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Artificial intelligence in clinical medicine and dentistry

Veštačka inteligencija u kliničkoj medicini i stomatologiji

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artificial intelligence; clinical medicine; dentistry; diagnosis, computer-assisted; algorithms; medical informatics, computing. Ključne reči: inteligencija, veštačka; medicina, klinička; stomatologija; dijagnoza, kompjuter-asistirana; algoritmi; informatika, medicinska, kompjuterizovana.

Introduction

The involvement of computer systems in clinical medicine and dentistry has of late become a necessity. These computer systems monitor the admission and treatment of patient, supported by health care professionals, from the moment of setting the time and date of examination, *via* opening a digital patient file (record), patient history taking, support in clinical diagnosis of a disease, analysis of radiographs, help in laboratory analyses, and all the way to the assistance in determination and administration of appropriate treatment. Although the field of use of computer systems in modern medicine and dentistry is very wide and diverse, the most sophisticated area is unquestionably artificial intelligence (AI)¹.

As the expression, it itself suggests that AI enables machines to think and present the results of such thinking. These are most commonly the suggestions regarding the choice among the existing options or solutions in insufficiently clear or doubtful situations, such as the selection of the most appropriate site in the jaw bone where dental implants could be placed without injury to the adjacent tissues and with maximum static product ², but also in identifying new, unknown solutions. This paper aims at informing the readers about contemporary achievements in the field of AI use in clinical medicine and dentistry.

The concept of AI

Roughly speaking, we may say that AI studies and projects intelligent systems are able to "experience" their own environment and take measures to maximize their own chances for success in it ^{1, 3}. AI is being used in various disciplines such as medical diagnosis, exchange market, control of robots, law, science, or entertainment. Although the origin of AI can be traced back to more distant past (e.g. to the machines and sketches of Leonardo da Vinci, to ancient Greek machines such as the Antikythera mechanism), it is usually associated with the invention of first usable computers after the Second World War, or in the year 1956 when John McCarthy used the term in its full meaning for the first time³. In general, AI consists of the knowledge base, research methods, problemsolving systems, reasoning systems, planning systems, learning systems (from previous examples/instances and from the knowledge base), genetic programming, and decision-making or conclusion-drawing systems ^{3, 4}. In fact, since ancient times, philosophers and mathematicians have presented their own interpretations of the course of human thinking and decisionmaking, striving to delineate general patterns and rules underlying the process. Although there have been attempts throughout history to create "intelligent" machines based on mechanical scientific achievements, the first real successes have occurred only with the discovery of digital electronic computers and scientific papers of Alan Turing⁵, a British mathematician, who laid the groundwork of artificial intelligence and created the Turing test - the test measuring a machine's ability to imitate human intelligence.

Since the 1950s, supported by numerous discoveries in neurology, information technology and cybernetics, statistics and mathematics, and by reviewing and summarizing the avai-

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lable knowledge in the fields of logic and philosophy, AI has made a huge progress. Perhaps the best example in that regard are the modern systems for the game of chess, where even the world chess champions, such as Garry Kasparov, have lost the matches playing against computers. Further on, there are modern Internet browsers able to predict the users wishes, and various other systems such as logic games, software packages assisting planning and construction in mechanical engineering, electronic engineering, simulations in aircraft industry, and so on.

The difference between human and AI is still a huge one. AI still bases mainly on the algorithms that rely on stepby-step reasoning, similar to the human brain solving a puzzle or making logical deductions ^{3, 6}. That is the reason why more difficult tasks require huge computer resources. In order to cope with the situation, researchers have created the methods and algorithms able to process uncertain and incomplete information, involving the concepts of the probability theory.

In contrast to machines, humans employ intuitive decision-making to resolve a large number of problems and do not always employ their thinking skills and probability consideration and reasoning (consideration of all possible situations; in computer science commonly called the brute force method). AI tries to get as close as possible to this "subsymbolic" way of thinking ^{7–9}. Perhaps the biggest step in that direction has been made in programming of logic games, when instead of considering all the possible combinations from the ongoing moment to the end, consideration of only the few steps in advance is used according to predetermined value functions (the Minimax procedure employed for searching the tree of moves) or the move is chosen based on the table prepared in advance ¹⁰.

