Original article
https://doi.org/10.18019/1028-4427-2025-31-2-237-244

Prediction of impaired consolidation of limb long-bone fractures using neural network analysis

A.M. Miromanov✉, **K.A. Gusev, A.N. Staroselnikov, V.A. Mudrov**

Chita State Medical Academy, Chita, Russia

Corresponding author: Alexander M. Miromanov, miromanov_a@mail.ru

Abstract

Introduction Impaired reparative regeneration in patients with fractures is the most common complication; immunogenetic mechanisms play a leading role in its pathogenesis. Many researchers are engaged in the search for an "ideal" diagnostic marker. For this purpose, neural networks have been increasingly used, which allow not only to predict various pathological conditions but also to determine reliable options for prevention and treatment.

The **purpose** of the study was to evaluate the effectiveness of predicting impaired consolidation of long-bone fractures of the extremities using the neural network data analysis.

Material and methods We examined 108 young patients (WHO classification) with fractures of lower limb long bones. The clinical comparison group consisted of 62 patients without complications at the age of 34.5 [18; 44] years. The study group included 46 patients of similar age (36 [18; 44]) years and gender with delayed consolidation. The control group included 92 practically healthy individuals. Exclusion criteria from the study were any concomitant disease, other location and nature of injuries, alcoholism, as well as inaccurate reduction of bone fragments, and repeated operations. Patients who received antiresorption therapy and calcium supplements in the prehospital stage were also excluded. Laboratory (genetic) studies included determination of carriage of polymorphic molecules — *TNFRSF11B-1181(G>C), IL6-174(C>G)*, *TGFβ1-25(Arg>Pro), EGFR-2073(A>T)* and *VDR(BsmI283G>A)*. Amplification was carried out using primer sets Litekh-SNP (Russia). The risk of developing delayed consolidation was assessed using SPSS Statistics Version 25.0 (Neural Networks module). The predictive performance of the neural network was assessed using ROC analysis.

Results For determining the importance of the independent variable, the following gradation was noted: *TGFβ1-25(Arg>Pro)* gene polymorphism — 100 %; gene polymorphism *TNFRSF11B-1181(G>C)* — 97.1 %, gene polymorphism *VDR-BsmI283(G>A)* — 34.7 %; *IL6-174(C>G)* gene polymorphism — 31.5 %; polymorphism of the *EGFR-2073(A>T)* gene — 15.3 %. The percentage of incorrect predictions was 8.3 %. Area under the curve of ROC analysis (AUC) = 0.91[0.85–0.98], $p < 0.001$. The specificity of the resulting model is 0.95 %, sensitivity is 0.87 %, accuracy is 91.7 %.

Conclusion The use of the neural network for predicting delayed consolidation of fractures using data on the carriage of certain gene polymorphisms has a sufficient degree of accuracy (91.7 %), which indicates that the introduction of the neural network analysis into practical medicine is promising.

Keywords: consolidation disorder, genetic markers, polymorphism, neural network analysis, neural network

For citation: Miromanov AM, Gusev KA, Staroselnikov AN, Mudrov VA. Prediction of impaired consolidation of limb long-bone fractures using neural network analysis. *Genij Ortopedii*. 2025;31(2):237-244. doi: 10.18019/1028-4427-2025-31-2-237-244.

INTRODUCTION

Despite advances in surgical treatment of patients with musculoskeletal injuries, slow bone tissue reparation processes are quite frequent, and about 10 % of fractures end in nonunion [1, 2, 3]. The issue of reparative regeneration disorders in patients without systemic and local risk factors remains open. Currently, studies have been conducted that show the leading role of human immunogenetics in this complication, and certain variants of polymorphic gene carriage and their abnormal expression can be decisive in the mechanism of consolidation disorders [4, 5, 6, 7]. However, the range of such studies is still not so wide and requires further research.

In the modern world, the role of innovative technologies for analyzing the data obtained is increasing. The use of neural networks and artificial intelligence (AI) in contemporary healthcare may solve many problems, in particular, not only predict various diseases/complications but also to determine reliable options for the prevention and treatment of these pathological conditions [8, 9, 10].

