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Artificial intelligence – an aid for physicians in chordoma management? A systematic review of current applications

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Abstract

Introduction. Chordoma, a rare neoplasm originating from the notochord, poses diagnostic and therapeutic challenges due to its slow growth and complex anatomical locations. The advent of artificial intelligence (AI) offers promising avenues for improving chordoma management through enhanced diagnosis, prognostication, and treatment optimization.

Methods. This systematic review adhered to the PRISMA guidelines and focused on AI applications in chordoma management. A comprehensive literature search was conducted across seven major databases, and relevant data were extracted, including publication details, study aims, AI techniques employed, validation methods, and study results.

Results. AI techniques, including machine learning and deep learning, demonstrated efficacy in differentiating chordomas from other neoplasms, segmenting tumor boundaries, predicting patient survival and recurrence, and guiding therapeutic strategies. Integration of radiomic features, clinical characteristics, and imaging modalities facilitated accurate diagnosis and prognostication. Additionally, AI-driven approaches enabled drug repurposing and optimized treatment planning, particularly in radiation therapy.

Conclusions. The findings highlight the transformative potential of AI in revolutionizing chordoma management, offering personalized and precise approaches for diagnosis, prognostication, and therapeutic intervention. Collaborative efforts between clinicians, researchers, and technologists are essential to validate AI-driven algorithms and introduce them into clinical practice. Further research is warranted to address limitations and ensure the ethical deployment of AI technologies in healthcare to improve outcomes for chordoma patients.

Keywords: artificial intelligence, machine learning, deep learning, LASSO, SVM, chordoma, automated tumor diagnosis, tumor survival prediction

Introduction

Chordoma, a neoplasm of rare occurrence (incidence rate of 1:1 000 000), was first identified by Virchow and Luschka in 1856 [1]. This neoplasm is typically characterized as low-grade and exhibits slow growth. The origin of chordomas can be traced back to the notochord, an embryonic structure that subsequently develops into the nucleus pulposus. Despite extensive research, no definitive genetic marker has been established; however, several factors have been implicated in the tumor's development, including the mTOR signaling pathway, PTEN deficiency, INI-1, PDGFR-beta, and the brachyury gene [2].

In terms of anatomical location, approximately half of all chordomas are found in the sacral area (50%),

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with one-third located at the skull base, and a minority (15%) appearing in the vertebral bodies [3–5]. The diagnostic process for this rare malignant tumor typically involves biopsy, magnetic resonance imaging (MRI), and computed tomography (CT). Computed tomography scans offer superior lesion information, while MRI provides a more comprehensive analysis of the extent of this neoplasm.

The primary treatment strategy is complete en-bloc resection of the chordoma. However, in cases where complete resection is not feasible (for instance, due to the tumor's complex location), alternative approaches such as intratumoral resection, piecemeal resection, and local debulking are employed. Given the high recurrence rate of chordomas, high-dose radiation therapy is often necessary, as these tumors exhibit relative resistance to radiation. With a high mortality rate (5-year survival rate of 50%), proactive measures are essential to prevent the further progression of this locally aggressive tumor [6].

The advent of artificial intelligence (AI), a rapidly evolving technology, has seen its application across various medical fields, including oncology. It has been tested in a range of cancers, including gliomas, adenomas, colorectal cancer, and more [7–9]. Artificial intelligence holds potential not only in neoplasm detection from imaging but also in predicting recurrence, tumor segmentation, biomarker detection, and beyond. The implementation of machine learning and deep learning (DL) techniques has led to increasingly more and more accurate algorithms, potentially paving the way for comprehensive implementation in the medical sector in the near future.

This review aims to explore current clinical applications of AI technology for chordoma. This article will systematically collate and present literature findings to organize the existing knowledge on this subject. Our objective is not only to describe the types of algorithms used in the studies but also to elucidate the methodology and performance of AI, and how this technology can AI physicians on chordoma management.

Methodology

In this systematic review, we adhered to the PRISMA guidelines for reporting systematic reviews and meta-analyses [10]. The literature search process was conducted across seven major databases, including PubMed, Embase, Cochrane Reviews, Scopus, Web of Science, Ovid, and Ebsco. We utilized appropriate medical subject headings (MeSH) terminology to identify pertinent studies, employing the following search terms: artificial intelligence OR convolutional neural network OR deep learning OR machine learning OR decision tree OR support vector machine OR lasso OR k-means AND chordoma. The full search strategy is delineated in Appendix 1.