The ability to learn and acquire new knowledge is an essential component of AI. AI has to be able to decide whether and in what degree the obtained pieces of information are true (correct), but also to learn to cope with false information, without endangering the aspect of the whole of applied resources.

AI primarily utilizes several basic forms of logic: mathematical logic, the statements of which can be true or false ¹¹; first-order logic or predicate calculus of the first order, representing a formal deduction system allowing the use of quantifiers and predicates, able to express the facts about objects, their characteristics, and relations with one another ^{12, 13}; fuzzy logic, allowing the truth of a statement to be represented as a value between 0 and 1, instead of simply true (1) and false (0). Fuzzy logic can be used for uncertain reasoning in the systems in which there are no certain or precise statements ¹⁴; other forms.

AI is required to cope successfully with incomplete and not always true information. That is the reason why it involves different methods and mechanisms that can be of use in that regard: Bayesian networks is a graphical model encoding the complete probability of association/relationships of the variables of interest ¹⁵; probability algorithms (Markov chain, Kalman filter, Coin-tossing, Monte Carlo and others) used in filtering, prediction, and understanding of a chain of information ^{16, 17}; others. AI requires excellent classifier behavior and utilizes: Naïve Bayes classifier, a simple probability classifier based on the Bayes' theorem, introducing simplification in the form of supposed independence of each other of the values of attributes in an ordered set of finite n-elements ¹⁸; knearest neighbors algorithm, a very intuitive method classifying unlabeled samples based on primer similarity ^{19, 20}; Gaussian Mixture Model (GMM), representing a parametric function of probability distribution ²¹; Decision Tree Classifiers, breaking down complex decision-making processes into a series of simple decisions, enabling solutions that can be easily understood and used ^{22, 23}, others.

In the processes of artificial reasoning, an essential part of AI are artificial neural networks, as an alternative to traditional analytics. Artificial neural networks are modelled based on the discovery of biological mechanisms of operation of the human brain ²⁴. The concept itself is similar to the transmission of neural signals and operation of the human brain ²⁴. Programming languages for AI are the principal tool in the assessment and creation of computer programms and understanding of symbolic information in a context. Although for a lower level of symbolic programming the use of standard programming languages is appropriate (such as C/C++, C#, Fortran, Pascal, and similar), for Rapid Application Development of AI applications, the following specialized programming languages are commonly used: Prolog; Lisp; others ²⁵.

Overview of AI application in clinical and dental medicine

The use of AI in medicine is a more recent phenomenon, and it has been developing very quickly; nowadays, it is the focus of interest of many scientists in the field of computer use and applications of robotics in medicine. The following references present the latest advancements and available achievements in the field.

Azarkhish et al.²⁶, investigating alternative options of determination of iron in serum, have shown that by way of analysis of other standard laboratory data, such as mean carpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular Hb concentration (MCHC), Hb/ red blood cell (RBC), using the system of artificial neural network (ANN) and adaptive neuro-fuzzy inference system (ANFIS), the level of iron in serum can be predicted with an acceptable degree of precision. This analysis illustrated how an AI system, based on peripheral laboratory results, drew conclusions and guided physicians regarding the possible presence of anemia as the consequence of iron deficiency. Qidwai et al.²⁷ have proposed a new strategy to be of use to neurologists, neurosurgeons, and orthopedic surgeons, aiming to predict the recovery and health status of a patient after surgery of the spinal column, based on the analysis of preoperative data by the Standard Fuzzy Inference System. The results suggested a high precision rate of predictions (of about 88%) in the population of 501 patients. The system was thus able to contribute to quality decision-making regarding whether to administer or not surgical treatment,

especially for benign lesions, where surgery could be avoided. Tsuchihashi²⁸ has found the accuracy of 95% in automatized diagnosis of prostate cancer by an AI system and automatized marking of cancerous regions. Syed et al. ²⁹ have proposed and evaluated a system of fully automatic nonparametric learning and drawing conclusions using the AI method, supported by support vector machines (SVMs) on large datasets, in order to calculate the probability of risk for perioperative patient complications, morbidity, and mortality. The system translated individual Current Procedural Terminology (CPT) codes into procedural risk values, and analyzed the robust risk model producing more reliable assumptions compared to the National Surgical Quality Improvement Program (NSQIP) - traditional, individual programme created by the American College of Surgeons (ACS).