The **purpose** of the study was to evaluate the effectiveness of predicting impaired consolidation of long-bone fractures of the extremities using the neural network data analysis.

MATERIALS AND METHODS

The ethical principles of the Helsinki Declaration of the World Medical Association (amended in 1964, 2011) were followed in the work with the subjects of this study.

This report was prepared as part of the comprehensive research work RK 034 (02, 03), registration number AAAA-A16-116063010015-6.

A total of 108 young patients (according to WHO grading of age) with long-bone fractures of the lower extremities were examined. The clinical comparison group consisted of 62 patients without complications aged 34.5 years [18; 44], the main study group were 46 patients of the same age (36 [18; 44]) with delayed consolidation, the control group included 92 practically healthy people comparable in age (35.0 [18; 44]) and gender. The criteria for non-inclusion in the study were any concomitant diseases, other locations and nature of injuries, alcoholism, as well as incomplete alignment of bone fragments during reduction and repeated operations. Patients who received antiresorptive therapy and calcium preparations at the prehospital stage were also excluded.

The diagnosis of delayed consolidation was made based on the RUST consolidation assessment [11] and radiographic criteria described in the clinical guidelines. Patients were treated in accordance with the clinical guidelines approved by the Russian Ministry of Health (Femur fractures (except for the proximal femur), 2021; Tibial fractures, 2021).

The material for molecular genetic analysis was DNA samples isolated from the peripheral blood leukocytes of the study subjects. For the study of SNV (Single Nucleotide Variant) point mutations of tumor necrosis factor receptor (TNFRSF11B) at position 1181 (G>C), interleukin-6 (IL6) at position 174 (C>G), transforming growth factor β_1 ($TGF\beta_1$) at position 25 (Arg>Pro), epidermal growth factor receptor (EGFR) at position 2073 (A>T) and vitamin D (VDR) (BsmI 283G>A) were selected. Amplification of gene fragments was performed in a Bis-M111 thermal cycle (Bis-N Ltd, Novosibirsk). Litekh-SNP primer sets (Russia) were used in the work. Visualization of amplification products was performed using electrophoresis in 3 % agarose gel with the addition of ethidium bromide in transmitted ultraviolet light. The results were interpreted according to the manufacturer's instructions.

The risk of delayed consolidation was assessed using SPSS Statistics Version 25.0 (Neural Networks module). The prognostic characteristics of the neural network were assessed using ROC analysis. For conducting statistical analysis, the authors were guided by the principles of the International Committee of Medical Journal Editors (ICMJE) and the recommendations on Statistical Analysis and Methods in Published Literature (SAMPL) [12].

To test the significance of differences in quantitative parameters between the groups, descriptive statistics methods and a number of nonparametric criteria were used. The distribution law of that considers the sample number in groups was assessed using the Shapiro – Wilk criterion. The analysis of differences in quantitative parameters of the studied samples was performed using the Mann – Whitney U-test. Qualitative data were described as absolute (*n*) and relative (%) values. To compare the nominal data of the two study groups, the Pearson χ^2 criterion was used. If the number of expected cases was less than 10, the Pearson χ^2 test with Yates's correction for continuity was used for comparison; if less than 5, the Fisher exact test was used. A value of $p < 0.05$ was considered statistically significant [13].

RESULTS

The prediction model used only genotypes of the studied gene polymorphisms (*TNFRSF11B, IL6, TGFβ$_1$, EGFR, VDR*) (Table 1, Table 2).

Table 1

Frequency of carriage of the studied SNVs among healthy individuals and groups of patients with long bone fractures