Our search was confined to original articles that concentrated on the application of AI technologies to chordoma. We excluded all review articles, abstract-only articles, conference papers, and other non-original articles. We included only articles published in English, without any restrictions on the publication date. The articles were independently screened by two reviewers. The entire screening process was facilitated by the bibliography manager (ZOTERO).

From each included study, we extracted the following data: publication date and origin of the study; aim of the study; artificial intelligence technique employed; validation used in the study; and the results. Given that researchers often employ diverse methods to assess the performance of the algorithm and considering that this study did not aim to target specific applications of AI in chordomas, we did not establish any stringent criteria for such extraction. We incorporated all relevant results that described the performance of the algorithm, such as the area under the receiver operating characteristic curve (AUC), sensitivity, specificity, accuracy, or the concordance index (C-index), which is analogous to the AUC.

Results

Overview of the studies

The screening process is visualized in Figure 1 [10]. We found 35 articles from PubMed, 68 from Embase, 31 from Web of Science, 41 from Scopus, 27 from Ebsco, 95 from Ovid, and 1 from Cochrane reviews. In total, we have managed to find 298 articles. The bibliography manager, which we have used in the study, initially marked 148 duplicates for removal. In total,150 articles underwent the process of screening. Afterward, we removed 101 articles, as they were irrelevant to the topic of our study. For full-text screening, 49 articles were assessed. Finally, for this systematic review, 25 articles were included [11–35]. We excluded 24 articles after full-text screening: 12 studies were not relevant to the topic of the analysis, and for 11 studies only abstracts were available; we also excluded 1 review article.

We have found 14 articles related to differentiation, classification, and segmentation (diagnostics), 9 articles related to survival and recurrence prediction, and finally 2 articles related to drug and dosimetry. Publication dates ranged from 2018 to 2023 (4 articles from 2018, 3 from 2019, 3 from 2020, 4 from 2021, 6 from 2022, and 5 from 2023). Publications also varied by country of origin — the majority of the articles were from the People's Republic of China (15), 5 from the USA, 2 from Italy, and there was 1 article from each of these countries: Japan, Canada, and the Netherlands. Studies also varied in

