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# Responsible and ethical application of artificial intelligence systems in healthcare through a case study in diagnostics and personalized medicine

**Abstract:** The paper discusses new challenges of responsible and ethical application of artificial intelligence (AI) systems in healthcare. Academic research and commercial development focused on medicine are showing exponential growth; however, regulatory requirements for clinical use and commercial introduction are progressing more slowly. After classifying AI applications and identifying challenges and risks, a case study in diagnostics and personalized medicine is presented. The main result is a clear overview of the upcoming trends in medicine that can help legislators prepare to create new regulations and ethical principles of practice for new AI technologies. It is essential that technical experts, policy makers, legislators and other decision-makers accept responsibility.

**Keywords:** artificial intelligence, regulation, case study, medicine

## Introduction

The use of artificial intelligence (AI) systems and software in medicine and healthcare is expanding. Academic research and commercial development are growing exponentially, but regulations for clinical application and global commercial market are growing much more slowly. The application of AI brings specific advantages, but also risks, so that there is a need for responsible and transparent systems which fulfil regulatory and ethical standards (Milovanović & Terzić, 2023).

Ethical guidelines of the development, application and use of reliable and responsible artificial intelligence are aimed at introducing a preventive mechanism which enables responsible development and verification procedures. There is a need for AI systems in compliance with the highest ethical and security standards regarding personal data protection, protection against discrimination in the

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application of machine learning and the establishment of responsible development of artificial intelligence in compliance with international ethical principles. We stress the importance of policy options the aims of which are the minimization of medical artificial intelligence risks, improvement of management and strengthening of responsible development. It is essential that technical experts, policy makers, legislators and other decision-makers accept responsibility (Milovanović, Terzić, Vučetić, 2023).



The EU strategy is based on high standards of protection against social risks represented by AI, unlike the US strategy which is developed mainly through private sector initiatives and self-regulation, and China's strategy which is essentially run by the government and characterized by a strong coordination of private and public investments in AI technologies (Papakonstantinou & DeHert, 2024). At the beginning of 2024, the EU Parliament adopted the Artificial Intelligence Act which imposes significant penalties for the failure to observe the regulations about the use of the forbidden AI systems as of the beginning of next year (Müller & Kettemann, 2024). This Law applies to AI providers in the EU market, but also to users in the EU and the providers and users in a third country if output results are used in the EU. The Law contains substantial assessment elements for high-risk systems which are completely forbidden, then high-risk systems which are not forbidden in themselves, but are significantly regulated and, finally, transparency and innovation support measures are introduced for all systems. The EU guidelines promote a reliable AI system which, in line with all the applicable laws and regulations, ensures respect for ethical principles and values, both from technical and social perspectives robust in avoiding unintentional causing of damage. It is essential that software and hardware artificial intelligence systems are directed towards man, that they are developed, applied and used in compliance with the key ethical requirements of human action: supervision, robustness and safety, data privacy and management, transparency, diversity, non-discrimination and fairness, social and ecological prosperity and responsibility (Coeckelbergh, 2020).

> Serbia has adopted a strategy of artificial intelligence development by 2025, an action plan and ethical guidelines for the development, application and use of reliable and responsible artificial intelligence. A draft strategy is currently being prepared for the period by 2030.

## Challenges of responsible and ethical application

AI technology is being progressively developed and introduced in almost all areas of medicine, from primary protection to rare diseases and biomedical research. It is expected that many aspects of management regarding healthcare administration (increased efficiency, quality control, more conscientious business operations) and policy benefit from the new tools mediated by artificial intelligence (Gerke, Minssen, Cohen, 2020).

AI systems in healthcare can be classified on the basis of user groups of stakeholders: patients and citizens, clinicians and carers, medical workers, public health experts and policy makers. The basic domains of AI technology application in healthcare are clinical practice, clinical research, new medications, personalized medicine, public healthcare and global health, and healthcare administration. The classification of medical AI tools can also be based on the environment in which the tools are used: clinical environments (hospitals, primary healthcare centres, emergency centres), clinical processing and setting management (laboratory, pharmacy, radiology) and administration. We will adopt a more comprehensive classification of AI applications clinical practice, research, public health and administrative applications.