Genotype		Control group (*n* = 92)	Comparison group (*n* = 62)	Main study group (*n* = 46)
TNFRSF11B-1181G>C	Genotype GG OR [95 % CI]	0.511	0.161 0.18 [0.08–0.41]	0.696 2.19 [1.03–4.63]
	Genotype GC OR [95 % CI]	0.326	0.452 1.7 [0.88–3.30]	0.196 0.5 [0.22–1.17]
	Genotype CC OR [95 % CI] χ^2 *p*	0.326	0.387 3.24 [1.53–6.88] 21.12 < 0.001	0.109 0.63 [0.21–1.84] 4.3 0.12
IL6-174C>G	Genotype CC OR [95 % CI]	0.326	0.323 0.98 [0.49–1.96]	0.174 0.44 [0.18–1.05]
	Genotype CG OR [95 % CI]	0.467	0.468 1.00 [0.53–1.91]	0.391 0.37 [036–1.5]
	Genotype GG OR [95 % CI] χ^2 *p*	0.207	0.210 1.02 [0.46–2.25] 0.00 1	0.435 2.96 [1.37–6.39] 8.63 0.01
TGFβ$_1$-25Arg>Pro	Genotype ArgArg OR [95 % CI]	0.630	0.581 0.81 [0.42–1.57]	0.282 0.23 [0.11–0.5]
	Genotype ArgPro OR [95 % CI]	0.240	0.371 1.88 [0.93–3.79]	0.196 0.77 [0.32–1.85]
	Genotype ProPro OR [95 % CI] χ^2 *p*	0.130	0.048 0.34 [0.09–1.26] 4.91 0.09	0.522 7.27 [3.14–16.82] 25.47 < 0.001
EGFR-2073A>T	Genotype AA OR [95 % CI]	0.315	0.306 0.96 [0.48–1.93]	0.13 0.33 [0.12–0.85]
	Genotype AT OR [95 % CI]	0.598	0.597 1.00 [0.52–1.92]	0.37 0.39 [0.19–0.82]
	Genotype TT OR [95 % CI] χ^2 *p*	0.087	0.097 1.13 [0.37–3.42] 0.05 0.98	0.5 10.5 [4.15–26.54] 30.48 < 0.001
VDR-BsmI283G>A	Genotype GG OR [95 % CI]	0.359	0.468 1.57 [0.82–3.03]	0.196 0.43 [0.19–1.01]
	Genotype GA OR [95 % CI]	0.446	0.435 0.96 [0.5–1.84]	0.5 1.24 [0.61–2.53]
	Genotype AA OR [95 % CI] χ^2 *p*	0.196	0.097 0.44 [0.16–1.18] 3.43 0.18	0.304 1.8 [0.8–4.05] 4.44 0.11

Note: *p* — statistical significance of differences with control group

Table 2

Frequency of carriage of the studied SNVs among groups of patients with long bone fractures

Genotype		Group I (n = 62)	Group II (n = 46)	χ^2	p	OR [95 % CI]
TNFRSF11B-1181G>C	Genotype GG	0.161	0.696	32.06	< 0.001	11.89 [4.72–29.92]
	Genotype GC	0.452	0.196			0.3 [0.12–0.71]
	Genotype CC	0.387	0.109			0.19 [0.07–0.56]
IL6-174C>G	Genotype CC	0.323	0.174	6.99	0.03	0.44 [0.17–1.12]
	Genotype CG	0.468	0.391			0.73 [0.34–1.59]
	Genotype GG	0.210	0.435			2.9 [0.89–6.75]
TGFβ$_1$-25Arg>Pro	Genotype ArgArg	0.581	0.283	23.73	< 0.001	0.05 [0.01–0.17]
	Genotype ArgPro	0.371	0.196			2.42 [0.99–5.92]
	Genotype ProPro	0.048	0.522			3.51 [1.55–7.95]
EGFR-2073A>T	Genotype AA	0.306	0.13	22.25	< 0.001	0.34 [0.12–0.94]
	Genotype AT	0.597	0.37			0.4 [0.18–0.87]
	Genotype TT	0.097	0.5			9.33 [3.36–25.92]
VDR-BsmI 283 G>A	Genotype GG	0.468	0.196	11.94	0.003	0.28 [0.11–0.67]
	Genotype GA	0.435	0.5			1.3 [0.6–2.79]
	Genotype AA	0.097	0.304			4.08 [1.43–11.67]

Note: p — statistical significance of differences with control group

The analysis of SNV genotypes carriage frequency in patients with delayed consolidation revealed a prevalence of the mutant genotype of the *IL6* gene *(C174G), TGFβ$_1$ (A25P), EGFR (A2073T)* and *VDR (BsmI G>A)* by 2.1, 10.1, 5.1 and 3.1 times, respectively, in comparison with the clinical comparison group. In contrast, determination of the distribution frequency of the genotype of the *TNFRSF11B (G1181C)* gene polymorphism in the group with delayed consolidation revealed a significant prevalence of the normal homozygous variant in comparison with the first group by 4.3 times (Tables 1, Table 2).