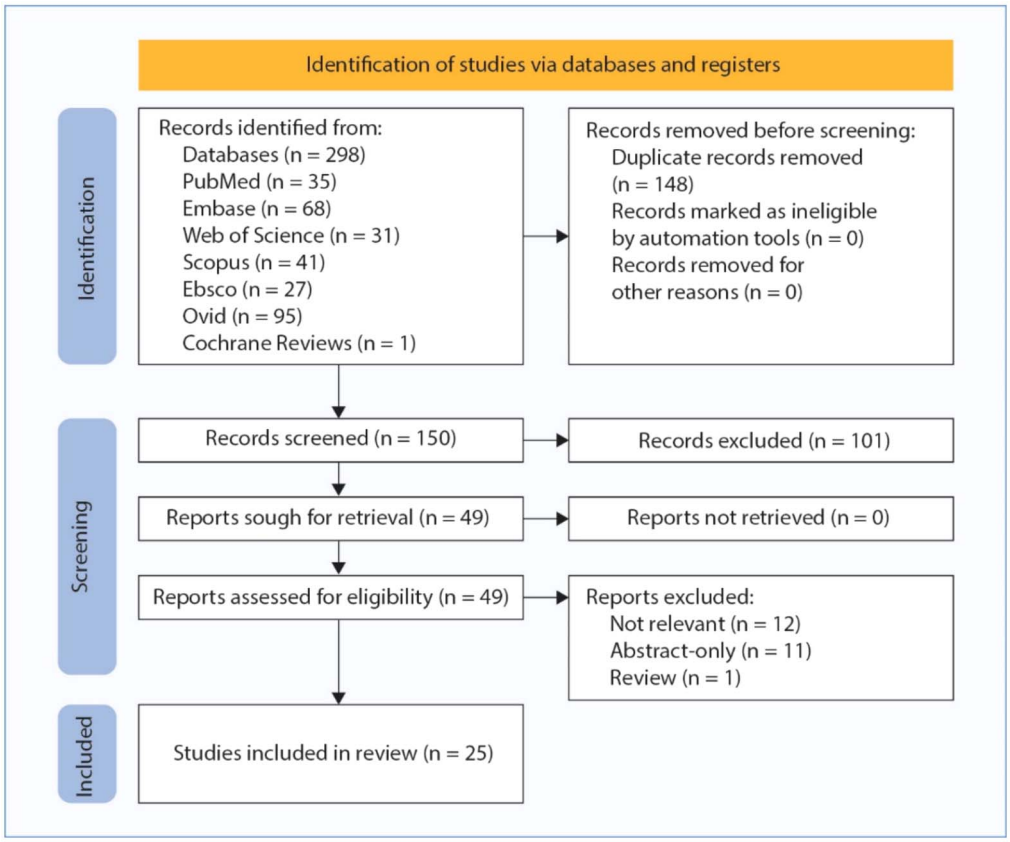

Figure 1. PRISMA flow diagram [10]

the artificial intelligence used: some studies used machine learning, others used deep learning, and there were also studies using both AI methods. Validation was reported in 23 articles used for this review. More details about each study included in this review are provided in Tables 1–3 after each section.

Differentiation, classification, and segmentation [11–24]

Chordoma, as previously noted, is classified as a rare neoplasm. Consequently, residents specializing in diagnostics, such as radiologists, along with less experienced physicians from other departments, may face challenges in differentiating this uncommon tumor. The application of artificial intelligence can significantly enhance the quality of a physician's work by eliminating potential life-threatening misdiagnoses, which is particularly advantageous for junior specialists.

In their study on the classification of nasopharyngeal tumors, Song et al. experimented with varying sizes of MRI images (112 × 112, 224 × 224, and 512 × 512), as well as different proportions of datasets used for model training (25%, 50%, and 100%) [13]. Among the models trained with the full dataset, the model using 112 × 112 image size achieved the highest AUC performance of 0.94, while the model using 512 × 512 image size yielded the lowest score of 0.935. A similar trend was observed in the models trained with the 25% dataset: the highest performance was achieved with the 112 × 112 model (0.823), and the 512 × 512 model achieved the lowest score in the study (0.640). Another study by Yamawaza et al. demonstrated that the application of radiomic features from multiple types of scans leads to higher AUC performance than extraction from only one type of MRI scan [22]. Meanwhile, Yin et al. [20] compared the performance of algorithms between standard CT scans and iodine-contrast CT scans in the differentiation of sacral tumors. Models differentiating chordomas on the enhanced scans achieved greater performance (AUC 0.875–0.984) than those on standard CT scans (AUC 0.639–0.883) on the validation set.

To further improve the performance of the DL model, Liu et al. [14] incorporated patient clinical characteristics into the XGBoost machine classifier, such as age, erythrocyte sedimentation rate, sex, or pain information. In the three-category testing set for the differentiation of bone tumors, the model incorporating these characteristics (fusion model) was superior (AUC of 0.872) to the standard MRI-based-only classification model (AUC of 0.813). This allowed

Table 1. Differentiation, classification, and segmentation studies reported in this review

