Baština Akademije nauka i umjetnosti Bosne i Hercegovine

Artificial Intelligence in Industry 4.0: The future that comes true: AI

Karabegović, Isak; editor

2024-09-17

https://bastina.anubih.ba/handle/123456789/791

Preuzeto s Baštine Akademije nauka i umjetnosti Bosne i Hercegovine

https://bastina.anubih.ba/

DOI: 10.5644/PI2024.215.15

Integration of Artificial Intelligence-Based Systems in Diagnostic Pathways: TRUEAID Case Study

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Abstract: *Neurological impairment disorders in fetuses, such as cerebral palsy, epilepsy, and autism spectrum disorder, can arise from numerous factors impacting the development of the fetal nervous system. Although diagnosing these disorders early is difficult, it is essential for prompt intervention. Recent progress in deep learning and ultrasound technology offers the potential to create a tool for early detection. Development of the TRUEAID system is based on combining the meticulously tuned Kurjak Antenatal Neurodevelopmental Test (KANET) with a sophisticated convolutional neural network for construction of an AI empowered ultrasound module capable of automated diagnostic decision support in the field of fetal neurodevelopmental risk assessment. The model's performance was evaluated using accuracy metrics, precision, sensitivity, specificity, F1 score, and Mathesson Correlation Coefficient (MCC). The custom CNN architecture achieved an overall accuracy of 93.83%. This pilot study lays the foundation for AI-based fetal neurobehavioral assessment, providing a promising tool for the early detection of fetal neurological impairment disorders. The research holds implications for improving outcomes for affected children and making advanced diagnostic capabilities accessible in diverse healthcare settings.*

Keywords: *fetal neurodevelopment, artificial intelligence, KANET, ultrasound, diagnostic support system*

1. Introduction

Fetal neurological impairment disorders constitute a category of conditions impacting the nervous system's development in fetuses. These disorders can arise from various causes, such as genetic anomalies and environmental influences. Moreover, complications during pregnancy and childbirth also pose a significant risk. Each type of fetal neurological impairment disorder has distinct symptoms and causes. Notable examples include cerebral palsy, intellectual disabilities, epilepsy, and autism spectrum disorder.

The causes of fetal neurological impairment disorders are not always clear, and can vary depending on the specific disorder. However, some common risk factors include maternal infections, exposure to toxins or radiation during

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pregnancy, and complications during delivery such as birth asphyxia or trauma. Diagnosing fetal neurological impairment disorders can be challenging, and may involve a combination of medical imaging, genetic testing, and neurological evaluations. Fetal neurological impairment disorders pose significant challenges to affected individuals, their families, and healthcare systems. Comprehensive understanding, early diagnosis, and targeted interventions are essential in mitigating the impacts of these disorders and improving the quality of life for affected individuals. Early diagnosis is important, as it can help ensure that affected children receive the appropriate medical care and therapies to help manage their symptoms and improve their overall quality of life. Treatment for fetal neurological impairment disorders typically involves a multidisciplinary approach, with a team of healthcare professionals working together to address the child's specific needs. This may include physical therapy, occupational therapy, speech therapy, and medications to manage symptoms such as seizures or behavioral problems.

The diagnostics of fetal neurological impairment disorders is a delicate and complex process, marked by the integration of advanced technologies and multidisciplinary expertise to assess the developing nervous system within the womb. These disorders, which can arise due to genetic anomalies, environmental factors, or a combination of both, necessitate precise and sensitive diagnostic approaches to facilitate early intervention and optimal management [1]. The complexity of diagnosing fetal neurological impairments requires a collaborative approach. Each professional, from the obstetrician conducting initial screenings to the pediatric neurologist interpreting advanced neuroimaging, plays a pivotal role. Genetic counselors translate complex genomic data into actionable insights, while perinatologists oversee the management of high-risk pregnancies. This collaborative effort extends to parental involvement as parents are integral partners in the diagnostic journey. Their insights, observations, and decisions central to the personalized and ethical management of fetal neurological impairments.