Model of predicting consolidation disorders

In order to verify the obtained results of delayed consolidation prediction, we additionally performed neural network data analysis. As a model, we used a multilayer perceptron system based on the dependent variable (delayed consolidation), which is determined during the analysis of independent data (possible predictors). As independent variables (15 input neurons), we used the genotypes of the studied SNPs that have significant prognostic value. During the calculation, the neural network showed an architecture with an optimal number of hidden layers (5 and 4, respectively), which realize the prediction (Fig. 1). The creation of a relationship between the weighted sums of objects with the subsequent layer of values of these objects in both hidden layers is carried out by activating the sigmoid function. A similar function is recorded in the output layer (0; 1), which corresponds to the original study design. The sum of squares served as the error function. The output layer contained 1 target (dependent) variable (delayed consolidation is present / not present) (Fig. 1).

By determining the importance of an independent variable, the following gradation is noted: gene polymorphism *TGFβ$_1$-25(Arg>Pro)*; gene polymorphism *TNFRSF11B-1181(G>C)*; gene polymorphism VDR-BsmI283(G>A); gene polymorphism *IL6-174(C>G)*; gene polymorphism *EGFR-2073(A>T)* (Fig. 2).

The normalized importance was 100 %, 97.1 %, 34.7 %, 31.5 %, and 15.3 %, respectively. The percentage of incorrect predictions was 8.3 %.

The prognostic value of this neural network was assessed using ROC analysis (Fig. 3).

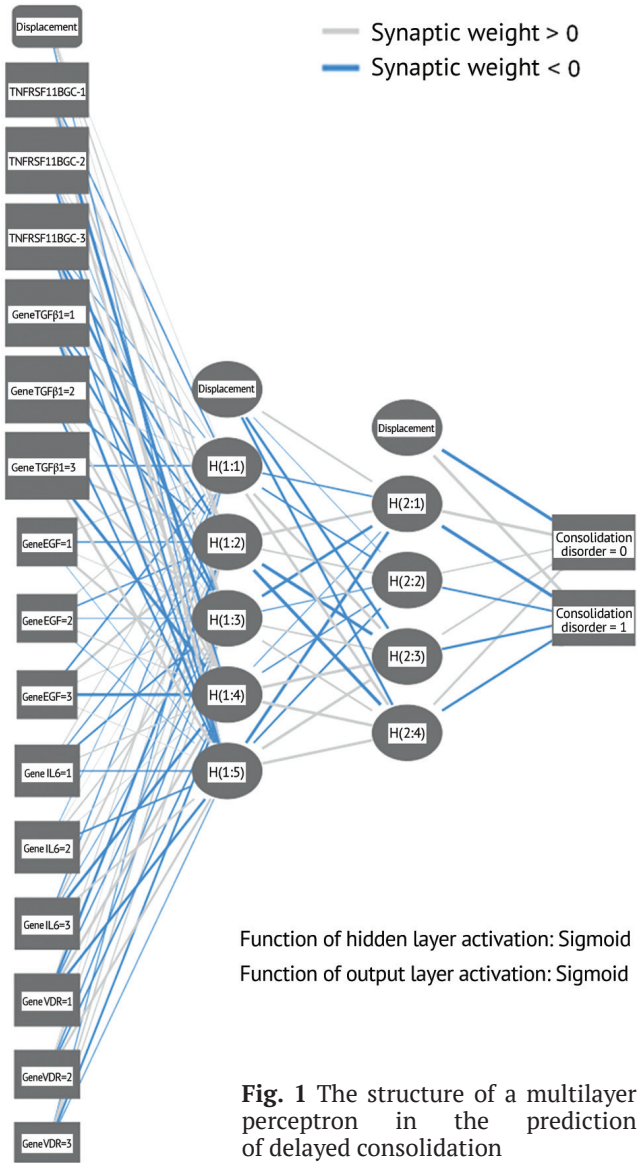

Fig. 1 The structure of a multilayer perceptron in the prediction of delayed consolidation