Study	Aim of the study	AI technique	Validation	Results
Boussioux 2023, USA [11]	Segmentation of sacral chordoma & surrounding muscles (CT)	DL — 3D U-Net and residual 3D U-Net with Dice loss, standard cross-entropy loss, and class-weighted cross-entropy loss functions	Random split	Dice: 85.5% (gross tumor volume)
Li 2019, China [12]	Differentiating skull base chordoma and chondrosarcoma (MRI)	ML —SVM model with a radial basis function kernel	10-fold	AUC: 0.872 Sensitivity: 89.47% Accuracy: 72.85%
Song 2022, China [13]	Classification and segmentation of tumors in the nasopharyngeal area (MRI)	DL — U-net and the Deeplabv3 (segmentation); EfficientNet-B0, Legacy SE-ResNet34, MobileNetV3 Large100, and DenseNet121 (detection)	N/A	AUC: 0.935–0.949 (100% dataset used), 0.64–0.823 (25% dataset used)
Liu 2022, China [14]	Classification of benign, malignant, and intermediate bone tumors (MRI)	DL — inception_v3 with XGBoost classifier; developed with PyTorch	Random split	AUC: 0.813 (radiological model), 0.872 (fusion model)
Nie 2023, China [15]	Nomogram for differentiating chordoma from giant cell tumor (CT)	ML — LASSO and RadCloud (feature extraction)	10-fold cross	AUC: 0.830 (radiomics), 0.980 (nomogram)
Sun 2021, China [16]	Differentiating between benign and malignant bone tumours (CT)	ML — LASSO	Random split	AUC: 0.781 (radomics), 0.823 (nomogram)
Yin 2018, China [17]	Differentiation of primary chordoma, giant cell tumor, and metastatic tumor of sacrum (MRI)	ML — analysis of variance (ANOVA), LASSO regression with Pearson correlation, and RF	Random split	AUC: 0.773 Accuracy: 71.1%
Yin 2019, China [18]	Differentiation of sacral chordoma and sacral giant cell tumor (CT)	ML — LASSO with GLM and Spearman correlation	10-fold cross	AUC: 0.942 (combined radiomics), 0.948 (nomogram)
Yin 2021, China [19]	Differentiation of the types of pelvic and sacral tumors (CT)	ML — GBDT and Spearman correlation	10-fold cross	AUC: 0.923
Yin 2018, China [20]	Differentiation of sacral chordoma and sacral giant cell tumour (CT)	ML — relief, LASSO, RF, GLM, SVM	N/A	AUC: 0.984 (LASSO + classifier GLM for CT enhanced), 0.889 (RF + GLM for standard CT)
Yin 2020, China [21]	Differentiation between benign and malignant sacral tumors (CT)	ML — LR, RF, SVM, k-nearest neighbor (KNN); DL — DNN	10-fold cross	AUC: 0.84 (LR model) AUC: 0.83 (DNN model)
Yamazawa 2022, Japan [22]	Differentiating skull base chordoma and chondrosarcoma (MRI)	ML — LR, SVM	2-fold cross	AUC: 0.87–0.95 (LR model) AUC: 0.86–0.92 (SVM model)
Herrgott 2022, USA [23]	Differentiation between pituitary neuroendocrine tumors from other CNS tumors or conditions	ML — RF	10-fold cross	Accuracy: 93%
Zuccato 2021, Canada [24]	Identification of epigenetic chordoma subtypes with plasma methylome-based biomarkers	ML — k-means clustering Cox regression model	10-fold cross	AUC: 0.84

AI — artificial intelligence; AUC — receiver operating characteristic curve; CT — computed tomography; DL — deep learning; DNN — deep neural network; GBDT — gradient boosting decision tree; GLM — generalized linear model; LASSO — Least Absolute Shrinkage and Selection Operator; LR — logistic regression; ML — machine learning; MRI — magnetic resonance imagining; N/A — not applicable; RF — random forest; SVM — support vector machine

the fusion model to achieve performance comparable with senior radiologists. A similar procedure was conducted by Nie et al. in their study differentiating chordoma from the giant cell tumor; the combination of age, tumor location, and Rad-score in the nomogram model allowed for superior performance compared to the standard radiomics model (AUC of 0.98 and 0.83, respectively) on the 48 patients in the