Ultrasound imaging is a crucial tool for real-time visualization of fetal development. Advanced sonographic technologies enable detailed imaging of the fetal brain, spinal cord, and associated structures. Ultrasound examinations, particularly the mid-pregnancy anatomy scan, offer a visual assessment of the fetus’s developing structures. Special attention is given to the brain and spinal cord, where structural anomalies can often be visualized. Neurosonographers carefully assess ventricular sizes, cortical folding patterns, and other structural markers to identify anomalies indicative of neurological impairments. In cases of suspected neural tube defects, spina bifida, or other structural anomalies, targeted ultrasounds provide enhanced imaging resolution, facilitating detailed anatomical assessments and diagnostic precision. These insights are instrumental in prenatal counseling, intervention planning, and parental decision-making

(Abu-Rustum & Daou, 2020). The integration of maternal health data, family history, and environmental factors enriches the interpretative precision of these screenings, offering a preliminary risk profile that guides subsequent diagnostic steps [2].

The Kurjak Antenatal Neurodevelopmental Test (KANET) represents a significant advancement in non-invasive prenatal neurodevelopmental testing. Developed by a team led by Dr. Asim Kurjak, KANET has made a notable impact in perinatal neurology. This test combines advanced technology with clinical expertise to offer unprecedented insights into fetal neurobehavior. Central to KANET's innovative method is the use of four-dimensional (4D) ultrasound technology. This technology allows for dynamic, multi-dimensional visualizations of the fetus in utero, enhancing our understanding of fetal neurological development [3,4].

KANET's uniqueness lies in its ability to conduct detailed, real-time analysis. The 4D ultrasound provides a dynamic observational platform, enabling the detailed study of every fetal movement and behavioral moment. This approach goes beyond mere observation; it deeply examines the spectrum of neurobehavioral indices that reflect the intricate neurodevelopmental processes occurring in the fetal environment. KANET operates on the premise that specific fetal movements and behaviors directly indicate the integrity and functionality of developing neural structures and pathways [5].

2. Decision Support Systems in Healthcare

Decision Support Systems (DSS) in healthcare are essential tools that aid clinicians and healthcare professionals in making well-informed and accurate decisions. These systems utilize a combination of technologies, data, and algorithms to provide insights and recommendations, thereby enhancing the quality and efficiency of healthcare delivery. Healthcare DSS incorporate a wide range of data sources, such as Electronic Health Records (EHRs), laboratory results, and medical imaging data. For example, research by Kawamoto et al. (2005) [6] showed that integrating clinical data into DSS significantly improves clinical practice and patient outcomes. These systems employ advanced algorithms and artificial intelligence to analyze complex datasets, providing personalized patient care recommendations. Clinical Decision Support (CDS) systems, a specific type of DSS, play a crucial role in diagnosis and treatment by analyzing patient-specific data to offer evidence-based recommendations. A study by Osheroff et al. (2012) [7] highlighted the impact of CDS in reducing medical errors, improving healthcare quality, and lowering costs. However, implementing DSS in healthcare presents certain challenges.

Artificial intelligence continues to transform medical diagnosis, with machine learning and deep learning leading the advancements. These technologies have significantly improved the accuracy, speed, and efficiency of diagnosing various medical conditions. The integration of AI in healthcare has been a focal point of research and development in recent years [8]. AI systems, particularly those using machine learning (ML) and deep learning (DL) algorithms, have shown remarkable capabilities in diagnosing diseases, sometimes surpassing human clinicians. AI has also made progress in the field of neurodegenerative disease diagnosis [9].

AI has also made advancements in neurodegenerative diseases. A study by Ding et al. (2021) [10] shows an example of a machine learning model that predicted the progression of Alzheimer's disease. By analyzing multimodal data, including genetic, imaging, and clinical data, the model could identify patients at risk of progression from mild cognitive impairment to Alzheimer's disease. Maroco et al. (2011) [11] demonstrated a machine learning model that utilized data from cognitive tests to identify patients in the early stages of Alzheimer's, enabling timely interventions. The diagnosis of Parkinson's disease is being revolutionized by AI, which analyzes clinical, imaging, and genetic data to identify the disease with superior accuracy. Athey et al. (2021) [12] employed machine learning to analyze voice recordings, effectively differentiating between individuals with and without Parkinson's, paving the way for non-invasive, cost-effective diagnostic tools. AI technologies, particularly deep learning, have demonstrated remarkable accuracy in analyzing PET scans to diagnose Parkinson's disease. Models can identify subtle metabolic changes in the brain, offering insights into disease onset and progression. Sarraf et al. (2020) [13] presented a that effectively distinguished between Parkinson's patients and controls based on PET images. Machine learning algorithms are utilized in the analysis of structural MRI data for the early detection of Huntington's disease. These algorithms can identify and measure specific brain structure changes, aiding in early diagnosis and monitoring of disease progression. Eskildsen et al. (2013) [14] applied a machine learning approach to analyze structural MRI scans to distinguish between early-stage Huntington's patients and controls. AI's role in monitoring and managing multiple sclerosis (MS) is also growing. AI algorithms analyze MRI scans to identify and quantify MS lesions, providing insights into disease progression and treatment effectiveness. Eitel et al. (2019) [15] illustrated how deep learning could precisely delineate and measure MS lesions over time, offering a reliable tool for personalized treatment monitoring while Brown & Hamarneh (2016) [16] illustrated how machine learning could analyze MRI data to identify and quantify brain lesions in multiple sclerosis patients, offering insights into disease progression and treatment response. AI is proving to be instrumental in utilizing diffusion tensor imaging (DTI) for the diagnosis and monitoring of multiple sclerosis (MS). Deep learning models can

