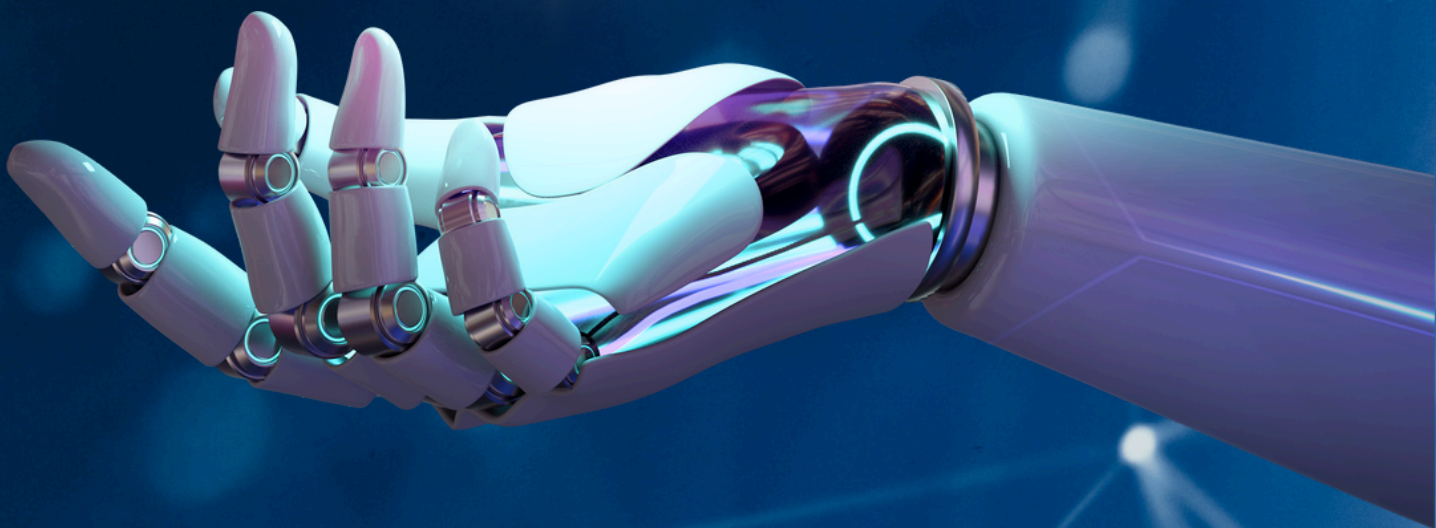


ISSN: 3023 - 8609

**VOLUME 2, ISSUE 1, JANUARY 2025**  
AN INTERDISCIPLINARY JOURNAL OF  
MEDICAL TECHNOLOGIES

# COMPUTERS AND ELECTRONICS IN MEDICINE



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**Computers and Electronics in Medicine**  
Volume: 2 – Issue No: 1 (January 2025)

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# Collaborative Care: Multi-Agent Systems in Healthcare

David Power <sup>\*</sup>,<sup>1</sup>

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**ABSTRACT** Everyday thousands of IoT devices are added to networks globally. Medical IoT (IoMT) is a subdomain, which has had much success over recent years and is expanding rapidly. However, interoperability is poor with IoMT devices, and even the sharing of basic patient data is generally poor between healthcare systems. There is considerable waste and unnecessary duplication of data across devices, which grows exponentially across healthcare systems. Multi-agent systems have the potential to reduce waste and expenditure while improving efficiency and personalizing patient care and may offer the potential to realize both organizational and patient care benefits.

## KEYWORDS

Healthcare  
Collaborative  
care  
IoT  
IoMT

## INTRODUCTION

The advent of the internet as we know it today began in 1991, changing the world almost immeasurably. In 1991, there were 1 million worldwide users of the internet, and today in 2023, this number has risen to over 5.16 billion users, with users steadily increasing daily. This figure is representative of 64.4% of global inhabitants who interact with the internet daily (Petrosyan 2023). All these users are generating massive amounts of data through their connected devices. By the year 2019, there were 8.6 billion internet-of-things (IoT) devices connected to the internet. By the end of this year, 2023, there is expected to be 15.14 billion, and by the year 2030, it is forecast that almost 30 billion IoT devices will be connected to the internet (Vailshery 2023). Every second, 127 new IoT devices are connected to the internet.

IoT devices are networked over the internet and allow monitoring and the exchange of data without human intervention. All these devices are generating massive amounts of data. Collecting and storing such volumes of heterogeneous data creates all kinds of challenges. One subtype of IoT is in the healthcare domain, often referred to as the Internet-of-Medical-Things (IoMT). IoMT devices connect and communicate with healthcare IT systems over the internet, or with other IoMT devices, either through IoT or Machine-to-Machine (M2M) technologies. M2M technology describes when two or more machines are connected together to capture and share data, with the ability to respond without human intervention. M2M is usually for monitoring and control purposes. IoT builds on and expands this idea, by connecting disparate wire-

less technologies to create a more fully connected environment that encompasses people, devices, and applications (Monteiro *et al.* 2023).

The IoMT is a massive growth market with a value of USD 41.17 billion in 2020, with a CAGR of 29.5%. Estimated growth by 2028 is USD 187.60 billion. Similar forces that are driving IoT are driving IoMT, such as lower costs of storage, memory, computing power, and sensors, in addition to massive amounts of data, hugely improved network speeds, and the availability of cloud computing resources. Furthermore, IoMT has the potential to drive down healthcare costs, improve patient monitoring, treatment, and services. It is estimated that 40% of all IoT devices will be health-related in the future (Sudarmani *et al.* 2022). However, most IoMT devices currently work as standalone devices or as part of a small network of connected similar devices. Interoperability is poor with IoMT devices, and even the sharing of basic patient data is generally poor between healthcare systems. Improving interoperability of devices and the sharing of health data allows for devices and health systems to improve patient monitoring and the delivery of healthcare services (Aledhari *et al.* 2022).

## BACKGROUND

It would seem that this environment would be ideal for the use of multi-agent systems. An agent can be described as a computer system capable of autonomous action to meet certain design objectives within its working environment (Wooldridge 2002). The agent may be a physical or virtual entity. The agent's environment may be accessible, that is one which the agent can use its sensors to detect the complete environment state. The environment may be deterministic, which means that the next state within the environment is completely determined by the current state and the agents current action. The environment may be episodic which is

Manuscript received: 23 October 2024,

Revised: 7 January 2025,

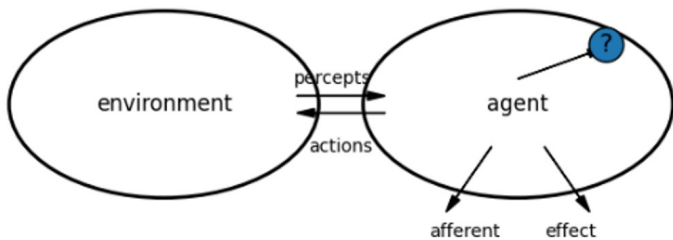
Accepted: 21 January 2025.

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to say that the environment is non-sequential and independent of other episodes. A dynamic environment describes one in which it changes while the agent is receiving inputs and/or performing actions (Fig. 1). A static environment does not change. A discrete environment refers to one which an agent can perform a finite number of actions, otherwise it is a continuous environment (Gupta et al. 2022).

The agent performs actions to solve goals, and these actions can be either discrete or continuous. Discrete actions are a limited response and number of actions to sensed information, while continuous refers to unconstrained actions. The purpose of the agent is to solve a task within its environment, therefore it must learn parameters and information about its environment. Using this knowledge and past experiences from previous actions the agent performance should improve at solving its task. Agents operate have autonomy of control over their own internal states and actions. Agents have the ability to sense changes and react to changes within their environment (Wooldridge 2002; Gupta et al. 2022). Agents display pro-active goal-directed behaviour. Agents have the ability to interact with other agents.

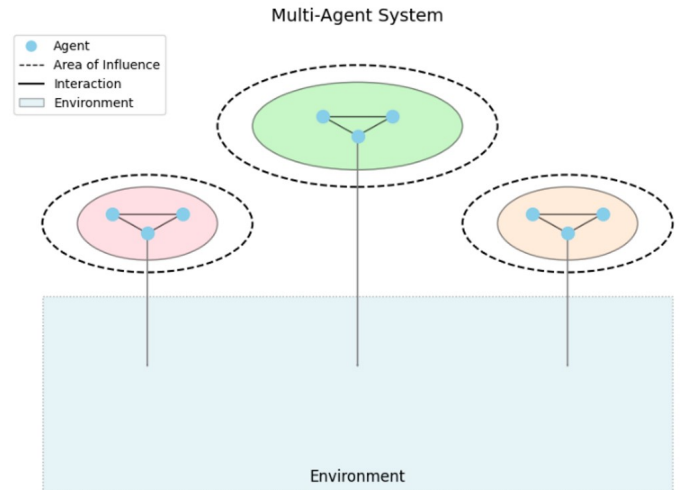
Agents may be simple reflex agents which make decisions based only on the current precept and react only on to predefined rules, or they may be model-based agents where actions are based on both the current and historical precepts. Goal-based agents use search and planning to achieve future goals and this directs its currents actions. Utility-based agents use performance metric such as a utility function to optimise its actions, calculating different paths and performance metrics to reach its goal. Learning agents can be any of the above types of agent that interacts with its environment and learns from its experience, adapts its behaviour and improves its performance (Goonatilleke and Hettige 2022). Multi-agent systems can be referred to as multiple interacting intelligent agents which can communicate with each other and their environment, and work towards solving a common goal. These systems interact by sharing data and information and must coordinate, collaborate, cooperate, negotiate and conflict resolution between agents to successfully meet their design objectives (Gupta et al. 2022).



**Figure 1** Agent interacting with environment

Multi-agent systems differ significantly from non-agent systems in their structure, behaviour, and capabilities. Multi-agent systems operate in a decentralized environment where each agent independently makes decisions based on its local knowledge and design goals. This decentralized nature allows for greater flexibility and adaptability as agents can respond dynamically to changes within their environment. By contrast, non-agent systems rely on centralized decision-making and control, making them less responsive to dynamic and unpredictable conditions. One of the defining features of multi-agent systems is their emergent behaviour, which arises from complex interactions between agents and their environment. Unlike non-agent systems, where behaviours are explicitly programmed, multi-agent systems exhibit behaviours that are not

directly coded but emerge as a result of these interactions. While this emergent behaviour can lead to unpredictability and challenges in system control and verification, it also opens opportunities for novel and unexpected outcomes that can prove beneficial. For instance, emergent behaviours enable multi-agent systems to discover innovative solutions to problems, enhancing system efficiency and adaptability in dynamic and uncertain scenarios.



**Figure 2** Multi-agent system interacting with environment

Agents within multi-agent systems demonstrate adaptability by learning from their experiences and evolving with changing conditions, leading to improved individual and collective performance over time. This capacity for adaptation distinguishes multi-agent systems from non-agent systems, which can only react within the constraints of their pre-programmed rules. Furthermore, multi-agent systems tend to be more robust and fault tolerant. In the event of an agent's failure, the system can continue to function as the overall behaviour emerges from the interactions of other agents rather than depending on a single component. In contrast, non-agent systems are more vulnerable to single points of failure, where the breakdown of a device or module may result in system-wide collapse. Scalability is another advantage of multi-agent systems.

Adding more agents allows the system to scale and handle larger, more complex tasks without requiring significant architectural changes. Non-agent systems, on the other hand, often require extensive redesign to accommodate greater complexity or workload. These advantages make multi-agent systems particularly well-suited for dynamic and decentralized applications such as swarm robotics, traffic management, and disaster response, and indeed the complex, dynamic and distributed environment of healthcare. However, fully realizing the potential of multi-agent systems requires addressing the inherent challenges of emergent behaviour, including unpredictability, coordination bottlenecks, and the computational complexity of validation and control. Ongoing research into advanced tools for modelling and controlling emergent behaviour, as well as interdisciplinary approaches, will be of the utmost importance for the continued development of multi-agent systems, especially in safety critical domains such as healthcare (Wooldridge 2002; Gupta et al. 2022; Goonatilleke and Hettige 2022).