Table 2. Survival and recurrence prediction studies reported in this review

Study	Aim of the study	AI technique	Validation	Results
Buizza 2021, Italy [25]	Predicting local control after carbon-ion radiotherapy in skull-base chordoma	ML — linear survival support vector machines (s-SVM), Cox proportional hazards model with elastic net penalty (r-Cox)	5-fold cross	C-index: 0.73–0.80
Cheng 2023, China [26]	Prediction of cancer-specific survival in patients with spinal chordoma	DL — DeepSurv and NMLTR	3-fold cross	C-index: 0.830 (DeepSurv) C-index: 0.804 (NMLTR)
Peng 2023, China [27]	Predicting overall survival in chordoma	DL — DeepSurv and NMLTR; ML — RSF	5-fold cross	C-index: 0.79 (DeepSurv)
Karchade 2018, USA [28]	Predicting 5-year survival in spinal chordoma	ML — boosted Decision Tree, SVM, bayes point machine; DL — Unnamed Neural Network	10-fold cross	C-index: 0.80 (Bayes Point Machine) AUC: 0.801 (Bayes Point Machine)
Morelli 2022, Italy [29]	Prediction of local recurrence in sacral chordomas after carbon-ion radiotherapy	ML — s-SVM, r-Cox with LASSO regression	5-fold cross	C-index: 0.80–0.86 (r-Cox models)
Wei 2019, China [30]	Characterization and local recurrence prediction in particle therapy of skull-base chordoma from microstructure	ML — radiomics, ridge regression-based Cox proportional hazards model	3-fold cross	C-index: 0.745
Zhai 2022, China [31]	Prediction of progression-free survival in patients with clival chordomas	ML — radiomics, LASSO, Elastic-Net, Cox regression	5-fold cross	AUC: 0.582 (1-year), 0.852 (3-years), and 0.914 (5-years)
Li 2020, China [32]	Prediction of clinical outcome of patients with spinal chordoma	ML — LASSO Cox regression	10-fold cross	AUC: 0.763 (1-year local relapse-free survival), 0.797 (5-year overall survival)
Ghaith 2023, USA [33]	Prediction of recurrence after clival and spinal chordoma resection	ML – DT, RF	10-fold cross	Accuracy: 77% Specificity: 83% Sensitivity: 75%

AI — artificial intelligence; AUC — receiver operating characteristic curve; DL — deep learning; DT — decision tree; LASSO — Least Absolute Shrinkage and Selection Operator; ML — machine learning; NMLTR — neural network multitask logistic regression; RSF — random survival forest

Table 3. Dosimetry and drug studies reported in this review

Study	Aim of the study	AI technique	Validation	Results
Dinkla 2018, Netherlands [34]	Accurate calculations of MRI-based dose in the brain with DNN and synthetic computed tomography (sCT)	DL — dCNN	2-fold cross	Mean dose deviations: 0.00% ± 0.02% (dose within the body contours), 0.13% ± 0.39% (inside the planning target volume)
Anderson 2020, USA [35]	Drug repurposing with synergistic drug combinations for chordoma	ML — BayesianML	5-fold cross	AUC: 0.67–0.81 (see subchapter)

AI — artificial intelligence; dCNN — dilated convolutional neural network; DL — deep learning; DNN — deep neural network; ML — machine learning; MRI — magnetic resonance imagining; sCT — synthetic computed tomography

test cohort [15]. Sun et al. [16] reported the use of age, ground-glass appearance, rim sclerosis, cortical integrity, residual bony ridge, and the presence or absence of a soft tissue mass as clinical features for the nomogram; this again allowed for better performance than the standard radiomics model (AUC of 0.823 vs. 0.781) from the CT scans for bone tumor classification.

Researchers are not confined to deep learning techniques alone; Li et al. [12], with multiparametric machine-learning-based (support vector machine) radiomics, analyzed the differentiation performance of chordoma and chondrosarcoma. On the validation set with 70 MRI images, the algorithm yielded an AUC of 0.8242, allowing for accurate differentiation. Other machine learning (ML) techniques include least ab-

solute shrinkage and selection operator (LASSO), analysis of variance (ANOVA), k-nearest neighbor (KNN), or random forest [15–22].

In the study conducted by Yin et al. [20], an assessment was made of various combinations of machine-learning techniques. The researchers implemented a diverse array of ML techniques, including relief, LASSO, random forest (RF), generalised linear models (GLM), and support vector machine (SVM). The combination of GLM and LASSO was the only one to achieve an AUC performance exceeding 0.91 in the differentiation of neoplasms from contrast-enhanced CT scans, with a score of 0.984. The second highest performance was achieved by the combination of GLM with Relief (0.908), followed by the double RF combination (0.904). In the case of standard CT scans, the superior performance was again attributed to GLM, but this time in combination with RF and a score of 0.889.

Herrgott et al. [23] undertook an analysis of methylation markers to distinguish pituitary neuroendocrine tumors from other central nervous system (CNS) tumors or conditions. A RF ML model was employed, utilizing 59 methylation signatures identified in serum and 49 in plasma, profiled with the cfDNA methylome EPIC array. Following a 10-fold cross-validation in the independent cohort, the RF model achieved an accuracy of 93% in distinguishing these neoplasms. Zuccato et al. [24] also utilized methylation profiles in their efforts to distinguish between chordoma subtypes. Employing a Cox regression model, they achieved an AUC of 0.84 for the algorithm in the testing set.