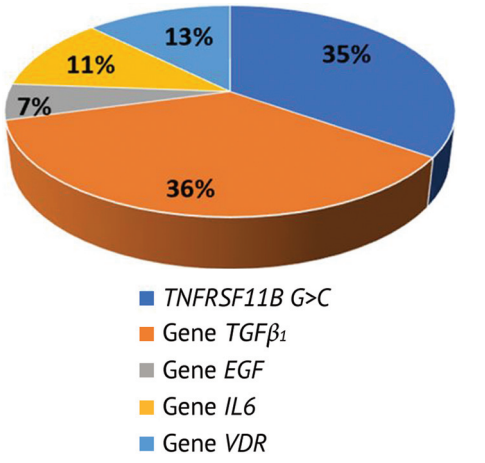

Fig. 2 Gradation in determining the importance of the independent variable

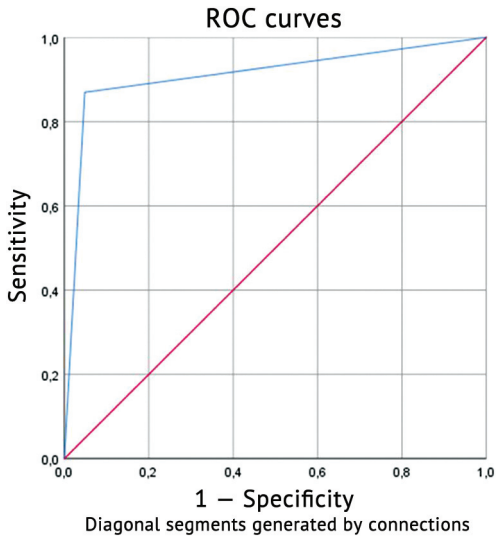

Fig. 3 ROC analysis of the possible delayed consolidation based on neural network data analysis

The area under the curve (AUC) = 0.91 (95 % CI = 0.85–0.98). The prediction accuracy of the prognostic model was 91.7 %, sensitivity was 0.87 %, specificity was 0.95 %. AUC was 0.91 (95 % CI = 0.85–0.98), $p < 0.001$.

DISCUSSION

Dominance of the mutant genotype of the gene I*L6(C174G), TGFβ$_1$(A25P), EGFR(A2073T), VDR (BsmI G>A)* and normal homozygous variant *TNFRSF11B(G1181C)* in the group with delayed consolidation indicate a high risk of consolidation disorders in case of their carriage [4].

The results of scientific works of the last decades show that hereditary factors play an important role in the development of improper functioning of the immune system. Programmed, genetically reduced or increased production of proteins in the macroorganism contributes to the ability of the immune system to respond differently to pathogens [4, 14]. In particular, the role of gene polymorphism of many cytokines was proven both in the development of pathological conditions and in their protective effect [15, 16].

However, these studies are not so many and they do not reveal the immunogenetic mechanisms of diseases and/or complications of the musculoskeletal system sufficiently [4].

To date, there are few studies where SNV genes act as "markers" of the risk of consolidation disorders. In particular, SNV of the SMAD6 transcription factor gene (T/T rs2053423) and the gene of the protein inhibitor of some morphogenetic proteins NOGGIN (G/G rs1372857) are associated with the development of atrophic pseudoarthrosis. Nonunion of the femoral and tibial diaphysis is more often observed in carriers of the platelet-derived growth factor (PDGF) haplotype A (rs1800814, rs62433334, rs13309625; CCG). A predisposition to inflammatory complications and impaired bone tissue reparation has been established in the carriage of the allele T and C/T codon 10 of the gene of the transforming growth factor-β (TGF-β) and the mutant gene of toll-like receptor-4 (TLR4) W/1. Also, the risk factors for consolidation disorders include carriage of the T/T genotype of the IL1β gene (rs2853550) and the nitric oxide synthase gene NOS2 (rs2297514). Moreover, the disruption of normal reparative regeneration is facilitated by the carriage of the haplotype A of the gene of the morphogenetic protein BMP4 (rs2761884, rs17563, rs2071047, rs762642; GTAA), the T/G genotype of the gene of the angiogenic inducer, rich in cysteine CYR61 (rs3753793), as well as the C allele of the gene of the fibroblast growth factor receptor FGFR1 (rs13317) [17].

