# **Artificial intelligence in pancreatic cancer**

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## **Abstract**

Pancreatic cancer is the deadliest disease, with a five-year overall survival rate of just 11%. The pancreatic cancer patients diagnosed with early screening have a median overall survival of nearly ten years, compared with 1.5 years for those not diagnosed with early screening. Therefore, early diagnosis and early treatment of pancreatic cancer are particularly critical. However, as a rare disease, the general screening cost of pancreatic cancer is high, the accuracy of existing tumor markers is not enough, and the efficacy of treatment methods is not exact. In terms of early diagnosis, artificial intelligence technology can quickly locate high-risk groups through medical images, pathological examination, biomarkers, and other aspects, then screening pancreatic cancer lesions early. At the same time, the artificial intelligence algorithm can also be used to predict the survival time, recurrence risk, metastasis, and therapy response which could affect the prognosis. In addition, artificial intelligence is widely used in pancreatic cancer health records, estimating medical imaging parameters, developing computer-aided diagnosis systems, etc. Advances in AI applications for pancreatic cancer will require a concerted effort among clinicians, basic scientists, statisticians, and engineers. Although it has some limitations, it will play an essential role in overcoming pancreatic cancer in the foreseeable future due to its mighty computing power.

**Keywords:**Artificial intelligence, machine learning, pancreatic cancer, early detection, prognosis prediction

## **Introduction**

Pancreatic cancer (PC) is the deadliest form of all cancer. The five-year relative survival rate for PC is only 11% in the USA, which is the lowest among all cancers [1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B1). There were 495773 new cases and 466003 deaths from PC worldwide in 2020, accounting for 2.6% of all new cancer diagnoses and 4.7% of all cancer deaths, respectively [2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B2). In China, the incidence and mortality of PC among tumors are 2.47% and 3.64%, respectively [3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B3). The main reason for such a poor prognosis of PC is the late diagnosis, with only about 20% of patients being diagnosed at an early stage. Most patients have non-specific first symptoms, such as jaundice, fatigue, change in bowel habits, and indigestion, that make it difficult to distinguish from non-cancer diseases [4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B4). Most chemotherapy [5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B5)-[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B7), targeted therapy [8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B8), and immunotherapy [9](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B9)-[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B11) are ineffective because most patients are already in the progressive stage with local invasion and distant metastases at the detection time [12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B12),[13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B13). A multicenter study demonstrated that patients with PC detected by screening had a 5-year survival rate of 73.3% and a median survival time of 9.8 years, compared with 1.5 years for patients with PC seen by non-screening [14](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B14). To diagnose early-stage PC accurately is desperately needed [15](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B15),[16](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B16).

## **State-of-the-art AI Algorithms involved in Pancreatic Cancer**

### **Machine Learning**

Machine learning (ML) is a subfield of AI that solves the problem of how to build computers that improve automatically through experience (**Figure**[**​Figure11**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/figure/F1/?report=objectonly)). Based on a large amount of feature data, ML can use specific algorithms to learn how to accomplish a task [45](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B45). In today's medical field, there is a massive amount of data generated every day, and it becomes a challenge to integrate this data to make predictions. The most significant advantage of ML is the ability to integrate vast amounts of data and combine the observed and predicted quantities in nonlinear and highly interactive ways [46](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B46). ML techniques can be broadly classified based on the type of labels. Based on labels, machine learning can be classified as supervised, unsupervised, semi-supervised, and reinforcement learning. There is also ensemble learning that integrates multiple algorithms

Receiver operating characteristics (ROC) curves help organize ML classifiers and visualize their performance. ROC curve is a line graph plotted with sensitivity as the vertical coordinate and (1-specificity) as the horizontal coordinate. The area under the ROC curve (AUC) is the evaluation metric, and the larger the AUC value, the better the corresponding algorithm performs [47](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B47). Other metrics, including accuracy, sensitivity, specificity, F1-Score, positive predictive value (PPV), and negative predictive value (NPV), are also commonly used to evaluate the result of the ML [48](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B48).

#### **Supervised Learning**

Supervised learning is constructing a model in which each observation vector has a corresponding response variable. In other words, all data is labeled. By fitting a model that relates responses to predictors, supervised learning can accurately predict future observed responses or better understand the relationship between responses and predictors [49](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B49),[50](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B50). Examples of such algorithms include Logistic Regressions (LR), Decision Trees (DT), Support Vector Machines (SVM), Naïve Bayes (NB), Artificial Neural Networks (ANN), etc., and the best application scenario for each algorithm varies [51](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B51). In this review, most of the algorithms used in PC are supervised learning. A typical application of supervised learning algorithms is the precise diagnosis, including detection, grading, and differential diagnosis, using radiomics, digital pathology slides, or biomarkers. The prognosis of PC is also widely used to predict survival time, recurrence rate, metastasis, and therapy response.

