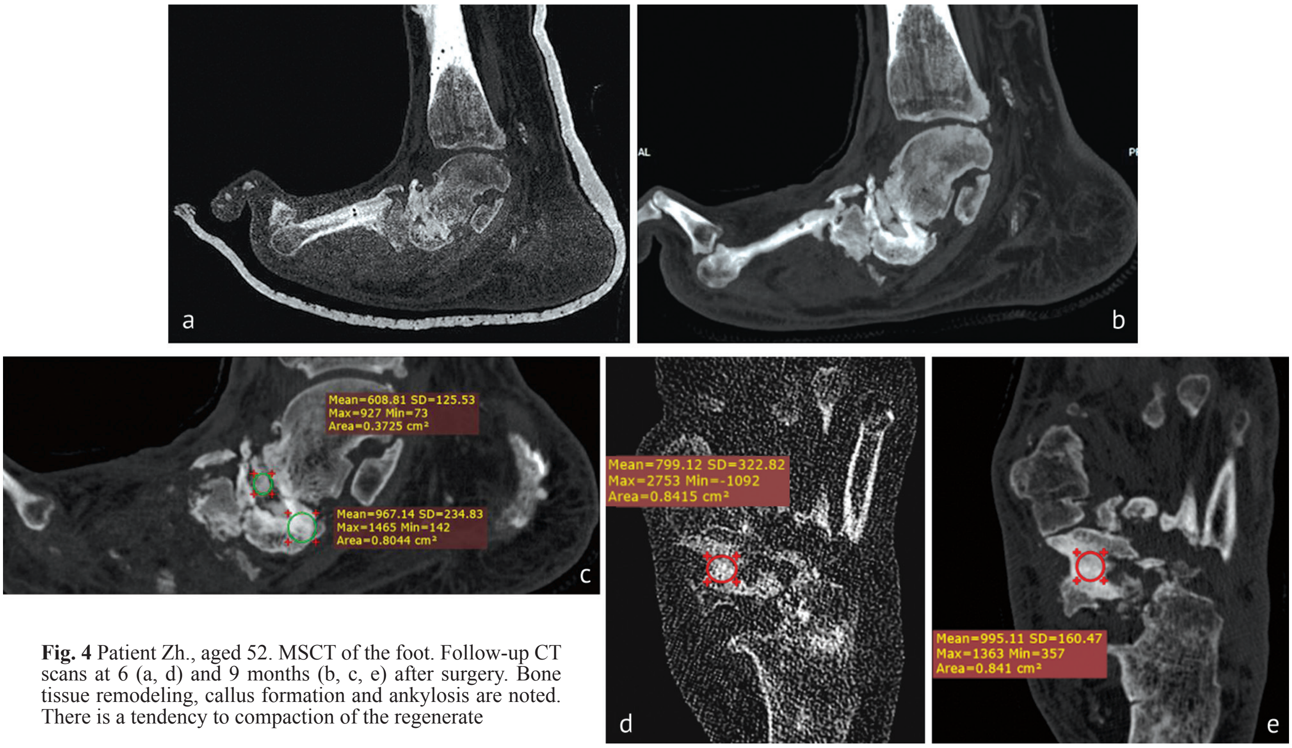


Fig. 4 Patient Zh., aged 52. MSCT of the foot. Follow-up CT scans at 6 (a, d) and 9 months (b, c, e) after surgery. Bone tissue remodeling, callus formation and ankylosis are noted. There is a tendency to compaction of the regenerate

DISCUSSION

According to the available literature, computed tomography has not been currently recognized as the leading method for diagnosing Charcot neuroarthropathy. Along with radiography, ultrasound and MRI, this method is the main procedure for evaluating foot complications associated with diabetes [26]; however, each of the methods is not sufficient to obtain complete information about the pathology. Therefore, an ideal diagnosis should use a multimodal approach [27, 28]. We share the opinion of the colleagues about the importance of using CT at the stages of preoperative planning and postoperative monitoring of patients with Charcot foot in order to assess the changes in the architectonics of bone tissue, bone regenerate formation and to determine its density, as well as for a reliable qualitative assessment of developed ankylosis [29].