## DISCUSSION

Potentially multi-agent systems can solve more complex problems because multiple agents can divide the workload and work together to break the problem down and then solve different parts of the problem (Table 1). Multi-agent systems may be more flexible, adaptable, and resilient than non-agent systems, but they may also be more complex and difficult to design and manage. There is also a significant communication overhead and complexity to consider as each agent must interact and communicate with each other and the environment, which may affect the performance of the overall system. There is also the potential for conflicts to arise between agents if interpretations of a problem vary or there is conflicting goals, leading to system problems (Wooldridge 2002; Gupta *et al.* 2022; Goonatilleke and Hettige 2022).

Healthcare may benefit from a multi-agent system approach to the distribution of complex learning and decision-making problems. Within this system each agent contributes with its own knowledge and capabilities, sharing information, contributing to the decision-making process and coordinating behaviour with other agents towards an overall goal, within the multi-agent system. These agents may consist of a combination of software agents and hardware agents from patient monitoring devices, electronic patient records, and therapy devices working together for shared goals. A multi-agent approach to remote monitoring and intervention of the elderly is proposed by researchers utilising 5G technology and collaborative approaches. The system measured several vital signs and diabetic markers and alerted both patients and healthcare providers with alarms and when to take necessary interventions, with initial results outperforming existing mHealth technology (Humayun *et al.* 2022). Such multi-agent systems have been demonstrated to be highly accurate such as the activity-aware vital signs patient monitoring system proposed by researchers which demonstrated adaptability across various monitoring signals via disparate sensors in response to adapting physical activities ensuring accurate health assessments and timely alerts to patients and healthcare providers (Ivascu and Negru 2021). This distributed approach can improve the overall performance, especially when used in conjunction with machine learning approaches to enable the agents to learn from experiences and adapt to their environments more efficiently. Reinforcement learning can provide the agents with feedback based on the outcomes of their actions, therefore leading to improved performance and decision-making over time (Lim *et al.* 2022; Hassanien *et al.* 2021).

Multi-agent systems have demonstrated effectiveness managing complex manufacturing tasks in industrial applications with enhanced flexibility, robustness and reconfigurability in manufacturing processes (Pereira *et al.* 2012). In supply chain management multi-agent systems have been used to improve decision-making and coordination of complex logistics and supply chains (Lee and Kim 2007). Multi-agent systems are employed successfully to coordinate multiple robots for tasks such as assembly and material handling (Luo and Xue 2010).

The industrial application of multi-agent systems to manage complex, dynamic and distributed systems, makes for a compelling case for their adoption in healthcare to improve patient monitoring, resource management, and decision support systems. Multi-agent systems are well-known for their use in improving information retrieval systems (Luo and Xue 2010). Their use in improving search results for medical purposes and improving security is a recent application of multi-agent systems in healthcare (Evtimova-Gardair 2019). Multi-agent systems have also been applied to improving the performance of medical chat-bots and

medical decision support tools (Kumar 2022; Frikha *et al.* 2023).

The idea is that machines can either make better decisions in some situations than humans or can assist humans in making better decisions (Luo and Xue 2010). Multi-agent systems have also been proposed for use in healthcare wireless sensor networks. Wireless sensor networks are a large collection of homogenous nodes which work together within a cooperative network. Each node can sense, process and communicate data (Sreedevi *et al.* 2022). Another area of proposed use of multi-agent systems within healthcare is with body area sensor networks, which are IoT devices which collect, process and analyse data on or, from within the human body. These agents are typically heterogeneous. Typically, these IoT devices do not share information or interact in a cooperative manner (Gupta *et al.* 2022; Humayun *et al.* 2022; Lim *et al.* 2022).

A key driver to the huge investment in IoMT is concerns regarding a worldwide aging population. Chronic diseases will inflate healthcare expenses as those over 65 will number 1.5 billion by the year 2050 (Lim *et al.* 2022). Furthermore, there is significant shift in focus from treating disease to prevention-orientated healthcare, where health-surveillance via IoMT can play a key role (Shakahuki and Reid 2015). There have been some notable successes in IoMT with monitoring electrocardiogram (ECG), where the ECG is monitored, stored and notifications sent to healthcare workers using sensors and fog computing (Ivascu and Negru 2021). Alzheimer's disease is a chronic disease that deteriorates memory and judgement, sensors have been successfully embedded in clothing to track and monitor patient's behaviour and movements. Fall detection using a camera, fall sensor and Amazon Echo device has been successfully reported for aged adults (Ivascu and Negru 2021; Shakahuki and Reid 2015).

Medication monitoring can track the distribution and dosing of medication, and medicine boxes linked by IoMT will be able to monitor specific patient patterns and compliance. There is even research ongoing into using IoMT sensors for biomedical tracing of secretions from potential cancers given a patient's risk factors. There has been the development of a washable T-shirt with multiple IoMT sensors, such as ECG, temperature, respiratory rate and patient activity classification and monitoring (Gupta *et al.* 2022; Goonatilleke and Hettige 2022; Ivascu and Negru 2021; Shakahuki and Reid 2015; Humayun *et al.* 2022). Other successful applications have been described measuring glucose levels, oxygen saturation, blood pressure (Aledhari *et al.* 2022). During the Covid-19 pandemic IoMT came to the fore, with connected diagnostics such as blood gas analyzers and biological services, imaging such as CT, MRI and X-ray, smart instruments, smart patient beds and smart facilities (Somani *et al.* 2022).

Multi-agent systems are a group of autonomous agents that cooperate with each other, share information, reason together and coordinate their activities, collectively solving problems that would be impossible to solve alone (Aledhari *et al.* 2022). The environment of monitoring patients remotely would seem to benefit greatly from a multi-agent system approach, which differs from the current situation where devices collect and send information, but rarely work collectively or take action. Sharing information and working towards common goals while using historic data to gather patient patterns and real-time data between intelligent nodes could reduce healthcare workload by monitoring patients closely and increase patient safety by sending alerts in emergencies (Alshamrani 2022). Likewise, using a multi-agent systems approach to in-patients has several benefits also, and builds on the idea of the smart hospital.

■ **Table 1 Comparison of multi-agent systems and centralized control systems**

Aspect	Multi-Agent Systems	Centralized Control Systems
Flexibility	High flexibility due to decentralized decision-making and adaptability.	Low flexibility as decisions are made centrally and require reprogramming.
Scalability	Easily scalable by adding more agents.	Difficult to scale as system architecture needs significant redesign.
Fault Tolerance	High fault tolerance; failure of one agent doesn't affect the entire system.	Low fault tolerance; single point of failure can disrupt the entire system.
Emergent Behaviour	Exhibits emergent, unpredictable behaviour, which can lead to novel solutions.	No emergent behaviour; all outcomes are predefined and deterministic.
Complexity of Control	Complex to predict and control due to decentralized interactions.	Easier to control and predict due to centralized decision-making.
Resource Utilization	Efficient utilization by distributing tasks among agents.	Less efficient resource utilization as tasks are centrally allocated.
Communication Overhead	High communication overhead for coordination between agents.	Minimal communication overhead due to centralized control.
Adaptability	Learns and adapts to changing environments dynamically.	Limited adaptability; only reacts to predefined conditions.
Development Complexity	More complex to design, implement, and debug.	Easier to design, implement, and debug due to simpler architecture.
Cost	Potentially higher initial development and deployment costs.	Lower initial cost but higher cost to scale and adapt.

The concept of the smart hospital can find its origins from Korea in the early 2000's with the notion of the digital hospital. At the time Korea pioneered digitalisation of hospital workflow with the concept of the 4-lesses, which is filmless, chartless, slipless and paperless operations with the introduction of complete electronic medical record system. By the end of that decade radiofrequency identification systems were widespread throughout the USA, Korea and Japan, allowing the real-time tracking and tracing of patients, medicines, equipment and other assets around the health system. More recently the introduction of 5G and Wi-Fi 6, have overcome network bottlenecks, and introduction of IoMT devices to the network working with AI and intelligent building technologies have the potential to drive efficiencies up and cost down in the era of the smart hospital (Kwon *et al.* 2022).

## CONCLUSION

As mentioned earlier in most instances IoMT devices have poor interoperability, this would lead to unnecessary duplication of data, and significant waste in processing, transfer and storage of data. Also, a significant concern with IoMT devices is minimising power consumption (Sharma and Tripathi 2022). By introducing a multi-agent systems approach to the smart hospital concept may help alleviate some of these issues as each IoMT device will

work as a node within the larger multi-agent system, sharing data, responding to changing stimuli in the environment, updating and sharing this information with other nodes, reasoning together and making decisions together to reduce duplicate data, improve efficiencies and performance of the overall system. Most likely, for a system like this to preform efficiently it will have to learn through reinforcement learning (Ivascu and Negru 2021).

Reinforcement learning is where agents learn through trial and error and receive feedback in the form of rewards or punishments. Reinforcement learning has been successfully used to personalise patient treatment plans, optimise healthcare facility operations and allocate healthcare resources. However, reinforcement learning is not without challenges especially in the healthcare setting where there are more stringent ethical and regulatory concerns to protect patients from harm. These models can be complex and difficult to interpret. Therefore, significant simulations would first have to be developed before such systems could ever be used in real-world (Gupta *et al.* 2022; Goonatileke and Hettige 2022; Ivascu and Negru 2021). The future is likely to be one where the smart hospital is common-place, multi-agent systems and reinforcement learning have the potential if used appropriately and safely to bring increased efficiencies to healthcare systems, and reduce expenditure while optimising patient care and personalising healthcare.

## Availability of data and material

Not applicable.

## Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

## Ethical standard

The author has no relevant financial or non-financial interests to disclose.

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**How to cite this article:** Power, D. Collaborative Care: Multi-Agent Systems in Healthcare. *Computers and Electronics in Medicine*, 2(1), 1-5, 2025.

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# Bibliometric Analysis of Publications on Clinical Studies Leveraging Natural Language Processing During 2000 - 2023

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**ABSTRACT** The number of clinical studies using natural language processing is quite large. Therefore, it is important to examine in depth the development of clinical studies using Natural Language Processing over the years. However, there are a limited number of studies in the literature examining the research status of this field. The article presents a bibliometric analysis of studies on the keywords "clinical AND studies AND natural AND language AND processing" indexed in Scopus between 2000 and 2023. This study aims to evaluate academic outputs in the relevant field quantitatively, make sense of the data, reveal the state of scientific knowledge in the field, and give scientists a general perspective on the subject. Bibliometrix and Microsoft Excel programs were used for bibliometric analysis. Nineteen thousand two hundred seventy-three different authors identified a total of 4535 studies. 77.5% of these studies were research articles (3516), 14.8% were conference papers (669), 6.8% were reviews (307), and 0.9% were book chapters (43). Journal of Biomedical Informatics was the journal in which the most studies were published, with 226 articles. Only the United States (2637) contributed 58.1% to the studies. Liu, H. was the most prolific author, with 85 articles. Harvard Medical School was the most productive institution, with 304 studies. The most cited article was Discontinuation of Statins in Routine Care Settings, A cohort study.

## KEYWORDS

Clinical studies  
Natural language processing  
Bibliometric analysis  
Citation analysis  
Network analysis

## INTRODUCTION

Natural Language Processing (NLP) is a branch of artificial intelligence and linguistics that enables computers to understand expressions or words written in human languages (Khurana *et al.* 2023). In the 1950s, NLP initially focused on rule-based methods to enable computers to understand natural language. However, these insufficient methods have transformed over time with the developments in machine learning methods (Nadkarni *et al.* 2011). NLP studies have recently been included in various fields, such as machine translation, e-mail spam detection, information extraction, summarization, and medical question-answering (Khurana *et al.* 2023).

Most clinical information sources contain significant amounts of information. But most of this information comes in unstructured form (Meystre and Haug 2005). NLP is extremely important in transforming unstructured information into structured information, improving healthcare, and advancing medicine (Wang *et al.* 2017). NLP has applications in medical information processing and rich research achievements (Chen *et al.* 2018). NLP medical applications include numerous research topics, such as its use for mental health (Le Glaz *et al.* 2021; Corcoran and Cecchi 2020), extraction of structured information from radiology reports (Casey *et al.* 2021), coding clinical notes (Tavabi *et al.* 2022), and monitoring Alzheimer's disease (Garcia *et al.* 2020).