Furthermore, AI has been applied to the procedures of neoplasm segmentation. Boussioux et al. developed 3D U-Net deep-learning architectures to perform this automated operation on sacral chordoma CT scans [11]. Six models were trained on a set of 30 images and subsequently validated on a new set of 5 images. The automated segmentation of the neoplasm yielded an expert-level Dice segmentation score of 85.5%. The continued development of AI in this field will undoubtedly enhance the accuracy of the algorithms, thereby optimizing the process of this highly time-consuming manual segmentation.

Survival and recurrence [25–33]

The prediction of survival and recurrence prognosis can be particularly beneficial for the patient, as it can guide the subsequent steps of treatment. At present, numerous proportional hazard prediction models, such as the Cox model, are being utilized. While these models are not considered machine-learning algorithms in themselves, when coupled with LASSO, Elastic net, or Ridge, they form a comprehensive model capable of accurately analyzing hazard prediction.

Cheng et al. [26] developed deep-learning models for the prediction of patient survival with spinal chordoma. These models were developed using basic demographic information (ethnicity, adjuvant therapy, sex) as well as more specific tumor information (size of the tumor at diagnosis, extent of invasion, presence of metastasis). A 5- and 10-year survival prediction resulted in AUC of 0.843 and 0.880, respectively, as well as a C-index of 0.830 with the use of the DeepSurv model. In a study conducted by Peng et al. [27], researchers compared the standard Cox proportional hazards model with two deep learning and one machine learning model. The DL DeepSurv model was superior to the standard CoxPH as well as the other two models, yielding an AUC of 0.84 and 0.88 for 5-year and 10-year survival prediction, respectively. The Bayes point machine used in the Karchade et al. [28] study showed a comparable C-index but lower AUC values for 5-year prediction compared to the Peng study.

Zhai et al. [31] assessed progression-free survival for less than five years. Utilizing machine learning methods (LASSO, Elastic-Net), seven radiomic features from the MRI images, as well as clinical factors, a nomogram was constructed to predict survivability. In the test cohort of 53 cases, the nomogram achieved excellent results for 5-year and 3-year survivability, with an AUC of 0.914 and 0.852, respectively. However, survival prediction for 1 year showed poor performance of the algorithm (0.582), nearly equivalent to random guessing. Li et al. [32] also conducted a study for short-term prediction with the ML LASSO Cox regression. With the use of four immune features (sCD8+, sFoxp3+, tFoxp3+, and tPD-1+ TILs), in the validation cohort of 60 patients, they achieved significantly better 1-year local relapse-free survival (LRFS) prediction (AUC of 0.763); however, the performance of the algorithm in predicting 3-year LRFS as well as 3- and 5-year overall survival was lower than in the Zhai study.

Buizza et al. [25] implemented imaging (CT + + MRI), dosiomic features [heterogeneity at different spatial scales, shape properties (elongation, flatness)], and clinical characteristics of the patients (anatomical location, optic pathway involvement, or sex) to predict the local control after carbon-ion radiotherapy. With all these features combined, the models achieved a C-index of 0.73–0.80. Additionally, in the study, the r-Cox model showed better performance than the sSVM algorithm in the testing set (n = 12). These results, while promising, still require further development before full-scale application in clinical practice.

Ghaith et al. [33] applied the ML decision tree algorithm combined with immunohistochemical markers for the prediction of recurrence. A multivariate analysis showed that S100 and pan-cytokeratin were

more likely to predict the increased risk of recurrence [odds ratio = 3.67; 95% confidence interval (CI) 1.09–12.42; p = 0.03; and OR = 3.74; 95% CI 0.05–2.21; p = 0.02, respectively]. With the use of patient age, type of surgical treatment, location of the tumor, S100, epithelial membrane antigen (EMA), and pan-cytokeratin markers, the algorithm yielded an accuracy of 77%, specificity of 83%, and sensitivity of 75% on the testing set. The ML model was also tested without the markers, yielding a significantly lower accuracy of 62.5%.