**Clinical practice.** The potential of AI application in the clinical environment is huge and ranges from the automation of diagnostic processes to therapy decision-making and clinical research. The data necessary for diagnosing and treatment come from numerous sources, including clinical notes, laboratory tests, pharmacy data, medical imaging and genome information. Radiology is a branch of medicine primarily dealing with discovering diseases and injuries – namely diagnostics, and that is why it has undergone substantial development with AI application in the past few years. AI technologies for screens processing help radiologists in interpreting medical images. For example, image segmentation with limited human supervision has been achieved by using deep neural network (DNN) models for automatic localization and marking of anatomic structure borders. AI tools can suggest a priority and monitor findings which require early attention, and enable radiologists to concentrate on the most probable pathological images. Radiomix is yet another image processing technique I which AI has proved to be useful. Although the term is not strictly defined, the general goals are a quantitative analysis of diagnostic images and treatment planning (Larson et al., 2021). The features include the characteristics of tissues and lesions such as their heterogeneity and shape, and can be used for resolving clinical problems independently or in combination with demographic, histological, genomic or proteomic data, which refer to patient's proteins, including their expression, modification and interaction. The importance of Radiomix is even greater when a large amount of information is processed with the aid of AI techniques.

**Biomedical research.** Medical research has numerous benefits from the solutions derived from artificial intelligence in comparison to clinical applications, while recent progress also show promising AI applications in discovering clinical knowledge. For example, the main sources of medical knowledge still use MI, algorithms for search result ranging, including algorithms which permanently learn from the users' behaviour in the search. For example, PubMed is a widely-used browser for biomedical literature. BestMatch search algorithm uses users' intelligence and most modern MI, technology as an alternative to the traditional data sorting sequence. BestMatch algorithm is "trained" by using previous user searches with dozens of signals (factors) of relevance ranging (the most important are the previous use of an article, its publication date, relevance grading and

article category). The algorithm significantly improves finding relevant information in relation to the implied time sequence in PubMed and with time it has increased the use of relevance search. Thanks to techniques such as information extraction, automatic summing and deep learning (DL) artificial intelligence has the potential to transform static narrative articles into patient-specific clinical evidence. Designers of medications intensively apply MMI techniques in searching chemical information in big data bases of compounds in order to discover new medications. The application focus is on the development of AI approach in implementing innovative modelling based on the diverse nature of data sets for medications. AI models contribute to a better understanding of the wide range of medications and clinical outcomes they may offer.



**Clinical research.** Randomized Controlled Research (RCT) is the most powerful method for risk assessment and benefiting from any medical intervention. However, the implementation of RCT is not always feasible. Common difficulties of unsuccessful RCT include the wrong selection of patients, inadequate randomization, insufficient sample size and wrong selection of end points. AI models are trained for a better selection of study participants by advanced statistical methods and for assessing the study end points by a data-based method. AI application generates a more efficient performance and a larger statistical strength than traditional RCT. Apart from the efficient selection process, a sufficiently large sample is critical for enabling the discovery of statistically significant differences between the groups.

**Personalized medicine.** It is important to understand scientifically how unique characteristics of an individual patient, such as molecular and genetic profiles, make the patient vulnerable to a disease and responsibe to a therapeutic treatment. The original concept of personalized medicine has been expanded to cover other properties and individual clinical characteristics, and a new concept has finally been formed and called expanded personalized medicine on the basis of additional sources of information such as clinical sources, demographic data, social data, lifestyle parameters (quality of sleep, physical activity, eating habits) and environmental conditions. AI tools improve progress in personalized medicine by assessing clinical benefits of various research methods and several types of data.