The work of Zimmermann et al. shows the role of gene expression in normal fracture consolidation and its disorders. Thus, excessive expression of the genes of cysteine dioxygenase-1 (CDO1), cartilage oligomeric matrix protein (COMP), fibromodulin (FMOD), fibronectin 1 (FN1), clusterin (CLU), two-component signaling pathway system (TCS22), actin (ACTA2) and phosphodiesterase 4D-interacting protein (PDE4DIP) contributes to an imbalance in the work of the structure and function of cells during reparative regeneration, which leads to consolidation disorder of the nonunion type [18].

Experimental studies of Waki et al. demonstrate the role of microRNA (miRNA) in reparative regeneration and bone tissue remodeling. It was found that consolidation disorders are noted with increased expression of miR-31a-3p, miR-31a-5p, miR-146a-5p, miR-146b-5p and miR-223-3p [19].

In contrast, the study by Wang et al. noted that bone morphogenetic protein receptor type Ib (BMPR1b) is a potential target of miR-125b, inhibits it and promotes better restoration of bone tissue defects [20]. Thus, eleven miRNAs that can contribute to the disruption of reparative regeneration processes were experimentally identified [21].

There are also data on the carriage of SNV that is protective. It was established that the carriage of the G/T and G/G genotype of the neuronal specific retinoic acid-induced gene (FAM5C (rs1342913)), the G/G genotype of the bone morphogenetic protein 6 gene (BMP6 (rs270393)) and the G/G genotype of the matrix metallopeptidase gene 13 (MMP13 (rs3819089)) is associated with a favorable course of consolidation [22].

However, in order to confirm the significant role of the above SNVs in the processes of impaired fracture consolidation, the above data require further studies with a large number of patients and strict inclusion/exclusion criteria regarding concomitant pathology.

It has been shown that AI can fulfill key healthcare tasks, including disease diagnostics. A mathematical model based on sample data (training) is built using machine learning (ML) algorithms, which leads to the construction of predictions and/or specific solutions [23, 24, 25]. In particular, ML algorithms are most frequently used in personalized medicine. Such ML programs necessarily require supervised learning using an outcome variable [23].

Complex forms of ML, such as neural networks, are now increasingly used in medicine. Such technologies are also used in the diagnosis (prediction) of various pathological conditions [26]. As for the multilayer perceptron used in this work, it is classified as a feedforward network (from layer

to layer). The final calculation result is formed as a result of the difference between the responses of each layer. The accuracy of this model increases with an increase in the number of perceptron layers [27].

Thus, further studies of personalized immunogenetic mechanisms in a unfavorable course of the traumatic disease in fractures of long bones of the extremities, including the use of modern digital systems, can serve as a basis for detecting a predictor of complications and will allow making the necessary preventive corrections to treatment, which will contribute to a significant decrease in adverse outcomes.

Currently, the use of such technological solutions in practice is limited due to the lack of universal software and the initial stages of digitalization in the medical sphere. However, the creation of a unified digital contour and the introduction of AI which is gaining momentum within the framework of the federal project "Digital Healthcare Services" demonstrates the importance of digitalization of scientific medical technologies in all fields. In the near future, with the development of research on genetic predisposition to various diseases/complications, this technology, in our opinion, will be widely used.

The data we obtained are preliminary. We hope that further full-scale studies will substantiate the introduction of immunogenetic markers based on digital services in the diagnosis of complications in the pathology of the musculoskeletal system.