Uzuner et al. ³⁰ have observed the relationships of medical complaints of patients in the context of semantic relation (SR) and cross-interference of diagnoses, tests, and therapies. These were classified according to the Unified Medical Language System (UMLS) and organized according to their meaning ³¹. Each medical complaint in a patient was represented as a disease or a symptom, creating a unique SR relation for the classification and processing of medical records. In this way, a significant help in drawing inferences was provided to AI systems, and the consequences were new scientific insights and discoveries. Roberts et al. 32 have demonstrated that it is possible to extract meaning from medical texts in patient records and set meaningful relations in order to use the algorithms of machine learning (ML). Large datasets could thus be analyzed in order to identify patterns of interest. This study was performed on the Clinical E-Science Framework (CLEF) system for storing, integration, and presentation of clinical information for research purposes. The study utilized clinical data from 20,000 patients of the Royal Marsden Hospital (Great Britain). Zolnoori et al. ³³ have created an extensive classification of AI applications in asthmalike diseases. They looked into the use of AI in the techniques of diagnosis and work-up of patients with asthma, but also in the automated production of new knowledge and prediction of major events and exacerbations in such patients. Kim et al. ³⁴, using an AI system based on the neural network model, have been able to predict toothache in 80% of the examined cases. Nieri et al. 35 using the Bayesian network analysis, have been able to successfuly identify several substrates with direct effect on the final outcome of treatment of impacted maxillary canines. Xie et al. 36 assisted by the ANN, have been able to use a decision-making expert system in order to identify the factors of prevailing influence in decision-making, evaluating the need for tooth extraction before orthodontic treatment of patients with malocclusion. They were able to reach a decision with the success rate of 80% whether a treatment with tooth extraction should be preferred to a treatment without it in a given situation.

Kitporntheranunt and Wiriyasuttiwong ³⁷ created a software medical expert system of assistance in diagnosing ectopic pregnancy. Using an interactive backward chaining inference algorithm, the system analyzed patient medical re-

cords and the available information, successfully detecting ectopic pregnancy in 31 out of 32 cases, while recognizing all cases of normal pregnancy. Tamaki et al. ³⁸ formed a data mining tool to identify associations, anomalies, and statistically significant patterns in large datasets, using a system of AI. The system successfully identified a high level of Streptococcus mutans and Lactobacillus as the factors of high risk for caries development in school children. Sakai et al.³⁹ studied the possibility of prediction of acute inflammation of the appendix using a Bayesian model. Based on the data about conditions preceding the disease in patient medical records, the AI system created a model and evaluated probability of the disease in new cases. Käkilehto et al.⁴⁰. using the data mining AI technique, analyzed a large set of patient electronic dental records in order to obtain scientifically acceptable conclusions about the duration of dental restorations. The results showed that the life span of dental amalgams and composite fillings was over 15 years, while 60% of silicate dental cement restorations were replaced as early as 5 years after the initial placement, and more than 50% of glass ionomer cement restorations were replaced after 7 years. Korhonen et al. 41, using the data mining technique, have established that dentists more successfully detect caries in their new patients, compared to their old patients. The study was done using an AI system with the data obtained at general physical examinations. Kawaguchi et al.⁴² used the data mining technique in order to find complex interactions between the risk factors and clinical evidence of non-hepatitis B virus/non-hepatitis C dependent hepatocellular carcinoma (NBNC-HCC). Since the disease is usually diagnosed in more advanced stages, in order to identify the risk factors, in a cohort of 663 patients with the diagnosis of NBNC-HCC, the Milan criterion was used and artificial analysis was done using the decision tree algorithm. Six factors were identified: date of diagnosis of hepatocellular carcinoma, the diagnosis of cirrhosis of the liver, values of serum aspartate transaminase, alanin aminotransferase, α -fetoprotein, and the level of des- γ -carboxy prothrombin. Miladinović et al.⁴ demonstrated that the use of AI enabled successful collection, triage, sorting, numbering, and analysis of raw electronic data related to tooth extraction samples, and that the applied AI algorithms were able to execute nonparametric evaluation of impact of possible non-dental attributes, drawing scientifically acceptable conclusions. In this way, an AI system was able to "understand" and communicate the reasons for tooth extraction, i.e. to indicate the principal substrates that may have influence on such an outcome. Miladinović et al. 43 have also assessed possible use of medical data usage for research purposes and analysis using the AI methods. They suggested a design model of a huge medical data base of collected medical information which would make possible subsequent precise analysis using AI algorithms. In his PhD Thesis, Miladinović 44 presented an AI model of automatization of numerous scientific processes using an AI system, suggesting that AI systems can be of significant diagnostic help in oral surgery, identification of potentially successful measures of disease prevention, and giving new insights into the diseases and health in oral surgery.