**Global health.** Public health covers disease prevention, life extension and health improvement through organized efforts and informed choices of society, public and private organizations, communities and individuals. Experiments with relevant AI solutions are currently underway within many areas of public health. AI can help to identify specific demographic or geographical locations with a distributed disease or high-risk behaviour. The scope of AI solutions which can improve supervision of a disease is also significant. Digital epidemiological supervision refers to integration of supervision based on cases and events (news ad online media, sensors, digital traces, mobile devices, social media, microbiological laboratories and clinical reporting) for the purpose of analysing the approach to threat verification. The aim is to build early warning systems for undesired events in relation to med-

ications and low air quality. AI has the potential to intensify contact with patients, as well as to personalize services. The essential component of the initiatives involves contacting a large number of patients via different automated, simply scalable methods, such as text messages and portals for patients. AI application in public health also includes a broader perspective of healthcare policy and management. Studies cover the research of artificial intelligence with the aim of improving the performances of healthcare institutions and allocating resources from the system perspective.

**AI healthcare administration.** Healthcare systems are characterized by a complex administrative work flow with a wide range of actors and institutions, including patients (insurance collection management), healthcare workers, healthcare institutions and organizations (patient flow), laboratories (supply chain of consumables), pharmacies, taxpayers and regulators. Within primary healthcare, potential problems have been identified as follows: time necessary for financial compensation, data input into various non-integrated information systems based on practice, processing information from hospitals and other external service providers and helping patients in the fragmented healthcare system. AI can perform routine tasks in a more efficient, accurate and impartial manner. One of the arguments in favour of its use in administrative practice is that errors in these activities are less serious than those in the clinical environment. Nevertheless, the questions of security and lack of privacy still remain. AI applications may be critical in the organization of the patient flow. For example, the lack of availability of hospital beds is an important cause of cancelling surgical interventions; however, it may constitute an administrative error which may be avoided in the patient flow. The problem frequently occurs and is also related to delayed release from the clinical department.

Below we will identify the main risks and potential consequences of AI application in medicine and healthcare:

- Patients' injury due to AI errors (main causes are noise and artefacts in clinical inputs and measurements, unexpected variations in clinical contexts and environments; medical consequences are inadequate treatment and wrong appointments or determining the priority of interventions);
- Abuse of medical AI tools (potential causes are the lack of training and sufficient explanation and information; improper use of AI tools may lead to wrong medical assessment and decision-making and, subsequently, to potential harm to patients);
- AI partiality and continuance of existing inequalities (most frequent causes are the lack of transparency, imbalanced data sets based on structural partiality and discrimination, as well as the lack of diversity and interdisciplinarity in technological, scientific, clinical and policy-making teams);
- Issues of privacy and security (the cause of which is the lack of transparency regarding the design, development, evaluation and application of AI tools; specific risks include the lack of understanding and trust, difficulties in the autonomous work

of reproducing and assessing algorithms, difficulties in identifying the source of errors and defining responsibility);
- Gaps in responsibility (main risks include sharing personal data without a fully informed consent, data requalification without the patient's knowledge, data violation both at the individual level and at the hospital or healthcare system level);
- Algorithm responsibility (the key aspect of reliable and applicable AI, legal gaps still existing in the current national and international regulations, not being simple to define roles and responsibilities due to multiple actors involved in the process, from design to application, particularly if the used AI model is not fully transparent);
- Obstacles in the implementation (limited data quality, structuring and interoperability of AI tools with the existing clinical work flows and electronic healthcare systems).



We have clarified basic clinical, social and ethical risks of AI application in healthcare: potential errors and harm suffered by patients, risk of impartiality and increased healthcare inequalities, the lack of transparency and trust, as well as vulnerability to hacking and violation of data privacy. Challenges must be addressed and prevented, so that it is necessary to monitor the processes of international standardization and patent registration.

Analyzing international registered patents with AI application in medicine it is possible to predict the trends of new technologies by specialities which require new regulations. A relatively recent study from 2022 identifies more than 10,000 healthcare patients in the past ten years, which has enabled regulators to perceive clear trends of the upcoming AI technologies and necessary strategic activities. First, it is possible to predict the areas on which to direct the regulatory focus, how patents are followed by products/devices ready for the market with a predictable delay. Medical specialties emphasized by a significant number of registered patents are radiology, oncology and ophthalmology, and therefore these areas will have the largest number of new technologies in clinical practice in the following years.