analyze DTI data to detect white matter lesions and abnormalities, essential for MS diagnosis as described by Danelakis et al. (2019) [17]. They have described a CNN that efficiently processed DTI data to classify MS patients and healthy controls. By analyzing complex datasets including neuroimaging, genomic, and clinical data, AI models can predict the onset and progression of Alzheimer's with high accuracy (Danelakis et al., 2019) [17]. AI applications extend to the analysis of functional MRI (fMRI) data for the diagnosis and monitoring of Amyotrophic Lateral Sclerosis (ALS). By analyzing brain activity patterns, AI models can identify functional anomalies indicative of ALS. Welsh et al. (2013) [18] implemented machine learning to classify ALS patients and healthy individuals based on resting-state fMRI data.

3. Trueaid Development

The dataset used to develop the AI-driven decision support system, named TRUEAID, consisted of 3D ultrasound images. From 2021 to 2023, a total of 10,452 samples were collected for the development of TRUEAID, which stands for TRUstworthy Artificial IntElligence system for fetal neurological risk assessment and Diagnostic support. These images were extracted from 4D ultrasound recordings of fetuses obtained during the KANET test, a prenatal evaluation of neurological development conducted in the third trimester of pregnancy. KANET assessments are conducted on pregnancies both healthy and suspected to have pathology, with a larger dataset available from normally developing fetuses in healthy pregnancies utilized for developing the TRUEAID system. The dataset used in this project was graciously provided by Dr. Panos Antsaklis from Alexandra Maternity Hospital in Athens, a prominent testing center within the KANET network known for its extensive data resources.

The methodology employed in this study was systematic and adhered to rigorous scientific standards, involving four key stages: data preprocessing, data augmentation, development of Convolutional Neural Network (CNN) models, and interface development. The workflow of TRUEAID's development has been detailed in the work of Spahić et al. [19].

The next step is integrating the AI model with the ultrasound device. This requires developing software that allows the AI to process images in real-time or near real-time, designing an intuitive user interface, and ensuring compatibility with different ultrasound machines and PACS systems. Following integration, the system undergoes extensive testing and validation. This includes bench testing in a controlled environment and clinical trials to assess its effectiveness in real-world settings. Feedback from clinicians is crucial during this phase to refine the system further.

Regulatory approval is a critical milestone. Detailed documentation covering all aspects of the AI-DSS, including design, development, validation, and risk management, is prepared and submitted to relevant regulatory bodies. Ongoing compliance with standards, such as ISO 13485, is maintained. Once approved, the system is deployed in clinical settings. Comprehensive training is provided to clinicians and technicians to ensure they can use the new system effectively. A robust support system is also established to address any issues that arise.

Finally, the system's performance is continuously monitored, with regular updates and improvements made based on new data and user feedback. An ongoing feedback loop with users helps gather insights for further enhancements, ensuring the AI-DSS remains effective and reliable in supporting clinical decisions.

4. Trueaid Concept Validation and Integration

Upon development of the AI-based decission support system, its performance was evaluated in a two fold way in order to ensure its ability to be implemented in a realistic setting. The first validation pathway relied on conventional validation with a subset of 3D ultrasound images extracted from the initial dataset and intended for subsequent validation while the second pathway relies on a near real-time validation setup that allows for accurate simulation of decission making durring a diagnostic process.
Durring conventional validation the system has achieved an overall accuracy of 96% making it surpass the accuracy treshold set for AI-based decission support systems used in healthcare.