Drug and dose delivery [34, 35]

Drug repositioning, also known as repurposing, is a prevalent strategy in pharmaceutical research, wherein a drug developed for one condition is tested for its efficacy in treating other diseases. Anderson et al. employed a machine learning Bayesian model in their research [35]. This model was trained on several studies that focused on the compounds screened against chordoma cell lines. The Bayesian model evaluated the activity of these compounds against chordoma based on their chemical features and known activities from previous screenings. This trained Bayesian model was subsequently utilized to score and predict the activity of new compounds that were not part of the training sets. Three molecules, namely AZD2014, RDEA119, and AZD4054, were selected for testing based on the predictions of the model. The scores provided by the Bayesian model were used to assess the potential activity of these compounds against chordoma. The authors then proceeded to conduct *in vitro* testing against chordoma cell lines (U-CH1 and U-CH2). The performance of the Bayesian model was evaluated based on its predictive accuracy of the activity of these molecules in the experimental set. AZD2014 was identified as the most potent against chordoma cell lines, with IC50 values of 0.35 μM for U-CH1 and 0.61 μM for U-CH2. Additionally, substantial synergy was observed between afatinib and palbociclib (EGFR and CDK4/6 inhibitors, respectively), as well as between afatinib and AZD2014.

In light of the current exponential growth in the importance of MRI in intracranial tumor diagnosis, Dinkla et al. [34] investigated one of the challenges associated with this technology. While MRI provides superior soft-tissue contrast, it lacks electron density information, which is crucial for precise dose calculation. The generation of synthetic CT scans (sCT) can be used for accurate dose calculation for radiation therapy. To address this issue, a dilated convolutional neural network, a deep-learning technique, was employed to create sCT scans. The algorithm was tested on a cohort of 26 patients. Dosimetric analysis showed mean deviations of 0.00% ± 0.02% for dose within the body contours and 0.13% ± 0.39% inside the planning target volume. The network demonstrated low deviations in the dose calculations as well as rapid sCT scan generation — approximately one minute for each scan — thus facilitating fast and accurate treatment planning.

Discussion

Chordoma presents a significant clinical challenge due to its rarity, slow growth, and complex anatomical locations, often necessitating intricate surgical approaches. The integration of artificial intelligence into chordoma management holds substantial promise, offering avenues for improved diagnosis, treatment planning, and prognostication. To our knowledge, this is the very first systematic review describing the application of artificial intelligence to this rare tumor management.

Artificial intelligence has the potential to enhance the accuracy and efficiency of chordoma diagnosis and segmentation. Various machine-learning and deep-learning techniques have been applied to differentiate chordomas from other neoplasms, leveraging diverse imaging modalities and clinical data. Notably, the integration of radiomic features and clinical characteristics has demonstrated superior performance compared to traditional imaging-based approaches. Artificial intelligence-driven segmentation algorithms, such as 3D U-Net architectures, offer automated and precise delineation of chordoma boundaries, mitigating the subjectivity and time constraints associated with manual segmentation. Both machine learning and deep learning models show promising results in the diagnostic sector of rare neoplasms. Some studies reported that the major limitation of this technology is the small dataset of chordoma scans publicly available, which currently hinders the improvement of the accuracy of the networks. Such an increase in scans would be significantly beneficial, especially for deep-learning networks.

Accurate prediction of survival and recurrence is paramount for guiding treatment decisions and optimizing patient outcomes. Artificial intelligence models, particularly deep learning approaches, have shown promise in prognosticating patient survival and disease recurrence based on demographic data, tumor characteristics, and radiomic features. Despite promising results, challenges remain in achieving robust predictions, particularly in short-term survival prognosis. Further refinement of AI models through incorporating additional clinical variables and validation of predictive performance in diverse patient cohorts is warranted.

Artificial intelligence-driven approaches have the potential to guide therapeutic strategies for chordoma,

including drug repurposing and treatment optimization. Machine learning models have been utilized to predict the efficacy of existing compounds against chordoma cell lines, facilitating the identification of novel therapeutic candidates. Moreover, deep learning techniques enable the generation of synthetic CT scans from MRI data, addressing the challenge of accurate dose calculation in radiation therapy planning. These advancements highlight the transformative potential of AI in tailoring personalized treatment regimens and optimizing therapeutic outcomes for chordoma patients.