NLP has significant potential in clinical trials. This technology is expected to help increase the efficiency and effectiveness of medical research. NLP-supported medical research is rapidly increasing and becoming more attractive. However, there are a limited number of studies examining the research status of clinical studies on NLP. Therefore, it is essential to conduct an in-depth

**Manuscript received:** 13 December 2024,

**Revised:** 24 January 2025,

**Accepted:** 24 January 2025.

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analysis to understand the latest developments in this field. This study aims to examine the academic output of NLP in clinical studies.

Bibliometric analysis is a field of research that deals with numerical analysis of scientific literature, used to search and analyze comprehensive scientific data. This analysis may include research publication frequency, citations, authors, and topics. The state of the art in a field of current scientific knowledge can be mapped using bibliometrics. Bibliometrics is an important tool for analyzing the output of scientists, collaborations between universities, the effects of science funding on research and development performance, and educational productivity. Therefore, theoretical and practical tools are needed to measure experimental data. Bibliometric analysis has increased in popularity in recent years as the availability and accessibility of software such as Gephi, Leximancer, VOSviewer, and Bibliometrix and scientific databases such as Scopus and Web of Science have increased. Bibliometric analysis can measure research outputs, identify trends, and evaluate research performance (Akmese 2022; Falagas et al. 2006; Moral-Muñoz et al. 2020; Sengupta 1992; Donthu et al. 2021).

Bibliometric methods are now considered scientific expertise and have become integral to research evaluation methodology, especially in scientific and applied fields (Ellegaard and Wallin 2015). Bibliometric methods are often used to process data (Wallin 2005). These methods have greatly benefited from computerized data processing. Accordingly, there has been a great increase in the number of publications in this field in recent years. Increasing data volume and more widespread use of computers were effective in this increase (Ellegaard and Wallin 2015).

This study covers top journals, institutions, keyword features in the field, citation network analysis, and review of top articles, and offers the potential to illustrate historical and geographic trends. This study aims to make sense of the large number of data obtained, to quantitatively evaluate the academic outputs of relevant research, to provide scientists in this field with a general perspective on the subject, and to reveal the state of scientific knowledge.

This study can make various contributions to the field of research in question. It can provide domain experts with a comprehensive overview of the research topic. It can help better understand research outcomes. In addition, it can provide researchers with the most important information about potential authors, institutions, journals, and countries. It can help identify research trends or track the popularity and importance of topics. Moreover, it can increase researchers' awareness when deciding on topic selection. It can also help improve the quality and efficiency of research. Finally, it can explain how the topic has developed over time.

## MATERIAL AND METHODS

The Scopus database was preferred to collect bibliometric information. All journals in the Scopus database are reviewed annually to maintain high-quality standards (Kokol et al. 2021). It has been determined that Scopus offers its users a more comprehensive journal profile than other databases and provides faster results from more articles in citation analysis.

All publications indexed in Scopus (access date: 18.12.2023) between 2000 and 2023 regarding clinical studies using natural language processing were analyzed using bibliometric methods. "clinical AND studies AND natural AND language AND processing" were used as search keywords. Documents were searched by article title, abstract, and keywords. Scopus codes used in the search are as follows: TITLE-ABS-KEY ( clinical AND studies AND natural AND language AND processing ) AND PUBYEAR > 1999

AND PUBYEAR < 2024 AND ( LIMIT-TO ( DOCTYPE , "ar" ) OR LIMIT-TO ( DOCTYPE , "cp" ) OR LIMIT-TO ( DOCTYPE , "re" ) OR LIMIT-TO ( DOCTYPE , "ch" ) )

This search method found all articles published between 2000 and 2023 in the studies' title, abstract, and keywords in the Scopus database. The number of studies may increase when 2023 is completed. Microsoft Excel and Bibliometrix (Aria and Cuccurullo 2017) were used for bibliometric network visualizations.

## ANALYSIS

### Literature Distribution

Four thousand five hundred thirty-five publications of different genres from 2000 to 2023 were evaluated. These publication types are articles (3516, 77.5%), conference proceedings (669, 14.8%), reviews (307, 6.8%), and book chapters (43, 0.9%).

As seen in Figure 1, clinical studies using Natural Language Processing, "Medicine" (3534, 45%), "Computer Science" (1113, 14%), "Health Professions" (584, 7%), "Engineering" (536, 7%), "Biochemistry, Genetics and Molecular Biology" (435, 6%), "Neuroscience" (275, 3%) and "Others" (1431, 18%). The total number of studies is more than 4535 because a study can be matched in more than one category.

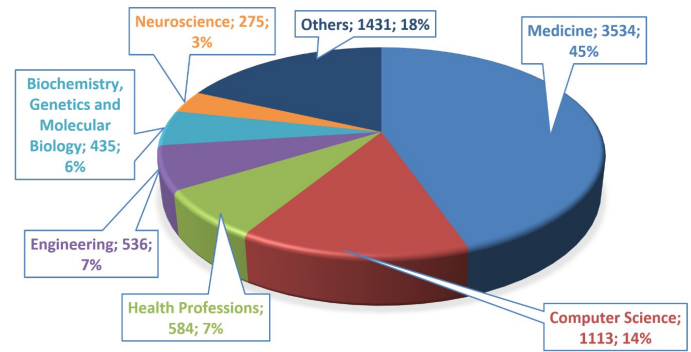


Figure 1 The distribution of subject areas

### Development of Publications

The annual production graph of scientific studies of 4535 studies is shown in Figure 2. Despite some fluctuations, there has been an increase in the number of scientific studies in general. It is seen that the number of studies decreased in 2016. In the following years, the number of publications tends to increase continuously.

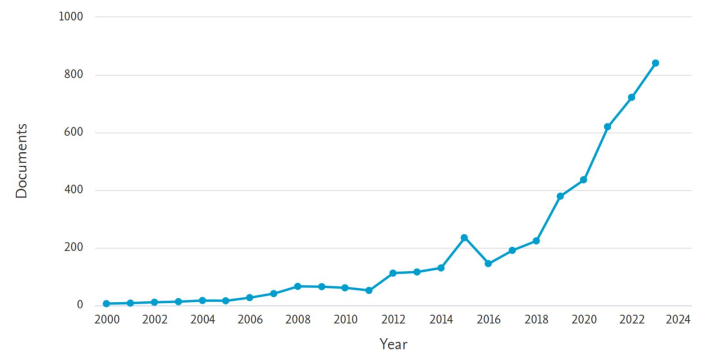


Figure 2 Document by year

### Active Authors

Nineteen thousand two hundred seventy-three authors produced a total of 4535 works. The top five producing authors are Liu H. (85, 1.9%), Xu H. (74, 1.6%), Denny J.C. (47, 1%), Stewart R. (44, 1%), and Wu Y. (41, 0.9%). These authors were important research pioneers in their respective fields. Figure 3 shows the top 15 authors with the highest number of studies.

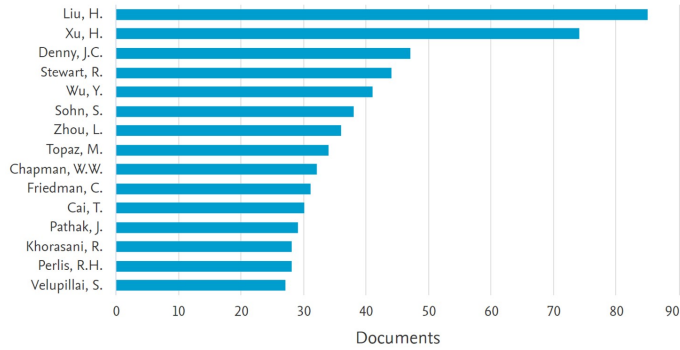


Figure 3 Top 15 authors with the highest number of studies

The collaboration network of the top 50 authors is shown in Figure 4. The size of the circles is directly proportional to the number of studies and collaboration between authors. Colors represent different clusters. The thickness of the lines expresses the strength of the collaboration between writers.

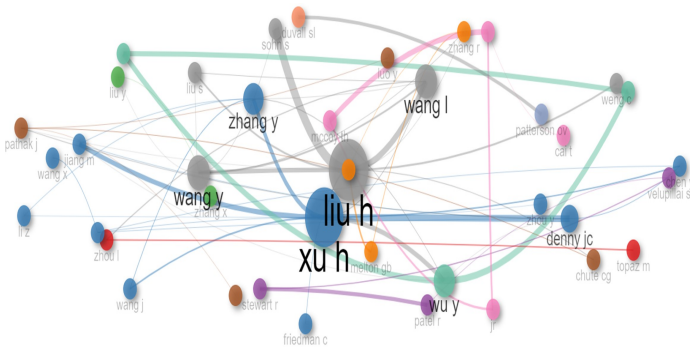


Figure 4 Authors Collaboration Network

### Active Affiliation

The top 5 institutions that contributed the most to the literature were Harvard Medical School (304, 6.7%), Brigham and Women’s Hospital (196, 4.3%), Massachusetts General Hospital (173, 3.8%), Mayo Clinic (169, 3.7%) and The University of Utah (137, 3%). Figure 5 shows the top 15 institutions that contributed the most according to the number of studies published by the institutions in the 2000-2023 period.

The collaboration network of the top 50 institutions is seen in Figure 6. The size of the circles is directly proportional to the number of studies and cooperation between institutions. Different colors represent clusters. The thickness of the lines expresses the strength of cooperation between institutions.

### Active Journals

Table 1 shows the top 25 journals with the highest *h\_index*. A total of 4535 studies were published in 1335 sources. 18.9% of the

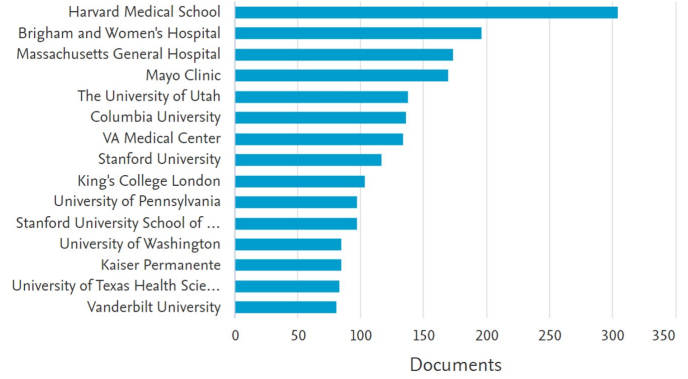


Figure 5 The top 15 organizations that contribute the most, according to the number of studies

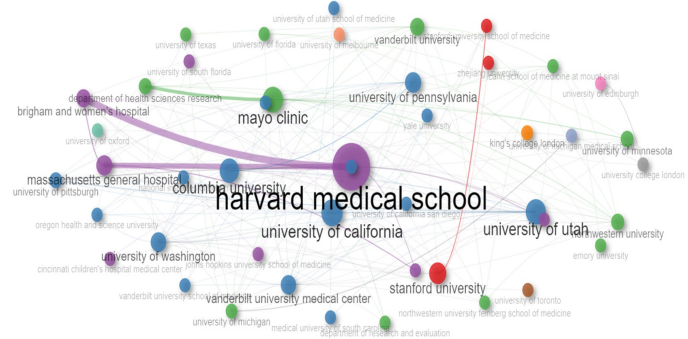


Figure 6 Institutions collaboration network

studies consist of the first five sources, and 38.5% comprise the 25 sources in Table 1.

Figure 7 shows the increase in the number of publications of the top five journals according to their number of publications between 2000 and 2023. According to the chart, the Journal of Biomedical Informatics, Journal of the American Medical Informatics Association, Studies In Health Technology and Informatics, Journal of Medical Internet Research, and Jmir Medical Informatics sources are the most productive.