CONCLUSION

The use of a neural network to predict delayed fracture consolidation using data on the carriage of certain gene polymorphisms has proven to be quite effective, since it has a high degree of accuracy (91.7 %). It indicates the prospects for introducing neural network analysis into the field of traumatology and orthopaedics.

Conflict of interest *None declared.*
Funding *No sponsorship.*

REFERENCES

1. Bondarenko AV, Guseynov RG, Gerasimova OA, et al. Frequency, risk factors, and features of diaphyseal non-unions of the long bones of the lower extremities. *Polytrauma*. 2023;(2):36-44. (In Russ.) doi: 10.24412/1819-1495-2023-2-36-44.
2. Fedorov VG, Kuzin IV. The results of treatment of femoral diaphysis fractures using locked intramedullary osteosynthesis and extramedullary osteosynthesis (results for 10 years). *Acta biomedica scientifica*. 2023;8(5):166-173. (In Russ.) doi: 10.29413/ABS.2023-8.5.18.
3. Wildemann B, Ignatius A, Leung F, et al. Non-union bone fractures. *Nat Rev Dis Primers*. 2021;7(1):57. doi: 10.1038/s41572-021-00289-8.
4. Miromanov AM, Gusev KA, Staroselnikov AN, et al. Modern genetic and immunological aspects of the pathogenesis of impaired consolidation of fractures (literature review). *Acta Biomedica Scientifica*. 2022;7(2):49-64. (In Russ.) doi: 10.29413/ABS.2022-7.2.6.
5. Afrasiabian B, Eftekhari M. Prediction of mode I fracture toughness of rock using linear multiple regression and gene expression programming. *J Rock Mech Geotech Eng*. 2022;14(5):1421-1432. doi: 10.1016/j.jrmge.2022.03.008.
6. Cui Y, Hu X, Zhang C, Wang K. The genetic polymorphisms of key genes in WNT pathway (LRP5 and AXIN1) was associated with osteoporosis susceptibility in Chinese Han population. *Endocrine*. 2022;75(2):560-574. doi: 10.1007/s12020-021-02866-z.
7. Ding ZC, Lin YK, Gan YK, Tang TT. Molecular pathogenesis of fracture nonunion. *J Orthop Translat*. 2018;14:45-56. doi: 10.1016/j.jot.2018.05.002.
8. MacEachern SJ, Forkert ND. Machine learning for precision medicine. Genome. 2021;64(4):416-425. doi: 10.1139/gen-2020-0131.
9. Pasini A. Artificial neural networks for small dataset analysis. *J Thorac Dis*. 2015;7(5):953-960. doi: 10.3978/j.issn.2072-1439.2015.04.61.
10. Curchoe CL, Bormann CL. Artificial intelligence and machine learning for human reproduction and embryology presented at ASRM and ESHRE 2018. J *Assist Reprod Genet*. 2019;36(4):591-600. doi: 10.1007/s10815-019-01408-x.
11. Plumarom Y, Wilkinson BG, Willey MC, et al. Sensitivity and specificity of modified RUST score using clinical and radiographic findings as a gold standard. *Bone Jt Open*. 2021;2(10):796-805. doi: 10.1302/2633-1462.210.BJO-2021-0071.R1.