Despite the promising findings, several limitations and avenues for future research should be acknowledged. The majority of the reviewed studies were retrospective, emphasizing the need for prospective validation of AI-driven algorithms in clinical settings. Additionally, the generalizability of AI models across diverse patient populations and healthcare settings warrants further investigation. Algorithms still need to be developed in larger testing sets; in the majority of our articles, they were tested on datasets of fewer than 70 patients. Furthermore, not all the articles implemented validation procedures in their analyses, which could have affected the reliability of the results. Ethical considerations, including data confidentiality, algorithm transparency, and bias mitigation, are paramount in developing and deploying AI technologies in healthcare. Future randomized trials could showcase the effectiveness of this technology, compared to conventional methods.

Conclusions

Using artificial intelligence holds immense potential in revolutionizing the management of chordoma, ranging from accurate diagnosis and segmentation to prognostication and therapeutic optimization. Collaborative efforts between clinicians, researchers, and technologists are essential to harness the full capabilities of AI and translate these advancements into tangible clinical benefits for chordoma patients. As AI continues to evolve, its role in empowering precision medicine approaches for rare cancers like chordoma is poised to expand, offering renewed hope for improved patient outcomes and quality of life.

Article Information and Declarations

Author contributions

P.M.Ł. and K.J. Paweł Łajczak equally contributed to this work (screening, writing, methodology, final review).

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Conflict of interest

Authors declare no conflict of interest.

Supplementary material

Appendix 1. Search strategy used in this systematic review

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SUPPLEMENTARY MATERIAL

Appendix 1. Search strategy used in this systematic review

PubMed: ((artificial intelligence) OR (convolutional neural network) OR cnn OR (deep learning) OR (machine learning) OR (decision tree) OR (neural network) OR (support vector machine) OR lasso OR (k-means) OR knn) AND (chordoma)
Embase: ('artificial intelligence'/exp OR 'artificial intelligence' OR (artificial AND ('intelligence'/exp OR intelligence)) OR 'convolutional neural network'/exp OR 'convolutional neural network' OR (convolutional AND neural AND ('network'/exp OR network)) OR cnn OR 'deep learning'/exp OR 'deep learning' OR (deep AND ('learning'/exp OR learning)) OR 'machine learning'/exp OR 'machine learning' OR (('machine'/exp OR machine) AND ('learning'/exp OR learning)) OR 'decision tree'/exp OR 'decision tree' OR (('decision'/exp OR decision) AND ('tree'/exp OR tree)) OR 'neural network'/exp OR 'neural network' OR (neural AND ('network'/exp OR network)) OR 'support vector machine'/exp OR 'support vector machine' OR (('support'/exp OR support) AND ('vector'/exp OR vector) AND ('machine'/exp OR machine)) OR 'lasso'/exp OR lasso OR 'k means'/exp OR 'k means' OR knn) AND ('chordoma'/exp OR chordoma)
Web of Science: ((artificial intelligence) OR (convolutional neural network) OR cnn OR (deep learning) OR (machine learning) OR (decision tree) OR (neural network) OR (support vector machine) OR lasso OR (k-means) OR knn) AND (chordoma)
Scopus: ((artificial intelligence) OR (convolutional neural network) OR cnn OR (deep learning) OR (machine learning) OR (decision tree) OR (neural network) OR (support vector machine) OR lasso OR (k-means) OR knn) AND (chordoma)
Cochrane Reviews: ((artificial intelligence) OR (convolutional neural network) OR cnn OR (deep learning) OR (machine learning) OR (decision tree) OR (neural network) OR (support vector machine) OR lasso OR (k-means) OR knn) AND (chordoma)
Ebsco: ((artificial intelligence) OR (convolutional neural network) OR cnn OR (deep learning) OR (machine learning) OR (decision tree) OR (neural network) OR (support vector machine) OR lasso OR (k-means) OR knn) AND (chordoma)
Ovid: (chordoma and (artificial intelligence or deep learning or machine learning)).mp. [mp=tx, bt, ti, ab, ct, sh, ot, nm, hw, fx, kf, ox, px, rx, an, ui, ds, on, sy, ux, mx]