Despite all the obvious advantages of magnetic resonance imaging, especially for detecting an early stage of diabetic Charcot osteoarthropathy, this method does not allow a reliable assessment of bone tissue formation and regeneration due to low differentiation of calcium caused by postoperative changes.

The bone, despite its high degree of mineralization, continuously rebuilds, restores and adapts to certain functional conditions. This constant dynamic process of adaptive remodeling depends mainly on optimal blood supply, metabolic activity and the coordinated work of bone cell elements. As is known, bone remodeling has two processes: resorption of bone tissue by osteoclasts and its new formation by osteoblasts [30, 31].

The remodeling of auto- and allograft (demineralized bone matrix) runs according to the same algorithm, which was demonstrated in histological studies by Bouaicha et al. [32]. The first step is the resorption of the allograft by osteoclasts, revascularization, and then the synthesis of a new bone by activating osteoblasts from the autograft and preserved healthy bone fragments. Traditionally, this process is called a creeping substitution line [32-34].

Brcic et al. showed revascularization of the bone allograft and its remodeling, including osteoclastic and osteoblastic activity, after 10 weeks [34].

Drawing an analogy with distraction regenerates in the correction of foot bone shortening, according to MSCT data, a similar gradual remodeling of the distraction regenerate was also noted and was associated with a gradual increase in the density of the regenerate [35].

Thus, the density of the distraction regenerate changed from a density equal to the density of adipose tissue to the density exceeding of the surrounding bone tissue [36]. This thesis is confirmed by a clinical case of patient M., 50 years old, MSCT and MRI studies 6 months after surgery (Fig. 5).

The difference between autologous bone grafting and the distraction regenerate was the possibility of intraoperative compaction of the material, which, according to early CT data, showed a higher density of the graft; and only in cases of insufficient compaction with extensive bone defects, low bone density was noted, corresponding to the density of granulation tissue (adipose), the same as in the early stages of the distraction regenerate formation. The presence of angiotrophic disorders in patients with Charcot foot under the conditions of transosseous osteosynthesis and the use of free bone allo- and autografts did not exclude the possibility of foot reconstruction in defects in its middle section and root with the formation of bone blocks undergoing complete organotopic remodeling. The data obtained allow us to make an assumption about the remodeling of the graft into a compact bone and the presence of angiogenesis in this area. However, it should be noted that there is a reserved attitude towards the use of external fixation in reconstructive operations in patients with Charcot foot; there are publications in the literature in which the authors share their results that describe only one clinical case [37, 38].

Fig. 5 MRI (a) and MSCT (b, c), sagittal plane, identical sections. The study was performed with a difference of several days. MRI PDW, sagittal plane (a): disorganization of the midfoot is determined, in the bed of the navicular bone there is a reduced density of the regenerate, corresponding to the optical density of the fibrous/granulation tissue with inclusions in the structure of the bone regenerate. The latter is weakly visualized. MSCT MPR in the sagittal plane (b, c): the sizes and morphology (architectonics) of bone fragments in the biomaterial are more differentiated, as well as the qualitative indicators of graft maturation (566.6 ± 105.2 HU, the minimum and maximum values are 461.4 and 671.7HU)

CONCLUSION

The inclusion of allobone in the combined bone graft does not decrease the likelihood of complete remodeling of the newly formed bone tissue. A higher bone density achieved by filling a defect with this graft differs it from distraction regenerate that has an initially low bone density. The degree of structural reorganization of bone grafts according to CT and/or MRI data in patients with bone defects in Charcot neuroosteoarthropathy should considered for preoperative planning and assessing the volume of the defect throughout the entire process of external fixation treatment, for planning the time of the termination of external fixation and loading mode and rehabilitation in the condition of increasing physiological load on the foot.

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