12. Lang TA, Altman DG. Statistical analyses and methods in the published literature: The SAMPL guidelines. *Medical Writing*. 2016;25(3):31-36. doi: 10.18243/eon/2016.9.7.4.
13. Mudrov VA. ROC curve analysis algorithm in biomedical research using SPSS software package. *Transbaikal Medical Bulletin*. 2021;1:148-153. (In Russ.) doi: 10.52485/19986173_2021_1_148.
14. Simbirtsev AS. Immunopharmacological aspects of the cytokine system. *Bulletin of Siberian Medicine*. 2019;18(1):84-95. (In Russ.) doi: 10.20538/1682-0363-2019-1-84-95.
15. Schaettler MO, Richters MM, Wang AZ, et al. Characterization of the Genomic and Immunologic Diversity of Malignant Brain Tumors through Multisector Analysis. *Cancer Discov*. 2022;12(1):154-171. doi: 10.1158/2159-8290.CD-21-0291.
16. Akbarov AN, Ziyadullayeva NS, Reimnazarova GD, Nurullaeva MU. Peculiarities of osteoreparation in case of bone defect replacement with bioactive glass in combination with an antibiotic. *British View*. 2022;7(1):101-105. doi: 10.5281/zenodo.6571286.
17. Ding ZC, Lin YK, Gan YK, Tang TT. Molecular pathogenesis of fracture nonunion. *J Orthop Translat*. 2018;14:45-56. doi: 10.1016/j.jot.2018.05.002.
18. Zimmermann G, Schmeckenbecher KHK, Boeuf S, et al. Differential gene expression analysis in fracture callus of patients with regular and failed bone healing. *Injury*. 2012;43(3):347-356. doi: 10.1016/j.injury.2011.10.031.
19. Waki T, Lee SY, Niikura T, et al. Profiling microRNA expression in fracture nonunions: Potential role of microRNAs in nonunion formation studied in a rat model. *Bone Joint J*. 2015;97-B(8):1144-1451. doi: 10.1302/0301-620X.97B8.34966.
20. Wang H, Xie Z, Hou T, et al. MiR-125b Regulates the Osteogenic Differentiation of Human Mesenchymal Stem Cells by Targeting BMPR1b. *Cell Physiol Biochem*. 2017;41(2):530-542. doi: 10.1159/000457013.
21. He B, Zhang ZK, Liu J, et al. Bioinformatics and microarray analysis of mirnas in aged female mice model Implied new molecular mechanisms for impaired fracture healing. *Int J Mol Sci*. 2016;17(8):1260. doi: 10.3390/ijms17081260.
22. Guimarães JM, Guimarães IC, Duarte ME, et al. Polymorphisms in BMP4 and FGFR1 genes are associated with fracture non-union. *J Orthop Res*. 2013;31(12):1971-1979. doi: 10.1002/jor.22455.
23. Komkov AA, Mazaev VP, Ryazanova SV, et al. The main directions of development of artificial intelligence in medicine. Medical sciences. *Scientific review*. 2020;(5):33-40. (In Russ.) doi: 10.17513/srms.1141.
24. Bernard de Villeneuve F, Jacquet C, El Kadim B, et al. An artificial intelligence based on a convolutional neural network allows a precise analysis of the alignment of the lower limb. *Int Orthop*. 2023;47(2):511-518. doi: 10.1007/s00264-022-05634-4.
25. Memiş A, Varlı S, Bilgili F. Semantic segmentation of the multiform proximal femur and femoral head bones with the deep convolutional neural networks in low quality MRI sections acquired in different MRI protocols. *Comput Med Imaging Graph*. 2020;81:101715. doi: 10.1016/j.compmedimag.2020.101715.
26. Lee SI, Celik S, Logsdon BA, et al. A machine learning approach to integrate big data for precision medicine in acute myeloid leukemia. *Nat Commun*. 2018;9(1):42. doi: 10.1038/s41467-017-02465-5.
27. Ziganshin AM, Dikke GB, Mudrov VA. Predicting a clinically narrow pelvis using neural network data analysis. *Obstetrics, Gynecology and Reproduction*. 2023;17(2):211-220. (In Russ.) doi: 10.17749/2313-7347/ob.gyn.rep.2023.382.

The article was submitted 18.09.2024; approved after reviewing 10.10.2024; accepted for publication 05.02.2025.

Information about the authors:

Alexander M. Miromanov — Doctor of Medical Sciences, Professor, First Vice-Rector, Vice-Rector for Medical Work, Head of Department, miromanov_a@mail.ru, https://orcid.org/0000-0003-1432-1844;

Kirill A. Gusev — Candidate of Medical Sciences, Associate Professor of the Department, kirill.gusev.86@mail.ru, https://orcid.org/0000-0003-3375-9956;

Artem N. Staroselnikov — Assistant of the Department, a.staroselnikov@mail.ru, https://orcid.org/0000-0003-4400-0750;

Viktor A. Mudrov — Specialist in the Scientific Department for Patent work, mudrov_viktov@mail.ru, https://orcid.org/0000-0002-5961-5400.