Stanley et al. 45 presented their model of automated search and ordering of clinically obtained diagnostic images (histograms, x-rays, etc.) with an image data base for known diseases. In this way, independent computer search is performed, someting similar to fingerprint identification, facilitating the job of a clinician in diagnosis and confirmation of a disease. Korhonen et al. ⁴⁶ have created and tested a data mining system able to determine independently the life-long mean index of carious teeth, extracted teeth, and/or filled permanent teeth. They found the method feasible, but not suitable for persons below 20 years of age. De Bruijn et al.⁴⁷ investigated the applicability of ANN in their analysis of speech nasalization in patients treated for oral or oropharyngeal cancer in order to evaluate hypernasalization in their speech. After the speech sound samples were recorded from 51 patients, using 18 control sounds, they evaluated hypernasalization, articulation, intelligibility, etc. The analysis of nasalization properties was done in the whole speech range, and based on their final results the study was considered feasible, while parameter prediction was graded as medium to poor. Bas et al. 48 have used ANN to predict two subgroups of internal disturbances of the temporomandibular joint and normal joint using characteristical clinical signs and symptoms of disease. Clinical symptoms and diagnoses of 161 patients with temporomandibular joint disorders were set as a gold standard and used for learning by the neural network. After the learning process, AI was presented for analysis with the results from 58 new patients for proper diagnosis to be made. The experiment was successfully finished in about 90% of cases, with the conclusion that ANN application in the diagnosis of subtypes of the disease can be a valuable diagnostic tool especially to dentists. Cilia et al.⁴⁹ obtained some promising results in the prediction of viral mutations. They used machine learning methods on the experience of existing viral resistencies developed against the present drugs. Wright et al. 50, using the Constrained Sequential Pattern Discovery using Equivalent Class (CSPADE) algorithm with 90% success rate, have made predictions as to which would be the next drug in the treatment of diabetic patients, based on the patterns observed for present drugs. Wu et al. ⁵¹, evaluating computer-aided diagnosis of early knee osteoarthritis from magnetic resonance imaging (MRI) findings, have concluded that AI methods alone were able to make the accurate diagnosis in 75% of cases.

We have to bear in mind that the use of AI in clinical medical and dental practice is still at an early stage of development and still in the investigation phase. The above studies could serve to foretell the bright future for AI in clinical medicine and dentistry. However, despite sky-high

- Mihailović B, Miladinović M, Mladenović D, Lazić Z, Janković A, Živković D, et al. Computerized dentistry. Beograd: 211–49. Obeležja. 2009.
- Miladinović M, Mihailović B, Živković D, Vujičić B. Computerized technology in the management of edentulous patients. PONS Med J 2010; 7(4): 150–6. (Serbian)

expectations, we should always remember to be patient but firm in our purpose in these developmental stages. If we do, we will be rewarded with the full capacity AI used in the resolution of many clinical problems. We should look at some concrete examples of practical use of AI. The AI within the Secretary-Mimicking Artificial Intelligence (SMILE) system designed to aid pathologists is able to listen to voice commands and perform numerous supplementary tasks in the analysis of pathological sections, creating semiautomatically pathological reports ⁵². AI softwares are able to make the diagnosis of dementia easily and reliably from structural MRI images 53, 54. AI softwares process electronic patient records and identify those with systemic sclerosis with the risk of scleroderma renal crisis ⁵⁵. In computerized drug prescription systems, AI improves system efficiency and reduces the risk of wrong drug choice by a physician ⁵⁶.