#### **Unsupervised Learning**

Unsupervised learning means we can know the observation vector, not the associated response. In other words, all data is unlabeled. Using the observation vector's data makes it possible to perform clustering, correlation evaluation, dimensionality reduction, etc. [50](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B50),[52](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B52). Examples of such algorithms include K-mean clustering [53](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B53), Principal Component Analysis (PCA) [54](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B54), Non-negative Matrix Factorization (NMF) [55](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B55), etc. The application of unsupervised learning in PC is relatively rare, but there have been attempts to do so, including classification [56](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B56), feature extraction of CT images [57](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B57),[58](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B58) or pathological slides [59](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B59), and estimation of medical imaging parameters [60](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B60).

#### **Semi-supervised Learning**

As its name suggests, semi-supervised learning is somewhere between supervised and unsupervised learning, allowing the use of large amounts of available unlabeled data in combination with small labeled datasets in many use cases. Semi-supervised learning can utilize a small amount of labeled data to obtain better performance than supervised learning while utilizing less labeled data to achieve the same level of performance close to that of supervised learning [61](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B61),[62](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B62). Examples of such algorithms include generative models, self-training, co-training, graph-based learning, Semi-supervised support vector machines, etc. [61](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B61),[63](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B63).

The application of semi-supervised learning is mostly seen in medical imaging. Supervised learning algorithms may lack annotated data because annotation of medical imaging data is time-consuming and requires a high level of expertise. By using semi-supervised learning algorithms, the task of segmentation or diagnosis using medical images can be accomplished with fewer annotations [64](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B64). For example, CT images of PC can be used for segmentation and diagnosis [65](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B65).

#### **Reinforcement Learning**

The reinforcement learning process is guided by a specific goal. Agents interact with the unknown environment and get reward or punishment feedback from the environment. Then, it uses this feedback to train itself and collect experience and knowledge about the environment to achieve specific goals [66](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B66). Reinforcement learning can also be combined with deep learning to become deep reinforcement learning. It uses dynamic data and labels to bring feedback signals into the learning process rather than constructed, static dataset labels as in traditional machine learning [67](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B67).

Reinforcement learning algorithms are commonly used in decision-making in the medical field. Due to the heterogeneity of patients' conditions and treatment responses, it is challenging to realize precision medicine. Reinforcement learning can construct dynamic treatment regimens that consider the immediate effect of treatment and the long-term benefit to the patient [68](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B68),[69](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B69). For PC, reinforcement learning algorithms can generate high-quality treatment plans for pancreas stereotactic body radiation therapy (SBRT) to achieve optimal metering distribution [70](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B70).

#### **Ensemble Learning**

Rather than a single algorithm, ensemble learning seamlessly integrates various machine learning algorithms into a unified framework, typically for supervised learning. Specifically, ensemble learning samples the data and produces prediction results using multiple learners. The above results are combined, and the errors of individual learners are potentially compensated by other learners, resulting in better prediction performance [71](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B71),[72](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B72). Depending on whether the different learners are independent of each other, the ensemble approach can be divided into two main frameworks: the dependent and independent [71](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B71). The output of each learner of the dependent framework affects the next learner, which is represented by AdaBoost in the “Boosting” algorithm [73](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B73). In an independent framework, individual learners can output in parallel, which is represented by Random Forest (RF) in the “Bagging” algorithm [74](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B74). Both dependent and independent frameworks have applications in diagnosing [75](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B75)-[77](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B77) and prognosis [78](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B78)-[81](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B81) PC.

### **Deep Learning**

Deep learning (DL) is a subset of ML algorithms (**Figure**[**​Figure11**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/figure/F1/?report=objectonly)). It allows a machine to feed raw data and automatically build complex concepts. Take image recognition as an example. The mapping from many different pixels to an image is very complex. DL solves this difficulty by decomposing the complex mappings required to recognize an image into a series of simple nested mappings. The algorithm can be divided into one visible layer and several hidden layers. The visible layer is where the image is fed, while hidden layers are where the algorithm gradually extracts the features from the image [82](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B82),[83](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B83). Compared to shallow ML and traditional data analysis methods, DL models have superior performance in many applications, especially in domains with extensive and high-dimensional data. However, shallow ML performs better for low-dimensional data, especially when a limited training set [84](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B84). With the significant development of computer technology, many DL algorithms, such as Convolutional Neural Networks (CNN), Recurrent Neural Networks (RNN), MultiLayer Perceptron (MLP), Generative Adversarial Networks (GAN), and Deep Belief Networks (DBN), have been widely used in the field of oncology (**Figure**[**​Figure33**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/figure/F3/?report=objectonly)) [85](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B85)-[87](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9576619/#B87).