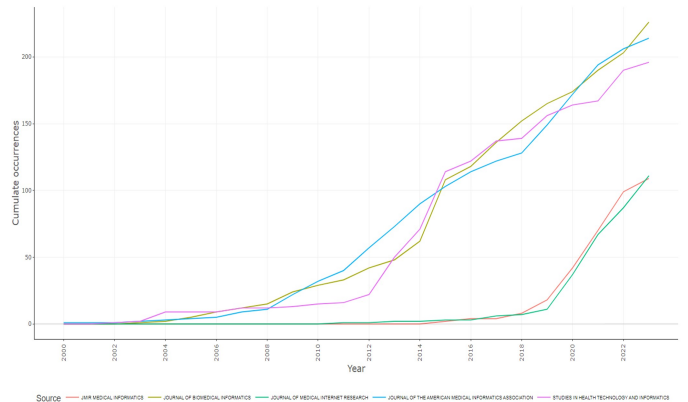


Figure 7 Top 5 journals with the highest number of articles

■ **Table 1 Top 25 journals with h-index**

No	Journal	h-index	g-index	m-index	TC	NP	PY_start
1	JOURNAL OF THE AMERICAN MEDICAL INFORMATICS ASSOCIATION	53	90	2.208	9816	214	2000
2	JOURNAL OF BIOMEDICAL INFORMATICS	50	80	2.381	8374	226	2003
3	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	34	56	2.125	3228	65	2008
4	INTERNATIONAL JOURNAL OF MEDICAL INFORMATICS	27	44	1.286	2279	97	2003
5	BMC MEDICAL INFORMATICS AND DECISION MAKING	26	43	1.3	2241	94	2004
6	AMIA ... ANNUAL SYMPOSIUM PROCEEDINGS / AMIA SYMPOSIUM	26	39	1.368	1889	90	2005
7	PLOS ONE	25	37	1.786	1668	94	2010
8	JOURNAL OF MEDICAL INTERNET RESEARCH	23	38	1.769	1785	111	2011
9	JMIR MEDICAL INFORMATICS	19	33	2.111	1383	109	2015
10	STUDIES IN HEALTH TECHNOLOGY AND INFORMATICS	16	29	0.727	1353	196	2002
11	RADIOLOGY	15	16	0.682	1656	16	2002
12	BMJ OPEN	13	32	1.444	1053	49	2015
13	AMIA ... ANNUAL SYMPOSIUM PROCEEDINGS. AMIA SYMPOSIUM	13	24	0.929	644	45	2010
14	ARTIFICIAL INTELLIGENCE IN MEDICINE	13	22	0.619	511	41	2003
15	JOURNAL OF THE AMERICAN COLLEGE OF RADIOLOGY	13	20	0.813	438	28	2008
16	JCO CLINICAL CANCER INFORMATICS	12	18	1.714	386	41	2017
17	METHODS OF INFORMATION IN MEDICINE	12	17	0.667	326	31	2006
18	COMPUTERS IN BIOLOGY AND MEDICINE	12	24	0.632	628	30	2005
19	COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE	11	14	0.733	221	18	2009
20	BMC BIOINFORMATICS	11	17	0.647	490	17	2007
21	JAMA NETWORK OPEN	10	18	1.667	371	32	2018
22	NPJ DIGITAL MEDICINE	10	19	1.667	454	19	2018
23	JAMIA OPEN	9	14	1.5	253	34	2018
24	APPLIED CLINICAL INFORMATICS	9	14	0.643	241	26	2010
25	IEEE JOURNAL OF BIOMEDICAL AND HEALTH INFORMATICS	9	18	1	324	21	2015

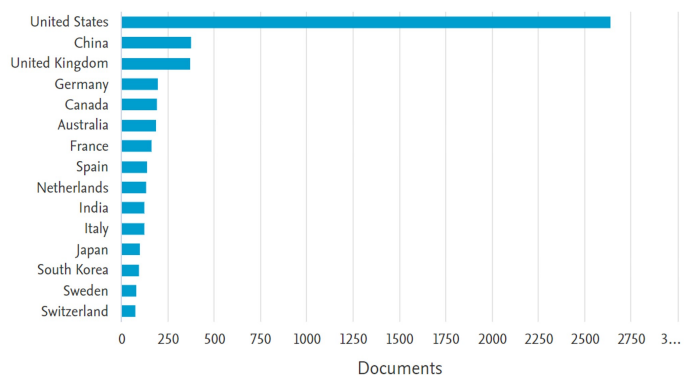
TC: Total Citation, NP: Number of Publication, PY\_start: Start of Publication Year

### Active Countries

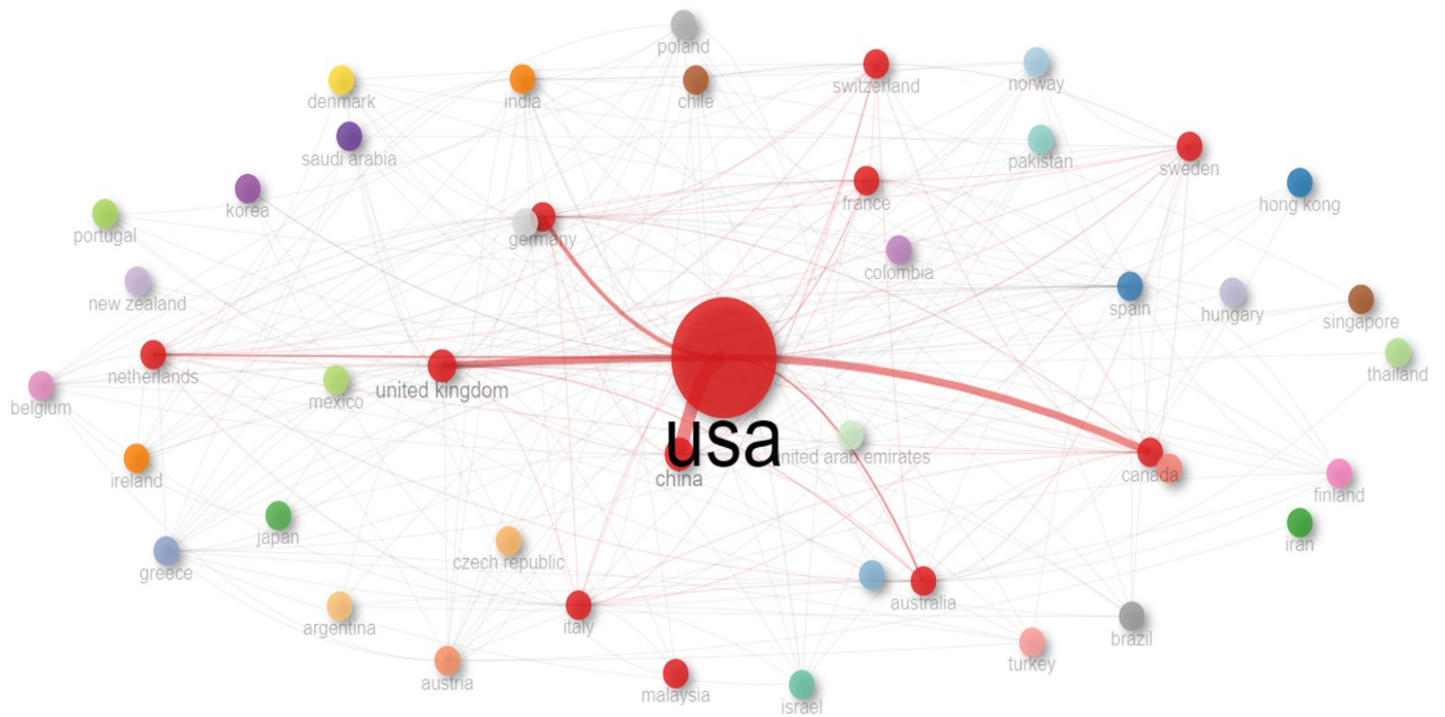
Analysis showed that the articles covered 95 countries or territories. The publication numbers of the first 15 countries are shown in Figure 8. The United States ranked first with 2637 (58.4%) studies, considering the number of publications. China ranked second with 374 (8.3%) studies. The United Kingdom ranked third with 366 (8.1%) studies. Germany ranked 4th with 194 (4.3%), and Canada ranked 5th with 191 (4.2%).

The network visualization map for countries' international cooperation can be seen in Figure 9. The size of the circles is directly proportional to the number of studies and cooperation between countries. Colors represent different clusters. The thickness of the lines expresses the strength of cooperation between countries.

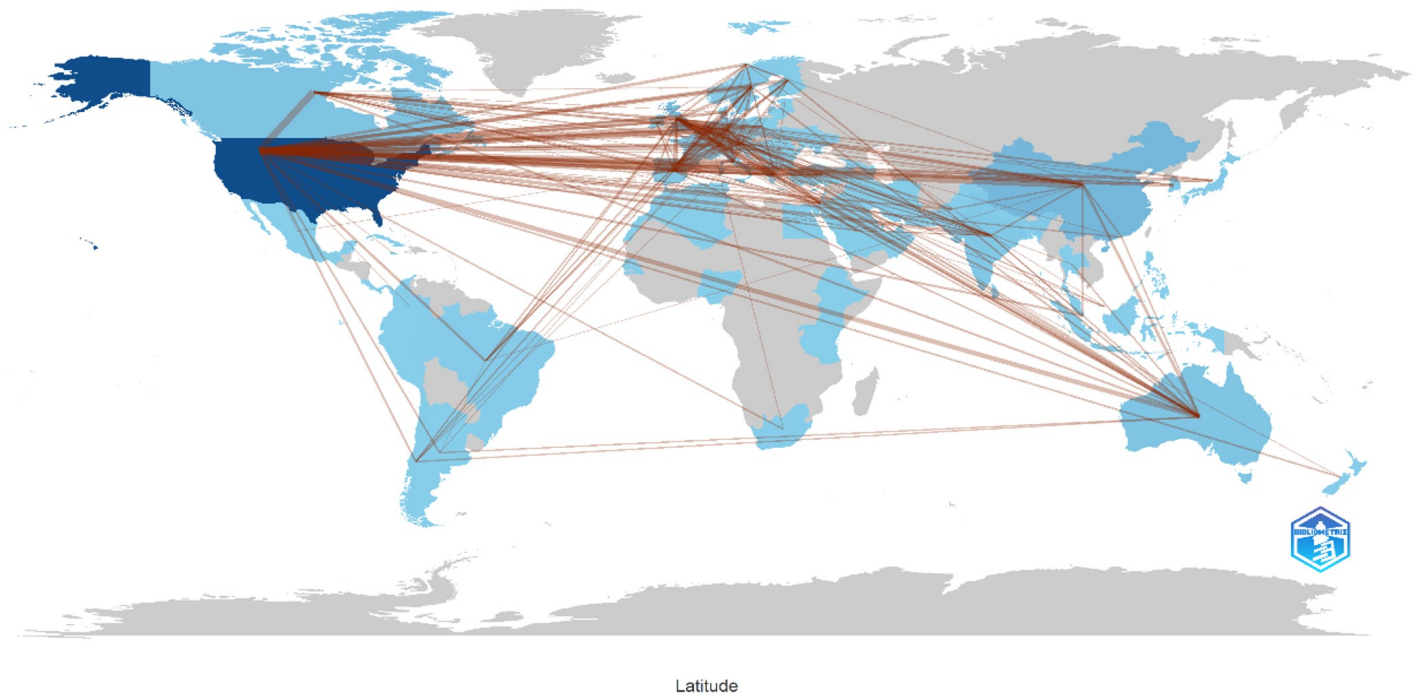
The geographical distribution of country collaboration for the overall study period is shown in Figure 10.



**Figure 8** Bar chart showing the 15 most productive countries in the world



**Figure 9** Network visualization map of countries' international cooperation



**Figure 10** Country collaboration map

### Citations

Citation status by publications is shown in Table 2. Figure 11 shows the co-citation network of the top 50 authors. As the size of the circle increases, the number of citations also increases. Colors represent different clusters. The thickness of the lines expresses the strength of the citation collaboration between authors.