Suggestions for possible further research directions

We believe that the scope of further research in the field should be increased. The research should be integrated with clinical practice as much as possible, thus obtaining benefits of this technology of the future as early as possible. All patient medical records should be stored in digital form, adequately processed and prepared, ready to be subjected to AI algorithm analysis. AI systems should constantly, repeatedly process and develop such data sets. Numerous essential correlations between the data items could thus emerge and new knowledge breakthroughs are certain without even starting individual targeted studies. This could help us save our resources and capacities, creating at the same time the basis for continual monitoring of patient health and longterm surveillance of the effects of drugs and therapeutic procedures. This type of research also constitutes the basis for identification of health risks which could be monitored using patient electronic medical records.

Conclusion

Results of the studies undertaken so far to investigate the use of AI in clinical medicine and dentistry have shown that this, most sophisticated area of computer use in health care, has some excellent prospects, but that further research and advancements in the field are required, even more intense than at present. The research has to be extensive and strong, so that high quality automation processes could be devised in the discovery of new drugs and new therapeutic methods.

REFERENCES

- 3. Russell S, Norvig P. Artificial intelligence: a modern approach. 3rd ed. New Jersey: Pearson Education; 2010.
- Miladinović M, Mihailović B, Janković A, Tošić G, Mladenović D, Živković D, et al. The reasons for the extraction obtained by artificial intelligence. Acta Fac Med Naiss 2010; 27(3): 143-58.

- Turing AM. Computing machinery and intelligence summary. Mind 1950; 59(236): 433–60.
- Poole D, Mackworth A, Goebel R. Computational intelligence: a logical approach. New York: Oxford University Press; 1998.
- 7. Wason C, Shapiro D. Foss B. Reasoning. In: Foss B, editor. New horizons in psychology. Harmondsworth: Penguin; 1966.
- Kahnemand , Slovic P, Tversky A. Judgment under uncertainty: Heuristics and biases. New York: Cambridge University Press; 1982.
- Lakoff G, Núñez R. Where mathematics comes from: How the embodied mind brings mathematics into being. New York: Basic Books; 2000.
- Shannon C. Programming a Computer for Playing Chess. Philosoph Mag 1950; 41(7): 256–75.
- Moconja S. Mathematical Logic in Computer Engineering -Tasks 1. Belgrade: Faculty of Mathematics; University of Belgrade; 2011 Available from: http://poincare.matf.bg.ac.rs/~slavko//mlur.vezbe.pdf. (Serbian)
- Marie F. Automated Reasoning-lecture notes: The reasoning in first-order logic. Belgrade: Faculty of Mathematics, University of Belgrade; 2012. Available from: <u>http://poincare.matf.bg.ac.rs/~filip/ar/ar-logika-prvog-reda.pdf.</u> (Serbian)
- Janičí P, Nikolić M. Artificial intelligence. Belgrade: Faculty of Mathematics, University of Belgrade; 2010. Available from: <u>http://poincare.matf.bg.ac.rs/~janicic/courses/vi.pdf.</u> (Serbian)
- Olivero J, Márquez AL, Real R. Integrating fuzzy logic and statistics to improve the reliable delimitation of biogeographic regions and transition zones. Syst Biol 2013; 62(1): 1–21.
- Heckerman D. A tutorial on learning with bayesian networks. Redmond, Washington: Technical Report MSR-TR-95-06, Microsoft Research; 1995.
- 16. *Mitzernmacher M, Upfal E.* Probability and Computing: Randomized algorithms and probabilistic analysis. Cambridge: Cambridge University Press; 2005.
- 17. Tzeng W. Learning probabilistic automata and Markov chains via queries. Mach Learn 1992; 8(2): 151-66.
- Kevin M. Naive Bayes classifiers. Vancouver: Department of Computer Science, University of British Columbia; 2006.
- Gutierrez-Osuna R. Introduction to Pattern Recognition. Dayton: Wright State University; 2000.
- 20. Jović A. Methodsof data mining. Zagreb: Faculty of Electrical Engineering and Computing; 2010. (Croatian)
- 21. *Reynolds D.* Gaussian Mixture Models. Lexington: MIT Lincoln Laboratory; 2002.
- 22. Safavian R, Landgrebe D. A survey of decision tree classifier methodology. West Lafayette: Purdue University, School of Electrical Engineering; 1991
- 23. Li J. Classification/Decision Trees. Harrisburg: The Pennsylvania State University; 2010.
- Khajanchi A. Artificial Neural Networks: The Next Intelligence. Los Angeles: University of Southern California, Technology Commercalization Alliance; 2012.
- Neumann G. Programming Languages in Artificial Intelligence. Kaiserslautern: German Research Center for Artificial Intelligence (LT-Lab, DFKI); 2001.
- Azarkhish I, Raoufy MR, Gharibzadeh S. Artificial intelligence models for predicting iron deficiency anemia and iron serum level based on accessible laboratory data. J Med Syst 2012; 36(3): 2057–61.
- Qidwai U, Shamim S, Enam A. Fuzzy prediction for failed back surgery syndrome. Appl Artif Intell 2010; 24(10): 881–95.
- Tsuchihashi Y. Expanding application of digital pathology in Japan--from education, telepathology to autodiagnosis. Diagn Pathol 2011; 6(Suppl 1): S19.
- 29. Syed Z, Rubinfeld I, Patton JH, Ritz J, Jordan J, Doud A, et al. Using Procedural Codes to Supplement Risk Adjustment: A