Table 1. Performance evaluation of TRUEAID

Class	Specificity	Sensitivity	Accuracy
Face	0.98	1.00	0.94
Hand to face	0.97	0.89	0.95
Legs	1.00	0.94	0.98
Thumb	0.98	0.93	0.97
Overall	0.98	0.94	0.96

The second validation pathway required development of a GUI for seamless interaction with the system. A GUI was developed and implemented as described in Spahic et al., Once developed and proven, TRUEAID can be used anywhere in the world, from low resource to high resource settings enabling better care of affected populations and supporting the fight against non-communicable neurological diseases.

The integration pathway is described through Figure 2.

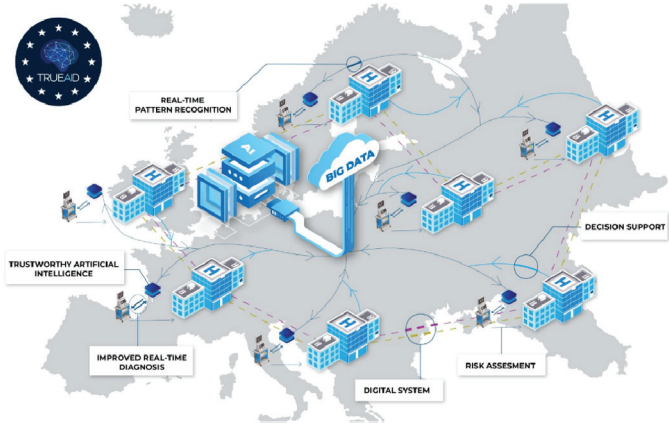


Figure 2. Implementation of TRUEAID throug integration in ultrasound devices

TRUEAID is envisioned as a cloud-based system that runs on high-performance computers located off-site from the testing premises. The reason for this is ensuring its availability everywhere from high to low computational-resource settings. As it can be infered from Fig. 2, TRUEAID will be integrated as a module of an ultrasound device that has the 4D ultrasound modality. Durring the conduction of a general pregnancy exam using a 4D ultrasound, the obstetritian will be able to run the module with a single click. This will result in initiation of a feedback loop with the cloud-based TRUAID where the 4D recording will be loaded frame by frame. Each time a characteristic fetal movement is detected, the physician will get a pop-up. The detected movements will be recorded, summed and fed into an if-else algorithm that will mimc the decission making process that trained KANET experts perform durring examination. In the end of the recording, the physician will be able to click on „results“ button where an entire record of recognized characteristic movements, their incidence and test-result interpretation will be displayed. Upon analyzing the record, the physician will give the overall result to the mother.

5. Conclusion

TRUEAID is envisioned as an AI-based platform for neurological impairment disease detection from fetal 4D ultrasound recordings. Initially, the prototype is planned to be tested in Ian Donald Schools of Medical Ultrasound in Bosnia and Herzegovina, Croatia, Slovenia, Czech Republic and Greece. TRUEAID will be integrated into the 4D ultrasound screening and KANET test, enabling the 4D recordings to be uploaded to the platform and AI-based evaluation to be performed. Advances beyond the state of the art are seen in the developed

predictive model that employs deep learning architectures for easier and faster decision making process in terms of neurological disease detection. The benefit of the integrated trustworthy AI-based system that will differentiate normal and abnormal neurological development of the fetuses, by constantly monitoring the intrauterine movements and predicting the risk of neurological impairment disorders in fetuses is in its objectiveness, compared to the subjective evaluation by doctors. This system will aid doctors in determining any pattern that could lead to potential neurological impairment in both, prenatal and postnatal neonatal period. The system will specially be beneficial for pregnant women, as they will have insight in the fetal diagnosis, resulting in the better treatment. With the reliable and ethical detection diagnosis of the neurological impairment diseases in the prenatal period, doctors would be able to investigate the proper treatment to potentially overcome the neurological impairment while the baby is still in utero the mother's belly.

TRUEAID solution can revolutionize the detection of neurological impairment enabling early possible and preliminary diagnosis during the antenatal period, allowing investigation of possible treatments in this phase as well.

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