### Keyword Analysis

The 50 most used keywords in 4535 articles were visualized. The network visualization map of trend keywords obtained according to the topicality of publications is shown in Figure 12. As the size of the circle increases, the number of keyword uses also increases. The thickness of the lines expresses the strength of the connection

■ **Table 2 Top 25 Papers by Total Citations (TC)**

No	Paper	DOI	Total Citations	TC per Year	Normalized TC
1	ZHANG H, 2013, ANN INTERN MED	10.7326/0003-4819-158-7-201304020-00004	461	41.91	14.99
2	WANG Y, 2018, J BIOMED INFORMATICS-a	10.1016/j.jbi.2017.11.011	405	67.50	13.03
3	GOULD MK, 2015, AM J RESPIR CRIT CARE MED	10.1164/rccm.201505-0990OC	382	42.44	11.08
4	MILLER DD, 2018, AM J MED	10.1016/j.amjmed.2017.10.035	382	63.67	12.29
5	BEDI G, 2015, NPJ SCHIZOPHR	10.1038/npjschz.2015.30	380	42.22	11.02
6	LIANG H, 2019, NAT MED	10.1038/s41591-018-0335-9	349	69.80	13.51
7	MURFF HJ, 2011, J AM MED ASSOC	10.1001/jama.2011.1204	349	26.85	7.02
8	FRIEDMAN C, 2004, J AM MED INFORMATICS ASSOC	10.1197/jamia.M1552	343	17.15	7.25
9	BATES DW, 2003, J AM MED INFORMATICS ASSOC	10.1197/jamia.M1074	338	16.10	3.77
10	PONS E, 2016, RADIOLOGY	10.1148/radiol.16142770	337	42.13	9.61
11	PERERA G, 2016, BMJ OPEN	10.1136/bmjopen-2015-008721	323	40.38	9.21
12	SHIVADE C, 2014, J AM MED INFORMATICS ASSOC	10.1136/amiajnl-2013-001935	304	30.40	9.67
13	MEHTA N, 2018, INT J MED INFORMATICS	10.1016/j.ijmedinf.2018.03.013	284	47.33	9.13
14	HANAUER DA, 2015, J BIOMED INFORMATICS	10.1016/j.jbi.2015.05.003	282	31.33	8.18
15	CALVERT GA, 2003, J COGN NEUROSCI	10.1162/089892903321107828	280	13.33	3.12
16	SARKER A, 2015, J BIOMED INFORMATICS	10.1016/j.jbi.2014.11.002	273	30.33	7.92
17	TING DSW, 2019, PROG RETINAL EYE RES	10.1016/j.preteyeres.2019.04.003	273	54.60	10.57
18	TANG C, 2014, INT J RADIAT ONCOL BIOL PHYS	10.1016/j.ijrobp.2014.04.025	270	27.00	8.59
19	TITANO JJ, 2018, NAT MED	10.1038/s41591-018-0147-y	268	44.67	8.62
20	BOSELER A, 2003, J AUTISM DEV DISORD	10.1023/B:JADD.0000006002.82367.4f	263	12.52	2.93
21	KISSLER J, 2006, PROG BRAIN RES	10.1016/S0079-6123(06)56008-X	260	14.44	4.62
22	NEAMATULLAH I, 2008, BMC MED INFORMATICS DECIS MAK	10.1186/1472-6947-8-32	258	16.13	7.23
23	RITCHIE MD, 2010, AM J HUM GENET	10.1016/j.ajhg.2010.03.003	250	17.86	5.02
24	HARKEMA H, 2009, J BIOMED INFORMATICS	10.1016/j.jbi.2009.05.002	247	16.47	5.34
25	KHO AN, 2011, SCI TRANSL MED	10.1126/scitranslmed.3001807	242	18.62	4.87



and (Bedi *et al.* 2015), *npj Schizophrenia* journal "Automated analysis of free speech predicts psychosis onset in high-risk youths", respectively.

The articles' first five most frequently used keywords were *Natural Language Processing, Human, Article, Humans, and Female*. Limitations of the study: Although the Scopus database is advantageous compared to other databases regarding the number of publications, not all could be included. Additionally, since 2023 has not been completed, there may be a slight deficiency in the number of publications.

## CONCLUSION

This study provides a holistic review of studies on clinical trials using Natural Language Processing between 2000-2023. According to the findings, it was observed that there was a decrease in the annual number of studies produced in 2016 and an increase in the following years. It was seen that the author with the most publications on the subject was Liu H., most articles were published in the JOURNAL OF BIOMEDICAL INFORMATICS, and the institution that contributed the most to the literature was Harvard Medical School. The most cited article (Zhang *et al.* 2013) was published in the Annals of Internal Medicine titled "Discontinuation of statins in routine care settings: a cohort study". The most productive countries in terms of the number of publications are developed or overpopulated countries. Participation of researchers in developing or underdeveloped countries in multinational studies may allow them to conduct further research on this subject.

### Availability of data and material

Not applicable.

### Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

### Ethical standard

The authors have no relevant financial or non-financial interests to disclose.

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**How to cite this article:** Akmeşe, Ö. F., and Bağcı, B. Bibliometric Analysis of Publications on Clinical Studies Leveraging Natural Language Processing During 2000 - 2023. *Computers and Electronics in Medicine*, 2(1), 6-14, 2025.

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# Investigation of the Effect of Alloying Elements on the Density of Titanium-Based Biomedical Materials Using Explainable Artificial Intelligence

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**ABSTRACT** Titanium alloys are widely preferred in the healthcare sector as biocompatible materials due to their superior properties such as low density and exceptional mechanical strength. Their low density provides lightweight solutions, and their density is closer to that of human bone compared to other metallic alloys with similar strength. This similarity facilitates a balanced load distribution between the bone and the implant, enhancing biomechanical compatibility. This study investigates the effects of alloying elements on the density of titanium-based biomedical materials using a computational materials science approach. A total of 72 different compositions of Ti-Al-V alloys were modeled using JMatPro software, and their densities were simulated at room temperature (25 °C). The simulation produced a comprehensive dataset, which was utilized to train an explainable artificial intelligence (XAI) model. Advanced interpretability techniques, including SHAP (SHapley Additive exPlanations), LIME (Local Interpretable Model-agnostic Explanations), and Partial Dependence Plots (PDP), were employed to elucidate the influence of each alloying element on the density. The dataset was analyzed using an XAI-based regression model implemented with the Artificial Neural Network (ANN) algorithm. The interpretability graphs provided insights into the individual contributions of the alloying elements, revealing their positive or negative effects on the density. The findings offer a deeper understanding of the role of alloying elements in optimizing the performance of titanium-based biomedical materials, particularly in achieving lightweight designs. This study highlights the potential of integrating computational material modeling with explainable AI to advance the design and development of high-performance lightweight materials for biomedical applications.

## KEYWORDS

Explainable artificial intelligence  
Computational materials science  
Biomedical materials  
Titanium alloys

## INTRODUCTION

Titanium and its alloys are widely recognized for their superior properties, such as low density, excellent mechanical strength, high corrosion resistance, and outstanding biocompatibility, which make them ideal candidates for biomedical applications. Among metallic materials, titanium's similarity in density to human bone allows for better load distribution, significantly enhancing its biomechanical compatibility as an implant material (Niinomi 2008). Over the years, extensive research has been conducted to improve the performance of titanium alloys by modifying their chemical compositions with alloying elements, focusing on achieving optimized mechanical properties and enhanced biological compatibility (Madalina Simona *et al.* 2019; Ikeda *et al.* 2020).

Alloying elements such as niobium (Nb), tantalum (Ta), and zirconium (Zr) have been shown to positively influence the properties of titanium alloys. These elements not only reduce the elastic mod-

ulus, which minimizes the stress shielding effect, but also improve the alloys' strength, wear resistance, and corrosion resistance. This is particularly important in biomedical contexts where the implant material must integrate effectively with surrounding tissues while maintaining structural integrity under physiological loads (Zhou *et al.* 2007; Hayyawi *et al.* 2022). For instance, beta-titanium alloys incorporating Nb and Ta exhibit low Young's modulus and excellent biocompatibility, making them ideal for orthopedic and dental applications (Phume *et al.* 2012; Ivanov *et al.* 2018).

The development of titanium-based biomedical materials also addresses concerns regarding the cytotoxicity of conventional alloys such as Ti-6Al-4V, where the presence of vanadium and aluminum may pose health risks. Research has shifted towards creating non-toxic titanium alloys by incorporating elements such as niobium and zirconium, which maintain high mechanical performance while eliminating adverse biological effects (Manojlović and Marković 2023; Li *et al.* 2011). Furthermore, advanced manufacturing techniques like additive manufacturing enable the production of patient-specific implants, providing opportunities to tailor the properties of titanium alloys to meet specific clinical needs (Alqattan *et al.* 2020; Niinomi *et al.* 2016).

**Manuscript received:** 20 December 2024,

**Revised:** 25 January 2025,

**Accepted:** 26 January 2025.

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Recently, computational materials science and machine learning approaches have emerged as powerful tools for exploring the effects of alloying elements on the performance of titanium alloys. Explainable Artificial Intelligence (XAI) methods, such as SHAP and LIME, provide valuable insights into how each alloying element contributes to key properties, guiding the development of lightweight and biocompatible titanium materials (Bărbîntă *et al.* 2013; Toğaçar *et al.* 2022, 2021). By integrating experimental and computational findings, researchers are now better equipped to design high-performance titanium alloys for biomedical applications, further advancing the field of implant materials science.

## MATERIALS AND METHODS

This study investigates the effects of alloying elements on the density of titanium-based biomedical materials through a computational and data-driven approach. A total of 72 different compositions of Ti-Al-V alloys were modeled using JMatPro software, enabling accurate simulation of material densities at room temperature (25°C). The simulation results formed a comprehensive dataset, which was subsequently used to train an Artificial Neural Network (ANN)-based explainable AI (XAI) model. Advanced interpretability techniques, including SHAP (SHapley Additive exPlanations), LIME (Local Interpretable Model-agnostic Explanations), and Partial Dependence Plots (PDP), were applied to analyze the influence of individual alloying elements on density. This integrated methodology combines computational material science and machine learning to provide insights into the relationship between composition and material properties, guiding the optimization of lightweight titanium alloys for biomedical applications.

### Dataset Preparation

The dataset utilized in this study comprises 72 different Ti-Al-V-based alloy compositions, which were modeled within the compositional ranges provided in Table 1. The titanium content ranged from 77% to 94%, while aluminum (Al) and vanadium (V) varied between 3–7% and 2.5–5.4%, respectively. Trace elements such as tin (Sn), zirconium (Zr), and molybdenum (Mo) were included within limited ranges (0–2%, 0–4%, and 0–4%). These specific composition ranges were selected based on their prominence in biomedical alloy design, particularly to achieve optimal density and mechanical properties (Brusewitz Lindahl *et al.* 2015). Each of the 72 alloy compositions was modeled using JMatPro software, and the density values at room temperature (25°C) were calculated and recorded for each entry.

The choice of these composition ranges stems from the widespread use of titanium-based alloys, particularly Ti-Al-V combinations, in biomedical applications such as orthopedic and dental implants (Kartamyshev *et al.* 2020). Titanium, as the base material, offers excellent biocompatibility, corrosion resistance, and a density closer to that of human bone (Li *et al.* 2024). Aluminum is included to stabilize the  $\alpha$ -phase, providing strength and reducing weight, while vanadium contributes to the  $\beta$ -phase, improving the alloy's flexibility and toughness (Luan *et al.* 2017). However, excessive amounts of V and Al may lead to biocompatibility concerns, prompting exploration of their optimal content (Bodunrin *et al.* 2020). Elements like Zr, Sn, and Mo were introduced to further enhance specific properties, such as strength, corrosion resistance, and stability, without compromising biocompatibility (Sun and Mi 2023). The simulation of density values at room temperature was essential to evaluate the lightweight nature of the modeled alloys.

Room temperature properties are particularly relevant for biomedical applications where implants must retain consistent structural and mechanical integrity under physiological conditions (Alipour *et al.* 2022). By systematically analyzing 72 alloy compositions, this study provided a comprehensive dataset for training an explainable AI model to elucidate the contributions of individual elements to the density of titanium-based materials. Such insights are critical for advancing the design of lightweight, high-performance biomedical materials optimized for biomechanical compatibility (Wan *et al.* 2020).

**Development of the Explainable Artificial Intelligence Model** In this study, an Artificial Neural Network (ANN)-based regression model was employed to predict the density of titanium-based biomedical materials, replacing conventional machine learning algorithms such as XGBoost. ANNs are widely recognized for their capability to model complex, non-linear relationships in high-dimensional datasets, making them ideal for applications in material science where properties depend on intricate compositional interactions (Valipoorsalimi 2023). The use of ANN ensures robust predictions by simulating material density for the 72 compositions of titanium alloys. This approach was particularly advantageous given the non-linear and multivariable nature of the relationship between alloying elements and material properties (Maitra *et al.* 2024).