## Case study

Artificial intelligence possesses significant potential for improving various aspects of healthcare and it covers diagnostics, treatment, data management and increasing efficiency of healthcare systems (Recht et al., 2020). We emphasize the trends of AI effects on healthcare:

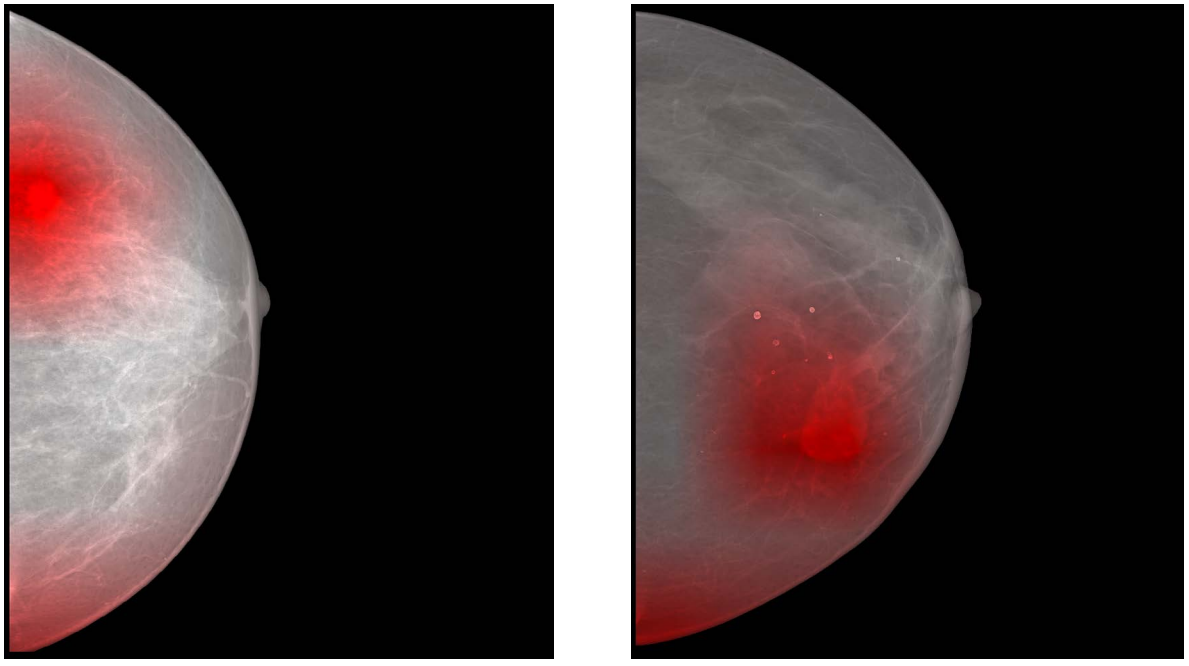
- **Diagnostics.** The development of AI systems for analyzing and interpreting medical screens (US, RO, CT, NMR, PET) may improve diagnosis speed and accuracy and be helpful in the work of clinical doctors.
- **Personalized treatment.** The use of AI for the analysis of genetic data and other factors in order to adjust the treatment to patients' individual needs.
- **Predictive analytics.** The implementation of AI systems in the analysis of a large amount of data in order to predict the risk of certain diseases or complications, enabling preventive measures.

- **Telemedicine and mobile applications.** The AI integration in the applications for health monitoring and telemedical platforms ensures better monitoring of patients and providing remote personalized care.
- **Automation of administrative processes.** The use of AI in the automation of administrative tasks, such as making appointments for examinations, invoicing and data management.

Together with the partners from the healthcare sector, they work on the development of AI tools for diagnostics, personalized medicine and improvement of efficiency of healthcare services, as well as the design of new medications. The aim is to ensure faster and simpler carcinoma detection, to reduce the complexity of rare disease diagnostics and to shorten the time until giving an

The researchers from the Institute for Artificial Intelligence Research and Development of Serbia (IVI, 2024) implement a number of projects in the area of healthcare: diagnostics of cancer and rare diseases, as well as the development of new medications.