Nonparametric Learning Approach. J Am Coll Surg 2011; 212(6): 1086–93.e1.

- Uzuner O, Mailoa J, Ryan R, Sibanda T. Semantic relations for problem-oriented medical records. Artif Intell Med 2010; 50(2): 63-73.
- Unified Medical Language System. Bethesda: U. S. National Library of Medicine. 2009. Available from: <u>http://www.nlm.nih.gov/research/umls</u>
- Roberts A, Gaizauskas R, Hepple M, Guo Y. Mining clinical relationships from patient narratives. BMC Bioinformatics 2008; 9(Suppl1): S3.
- Zolnoori M, Zarandi MH, Moin M. Application of intelligent systems in asthma disease: designing a fuzzy rule-based system for evaluating level of asthma exacerbation. J Med Syst 2012; 36(4): 2071–83.
- Kim EY, Lim KO, Rhee HS. Predictive modeling of dental pain using neural network. Stud Health Technol Inform 2009; 146: 745-6.
- Nieri M, Crescini A, Rotundo R, Baccetti T, Cortellini P, Pini PG. Factors affecting the clinical approach to impacted maxillary canines: A Bayesian network analysis. Am J Orthod Dentofacial Orthop 2010; 137(6): 755–62.
- Xie X, Wang L, Wang A. Artificial neural network modeling for deciding if extractions are necessary prior to orthodontic treatment. Angle Orthod 2010; 80(2): 262–6.
- Kitporntheranunt M, Wiriyasuttiwong W. Development of a medical expert system for the diagnosis of ectopic pregnancy. J Med Assoc Thai 2010; 93 Suppl 2: S43–9.
- Tamaki Y, Nomura Y, Katsumura S, Okada A, Yamada H, Tsuge S, et al. Construction of a dental caries prediction model by data mining. J Oral Sci 2009; 51(1): 61–8.
- Sakai S, Kobayashi K, Nakamura J, Toyabe S, Akazawa K. Accuracy in the diagnostic prediction of acute appendicitis based on the Bayesian network model. Methods Inf Med 2007; 46(6): 723–6.
- Käkilehto T, Salo S, Larmas M. Data mining of clinical oral health documents for analysis of the longevity of different restorative materials in Finland. Int J Med Inform 2009; 78(12): 68–74.
- Korhonen M, Gundagar M, Suni J, Salo S, Larmas M. A Practice-Based Study of the Variation of Diagnostics of Dental Caries in New and Old Patients of Different Ages. Caries Res 2009; 43(5): 339–44.
- 42. Kawaguchi T, Kakuma T, Yatsuhashi H, Watanabe H, Saitsu H, Nakao K, et al. Data mining reveals complex interactions of risk factors and clinical feature profiling associated with the staging of non-hepatitis B virus/non-hepatitis C virus-related hepatocellular carcinoma. Hepatol Res 2011; 41(6): 564-71.
- Miladinović M, Mihailović B, Kavarić N. The model of computer medical system for the collection of scientific information in the Serbian health care system. HealthMED 2013; 7(1): 35–40.
- Miladinonić M. The model of artificial intelligence in discovering the causes of disease and modes of healing in oral surgery. Kosovska Mitrovica: School of Medicine, University of Pristina;. 2013. (Serbian)
- 45. Stanley RJ, De S, Demner-Fushman D, Antani S, Thoma GR. An image feature-based approach to automatically find images for application to clinical decision support. Comput Med Imaging Graph 2011; 35(5): 365–72.
- Korhonen M, Salo S, Suni J, Larmas M. Computed online determination of life-long mean index values for carious, extracted, and/or filled permanent teeth. Acta Odontol Scand 2007; 65(4): 214–8.
- 47. de Bruijn MJ, ten Bosch L, Kuik DJ, Langendijk JA, Leemans CR, Verdonck-de Leeuw IM. Artificial neural network analysis to assess hypernasality in patients treated for oral or oropharyngeal cancer. Logoped Phoniatr Vocol 2011; 36(4): 168–74.