The ANN regression model was trained on a comprehensive dataset generated through simulations using JMatPro software, where the density values of titanium-based alloys were computed at room temperature (25°C). The network architecture was optimized by fine-tuning hyperparameters such as the number of hidden layers, neurons per layer, activation functions, and learning rates to minimize errors and improve generalization capability (Hagan *et al.* 2014). To prevent overfitting, regularization techniques such as dropout and L2 weight penalties were incorporated, ensuring that the ANN model remained robust across the dataset. The high predictive accuracy achieved by the ANN highlights its suitability for capturing complex relationships within the data (Goodfellow *et al.* 2016).

To ensure the transparency and interpretability of the developed ANN model, Explainable Artificial Intelligence (XAI) methods, including SHAP (SHapley Additive exPlanations), LIME (Local Interpretable Model-agnostic Explanations), and Partial Dependence Plots (PDP), were integrated into the analysis. XAI techniques address the "black-box" nature of neural networks, providing insights into how the input features (alloying elements) influence the model's predictions (Lundberg and Lee 2017). This step is particularly crucial in material design and biomedical applications, where understanding the effect of alloying elements on density can guide the development of lightweight, high-performance materials (Ribeiro *et al.* 2016).

SHAP was utilized to quantify the contribution of each alloying element to the predicted density. By leveraging Shapley values from cooperative game theory, SHAP ensures fair attribution of feature importance to the model's predictions (Scavuzzo *et al.* 2022). This method offers both local (individual predictions) and global (model-wide) interpretability, enabling a detailed analysis of how elements like aluminum, vanadium, zirconium, and tin influence the material density. For example, it was observed that increasing the vanadium content consistently reduced density, while aluminum showed a more complex interaction, stabilizing density within a specific range (Sun and Mi 2023).

LIME was implemented to further enhance local interpretability by generating simplified surrogate models for individual predic-

**Table 1 Elemental Composition Ranges of Alloys in the Dataset (values represent wt%)**

Ti (%)	Al (%)	V (%)	Sn (%)	Zr (%)	Mo (%)	Fe (%)	N (%)	C (%)	H (%)	O (%)
77–94	3–5–7	2.5–3.5–4.5	0 and 2	0 and 4	0 and 4	0.3	0.05	0.08	0.015	0.2

tions. LIME creates perturbations around specific alloy compositions and fits an interpretable model, such as linear regression, to approximate the behavior of the ANN model locally (Ferdib-Al-Islam et al. 2023). This approach allowed for a clearer understanding of the decision-making process for specific alloy compositions, ensuring that model predictions aligned with physical and chemical principles. The combination of SHAP and LIME provided a multi-faceted view of model behavior, improving confidence in the ANN predictions.

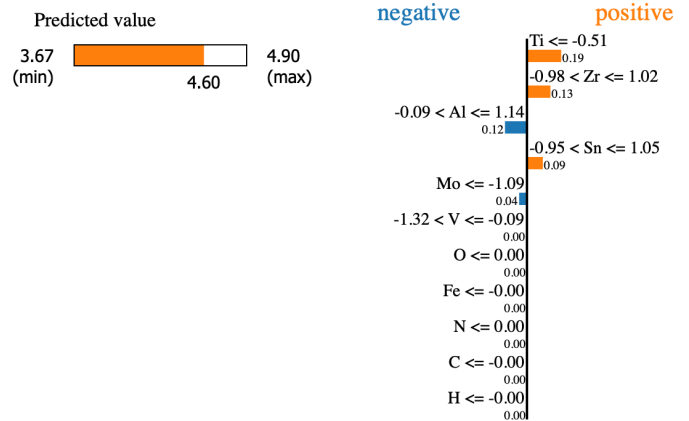
Finally, Partial Dependence Plots (PDPs) were employed to visualize the global effects of individual features on the predicted density. PDPs reveal the average influence of an alloying element while holding other elements constant, enabling the identification of critical compositional ranges for density optimization (Friedman 2001). By integrating PDPs into the analysis, it was possible to uncover non-linear dependencies and interactions, offering valuable insights into the optimal ranges for alloying elements. For example, Zr and Sn demonstrated significant effects on density only within specific intervals, highlighting their potential for fine-tuning material properties.

## RESULTS AND DISCUSSION

In this study, the influence of alloying elements on the density of titanium-based biomedical materials was analyzed using an explainable artificial intelligence (XAI) approach. The ANN-based regression model demonstrated high predictive accuracy for density values, supported by advanced interpretability techniques such as SHAP, LIME, and Partial Dependence Plots (PDP). These methods provided comprehensive insights into the individual and combined effects of alloying elements, enabling the identification of critical ranges and interactions. The results revealed that certain alloying elements, such as zirconium (Zr) and tin (Sn), play a significant role in enhancing the density, while others, such as molybdenum (Mo) and vanadium (V), contribute to reducing the density. These findings underline the potential of integrating computational materials science with XAI to optimize the design of lightweight titanium alloys for biomedical applications.

The results of the XAI analysis are illustrated in Figure 1, which presents the predicted density value and the contribution of each alloying element. The predicted density of the alloy composition is approximately 4.60 g/cm<sup>3</sup>, as shown on the horizontal bar. The SHAP plot highlights the positive (orange) and negative (blue) contributions of individual elements. Notably, Zr (0.98 ≤ Zr ≤ 1.02 wt%) and Sn (-0.95 ≤ Sn ≤ 1.05 wt%) exhibit the most significant positive effects on density, while Mo and Al negatively impact the overall density. This visualization underscores the critical role of individual alloying elements and their optimized compositions in achieving the desired material properties for biomedical applications.

Figure 2 highlights the contributions of key alloying elements to the density of titanium-based biomedical materials. The analysis reveals that zirconium (Zr), tin (Sn), and aluminum (Al) have the most significant positive impacts, with feature values of 1.02, 1.05,



**Figure 1** Predicted density and SHAP-based contributions of alloying elements in titanium-based biomedical materials

and 1.14, respectively. These elements play a vital role in optimizing the density while maintaining the mechanical properties of the alloy. Conversely, molybdenum (Mo) and vanadium (V) exhibit slight negative contributions (-1.09 and -0.09), reflecting their density-reducing characteristics. Titanium (Ti), as the base element, demonstrates a moderate negative impact (-0.80), consistent with its lightweight nature. The negligible contributions of other elements (O, Fe, N, C, H) suggest their minimal influence on the alloy's density within the studied composition. These insights provide a comprehensive understanding of how specific elements contribute to achieving desired material properties for biomedical applications.

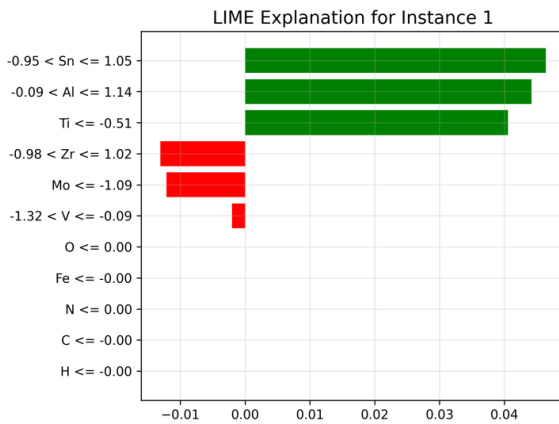
### Feature Value

Ti	-0.80
Zr	1.02
Al	1.14
Sn	1.05
Mo	-1.09
V	-0.09
O	0.00
Fe	-0.00
N	0.00
C	-0.00
H	-0.00

**Figure 2** Contributions of Alloying Elements to Density

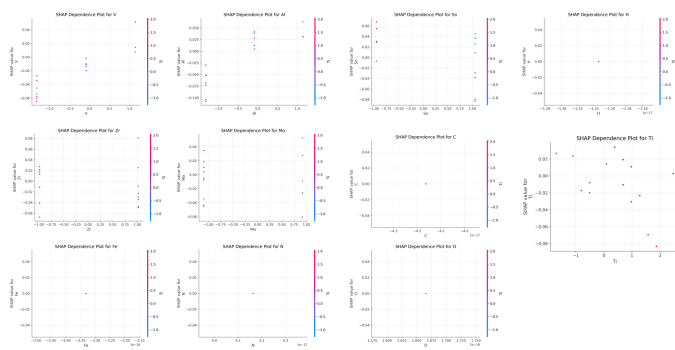
Figure 3 presents the LIME (Local Interpretable Model-Agnostic Explanations) analysis for the contributions of individual alloying elements to the density of a specific titanium-based composition. Positive contributions are shown in green, while negative ones are indicated in red. Tin (Sn) and aluminum (Al) are the most

significant positive contributors, with their effects observed within the ranges  $-0.95 < \text{Sn} \leq 1.05$  and  $-0.09 < \text{Al} \leq 1.14$ , respectively. Titanium (Ti) also exhibits a moderate positive impact. Zirconium (Zr) shows a neutral to slightly positive influence, whereas molybdenum (Mo) and vanadium (V) contribute negatively, reducing the density. Elements such as oxygen (O), iron (Fe), nitrogen (N), carbon (C), and hydrogen (H) display negligible contributions, highlighting their limited role in this specific alloy composition. These results provide localized insights into the effects of alloying elements, enabling targeted optimizations for biomedical material design.



**Figure 3** LIME Explanation of Alloying Element Contributions

Figure 4 presents the SHAP dependence plots for various alloying elements, providing insights into their individual contributions to the predicted density of titanium-based biomedical materials. The plots reveal that aluminum (Al) and tin (Sn) have strong positive effects on density, showing a direct relationship as their values increase. Zirconium (Zr) exhibits a nonlinear contribution, with its optimal effect occurring within a specific range. Conversely, vanadium (V) and molybdenum (Mo) contribute negatively, reducing density as their values increase. Elements like oxygen (O), nitrogen (N), carbon (C), and hydrogen (H) show negligible SHAP values, indicating minimal influence on density. These results highlight the importance of optimizing the composition of critical elements such as Al, Sn, and Zr to achieve desired density properties in biomedical applications.



**Figure 4** SHAP Dependence Plots for Alloying Elements

## CONCLUSION

This study investigated the effects of alloying elements on the density of titanium-based biomedical materials using a computational materials science approach integrated with explainable artificial intelligence (XAI). The findings demonstrated that specific elements, such as aluminum (Al), tin (Sn), and zirconium (Zr), play a critical role in enhancing density, while others like molybdenum (Mo) and vanadium (V) reduce it. SHAP and LIME analysis provided valuable insights into the contributions of individual elements, revealing their importance in achieving optimal density for lightweight and biocompatible materials. The integration of computational modeling with XAI enables precise evaluation of complex relationships between alloy compositions and material properties, offering a systematic approach to improving implant designs.

Future studies should explore a broader range of alloying elements and their interactions to optimize additional properties such as mechanical strength, corrosion resistance, and biocompatibility. Advanced machine learning techniques combined with experimental validation can further enhance the reliability of predictions and provide a more comprehensive understanding of material performance under physiological conditions. The adoption of such data-driven methodologies holds significant potential for advancing the development of high-performance titanium alloys tailored for specific biomedical applications.

### Availability of data and material

Not applicable.

### Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

### Ethical standard

The authors have no relevant financial or non-financial interests to disclose.

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**How to cite this article:** Alaca, Y., Uzunoğlu, Y., and Emin, B. Investigation of the Effect of Alloying Elements on the Density of Titanium-Based Biomedical Materials Using Explainable Artificial Intelligence. *Computers and Electronics in Medicine*, 2(1), 15-19, 2025.