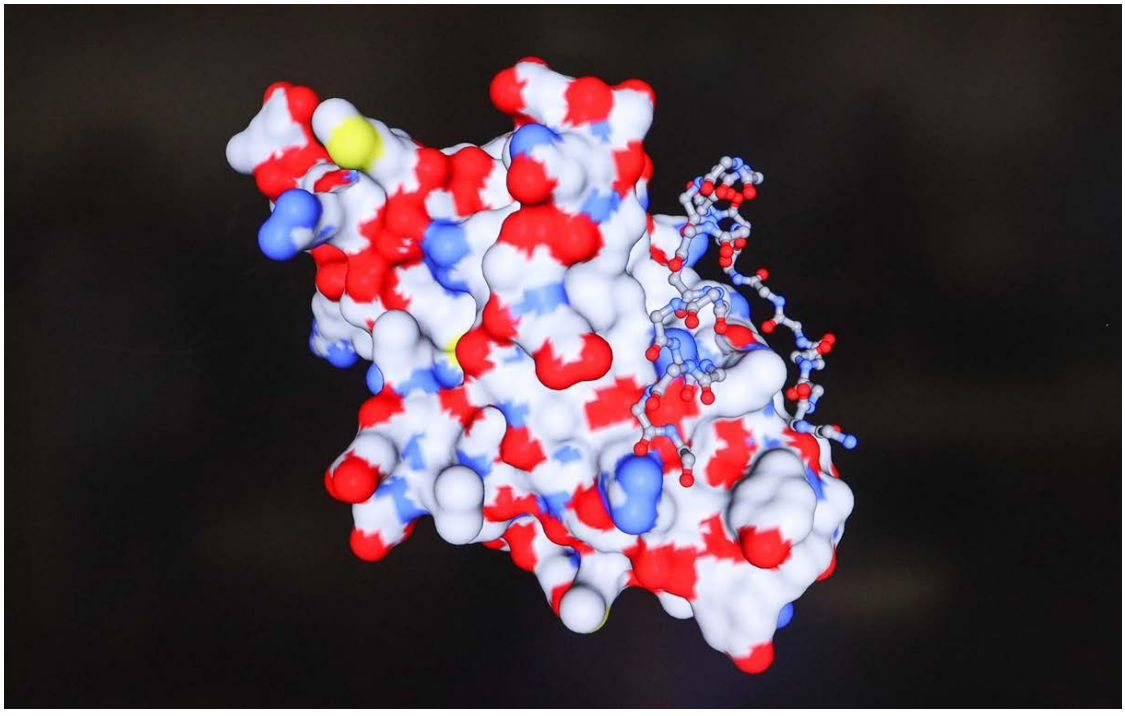
The Institute for Artificial Intelligence Research and Development of Serbia, with the aid of artificial intelligence, analyzes and ranks patients' mammographic images with the aim of faster diagnosis of carcinomas.
Photo: Institute for Artificial Intelligence Research and Development

accurate diagnosis, to reduce the pressure on the healthcare system and, consequently, to redirect treatment costs towards an adequate innovative therapy, as well as to accelerate the process of finding and developing mediations and to reduce pharmaceutical research costs.

The first project includes AI analysis and ranging of patients' mammographic screens. The procedure is that early screening results indicate that no further monitoring of the patient is required or that additional analyses are necessary. The solution is to range screens by their importance: the first place is for the screens which need further attention, interpretation, analysis or biopsy, while the last place is for the patients who do not need an urgent examination and who are probably healthy. Of course, a radiologist makes the final decision and that is why AI tools only ensures better organization and optimization of doctors' working hours.

The project of diagnosing rare diseases is important due to the observed long time interval between the patient's registrations of the first symptoms to the actual diagnosis. The use of





The Institute for Artificial Intelligence Research and Development of Serbia, in cooperation with a startup from the United States of America, develops a platform based on generative artificial intelligence for the design of binding peptides to a desired protein.