Miladinović M, et al. Vojnosanit Pregl 2017; 74(3): 267-272.

- Bas B, Ozgonenel O, Ozden B, Bekcioglu B, Bulut E, Kurt M. Use of artificial neural network in differentiation of subgroups of temporomandibular internal derangements: a preliminary study. J Oral Maxillofac Surg. 2012; 70(1): 51–9.
- 49. *Cilia E, Teso S, Ammendola S, Lenaerts T, Passerini A*. Predicting virus mutations through statistical relational learning. BMC Bioinformatics 2014; 15(1): 309.
- Wright AP, Wright AT, Many AB, Sittig DF. The use of sequential pattern mining to predict next prescribed medications. J Biomed Inform 2015; 53: 73–80.
- Wu Y, Yang R, Jia S, Li Z, Zhou Z, Lou T. Computer-aided diagnosis of early knee osteoarthritis based on MRI T2 mapping. Biomed Mater Eng. 2014; 24(6): 3379–88.
- 52. *Ye JJ*. Artificial Intelligence for Pathologists Is Not Near- It Is Here: Description of a Prototype That Can Transform How We Practice Pathology Tomorrow. Arch Pathol Lab Med 2015; 139(7): 929–35.
- 53. Bron EE, Smits M, van der Flier WM, Vrenken H, Barkbof F, Scheltens P, et al. Standardized evaluation of algorithms for

computer-aided diagnosis of dementia based on structural MRI: The CADDementia challenge. Neuroimage 2015; 111: 562–79.

- Klöppel S, Abdulkadir A, Jack CR, Koutsonleris N, Mourão-Miranda J, Vemuri P. Diagnostic neuroimaging across diseases. Neuroimage 2012; 61(2): 457–63.
- Redd D, Frech TM, Murtaugh MA, Rhiannon J, Zeng QT. Informatics can identify systemic sclerosis (SSc) patients at risk for scleroderma renal crisis. Comput Biol Med 2014; 53: 203–5.
- Syed-Abdul S, Nguyen A, Huang F, Jian W, Iqbal U, Yang V, et al. A smart medication recommendation model for the electronic prescription. Comput Methods Programs Biomed 2014; 117(2): 218–24.

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