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# Deep Learning-Based Detection of Abdominal Diseases Using YOLOv9 Models and Advanced Preprocessing Techniques

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**ABSTRACT** Artificial intelligence has emerged as a transformative tool in medical imaging, enabling automated diagnosis and analysis across various domains. While significant advancements have been made in abdominal imaging, many studies struggle to achieve robust detection of diseases. The complexity and variability in abdominal structures present unique challenges for traditional machine learning models, necessitating the adoption of more advanced object detection frameworks. Motivated by these challenges, this study focuses on leveraging the YOLOv9 object detection architecture to enhance the identification of abdominal diseases using the TEKNOFEST 2022 Abdomen Dataset. Advanced preprocessing techniques, including CLAHE (Contrast Limited Adaptive Histogram Equalization) and Gaussian noise augmentation, were applied to improve image contrast and model robustness. The dataset was processed into YOLO-compatible formats, and multiple training configurations were evaluated using YOLOv9c and YOLOv9s variants. These configurations included variations in batch size, optimizer type (SGD and Adam), dropout rate, and frozen layers. Among the configurations tested, the YOLOv9s model with 32 batch size, SGD optimizer, and a 35% dropout rate demonstrated the best performance, achieving a Recall of 0.7698, Accuracy of 0.7698, and F1 Score of 0.8228. The highest mAP50 of 0.9385 was observed with the YOLOv9c model trained using the Adam optimizer and a 35% dropout rate. Confusion matrix analysis revealed strong detection capabilities for conditions like acute cholecystitis and abdominal aortic aneurysm. This study highlights the potential of YOLOv9 models in medical imaging and emphasizes the importance of high-resolution datasets and advanced feature extraction techniques for improving diagnostic accuracy in abdominal disease detection. These findings lay a foundation for the development of reliable and efficient AI-driven diagnostic tools.

## KEYWORDS

Abdominal disease detection  
YOLOv9  
Medical image analysis  
Preprocessing techniques  
Deep learning for diagnosis

## INTRODUCTION

Artificial intelligence (AI) has brought about transformative changes in the diagnosis and treatment processes within the medical field. AI technologies, such as machine learning and deep learning, have significantly enhanced accuracy in medical imaging, thereby improving the efficiency of healthcare services (El-Tanani *et al.* 2025). In the analysis and processing of medical data, AI has enabled the early detection of diseases and the development of personalized treatment approaches (Shaikh *et al.* 2025). Moreover, the application of AI in genomic research has deepened the understanding of genetic disorders, offering innovative solutions in treatment strategies (Zhou *et al.* 2025; Chen *et al.* 2025).

The integration of AI into healthcare services through automated machine learning (AutoML) applications has allowed for reduced error rates and faster processing of healthcare workflows (Shujaat 2025). These advancements have not only optimized diagnostic and treatment processes but also increased the overall

efficiency of healthcare systems (Donovan *et al.* 2025). Furthermore, the necessity to uphold data privacy and ethical standards in healthcare systems remains a critical priority to ensure the safe and equitable application of AI.

Abdominal diseases, which encompass pathological conditions affecting organs in the abdominal region, involve complex processes in both diagnosis and treatment. AI-based approaches offer significant opportunities to enhance accuracy, save time, and support clinical decision-making mechanisms in these processes. In particular, machine learning and deep learning techniques have demonstrated high performance in analyzing abdominal imaging data, enabling the early detection of conditions such as appendicitis, pancreatic cancer, and abdominal aortic aneurysm. Recent studies show that AI-based image processing algorithms can be utilized not only for diagnosis but also in conjunction with verification systems that ensure the security of patient data. The increasing adoption of these technologies in clinical applications facilitates more precise disease management and drives transformation in healthcare services (Zhou *et al.* 2025; Boyraz *et al.* 2022; Santos *et al.* 2024).

Manuscript received: 3 January 2025,

Revised: 25 January 2025,

Accepted: 27 January 2025.

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Object detection algorithms have significantly advanced the field of medical diagnosis by enabling the rapid and accurate identification of diseases in medical imaging data. Deep learning-based models like YOLO have made it possible to identify thyroid nodules in ultrasound images with high accuracy (Wang *et al.* 2025). Moreover, multi-object detection algorithms have contributed to the precise differentiation of reactive lymphocytes in blood samples, playing a crucial role in the diagnosis of hematological diseases (Liu *et al.* 2025). In another study, YOLO-based deep learning models were employed to detect extrahepatic common bile duct obstruction in MRCP images, allowing for the clinical diagnosis of these complex conditions with high accuracy (Tho *et al.* 2025). Additionally, multi-scale feature fusion algorithms used in the staging of occupational diseases such as pneumoconiosis have enhanced diagnostic precision while improving the understanding of disease progression (Ren *et al.* 2025). These studies demonstrate that object detection algorithms not only improve the accuracy of image analysis but also make patient care processes more efficient.

In this study, a YOLOv9-based (Wang *et al.* 2024) object detection model was developed to enable the early and accurate detection of acute abdominal diseases using the Abdomen Dataset presented in the TEKNOFEST 2022 Artificial Intelligence in Health Competition (Koç *et al.* 2024). Detailed preprocessing steps were conducted for the dataset classes, including the enhancement of image contrast through the CLAHE method (Pisano *et al.* 1998) and the addition of noise at varying levels. The model training was performed using the s and c variants of YOLOv9 with different hyperparameter combinations. Furthermore, the model's performance was evaluated using metrics such as precision and accuracy, emphasizing the effectiveness of AI-based methods in medical image analysis.

The main contributions of this paper are as follows:

- An object detection-based model for the detection of abdominal diseases was developed using the Abdomen Dataset from the TEKNOFEST 2022 Artificial Intelligence in Health Competition.
- Image contrast was enhanced through the CLAHE method, and preprocessing techniques such as noise addition at varying levels enriched the diversity of the training data.
- The model was trained using different variants of YOLOv9 (YOLOv9s and YOLOv9c) and hyperparameter combinations, with optimization techniques analyzed in detail.
- The effects of different optimization algorithms (SGD and Adam) and hyperparameters on the classification accuracy of medical image data were thoroughly analyzed.
- The proposed method offers the potential for faster and more accurate diagnosis in medical imaging, making a significant contribution to clinical decision support systems.

The remainder of this paper is organized as follows. The Related Work section reviews previous studies utilizing object detection models for analyzing abdominal medical images and detecting related diseases. The Dataset section introduces the TEKNOFEST 2022 Abdomen Dataset, describing its class structure, annotations, and preprocessing steps. The Methodology section explains the proposed workflow in detail, including preprocessing techniques like CLAHE for enhancing image contrast and noise augmentation, along with the training steps of YOLOv9 models with varying hyperparameters. The Experiments and Results section presents quantitative evaluations of model performance, including precision, recall, and overall accuracy, f1-score across different configurations. The Discussion section interprets these results, highlights

the significance of the findings, and compares the proposed approach with existing methods. Lastly, the Conclusion and Future Work section summarizes the study's contributions and provides insights into potential future developments for improving disease detection in abdominal images using advanced object detection techniques.

Object detection algorithms play a crucial role in the diagnosis and classification of abdominal diseases in medical image analysis. Ramamoorthy *et al.* (2024) employed deep learning methods for early cancer detection and ulcer classification in endoscopy videos. In this study, cancer and ulcer lesions were automatically detected. The research demonstrated that object detection models could precisely identify small and ambiguous lesions in endoscopic images. Moreover, this approach ensured the accurate classification of lesions. Maity *et al.* (2024) integrated explainable artificial intelligence (XAI) with object detection methods for the diagnosis of gastroesophageal reflux disease (GERD). The study identified different stages of the disease through segmentation and classification processes. Using object detection models, anatomical abnormalities caused by GERD were automatically detected, thereby supporting clinical decision-making processes.

Su *et al.* (2023) compared Faster RCNN, Cascade RCNN, and Mask RCNN models for the diagnosis of early gastric cancer in gastroscopic images. This study successfully detected and localized cancerous regions using object detection algorithms. The results showed that RCNN-based models achieved high accuracy rates in lesion detection in gastroscopic images. Jin *et al.* (2022) performed segmentation and detection of gastric cancer lesions in endoscopic images using the Mask RCNN model. Object detection algorithms optimized the diagnostic process by accurately identifying cancerous regions. This study demonstrated that Mask RCNN is an effective method for improving detection accuracy in endoscopic images.

In the study conducted by Koçer *et al.* (2024), the YOLOv5 algorithm was employed to detect and classify various diseases in abdominal CT images. The study was carried out on a dataset containing 11 different disease conditions from 1200 patients. The YOLOv5 algorithm demonstrated high accuracy, particularly in detecting conditions such as acute appendicitis, kidney stones, gallstones, and ureteral stones. The data were converted from DICOM format to formats required by the YOLO algorithm, making them compatible with the deep learning model. The object detection algorithm was equipped with class labels and bounding boxes to pinpoint the exact locations of disease regions. The study highlighted that YOLOv5 is a promising tool for fast and accurate diagnosis in medical imaging and can expedite diagnostic processes while reducing the workload of radiologists. These studies emphasize the significant advantages of object detection algorithms in medical image analysis, particularly in the early diagnosis and accurate classification of abdominal diseases. Models such as YOLO, RCNN, and Mask RCNN have been observed to contribute to faster and more precise diagnostic processes on abdominal images.

## DATASET

In this study, the TR\_ABDOMEN\_RAD\_EMERGENCY dataset (Koç *et al.* 2024), used in the TEKNOFEST-2022 Artificial Intelligence in Healthcare Competition, was utilized. The dataset aims to classify abdominal emergencies into six distinct categories: (i) acute cholecystitis, (ii) kidney and/or ureter stones, (iii) acute pancreatitis, (iv) abdominal aortic aneurysm/dissection/rupture, (v) acute appendicitis, and (vi) acute diverticulitis.

The dataset was collected through the infrastructure of the e-Nabız (Pulse) and National Teleradiology System (NTS) managed by the Ministry of Health of the Republic of Türkiye (Koç *et al.* 2024). DICOM-format images recorded between 2019 and 2021 underwent a centralized screening and selection process. These anonymized images were meticulously labeled by 10 radiologists with 5 to 10 years of professional experience. During the labeling process, bounding boxes were used to ensure the accurate classification of radiological data.

The dataset is divided into two distinct parts for training and competition phases:

- Training data: 1,209 cases and 357,428 images.
- Competition data: 308 cases and 98,101 images.

The distributions and detailed information for each class are presented in Table 1.

## METHODOLOGY

This section outlines the methodology employed for detecting abdominal diseases using the TEKNOFEST 2022 Abdomen Dataset. The Preprocessing step focuses on enhancing the quality and contrast of medical images by applying CLAHE (Contrast Limited Adaptive Histogram Equalization), which improves visibility in low-contrast regions. To further simulate real-world variability and increase model robustness, various levels of Gaussian noise were added to the dataset. The Training Step involves utilizing the YOLOv9 model, which was trained with multiple configurations, including variations in hyperparameters such as batch size, optimizer type, and dropout rates.

### Preprocessing Step

The preprocessing phase is a critical step in preparing the TEKNOFEST 2022 Abdomen Dataset for training. Several preprocessing techniques were employed to enhance the dataset and prepare it for training with the YOLOv9 model. These steps include:

- **DICOM to JPG Conversion:** The medical images in DICOM format were converted to JPG format to ensure compatibility with the YOLO framework.
- **Bounding Box Conversion:** The bounding box annotations provided in the dataset were converted to YOLO-compatible coordinates.
- **Image Resizing:** Each image was resized to a resolution of  $640 \times 640$  pixels, adhering to the YOLO model's input requirements.
- **Contrast Enhancement (CLAHE):** CLAHE (Contrast Limited Adaptive Histogram Equalization) was applied to improve the visibility of critical details, especially in low-contrast regions.
- **Noise Addition:** Gaussian noise was added at varying levels to simulate real-world variability and increase model robustness. Four variations were tested: CLAHE without noise, CLAHE with 0.03 noise, CLAHE with 0.1 noise, and CLAHE with 0.3 noise.

Among the tested preprocessing methods, CLAHE with 0.03 Gaussian noise yielded the best results in terms of model accuracy, as it provided an optimal balance between noise robustness and enhanced contrast. This highlights the importance of careful tuning of preprocessing parameters to achieve superior performance.

As demonstrated in Figure 1, the original image (left) has relatively low contrast, which is significantly improved after applying

CLAHE (middle). When Gaussian noise is combined with CLAHE (right), the contrast is further enhanced, with CLAHE + 0.03 noise providing the best results. This combination ensures that the processed images retain their clinical significance while providing robust input for the YOLO model.