Photo: Institute for Artificial Intelligence Research and Development

modern AI techniques is examined in terms of reducing the complexity of diagnosing Fabry disease, shortening the time for giving an accurate diagnosis, reducing the pressure on the healthcare system and, consequently, on redirecting treatment costs towards an adequate innovative therapy. Exceptionally rare diseases are on the increase, but there is still a problem of doctors not examining frequently the patients suffering from rare diseases and, in addition, the symptoms are quite different. Thanks to NLP models, the researchers from the Institute have examined huge amounts of medical data about 50,000 patients and a certain knowledge corpus has been generated about the patients potentially diagnosed with Fabry disease. The ranking list has been made on the basis of the criteria of the speciality doctors about the most important symptoms, as well as the minor ones. The ranking of the patients has been generated for testing at the doctor's invitation. Early detection of rare diseases significantly extends and improves the quality of patients' lives, so that the development of AI tools also contributes to substantial savings in the healthcare system.

The Institute works on AI application projects in cooperation with pharmaceutical industry on discovering and producing new medications. With the advanced techniques of machine learning of PL and AI, huge data sets from biomedical research are analyzed. Trained AI systems then identify patterns and relations of different biological entities and molecules, which further enables the evaluation of the efficiency of molecules as potential medications. There is also an emphasis on the development of generative AI models in creating molecules which are not present in standard libraries of known molecules used for therapeutic purposes. Models expand the chemical space of searching for new medications on a large scale and support therapies for the so far untreated diseases. The project is rather complex and also includes the analysis of a large amount of biomedical data, as well as the development of generative AI models which re3quire laboratory corroboration of potential molecules as candidates for the evaluation of the model quality.



## Conclusion

The paper considers current regulatory and socio-ethical aspects of AI in medicine and healthcare. Artificial intelligence may make a revolutionary transformation in the way we provide and receive healthcare services, through personalized medicine, more efficient diagnoses and treatment, better outcomes for patients and the optimization of the healthcare system. Predicting AI trends in healthcare is challenging and exciting.

With responsible development and application, AI can support a more precise, efficient and available medical service. It is difficult to overcome technical and ethical challenges of the AI system application in order to use maximally the potential and avoid potential risks. The future of healthcare is inevitably related to AI and it is our task to shape it in the way that brings benefits to society.

# References

Coeckelbergh, M. (2020). *AI ethics*. Cambridge. MA: MIT Press.

Gerke, S., Minssen, T., Cohen, G. (2020). Ethical and legal challenges of artificial intelligence-driven healthcare. In: A. Bohr, K. Memarzadeh (eds.) *Artificial Intelligence in Healthcare* (295–336). Cambridge, MA: Academic Press.

IVI, *Institute for Artificial Intelligence Research and Development of Serbia* (2024). Available at https://ivi.ac.rs/en/news/.

Larson, D. B. et al. (2021). Regulatory frameworks for development and evaluation of artificial intelligence–based diagnostic imaging algorithms: summary and recommendations. *Journal of the American College of Radiology*, XVIII (3), 413–424. DOI: https://doi.org/10.1016/j.jacr.2020.09.060.

Milovanović, D., Terzić, R. (2023). Responsible application of Artificial Intelligence in healthcare: ethical principles of practice and new regulations. In: M. Ivković, D. Drašković (eds.) *Proceedings of the 29th ICT Conference YU INFO 2023* (46–49). Beograd: Informaciono društvo Srbije. [In Serbian]

Milovanović, D., Terzić, R., Vučetić, Č. (2024). Trends of application Artificial Intelligence in healthcare: challenges and regulation issues. In: *Proceedings of the 30th ICT Conference YU INFO 2024.* In preparation [In Serbian]

Müller, M., Kettemann, M.C. (2024). European approaches to the regulation of digital technologies. In: H. Werthner et al. (eds.) *Introduction to Digital Humanism* (623–637). Cham: Springer.

Papakonstantinou, V., DeHert, P. (2024). *The Regulation of Digital Technologies in the EU*, Oxfordshire, England, UK: Routledge.

Recht, M. P. et al. (2020). Integrating artificial intelligence into the clinical practice of radiology: challenges and recommendations. *European Radiology*, XXX (6), 3576–3584. DOI: https://doi.org/10.1007/s00330-020-06672-5