### Training Step

The training phase involved the application of the YOLOv9 model, specifically using its two variants: YOLOv9c and YOLOv9s. These models were trained using a variety of configurations to identify the best-performing setup for abdominal disease detection. The training process utilized several key hyperparameters and techniques, as summarized in Table 2.

In this study, the models were trained using batch sizes of 16 and 32 to examine the effect of batch size on training stability and performance. Two optimization algorithms, SGD and Adam, were employed to compare convergence rates and generalization. Each model was trained for 90 epochs, with input images resized to  $640 \times 640$  pixels to meet YOLO requirements.

Additional techniques included applying dropout rates of 35% to reduce overfitting and freezing the first 10 layers in some configurations to leverage pre-trained weights. The models were evaluated using 5-fold cross-validation, ensuring reliable and robust results across different data splits.

This systematic experimentation allowed for the identification of the optimal configuration, which utilized YOLOv9c, a batch size of 32, SGD optimizer, and a dropout rate of 35%, achieving the highest performance with a mean average precision (mAP) of 83.1%.

## RESULTS AND DISCUSSION

The results obtained from training YOLOv9c and YOLOv9s models using various configurations are summarized in Table 3. The evaluation metrics, including Precision, Recall, Accuracy, F1 Score, and mAP50, were calculated for each configuration to assess the performance of the models.

As shown in Table 3, the performance of the models varied across different configurations. The following observations can be made:

### Performance of YOLOv9c and YOLOv9s Models

The results indicate that the YOLOv9s variant, when trained with 32 batch size, SGD optimizer, and a 35% dropout rate, achieved the highest F1 Score (0.8228) and mAP50 (0.8738) among SGD-based configurations. On the other hand, the YOLOv9c model, trained with the Adam optimizer and a 35% dropout rate, achieved the highest overall mAP50 (0.9385) and Precision (0.9530).

### Effect of Dropout and Freezing Layers

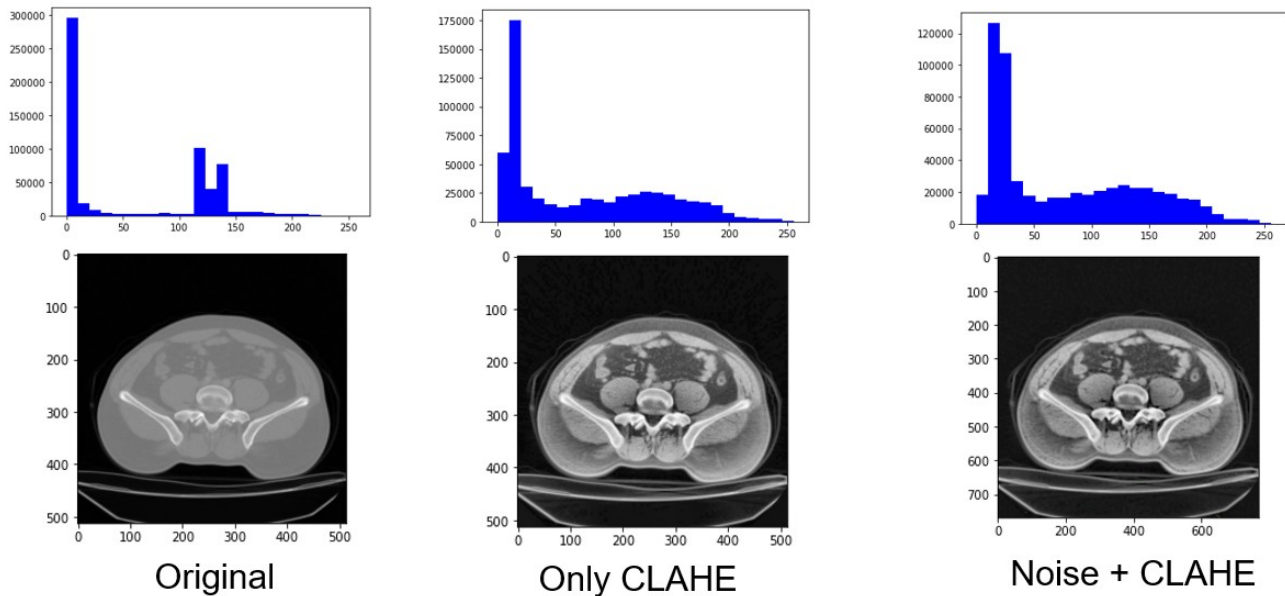
Applying a 35% dropout rate improved the generalization performance, as evidenced by higher F1 Scores and mAP50 values compared to configurations without dropout. However, freezing the first 10 layers in the models led to slight reductions in Recall and Accuracy metrics, suggesting that freezing may limit the model's ability to adapt to new data.

### Comparison of Optimizers

The Adam optimizer showed superior performance in terms of Precision and mAP50, particularly for the YOLOv9c model. However, SGD provided more balanced results across all metrics, making it a reliable choice for configurations focused on generalizability.

■ **Table 1 Distribution of Dataset**

Class	Training Cases	Test Cases	Total Images
Acute Appendicitis	221	83	7,541
Acute Cholecystitis	124	34	6,345
Acute Pancreatitis	146	48	8,841
Kidney/Ureter Stones	283	97	3,488
Acute Diverticulitis	76	16	1,403
Abdominal Aortic Aneurysm	159	49	12,667



**Figure 1** The comparison of original, CLAHE-applied, and Gaussian noise + CLAHE-applied abdominal images

■ **Table 2 Training Parameters and Configurations**

Parameter	Values Used
Batch Size	16, 32
Optimizer	SGD, Adam
Epochs	90
Input Size	640 × 640 pixels
Dropout	0%, 35%
Frozen Layers	0, 10
Model Variants	YOLOv9c, YOLOv9s
Cross-Validation	5-fold

**Best Configuration Performance Evaluation**

The best-performing configuration in terms of Recall, Accuracy, and F1 Score was achieved using the **YOLOv9s model** with a batch size of 32, the SGD optimizer, and a 35% dropout rate. This configuration produced a Recall of **0.7698**, an Accuracy of **0.7698**, and an F1 Score of **0.8228**, demonstrating its robust ability to detect and classify abdominal diseases effectively. The mAP50 value of **0.8738** further supports the strong generalization of this model across all test cases.

Figure 2 presents the normalized confusion matrix for this configuration, providing a detailed view of the model’s performance across different classes. Notably, the model achieved high classification accuracy for categories such as **"Compatible with acute cholecystitis"** (0.78) and **"Abdominal aortic aneurysm"** (0.89), indicating its capability to identify larger and more distinct features associated with these conditions. However, the matrix reveals that the classification performance for **"Kidney stone"** was notably lower, with a Recall of **0.48**.

The low performance for the **"Kidney stone"** category can be attributed to the small size of these stones, which makes them challenging to detect even with advanced object detection mod-

■ **Table 3 Training Results and Metrics for YOLOv9 Configurations**

Configuration	Precision	Recall	Accuracy	F1 Score	mAP50
YOLOv9c, 16 Batch, SGD, No Dropout	0.8758	0.7619	0.7619	0.8149	0.8651
YOLOv9c, 16 Batch, SGD, 35% Dropout	0.8781	0.7639	0.7639	0.8170	0.8689
YOLOv9c, 16 Batch, SGD, 35% Dropout, 10 Freeze	0.8658	0.7564	0.7564	0.8074	0.8574
YOLOv9c, 32 Batch, SGD, No Dropout	0.8713	0.7583	0.7583	0.8109	0.8628
YOLOv9c, 32 Batch, SGD, 35% Dropout	0.8744	0.7609	0.7609	0.8137	0.8665
YOLOv9c, 32 Batch, SGD, 10 Freeze	0.8603	0.7637	0.7637	0.8091	0.8532
YOLOv9c, 32 Batch, SGD, 35% Dropout, 10 Freeze	0.8594	0.7629	0.7629	0.8083	0.8531
YOLOv9s, 32 Batch, SGD, No Dropout	0.8795	0.7662	0.7662	0.8190	0.8672
YOLOv9s, 32 Batch, SGD, 35% Dropout	0.8836	<b>0.7698</b>	<b>0.7698</b>	<b>0.8228</b>	0.8738
YOLOv9s, 32 Batch, SGD, 35% Dropout, 10 Freeze	0.8790	0.7574	0.7574	0.8137	0.8715
YOLOv9c, 32 Batch, Adam, No Dropout	0.9499	0.7002	0.7002	0.8061	0.9347
YOLOv9c, 32 Batch, Adam, 10 Freeze	<b>0.9551</b>	0.6871	0.6871	0.7992	0.9372
YOLOv9c, 32 Batch, Adam, 35% Dropout	0.9530	0.7024	0.7024	0.8088	<b>0.9385</b>

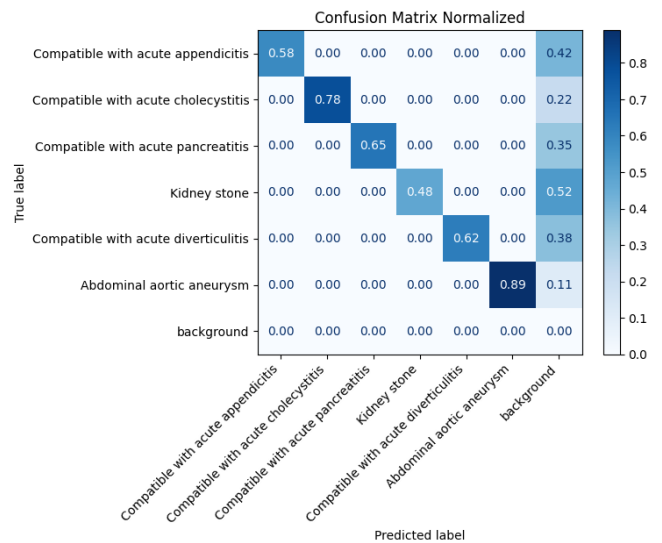
els. Their subtle appearance in medical images often results in misclassification or lower detection confidence. This observation highlights the need for higher-resolution datasets or more advanced preprocessing techniques tailored to enhance the visibility of smaller objects.

In summary, the YOLOv9s model with the aforementioned configuration provided strong results for most abdominal disease categories, but certain challenges, such as detecting small-sized features like kidney stones, emphasize the necessity for further dataset improvements and potential model fine-tuning.

## CONCLUSION

In this study, a YOLOv9-based object detection approach was implemented to identify abdominal diseases using the TEKNOFEST 2022 Abdomen Dataset. The dataset was enhanced through advanced preprocessing techniques, including CLAHE and Gaussian noise augmentation, to improve image contrast and robustness. Multiple training configurations were evaluated using YOLOv9c and YOLOv9s variants, with variations in batch size, optimizer, dropout rate, and frozen layers. The results demonstrated that the YOLOv9s model, trained with a batch size of 32, the SGD optimizer, and a 35% dropout rate, provided the best performance in terms of Recall (0.7698), Accuracy (0.7698), and F1 Score (0.8228). Additionally, the highest mAP50 (0.9385) was achieved using the YOLOv9c model with the Adam optimizer and a 35% dropout rate.

The confusion matrix analysis highlighted the strong performance of the proposed approach in identifying diseases such as acute cholecystitis and abdominal aortic aneurysm. However, the detection of smaller objects, such as kidney stones, remained challenging due to their subtle appearance in medical images. This



**Figure 2** Normalized Confusion Matrix for YOLOv9s, 32 Batch, SGD, 35% Dropout Configuration.

observation emphasizes the need for higher-resolution datasets and advanced preprocessing methods in future studies.

As part of future work, several enhancements can be considered. First, incorporating higher-resolution medical images and exploring multi-scale feature extraction techniques could improve the detection of small-sized objects. Second, leveraging ensemble learning by combining YOLO models with other object detection frameworks could enhance overall performance. Lastly, expanding

the dataset with diverse samples and annotating additional classes would further strengthen the model's robustness and applicability in clinical settings.

#### Availability of data and material

TEKNOFEST 2022 Abdomen Dataset were used in this study.

#### Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

#### Ethical standard

The author has no relevant financial or non-financial interests to disclose.

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**How to cite this article:** Kiran, H. E. Deep Learning-Based Detection of Abdominal Diseases Using YOLOv9 Models and Advanced Preprocessing Techniques. *Computers and Electronics in Medicine*, 2(1), 20-25, 2025.

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